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NONPRESCRIPTION DRUGS

Over the Counter and Underemphasized

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Mr. Chairman and Members of the Subcommittee:

It is a pleasure to be here this morning to discuss our evaluation of the Food and Drug Administration's (FDA's) procedures for approving and monitoring over-the-counter (OTC) drugs sold in the United States.

OTC drugs are a common part of our daily lives. Products such as cold remedies, analgesics, and sleep-aids are used for the relief of symptoms and improve the quality of life for many. Similar to other developed nations, Americans take only a small percent of their health complaints to doctors -- about 10 percent. More often, minor health problems are treated by self-medication. Estimated OTC drug sales in the United States for 1990 were \$11.2 billion, or nearly 2 percent of all national health care expenditures. FDA has estimated that there are between 125,000 and 300,000 different OTC products currently being marketed.

However, not all OTC drugs that reach the marketplace are safe or effective. When FDA has evidence of potentially unsafe or ineffective drugs, they have removed products or entire classes of drugs from the market. In 1990 FDA published final rules in the Federal Register banning from the OTC marketplace more than 200 unsafe and ineffective active ingredients for various problems. According to FDA, further action to remove over 400 additional ingredients in 13 drug categories is underway at this time.

In February 1991, we were asked to examine FDA's procedures for approving and monitoring over-the-counter drugs in order to identify potential vulnerabilities in these procedures that could result in the approval and marketing of unsafe and ineffective drugs. We provided the results of our efforts in a report issued earlier this year.¹ In this testimony, I will concentrate on our findings.

In our comparison of FDA regulation of OTC and prescription drugs, we found several differences in how FDA ensures the safety and effectiveness of each. Specifically, we found that (1) unlike prescription drugs, many OTC drug products have not been required to demonstrate their safety and effectiveness before being made available to the public; (2) during FDA inspections for compliance with current good manufacturing practices (CGMP), FDA has statutory authority to inspect records and documents of prescription drug manufacturers, but not those of OTC drug manufacturers; and (3) FDA collects less postmarketing surveillance information and conducts less product performance analysis for OTC drugs than for prescription drugs.

¹Nonprescription Drugs: Over the Counter and Underemphasized
(GAO/PEMD-92-9, February 28, 1992).

I will now turn to a more detailed description of the policies and procedures for approving and monitoring over-the-counter drugs.

Premarket Approval

There are four principal routes through which a manufacturer may market an OTC drug product. These methods are illustrated in our diagram of the approval process (see appendix I). The first route is compliance with an FDA regulatory statement (called a monograph) that specifies the ingredients, dosage, labeling, mode of administration, and the combination of generally recognized safe and effective ingredients permissible in the product.² The second route is the submission of an abbreviated new drug application (ANDA) for products with the same or nearly identical active ingredients, dosage form, strength, administration route, use, and labeling as a product that is currently on the market and has already been approved as safe and effective. These types of drugs are often referred to as "generic drugs." For drugs new to the market, a manufacturer must submit a new drug application (NDA) that includes data from clinical studies sufficient to permit its evaluation from specific technical viewpoints. Drugs approved by this method have been determined safe and effective for their intended use by FDA. In the fourth route, a manufacturer may submit a new drug application supplement for changes in a product that already has an approved new drug application. This method would include product changes, such as the introduction of a capsule form of a product already approved as a tablet, or the use of new technology in the manufacturing process.

In 1972, FDA began a review of OTC drugs as part of the 1962 congressional mandate to review drugs approved between 1938 and 1962.³ This review, also known as the monograph program, is the principal route to market for OTC drugs. Drug products that the manufacturer determines meet the requirements of the relevant monograph may be marketed without any FDA review. For example,

²This route is applicable only to OTC drug products.

