The Prescription Drug Marketing Act

Report to Congress

Department of Health and Human Services
U.S. Food and Drug Administration
June 2001

TABLE OF CONTENTS

ATTACHMENT E: THE 1988 GUIDANCE LETTER

ATTACHMENT F: QUESTIONS ON PDMA FOR THE PRIMARY WHOLESALERS

ATTACHMENT G: PROFILE OF THE PRESCRIPTION DRUG WHOLESALING INDUSTRY

EXECUTIVE SUMMARY

Introduction

On May 16, 2000, in its report accompanying the Food and Drug Administration (FDA or Agency) appropriations bill for 2001,[1] the House Committee on Appropriations stated that the FDA should thoroughly review the potential impact of certain provisions of the Prescription Drug Marketing Act (PDMA) of 1987 on the secondary wholesale pharmaceutical industry.[2] The Committee directed the FDA to provide a report to the Committee by January 15, 2001, summarizing the comments and issues raised and FDA's plans to address those concerns.[3] This report is intended to fulfill the Committee's request.

The report briefly summarizes the history of the PDMA; discusses concerns that have been raised by industry, industry associations, and Congress; and outlines possible ways to address those concerns.

Background[4]

The PDMA, which was signed by the President on April 22, 1988, was enacted to ensure that prescription drug products purchased by consumers would be safe and effective and to avoid an unacceptable risk that counterfeit, adulterated, misbranded, subpotent, or expired drugs were being sold to the American public. Congress decided that legislation was necessary because there were insufficient safeguards in the prescription drug distribution system to prevent the introduction and retail sale of substandard, ineffective, or counterfeit drugs and that a wholesale drug diversion submarket had developed that prevented effective control over, or even routine knowledge of, the true sources of drugs.

---

[1] Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations Bill, 2001 (H. Report 106-619), enacted into law in P.L. 106-387, 114 Stat. 1549.

[2] For purposes of this report, *secondary wholesale distributor* (or *secondary wholesaler*) refers to a distributor of prescription drugs who buys prescription drugs primarily from other wholesale distributors, rather than directly from manufacturers. A *primary wholesale distributor* (or *primary wholesaler*) is a distributor of prescription drugs who buys prescription drugs primarily from manufacturers. Primary wholesale distributors usually have on-going relationships with manufacturers because of purchasing patterns and, therefore, in most cases are *authorized distributors* within the meaning of the PDMA. It should be noted, however, that primary, or authorized, distributors sometimes purchase prescription drugs from secondary wholesale distributors, and secondary wholesale distributors sometimes purchase drugs directly from a manufacturer.

[3] The Agency was granted an extension on the report due date.

[4] Attachment C contains a summary list of events related to the PDMA.

The PDMA, as amended,[5] requires State licensing of wholesale distributors of prescription drugs; requires unauthorized wholesale distributors to provide purchasers a statement (also called a pedigree) identifying each prior sale of the drug; and with certain exceptions, prohibits the sale of, or offer to sell, prescription drugs that have been purchased by a hospital or other health care entity or that have been donated or supplied at a reduced price to a charitable organization.[6]

On August 1, 1988, the Agency issued a letter that provided guidance on the PDMA for industry pending the issuance of implementing regulations (see Attachment E and discussion in section II.C).

On March 14, 1994, the Agency published a proposed rule that would, when finalized, implement many of the provisions of the PDMA including the pedigree requirement. The proposed rule called for the submission of comments by May 30, 1994; the comment period was subsequently extended to August 15, 1994. The Agency received very few comments reflecting concern about the pedigree and related requirements: one comment objected to the requirement that the pedigree show all previous sales; two comments objected to the definition of the term *on-going relationship*, which is key in determining whether one is an authorized or unauthorized distributor.

The Agency also received several comments on the proposed regulation's potential effects on certain blood centers that function both as health care entities and as distributors of blood derivative products. The comments noted that, under the proposed regulation, these blood centers would not be permitted to continue operating in both capacities. Among other suggestions, the comments urged the exclusion of blood derivative products from the scope of the rule. Comments also objected to the statement in the proposed definition of *health care entity* that "[a] person cannot simultaneously be a 'health care entity' and a retail pharmacy or wholesale distributor."

On December 3, 1999, the Agency published final regulations in 21 CFR part 203 implementing the provisions of the PDMA as amended. In the preamble to the final rule, the Agency responded in detail to the comments submitted on the proposed rule.

After publication of the final rule, the Agency began to receive comments on the provisions concerning the pedigree requirement and the definition of health care entity. Comments came in the form of letters and petitions and other communications from industry, industry trade associations, and members of Congress objecting to certain provisions in the regulation. In addition, FDA received a petition for stay of action requesting that the

[5] The PDMA was modified by the Prescription Drug Amendments of 1992 (P. L. 102-353, 106 Stat. 941) on August 26, 1992.

[6] The state licensing provisions of the PDMA (part 205 (21 CFR 205)) were implemented by a final FDA rule, which published in the *Federal Register* of September 14, 1990 (55 FR 38012).

relevant provisions in the final rule be stayed until October 1, 2001. That petition was supported by several letters submitted to the docket from entities that would be considered unauthorized distributors under the final rule.

On March 29, 2000, the Agency met with representatives from the wholesale industry to discuss their concerns. The Agency also received several letters on the implications of the final regulations for blood centers that distribute blood derivative products and provide certain blood-related health care services.

Based on the concerns expressed by industry, industry associations, and Congress about implementing certain provisions of the regulation by the December 4, 2000, effective date, the Agency published a notice in the May 3, 2000, *Federal Register* delaying the effective date for §§ 203.3(u) and 203.50 until October 1, 2001. In addition, the notice delayed the applicability of 203.3(q) to wholesale distribution of blood derivatives by health care entities until October 1, 2001.[7]

The *Federal Register* notice also reopened the administrative record and gave interested persons until July 3, 2000, to submit written comments. As stated in the notice, the purpose of delaying the effective date for these provisions was to give the Agency time to obtain more information about the possible consequences of implementing them and to further evaluate the issues involved. To that end, the Agency also decided to schedule a public hearing[8] for the fall of 2000 to solicit information from interested persons and help develop a factual basis that the Agency could use to determine whether it is in the public interest to take steps to modify or change the requirements in the final regulations.

On May 16, 2000, the House Committee on Appropriations stated in its report (accompanying FDA's 2001 appropriations bill) that it supported FDA's decision to delay the effective date for implementing those sections of the regulations and to reopen the administrative record to receive additional comments. In addition, the Committee asked that the Agency thoroughly review the potential impact of the proposed regulations on the secondary wholesale pharmaceutical industry. The Committee directed the Agency to provide a report to the Committee by January 15, 2001, summarizing the comments and issues raised and Agency plans to address the concerns.

Summary of Comments to the Docket and Hearing Testimony

A detailed discussion of the hearing testimony and comments is included in the body of the report. In addition to presentations at the public hearing, FDA received more than 60 written comments in response to the May 3, 2000, and September 19, 2000, *Federal*

[7] The Agency further delayed the effectiveness date for §§ 203.3(u), 203.50, and 203.3(q) until April 1, 2002.

[8] The FDA holds public hearings according to the requirements in 21 CFR part 15, Public Hearing Before the Commissioner. In accordance with those requirements, the public hearing was announced in the *Federal Register* of September 19, 2000 (65 FR 56480) (see Attachment D).

Register notices pertaining to wholesale distribution (i.e., the definition of on-going relationship and the pedigree requirement) and blood derivative distribution issues (e.g., the definition of *health care entity* and the inclusion of blood derivative products). Comments were submitted by industry groups and associations, secondary wholesale distributors (i.e., distributors who would be considered unauthorized under the final rule for some or all of the products they sell), public interest groups, and individual physicians.

Comments Opposing the Final Rule

The vast majority of comments received as well as the presentations made at the public hearing opposed the specific provisions of the regulations discussed above and were consistent with the letters and petitions and other communications the Agency had received from industry, industry trade associations, and members of Congress.

Secondary Wholesalers

The general perception among secondary wholesalers, as expressed in the comments and the presentations made at the public hearing, is that a significant number of prescription drug wholesale distributors would be adversely affected economically by the requirements in the final regulations. Secondary distributors assert that a significant portion of their business would be eliminated by implementation of the final regulations because (1) they cannot obtain authorized distributor of record status from manufacturers for many of the drugs they sell and (2) primary wholesalers are not willing to provide pedigrees for drugs they sell to secondary wholesalers. The secondary wholesalers indicated that, when they do not qualify as authorized distributors under the *status quo*, they supply pedigrees, back to the last authorized distributor.[9]

Primary Wholesalers

There are five primary wholesale distributors, who buy most of their prescription drugs directly from manufacturers.[10] Primary wholesale distributors usually have on-going relationships with manufacturers and, therefore, are considered *authorized distributors* within the meaning of the PDMA. Although none of the primary wholesaler distributors initially submitted individual comments to the docket or attended the October public hearing, their views were presented in statements submitted to the docket by their trade

[9] Transcript of the FDA Part 15 Hearing, Prescription Drug Marketing Act, Friday, October 27, 2000, p. 56.

[10] The five largest wholesale distributors include McKesson HBOC, Inc.; Bergen Brunswig Drug Company; Cardinal Health, Inc.; AmeriSource Corporation, and Bindley Western Drug Company. These companies generate revenues of between $7.6 to 21.5 billion per year each (see Attachment G, ERG rept. pp. 1-10 and table 1-3).

association[11] and in responses to questions the Agency submitted to them after the public hearing.

The statements submitted to the docket by the primary distributors are generally consistent with those submitted by the secondary distributors, indicating that they generally are not providing pedigrees. In addition, several primary distributors stated that their warehouse operations are not currently set up in a way that facilitates providing pedigrees, and it would be expensive for them to do so. Therefore, as a practical matter, the large distributors do not appear to be willing to voluntarily provide pedigrees. Like the secondary wholesalers, primary wholesalers cite the low profit margin associated with their business as a reason why they purchase drugs from secondary wholesalers, and they say they cannot afford the costs associated with passing on the pedigree.[12]

Individuals Who Purchase from Secondary Distributors

Comments and hearing testimony from some individuals who purchase drugs from secondary distributors, such as retail grocery stores, pharmacies, and physicians, indicated that it would be more difficult and expensive to obtain prescription drugs if secondary distributors could not continue distributing them. Pharmacists frequently use more than one distributor to meet their supply needs, and secondary wholesale distributors are used extensively by pharmacies — particularly, to obtain unusual products or to purchase products when a pharmacy is in a remote area not served by one of the larger distributors. Although pharmacies purchase directly from manufacturers and authorized distributors, secondary distributors are often used as backups to ensure access to a full range of products when they are needed.[13]

Competition in the Marketplace

It was argued that implementation of the wholesale distribution requirements in the final rule would generally decrease competition in the marketplace and result in higher prescription drug prices for retailers and, ultimately, consumers.[14]

Public Health Concerns

[11] The National Wholesale Druggists' Association (NWDA) represents the health care product distribution industry, including specialty and secondary source distributors.

[12] Data show that for every dollar of prescription drugs sold in 1997, 76 cents went to the manufacturer, 20 cents to the dispenser (e.g., the pharmacy), and only 4 cents to the wholesale distributor. After-tax net profit expressed as a percentage of sales was only 0.62 percent for 1998 (ERG rept. 2001).

[13] Ibid., 19, 23, 98.

[14] Ibid., 20, 40, 67, 70, 99.

Some testimony and comments argued that the final rule would not significantly help to enhance the public health. The commenters stated that existing requirements for State licensing of wholesale distributors in 21 CFR part 205 of the Agency's regulations provide adequate record keeping for the purposes of conducting recalls and ensuring that diverters of prescription drugs can be readily identified by the Agency. Commenters indicated at the hearing that recalls are done by broadcast messages rather than direct notification of particular purchasers of specific lots of drug. The presenters did not believe that a pedigree accompanying the drug would provide significant additional assurance of drug quality.[15]

Criminal Activity

When asked whether the pedigree requirement helps deter criminal activity, several presenters stated that sales records without a pedigree are sufficient to identify individuals in the distribution chain of a drug who may be responsible for counterfeiting or other diversion activities.[16]

Secondary Wholesaler Recommendation

Most of the comments and testimony supported maintaining the *status quo* – that is, the way the wholesale industry has been operating during the 12 years since the PDMA was passed. Apparently, the industry has been operating under its interpretation of the guidance letter issued by the Agency in 1988. However, industry has interpreted the guidance letter very broadly.

Industry has interpreted the guidance letter as defining the term *authorized distributor* as a distributor who conducts at least two transactions with the manufacturer within any two-year period. In fact, the guidance letter says that to qualify as an authorized distributor, a distributor must have an on-going relationship with a manufacturer, that is, show evidence of two sales in a two-year period ***and*** have "evidence of a written franchise, license, or other distribution agreement." In addition, the guidance letter stated that a pedigree should show all sales of a drug starting with "the manufacturer or authorized distributor of record" (see Attachment E and discussion in section II.C). Secondary wholesalers have interpreted this to mean that the pedigree need only go back to the ***most recent*** authorized distributor who handled the drug .

The Blood Centers

According to the comments and testimony, implementation of the final rule as published would be detrimental to the public health because it would disrupt distribution of blood derivative products and interfere with longstanding relationships between blood centers and other health care providers. Comments asserted that the final rule would hinder blood

[15] Transcript 20, 24, 60, and 105.

[16] Ibid., 41 and 42, 211 to 213.

centers' ability to provide blood derivative products and medical services associated with those products to hospitals, hemophilia treatment centers, and other providers.

Comments Favoring the Final Rule

The comments and testimony supporting the final rule as written came from pharmaceutical manufacturers and one public interest group. They stated that the requirements in the regulations are consistent with Congress' objectives in enacting the PDMA and would be helpful in supporting those objectives. They indicated that without a legally required document ensuring traceability back to the manufacturer, the public has no guarantee that the pharmaceutical products being sold are not counterfeit or that they were stored under appropriate conditions throughout their shipment chain.

One presenter at the hearing said that Congress should have required a universal pedigree because the pedigree as conceived would provide the opportunity for unscrupulous distributors to launder counterfeit or substandard drugs through authorized distributors. The presenter argued that logistical problems in tracking the pedigree of drugs is not a legitimate reason for not requiring all distributors to maintain a pedigree.[17]

Agency Conclusions

After carefully reviewing all of the comments, the Agency believes that by revising its regulations, it would be able to address some, but not all, of the concerns raised by both the secondary wholesale industry and the blood industry. Four issues seem to be the focus of most concerns.

Key Issues

Most concerns about the final rule focus on four key issues:

1. Who qualifies as an authorized distributor?
2. Should authorized distributors be exempt from maintaining and passing on a pedigree?
3. What is the meaning of the phrase *each prior sale*?
4. Should blood centers that provide some health care services be permitted to distribute blood derivative products?

By changing its regulations, the Agency would be able to address issues 1 and 4. It would take statutory changes, however, to address concerns raised regarding issues 2 and 3.

1. Who qualifies as an authorized distributor?

[17] Transcript 130, 133.

Current § 203.3(u) of the final regulations requires a written agreement between a manufacturer and each of its authorized distributors. The Agency agrees that this requirement is restrictive and places control of who can be an authorized distributor in the hands of manufacturers. It could prohibit many secondary distributors, including those who make regular purchases from manufacturers, from qualifying as authorized distributors of record. This could have anticompetitive consequences without the corresponding benefit of protecting the public health.

The Agency believes that changing the regulations to broaden the definition of *on-going relationship* could enable more wholesale distributors to qualify as authorized distributors. FDA believes that an on-going relationship could be demonstrated by evidence of two sales within the previous 24-month period. With such a change, a distributor who is able to provide such evidence would be considered an authorized distributor. If the definition in the regulation were revised, a greater number of wholesale distributors would be able to qualify as authorized distributors and would not have to maintain or pass on a pedigree as required under the PDMA and FDA's implementing regulations. One possible consequence of this change would be that it could reduce the extent to which pedigrees currently are maintained and passed on during the distribution of prescription drugs.

Despite this change, some wholesale distributors would still not qualify as authorized distributors. For these wholesale distributors, the pedigree requirement would remain problematic because under the regulations, they would have to obtain a pedigree showing each prior sale and pass it on when reselling prescription drugs. As discussed in the next section, they still might not be able to obtain a pedigree, unless the PDMA were changed.

2. Should authorized distributors be exempt from maintaining and passing on a pedigree?

In 1987, when the PDMA was enacted, the general understanding of the prescription drug distribution system was that most prescription drugs pass in a linear manner from a manufacturer to a retail outlet through a primary, or authorized, distributor of record (an identifiable group of distributors who could be characterized by their on-going relationships with manufacturers). Congress exempted authorized distributors from the pedigree requirements in the PDMA. As a result, most authorized distributors do not maintain or pass on pedigrees. This creates a substantial problem for unauthorized distributors wishing to purchase prescription drugs from an authorized distributor and resell them. Under the PDMA, without a pedigree, an unauthorized distributor cannot legally resell prescription drugs. The secondary wholesale distributor might be able to create an incomplete pedigree that indicates whom he or she purchased the drugs from, but that

pedigree would not reflect each sale back to the manufacturer as required by the PDMA.

The wholesale prescription drug distribution system has changed considerably since 1988 when the PDMA was enacted. According to the testimony and other comments, today, between 5 and 10 percent of the $100 billion wholesale pharmaceutical market is handled by secondary wholesalers (see Attachment G, table 1-7). In many cases, a primary distributor purchases prescription drugs from a manufacturer and resells them to one or more secondary wholesalers, who subsequently resell them to other wholesalers. In some cases, manufacturers sell directly to secondary distributors. Some drugs may go through several transaction cycles involving multiple primary and secondary wholesalers before arriving at their retail destination.

Furthermore, the volume of drugs that authorized distributors purchase from secondary wholesalers is significant. The National Wholesale Druggists' Association (NWDA) told the Agency that the big five distributors purchase 2 to 4 percent of their products from sources other than manufacturers. One of the big five reported that of the approximately $16 billion total inventory purchased in 2000, approximately $350 million came from nonmanufacturer vendors.

Authorized distributors are not required to maintain a pedigree or pass one along when they resell prescription drugs to another wholesaler or retail outlet. As a result, an unscrupulous wholesale distributor seeking to introduce a counterfeit or diverted drug into commerce may do so by selling it to an unknowing authorized distributor who may or may not know the true origins of the drug and who is not required to maintain or pass on a pedigree when the drugs are resold.

The PDMA pedigree exemption for authorized distributors not only puts unauthorized distributors at a disadvantage, but also has the effect of *wiping the slate clean* each time prescription drugs pass through an authorized distributor. Today under the *status quo*, a large volume of prescription drugs move through the system without pedigrees, or with incomplete pedigrees, because they have passed through an authorized distributor at least once before reaching their retail destination.

FDA believes that maintaining and passing on a pedigree on prescription drugs provides a valuable tool — even if this is required of only those secondary distributors unable to attain authorized distributor status. The pedigree requirement is a deterrent to the introduction and retail sale of substandard, ineffective, and counterfeit drugs. Although a pedigree can be, and sometimes is, falsified to disguise the true source of prescription drugs,

FDA believes that requiring a pedigree makes it more difficult for someone planning to introduce counterfeit or diverted drugs into commerce. Requiring a pedigree also facilitates the efforts of law enforcement personnel seeking to identify the source of a counterfeit or diverted drug shipment and take action against those responsible.

The Agency also believes that, given today's prescription drug distribution system, the PDMA provision that exempts authorized distributors from having to maintain and pass on a pedigree undermines the purpose of the pedigree by allowing for potential gaps in the distribution history. If the definition of *authorized distributor* were broadened, fewer wholesalers than before would be required to maintain and pass on pedigrees on prescription drugs.

FDA does not have the authority to require authorized distributors to maintain and pass on a pedigree. Such a requirement would necessitate a statutory change. Therefore, Congress may want to consider whether the benefits of requiring authorized distributors to maintain and pass on pedigrees to deter the introduction of counterfeit or diverted drugs outweigh the costs to the primary and secondary distributors of maintaining and passing along such pedigrees.

3. What is the meaning of the phrase *each prior sale*?

Section 503(e)(1)(A) of the Federal Food, Drug, and Cosmetic Act requires that the pedigree must identify "each prior sale, purchase, or trade."

The Agency's 1988 guidance letter stated that the pedigree could start with the "manufacturer or authorized distributor of record." It was the Agency's understanding at the time that the authorized distributor of record would be the distributor to whom the manufacturer first sold the drugs, not just any authorized distributor who happened to purchase the drugs somewhere along the distribution chain.

Authorized distributors are exempt from the pedigree requirement and in most cases will not provide a pedigree to a distributor to whom they sell prescription drugs. In the years since issuance of the 1988 guidance letter, unauthorized distributors have interpreted the Agency's guidance letter to mean that the pedigree need only go back to the ***most recent*** authorized distributor who handled the drug. This interpretation is what pharmaceutical distributors consider the *status quo*.

The language in the current regulation, which is based on the statute, clarifies that the pedigree must identify "each prior sale, purchase, or trade of such drug" (§ 203.50(a)) and include "all parties to each prior transaction...starting

with the manufacturer" (§ 203.50(a)(6)). Consistent with Congress' intent in enacting the PDMA, this requirement ensures that a complete history of a prescription drug is created and passed along.

As stated in the comments to the docket and in testimony given at the public hearing, the regulation, although consistent with the statute, is inconsistent with the *status quo* as understood by wholesalers. As a result, under the *status quo,* whenever a prescription drug is sold to an authorized distributor of record, the transaction history prior to that sale is no longer maintained. Secondary wholesale distributors have asked the Agency to amend the regulations to be consistent with their interpretation of the *status quo* (i.e., the pedigree need only go back to the most recent authorized distributor who handled the drug).

Because § 203.50 reflects the language of the statute, the FDA believes that it cannot revise the regulation to make it consistent with the *status quo*. Such a requirement would necessitate a statutory change. Congress may want to consider this issue in conjunction with the issue of granting authorized distributors an exemption from the pedigree requirement. Congress could require that the pedigree go back only as far as the last authorized distributor, rather than to the manufacturer. This would, however, as pointed out in the previous section, leave gaps in the pedigree and encourage the laundering of drugs through unknowing authorized distributors. Congress may wish to consider whether the benefits of requiring that a complete pedigree be maintained and passed along outweigh the costs to the primary and secondary distributors of maintaining and passing along such a pedigree.

4. Should blood centers that provide some health care services be permitted to distribute blood derivative products?

Based on the comments it has received, the Agency is reconsidering its previous position with respect to blood centers that provide certain health care services and distribute blood derivative products. The Agency is considering whether blood centers that provide some blood-related health care services should be able to continue to distribute blood derivative products.

The Agency is considering whether it should modify the regulation to allow blood centers that offer certain limited health care services and also function as wholesale distributors of blood derivative products to continue operating in both capacities.

Summary of Conclusions

After carefully reviewing all of the comments, the Agency believes that it would be able to address some, but not all, of the concerns raised by both the secondary wholesale industry and the blood industry.

- By changing its regulations, the Agency could broaden the definition of *authorized distributor* — although this change could result in even fewer wholesalers than before maintaining and passing on pedigrees for prescription drugs.

- The Agency is considering whether it should amend the regulation to permit those blood centers that provide certain limited health care services to distribute blood derivative products.

- The Agency believes, as discussed above, that concerns related to continuing to exempt authorized distributors from the pedigree requirement and to the exact meaning of the phrase *each prior sale*, can be addressed only through statutory remedies.

- The Agency has further delayed the effective date for §§ 203.3(u) and 203.50, and the applicability of § 203.3(q) to wholesale distribution of blood derivatives by health care entities until April 1, 2002.

The Prescription Drug Marketing Act

Report to Congress

I. INTRODUCTION

On May 16, 2000, in its report accompanying the Food and Drug Administration (FDA or Agency) appropriations bill for 2001,[1] the House Committee on Appropriations stated that the FDA should thoroughly review the potential impact of certain provisions of the Prescription Drug Marketing Act (PDMA) on the secondary wholesale pharmaceutical industry. The Committee directed FDA to provide a report to the Committee by January 15, 2001, summarizing the comments and issues raised by the public and proposing FDA plans to address those concerns.[2] This report is intended to fulfill the Committee's request.

Since the issuance of final regulations implementing the PDMA in December 1999, representatives primarily of the secondary wholesale distribution industry have expressed concerns about the effects those regulations may have on the industry. Although not the only concern, a primary concern has been that, as a result of factors discussed in detail below, as many as 4,000 unauthorized, secondary wholesale pharmaceutical distributors could be adversely affected as a result of certain requirements in the regulations.[3]

Members of the blood community also have expressed concerns that implementing the final regulations as written may disrupt effective distribution and create shortages of blood derivatives and add to health care costs.

II. BACKGROUND

The evolution of the PDMA spans almost two decades. The following paragraphs provide a brief background of the legislation and a discussion of the two key areas of concern: (1) the secondary wholesale distribution of human pharmaceuticals and (2) restrictions on the

[1] Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations Bill, 2001 (report 106-619).

[2] The Agency was granted an extension.

[3] Transcript of the FDA Part 15 Hearing, Prescription Drug Marketing Act, October 27, 2000, p. 38.

distribution of prescription blood derivative products by blood establishments that offer limited health care services.

A. Congressional Findings Prompting Passage of the PDMA

The congressional findings, which were made part of the text of the legislation, explain that the PDMA was intended (1) to ensure that drug products purchased by consumers would be safe and effective and (2) to avoid an unacceptable risk that counterfeit, adulterated, misbranded, subpotent, or expired drugs were being sold to American consumers.[4] Congress found, among other things, that legislation was necessary because there were insufficient safeguards in the drug distribution system to prevent the introduction and retail sale of substandard, ineffective, or counterfeit drugs, and that a wholesale drug diversion submarket had developed that prevented effective control over, or even routine knowledge of, the true sources of drugs.[5]

Congress found that large amounts of drugs had been re-imported into the United States as American goods returned (AGRs), causing a health and safety risk to American consumers because the drugs may have become subpotent or adulterated during foreign handling and shipping.[6] Congress also found that a ready market for prescription drug re-imports had been the catalyst for a continuing series of frauds against American manufacturers and had provided the cover for the importation of foreign counterfeit drugs.[7]

The congressional findings also stated that the then-existing system of providing drug samples to physicians through manufacturers' representatives had been abused for decades and had resulted in the sale to consumers of misbranded, expired, and adulterated pharmaceuticals.[8]

According to congressional findings, the bulk resale of below-wholesale-priced prescription drugs by health care entities for ultimate sale at retail helped to fuel the diversion market and was an unfair form of competition to wholesalers and retailers who had to pay otherwise prevailing market prices.[9]

---

[4] See section 2(8) of the PDMA.

[5] See sections 2(2) and 2(3) of the PDMA.

[6] The 106th Congress tried to address issues related to the reimportation of drug products when it enacted the Medicine Equity and Drug Safety Act of 2000 (P.L. 106-387, § 1(a), 114 Stat. 1549).

[7] See section 2(4) of the PDMA.

[8] See section 2(6) of the PDMA.

[9] See section 2(7) of the PDMA.

B. The Effects of the PDMA on the Federal Food, Drug, and Cosmetic Act

As a result of its findings, Congress passed the Prescription Drug Marketing Act of 1987 (Pub. L. 100-293), which the President signed into law on April 22, 1988. Most PDMA provisions became effective on July 22, 1988. On August 26, 1992, the Prescription Drug Amendments (P. L. 102-353, 106 Stat. 941) were passed, which amended several parts of the PDMA.

The PDMA, as amended by the Prescription Drug Amendments, modified sections 301, 303, 503, and 801 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 331, 333, 353, and 381) to:

1. Ban the sale, purchase, or trade of, or the offer to sell, purchase, or trade, drug samples and drug coupons.

2. Restrict re-importation of prescription drugs to the manufacturer of the drug product or for emergency medical care.

3. Establish requirements for drug sample distribution and the storage and handling of drug samples.

4. Require a wholesale distributor of prescription drugs to be State licensed, and require FDA to establish minimum requirements for State licensing.

5. Establish requirements for wholesale distribution of prescription drugs by unauthorized distributors.

6. Prohibit, with certain exceptions, the sale, purchase, or trade of (or the offer to sell, purchase, or trade) prescription drugs that were purchased by hospitals or other health care entities, or donated or supplied at a reduced price to charities.

7. Establish criminal and civil penalties for PDMA violations.

C. 1988 Agency Guidance Letter

On August 1, 1988, the Agency issued a letter that provided guidance on the PDMA for industry pending the issuance of implementing regulations (see Attachment E). The letter provides detailed guidance on the Agency's interpretation of the PDMA, including clarifying definitions and explanations of specific sections.

For example, in section VII, Wholesale Distribution, under part B, Requirements for Unauthorized Distributors, the letter explains that the PDMA (section 503(e)(1)(A) of the Act) requires that a

> person who is engaged in the wholesale distribution of prescription drugs and who is not an authorized distributor of record of such drugs shall provide to each wholesale distributor of such drugs a statement identifying each sale of the drug (including the date of sale) before the sale to such wholesale distributor.

The letter also states that the phrase *authorized distributors of record* is defined in the Act[10] as "those distributors with whom a manufacturer has established an on-going relationship to distribute such manufacturer's products."

Under part C, Guidance Information, the letter explains that *on-going 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. Evidence of such intent would include, but 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 on-going sales by the manufacturer to the distributor, either directly or through a jointly agreed upon intermediary. The Agency would consider two transactions in any 24-month period to be evidence of a continuing relationship.

Part C also explains that the statement identifying prior sales (pedigree) should include "all necessary identifying information regarding all sales in the chain of distribution of the product, starting with the manufacturer ***or*** authorized distributor of record [emphasis added]."

The wholesale distribution industry has been operating under its interpretation of the guidance letter for the past 12 years and considers this to be *the status quo*. Although the guidance letter clearly contemplates some sort of a written agreement ***as well as*** some actual sales to demonstrate an on-going relationship that would qualify a distributor to be an authorized distributor exempt from the pedigree requirement, the secondary wholesale industry, as indicated in its comments, has apparently not been obtaining such written agreements. Instead, many distributors consider themselves to be authorized distributors exempt from the pedigree requirement based on sales alone.[11] As a result, much of the industry has interpreted the requirement to provide a pedigree as applying to only a relatively small number of secondary distributors.

---

[10] Section 503(e)(4)(A) of the Act (21 U.S.C. 353(e)(4)(A).

[11] Transcript 22.

Industry's interpretation of the phrase *each prior sale* also is inconsistent with the PDMA (section 503(e)(1)(A) of the Act) and the regulation (§ 203.50). In 1988, when PDMA was enacted, the general understanding of the prescription drug distribution system was that most prescription drugs pass in a linear manner from a manufacturer to a retail outlet through a primary, or authorized, distributor of record (an identifiable group of distributors who could be characterized by their on-going relationships with manufacturers). The 1988 guidance letter states that the necessary identifying information regarding all sales in the chain of distribution may start with the manufacturer or authorized distributor of record. It was the Agency's understanding at the time that the authorized distributor of record would be the distributor to whom the manufacturer first sold the drugs, not just any authorized distributor who happened to purchase the drugs somewhere along the distribution chain.

Authorized distributors are exempt from the pedigree requirement and in most cases will not provide a pedigree to a distributor to whom they sell prescription drugs. In the years since issuance of the 1988 guidance letter, unauthorized distributors have interpreted the Agency's guidance letter to mean that the pedigree need only go back to the ***most recent*** authorized distributor who handled the drug.[12] This interpretation is what pharmaceutical distributors consider the *status quo*. As a result, under the *status quo*, whenever a prescription drug is sold to an authorized distributor of record, the transaction history prior to that sale is no longer maintained.

D. Today's Pharmaceutical Wholesale Distribution System

A report prepared for the FDA's Office of Policy, Planning, and Legislation (ERG rept., 2001) provides a profile of the prescription drug wholesaling industry (see Attachment H). Excerpts from that report have been included here to provide a brief overview of the U. S. prescription drug distribution industry.[13]

The prescription drug wholesale industry in the United States is highly concentrated. Ninety (90) percent of the sales of prescription drugs are made by five major full-line companies, referred to as the *big five*.[14] These companies each generate from $7.6 to $21.5 billion per year in revenue. They control the movement of most of the medical products from the manufacturers to the dispensers. The big five distribute a full line of drug products nationwide. The big five purchase the large majority of their drugs directly from the drug manufacturers, making them *primary distributors*. Because the big five have formal, written distribution contracts with the drug manufacturers, they would be considered

[12] Transcript 38.

[13] ERG rept. pp. 1-10 to 1-32.

[14] The five largest wholesale distributors include McKesson HBOC, Inc.; Bergen Brunswig Drug Company; Cardinal Health, Inc.; AmeriSource Corporation, and Bindley Western Drug Company.

authorized distributors as the term is defined under either the 1988 guidance letter or the final rule.

Their traditional mode of operation is to purchase prescription drugs in large quantities from manufacturers, take ownership of the drugs in their own warehouses, and resell them directly to the retail chains or hospitals in desired allotments. Increasingly, however, the big five use other methods of distribution. For example, they may arrange for a manufacturer to ship the products directly to the customer, but with the order and payment submitted through the wholesaler.

Although the big five are very large business entities, price and competitive conditions dictate that they operate on narrow profit margins. In general, the wholesale markup is modest. According to data generated in a recent U. S. Court case, for every dollar of prescription drugs sold in 1997, 76 cents went to the manufacturer, 20 cents went to the dispenser, and 4 cents went to the wholesale distributor.[15] The NWDA reported that the after-tax net profit, expressed as a percent of sales, was only 0.62 percent for 1998.[16]

Secondary wholesalers, who generally purchase their products from other wholesalers, come in a variety of types and sizes. Regional wholesalers, probably the largest of the secondary industry, are at least an order of magnitude smaller than the big five. These companies generate revenues of approximately $500 million to $900 million per year.[17] It is estimated that there are approximately 70 regional prescription drug wholesalers.[18] Numerous additional, and generally smaller, wholesalers also distribute pharmaceutical products. Many viable drug wholesalers are quite small. Some small companies generate over $10 million in annual revenues with fewer than 10 staff dedicated to drug distribution. Smaller wholesalers generally are willing to deal in smaller volumes than regional wholesalers and serve the individual independent pharmacies and physicians' offices.

Secondary wholesalers seldom offer a full line of pharmaceutical products and often specialize in purchasing and selling selected discounted drug products. Although the big five also purchase and sell discounted products, secondary wholesalers are distinguished by their willingness to risk substantial capital in buying and trading discounted drugs. Their activities are built around the rapid turnover of discounted drugs in a fashion similar to that of discounters in other industries.

---

[15] U.S. District Court for the District of Columbia, 1998, Civil Action No. 98-595: Federal Trade Commission v. Cardinal Health, Inc. and Bergen Brunswig Corp. and Civil Action No. 98-596: Federal Trade Commission v. Mc Kesson Corp. and Amerisource Health Corp.

[16] National Wholesale Druggists' Association (NWDA), 1999, 1999 NWDA Industry Profile and Healthcare Factbook, National Wholesale Druggists' Association, Reston, VA.

[17] Ibid.

[18] This number is based on the membership roster of the NWDA.

For example, occasionally, pharmaceutical manufacturers offer drug products for a limited time at a discounted price. This often occurs when they strive to meet a quarterly sales goal or wish to sell off inventory in advance of a price increase. Cash customers can often receive additional discounts. In response to such a sale, a secondary wholesaler might purchase quantities of the sale products. The secondary wholesaler would in turn offer the discounted products to other wholesalers, including the big five, undercutting the regular prices being offered by the manufacturer. These companies do very little advertising or sales promotion work other than publishing and advertising their sale prices. Additionally, these wholesalers (as do the big five when appropriate) often engage in trading of pharmaceutical products to take advantage of price differentials.

Like the majority of regional and smaller wholesalers, most secondary wholesalers do not have written distribution agreements with drug manufacturers whose products they purchase and resell. Some of the reasons why drug manufacturers decline to enter into written distribution agreements with the secondary wholesalers include (1) the inability of these wholesalers to carry the full line of manufacturers' products and maintain a required line of credit and (2) manufacturers' unwillingness to open new accounts . Furthermore, secondary wholesalers are usually irregular customers and do not represent an avenue for routine distribution of the manufacturers' products. [19]

It is estimated, based on available data, that there are more than 6,500 wholesalers. Of these, 83 percent are small (fewer than 20 employees), 11 percent are medium-sized (with 20 to 99 employees), and 6 percent are large (with more than 100 employees).[20]

E. Concerns of Secondary Wholesale Distributors

On March 14, 1994, the Agency issued a proposed rule implementing the PDMA as amended. The proposed rule called for the submission of comments by May 30, 1994, and the comment period was subsequently extended to August 15, 1994. The Agency published final regulations in 21 CFR part 203 implementing the provisions of the PDMA, as amended, on December 3, 1999.

The provision in the final regulations that has attracted the most attention from industry is § 203.50, which requires that, 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 must provide to the purchaser a statement (or pedigree) identifying each prior sale, purchase, or trade of the drug. The identifying statement must include the proprietary and established name of the drug, its dosage, the container size, the number of containers, lot or control numbers of the drug being distributed, the business name and address of all parties to

[19] ERG rept. pp. 1-19 to 1-20.

[20] ERG rept. pp. 1-20 to 1-21.

each prior transaction involving the drug, starting with the manufacturer, and the date of each previous transaction.[21]

Section 203.3(b) of the regulation defines *authorized distributor of record* as a distributor with whom a manufacturer has established an on-going relationship to distribute the manufacturer's products. This definition, too, mirrors the statutory definition of authorized distributor.[22] Congress left it up to FDA to define what constitutes an on-going relationship.

Ongoing relationship is defined in § 203.3(u) of FDA's regulations to mean 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.

The provisions in the final rule related to wholesale distribution of prescription drugs by unauthorized distributors (i.e., §§ 203.3(u) and 203.50) were adopted from the provisions in the proposed rule published in the *Federal Register* of March 14, 1994 (59 FR 11842) and are essentially the same as the proposed provisions, except the definition of *on-going relationship* in the proposed rule was revised to eliminate certain requirements.[23]

When FDA published its final rule, the Agency responded to comments submitted on the proposed rule, explaining that the PDMA required the provision of a statement of all sales going back to the manufacturer.[24] The Agency also said that a written agreement is necessary to facilitate compliance with the Act by providing a formalized way of establishing on-going relationships between manufacturers and authorized distributors.

---

[21] The requirement that the pedigree include the names and addresses of all parties to each prior transaction involving the drug and the requirement that it identify "each prior sale, purchase, or trade of such drug" are taken directly from the statute. Section 503(e)(1)(A) of the Act says that the statement [pedigree] must identify "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)."

[22] Section 503(e)(4)(A) of the Act 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."

[23] The proposed rule defined *on-going relationship* to require a written agreement and the following additional two requirements, which were eliminated in the final rule: (1) That a sale be completed under the written agreement and (2) that the distributor be listed on the manufacturer's list of authorized distributors.

[24] The Agency received very few comments on the proposed requirements related to the provision of a pedigree. Only one comment objected to the requirement of a statement identifying all previous sales. Two comments objected to the definition of the term *on-going relationship* as it relates to the identification of authorized distributors.

As discussed in the preamble to the final rule (64 FR 67720 at 67747), manufacturers and authorized distributors of record are ***not required*** to provide an identifying statement when selling a drug, although the Agency encouraged them to do so voluntarily to permit unauthorized distributors to continue to be able to purchase products from them.[25]

Subsequent to publication of the final rule, the Agency began to receive letters and petitions and had other communications with industry, industry trade associations, and members of Congress objecting to the provisions in §§ 203.3(u) and 203.50.

On March 29, 2000, the Agency met with representatives from the wholesale industry and industry associations. The industry representatives discussed their concerns with both (1) the requirement in § 203.3(u) that there be a written authorization agreement between a manufacturer and distributor for the distributor to be considered an authorized distributor of record under § 203.3(b), and (2) the requirement in § 203.50 that unauthorized distributors provide a pedigree showing all prior sales going back to the manufacturer.

The industry representatives asserted that manufacturers are unwilling to enter into written authorization agreements with the majority of smaller wholesalers.[26] As a result, wholesalers cannot become authorized distributors of record for the drugs they sell. The industry representatives also said that smaller wholesalers cannot obtain the required pedigree showing all prior sales of the drugs they purchase for sale, because a large portion of these drugs are purchased from authorized distributors who are not required to provide pedigrees and who are unwilling to voluntarily provide them.[27] The industry representatives asserted that authorized distributors will not voluntarily provide pedigrees when they sell drugs to unauthorized distributors because it would require them to change their warehouse and business procedures, which would entail additional effort and expense.[28]

The industry representatives said that implementation of the final rule could prevent as many as 4,000 smaller, unauthorized distributors from distributing many drugs to their customers and could put them out of business, at least with respect to their prescription

---

[25] An unauthorized wholesale distributor who purchases a product from a manufacturer or authorized distributor of record without an identifying statement showing the prior sales of the drug could not provide an identifying statement to its purchasers and, therefore, could not conduct further wholesale transactions of the drug in compliance with § 203.50.

[26] According to the ERG rept. (pp. 1-19 and 1-20), there are several reasons for this. First, many wholesalers cannot carry the full line of a manufacturer's products and cannot maintain the required line of credit. In addition, many secondary wholesalers will only purchase products from a manufacturer under certain conditions. As a result, they do not represent "an avenue for routine distribution of a manufacturer's products."

[27] Testimony at the hearing indicated that there are five large full-line wholesalers that carry most if not all of the drugs distributed in the United States and distribute 90 percent or more of all drugs (Transcript 36).

[28] Apparently, few distributors track prescription drugs by lot number (10 percent, ERG rept. p 1-29).

drug wholesale business. They also asserted that because many of their customers are small retail outlets not served by larger distributors, implementation of the final rule may leave certain markets for prescription drugs, and ultimately consumers of prescription drugs, underserved.

In addition to the meeting discussed above and other informal communications that FDA has had with industry, industry associations, and Congress, FDA received a petition for stay of action requesting that the relevant provisions of the final rule be stayed until October 1, 2001. That petition was supported by several letters submitted to the docket from entities that would be considered unauthorized distributors under the final rule.

The Agency also received a petition for reconsideration from the Small Business Administration (SBA) requesting that FDA reconsider the final rule and suspend its effective date based on the projected severe economic impact it would have on over 4,000 small businesses. The petitions argued that the requirement for a written agreement in § 203.3(u) is unreasonable because manufacturers are unwilling to enter into such agreements with the majority of smaller distributors. The petitions also asserted that authorized wholesalers are not now able and could not provide, at a reasonable cost, a pedigree to their unauthorized distributor customers that meets the requirements of § 203.50 of the final rule. The SBA petition asserted that, if the effective date of the final rule is not stayed, drug products now in the inventory of wholesalers will have to be cleared, and new orders will have to cease or be severely limited to comply with the final rule's original December 4, 2000, effective date, with corresponding disruptions in the distribution of drugs possible by summer of 2000.[29]

F. Concerns of Blood Centers

Section 503(c)(3)(A) of the Act states that no person may sell, purchase, or trade, or offer to sell, purchase, or trade, any prescription drug that was purchased by a public or private hospital or other health care entity. Section 503(c)(3)(B) of the Act states several exceptions to § 503(c)(3)(A), none of which are relevant to this discussion. Section 503(c)(3) also states 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."

Section 203.22 of the PDMA final rule provides, with certain exceptions, that no person may sell, purchase, or trade, or offer to sell, purchase, or trade any prescription drug that was purchased by a public or private hospital or other health care entity or donated or supplied at a reduced price to a charitable institution. In § 203.3(q) of the PDMA final rule, *health care entity* is defined as any person that provides diagnostic, medical, surgical, or dental treatment, or chronic or rehabilitative care, but does not include any retail pharmacy

[29] The Agency has decided to delay further the effectiveness date for §§ 203.3(u), 203.50, and 203.3(q) until April 1, 2002.

or wholesale distributor. Under the final rule, a person could not simultaneously be a health care entity and a retail pharmacy or wholesale distributor.

Thus, under the PDMA final rule, blood centers functioning as health care entities could not engage in wholesale distribution of prescription drugs, except for blood and blood components intended for transfusion, which are exempt from the PDMA regulations under § 203.1 of the final rule. Blood and blood components include whole blood, red blood cells, platelets, and cryoprecipitated antihemophilic factor, which are prepared by blood banks that collect blood from donors and separate out the components using physical or mechanical means. In contrast, blood derivative products are derived from human blood, plasma, or serum through a chemical fractionation manufacturing process; blood derivative products fall within the scope of the PDMA final rule. Examples of blood derivative products include albumin, antihemophilic factor, immune globulin, and alpha-1 anti-tripsin. As discussed in the preamble to the final rule, blood derivative products are not blood or blood components intended for transfusion and, therefore, could not be distributed by health care entities, including certain blood centers, after the final rule goes into effect.

After publication of the final rule, the Agency received several letters on the implications of the final regulations for blood centers that distribute blood derivative products and provide certain health care services. The blood industry asserts that the regulations, in particular, the definition of *health care entity* and the inclusion of blood derivative products within the scope of this rule, will severely inhibit the blood industry's ability to provide health care and may disrupt the distribution of blood derivative products to the public.

G. Decision to Delay the Effective Date; Hold a Public Hearing

Based on the concerns expressed by industry, industry associations, and Congress about implementing §§ 203.3(u) and 203.50 by the December 4, 2000, effective date, the Agency published a notice in the May 3, 2000, *Federal Register* (65 FR 25639) delaying the effective date for those provisions until October 1, 2001. In addition, the notice delayed the applicability of § 203.3(q) to wholesale distribution of blood derivative products by health care entities until October 1, 2001. The *Federal Register* notice also reopened the administrative record and gave interested persons until July 3, 2000, to submit written comments. As stated in the notice, the purpose of delaying the effective date for these provisions was to give the Agency time to obtain more information about the possible consequences of implementing them and to further evaluate the issues involved. In addition, the Agency decided to hold a public hearing[30] to solicit information from, and the views of, interested persons, including professional groups and associations, the regulated industry, health care professionals, and consumers. The Agency believed such a hearing would help develop a factual basis that the Agency could use to determine whether it is in

[30] The FDA holds public hearings according to the requirements in 21 CFR part 15, Public Hearing Before the Commissioner.

the public health interest to take steps to modify or change the requirements in the final rule.

On May 16, 2000, the House Committee on Appropriations stated in its report accompanying the Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations Bill, 2001 (report 106-619) that it supported the "recent FDA action to delay the effective date for implementing certain requirements of the Prescription Drug Marketing Act until October 1, 2001, and to reopen the administrative record in order to receive additional comments." In addition, the Committee stated it "believes the Agency should thoroughly review the potential impact of the proposed provisions on the secondary wholesale pharmaceutical industry." The Committee directed the Agency to provide a report to the Committee by January 15, 2001,[31] summarizing the comments and issues raised and proposing Agency plans to address the concerns.

The public hearing was held on October 27, 2000 (see Attachments A and B). The Agency left the docket open to receive additional comments after the hearing until November 20, 2000. Although none of the primary wholesaler distributors submitted individual comments to the docket or attended the October public hearing, their views were presented in statements submitted to the docket by their trade association[32] and in responses to questions the Agency submitted to them after the public hearing (see Attachment F). The questions and received responses have been placed in the docket.

III. ANALYSIS OF PUBLIC COMMENTS

At the October 27, 2000, public hearing, various associations, industry groups, and individuals made presentations to an FDA panel (see Attachments A and B). The presenters that addressed prescription drug wholesale distribution issues included the American Pharmaceutical Association, the Pharmaceutical Distributors Association, Purity Wholesaler, Inc., the Food Marketing Institute, the American Veterinary Distributors Association, the Pharmaceutical Research and Manufacturers of America (PhRMA), Public Citizen Health Research Group (Public Citizen), R&S Sales, a wholesale distributor based in Kentucky, and a representative of the National Wholesale Druggists' Association. The presenters that addressed blood derivative issues included the American National Red Cross, America's Blood Centers, and the Blood Centers of America, Inc.

In addition to testimony at the public hearing, FDA received more than 60 written comments and other submissions in response to the May 3, 2000, and September 19, 2000, *Federal Register* notices pertaining to wholesale distribution (i.e., the definition of *on-going relationship* and the pedigree requirement) and blood derivative distribution

[31] The Agency further delayed the effectiveness date for §§ 203.3(u), 203.50, and 203.3(q) until April 1, 2002.

[32] The National Wholesale Druggists' Association (NWDA) represents the health care product distribution industry, including specialty and secondary source distributors.

issues (e.g., the definition of *health care entity* and the inclusion of blood derivative products). Comments on the wholesale distribution requirements were received from industry groups and associations, wholesale distributors that would be considered unauthorized distributors under the final rule for some or all of the products they sell, and individual physicians. The vast majority of comments received opposed the Agency's definition of *on-going relationship* and/or the pedigree requirement in the final rule.

The general perception, as expressed in the comments and the presentations made at the public hearing, is that a significant number of prescription drug wholesale distributors would be adversely affected economically, and might be put out of business, by the requirements in the final rule, because the requirements would prohibit them from distributing some or all of the drugs they currently are distributing.[33]

According to the information provided, there are five large, full-line wholesale distributors, who carry most, if not all types, of pharmaceutical products; purchase the majority, but not all, of their drugs from manufacturers; distribute nationwide to a variety of customers; and handle perhaps 90 percent or more of the $100 billion pharmaceutical product distribution in the United States.[34] Although it was not stated explicitly in the testimony or comments, the Agency assumes that these large distributors would be authorized distributors of record under the final rule for most, or all, of the drugs they sell. The remaining 6 to 10 percent of drugs distributed in the United States that are not distributed by the five large distributors are distributed by 4,000 *secondary distributors*. These secondary distributors in many cases serve smaller areas than the big five distributors and, in some cases, distribute only a limited line of pharmaceuticals.

A. Comments From Those Opposed to the Pedigree/Wholesale Distribution Regulations

1. Secondary Distributors

Although secondary distributors apparently purchase some of their inventory directly from manufacturers, much of their inventory is purchased from other wholesale distributors. The secondary wholesale distributors said they have tried and, for the most part, have been unable to obtain written agreements from manufacturers so they can be considered authorized distributors of record for manufacturers' products. For example, one distributor stated at the hearing that out of 59 manufacturers with whom it does business and contacted to obtain a written authorization agreement, 51 did not respond at all, 1 denied the request, and 7 provided the written agreement.[35]

[33] Transcript 19, 20, 38, 39, 69.

[34] Ibid., 36.

[35] Transcript 73.

In addition, the secondary distributors state that when they purchase drugs from other distributors, it is difficult to obtain pedigrees for them. This is due to the fact that the majority of drugs are distributed through one of the five large distributors, who most likely are authorized distributors of record and, therefore, are not required to provide pedigrees for the drugs they sell.

Secondary distributors assert that because they cannot obtain authorized distributor of record status for many of the drugs they sell or obtain a pedigree for drugs purchased from sources other than a manufacturer, a significant portion of their business would be eliminated by implementation of the final rule.

They testified that they have been operating under the 1988 guidance letter and believe that the Agency should maintain the *status quo* (see discussion of the 1988 guidance letter and the *status quo* in section II.C).

2. Primary or Authorized Distributors

The five primary wholesale distributors most likely have on-going relationships with manufacturers and, therefore, would be considered *authorized distributors* within the meaning of the PDMA. None of the primary wholesaler distributors submitted individual comments to the docket or attended the October public hearing; however, their views were presented in statements submitted to the docket by the NWDA.

The NWDA stated that the typical authorized distributor center carries approximately 14,000 different prescription drug products and that each of these 14,000 products includes an average of three different manufacturer lot numbers at any given time. The NWDA stated further that a distribution center processes an average of 14,600 *order lines* per day. Thus, the burdens and resulting costs associated with requiring records of distribution of individual products by lot number, source, date, or other particulars required under the pedigree requirement would be extremely high.[36] The NWDA estimated that tracking distribution of drug products by lot number would cost approximately $1 million per year per distribution center, which, for NWDA member distribution centers alone, would total $200 million per year. The NWDA stated that it would "vigorously oppose" any effort to impose additional requirements on authorized distributors.[37]

Because no individual comments were received from the primary distributors and they did not attend the Agency's public hearing, the Agency solicited comments from the primary distributors on five specific questions (see Attachment F). The comments submitted by the

[36] Apparently, only 10 percent of distributors can track products by lot number (ERG rept., p. 1-29). In answers to questions posed by the Agency after the hearing, primary distributors said that the costs of implementing a system to maintain a pedigree would be significant.

[37] NWDA comment to September 19, 2000, *Federal Register* notice, comment # EC-2, November 20, 2000, pp. 5, 6.

primary distributors are generally consistent with those submitted by the secondary distributors. Like the secondary wholesalers, primary wholesalers cite the low profit margin associated with their business as a reason why they purchase drugs from secondary wholesalers, and they say they cannot afford the costs associated with passing on the pedigree.