³The OTC monograph program is FDA's response to the 1962 Harris-Kefauver Amendments to the Federal Food, Drug, and Cosmetic Act of 1938 (P.L. 87-781). It is a three-phase rule-making process that includes an advance notice of proposed rule-making (advisory panel recommendation on the safety and effectiveness of active ingredients and on labeling), proposed rule-making (tentative conclusions based on advisory panel's findings, public comment, available data, and tentative final monograph), and a final rule that identifies those active ingredients that are generally recognized as safe and effective for specified uses and that may be marketed in OTC drug products for each therapeutic class (for example, antacid and analgesic).

since FDA has completed the monograph that prescribes the requirements for antiemetics, nighttime sleep aids, and stimulants, a manufacturer may produce and market a conforming product without FDA approval.

However, as of April 1992, nearly 30 years after the legislation was enacted, FDA had promulgated only 36 (or fewer than half) of the 88 drug categories under consideration into final rules. In addition, FDA has adopted a policy that extends the coverage of the monograph program to all OTC drugs that were marketed up to 1972. As a result of this extension, FDA has exempted an undetermined number of individual OTC drug products first marketed between 1962 and 1972 from the new drug application requirement to show proof of their safety and effectiveness. What this means is that the monograph program, as it is implemented, makes the adequacy of FDA's regulation and monitoring of production quality assurance and postmarketing surveillance activities critical to protecting the public health.

In contrast to the OTC monograph program, the new drug application, abbreviated new drug application, and new drug application supplement routes apply to all requests to market a prescription drug or OTC product first introduced into commercial distribution after 1972.⁴ All of these programs require a review by FDA of the safety and effectiveness data for each drug product before it is approved for marketing.

In addition to the routes for initial marketing approval for prescription and OTC drugs, there are several options available to FDA or a drug manufacturer to change the marketing status of a product from prescription to OTC.⁵ Two recent examples of drugs that were initially available to the public only by prescription and are now OTC are Ibuprofen (200 mg strength), found in a variety of analgesics for the relief of pain and fever, and topical hydrocortisone, used for minor skin rashes and itching. Since 1972, about 46 prescription drug ingredients, many of them in cough or cold remedies, have been switched to OTC status.

For the public, the change of a drug's marketing status from prescription to OTC has historically meant an increase in the availability of more effective drugs for self-medication and a reduction in health care expenses. However, OTC status also means

⁴Insulin and antibiotic drugs are exceptions in that they follow a procedure that combines parts of the NDA and monograph programs.

⁵FDA can switch a drug's marketing status under its own initiative, which may include incorporating that drug into the development of an OTC monograph. Manufacturers may obtain an approved NDA supplement from FDA or petition FDA to modify an existing OTC monograph to include the prescription drug.

reduced supervision by health care professionals with the potential for overuse and misuse of the drug and decreased FDA monitoring.

Having described the routes by which an OTC drug may be marketed and the vulnerabilities within the current status of the monograph process, let me now proceed to a detailed description of production quality assurance.

Production Quality Assurance

As our figure on regulatory components illustrates, the current good manufacturing practices regulation requires manufacturers of both OTC and prescription drugs to maintain customer complaint files, equipment maintenance logs, and other manufacturing records (see appendix II). However, FDA does not have the statutory authority to inspect the records of OTC drug manufacturers as it does those of prescription drug manufacturers. This means that the agency is only able to inspect records that are on display at the time of the inspection or that are voluntarily provided by the manufacturer.

Although we were told by FDA officials that drug manufacturers will generally provide access to their records upon request, we found that large manufacturers are more likely than small ones to refuse or to provide limited access to production quality assurance documents. When access is denied, FDA inspectors interpret this as an indication of a potential problem situation. In an effort to compensate for the manufacturer's failure to provide access to records, FDA may use such techniques as increasing the scope and depth of their observational inspection of the production facility.

Although an individual manufacturer of OTC drugs may receive information about adverse effects associated with its products, may record that information in its complaint files, and may take remedial action, its efforts -- as a single manufacturer -- may not be sufficient to protect the public health against a problem that is more widespread.

As a result, FDA's lack of full access to an OTC drug manufacturer's records and files denies the agency a critical source of information on the nature and scope of postmarketing problems associated with OTC drug products. Moreover, this lack of full access limits FDA's ability to evaluate the effectiveness of the manufacturer's efforts to analyze complaints, remedy problems, and generally produce a safe and effective product. This situation hinders FDA from fully carrying out its mandate to protect the public health and to provide reasonable assurance of the safety and effectiveness of OTC drugs.