3. Individuals Who Purchase From Secondary Distributors

In addition to the potential economic harm to secondary distributors that implementation of the final rule could have, comments and hearing testimony from some individuals who purchase drugs from secondary distributors, such as retail grocery stores, pharmacies, and physicians, indicated it would be more difficult and expensive to obtain prescription drugs if secondary distributors could not continue distributing to them.[38] For example, the representative for the American Pharmaceutical Association, a group that represents pharmacists, stated that pharmacists frequently use more than one distributor to meet their supply needs and that secondary wholesale distributors are used extensively by pharmacies, particularly to obtain unusual products or to purchase drugs when a pharmacy is in a remote area not served by one of the larger distributors.[39] The representative said that although pharmacies do purchase directly from manufacturers and authorized distributors, secondary distributors are often used as backups to ensure access to a full range of products when they are needed.

4. Competition in the Marketplace

It was argued that implementation of the wholesale distribution requirements in the final rule would generally decrease competition in the marketplace and result in higher prescription drug prices for retailers and, ultimately, consumers.[40] As the secondary distributors explained to the Agency, the secondary wholesale market operates on an arbitrage system whereby secondary distributors, by purchasing and selling drugs at discounts offered by manufacturers and other distributors, help to keep drug prices lower overall for consumers than they would otherwise be without the presence of secondary distributors.[41] Under this system, secondary distributors apparently purchase from and sell drugs to large distributors (i.e., authorized distributors of record). For example, a secondary distributor might purchase a large volume of a discounted drug from a manufacturer prior to the end of the manufacturer's sales quarter and sell it at a later date to a large distributor below the cost the distributor could otherwise obtain it from the manufacturer, from whom it would

[38] Transcript 20.

[39] Ibid., 18, 19, 27.

[40] Ibid., 20, 60, 67-68.

[41] Ibid., 52-54, 65-67.

normally buy. The authorized distributor could then sell the same drug to another secondary distributor or retail outlet.

5. Public Health

Some testimony and comments argued that the final rule would not significantly help to enhance the public health. The comments and testimony stated that existing requirements for State licensing of wholesale distributors in 21 CFR part 205 of the Agency's regulations provide adequate record keeping for the purposes of conducting recalls and ensuring that diverters of prescription drugs can be readily identified by the Agency.[42] With respect to recalls, several presenters at the hearing stated that recalls are generally broadly broadcast by manufacturers, not only to distributors, but also to retail pharmacies and health care professionals.[43]

Several presenters also stated that, even where no pedigree exists for a drug, sales records required to be maintained under 21 CFR part 205 could be used to trace the distribution history of a drug for recall purposes.[44]

In response to the Agency's posthearing questions, which were sent through the NWDA to the major primary distributors, the primary distributors supported maintaining the pedigree requirement as implemented under the *status quo* (industry's interpretation of the Agency's 1988 guidance letter, see discussion in section II.C) because it helps authorized distributors make better purchasing decisions, helps provide a safe and efficient drug distribution system, and helps the primary distributors document where a product originated.

6. Criminal Activity

When asked whether the pedigree requirement helps deter criminal activity, several presenters stated that sales records without a pedigree are sufficient to identify individuals in the distribution chain of a drug who may be responsible for counterfeiting or other diversion activities.[45] Several presenters, including representatives of pharmacies, noted that established relationships exist between retailers and distributors of prescription drugs and that it is these relationships that provide the primary assurance of drug quality when a drug is purchased.[46] The speakers did not believe that a pedigree accompanying the drug would provide significant additional assurance of drug quality.

---

[42] Ibid., 21, 32-33.

[43] Ibid., 25, 60-61. See also ERG rept. pp. 1-28 and 1-29.

[44] Ibid., 42.

[45] Ibid., 51.

[46] Ibid., 105.

7. Recommended Solution

Most of the comments and testimony supported maintaining the *status quo* – that is, the way the wholesale industry has been operating in the 12 years since PDMA was passed. However, the *status quo* (industry's interpretation of the Agency's 1988 guidance letter, see discussion in section II.C) is inconsistent with the PDMA and the regulations. Industry's interpretation allows a broader definition of who is considered an authorized distributor than is contained in either the 1988 guidance letter or the final regulations and assumes that a pedigree need only show prior sales since the drug was last handled by an authorized distributor.

B. Comments From Those In Favor of the Pedigree/Wholesale Distribution Regulations

The comments and testimony that supported the final rule as written came from manufacturers and a public interest group. They stated that the requirements in the regulations are consistent with Congress' objectives in enacting the PDMA and would be helpful in supporting those objectives. The representative from PhRMA stated at the hearing that without a legally required document ensuring traceability back to the manufacturer, one has no guarantee that the pharmaceutical products being sold are not counterfeit or that they were stored under appropriate conditions throughout their shipment chain. The representative also stated that using a small number of sales, rather than a written authorization agreement, to confer authorized distributor of record status on a distributor does not meet the definition of an *on-going relationship* under the statute and argued that the final rule should be implemented as published.

The representative from Public Citizen stated that Congress erred in not requiring a universal pedigree, because the pedigree as conceived would provide the opportunity for unscrupulous distributors to launder counterfeit or substandard drugs through authorized distributors. The representative argued that logistical problems in tracking the pedigree of drugs is not a legitimate reason for not requiring all distributors to maintain a pedigree. He recommended that the Act be amended to also apply the pedigree requirement to authorized distributors.

C. Comments From Blood Centers

The Agency received comments on blood-related issues from Congress, various national, regional, and local blood centers, blood center associations, and individuals. Presenters that addressed issues related to blood derivative product distribution at the October 27, 2000, hearing included the American National Red Cross (Red Cross), America's Blood Centers, and Blood Centers of America.

According to the testimony, more than 15 percent of all U.S. blood derivative products are distributed by community and Red Cross blood centers, with the Red Cross alone

accounting for 10 percent. In the case of the Red Cross, the products distributed are prepared by contract manufacturers for Red Cross from plasma collected by Red Cross and distributed under the Red Cross label.

In addition to their role collecting blood and plasma and distributing blood derivative products, blood centers also provide certain health care services to the hospitals and health care entities they serve. These services include therapeutic phlebotomy, plasma exchange, and stem cell and cord blood collection and processing. In addition, blood centers work directly with physicians at hospitals and health care entities to provide medical expertise on the appropriate use of blood derivative products they are involved in distributing. It was argued that continued provision of these services is important to the public health, because it provides patients access to a higher level of medical expertise than would be possible to obtain or practical to maintain at individual community hospitals. It was argued that the value of the specialized medical expertise that exists in blood centers is critical to community health care and does not exist in the majority of local hospitals.

America's Blood Centers stated that the provision of medical expertise by blood centers is subsidized by the small margins that blood centers earn on sales of blood derivative products. Comments and testimony stated that there is no evidence that the current system of blood derivative product distribution results in any distribution of counterfeit, expired, adulterated, misbranded, or otherwise unsuitable blood derivative products to consumers. Finally, it was argued that manufacturers of blood derivative products are not granting centers special pricing that would not be available to other distributors and that blood centers are not unfairly competing with other distributors of these products.

According to the comments and testimony, implementation of the final rule as published would be detrimental to the public health because it would disrupt distribution of blood derivative products and interfere with longstanding relationships between blood centers and health care entities. The final rule would hinder centers' ability to provide blood derivative products and medical services associated with those products to hospitals, hemophilia treatment centers, and other providers.

The Red Cross stated that 85 percent of their anti-hemophilic factor is supplied directly to health care entities. They stated that implementation of the final rule would deny hemophilia patients access to this product because many treatment centers are smaller entities that are not supported by large distributors. Additionally, the Red Cross stated that 15 percent of their IVIG (intravenous immunoglobulin) products and 10 percent of their albumin product are provided directly to health care providers and account for 26,000 to 69,000 infusions annually.

It was argued that distribution of blood derivative products to hospitals and health care entities by blood centers is cost efficient because it relieves these entities of the burden of carrying inventory of specialized products that may only be needed on an infrequent basis. Also, it was stated that small or medium-size hospitals may have trouble negotiating with

larger distributors and, even if needed blood derivative products could be obtained from larger distributors, they would be more expensive.

It also was argued that blood centers, as neutral, not for profit entities, are able to distribute products in short supply equitably throughout the communities they serve, avoiding problems with hoarding of products and price gouging during times of shortages. The recent shortages of immunoglobulin and alpha-1 antitrypsin were cited as examples.

IV. AGENCY CONCLUSIONS

After carefully reviewing all of the comments, the Agency believes that by revising its regulations, it would be able to address some, but not all, of the concerns raised by both the secondary wholesale industry and the blood industry. Four issues seem to be the focus of most concerns.

A. Key Issues

Most concerns about the final rule focus on four key issues:

1. Who qualifies as an authorized distributor?

2. Should authorized distributors be exempt from maintaining and passing on a pedigree?

3. What is the meaning of the phrase *each prior sale*?

4. Should blood centers that provide some health care services be permitted to distribute blood derivative products?

By changing its regulations, the Agency would be able to address issues 1 and 4. It would take statutory changes, however, to address concerns raised regarding issues 2 and 3.

1. Who qualifies as an authorized distributor?

Current § 203.3(u) of the final regulations requires a written agreement between a manufacturer and each of its authorized distributors. The Agency agrees that this requirement is restrictive and places control of who can be an authorized distributor in the hands of manufacturers. It could prohibit many secondary distributors, including those who make regular purchases from manufacturers, from qualifying as authorized distributors of record. This could have anticompetitive consequences without the corresponding benefit of protecting the public health.

The Agency believes that changing the regulations to broaden the definition of *on-going relationship* could enable more wholesale distributors to qualify as authorized distributors. FDA believes that an on-going relationship could be demonstrated by evidence of two sales within the previous 24-month period. With such a change, a distributor who is able to provide such evidence would be considered an authorized distributor. If the definition in the regulation were revised, a greater number of wholesale distributors would be able to qualify as authorized distributors and would not have to maintain or pass on a pedigree as required under the PDMA and FDA's implementing regulations. One possible consequence of this change would be that it could reduce the extent to which pedigrees currently are maintained and passed on during the distribution of prescription drugs.

Despite such a change, some wholesale distributors would still not qualify as authorized distributors. For these wholesale distributors, the pedigree requirement would remain problematic because under the regulations, they would have to obtain a pedigree showing each prior sale and pass it on when reselling prescription drugs. As discussed in the next section, they still might not be able to obtain a pedigree, unless the PDMA were changed.

2. Should authorized distributors be exempt from maintaining and passing on a pedigree?

In 1987, when PDMA was enacted, the general understanding of the prescription drug distribution system was that most prescription drugs pass in a linear manner from a manufacturer to a retail outlet through a primary, or authorized, distributor of record (an identifiable group of distributors who could be characterized by their on-going relationships with manufacturers). Congress exempted authorized distributors from the pedigree requirements in the PDMA. As a result, most authorized distributors do not maintain or pass on pedigrees. This creates a substantial problem for unauthorized distributors wishing to purchase prescription drugs from an authorized distributor and resell them. Under the PDMA, without a pedigree, an unauthorized distributor cannot legally resell prescription drugs. The secondary wholesale distributor might be able to create an incomplete pedigree that indicates whom he or she purchased the drugs from, but that pedigree would not reflect each sale back to the manufacturer as required by the PDMA.

The wholesale prescription drug distribution system has changed considerably since 1987 when the PDMA was enacted. According to the testimony and other comments, today, between 5 and 10 percent of the $100 billion wholesale pharmaceutical market is handled by secondary wholesalers (see Attachment G, table 1-7). In many cases, a primary distributor purchases prescription drugs from a manufacturer and resells

them to one or more secondary wholesalers, who subsequently resell them to other wholesalers. In some cases, manufacturers sell directly to secondary distributors. Some drugs may go through several transaction cycles involving multiple primary and secondary wholesalers before arriving at their retail destination.

Furthermore, the volume of drugs that authorized distributors purchase from secondary wholesalers is significant. The NWDA told the Agency that the big five distributors purchase 2 to 4 percent of their products from sources other than manufacturers. One of the big five reported that of the approximately $16 billion total inventory purchased in 2000, approximately $350 million came from nonmanufacturer vendors.

Authorized distributors are not required to maintain a pedigree or pass one along when they resell prescription drugs to another wholesaler or retail outlet. As a result, an unscrupulous wholesale distributor seeking to introduce a counterfeit or diverted drug into commerce need only *launder* the product by selling it to an unknowing authorized distributor who may or may not know the true origins of the drug and who is not required to maintain or pass on a pedigree when the drugs are resold.

The PDMA pedigree exemption for authorized distributors not only puts unauthorized distributors at a disadvantage, but also has the effect of *wiping the slate clean* each time prescription drugs pass through an authorized distributor. Today under the *status quo*, a large volume of prescription drugs move through the system without pedigrees, or with incomplete pedigrees, because they have passed through an authorized distributor at least once before reaching their retail destination.

FDA believes that maintaining and passing on a pedigree on prescription drugs provides a valuable tool — even if this is required of only those secondary distributors unable to attain authorized distributor status. The pedigree requirement is a deterrent to the introduction and retail sale of substandard, ineffective, and counterfeit drugs. Although a pedigree can be, and sometimes is, falsified to disguise the true source of prescription drugs, FDA believes that requiring a pedigree makes it more difficult for someone planning to introduce counterfeit or diverted drugs into commerce. Requiring a pedigree also facilitates the efforts of law enforcement personnel seeking to identify the source of a counterfeit or diverted drug shipment and take action against those responsible.

The Agency also believes that, given today's prescription drug distribution system, the PDMA provision that exempts authorized distributors from having to maintain and pass on a pedigree undermines the purpose of the pedigree by allowing for potential gaps in the distribution history. If the

definition of *authorized distributor* were broadened, fewer wholesalers than before would be required to maintain and pass on pedigrees on prescription drugs.

FDA does not have the authority to require authorized distributors to maintain and pass on a pedigree. Such a requirement would necessitate a statutory change. Therefore, Congress may want to consider whether the benefits of requiring authorized distributors to maintain and pass on pedigrees to deter the introduction of counterfeit or diverted drugs outweigh the costs to the primary and secondary distributors of maintaining and passing along such pedigrees.

3. What is the meaning of the phrase *each prior sale*?

Section 503(e)(1)(A) of the Federal Food, Drug, and Cosmetic Act requires that the pedigree must identify "each prior sale, purchase, or trade."

The Agency's 1988 guidance letter stated that the pedigree could start with the "manufacturer or authorized distributor of record." It was the Agency's understanding at the time that the authorized distributor of record would be the distributor to whom the manufacturer first sold the drugs, not just any authorized distributor who happened to purchase the drugs somewhere along the distribution chain.

Authorized distributors are exempt from the pedigree requirement and in most cases will not provide a pedigree to a distributor to whom they sell prescription drugs. In the years since issuance of the 1988 guidance letter, unauthorized distributors have interpreted the Agency's guidance letter to mean that the pedigree need only go back to the ***most recent*** authorized distributor who handled the drug. This interpretation is what pharmaceutical distributors consider the *status quo*.

The language in the current regulation, which is based on the statute, clarifies that the pedigree must identify "each prior sale, purchase, or trade of such drug" (§ 203.50(a)) and include "all parties to each prior transaction...starting with the manufacturer" (§ 203.50(a)(6)). Consistent with Congress' intent in enacting the PDMA, this requirement ensures that a complete history of a prescription drug is created and passed along.

As stated in the comments to the docket and in testimony given at the public hearing, the regulation, although consistent with the statute, is inconsistent with the *status quo* as understood by wholesalers. As a result, under the *status quo,* whenever a prescription drug is sold to an authorized distributor of record, the transaction history prior to that sale is no longer maintained. Secondary wholesale distributors have asked the Agency to amend the

regulations to be consistent with their interpretation of the *status quo* (i.e., the pedigree need only go back to the most recent authorized distributor who handled the drug).

Because § 203.50 reflects the language of the statute, the FDA believes that it cannot revise the regulation to make it consistent with the *status quo*. Such a requirement would necessitate a statutory change. Congress may want to consider this issue in conjunction with the issue of granting authorized distributors an exemption from the pedigree requirement. Congress could require that the pedigree go back only as far as the last authorized distributor, rather than to the manufacturer. This would, however, as pointed out in the previous section, leave gaps in the pedigree and encourage the laundering of drugs through unknowing authorized distributors. Congress may wish to consider whether the benefits of requiring that a complete pedigree be maintained and passed along outweigh the costs to the primary and secondary distributors of maintaining and passing along such a pedigree.

4. Should blood centers that provide some health care services be permitted to distribute blood derivative products?

Based on the comments it has received, the Agency is reconsidering its previous position with respect to blood centers that provide certain health care services and distribute blood derivative products. The Agency is considering whether blood centers that provide some blood-related health care services should be able to continue to distribute blood derivative products.

The Agency is considering whether it should modify the regulation to allow blood centers that offer certain limited health care services and also function as wholesale distributors of blood derivative products to continue operating in both capacities.

B. Summary of Conclusions

After carefully reviewing all of the comments, the Agency believes that it would be able to address some, but not all, of the concerns raised by both the secondary wholesale industry and the blood industry.

- By changing its regulations, the Agency could broaden the definition of *authorized distributor* — although this change could result in even fewer wholesalers than before maintaining and passing on pedigrees for prescription drugs.

- The Agency is considering whether it should amend the regulation to permit those blood centers that provide certain limited health care services to distribute blood derivative products.

The Agency believes, as discussed above, that concerns related to continuing to exempt authorized distributors from the pedigree requirement and to the exact meaning of the phrase *each prior sale* can be addressed only through statutory remedies.

V. DECISION TO FURTHER DELAY THE EFFECTIVE DATE

The Agency has delayed the effectiveness date for §§ 203.3(u) and 203.50 and the applicability of § 203.3(q) to wholesale distribution of blood derivatives by health care entities until April 1, 2002.

ATTACHMENT A: LIST OF PRESENTERS AT THE HEARING

FDA Part 15 Hearing — Prescription Drug Marketing Act

October 27, 2000
5630 Fishers Lane, Rm 1061
Rockville, MD 20852

8:30 a.m. to 4:30 p.m.

8:30 Welcome and Introduction of Panelists

Jane Axelrad, Associate Director for Policy, Center for Drug Evaluation and Research (CDER)
Diane Maloney, Associate Director for Policy, Center for Biologics Evaluation and Research (CBER)

Scheduled Presenters

Susan Winckler, ***American Pharmaceutical Association***

Anthony L. Young, ***Pharmaceutical Distributors Association***

Salvatore Ricciardi, ***Purity Wholesaler***

Patrick C. O'Connor, ***International Warehouse Logistics Association***

BREAK

Ty Kelley, ***Food Marketing Institute***

Alan Goldhammer, ***Pharmaceutical Research and Manufacturers of America (PhRMA)***

Charles F. Franz, ***American Veterinary Distributors Association***

Larry Sasich, ***Public Citizen Health Research Group***

LUNCH

Shelley Capps, ***International Academy of Compounding Pharmacists***

Paul Devine, ***Truxton Incorporated (Pharmaceuticals and Medical Supplies)***

Chris Lamb, ***American Red Cross***

Jim MacPherson, ***America's Blood Center***

Laura McDonald, ***Blood Centers of America, Inc./hemerica***

<u>Unscheduled Presenters</u>

Steven Shirley, ***R&S Sales, Fountain Run, Kentucky***

Steve Sims, ***Lobbyist***

Derek Robertson, ***representing 15 hemophilia treatment centers.***

ATTACHMENT B: LIST OF AGENCY PANEL MEMBERS AT THE HEARING

Jane A. Axelrad
Associate Director for Policy
Center for Drug Evaluation and Research, FDA

Mary Elizabeth Jacobs
Associate Director for Regulatory Affairs
Office of Blood Research and Review
Center for Biologics Evaluation and Research, FDA

William McConagha
Associate Chief Counsel for Enforcement, FDA

Lana Ogram
Director, Division of Prescription Drug Compliance and Surveillance
Center for Drug Evaluation and Research, FDA

Margaret O'Rourke
Senior Regulatory Expert, Prescription Drug Marketing Act
Center for Drug Evaluation and Research, FDA

Seth Ray
Associate Chief Counsel for Drugs, FDA

Toni Stifano
Associate Director for Labeling Policy and Medical Communication
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research, FDA

John Taylor
Director, Office of Enforcement
Office of Regulatory Affairs, FDA

ATTACHMENT C: LIST OF KEY DATES

April 22, 1988: The Prescription Drug Marketing Act was signed by the President.

August 26, 1992: PDMA was modified by the Prescription Drug Amendments of 1992.

March 14, 1994: The Agency issued a proposed rule implementing the PDMA.

May 30, 1994: Comment period to close; comment period subsequently was extended to August 15, 1994.

December 3, 1999: The Agency published final regulations in 21 CFR part 203 implementing the provisions of the PDMA.

March 13, 2000: Received petition from U. S. Small Business Administration to reconsider final rule.

March 31, 2000: Received petition from Pharmaceutical Distributors Association to stay implementation of final regulation until October 1, 2001.

March 29, 2000: Met with industry representatives.

May 3, 2000: Agency delayed effective date for certain requirements of the final rule and reopened the administrative record.

May 16, 2000: House Committee on Appropriations issues report accompanying the Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations Bill 2001 (report 106-619)

September 19, 2000: Agency announced the public hearing

October 27, 2000: Agency held public hearing

November 20, 2000: Comment period on public hearing closed.

February 2001: Agency submits report to Congress.

ATTACHMENT D: NOTICE ANNOUNCING THE OCTOBER 27, 2000, HEARING

§ 314.445 Guidance documents.

(a) FDA has made available guidance documents under § 10.115 of this chapter to help you to comply with certain requirements of this part.

(b) The Center for Drug Evaluation and Research (CDER) maintains a list of guidance documents that apply to CDER's regulations. The list is maintained on the Internet and is published annually in the **Federal Register**. A request for a copy of the CDER list should be directed to the Office of Training and Communications, Division of Communications Management, Drug Information Branch (HFD–210), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

PART 316—ORPHAN DRUGS

40. The authority citation for 21 CFR part 316 continues to read as follows:

Authority: 21 U.S.C. 360aa, 360bb, 360cc, 360dd, 371.

41. Revise § 316.50 to read as follows:

§ 316.50 Guidance documents.

FDA's Office of Orphan Products Development will maintain and make publicly available a list of guidance documents that apply to the regulations in this part. The list is maintained on the Internet and is published annually in the **Federal Register**. A request for a copy of the list should be directed to the Office of Orphan Products Development (HF–35), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

PART 500—GENERAL

42. The authority citation for 21 CFR part 500 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 342, 343, 348, 351, 352, 353, 360b, 371.

§ 500.80 [Amended]

43. In § 500.80(a), remove the word "guidelines" wherever it appears and add in its place the words "guidance documents".

PART 514—NEW ANIMAL DRUG APPLICATIONS

44. The authority citation for 21 CFR part 514 continues to read as follows:

Authority: 21 U.S.C. 351, 352, 360b, 371, 379e, 381.

§ 514.1 [Amended]

45. In § 514.1(d)(2), remove the word "guidelines" wherever it appears and add in its place the words "guidance documents".

PART 601—LICENSING

46. The authority citation for 21 CFR part 601 continues to read as follows:

Authority: 15 U.S.C. 1451–1561; 21 U.S.C. 321, 351, 352, 353, 355, 360, 360c–360f, 360h–360j, 371, 374, 379e, 381; 42 U.S.C. 216, 241, 262, 263; sec. 122, Pub. L. 105–115, 111 Stat. 2322 (21 U.S.C. 355 note).

47. Add § 601.29 to subpart C to read as follows:

§ 601.29 Guidance documents.

(a) FDA has made available guidance documents under § 10.115 of this chapter to help you comply with certain requirements of this part.

(b) The Center for Biologics Evaluation and Research (CBER) maintains a list of guidance documents that apply to the center's regulations. The lists are maintained on the Internet and are published annually in the **Federal Register**. You may request a copy of the CBER list from the Office of Communication, Training, and Manufacturers Assistance (HFM–40), Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852–1448.

PART 803—MEDICAL DEVICE REPORTING

48. The authority citation for 21 CFR part 803 continues to read as follows:

Authority: 21 U.S.C. 352, 360, 360i, 360j, 371, 374.

§ 803.14 [Amended]

49. In § 803.14(b), remove the word "guidelines" and add in its place the words "guidance documents".

PART 814—PREMARKET APPROVAL OF MEDICAL DEVICES

50. The authority citation for 21 CFR part 814 continues to read as follows:

Authority: 21 U.S.C. 351, 352, 353, 360, 360c–360j, 371, 372, 373, 374, 375, 379, 379e, 381.

51. In § 814.20, revise paragraph (g) to read as follows:

§ 814.20 Application.

* * * * *

(g) FDA has issued a PMA guidance document to assist the applicant in the arrangement and content of a PMA. This guidance document is available on the Internet at http://www.fda.gov/cdrh/dsma/pmaman/front.html. This guidance document is also available upon request from the Center for Devices and Radiological Health, Division of Small Manufacturers Assistance (HFZ–220), 1350 Piccard Dr., Rockville, MD 20850, FAX 301–443–8818.

* * * * *

PART 860—MEDICAL DEVICE CLASSIFICATION PROCEDURES

52. The authority citation for 21 CFR part 860 continues to read as follows:

Authority: 21 U.S.C. 360c, 360d, 360e, 360i, 360j, 371, 374.

§ 860.3 [Amended]

53. In § 860.3(c)(2), remove the words "guidelines" and "guidelines for" and add in their place the words "guidance documents" and "guidance on", respectively.

Dated: September 1, 2000.

Margaret M. Dotzel,

Associate Commissioner for Policy.

[FR Doc. 00–23887 Filed 9–18–00; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 203 and 205

[Docket No. 92N–0297]

Prescription Drug Marketing Act of 1987; Prescription Drug Amendments of 1992; Policies, Requirements, and Administration Procedures; Public Hearing

AGENCY: Food and Drug Administration, HHS.

ACTION: Announcement of public hearing; request for comments.

SUMMARY: The Food and Drug Administration (FDA) is announcing a public hearing to discuss certain requirements of the final rule 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 (Modernization Act), which published in the **Federal Register** of December 3, 1999 (64 FR 67720), (hereinafter referred to as the PDMA final rule). The purpose of the hearing is to elicit comment from interested persons, including professional groups and associations, the regulated industry, health care professionals, and consumers, on the potential impact of certain requirements in the PDMA final rule relating to wholesale distribution of prescription drugs by distributors that are not authorized distributors of record, and distribution of blood derivatives by

entities that meet the definition of a "health care entity" in the PDMA final rule. The agency will use information obtained from the hearing and the comments to this document to determine what steps, if any, should be taken to modify the requirements in the PDMA final rule.

DATES: The public hearing will be held on Friday, October 27, 2000, from 8:30 a.m. to 4:30 p.m. Submit written notices of participation and comments for consideration at the hearing to the docket number listed in the heading of this document by October 13, 2000.[1] Written comments will be accepted after the hearing until November 20, 2000.

ADDRESSES: The public hearing will be held at 5630 Fishers Lane, rm. 1066, Rockville, MD 20852. Submit written notices of participation to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Comments should also be submitted to the Dockets Management Branch (address above). Transcripts of the hearing will be available for review at the Dockets Management Branch (address above).

FOR FURTHER INFORMATION CONTACT: Anne M. Henig, Center for Drug *Evaluation and Research (HFD–006)*, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–594–5410.

SUPPLEMENTARY INFORMATION:

I. Background

A. Legislative and Regulatory Requirements for Distribution of Prescription Drugs by Unauthorized Distributors

PDMA, as amended 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, among other things, establish requirements for the wholesale distribution of prescription drugs: and to prohibit, with certain exceptions, the sale or offer to sell prescription drugs that have been purchased by a hospital or other health care entity or that have been donated or supplied at a reduced price to a charitable organization.

Section 503(e)(1)(A) of the act states that each person who is engaged in the wholesale distribution of a prescription drug who is not the manufacturer or an authorized distributor of record for the drug must, before each wholesale distribution of a drug, provide to the person receiving the drug a statement, also known as a drug "pedigree," (in such form and containing such information as the Secretary may require) 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. Section 503(e)(4)(A) of the act states that, for the purposes of section 503(e), the term "authorized distributors of record" means those distributors with whom a manufacturer has established an "ongoing relationship" to distribute the manufacturer's products.

In the PDMA final rule, the agency published regulations in part 203 (21 CFR part 203) implementing these and other provisions of PDMA. Section 203.50 implements section 503(e)(1)(A) of the act and requires that, 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 must provide to the purchaser a statement identifying each prior sale, purchase, or trade of the drug. The identifying statement must include the proprietary and established name of the drug, its dosage, the container size, the number of containers, lot or control numbers of the drug being distributed, the business name and address of all parties to each prior transaction involving the drug, starting with the manufacturer, and the date of each previous transaction. Section 203.3(b) defines "authorized distributor of record" as a distributor with whom a manufacturer has established an ongoing relationship to distribute the manufacturer's products. "Ongoing relationship" is defined in § 203.3(u) to mean 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.

Thus, the PDMA final rule requires unauthorized distributors (i.e., those distributors who do not have a written authorization agreement) to provide a drug statement, or pedigree, to purchasers showing the entire prior sales history of the drug back to the first sale by the manufacturer. As discussed in the preamble to the PDMA final rule (64 FR 67720 at 67747), manufacturers and authorized distributors of record are not required to provide an identifying statement when selling a drug, although the agency encouraged them to do so voluntarily to permit unauthorized distributors to continue to be able to purchase products from them.[2]

The provisions in the PDMA final rule related to wholesale distribution of prescription drugs by unauthorized distributors (i.e., §§ 203.3(u) and 203.50) were adopted from the provisions in the proposed rule published in the **Federal Register** of March 14, 1994 (59 FR 11842), and are essentially the same as the proposed provisions, except the definition for "ongoing relationship" in the proposed rule was revised to eliminate certain requirements.[3] The agency received two comments on the proposed definition of ongoing relationship and one comment on proposed § 203.50, and responded in detail to those comments in the preamble to the PDMA final rule (see 64 FR 67720 at 67727, 67728, and 67747).

B. Legislative and Regulatory Requirements Restricting Distribution of Blood Derived Prescription Drug Products by Health Care Entities

Section 503(c)(3)(A) of the act states that no person may sell, purchase, or trade, or offer to sell, purchase, or trade, any prescription drug that was purchased by a public or private hospital or other health care entity. Section 503(c)(3)(B) of the act states several exceptions to section 503(c)(3)(A), none of which are relevant to this discussion. Section 503(c)(3) of the act also states 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 * * *."

Sections 203.20 of the PDMA final rule provides, with certain exceptions, that no person may sell, purchase, or trade, or offer to sell, purchase, or trade any prescription drug that was purchased by a public or private hospital or other health care entity or donated or supplied at a reduced price to a charitable institution. In § 203.3(q)

[1] Until recently, two dockets were being used to receive comments on issues related to PDMA. One docket, the docket established in 1988, will no longer be used. For simplicity, all comments related to any issues involving PDMA should be forwarded to the docket listed in the heading of this document.

[2] An unauthorized wholesale distributor that purchases a product from a manufacturer or authorized distributor of record without an identifying statement showing the prior sales of the drug could not provide an identifying statement to its purchasers and, therefore, could not conduct further wholesale transactions of the drug in compliance with § 203.50.

[3] The proposed rule defined "ongoing relationship" to require a written agreement and, in addition, the following two requirements that were eliminated in the final rule: (1) That a sale be completed under the written agreement and (2) that the distributor be listed on the manufacturer's list of authorized distributors.

of the PDMA final rule, "Health care entity" is defined as meaning any person that provides diagnostic, medical, surgical, or dental treatment, or chronic or rehabilitative care, but does not include any retail pharmacy or wholesale distributor. Under both the act and the PDMA final rule, a person could not simultaneously be a health care entity and a retail pharmacy or wholesale distributor. Thus, under the PDMA final rule, blood centers functioning as health care entities could not engage in wholesale distribution of prescription drugs, except for blood and blood components intended for transfusion, which are exempt from PDMA under § 203.1 of the PDMA final rule. Blood and blood components include whole blood, red blood cells, platelets, and cryoprecipitated antihemophilic factor, which are prepared by blood banks who collect blood from donors and separate out the components using physical or mechanical means. Blood derivatives are derived from human blood, plasma, or serum through a chemical fractionation manufacturing process. Examples of blood derivative products include albumin, antihemophilic factor, immune globulin, and alpha-1 anti-tripsin. As discussed in the preamble to the PDMA final rule in response to comments (64 FR 67720 at 67725 through 67727), blood derivative products are not blood or blood components intended for transfusion and therefore could not be distributed by health care entities, including full service blood centers that function as health care entities, after the final rule goes into effect. The agency received several comments on the proposed rule objecting to the applicability of the sales restrictions to the sale of blood derivatives by blood centers that function as health care entities, and responded in detail to those comments (see 64 FR 67720 at 67726).

C. Events Leading to the Delay of the Effective Date; Need for the Public Hearing

After publication of the PDMA final rule, the agency received letters and petitions and had other communications with industry, industry trade associations, and members of Congress objecting to the provisions in §§ 203.3(u) and 203.50. On March 29, 2000,[4] the agency met with representatives from the wholesale drug industry and industry associations. The meeting participants discussed their concerns with both: (1) The requirement in § 203.3(u) that there be a written authorization agreement between a manufacturer and distributor for the distributor to be considered an authorized distributor of record under § 203.3(b), and (2) the requirement in § 203.50 that unauthorized distributors provide a pedigree showing all prior sales going back to the manufacturer.

The meeting participants asserted that manufacturers are unwilling to enter into written authorization agreements with the majority of smaller wholesalers. As a result, these wholesalers cannot become authorized distributors of record for the drugs they sell. The meeting participants also said that smaller wholesalers cannot obtain the required pedigree showing all prior sales of the drugs they purchase for sale because a large portion of these drugs are purchased from authorized distributors who are not required to provide a pedigree and who are unwilling to voluntarily provide them. The meeting participants asserted that authorized distributors will not voluntarily provide pedigrees when they sell drugs to unauthorized distributors because it would require them to change their warehouse and business procedures, which would entail additional effort and expense.

The meeting participants asserted that implementation of the PDMA final rule will prevent over 4,000 smaller, unauthorized distributors from distributing drugs to their customers and may put them out of business, at least with respect to their prescription drug wholesale business. They also asserted that because many of their customers are smaller retail outlets that are not served by larger distributors, implementation of the PDMA final rule may leave certain markets for prescription drugs, and ultimately consumers for prescription drugs, underserved.

In addition to the meeting discussed above and other informal communications that FDA has had with industry, industry associations, and Congress, FDA received a petition for stay of action requesting that the relevant provisions of the PDMA final rule be stayed until October 1, 2001. That petition was supported by numerous letters submitted to the docket from entities that would be considered unauthorized distributors under the PDMA final rule. The agency also received a petition for reconsideration from the Small Business Administration (SBA) requesting that FDA reconsider the PDMA final rule and suspend its effective date based on the projected severe economic impact it would have on over 4,000 small businesses. The petitions argued that the requirement for a written agreement in § 203.3(u) is unreasonable because manufacturers are not willing to enter into such agreements with the majority of smaller distributors. The petitions also asserted that authorized wholesalers are not now able and could not provide, at a reasonable cost, a pedigree to their unauthorized distributor customers that meets the requirements of § 203.50 of the PDMA final rule. The SBA petition asserted that, if the effective date of the PDMA final rule is not stayed, drug products now in the inventory of wholesalers will have to be cleared and new orders will have to cease or be severely limited to comply with the PDMA final rule's December 4, 2000, effective date, with corresponding disruptions in the distribution of drugs possible by summer 2000.

In addition to the submissions on wholesale distribution by unauthorized distributors, the agency has received several letters on, and has held several meetings to discuss, the implications of the final regulations on blood centers that distribute blood derivative products and provide health care as a service to the hospitals and patients they serve. The blood center industry asserts that the regulations and, particularly the definition of "health care entity," will severely inhibit their ability to provide full service care to the detriment of client hospitals and the patients they serve, and may disrupt the distribution of these products to the public. The agency also received a letter from Congress on this issue.

Based on the concerns expressed by industry, industry associations, and Congress about implementing §§ 203.3(u) and 203.50 by the December 4, 2000, effective date, the agency published a document in the **Federal Register** of May 3, 2000 (65 FR 25639), delaying the effective date for those provisions until October 1, 2001 (the May 2000 document). In addition, the May 2000 document delayed the applicability of § 203.3(q) to wholesale distribution of blood derivatives by health care entities until October 1, 2001. The May 2000 document also reopened the administrative record and gave interested persons until July 3, 2000, to submit written comments. As stated in the May 2000 document, the purpose of delaying the effective date for these provisions was to give the agency time to obtain more information about the possible consequences of implementing them and to further evaluate the issues involved.

[4] In a document published in the **Federal Register** of May 3, 2000 (65 FR 25639 at 25640), the agency incorrectly stated that this meeting occurred in early February 2000.

On May 16, 2000, the House Committee on Appropriations (the Committee) stated in its report accompanying the Agriculture, Rural Development, Food and Drug Administration, and Related Agencies Appropriations Bill, 2001 (report 106–619) that it supported the "recent FDA action to delay the effective date for implementing certain requirements of the Prescription Drug Marketing Act until October 1, 2001 and reopen the administrative record in order to receive additional comments." In addition, the Committee stated that it "believes the agency should thoroughly review the potential impact of the proposed provisions on the secondary wholesale pharmaceutical industry." The Committee directed the agency to provide a report to the Committee by January 15, 2001, summarizing the comments and issues raised and agency plans to address the concerns.

In light of the complexity of the issues involved and the potentially serious economic and public health consequences that implementation of the relevant provisions of the PDMA final rule may have, the agency believes that it is appropriate to hold a public meeting to solicit information from, and the views of, interested persons, including professional groups and associations, the regulated industry, health care professionals, and consumers. This will help to develop an adequate factual basis that the agency can use to determine whether it is in the public health interest to take steps to modify or change the requirements in the PDMA final rule.

II. Scope of the Hearing

The PDMA final rule provisions discussed in this document raise many complex economic and public health issues. To promote a more useful discussion at the public hearing, FDA has developed the following list of questions, which are of specific interest. This list is not intended to be exclusive, and presentations and comments answering other questions or addressing other issues, to the extent that they are pertinent to the PDMA final rule provisions discussed in this document, are encouraged.

A. Questions on Distribution of Prescription Drugs by Unauthorized Distributors

1. How does the PDMA final rule, as published, affect the ability of unauthorized distributors to engage in drug distribution, i.e., what specific requirements would be difficult or impossible for unauthorized distributors to meet? Why?

2. If the PDMA final rule diminished the ability of unauthorized distributors to engage in drug distribution, what effect would this have on the drug distribution system? What, if any, adverse public health consequences would result? What would be the economic costs to manufacturers, distributors (authorized and unauthorized), and consumers of drugs?

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?

4. If the act were amended by Congress to require authorized distributors to provide a pedigree, what types of additional costs and burdens would they incur?

5. Could specific changes be made to the information that is required under § 203.50 to appear on a pedigree to make it more practical, from an authorized distributor's standpoint, to voluntarily provide a pedigree? Would use of a standardized government form be helpful?

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?

B. Questions on Distribution of Blood Derivatives by Blood Banks and Other Health Care Entities

1. What distribution systems are available for blood derived products? Do these distribution systems differ from those for other types of prescription drugs? If so, how?

2. What effect would the PDMA final rule, as published, have on the distribution system for blood derived products? What, if any, adverse public health consequences would result? What would be the economic costs to manufacturers, distributors, and consumers of blood derived products?

3. If blood derived products were excluded from the sales restrictions (i.e., if such products were permitted to be sold by health care entities), would there be an increased risk of distribution of counterfeit, expired, adulterated, misbranded, or otherwise unsuitable blood derived products to consumers and patients? Why or why not?

4. Do manufacturers of blood derived products provide these products to health care entities, particularly those that are also charitable organizations, at a lower price when compared to other customers? Do manufacturers sell these products to charitable or for profit health care entities with the understanding that the products will be used for patients of the purchasing health care entity and will not be resold to other health care entities, distributors, or retail pharmacies?

III. Notice of Hearing Under 21 CFR Part 15

The Commissioner of Food and Drugs (the Commissioner) is announcing that the public hearing will be held in accordance with part 15 (21 CFR part 15). The presiding officer will be the Commissioner or her designee. The presiding officer will be accompanied by a panel of FDA employees with relevant expertise.

Persons who wish to participate in the part 15 hearing must file a written notice of participation with the Dockets Management Branch (address above) prior to October 13, 2000. To ensure timely handling, any outer envelope should be clearly marked with the Docket No. 92N–0297 and the statement "FDA PDMA Hearing." Groups should submit two copies. The notice of participation should contain the person's name; address; telephone number; affiliation, if any; the sponsor of the presentation (e.g., the organization paying travel expenses or fees), if any; brief summary of the presentation; and approximate amount of time requested for the presentation. The agency requests that interested persons and groups having similar interests consolidate their comments and present them through a single representative. FDA will allocate the time available for the hearing among the persons who file notices of participation as described above. If time permits, FDA may allow interested persons attending the hearing who did not submit a written notice of participation in advance to make an oral presentation at the conclusion of the hearing.

After reviewing the notices of participation and accompanying information, FDA will schedule each appearance and notify each participant by telephone of the time allotted to the person and the approximate time the person's oral presentation is scheduled to begin. The hearing schedule will be available at the hearing. After the hearing, the hearing schedule will be placed on file in the Dockets Management Branch under Docket No. 92N–0297.

Under § 15.30(f), the hearing is informal, and the rules of evidence do not apply. No participant may interrupt the presentation of another participant. Only the presiding officer and panel members may question any person during or at the conclusion of each presentation.

Public hearings under part 15 are subject to FDA's policy and procedures for electronic media coverage of FDA's public administrative proceedings (part 10, subpart C (21 CFR part 10, subpart C)). Under § 10.205, representatives of the electronic media may be permitted, subject to certain limitations, to videotape, film, or otherwise record FDA's public administrative proceedings, including presentations by participants. The hearing will be transcribed as stipulated in § 15.30(b). The transcript of the hearing will be available on the Internet at http://www.fda.gov/ohrms/dockets and orders for copies of the transcript can be placed at the meeting or through the Freedom of Information Staff (HFI–35), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

Any handicapped persons requiring special accommodations to attend the hearing should direct those needs to the contact person listed above.

To the extent that the conditions for the hearing, as described in this document, conflict with any provisions set out in part 15, this document acts as a waiver of those provisions as specified in § 15.30(h).

IV. Request for Comments

Interested persons may submit to the Dockets Management Branch (address above) written notices of participation and comments for consideration at the hearing by October 13, 2000. To permit time after the hearing for all interested persons to submit data, information, or views on this subject, the administrative record of the hearing will remain open following the hearing until November 20, 2000. Persons who wish to provide additional materials for consideration should file these materials with the Dockets Management Branch (address above) by November 20, 2000. Two copies of any comments are to be submitted, except that individuals may submit one copy.

Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: September 12, 2000.

William K. Hubbard,

Senior Associate Commissioner for Policy, Planning, and Legislation.

[FR Doc. 00–24008 Filed 9–18–00; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF THE TREASURY

Internal Revenue Service

26 CFR Part 602

[TD 8892]

RIN 1545–AR97

TeleFile Voice Signature Test; Correction

AGENCY: Internal Revenue Service (IRS), Treasury.

ACTION: Correction to removal of temporary regulations.

SUMMARY: This document contains corrections to a removal of temporary regulations that provides that an individual Federal income tax return completed as part of the Telefile Voice Signature test will be treated as a return that is signed, authenticated, verified and filed by the taxpayer. This document was published in the **Federal Register** on July 18, 2000 (65 FR 44437).

DATES: This correction is effective July 18, 2000.

FOR FURTHER INFORMATION CONTACT: Beverly A. Baughman (202) 622–4940 (not a toll-free number).

SUPPLEMENTARY INFORMATION:

Need for Correction

As published, the removal of *temporary regulations (TD 8892)* contains errors that may prove to be misleading and is in need of clarification.

Correction of Publication

Accordingly, the publication of the removal of temporary regulations (TD 8892), which is the subject of FR Doc. 00–18116, is corrected as follows:

1. On page 44438, column 1, in amendatory instruction **Par. 6.**, line 1, the language, "**Par. 6.** Section 602.101(c) is amended" is corrected to read "**Par. 6.** Section 602.101(b) is amended".

§ 602.101 [Corrected]

2. On page 44438, column 1, the paragraph designation § 602.101(c) is correctly designated § 602.101(b).

Cynthia Grigsby,

Chief, Regulations Unit, Office of Special Counsel (Modernization and Strategic Planning).

[FR Doc. 00–23918 Filed 9–18–00; 8:45 am]

BILLING CODE 4830–01–U

DEPARTMENT OF TRANSPORTATION

Coast Guard

33 CFR Parts 100, 117 and 165

[USCG–2000–7757]

Safety Zones, Security Zones, Drawbridges and Special Local Regulations

AGENCY: Coast Guard, DOT.

ACTION: Notice of temporary rules issued.

SUMMARY: This document provides required notice of substantive rules adopted by the Coast Guard and temporarily effective between April 1, 2000 and June 30, 2000 which were not published in the **Federal Register**. This quarterly notice lists temporary local regulations, drawbridge regulations, security zones, and safety zones of limited duration and for which timely publication in the **Federal Register** was not possible.

DATES: This notice lists temporary Coast Guard regulations that became effective and were terminated between April 1, 2000 and June 30, 2000.

ADDRESSES: The Docket Management Facility maintains the public docket for this notice. Documents indicated in this notice will be available for inspection or copying at the Docket Management Facility, U.S. Department of Transportation, Room PL–401, 400 Seventh Street SW., Washington, DC 20593–0001 between 9 a.m. and 5 p.m., Monday through Friday, except Federal holidays. You may electronically access the public docket for this notice on the Internet at *http://dms.dot.gov.*

FOR FURTHER INFORMATION CONTACT: For questions on this notice, contact Lieutenant Bruce Walker, Office of Regulations and Administrative Law, telephone (202) 267–6233. For questions on viewing, or on submitting material to the docket, contact Dorothy Beard, Chief, Dockets, Department of Transportation (202) 866–9329.

SUPPLEMENTARY INFORMATION: District Commanders and Captains of the Port

ATTACHMENT E: THE 1988 GUIDANCE LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

Date: AUG 1 1988

re: Prescription Drug
Marketing Act of 1987

[Docket No. 88N-258L]

TO REGULATED INDUSTRY AND OTHER INTERESTED PERSONS

Dear Sir or Madam:

The purpose of this letter is to provide you information on the Prescription Drug Marketing Act of 1987 [Pub.L. 100-293, 102 STAT. 95], which was signed into law by the President on April 22, 1988.

The Food and Drug Administration (FDA) intends to propose rules, through notice and comment rulemaking, to implement this legislation. Until these rules are finalized, the information in this letter may be relied upon with assurance of its acceptability to FDA. This letter, however, is not intended to bind FDA should events occur prior to the issuance of a rule that require a change in FDA's policy. Changes in FDA policy will be announced in future letters or notices. In addition, except insofar as this letter describes legal requirements found in the legislation or existing regulations, this letter does not state legal requirements but, rather, FDA's interpretation of how the legislation should be implemented. (For example, use of the word "shall" indicates a legal requirement.)

I. BACKGROUND

The Prescription Drug Marketing Act of 1987 (the new law) amends the Federal Food, Drug, and Cosmetic Act (the Act) to: (1) require State licensing of wholesale distributors of prescription human drugs under Federal guidelines that include minimum standards for storage, handling, and recordkeeping; (2) ban the reimportation of prescription human drugs produced in the United States, except when reimported by the manufacturer or for emergency use; (3) ban the sale, trade, or purchase of drug samples; (4) ban trafficking in or counterfeiting of drug coupons; (5) mandate storage, handling, and recordkeeping requirements for drug samples; (6) require practitioners to request drug samples in writing; (7) prohibit, with certain exceptions, the resale of prescription human drugs purchased by hospitals or health care facilities; and (8) set forth criminal and civil penalties for violations of these provisions.

II. EFFECTIVE DATES

The effective date for most provisions of the new law is July 22, 1988, except that the requirements relating to the distribution of drug samples become effective on October 20, 1988, and the requirement for wholesale distributors to be licensed by the State becomes effective 2 years after the adoption of final rules by the Agency setting standards for State licensing. FDA is required to issue regulations establishing minimum guidelines for State licensing of wholesale distributors engaged in interstate commerce by October 20, 1988.

III. SCOPE

The new law applies to drugs subject to Section 503(b) of the Act — "prescription drugs."

"Prescription drug" may be interpreted to include any finished dosage form or active ingredient subject to Section 503(b) of the Act or any drug for human use required by Federal or State law or regulation to be dispensed only by a prescription.

"Active ingredient" may be interpreted to mean any drug or drug component 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 any function of the body of humans.

IV. REIMPORTATION OF U.S.-MANUFACTURED DRUGS

Congress found that large amounts of prescription drugs are being reimported into the United States as American goods returned, and that these reimports are a health and safety risk to American consumers because they may have become subpotent or adulterated during foreign handling and shipping. Accordingly, Congress amended Section 801 of the Act to prohibit the re-importation of U.S.-produced prescription drugs, except by the manufacturer of the product or as authorized by FDA for emergency purposes.

For the purpose of this letter, "manufacturer" may be interpreted to mean a person who is engaged in the manufacture, preparation, propagation, compounding, processing, packaging, or labeling of a drug or drugs, as used in Section 510 of the Act.

The Agency has issued an Import Alert (Import Alert #66-14) concerning reimportation of U.S.-manufactured prescription drugs. A copy of the Import Alert is attached to this letter. Applications to reimport prescription drugs for emergency medical care should be submitted to the

Director of the FDA District into which the person reimporting the drug is located (see 21 CFR 5.115). A list of FDA District Offices is attached to this letter.

V. DRUG SAMPLES AND DRUG COUPONS

The new law defines "drug sample" to mean a unit of a prescription drug which is not intended to be sold and is intended to promote the sale of the drug.

The new law defines "drug coupon" to mean a form which may be redeemed, at no cost or at a reduced cost, for a prescription drug.

Congress found that the existing system of providing drug samples to physicians through manufacturer's representatives has been abused for decades, and has resulted in the sale to consumers of misbranded, expired, and adulterated pharmaceuticals. In response to this problem, Congress amended Section 503 of the Act to prohibit sale, purchase, or trade of drug samples and drug coupons; the offer to sell, purchase, or trade drug samples and drug coupons; and the counterfeiting of drug coupons. The new law also includes in amended Section 503 specific requirements for the distribution of drug samples.

A. REQUIREMENTS FOR DRUG SAMPLE DISTRIBUTION BY MAIL OR COMMON CARRIER.

The manufacturer or distributor of a prescription drug may distribute prescription drug samples to a licensed practitioner—or to the pharmacy of a hospital or other health care entity at the request of a licensed practitioner—by mail or common carrier, provided that the licensed practitioner submits a written request setting forth certain specified information and the recipient of the drug sample executes a written receipt upon its delivery and returns the receipt to the manufacturer or distributor.

1. Submission of a written request for a drug sample for delivery by mail or common carrier. To request a drug sample for delivery by mail or common carrier, a practitioner shall submit a written request on a form setting forth the information required below:

(a) Name, address, professional designation, and signature of the practitioner making the request;
(b) The identity of the drug sample requested;
(c) The quantity requested;
(d) The name of the manufacturer of the drug sample requested; and
(e) The date of request.

2. Recordkeeping requirements for drug samples delivered by mail or common carrier. Each drug manufacturer or distributor who distributes samples by mail or common carrier shall maintain all sample request forms and all receipts for a period of 3 years, and shall maintain a drug sample distribution record identifying all drugs distributed and all

recipients of samples. These records shall be made available on request to FDA and other Federal, State, and local drug law enforcement officials by the manufacturer or distributor.

B. REQUIREMENTS FOR SAMPLE DISTRIBUTION BY REPRESENTATIVES

The manufacturer or distributor of a prescription drug may distribute prescription drug samples to a licensed practitioner—or to the pharmacy of a hospital or other health care entity at the request of a licensed practitioner—by means other than by mail or common carrier (e.g., by representatives or "detail persons"), provided that the manufacturer or distributor makes the distribution pursuant to a written request from a licensed practitioner setting forth certain information specified in paragraph 1 and carries out the activities specified in paragraphs 2 through 8.

1. Submission of written request for a drug sample for delivery by a representative. To request a drug sample for delivery by a representative, a practitioner shall submit a written request on a form setting forth the information required below:

(a) Name, address, professional designation, and signature of the practitioner making the request;
(b) The identity of the drug sample requested;
(c) The quantity requested;
(d) The name of the manufacturer or distributor of the drug sample requested; and
(e) The date of request.

2. Proper storage of drug samples. All drug samples shall be stored by manufacturers or distributors under conditions that will maintain their stability, integrity, and effectiveness, and will assure that the drug samples will be free of contamination, deterioration, and adulteration.