Lastly, I would like to address our findings on the existing postmarketing surveillance system. The purpose of a postmarketing system is to monitor drugs in widespread use and to provide an "early warning" of problems so that FDA can analyze the data and decide on an appropriate course of action.

Postmarketing Surveillance

We found that FDA obtains only limited information on the postmarketing performance of OTC drugs in comparison with that available on prescription drugs. The lack of postmarketing information is intensified in the case of OTC drugs subject to the monograph process. This finding is noteworthy because monograph-controlled OTC drugs represent the majority of all OTC drugs, yet they are the category of drugs for which FDA's postmarketing surveillance system provides the least amount of information. For example, FDA does not require manufacturers of OTC monograph drugs to report adverse reactions experienced by their customers.

Additionally, FDA does not know, and is unable to determine, the number of OTC products currently being marketed in the United States.⁶ FDA requires manufacturing firms to notify FDA of the products it markets.⁷ We have learned that in 1986, FDA assigned a low priority to maintenance of the OTC product listing files.⁸ Without information on the number of OTC products marketed, FDA is unable to evaluate the relative extent of any identified problem with an OTC product and, in addition, does not know how many OTC products are being marketed in therapeutic categories that still lack finalized monographs. The net effect is that FDA is unaware of (1) the number of individual OTC products currently being marketed and (2) whether these products are safe and effective as determined by any type of FDA review.

⁶We found the same problem in April 1982 and recommended that the Secretary of Health and Human Services "establish for each category of drug product a complete master list of firms manufacturing the drug and a list of the products as they are identified for each monograph." See FDA's Approach to Reviewing Over-the-Counter Drugs Is Reasonable, But Progress Is Slow (GAO/HRD-82-41, April 1982), p. iv.

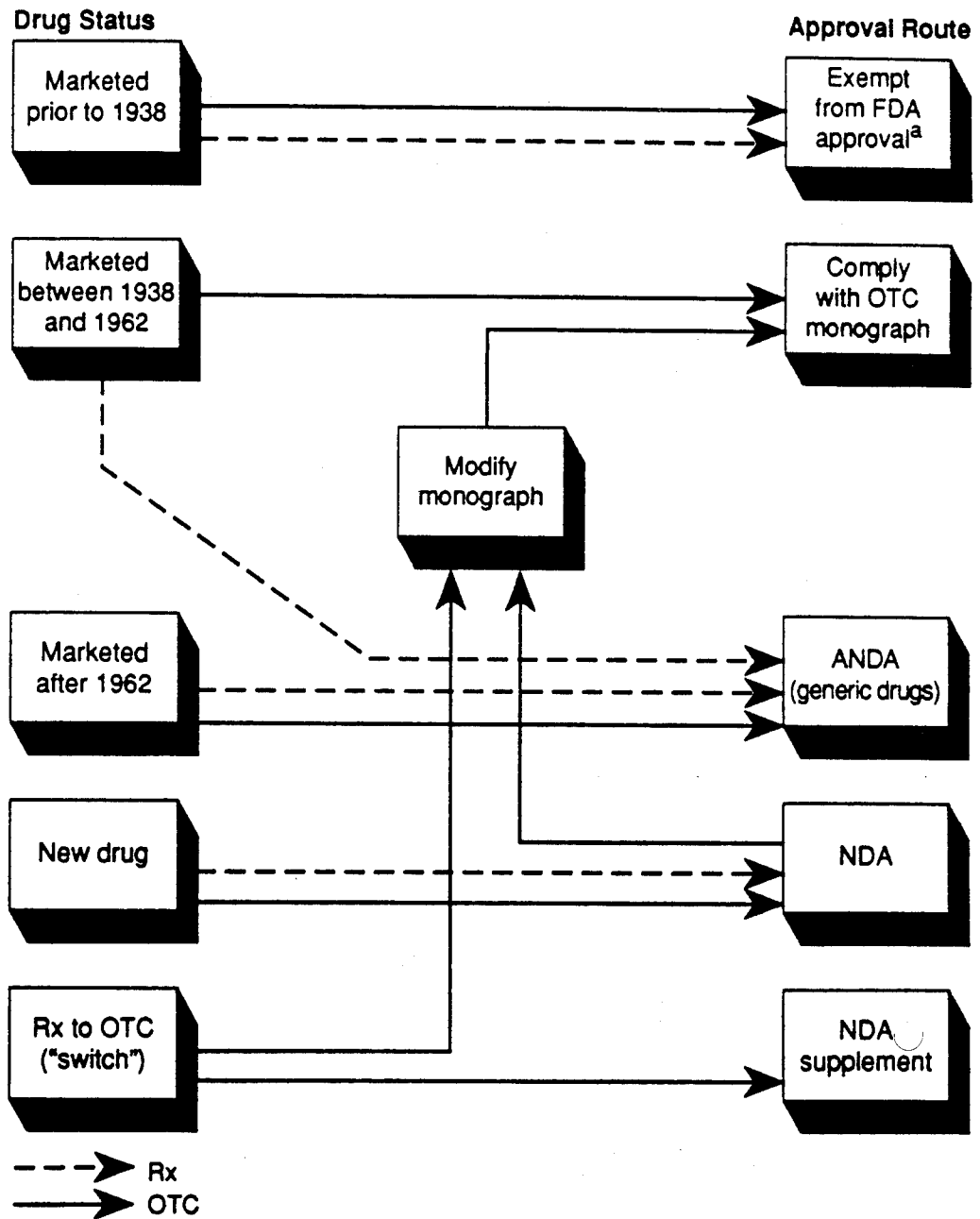
⁷A drug product is more specific than the brand. For example, 100-count bottles of 250 mg tablets and 100-count bottles of 500 mg tablets of aspirin made by one manufacturer would be considered by FDA as two products. Likewise, a manufacturer's 100-count bottles of 250 mg capsules and 100-count bottles of 250 mg tablets of aspirin would be considered two products.