3. Inventories of manufacturers' and distributors' representatives. Drug manufacturers or distributors shall conduct, at least annually, complete and accurate inventories of all drug samples in the possession of manufacturers' and distributors' representatives.

4. Lists of manufacturers' and distributors' representatives. Drug manufacturers or distributors shall maintain lists of the names and address of each of their representatives who distribute drug samples and of the sites where drug samples are stored.

5. Maintenance of records. Drug manufacturers or distributors shall maintain records for at least 3 years of all drug samples distributed, destroyed, or returned to the manufacturer or distributor; of all inventories maintained under this section; of all thefts or significant losses of drug samples; and of all requests for drug samples under this section. Records and lists maintained under this section shall be made available on request to FDA by the manufacturer or distributor.

6. Notification of significant loss or theft. Drug manufacturers or distributors shall notify FDA of any significant loss of drug samples and any known theft of drug samples.

7. Notification if representative convicted of drug law violations. Drug manufacturers or distributors shall report to FDA any conviction of their representatives for violations of the prohibitions against sale of drug samples in Section 503(c)(1) of the Act or a State law because of the sale, purchase, or trade of a drug sample or the offer to sell, purchase, or trade a drug sample.

8. Name and telephone number of responsible person required. Drug manufacturers or distributors shall provide to FDA the name and telephone number of the individual responsible for responding to a request for information respecting drug samples.

C. GUIDANCE INFORMATION

1. "Licensed practitioner" may be interpreted to mean any person authorized by State law to prescribe prescription drugs.

2. Standing requests. FDA requests that separate written requests be made for each sample or group of samples, and that open-ended or "standing" requests not be used to order drug samples.

3. Forms for drug sample requests. Forms developed by manufacturers and distributors for manufacturers to request drug samples that comply with the above requirements are acceptable to FDA.

4. Drug Enforcement Administration (DEA) and State identification and license numbers. FDA requests that the request form for a drug sample include, if applicable, the Drug Enforcement Administration identification number and the State license number of the practitioner making the request.

5. Samples to hospitals or health care entities. The Agency requests that a licensed practitioner requesting delivery of a sample to a pharmacy of a hospital or health care entity include the name and address of the intended recipient on the request form. When a sample is requested to be delivered by mail or common carrier, FDA requests that the licensed practitioner requesting the sample include the name of the responsible party who will sign the receipt acknowledging delivery.

6. Receipts for samples delivered by mail or common carrier. U.S. Postal Service return receipts, business reply cards, or similar forms that produce written receipts are acceptable to FDA for the verification of delivery of samples shipped by mail or common carrier.

7. Verification of delivery of samples delivered by representatives. FDA requests that the manufacturer or distributor verify by written receipt the delivery of a drug sample by a detail person to a licensed practitioner or to the pharmacy of a hospital or health care entity receiving samples at the request of a licensed practitioner. The Agency requests that a practitioner, hospital, or health care entity who is sent a sample but fails to execute a receipt be barred from receiving additional samples.

8. Proper storage of drug samples distributed by representatives. Compliance by manufacturers, distributors, and representatives with 21 CFR 205.50(a) through (e) and 205.50(i), the storage and handling sections of the FDA guidelines for State wholesale distributor licensing, which will be published shortly, is acceptable assurance to FDA of good storage and handling practices for drug samples.

9. Inventories of manufacturer's and distributor's representatives. FDA requests that inventories be conducted by independent personnel. Discrepancies should be carefully evaluated and full investigations made when circumstances warrant. FDA requests that the inventory include the following:

(a) The name of the drug and the dosage strength,
(b) The date of each shipment,
(c) The recipient of the drug,
(d) The quantity of drug shipped,
(e) The quantity of drug received, and
(f) The quantity of the drug on hand.

10. When to notify FDA of a significant loss or theft of drug samples. The agency requests that it be notified within 5 working days when a manufacturer or distributor becomes aware of a significant loss or theft of drug samples.

11. Whom to notify at FDA of a significant loss or theft. When a significant loss of drug samples or a theft is identified, the drug manufacturer or distributor should notify the Office of Compliance (HFD-300), Center for Drug Evaluation and Research (CDER), or the Office of Compliance (HFB-100), Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 5600 Fishers Lane, Rockville, Maryland 20857, as appropriate.

12. How to notify FDA of a significant loss or theft. The Agency will accept an initial notification by telephone, but asks that a telephone notification be followed by a written report as soon as practicable. A full report of any investigation into the loss or theft should be submitted in writing to the CDER or CBER Office of Compliance, as appropriate, upon completion. FDA may conduct an investigation regarding a significant loss or theft of drug samples.

13. Information leading to the conviction of a representative. FDA encourages reporting of information about suspected violations of Section 503(c)(1) or a State law regarding the sale, purchase, or trade of drug samples. A person or firm making such a report may be entitled to a reward if that information results in a conviction (see section VIII of this letter, Rewards).

14. How to report the conviction of a representative to FDA. The Agency requests that manufacturers and distributors report to the Office of Compliance in CDER or CBER, as appropriate, when one or more of their representatives is convicted of violating Section 503(c)(1) of the Act or any State law involving sale, purchase, or trade of a drug sample or the offer to sell, purchase, or trade a drug sample. Such a report should be made within 30 days of such information becoming known to a manufacturer or distributor.

15. How to advise FDA of a drug sample contact person. The Agency requests that a drug manufacturer or distributor who intends to distribute drug samples other than by mail or common carrier provide to the Office of Compliance in CDER or CBER, as appropriate, the name and telephone number of the individual designated to respond to requests for information relating to drug samples.

VI. SALES RESTRICTIONS FOR HOSPITALS, HEALTH CARE ENTITIES, AND CERTAIN CHARITABLE ORGANIZATIONS

Congress found that bulk resale of below-wholesale priced prescription drugs by health care entities for ultimate sale at retail helps fuel the drug diversion market and is an unfair form of competition to wholesalers and retailers that must pay otherwise prevailing market prices. Accordingly, Congress amended Section 503 of the Act to prohibit the sale, purchase, or trade (and the offer to sell, purchase, or trade) of prescription drugs by a hospital or health care entity; or the sale, purchase, or trade of prescription drugs donated or sold at reduced cost to charitable institutions operating under section 501(c)(3) of the Internal Revenue Code of 1954 (except for a sale to a nonprofit affiliate of the charitable organization).

A. EXCEPTIONS

Section 503(c)(3)(B) of the Act provides certain exceptions to the sales restrictions provisions. They include:

1. The purchase or other acquisition by a hospital or other health care entity which 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 which are members of such organization;

2. The sale, purchase, or trade of a drug or an offer to sell, purchase, or trade a drug by a charitable organization described in Section 501(c)(3) of the Internal Revenue Code of 1954 to a nonprofit affiliate of the organization to the extent otherwise permitted by law;

3. 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 which are under common control;

4. The sale, purchase, or trade of a drug or an offer to sell, purchase, or trade a drug for emergency medical reasons; and

5. The sale, purchase, or trade of a drug, an offer to sell, purchase, or trade a drug, or the dispensing of a drug pursuant to a valid prescription.

B. GUIDANCE INFORMATION

1. "Health care entity" may be interpreted to mean any organization or business entity that provides diagnostic, medical, surgical, or dental treatment and/or care, or chronic and/or rehabilitative care, but does not include any wholesale distributor or retail pharmacy licensed under State law to deal in prescription drugs.

2. "Group purchasing organization" may be interpreted to mean any entity established, maintained, and operated for the purchase of drugs for distribution exclusively to its members with such membership consisting solely of health care entities bound by written contract with the organization.

3. The new law states that "emergency medical reasons" include 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.

4. "Nonprofit affiliate" may be interpreted to mean 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.

5. Blood and blood components. Blood and blood components intended for transfusion are biological products licensable under Section 351 of the Public Health Service Act (the PHS Act) as well as being prescription drugs. Such blood and blood components, including whole blood, red blood cells, plasma, and platelets, are usually collected and processed by blood establishments or "blood banks," and are used at hospital transfusion services. A unique public-private distribution system has

evolved under the Federally sponsored National Blood Policy, whereby blood establishments and medical facilities share blood resources to avoid wastage of blood and blood components. A unit of blood or blood component may be sent to a transfusion service to be held in case of an emergency, then be sent to another facility to balance a diminishing inventory, and pass through several facilities before the unit is ultimately transfused.

An extensive system of regulation of the blood supply now exists to protect the public against substandard, ineffective, or counterfeit blood and blood components. Storage and shipment of blood and blood components are carefully controlled by FDA regulation. FDA believes that prohibiting resale of blood and blood components as it now takes place freely among hospitals and blood establishments would severely inhibit the current system of blood resources distribution, could result in local shortages and undue wastage of blood, and could have an adverse effect on public health.

Under its enforcement discretion, FDA has concluded, pending notice and comment rulemaking, that it will not take compliance action against blood establishments or hospitals which engage in the sale, purchase, trade, transfer, exchange, credit, barter or other trafficking in blood and blood components, as defined at 21 CFR 606.3(a) and (c), for violating the sales restriction requirements of the new law.

6. Government hospitals and health care entities. Congress has established an extensive system of public hospitals and health care entities. These include the hospitals, clinics, and dispensaries operated for the military by the Department of Defense; hospitals and clinics operated by the Veterans Administration; and hospitals and clinics operated by the U.S. Public Health Service (including Indian Health Service hospitals and clinics).

In addition, State and local governments have established public health hospitals, clinics, and dispensaries, including drug treatment inpatient and outpatient facilities. These facilities operate under several varieties of organization and control. They may be owned and operated by governmental entities; they may be organized as private corporations or associations under contract to State or local government agencies; and they may be organized under public-private partnerships under informal or formal contractual arrangements with local governmental authorities. These health care entities may have inter-agency arrangements for the purchase and exchange of prescription drugs. Such facilities operate because of Federal or State governmental commitments to provide certain kinds of health care to particular classes of patients in response to specific client needs. FDA believes that it would be unwise to unduly interfere with the established patterns of operation of these governmentally mandated health care facilities.

Under its enforcement discretion, FDA has concluded, pending notice and comment rulemaking, that it will not take compliance action against government hospitals or health care entities which engage in the sale, purchase, trade, transfer, exchange, credit, barter, or other trafficking in prescription drugs (including vaccines and other biological drugs) with other government hospitals and health care entities for violations of the sales restrictions of the new law.

7. Returns by hospitals, health care entities, and charitable institutions. A return of a prescription drug to a manufacturer or distributor by a hospital, health care entity, or charitable institution may be interpreted as falling outside the scope of a sale or trade, provided that:

(a) The return is made directly to the manufacturer, and the manufacturer notifies the person returning the product in writing that the returned prescription drug was received; or

(b) The return is made to a wholesale distributor, and the person returning the product receives a written statement from the manufacturer that the returned prescription drug was either destroyed by the wholesaler or forwarded to and received by the manufacturer.

VII. WHOLESALE DISTRIBUTION

Congress found that the existence and operation of a wholesale submarket, commonly known as the "diversion market," prevents effective control over or even routine knowledge of the true sources of prescription drugs for human use in a significant number of cases. Accordingly, Congress amended Section 503 of the Act by adding new paragraph 503(e), which regulates wholesale distribution of prescription drug products.

The new law defines "wholesale distribution" as the distribution of drugs subject to Section 503(b) of the Act to other than the consumer or patient, but does not include intracompany sales or the following distributions of prescription drugs:

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

(b) The sale, purchase, or trade of a prescription drug or an offer to sell, purchase, or trade a prescription drug by a charitable organization described in Section 501(c)(3) of the Internal Revenue Code of 1954 to a nonprofit affiliate of the organization to the extent otherwise permitted by law;

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

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

(e) The sale, purchase, or trade of a prescription drug, an offer to sell, purchase, or trade a prescription drug, or the dispensing of a prescription drug pursuant to a prescription executed in accordance with Section 503(b) of the Act.

A. REQUIREMENTS AFFECTING ALL WHOLESALE DISTRIBUTORS

Section 503(e)(2) prohibits the wholesale distribution of prescription drugs in interstate commerce unless the wholesale distributor is licensed by the State in accordance with Federally prescribed minimum standards, conditions, and terms, as set forth in guidelines to be issued by the FDA. These minimum standards, conditions, and terms are to include minimum requirements for storage, handling, and recordkeeping.

Section 503(e)(2) requires that the guidelines be promulgated as a regulation, through notice and comment rulemaking. The prohibition against distribution of prescription drugs by unlicensed wholesalers becomes effective 2 years after the final regulation setting forth the Federal guideline is published by the Agency in the FEDERAL REGISTER. FDA intends to implement Section 503(e)(2) shortly.

B. REQUIREMENTS FOR UNAUTHORIZED DISTRIBUTORS

Section 503(e)(1) requires that a person who is engaged in the wholesale distribution of prescription drugs and who is not an authorized distributor of record of such drugs shall provide to each wholesale distributor of such drugs a statement identifying each sale of the drug (including the date of sale) before the sale to such wholesale distributor. The Act also provides that each manufacturer shall maintain a current list of authorized distributors at its corporate offices.

The new law defines "authorized distributors of record" as those distributors with whom the manufacturer has established an ongoing relationship to distribute such manufacturer's products.

C. GUIDANCE INFORMATION

1. "Wholesale distributor" may be interpreted to mean any person engaged in wholesale distribution of prescription drugs, including, but not limited to, manufacturers; repackers; own-label distributors; private-label distributors; manufacturers' and distributors' representatives; 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. A transfer of prescription drugs by a retail pharmacy to another retail pharmacy to alleviate a temporary shortage may be interpreted not to be a wholesale distribution.

2. "Authorized distributors of record" may include, but would not be limited to, subsidiaries, franchisees, and distributors to whom the manufacturer distributes prescription drugs.

3. "Ongoing relationship," as used in the definition of "authorized distributors of record," 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. Evidence of such intent would include, but 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, either directly or through a jointly agreed upon intermediary. The Agency would consider two transactions in any 24-month period to be evidence of a continuing relationship.

4. "Unauthorized distributor" may be interpreted to mean a distributor with whom the manufacturer has not established an ongoing relationship to distribute such manufacturer's products.

5. Statement identifying prior sales. FDA requests that the statement identifying prior sales of prescription drugs by unauthorized distributors be in writing, that it bear the title "Statement Identifying Prior Sales of Prescription Drugs by Unauthorized Distributors Required by the Prescription Drug Marketing Act," and that it include all necessary identifying information regarding all sales in the chain of distribution of the product, starting with the manufacturer or authorized distributor of record. FDA also requests that the identifying statement accompany all products purchased from an unauthorized distributor, even when they are resold. Identifying statements are not required to include information about sales completed before July 22, 1988. FDA requests that the identifying statement include the following information:

(a) The business name and address of the source from which the drug was purchased,

(b) The date of the sale, and

(c) The identity, strength, container size, number of containers, and lot number(s) of the drug.

6. Forms for identifying statements. Forms developed by manufacturers and distributors for identifying statements that comply with the above requirements will be acceptable to FDA.

7. Identifying statements recordkeeping. The Agency requests that the identifying statements be retained in a secure manner by each party to the transaction for a period of 3 years after the expiration date of the drug involved, and that they be made available for inspection or photocopying on request to authorized representatives of Federal, State, and local agencies with drug law enforcement responsibilities. Statements should be maintained at the place of business, except that records may be kept at the principal domestic business office of an entity that conducts business in multiple locations.

8. Manufacturer's list of authorized distributors of record. The Agency requests that the manufacturer's list of authorized distributors of record be made available upon request to authorized representatives of Federal, State, and local agencies with drug law enforcement responsibilities. The Agency also requests that such list be made available at reasonable charge to any person requesting it.

VIII. REWARDS

The new law provides for a reward for information leading to the arrest and conviction of a person who sells, purchases, or trades drug samples or coupons. The reward is one-half the criminal fine imposed and collected, not to exceed $125,000. A person wishing to provide information intended to lead to the arrest and conviction of a person for such a violation may make a report to the Office of Compliance in CDER or CBER, as appropriate.

IX. REQUESTS FOR INFORMATION FROM FDA

Requests for further information about the Prescription Drug Marketing Act of 1987 or for clarifications of the new law should be directed to the Division of Regulatory Affairs (HFD-360), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, Maryland 20857, telephone: 301-295-8038.

X. COMMENTS

FDA is seeking comments on implementation of the Prescription Drug Marketing Act of 1987 and this letter. Comments should be sent to the Dockets Management Branch (HFA-305), Food and Drug Administration, Room 4-62, 5600 Fishers Lane, Rockville, Maryland 20857 (telephone 301/443-1751), identifying your comments with the docket number to be

found on the cover page of this letter. Please send comments to the Agency by September 30, 1988. Comments and other information in the docket will be available for review in that office during regular business hours, 9 a.m. to 4:30 p.m., Monday through Friday.

We hope the information in this letter is helpful in guiding affected persons seeking to comply with the new law. We are looking forward to seeing your comments and using them in developing FDA's implementing regulations.

Sincerely yours,

Daniel L. Michels
Director
Office of Compliance (HFD-300)
Center for Drug Evaluation and
Research

Sincerely yours,

for Thomas S. Bozzo
Director
Office of Compliance (HFB-100)
Center for Biologics Evaluation
and Research

ATTACHMENTS:
List of FDA District Offices
Import Alert #66-14

FINDING AID

ATTACHMENT F: QUESTIONS ON PDMA FOR THE PRIMARY WHOLESALERS

Because none of the primary wholesalers attended the October 27, 2000, Part 15 Hearing, the Agency decided to submit questions to them through their association the National Wholesale Druggists Association. Responses to the questions below have been placed in the Agency's docket 92N-0297.

1. At the Agency's Part 15 Hearing on October 27, 2000, we heard representatives of wholesalers of prescription drugs say that the largest wholesalers would oppose the requirement of a universal pedigree. Please state whether you would favor or oppose such a requirement and why.

2. We understand that there are computer software and systems readily available that can be used to create a pedigree. What do you believe it would cost to create a pedigree and provide it with the drugs that you sell? What would these costs be associated with specifically? Do you believe these costs could be accommodated without a significant increase in the cost or decrease in the availability of prescription drugs?

3. Do you believe it would be advisable to eliminate the pedigree requirement altogether? Please explain your answer.

4. Do you believe there would be any consequences to the public health and safety if the pedigree were eliminated?

5. What would your position be on the following requirement?

   All distributors (authorized and unauthorized) must maintain and pass on a pedigree for those prescription drugs that are bought from or sold to a secondary distributor.

ATTACHMENT G: PROFILE OF THE PRESCRIPTION DRUG WHOLESALING INDUSTRY

Examination of Entities Defining Supply and Demand in Drug Distribution

Final Report to

Economic Staff
Office of Policy, Planning, and Legislation
Food and Drug Administration
Department of Health and Human Services
Rockville, MD 20857

Prepared by
Eastern Research Group Inc.
110 Hartwell Avenue
Lexington, MA 02421

December 2000

PROFILE OF THE PRESCRIPTION DRUG WHOLESALING INDUSTRY

EXAMINATION OF ENTITIES DEFINING SUPPLY AND DEMAND IN DRUG DISTRIBUTION

Final Report

Task Order No. 13
Contract No. 223-98-8002

Prepared for
Economics Staff
Office of Policy, Planning, and Legislation
Food and Drug Administration
Department of Health and Human Services
Rockville, MD 20857

Prepared by
Eastern Research Group Inc.
110 Hartwell Avenue
Lexington, MA 02421

February 12, 2001

PROFILE OF THE PRESCRIPTION DRUG WHOLESALING INDUSTRY

EXAMINATION OF ENTITIES DEFINING SUPPLY AND DEMAND IN DRUG DISTRIBUTION

FINAL REPORT

Prepared for

Economics Staff
Office of Policy, Planning, and Legislation
Food and Drug Administration
Department of Health and Human Services
Rockville, MD 20857

Prepared by

Eastern Research Group, Inc.
110 Hartwell Avenue
Lexington, MA 02421

February 12, 2001

TABLE OF CONTENTS

LIST OF FIGURES AND TABLES

EXECUTIVE SUMMARY

The U.S. Food and Drug Administration (FDA) is examining the drug wholesaling and distribution industry as it reviews policies applying to the distribution of prescription drugs. This study profiles drug wholesalers and drug distribution patterns. It also characterizes the pharmaceutical purchasing organizations and their impact on prescription drug prices and distribution.

Drug wholesalers consist of the Big Five full-line wholesalers (including McKesson HBOC, Inc., Bergen Brunswig Drug Company, and Cardinal Health, Inc.), regional wholesalers, and numerous smaller sub-regional/specialty wholesalers. In addition, there are "secondary wholesalers" that take advantage of manufacturers' sales on drugs to purchase discounted products and then resell these products throughout the distribution chain.

ERG identified several models that apply to the distribution of pharmaceuticals. In the most common model, covering a majority of drugs, manufacturers sell drugs to the Big Five drug wholesalers, who then sell them to dispensing organizations, such as retail chain stores, independent drug stores, and health care facilities. These drugs reach the ultimate consumer with a minimum number of transactions or physical shipments. In some cases, manufacturers sell directly to health care facilities or drug stores, eliminating any role for wholesalers. According to a compilation by PhRMA, 20 percent of all pharmaceutical drug sales went directly to dispensing organizations.

A more complex model of distribution is initiated, however, when manufacturers offer price discounts on various prescription drugs. Frequently, manufacturers hold short-term sales for individual drugs in order to reduce inventories or to meet quarterly sales targets. Large distributors, and especially secondary wholesalers, who are willing to risk substantial capital to acquire the discounted goods, purchase these sale drugs. These purchasers then turn the product over quickly by selling it to their networks of customers, which might include both larger and smaller distributors, and some drug dispensing organizations. In this model of drug dispersion, however, the sale drugs might change hands more than one-half dozen times before reaching a drug dispenser (i.e., a retail pharmacy or a hospital).

SECTION ONE

PROFILE OF THE PRESCRIPTION DRUG WHOLESALING INDUSTRY— THE SUPPLY OF WHOLESALE DRUG PRODUCTS

This section examines the market characteristics of the prescription drug wholesaling and distribution industry. Section 1.1 outlines the applicable Federal and State regulations governing the distribution of prescription drugs. Subsequent sections describe the components and characteristics of the entities that distribute wholesale drug products. Section Two examines the organization of purchasers of wholesale drugs. These sections also provide data on the number of companies and distribution of sales for each of the market players addressed.

This report generally refers to the companies being profiled as "wholesalers," in keeping with the terminology most commonly used in the industry. In fact, it is recognized that most wholesalers also perform substantial distribution functions and, therefore, can also be called "distributors." This report, however, will generally use the term wholesalers to refer to the larger companies that engage in wholesale purchasing and reselling of pharmaceutical products. While most of these wholesalers also perform distribution functions, their activities do not always primarily involve distribution in the sense of moving products closer to their eventual point of consumption. For example, some discount wholesalers could theoretically purchase an entire lot of distressed product and resell it, in its entirety, to another company, without "distributing" the product to smaller companies. The term "distribution" will be used to refer to the physical activity that generally is one of the primary functions of the wholesalers, namely, to divide large-volume purchases among customers for them to eventually resell to retail customers or to smaller wholesalers.

Much of the material collected for this report is derived from conversations with industry sources that did not wish to be quoted or for whom their identification posed a possibility of revealing sensitive material. Thus, some statements about the operation of the drug distribution industry are not attributable to specific sources.

1.1 Regulatory Framework for the Distribution of Prescription Drugs

Federal regulations define distributor requirements for reporting on the source of their drug purchases to their customers. States impose basic licensing requirements on drug distributors.

1.1.1 Federal Regulations

At the Federal level, the Prescription Drug Marketing Act (PDMA) of 1988, as modified by the Prescription Drug Amendments of 1992, establishes requirements for the distribution of prescription drugs. Section 503 [e] [1] [A] of the Act requires each person, who is engaged in the wholesale distribution of a prescription drug and who is not the manufacturer or an authorized distributor of record for the drug, to provide the person receiving the drug a statement 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 before each wholesale distribution. Further Section 503 [e] [4] [A] of the Act 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. In a 1988 Guidance, FDA indicated that:

> "Ongoing relationship" as used in the definition of "authorized distributors of record," 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. Evidence of such intent would include, but 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, either directly or through a jointly agreed upon intermediary. The Agency would consider two transactions in any 24 month period to be evidence of a continuing relationship (FDA, 1988).

On December 3, 1999, the Agency published final regulations in 21 CFR Part 203 implementing these and other provisions of the PDMA as amended by the Prescription Drug Amendments of 1992 (64 FR 67720). Section 203.50 of these final regulations requires that, before the completion of any wholesale distribution transaction where the seller is not an authorized distributor of record, the seller must provide the purchaser with a statement

identifying each prior sale, purchase, or trade of the drug. The identifying statement, also known as the drug product's pedigree, must include the proprietary and established name of the drug, its dosage, the container size, the number of containers, lot or control numbers of the drug being distributed, the business name and address of all parties to each prior transaction involving the drug, starting with the manufacturer, and the date of each previous transaction. The Agency further refined its definition of "ongoing relationship" in Section 203.3 [u] of the final regulation to mean

> "... 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."

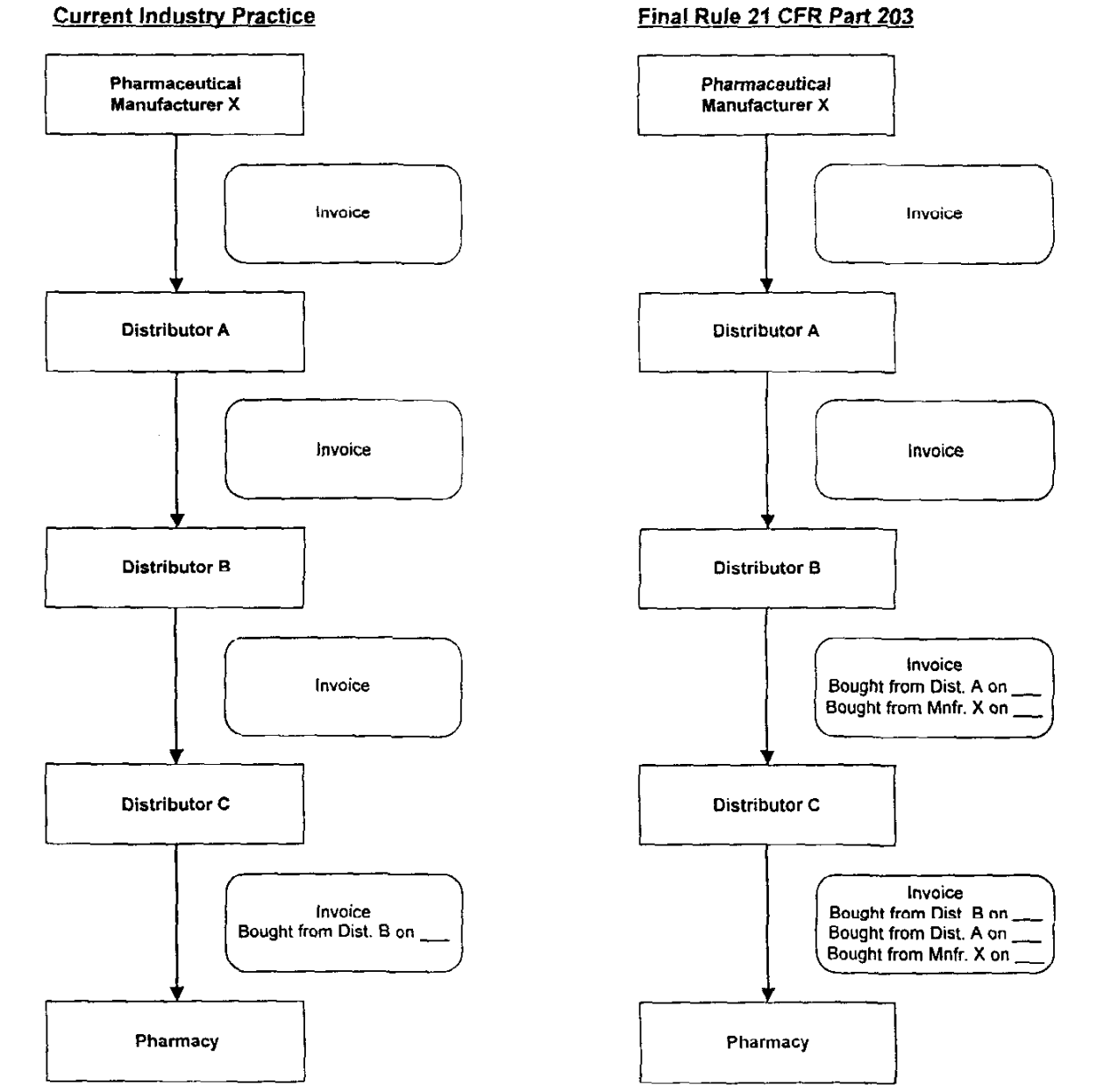
Based on concerns expressed by the industry and the Small Business Administration (SBA), FDA decided to delay the effective date for the above and other sections of the final rule (21 CFR Part 203) until October 1, 2001. At present, the prescription drug wholesale industry operates on the basis of its interpretation of the 1988 FDA Guidance regarding drug product pedigrees. Specifically, the wholesale distribution industry has interpreted the last sentence of the "ongoing relationship" definition (see p. 1-2) as indicating that it is sufficient for a wholesaler to have had two transactions within a 24-month period in order to be considered authorized. Figure 1-1 compares the distribution chain and the associated drug pedigrees under current industry practice and the final rule.

1.1.2 State Regulations

All drug wholesalers must be licensed under state licensing systems, which must in turn meet the FDA guidelines under State Licensing of Wholesale Prescription Drug Distributors (21 CFR Part 205). The regulations set forth minimum requirements for prescription drug storage (21 CFR Part 205.50 [a] and [c]) and security (21 CFR Part 205.50 [b]), as well as for the treatment of returned, damaged, and outdated prescription drugs (21 CFR Part 205.50 [e]). Further, under 21 CFR Part 205.50 [f], wholesale drug distributors must establish and maintain inventories and records of all transactions regarding the receipt and distribution of prescription

Figure 1-1

Views of the Distribution Chain and Drug Pedigrees Under Current Industry Practice and the Final Rule



Notes:
Distributor A has a written distribution agreement with Manufacturer X.
Distributor B has no written distribution agreement but has at least two transactions with Manufacturer X in any 24-month period.
Distributor C has neither a written distribution agreement nor at least 2 transactions with Manufacturer X in any 24-month period.

drugs and make these available for inspection and copying by authorized federal, state, or local law enforcement officials.

In most states, wholesale distributor licenses are issued by the State Boards of Pharmacy and require periodic renewal. The majority of states (approximately 80 percent) also require out-of-state wholesalers that distribute drugs within their borders to be licensed as well. Table 1-1 presents the available data on wholesale distributor licensure requirements, license renewal schedules, and the number of in-state and out-of-state licenses issued, by state.

1.2 Role and Functions of Wholesalers

Drug wholesalers serve as middlemen between drug manufacturers and prescription drug dispensers (i.e., retail outlets and institutions). Wholesalers provide a cost-effective means for the purchase, delivery, and sale of prescription drugs. They improve purchasing economies and lower manufacturer costs by reducing the number of small volume sales by drug manufacturers. They also relieve retailers and institutions from the burden of dealing with each individual manufacturer for drug purchases.

Typically, major wholesalers have sophisticated ordering systems that allow customers to place and confirm orders electronically and to determine the availability and prices of wholesalers' stock. Wholesalers' inventory management systems help customers minimize carrying costs while maintaining adequate supplies to meet patients' needs. In most cases, wholesalers can also provide products within 24 hours. In addition to the delivery of drugs, wholesalers also provide a broad range of value-added services to pharmaceutical manufacturers, dispensers, and other customers, such as pharmacy benefit management companies (PBMs), clinical research organizations (CROs), group purchasing organizations (GPOs), and integrated delivery networks (IDNs). The major supplemental services offered by wholesalers include the following:

- *Private label/Control label programs*—Number of wholesalers offer packaging and labeling operations in accordance with current Good Manufacturing Practices (CGMPs). The services offered typically include package configuration and product label design, filling and capping, labeling, and printing of bar coded product identification stickers.

Table 1-1

State Wholesale Distributor Licensure Requirements, Renewal Schedules, And the Number of In-State and Out-of-State Wholesale Distributor Licenses Issued by State

State	Does State License Out-of-State Wholesalers?	License Renewal Schedule	Number of Wholesale Licenses		
			In-State	Out-of-State	Total
Alabama	Yes	1 year	NA	NA	745
Alaska	No	2 years	9	147	156
Arizona	No [a]	2 years	15	185	200 [e]
Arkansas	Yes	1 year	NA	NA	495
California	Yes	1 year	427	276	703
Colorado	Yes [b]	1 year	NA	NA	282
Connecticut	Yes	1 year	NA	NA	362
Delaware	Yes	2 years	32	444	476
District of Columbia	Yes	1 year	NA	NA	0
Florida	Yes	2 years	530	764	1,294
Georgia	Yes	2 years	NA	NA	644
Hawaii	No [c]	2 years	NA	NA	45
Idaho	Yes	1 year	NA	NA	475 [e]
Illinois	Yes	2 years	NA	NA	685
Indiana	Yes	2 years	192	450	642
Iowa	Yes	1 year	NA	NA	579
Kansas	Yes	1 year	NA	NA	526
Kentucky	Yes	1 year	NA	NA	450
Louisiana	Yes	1 year	180	606	786
Maine	Yes	1 year	5	277	282
Maryland	Yes	1 year	NA	NA	1,500 [e]
Massachusetts	No	1 year	0	140	140 [e]
Michigan	Yes	2 years	NA	NA	580
Minnesota	Yes	1 year	NA	NA	352
Mississippi	Yes	2 years	NA	NA	726
Missouri	Yes	1 year	NA	NA	780
Montana	Yes	1 year	NA	NA	298
Nebraska	No	1 year	NA	NA	61
Nevada	Yes	2 years	83	340	423
New Hampshire	Yes	1 year	8	493	501
New Jersey	No	NA	NA	NA	1,000 [e]
New Mexico	Yes	1 year	NA	NA	482
New York	No	3 years	349	0	349
North Carolina	Yes	1 year	154	251	405
North Dakota	Yes	1 year	6	450	456
Ohio	Yes	1 year	491	599	1,090
Oklahoma	Yes	1 year	34	335	369
Oregon	Yes	1 year	825	325	1,150
Pennsylvania	NA [d]	1 year	525	0	525
Rhode Island	Yes	1 year	48	210	258
South Carolina	No	1 year	NA	NA	419

Table 1-1

State Wholesale Distributor Licensure Requirements, Renewal Schedules, And the Number of In-State and Out-of-State Wholesale Distributor Licenses Issued by State

State	Does State License Out-of-State Wholesalers?	License Renewal Schedule	Number of Wholesale Licenses		
			In-State	Out-of-State	Total
South Dakota	Yes	1 year	29	382	411
Tennessee	Yes	Cyclical	350	518	868
Texas	Yes [d]	1 year	1,832	604	2,436 [f]
Utah	No	2 years	52	0	52
Vermont	Yes	2 years	3	311	314
Virginia	Yes	1 year	238	432	670
Washington	Yes	1 year	72	301	373
West Virginia	Yes	1 year	NA	NA	412
Wisconsin	Yes	2 years	194	314	508
Wyoming	Yes	1 year	50	431	481
Total	**NA**	**NA**	**6,733**	**9,585**	**28,216 [g]**

Source: NABP, 1999, PDA, 2000a, and Texas Department of Health, 2001
"NA" = Not available

[a] Will begin licensing (permitting) non-resident wholesale drug distributors in the year 2000 pursuant to methamphetamine legislation requirement.

[b] For controlled substances only.

[c] However, per Board's informal interpretation, if the out-of-state wholesaler has a vendor-managed inventory system within the State, a wholesale distributor license is required.

[d] Wholesalers are regulated and licensed by Department of Health.

[e] Indicates that the figure is approximate.

[f] The figure represents the number of wholesale distributor licenses that are current as of January 17, 2001 (Texas Department of Health, 2001).

[g] The figure represents the total number of licenses for wholesale operation. Multi-state wholesalers presumably hold licenses in all states where they operate and are required. The total number of licenses does not represent an estimate of the number of unique wholesalers.

- *Voluntary and/or co-op advertising programs*—The cooperative advertising program is one in which the wholesaler provides marketing materials (i.e., store displays, flyers, etc.) to and reimburses the retail pharmacy for part or all of the retail pharmacy's advertising expenditures on selected products purchased from the wholesaler.

- *Special handling services for vaccines, frozen products, and orphan drugs.*

- *Generic source programs*—The program enables a wholesaler to combine the purchase volumes of its customers and negotiate prices with generic manufacturers. This results in competitive pricing of generic pharmaceuticals for the customers of the wholesaler.

- *Pharmacy computer systems*—The pharmacy computer system facilitates the processing of prescriptions, drug interactions monitoring and claims processing.

- *Third-party claims processing*—The claims processing system, which is integrated into the pharmacy computer system, facilitates real-time review and adjudication of prescriptions by third-party payers (i.e., health insurance companies). The system allows the pharmacist to establish patient eligibility, perform prospective drug utilization review (DUR), and notify the patient of any formulary requirements or prior authorization restrictions.

- *Retail-zone pricing systems*—The products are delivered to the retail pharmacy with price labels already affixed to the individual containers so that the products can be immediately shelved.

- *Point-of-sale (POS) systems*—The information technology (IT) system allows pharmacies to manage their inventory and ensure drug pricing accuracy. Typically, the POS systems feature bar code scanning and electronic credit card processing capabilities, which promote faster checkout at the cash register. The system also tracks product movement, identifying best and worst sellers, and facilitates better utilization of product shelf space. The system can generate a multitude of customized business management reports, including hourly product sales, monthly profit trends, and various cashier activities.

Table 1-2 describes the percentage of wholesalers providing each common type of value-added service discussed above.

Despite the broad range of services available from a full-line wholesaler, most dispensing customers of wholesalers use both a primary, usually a major full-line wholesaler and a backup wholesaler. The backup wholesaler provides products when the primary wholesaler cannot fill the order (U.S. District Court for the District of Columbia, 1998).

Table 1-2

Percent of Wholesalers Offering Each Type of Value-Added Service

Type of Service	Percent of Wholesalers (1998)
Private Label/Control Label Program	71%
Voluntary and/or Co-op Advertising Program	62%
Special Handling Services	
Vaccines	100%
Frozen Products	100%
Orphan Drugs	35%
Generic Source Programs	84%
Pharmacy Computer Systems	34%
Third Party Claims Processing	32%
Print Universal and Other Claim Forms	33%
Electronic Transmission	100%
Tape-to-tape Transmission	33%
On-line Adjudication	92%
Connectivity (Customer-to-customer communication)	33%
Retail Zone Pricing Systems	63%
Rx Drugs - Branded	38%
Rx Drugs - Generic	46%
OTC Drugs	96%
Health and Personal Care	96%
General Merchandise	54%
Durable Medical Equipment/Home Health Care	52%
Point-of-Sale (POS) Systems	34%

Source: NWDA, 1999

Notes:

[1] Based on a survey of NWDA member wholesalers.

[2] The total number of responses received is 39.

1.3 Major Categories of Wholesalers

Wholesalers can be classified into several categories based on their size, breadth of coverage and activity, and principal function. The following sections profile the "Big Five" wholesalers, regional wholesalers, smaller (i.e., sub-regional and/or specialty) wholesalers, and secondary wholesalers.

1.3.1 The Big Five Wholesalers

The prescription drug wholesaling industry in the United States is highly concentrated, with 90 percent of sales made by five major full-line companies, referred to as the "Big Five." This group consists of McKesson HBOC, Inc., Bergen Brunswig Drug Company, Cardinal Health, Inc., AmeriSource Corporation, and Bindley Western Drug Company (see Table 1-3) (NWDA, 1999 and U.S. District Court for the District of Columbia, 1998). These companies generate from $7.6 billion to $21.5 billion per year in revenue, and represent the principal pipeline of drug distribution from manufacturers to dispensers (NWDA, 1999). The Big Five sell to regional distributors but also supply some health care institutions and independent drug stores (i.e., those with no more than three pharmacies). The Big Five distribute a full-line of drug products.

Traditionally, these wholesalers purchased the prescription drugs in large quantities from drug manufacturers, took ownership of the drugs in their own warehouses, and then resold them directly to the retail chains or hospitals (i.e., large dispensers) in desired allotments. This traditional service is referred to as "direct store delivery." Increasingly, however, large purchasers (especially retail chains) prefer self-warehousing, where the retailer buys direct from the manufacturer, stores the drugs in one or more of its own warehouses, and then delivers them to its retail stores and hospitals as needed. Accordingly, the Big Five and various regional wholesalers now also offer "dock-to-dock" delivery and "drop shipment" charging, which are also known as "brokerage" services in the wholesale industry (U.S. District Court for the District

Table 1-3

Sales and Market Shares of the Big Five Wholesalers

Company	1998 Annual Sales ($ Million)	1998 Market Share	1998 Sales Ranking	Number of Distribution Centers	Types of Customers
McKesson HBOC, Inc.	$21,484	28%	1	35	Health care institutions - 32% Independent pharmacies - 37% Retail chain pharmacies - 31%
Bergen Brunswig Drug Company	$16,698	22%	2	31 [a]	Health care institutions - 50% Independent pharmacies - 27% Retail chain pharmacies - 16%
Cardinal Health, Inc.	$14,928	19%	3	26 [b]	Health care institutions - 52% Independent pharmacies - 16% Retail chain pharmacies (non-warehousing) - 29% Retail chain pharmacies (warehousing) - 3%
AmeriSource Corporation	$8,669	11%	4	19 [c]	Health care institutions - 47% Independent pharmacies - 33% Retail chain pharmacies - 20%
Bindley Western Drug Company	$7,623	10%	5	18	Direct store delivery - 58% [d] Retail chain pharmacies (warehousing) - 42%
Big Five Total	**$69,402**	**90.0%**	**NA**	**129**	**NA**

Source: NWDA, 1999; U.S. District Court for the District of Columbia, 1998; Bindley Western Industies, Inc., 2000

[a] Additionally, the company has alternate site and depot facilities.

[b] Additionally, the company has 4 specialty distribution centers, 1 medical/surgical distribution facility, 6 packaging facilities, and 4 specialty centers.

[c] The company also has 3 specialty products distribution facilities.

[d] The annual report of the company did not provide figures for the different types of direct store deliveries.

of Columbia, 1998). In dock-to-dock delivery, the wholesaler obtains drugs in large quantities from the manufacturer for direct delivery to retail chain or hospital warehouses and does not bring the drugs into its own inventory. In drop shipments, the manufacturer ships the product directly to the customer, but with the order and payment submitted through the wholesaler. In these brokerage operations, the wholesaler does not take ownership of the drugs in its own warehouse at any time. In 1998, these non-stock sales of the Big Five and regional wholesalers amounted to 17 percent ($12.7 billion) of total sales by wholesalers ($73.8 billion) (NWDA, 1999).

Wholesalers generate revenues from both ends of the wholesale transaction. From dispensers, they receive the "upcharge," which is the percentage fee paid by dispensers for the cost of distribution, and other brokerage fees. These revenues are generally described as the "sell-side" margins. From manufacturers they receive "buy-side" margins, consisting of cash rebates and discounts for prompt and/or early payment. Distributors also might generate revenues by using the time differential, known as the "float," between when they receive payment from the drug purchaser and when they pay their supplier.

While the Big Five are very large business entities, price and competitive conditions dictate that they operate on narrow profit margins. In general, the wholesale markup is modest. According to data generated during a recent U.S. court case, for every dollar of prescription drugs sold in 1997, 76 cents went to the manufacturer, 20 cents to the dispenser (i.e., pharmacy), and only 4 cents to the wholesale distributor (U.S. District Court for the District of Columbia, 1998).[1] The NWDA reported the after-tax net profit expressed as a percent of sales, was only 0.62 percent for 1998 (NWDA, 1999).

The Big Five purchase the large majority of their drugs directly from the drug manufacturers. Because the Big Five have formal, written distribution contracts and conduct more than 2 transactions in any 24-month period with the drug manufacturers, they are clearly considered authorized distributors as the Agency has defined the term. The Big Five also

[1]Based on the context of the discussion in the source, this estimate of the division of the average prescription dollar among manufacturers, wholesalers, and dispensers, reflects all rebates and markups applicable to the industry.

purchase drugs from other distributors who can occasionally offer lower prices. The role of price discounting in the industry is described in more detail below.

1.3.2 Regional Wholesalers

The next largest distributors after the Big Five are the regional wholesalers. While at least an order of magnitude smaller than the Big Five, these companies generate revenues of approximately $500 million to $900 million per year (NWDA, 1999). ERG estimates that there are approximately 70 regional prescription drug wholesalers, based on the membership roster of the National Wholesale Druggist Association (NWDA), an industry trade association, and comments submitted to the FDA docket by Purity Distributors (Riccardi, 2000). Table 1-4 presents the 1998 sales volumes and rankings of the top regional wholesalers.

Regional distributors are distinguished from the Big Five by a smaller volume throughput of drugs. Many regional distributors, however, offer a complete or nearly complete line of drugs. Unlike the Big Five, most regional wholesalers do not have formal written distribution contracts with the pharmaceutical manufacturers, although many conduct business with them on a regular basis. Thus, while these wholesalers could be considered authorized distributors under industry's interpretation of the 1988 FDA Guidance, they are not authorized according to the final rule, 21 CFR Part 203.

Regional distributors and the Big Five sell to the same industry sectors. The regional distributors can compete with the Big Five because they can provide better service to some of the areas in their region and because many of their drug purchases from manufacturers are on terms as or nearly as favorable as those offered to the Big Five. The main customers for the two groups combined include: (1) health care institutions (36.6 percent of total sales), (2) independent (non-chain) drug stores (31.6 percent of sales), (3) retail chains (25.7 percent of sales), and (4) other entities, such as surgical or dialysis centers and physicians' offices (6.1 percent) (Casteuble, 2000a). Table 1-5 summarizes the distribution of drug sales by type of customer.

Table 1-4

Top Regional Drug Wholesalers in the U.S., by 1998 Sales Volume and Market Share

Company	Sales ($ Million)	Market Share	Sales Ranking
Neuman Distributors, Inc.	$1,668	2%	6
Kinray, Inc.	$905	1%	7
C.D. Smith Healthcare Inc.	$798	1%	8
D & K Healthcare Resources, Inc.	$703	1%	9
Remo Drug Corp.	$508	1%	10
N.C. Mutual Wholesale Drug Co.	$480		11
The F. Dohmen Co.	$423		12
Walsh Distribution, Inc.	$387		13
Harvard Drug Group	$347		14
H.D. Smith Wholesale Drug Co.	$306		15
Bellco Drug Corporation	$300		16
Value Drug Company	$267		17
Smith/Smith/Texas	$235		18
FMC Distributors Inc.	$175		19
Rochester Drug Cooperative	$160		20

Source: NWDA, 1999

Table 1-5

1998 Net Sales of The Big Five and Regional Drug Wholesalers by Type of Customer

Type of Customer	Net Sales [a] ($ million)	Percent of Total Stock Sales	Percent of Total sales
Institutional Dispensers	$22,362	36.6%	30.3%
Hospitals	$17,902	29.3%	24.3%
Clinics and Nursing Homes	$4,460	7.3%	6.0%
Independent Drug Stores	$19,308	31.6%	26.2%
Retail Chains	$15,716	25.7%	21.3%
Chain Drug Stores	$7,027	11.5%	9.5%
Chain Drug Warehouses	$1,528	2.5%	2.1%
Mass Merchandisers and Food Stores	$7,161	11.7%	9.7%
Other Customers	$3,715	6.1%	5.0%
Total Stock Sales	**$61,101**	**100.0%**	**82.8%**
Non-Stock Sales [b]	$12,700	NA	17.2%
Total Sales	**$73,801**	**NA**	**100.0%**

Source: NWDA, 1999
"NA" = Not available
[a] Includes sales of prescription drugs, OTC drugs, health and beauty aids, general merchandise, and other products.
[b] Non-stock sales include brokerage sales, dock-to-dock, drop shipments, and any other form of sales not placed in inventory that are generally sold at a significantly lower margin. Most non-stock sales are to chain drug store warehouses.

Combined, the Big Five and the regional distributors operate a total of 235 distribution centers across the continental United States and U.S. Territories (NWDA, 1999 and Pharmaceutical Distributors Association, [PDA], 2000a). Based on data provided by the NWDA Industry Performance and Trend Reporting Program, the average number of suppliers (whether manufacturer or other wholesaler) per wholesaler among the Big Five and regional companies is 913 in 1998. This represents an increase of around 47 percent from its 1994 level of 620 (NWDA, 1999). The increase is at least partly due to the significant growth in the variety of products offered in many pharmacies, and especially by the increase in herbal products and remedies now being offered (Casteuble, 2000b).

1.3.3 Smaller Wholesalers

Numerous additional, and generally smaller, wholesalers also distribute pharmaceutical products. This category captures wholesalers of varying characteristics. For example, some of these companies carry a relatively full line of drug products and provide distribution service to small independent pharmacies and physicians. Other wholesalers distribute partial lines of pharmaceutical products, such as injectables, that require special handling. Still other wholesalers team with medical supply companies to provide the combination lines of drug and medical devices dispensed from physician's office, or supplies provided for veterinarians' offices.

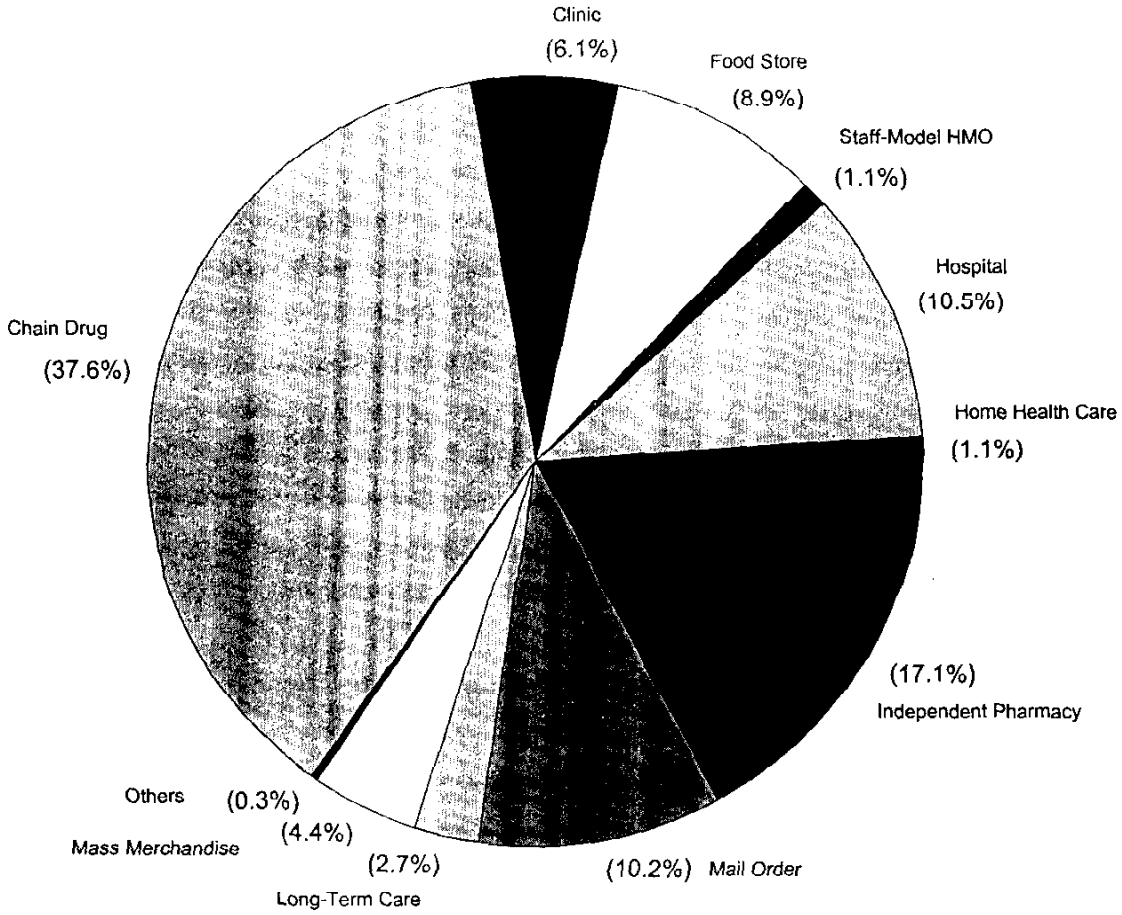
Many viable drug wholesalers are quite small. Some companies contacted for this study generated over $10 million in annual revenues with fewer than 10 staff dedicated to drug distribution.

Some of these wholesalers serve small drug dispensers, such as small, independent pharmacies, that are not part of buying groups or under contract to larger, full-line distributors.[2] Smaller wholesalers generally are willing to deal in smaller volumes than regional wholesalers and serve the individual independent pharmacies and physicians offices. Figure 1-2 presents the distribution of prescription drug sales by dispensing outlet. In the figure, physician's offices

[2]A small drug store's contract with a distributor might require that they purchase all pharmaceuticals or a specified range of pharmaceuticals from that distributor.