⁸According to an FDA official, the agency has since changed that policy. However, OTC manufacturers have been slow to comply with the listing requirement.

In summary, we found that FDA has been slow to develop monographs for OTC drugs. In the 30 years since the congressional mandate, FDA has moved fewer than half of the 88 monographs into final rules. Consequently, those OTC products that are marketed without final monographs have not been required to show evidence of their safety and effectiveness. In addition, FDA lacks the statutory authority to examine the records, including complaint files, of OTC drug manufacturers. Moreover, FDA does not require manufacturers of OTC monographs to report adverse reactions experienced by consumers. Since FDA may not know of adverse reactions and is unable to determine the magnitude of problems it is made aware of, it is difficult to be sure that the agency can fulfill its mission to protect the public health.

This concludes my statement, Mr. Chairman. I will be happy to respond to any questions that you or Members of the Subcommittee may have.

GAO OTC and Prescription Drug Approval Process



^aTo qualify for exemption, the product and labeling must be exactly the same as in 1938.

GAO Regulatory Components by Marketing Status

OTC and Rx Drugs

Regulatory component	Marketing status		
	Prescription	OTC NDA	Monograph
Premarket approval			
Clinical trials	Yes	Yes	No
FDA review	Yes	Yes	No
FDA approval	Yes	Yes	No
Product quality assurance			
CGMP	Yes	Yes	Yes
Access to complaint files	Yes	No	No
Postmarketing surveillance			
Listing file	Yes	Yes	Yes
Registration file	Yes	Yes	Yes
National drug code	Yes	Yes	Yes
Manufacturer drug distribution reports	Yes	No	No
Prescription reports	Yes	No	No
Drug Quality Reporting System	Yes	Yes	Yes
Adverse Drug Reaction reports	Yes	Yes	No
Consumer complaints	Yes	Yes	Yes
Pharmaceutical literature	Yes	Yes	No
NDA field alerts	Yes	Yes	No
Advertising	Yes	No	No
Label review	Yes	Yes	Yes
Product changes	Yes	Yes	No

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