Figure 1-2

1999 U.S. Prescription Drug Sales by Outlet



Source: PhRMA, 2000

are included in the "Other" category, which represents 0.3 percent of total sales. Small dispensers of various types (e.g., small clinics) are also found in the other dispenser categories as well.

Based on discussions with industry personnel, ERG concluded that virtually none of these smaller wholesalers have formal distribution contracts with drug manufacturers and thus, are not considered authorized distributors. Further, many of these wholesalers probably do not purchase products directly from manufacturers on a regular basis. For example, one wholesaler reports that 83 percent of its purchases are from 3 major full-line wholesalers, 8 percent are from other distributors, and only 9 percent are from 11 different manufacturers (Ford and Everly, 2000). Thus, most smaller wholesalers probably do not meet the requirement for 2 transactions with most pharmaceutical manufacturers in any 24-month period.

The customers of smaller wholesalers do not purchase pharmaceuticals from the major wholesalers (the Big Five or the regional distributors) because:

- They do not meet the minimum volume purchase requirements set by major wholesalers to qualify potential customers; or
- Some wholesalers sell prescription drugs in packages that are inconveniently large for these customers; (Ford and Everly, 2000, Everly, 2000, and Clark, 2000).

1.3.4 Secondary Wholesalers

Secondary wholesalers generally do not offer a full line of pharmaceutical products but specialize in purchasing and selling selected discounted drug products. Pharmaceutical manufacturers occasionally offer drug products for sale, such as when they strive to meet a quarterly sales goal or wish to sell off inventory in advance of a price increase (Riccardi, 2000). At such times, manufacturers offer products for a limited time at a discounted price. Cash customers often receive an additional discount. In response to such sales, secondary wholesalers (and some full-line national or regional wholesalers) will purchase quantities of the sale products.

Secondary wholesalers in turn offer the discounted products for sale, principally to other wholesalers. They sell products to many other wholesalers, including the Big Five and regional wholesalers, because their discounted price undercuts the regular prices being offered by the manufacturer. Thus, a manufacturer's special sale price for a given drug might undercut the price at which the drug is sold under contract to the Big Five and to regional wholesalers. The Big Five might then reduce their purchases under contract for selected drugs in order to take advantage of sale prices being offered by these secondary and other wholesalers.

While any distributor might be able to take advantage of manufacturer sale prices, secondary wholesalers are distinguished by their willingness to risk substantial capital in buying and trading discounted drugs. Their activities are built around the rapid turnover of discounted drugs in a fashion similar to that of discounters in other industries. One executive noted that his company will fax its inventory and current sale price list either daily or at least twice a week to potential customers. The companies do very little advertising or sales promotion work other than publishing and advertising their sale prices periodically. Industry contacts also noted that, while secondary wholesalers are able to build some customer loyalty, their relationships are built almost entirely on the competitiveness of their sale prices.

There is no formal definition or count of the number of secondary wholesalers. Like other wholesalers, some of these firms are very modest in size, with fewer than 10 staff handling drug orders. There are three prominent secondary wholesalers, each of which are fairly large companies, namely Supreme Distributors Company, Victory Wholesale Grocers Company, and Quality King Distributors, Inc. As their names indicate, these secondary wholesalers distribute other products, including food.

Additionally, a wide spectrum of wholesalers, including the Big Five companies, engage in trading of pharmaceutical products to take advantage of price differentials. Thus, even wholesalers that are primarily engaged in routine distribution services will sometimes trade in pharmaceuticals to take advantage of price differentials.

Like the majority of regional and smaller wholesalers, most secondary wholesalers do not have a written distribution agreement with drug manufacturers whose products they purchase and resell. Some of the reasons why drug manufacturers decline to enter into written

distribution agreements with the secondary wholesalers include (1) the inability of these wholesalers to carry the full line of manufacturers' products and maintain a required line of credit, and (2) manufacturers' unwillingness to open new accounts (PDA, 2000b). Furthermore, secondary wholesalers are only irregular customers of the manufacturers and thus do not represent an avenue for routine distribution of the manufacturers' products.

Many secondary wholesalers engage in numerous transactions with pharmaceutical manufacturers over the course of any 24-month period but usually lack formal written agreements with pharmaceutical manufacturers. Thus, while many secondary wholesalers have believed themselves to be authorized distributors under industry's interpretation of the 1988 FDA Guidance, they are not classified as such under the final rule (21 CFR Part 203).

There are believed to be numerous, smaller, secondary wholesalers as well as the large firms mentioned above. The small secondary wholesalers are entities that also engage substantially in trading of price discounted drugs. This group also resembles the smaller wholesalers described in the previous section, however, in that they service portions of the industry that are not supplied by the Big Five or by the larger regional wholesalers. Even these small secondary wholesalers participate in manufacturer sales of products and trade products aggressively to take advantage of price discounts. ERG lacks quantitative data or distinct industry statistics that allows it to characterize further the population of small secondary wholesalers.

1.4 Statistical Profile of Wholesalers

Government data sources address the drug wholesaling industry, but do little to differentiate drug distributors from other medical and consumer product distributors. According to the U.S. Standard Industrial Classification (SIC) system, businesses primarily engaged in the wholesale distribution of drugs and druggists's sundries, including over-the-counter (OTC) drugs, health and beauty products, vitamins, and in-vitro and in-vivo diagnostics, are classified in SIC 5122, Drugs, Drug Proprietaries, and Druggists' Sundries (NAICS 42221, Drugs and Druggists' Sundries, Wholesalers). Based on 1997 data from the Small Business Administration (SBA) (see Table 1-6), there are a total of 6,500 wholesalers in SIC 5122, of which 83 percent

Table 1-6

1997 SBA Data on Prescription Drug Wholesalers
(SIC 5122: Drugs, Drug Proprietaries, and Druggists' Sundries)

Firm Employment Size	Firms	Establishments	Employment	Annual Payroll ($1,000)	Estimated Receipts ($1,000)	Estimated Receipts Per Employee ($)
0 to 9 Employees	4,737	4,747	12,595	$500,975	$8,011,427	$636,080
10 to 19 Employees	670	689	8,798	$307,819	$3,898,071	$443,063
20 to 99 Employees	738	820	27,086	$957,207	$12,581,836	$464,514
100 to 499 Employees	201	354	26,981	$1,000,117	$15,208,338	$563,668
500 or More Employees	171	1,725	122,254	$6,047,119	$157,600,505	$1,289,124
[a] Small Entities - 0 to 100 Employees [a]	**6,145**	**6,256**	**48,479**	**$1,766,001**	**$24,491,334**	**$505,195**
Total	**6,517**	**8,335**	**197,714**	**$8,813,237**	**$197,300,177**	**$997,907**

Source: SBA, 2000
[a] According to the SBA size standards, firms employing 100 or fewer employees are small.

are small (with less than 20 employees), 11 percent are medium-sized (with 20 to 99 employees), and the remaining 6 percent are large (with more than 100 employees). The average estimated revenues per firm ranges from $2.2 million for small to over $0.9 billion for very large wholesalers.

ERG judged that the estimate of 6,500 wholesalers is, at best, a rough approximation of the actual number of U.S. drug wholesalers because SIC 5122 (1) does not include firms that distribute drugs but generate the majority of their revenues from other activities, such as the distribution of groceries, distribution of medical and surgical equipment, and the operation of retail pharmacies, and (2) includes firms that may not distribute prescription drugs (i.e., firms that distribute druggists' sundries such as health and beauty products).

According to the Robert Morris Associates (RMA) Annual Statement Studies,[3] the operating profits of wholesalers classified in SIC 5122 range from 3.4 percent to 4.9 percent of annual sales in 1999 (RMA, 2000).

1.5 Models of Prescription Drug Distribution

ERG identified four broadly defined models of drug distribution although numerous additional variations can be defined. The models are delineated according to the number of times the drug product is resold. Table 1-7 outlines the 1998 sales of prescription drugs by some of the distribution channels identified and by type of dispenser.

ERG did not consider mail-order distribution to be a separate and unique distribution model, but rather a separate dispensing model. Mail-order companies buy their drugs directly from manufacturers or, more commonly, from wholesalers. In either case, distribution occurs through a channel that is equivalent to Models 1 and 2 described below.

[3] Data provided in Robert Morris Associates Annual Statement Studies is compiled from bank loan requests of companies and includes ratios and common size financial statement percentages segregated by sales size and quartile.

Table 1-7

1998 Sales of Prescription Drugs to Dispensers, by Channel of Distribution

			Channel of Distribution					
	Total Sales		Manufacturer Direct		Chain Store Warehouse/ Mail Order		Wholesaler	
Type of Dispenser	$ Million	Percent	$ Million	Percent	$ Million	Percent	$ Million	Percent
Health Care Institutions	$24,959	24.5%	$6,270	25.1%	$22.4	0.1%	$18,669	74.8%
Hospitals	$12,980	12.8%	$2,622	20.2%	$0.0	0.0%	$10,358	79.8%
Clinics	$6,251	6.1%	$2,494	39.9%	$12.5	0.2%	$3,744	59.9%
Long Term Care/Home Health	$4,219	4.1%	$447	10.6%	$8.4	0.2%	$3,763	89.2%
Health Care Plans	$1,509	1.5%	$706	46.8%	$1.5	0.1%	$803	53.2%
Independent Drug Stores	$19,291	19.0%	$714	3.7%	$57.9	0.3%	$18,519	96.0%
Retail Chains	$46,171	45.4%	$1,031	2.2%	$29,245.7	63.3%	$15,924	34.5%
Chain Drug Stores	$30,288	29.8%	$1,000	3.3%	$22,292.0	73.6%	$7,027	23.2%
Mass Merchandisers	$7,573	7.4%	$15	0.2%	$4,543.8	60.0%	$3,014	39.8%
Food Stores	$8,310	8.2%	$17	0.2%	$2,409.9	29.0%	$5,863	70.6%
Mail-order Pharmacies	$10,972	10.8%	$417	3.8%	$7,153.7	65.2%	$3,401	31.0%
Others	$278	0.3%	$225	81.0%	$0.6	0.2%	$52	18.7%
Total	**$101,671**	**100.0%**	**$8,657**	**8.5%**	**$36,480.3**	**35.9%**	**$56,566**	**55.6%**

Source: NWDA, 1999

1.5.1 Model 1—Distribution Directly from Manufacturer to Dispensing Organization

Manufacturers sell a portion of their output directly to dispensing organizations, such as large retail pharmacy chains or healthcare organizations. Table 1-8 provides a breakdown of the drug purchases prescription drug sales of innovator drug companies (i.e., excluding generic drug manufacturers) by class of customer. According to a compilation by PhRMA, 20 percent of all pharmaceutical drug sales went directly to dispensing organizations. Specifically, 12.4 percent of manufacturer sales went to retailers, 2.1 percent to private hospitals, and 1.4 to healthcare practitioners. The data include sales of both branded and generic drugs, as sold by PhRMA members.

In the past decade, institutional consumers of pharmaceutical drugs, such as hospitals and retail pharmacy chains, as well as independent retail pharmacies, have significantly decreased the percentage of pharmaceuticals purchased directly from the manufacturer. For these institutions, the value-added services of the distributor are more valuable than the price savings from dealing directly with the manufacturer. Conversely, mail order pharmacies have increased the volume of pharmaceuticals they purchase directly from manufacturers. Mail order dispensing of pharmaceuticals is the fastest growing segment of the industry. From 1990 to 1997, the sale of pharmaceuticals by mail order increased from 5.1% to 9.7% of the total sales (U.S. District Court for the District of Columbia, 1998). Mail-order is often used to dispense "maintenance" drugs regularly used by patients over an extended period of time. There are approximately 63 mail-order pharmacies and 32 retail companies with mail-order pharmacy operations in the U.S. (NWDA, 1999).

Some large dispensing companies, especially chain drug stores, perform "self-warehousing" wherein they assume the task of distribution itself. Instead of relying upon an outside distributor, these retailers buy directly from the manufacturer; store the drugs in one or more of their own warehouses; and deliver the drugs to their retail stores as needed. Retail chains with four or more stores (including chain drug stores, mass merchandisers, and food stores) have increased the percentage of drugs they now self-warehouse to 66.1 percent of their total drug purchases (U.S. District Court for the District of Columbia, 1998).[4] Thus, retail

[4]Defined in terms of the total dollar volume of pharmaceuticals purchased.

Table 1-8

1998 Prescription Drug Sales of PhRMA Member Innovator Drug Manufacturers by Class of Customer

Class of Customer	Sales ($ million)	Market Share
Wholesalers	$64,015.1	80.0%
Retailers	$9,922.3	12.4%
Private Hospitals	$1,680.3	2.1%
Practitioners	$1,120.2	1.4%
Manufacturers, Repackagers	$1,200.2	1.5%
Federal Hospitals	$640.1	0.8%
Other Federal Government	$880.2	1.1%
State and Local Government Hospitals	$560.1	0.7%
Total	**$80,018.9**	**100.0%**

Source; PhRMA, 2000
Note: Sales are reported net of rebates and discounts. Numbers and percents may not add to totals because of rounding.

chains self-warehouse a majority of purchases made either directly from manufacturers or through wholesalers.

1.5.2 Model 2—Distribution Through Major Wholesalers

The second model of drug distribution characterizes the movement of the large bulk of pharmaceutical products. Most drug shipments move from the drug manufacturer to several large wholesalers (i.e., the Big Five and regional wholesalers) and then on to dispensers (i.e., health care organizations, retail pharmacy chains, etc.). For these drugs, the number of transactions and the times that the drug product is handled and physically moved is the minimum necessary to reach an eventual consumer. Specifically, perhaps 2 transactions (manufacturer to wholesale distributor to pharmacy chain or other dispenser) are made before the product is consumed.

1.5.3 Model 3—Distribution from Large to Small Wholesalers to Dispensers

Additional tiers of distribution exist for drugs that are shipped to some of the smaller drug dispensers. As has been noted, the Big Five and even regional wholesalers often have volume requirements that exclude some small dispensers from using their services. In the case of physicians' offices or small healthcare facilities, their demand for drugs is also somewhat limited and/or specialized so that they do not require the services of a full-line distributor. Thus, a hypothetical small wholesaler might report that his customer base consists of several hundred physicians' offices, selected Federal health facilities, selected health care clinics, and miscellaneous other dispensers.

For this case, the number of drug transactions made from manufacturer to dispenser might be three or four (full-line to regional to small sub-regional to perhaps smaller wholesaler).

1.5.4 Model 4—Distribution of Discounted Drugs, Via Secondary Wholesalers

Discounted drugs are sometimes sold in substantial volumes and, in order to absorb the supply, dispersed widely throughout the distribution network. In these cases, the number of transactions made before the drug product reaches a dispenser can be quite large.

Discounted products are often sold to secondary wholesalers, although the Big Five or regional wholesalers also participate in such sales. The secondary wholesalers are notable, however, for their willingness to absorb the risk of large purchases of discounted products.

Representatives of secondary wholesalers described a considerably lengthy set of transactions for many of the drug products they handle. First, while manufacturers sell the bulk of their output to the Big Five wholesalers, they sometimes wish to sell additional products separately from these relationships. As noted earlier, manufacturers will often announce short-term sales of products for various reasons, such as to meet quarterly sales goals, or to reduce inventory before a price increase. Wholesalers might also hold drug sales to eliminate slow-moving inventory.

Such discounted drugs are then purchased by wholesalers, with many purchases by wholesalers other than the Big Five. In making these sometimes large purchases of sale merchandise, the wholesalers incur a substantial capital investment and, less significantly, also use warehouse space to hold the drugs. Furthermore, many of these wholesalers do not have a normal or routine distribution channel that can absorb the discounted product quickly. The wholesalers are interested, therefore, in turning over products quickly and can do so by passing on a portion of the original discount to other wholesalers or drug purchasers. Thus, the original purchaser makes a large capital investment and attempts to recoup it as quickly as possible by selling portions of the sale product, at a still somewhat discounted price, to other wholesalers.

The second tier of wholesalers are largely in the same position as the original purchaser, although they are handling small volumes of sale products. Nevertheless, they make relatively large capital investments and wish to turn over the discounted product as quickly as possible. In this fashion, the sale product is distributed rapidly and with broad dispersion, throughout the drug distribution industry. This second tier might include any drug wholesale organization, including the Big Five, regional, mail order, or other organizations.

The breadth of dispersion is indicated by the number of transactions that might occur before the sale product reaches the dispenser. According to one secondary wholesaler, it is not uncommon for his company to be among the third tier of distributors to purchase some of the sale product. Further, this executive judged it likely that the product would trade hands two or three more times before reaching the eventual drug dispenser. Thus, from 5 to perhaps 7 transactions involving the sale product are commonplace.

1.6 Topics Related to the Functioning of the Distribution Models

1.6.1 Distribution of Branded vs. Generic Pharmaceuticals and Other Variations

Industry contacts indicated that the distribution patterns for drugs of almost all types are unaffected by the nature of the drug. Thus, the distribution models described are applicable to virtually any form of pharmaceutical. There are two areas, however, where there is some variation away from the distribution patterns described above.

First, generic drugs are less often offered in promotional sales at discounted terms. Generic drugs are substantially less expensive than brand name drugs and, thus, already represent a substantial discount from competing products. In any case, distributors mentioned that generic drugs are handled less frequently through secondary wholesalers. ERG did not identify quantitative data on this point.

Second, some products, such as many parenteral products, must be consumed within a relatively short period after manufacturing. Many parenteral products, due to their water content, are relatively bulky to handle and costly to distribute. As a result, these products are poor candidates for repeated reselling through the wholesaling industry. Most of these products are sold using routine distribution channels and generally would not be handled by secondary wholesalers.

1.6.2 Handling of Recalls

Drug distributors must participate with manufacturers and retailers in efforts to retrieve recalled drugs. ERG contacted several distributors about their approach to accomplishing recalls.

An estimated 10 percent of distributors can track products by lot number (Casteuble, 2000b). The large majority of distributors must rely on date of shipment information received from the manufacturer to determine when and whether they received the recalled materials. Using this information, wholesalers indicated that they can generally determine whether they still have the material and/or who among their customers might have received the product. Wholesalers store incoming products in their warehouses on shelves but, in most cases, do not track the flow of products through the warehouse on a lot-by-lot basis. Wholesalers also do periodic (e.g., monthly) inventories of the products on their shelves.

Some large wholesalers contacted for this study stated that their firms would use the lot and date information from manufacturer invoices to determine if and when they received the recalled product. One wholesaler also stated that the firms' employees perform a monthly inventory of the cases on their shelf. Thus, the wholesaler can determine in which month they shipped a recalled product, but cannot determine which of the customers (among those purchasing that product during the month) received the recalled lots.

Wholesalers reported that it was standard operating procedure to notify all customers of all recalls. Customers are then required to make their own checks to determine if they still have the recalled products and to notify their customers, as may be appropriate.

Some secondary wholesalers appear to have greater ability to track information by lot number than other wholesalers. For example, testimony at a recent FDA hearing indicated that secondary wholesalers are able to use lot numbers to identify the exact destination of shipments passing through their warehouses (FDA, 2000).

1.6.3 Combined Efficiency of Distribution Models

The first three models above describe fairly conventional models of distribution while the fourth model, distribution via secondary wholesalers, describes the use of unique sale-by-sale channels for distributing discounted products. This fourth channel provides an outlet for promotional or occasional inventory-reducing sales by drug manufacturers.

Many industries have both routine distribution channels which handle the bulk of product sales and "spot" markets that equilibrate supply and demand of product lots that are not distributed through contractual agreements. The spot market allows manufacturers to sell excess production, thereby avoiding inventory charges, product waste, or other costs. It also allows manufacturers to discriminate between buyers that require a guaranteed, predictable, supply of product for distribution and buyers (e.g., secondary wholesalers) that do not. This spot market, like spot markets in any industry, help equilibrate supply and demand and create a more efficient, smoothly functioning market. The spot market provides additional flexibility, through immediate price fluctuations, to both buyers and sellers of products.

SECTION TWO

ORGANIZATIONS PURCHASING WHOLESALE DRUGS PRODUCTS— THE DEMAND FOR WHOLESALE DRUGS

To further characterize drug distribution and drug pricing influences, this section profiles some of the organizations that purchase or are involved indirectly in the purchase of drugs. Separate discussions are provided below on health care institutions and integrated delivery networks (IDNs), pharmacy benefit management companies (PBMs), and retailers. The final section briefly addresses the influence of health maintenance organizations (HMOs) and PBMs on prescription drug prices.

2.1 Health Care Institutions and Integrated Delivery Networks (IDNs)

Health care institutions, including, hospitals, clinics, nursing homes, home health care providers, managed care providers (i.e., HMOs), government agencies, and various alternate care providers, collectively purchased around $25.0 billion in prescription drugs in 1998 (NWDA, 1999). Over 75 percent of these purchases were from wholesalers and the remaining volume from drug manufacturers (NWDA, 1999). Health care facilities generally demand a greater quantity of prescription drugs per location and a narrower range of items than retail stores.

Over the years, health care institutions have consolidated to form integrated delivery networks (IDNs), which are organized to provide efficient and cost-effective medical services to a community. According to data compiled by the SMG Marketing Group, Inc., there are a total of 604 IDNs in the United States as of April 1999 (NWDA, 1999). Some health care institutions, including individual hospitals, chains, and IDNs, have combined to form group purchasing organizations (GPOs). While the GPOs do not purchase the drugs themselves or provide drug distribution services, they use the aggregated purchasing power of their members to negotiate favorable contracts with manufacturers and wholesalers on behalf of their members (U.S. District Court for the District of Columbia, 1998).

SMG Marketing Group, Inc., estimates that as of April 2000, there were a total of 701 hospital GPOs in the United States. Further, of these 701 GPOs, 416 are multi-hospital systems that own, manage, or lease two or more hospitals (SMG Marketing Group, Inc., 2000).

2.2 Pharmacy Benefit Management Companies (PBMs)

Pharmacy benefit management companies (PBMs) administer the prescription drug part of health insurance plans on behalf of plan sponsors such as self-insured employers, insurance companies, and health maintenance organizations (HMOs). The objective of these companies is to provide high-quality drug care at the lowest possible cost (GAO, 1995). The development of PBMs in the U.S. coincides with the emergence of prescription drug benefits in health care plans in the 1970s and 1980s. The precursors of PBMs include pharmacy claims processors and mail-order pharmacies. While PBMs continue to provide pharmacy claims processing and mail-order pharmacy services to their customers, many now provide additional services, including

- Rebate negotiations with drug manufacturers,
- Development of pharmacy networks,
- Formulary management,
- Prospective and retrospective drug utilization reviews (DURs),
- Generic drug substitution, and
- Disease management programs (Levy, 1999).

Rebate Negotiations with Drug Manufacturers. PBMs represent health plans and their enrollees in dealing with drug manufacturers and pharmacies in the prescription drug market. For example, a PBM negotiates with drug manufacturers to obtain rebates for a plan sponsor in return for inclusion and low-cost designation of the manufacturers' drugs on the plan's formulary (GAO, 1997). These rebates usually take the form of a direct payment from the manufacturer to the PBM. For example, in a simple rebate arrangement, the PBM may periodically report to the drug manufacturer the number of prescriptions for a given drug filled by the PBM's enrollees; the manufacturer then pays the PBM an agreed-upon amount for each prescription.

Alternatively, the PBM and the drug manufacturer may negotiate an agreement where the PBM is reimbursed for moving market share (i.e., significant increases in the number of prescriptions for the manufacturer's drug) (DHHS, 2000). Although there are no published data available on the magnitude of manufacturers' rebates, they are estimated to range from 2 to 21 percent of acquisition price and can be as high as 35 percent for selected drugs (DHHS, 2000).

PBMs generally pass on the rebates they negotiate with drug manufacturers to their customers. Consequently, the insurer or the self-employed insurer typically receives 70 to 90 percent of the rebates (DHHS, 2000).

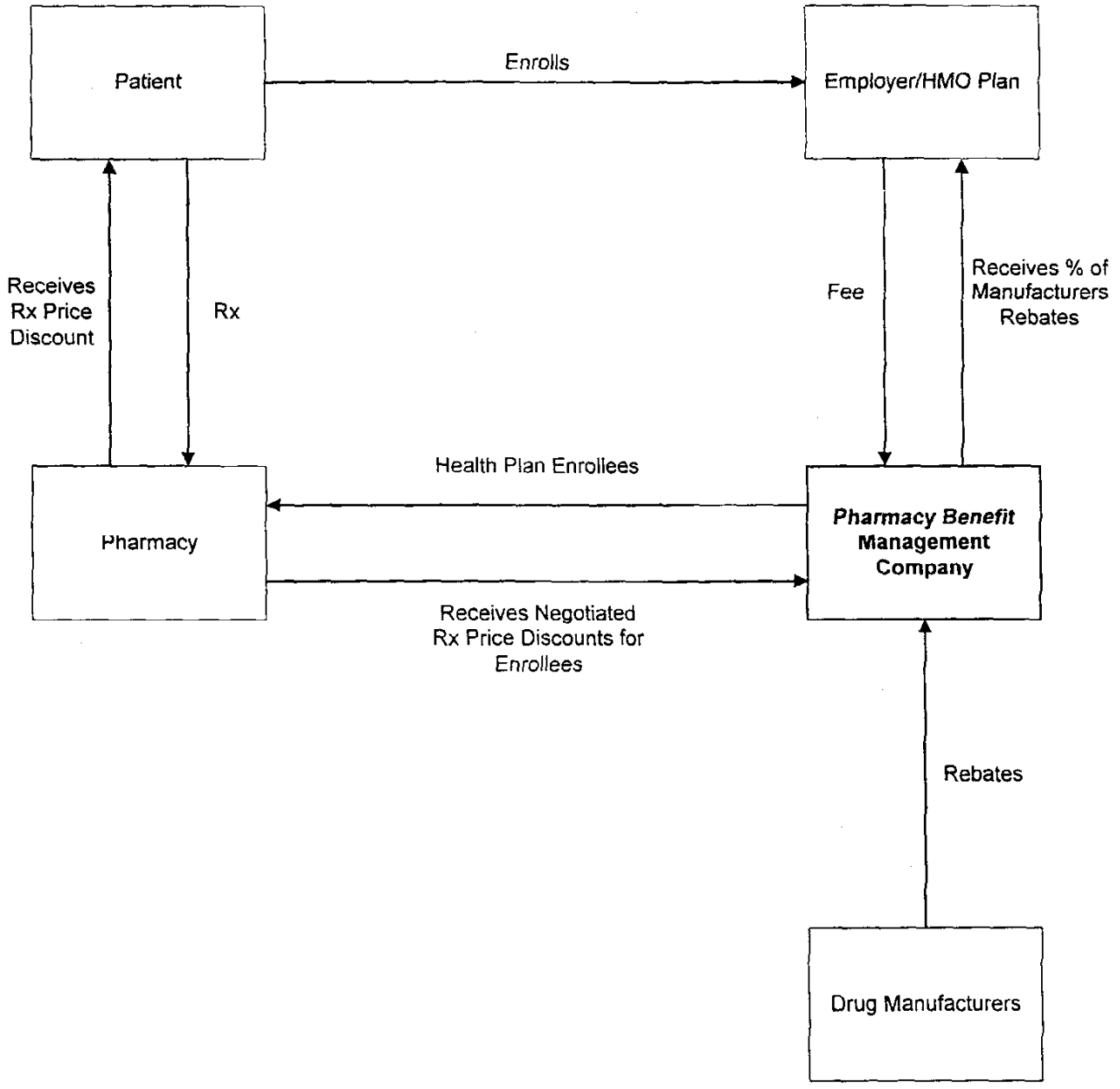
Development of Pharmacy Networks. In addition to drug manufacturers, PBMs also negotiate with retail pharmacies to obtain various discounts on prescription drug prices. Additionally, PBMs try to assure adequate sites for patients enrolled in the various health plans to obtain their prescription drugs. Thus, PBMs try to optimize their position by obtaining the widest geographic pharmacy coverage while keeping costs at their lowest. Figure 2-1 shows a typical network in which a PBM operates.

As part of their management functions, PBMs provide pharmacists information on a variety of issues before drugs are dispensed to the patients. The type of information provided includes (1) data on applicable co-payments, co-insurance, or deductibles; (2) details relevant to any online claims adjudication; (3) concurrent drug utilization review (DUR) data on basic eligibility requirements, drug interactions, and adverse drug reactions; (4) details about any formulary restrictions; (5) data about any generic substitution requirements; and (6) information on brand-name and generic drug dispensing fees (Levy, 1999).

Formulary Management. Formulary management involves the development of a drug formulary, which is a list of drugs that an insurance plan uses to make reimbursement decisions. Formularies help control drug costs by (1) encouraging the use of formulary drugs through compliance programs that inform physicians and enrollees about which drugs are on the formularies; (2) limiting the number of drugs a plan will cover; or (3) developing financial incentives to encourage the use of formulary products. PBMs rely on pharmacy and therapeutic (P & T) committees, consisting of pharmacists and physicians, to determine the number of drugs to include on the formulary (GAO, 1995).

Figure 2-1

Pharmacy Benefit Management Company (PBM) Network



Source: GAO, 1995

Formularies can be open, incentive-based, or closed. An open formulary usually implies that the plan will cover all drugs except those listed as exclusions to the drug reimbursement policy. An incentive-based formulary provides enrollees with financial benefits if their physicians prescribe formulary drugs. Under the arrangement, the health plan still reimburses enrollees for non-formulary drugs but requires them to make higher co-payments than for formulary drugs. A closed formulary details the specific drugs that meet the plan's reimbursement policy. Under a closed formulary, enrollees generally pay the full cost of non-formulary drugs prescribed (GAO, 1995 and DHHS, 2000).

Drug Utilization Reviews (DURs). PBMs conduct prospective DURs to control drug use before physicians write prescriptions. Under prospective DUR, PBMs use a computer link with network pharmacists to review each prescription before it is dispensed. Prospective DURs are designed to help PBMs to identify whether there is a generic or formulary alternative to the prescribed drug and whether the drug will duplicate an existing prescription or will adversely interact with other drugs the patient is using. For retrospective DURs, PBMs analyze the drug utilization statistics of a customer's enrollees to identify any instances in which physicians prescribed potentially inappropriate medications. If PBMs detect inappropriate patterns of prescribing or consumption, they then contact and educate physicians about more appropriate and potentially cost-effective treatments (GAO, 1995).

Generic Drug Substitution. Many PBMs offer incentives to their enrollees to select generic instead of brand-name drugs as these are less costly than their brand-name counterparts. PBMs facilitate these therapeutic substitution programs through the mail-order pharmacies they operate (Levy, 1999).

Disease State Management (DSM) Programs. PBMs also initiate disease state management (DSM) programs to contain spending for chronic conditions such as asthma, cystic fibrosis, hemophilia, and multiple sclerosis. In developing these programs, PBMs evaluate various treatment options, or therapies to identify those that are associated with better therapy management and low overall spending. PBMs then attempt to educate both health plan enrollees and their physicians about these more cost effective treatments and monitor the degree of their compliance with the related protocols over time (GAO, 1995).

There are an estimated 76 PBMs in the United States (SMG Marketing Group, Inc., 1999). The top five PBMs by number of covered lives include PCS Health Systems with 56.0 million, Merck-Medco Managed Care with 51.0 million, Diversified Pharmaceutical Services with 23.9 million, Express Scripts ValueR/X with 22.7 million, and WellPoint Pharmacy Management with 15.5 million (NWDA, 1999). SMG Marketing, Inc., reports that on average, 6.2 prescriptions are written per year for each covered life of which 55.7 percent are branded and 44.3 percent are generic drugs.

Some PBMs are privately owned companies whereas others are either owned by or affiliated with pharmaceutical manufacturers, health maintenance organizations, or pharmacy chains. Table 2-1 presents available data on selected PBMs in the United States as gathered from various sources.

The various purchasing methods (PBMs, IDNs, GPOs) affect the destination of drug products (i.e., they help determine eventual purchasers), but in general they do not affect the physical logistics of drug distribution. ERG did not investigate the extent to which purchasing organizations might indirectly affect the logistics of drug distribution by influencing purchasing patterns.

2.3 Retailers

The retailers, which include independent drug stores, retail chains pharmacies, and mail-order pharmacies, are the major customers of wholesalers with total prescription purchases of $76.4 billion in 1998 (NWDA, 1999).

Independent drug stores are defined as companies having three or fewer stores. There are currently an estimated 22,000 independent drug stores in the United States (ERG, 2000). Independent drug stores purchased $19 billion in prescription drug products in 1998, with the majority (96 percent) purchased from wholesalers (NWDA, 1999). Over the years, independent drug stores have joined group purchasing organizations (GPOs) in increasing numbers to gain greater leveraging power with wholesalers and manufacturers.

Table 2-1

Data on Selected Pharmacy Benefit Management Companies (PBMs)

Company	Ownership	Lives Covered (1999)	Sales ($ millions) (2000)	Employment (2000)	SICs Reported	Additional Information
PCS Health Systems	Rite Aid Corp.	56.0 million	$14,500	77,258	5912	Operates retail drug stores which sell health and beauty aids, proprietary drugs, housewares, tobacco products, sundries, and prescription medicines
Merck-Medco Managed Care	Merck & Co.	51.0 million	$35,500	62,300	2834, 2833, 2836, 2835	Develops, produces, and markets human health care products, including therapeutic and preventive agents generally sold by prescription; produces animal health products; provides pharmaceutical benefit services
Diversified Pharmaceutical Services	SmithKline Beecham	23.9 million	$12,300	47,200	2834, 2844, 8071	Researches, develops, manufactures, and markets a wide range of health and personal care products, including pharmaceuticals; provides disease management and pharmaceutical benefit management services; performs clinical laboratory testing services
Express Scripts Value R/X	Express Scripts	22.7 million	$5,520	4,606	5912, 8099, 8093	Provides broad range of pharmacy benefit management services to health benefit plan sponsors including pharmacy network administration, drug utilization review, and mail pharmacy service; and offers infusion therapy services and managed vision care programs
WellPoint Pharmacy Management	WellPoint Health Networks	15.5 million	$8,290	10,600	6324, 6719	Holding company with subsidiaries that offer managed healthcare plans through health maintenance and preferred provider organizations
Integrated Pharmaceutical Services	Foundation Health Pharm.	14.0 million	$8,790	12,000	6324, 6719	Holding company with subsidiaries that operate health maintenance organizations and offer managed health care product coordination for multi-region employers and administrative services for medical groups and self-funded benefits programs

Table 2-1

Data on Selected Pharmacy Benefit Management Companies (PBMs)

Company	Ownership	Lives Covered (1999)	Sales ($ millions) (2000)	Employment (2000)	SICs Reported	Additional Information
Advance Paradigm	Advance Paradigm, Inc.	13.0 million	$2,150	1,370	8099	Provides pharmacy benefit management services including clinical and benefit design consultation services to health plan sponsors
Caremark - Prescription Service Div.	Caremark Rx Inc.	10.0 million	$3,860	4,373	6324, 8099	Develops, organizes and manages integrated health care delivery systems that provide primary and specialty health care services to prepaid managed care enrollees and fee-for-service patients; performs prescription benefit management and therapeutic pharmaceutical services
First Health Services	First Health	8.0 million	$0.474	3,600	6324, 8742, 8099	Develops and manages payer-based PPO networks that incorporate both group health and workers' compensation medical providers; provides prescription drug benefit plan administration, drug utilization review, and a nationwide network of nearly 50,000 pharmacies; provides centralized clinical management programs and other medical consulting services

Source: Yahoo Business, 2000, Disclosure, 2000, and NWDA, 1999

Retail chains, defined as having four or more stores, include chain drug stores, mass merchandisers, and food stores. In 1998, retail chains purchased around $46 billion in prescription drugs (NWDA, 1999). While retail chains rely on wholesalers to deliver a certain percentage of their drug needs, the largest retail chains also maintain their own internal distribution system. Like wholesalers, self-warehousing chains receive the drugs from manufacturers in large quantities, store the drugs in their own warehouses, and deliver the drugs to their retail outlets through their own distribution systems. Retail chains are the only dispensers of prescription drugs that self-warehouse to any significant extent. Large chains, such as Rite-Aid and Eckerd, have the capacity to self-warehouse up to 90 percent or so of the prescription drugs that are sold in their stores. Over the years, retail chains have steadily decreased their reliance on wholesalers. At the same time, drug manufacturers, that used to sell exclusively or principally to wholesalers, sell increasing shares of their production directly to the chains. In 1998, over 63.3 percent of purchases by retail chains were for self-warehousing (NWDA, 1999).

Mail-order pharmacies are a hybrid between the distribution and retail ends of the pharmaceutical industry. Mail-order pharmacies receive prescriptions by fax or through the mail and dispense the drugs directly to consumers anywhere in the United States. Mail-order is often used to dispense "maintenance" drugs regularly used by patients over an extended period of time. Mail-order pharmacies often use the services of a wholesaler to buy their prescription drug inventories. They then store their inventories in one or more of their warehouses. There are approximately 63 mail-order pharmacies and 32 retail companies with mail-order pharmacy operations in the U.S. (NWDA, 1999).

2.4 The Influence of Pharmacy Benefit Management Companies (PBMs) and Health Maintenance Organizations (HMOs) on Prescription Drug Prices

Department of Health and Human Services conducted a major study, published in April 2000, assessing prescription drug pricing (DHHS, 2000). This section summarizes one set of findings of the study's profile of price setting.

Most drug purchasers, almost regardless of their health care coverage or insurance plan, eventually receive their prescription products at a pharmacy. Table 2-2 describes how the

Table 2-2

An Illustrative Example of Pricing for a Brand Name Prescription Drug

Data Element	Cash Customers (No 3rd Party Payment at Point of Sale)	Insurers and PBMs	HMOs [a]	Medicaid	Federal Supply Schedule
List Price (AWP)	$50	$50	$50	$50	$50
Manufacturer's price *(Manufacturer to wholesaler other entity)*	$40 (AWP - 20%)	$40 (AWP - 20%)	[b] $34 (AWP - 33%)	$40	[b] $24 (AWP - 52%)
Acquisition price *(Wholesaler to pharmacy)*	$41	$41	NA	$41	NA
Retail price at pharmacy *(Total of amounts paid by customer and reimbursed by 3rd party payer)*	$52 (AWP + 4%)	$46 (AWP - 13% + $2.50) [b]	NA	$43.50 ($41 + $2.50)	NA
Retail price, less typical manufacturer rebate	NA	$30 to $44 (5% to 35% rebate)	NA	$30 to $37 (15.1% to 30% rebate)	NA
Ultimate (net) amount paid by final purchaser *and/or* consumer	$52	$30 to $44	$30 to $37	$30 to $37	$24

Source: DHHS, 2000

"NA" = Not applicable

[a] The column refers only to those HMOs that buy directly from manufacturers.

[b] Without rebates

Notes:

[1] Prices are based on a composite of *several commonly* prescribed brand-name drugs for a typical quantity of pills. For some cells in the table, the relative relationships have been calculated based on relationships reported in the literature and on other relationships *widely reported by* industry sources.

[2] The prices are used for illustrative purposes only and do not represent and type of overall average.

[3] Prices reported in the table include both amounts paid by third-party payers and amounts paid by the consumer as cost sharing.

groups discussed above, including PBMs and HMOs, influence the prices set. The table provides an illustrative hypothetical example of how prices are set under different schemes for a brand name prescription product using a relatively simple set of wholesale transactions.

The table shows that the first transaction, that from manufacturer to wholesaler, occurs at a discount from the average wholesale price (AWP). The AWP serves as a list price for drugs, but most sales occur well below this list price. DHHS reports that average sales occur at a 20 percent discount from AWP as indicated by various industry sources. In the illustration provided in Table 2-2, the HMO has bought the drug directly from the manufacturer and negotiated a steeper discount than that received by insurers or PBMs. This deeper discount would be representative of some of the largest HMOs such as Kaiser Permanente that are running their own pharmacies. Other HMOs use PBMs to manage their clients' drug purchases.

The wholesaler's markup to the manufacturer's price is modest, generally at 2 to 4 percent. In this case, the wholesaler's markup is shown to increase prices from $40 to $41 dollars, where it is applicable.

Next, the price is marked up by the pharmacy by a percentage amount and, in some cases, by a fixed charge for the dispensing function. The study indicates that the pharmacy will commonly add 20 to 25 percent to the drug cost, or in this case $11 on a $41 drug, for a total $52 purchase for a cash customer. Where insurers or PBMs are involved, they will negotiate discounts from pharmacists (as well as from drug manufacturers), thereby lowering the price paid by consumers and/or insurers. The DHHS authors note that little is known about the average extent of such discounts offered by pharmacies though a $5 markup on the $41 drug is assumed in their example.

Insurers and PBMs generally negotiate manufacturer rebates on their drug purchases. DHHS estimates the possible range of such rebates as 5 to 35 percent, reducing the $46 drug cost to $30 to $44. PBMs that use restricted formularies are best able to negotiate rebates with manufacturers.

Federal programs pay for drugs according to the Federal Supply Schedule. As a very large purchaser of drugs, the Federal government can negotiate steep discounts from retail prices.

GLOSSARY

Authorized distributor (or authorized distributor of record). Any distributor of a prescription drug that has a written agreement with the manufacturer of the prescription drug and conducts at least two transactions with the manufacturer of the prescription drug within any 24-month period.

Average wholesale price (AWP). The AWP is a published wholesale price or "list price" suggested by the manufacturer of the drug. Although the AWP does not capture the actual transaction prices, it serves as a reference for pricing, negotiations, and reimbursements.

Brokerage. The combination of drop-ship and dock-to-dock delivery services provided by wholesalers. In brokerage services, wholesalers do not bring the products into their warehouses.

Buy-side margin. The term refers to the early payment discounts and other earned or negotiated rebates and discounts received by wholesalers from drug manufacturers. Further, increases in the value of wholesalers' inventories as manufacturers' prices rise are also considered buy-side margins.

Chain drug store. A company that owns and operates four or more pharmacies. Food store and mass merchandiser pharmacies are also considered chain drug stores. Examples include Shaw's, Wal-Mart, Rite-Aid, and CVS.

Dock-to-dock delivery. In dock-to-dock delivery, a wholesaler obtains the drugs from the manufacturer and delivers them to a dispenser's own warehouse without taking the drugs into its own inventory. Thus, dock-to-dock sales are also referred to as non-stock sales.

Drop shipment. In drop shipments, a drug manufacturer directly delivers the drugs to a dispenser, but the order and payment is made through a wholesaler.

Drug formulary. A list of drugs compiled by a government body, third-party insurer or health plan, or another institution that may or may not be dispensed or reimbursed. Some institutions or health plans develop closed (i.e., restricted) formularies where only those drug products listed can be dispensed in that institution or reimbursed by the health plan. Other formularies may have no restrictions (open formularies) or may have limited restrictions such as higher patient co-payments for non-formulary drugs.

Float. The time differential between when a wholesaler receives payment from its customer (i.e., retail dispenser, health care organization, etc.) and when the payment is due to its supplier (i.e., pharmaceutical manufacturer or other wholesaler).

Group purchasing organization (GPO). An entity consisting of two or more hospitals or other health care entities that is formed to offer its members access to purchasing contracts for health supplies (i.e., pharmaceuticals, biologics, medical/surgical equipment, laboratory supplies, and other capital equipment). GPOs actively negotiate contracts with manufacturers on behalf of their members, provide their members access to the purchasing contracts of other GPOs, and/or have central purchasing supply sites which are utilized by their members.

In-state wholesaler. A wholesaler that distributes drug products in a given state and is physically located in that state.

Independent drug store. A company that owns and operates three or fewer pharmacies. These are also referred to as community or neighborhood pharmacies.

Integrated delivery network (IDN). Also known as integrated healthcare delivery network (IHDN), integrated delivery system (IDS), or integrated health/healthcare system (IHS). A financial and management structure that unites hospitals, physicians, ambulatory care sites, and managed care plans through ownership or exclusive formal agreements to provide a system to deliver a continuum of healthcare services. The IDN appears totally integrated to the patient, provider, and payer throughout the healthcare system. Increasingly, a shared financial information system and optimization of resources connect the structural components of the IDN.

Mail-order pharmacy. A pharmacy that dispenses prescriptions to patients who submit their prescriptions by mail or fax. The pharmacy then mails the filled prescription to the patient. Mail-order pharmacies generally serve patients on long-term drug therapies and those without immediate drug needs. The average size of prescriptions (i.e., the number of capsules or tablets) dispensed by mail-order pharmacies is usually 3 times larger than those dispensed by retail pharmacies (NACDS, 2000).

Manufacturer-direct sale. The type of sale that bypasses the need for any intermediary distributor. The product is sold and shipped directly by the manufacturer to the dispenser.

Mass merchandiser. An establishment, also known as a department store, that is primarily engaged in retailing a wide range of merchandise, including apparel, furniture, appliances, paint, hardware, toiletries, cosmetics, and prescription drugs. Prescription drugs are dispensed through an on-site pharmacy. Examples of mass merchandisers include Wal-Mart, K-Mart, and ShopKo.

National Wholesale Druggists' Association (NWDA). The national trade association that represents pharmaceutical and related healthcare product distributors throughout North America.

Non-stock sales. Brokerage sales, dock-to-dock delivery sales, drop shipments, and any other form of sales not placed in inventory. These generally have a significantly lower margin than stock sales.

Out-of-state wholesaler. A wholesaler that distributes drug products in a given state but is physically located in another state.

Pharmaceutical Distributors Association (PDA). An industry trade association that represents secondary and smaller wholesalers. The association's membership includes Supreme-Purity Distributors Company, Quality King Distributors, Inc., and Victory Wholesale Grocers Company.

Pharmacy benefit management company (PBM). An entity that administers the prescription drug part of health insurance plans on behalf of plan sponsors, such as self-insured employers, insurance companies, and health maintenance organizations (HMOs). PBMs provide pharmacy

claims processing and mail-order pharmacy services in addition to other services, such as rebate negotiations with pharmaceutical manufacturers, development of pharmacy networks, formulary management, drug utilization reviews, generic drug substitution, and disease management programs.

Rebate. The amount that the manufacturer of the drug pays to an insurer or health plan for each unit of drug dispensed. Rebate arrangements exist between drug manufacturers and Medicaid agencies, HMOs, and other insurers or drug plans, and generally bypass the pharmacy. Rebates are also referred to as "after market" arrangements because they do not affect the prices paid at the time of service, but are implemented later, ultimately reducing the payer's expenditures or program costs (Kaiser Family Foundation, 1999)

Self-warehousing. A type of distribution system where the retail or the institutional dispenser take on the task of distribution itself. Instead of relying on an outside distributor, the retailer or the institutional dispenser buys direct from the manufacturer, stores the drugs in one or more of its own warehouses, and then delivers them to its retail stores or hospitals as needed. Self-warehousing is most prominent among the chain drug stores.

Sell-side margin. Wholesaler revenues that are generated from fees and other charges obtained from dispensers. During the 1980 to 1998 period, sell-side margins have declined from 5.5 percent to 0.35 percent (U.S. District Court for the District of Columbia, 1998).

Upcharge. The percentage fee that is paid by the dispenser to the wholesaler for the cost of distribution.

REFERENCES

Bindley Western Industries, Inc. 2000. 1999 Annual Report. Downloaded from http://www.bindley.com.

Casteuble, Tracy. 2000a. Telephone conversation between Tracy Casteuble (National Wholesale Druggists' Association) and Aylin Sertkaya (Eastern Research Group, Inc.) September 14.

Casteuble, Tracy. 2000b. Telephone conversation between Tracy Casteuble (National Wholesale Druggists' Association) and John Eyraud (Eastern Research Group, Inc.). November 2, 2000.

Clark, Sheila. 2000. Telephone conversation between Sheila Clark (Medical Specialties) and John Eyraud (Eastern Research Group, Inc.).August 23.

Department of Health and Human Services (DHHS). 2000. Report to the President: Prescription Drug Coverage, Spending, Utilization, and Prices. April. Downloaded from http://aspe.hhs.gov/health/reports/drugstudy/index.htm. June 29.

Eastern Research Group, Inc. (ERG). 2000. Cost Analysis of the Proposed Rule on Pharmacy and Physician Compounding of Drug Products: Draft Final Report. Prepared for the Office of Policy, Planning, and Legislation, Food and Drug Administration. August 11.

Everly, Conrad. 2000. Telephone conversation between Conrad Everly, President, (Mohawk Medical) and Aylin Sertkaya (Eastern Research Group, Inc.) September 14.

Food and Drug Administration (FDA). 1988. Letter from Daniel L. Michels, Director, Office of Compliance to Regulated industry, Docket No. 88N-258L. August 1.

Food and Drug Administration (FDA). 2000. FDA Part 15 Hearing—Prescription Drug Marketing Act. October 27. Http://www.fda.gov/ohrms/dockets/92n0297/tr00001.asc.

Ford, Steve and Conrad Everly. 2000. Letter from Steve Ford, Secretary/Treasurer and Conrad Everly, President, (Mohawk Medical) to the FDA Dockets Management Branch. May 9.

Kaiser Family Foundation. 1999. Prescription Drug Trends: A Chartbook. Kaiser Family Foundation.

Levy, Roy. 1999. The Pharmaceutical Industry: A Discussion of Competitive and Antitrust Issues in an Environment of Change. Bureau of Economics Staff Report. Federal Trade Commission. Washington, D.C. March. Downloaded from http://www.ftc.gov/

National Association of Boards of Pharmacy (NABP). 1999. 1999-2000 Survey of Pharmacy Law. National Association of Boards of Pharmacy. Park Ridge, IL.

National Association of Chain Drug Stores (NACDS). 2000. Industry Facts. Downloaded from http://www.nacds.org/industry/Pharmacy_Sales.pdf. September 22.

National Wholesale Druggists' Association (NWDA). 1999. 1999 NWDA Industry Profile and Healthcare Factbook. National Wholesale Druggists' Association. Reston, VA.

Pharmaceutical Distributors Association (PDA). 2000a. Comments of the Pharmaceutical Distributors Association Regarding the Final Rule Concerning Policies, Requirements, and Administrative Procedures; Prescription Drug Marketing Act of 1987; Prescription Drug Amendments of 1992. FDA Docket Nos. 92N-0927 and 88N-0258. June 30.

Pharmaceutical Distributors Association (PDA). 2000b. Petition for Stay of Action by the Pharmaceutical Distributors Association on the Final Rule Concerning Policies, Requirements, and Administrative Procedures; Prescription Drug Marketing Act of 1987; Prescription Drug Amendments of 1992. FDA Docket Nos. 92N-0927 and 88N-0258. March 29.

Pharmaceutical Research and Manufacturers of America (PhRMA). 2000. PhRMA Industry Profile 2000. Downloaded from http://www.phrma.org/publications/industry/profile00/tocnf.html. August 30.

Robert Morris Associates (RMA). 2000. Annual Statement Studies 1999-2000. RMA. Philadelphia, PA.

Riccardi, Sal. 2000. Statement of Sal Riccardi, President, Purity Wholesale Grocers, Inc., before the Subcommittee on Regulatory Reform and Paperwork Reduction of the Committee on Small Business. June 8.

Small Business Administration (SBA). 2000. *1997 Firm Size Data*. Office of Advocacy in contract with the U.S. Bureau of the Census. Downloaded from http://www.sba.gov/advo/stats/int_data.html. August 1.

Small Business Administration (SBA). 1999. Small Business Standards Matched to SIC Codes: As of June 14. Downloaded from http://www.sba.gov/regulations/siccodes. November 15.

SMG Marketing Group, Inc. 2000. 2000 Market Report: Multi-Hospital Systems (MHSs) & Group Purchasing Organizations (GPOs) by System. Chicago, IL.

SMG Marketing Group, Inc. 1999. PBMs Market Growth Slows Amid Restructuring. News Release. Downloaded from http://www.smg.com/pr/pbms.pdf. March 23.

Texas Department of Health. 2001. *Drugs and Medical Devices Division Establishment* Database. Downloaded from http://www.tdh.texas.gov/bfds/dmd/default.htm. January 17.

U.S. District Court for the District of Columbia. 1998. Civil Action No. 98-595: Federal Trade Commission (Plaintiff) v. Cardinal Health, Inc. and Bergen Brunswig Corp (Defendants) and Civil Action No. 98-596: Federal Trade Commission (Plaintiff) v. McKesson Corp. and Amerisource Health Corp. (Defendants). Downloaded from http://www.ftc.gov/os/1998/9807/98cv0595.htm. July.

U.S. General Accounting Office. 1997. Pharmacy Benefit Managers: FEHBP Plans Satisfied With Savings and Services, but Retail Pharmacies Have Concerns. Washington, D.C. Report Number GAO/HEHS-97-47.

U.S. General Accounting Office. 1995. Pharmacy Benefit Managers: Early Results on Ventures With Drug Manufacturers. Washington, D.C. Report Number GAO/HEHS-96-45.