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OVER THE COUNTER DRUGS

Gaps and Potential Vulnerabilities in the Regulatory System

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Mr. Chairman and Members of the Subcommittee:

It is a pleasure to be here this morning to present the findings from our review of the Food and Drug Administration's (FDA) system for approving and monitoring nonprescription drugs. Our study was undertaken at your request, and the testimony I am presenting this morning focuses on some of the gaps and potential vulnerabilities we found in that system. A complete description of our study and its findings can be found in our report entitled Nonprescription Drugs: Over the Counter and Underemphasized (GAO/PEMD-92-9).

Our study examined the critical regulatory areas associated with nonprescription drugs--approval for marketing, quality assurance in manufacturing, and monitoring for adverse effects after marketing.

With regard to the approval process, there are four principal routes through which a manufacturer may market a nonprescription drug product. Three of these routes apply to what are defined as "new drugs" and require FDA's approval of a manufacturer's application to market a specific drug product. FDA's approval of any of the three types of new-drug application, referred to as "NDAs," indicates that the product has been determined safe and effective for its intended use and does not violate any other applicable regulations.

While approximately 420 nonprescription drug products were marketed through NDAs following the passage of the 1938 act, the vast majority of nonprescription drug products (estimated in the hundreds of thousands of individual products) were not appropriate for any of the NDA routes. These drugs reached the market through a fourth route--compliance with an FDA regulatory statement called a drug review monograph. A monograph specifies the therapeutic categories of ingredients that are generally recognized as safe and effective and thus permissible in a given drug product, as well as dosage, labeling, and mode of administration.

It is the consensus of expert opinion that a product which complies with the relevant final monograph is as safe and effective as a product that reaches the market through the product-specific NDA route. However, nearly 30 years after the enabling legislation was enacted, FDA has promulgated final monographs for only 36 of the 88 therapeutic drug categories under consideration; this, of course, leaves 52 incomplete. The point here is that some undetermined number of products--whose active ingredients are included in therapeutic categories covered by any of the 52 incomplete monographs--may continue to be made available to the public, unless they violate some other applicable regulation such as those covering labeling and

adulteration. Included among these product categories are many that the general public assumes FDA has given its stamp of approval--such as certain cough and cold preparations, vaginal drug products, remedies for diaper rash, oral health care products, and sun screens--when, in fact, they have not received such a safety and effectiveness declaration.

In addition, FDA has adopted a policy extending the coverage of the monograph program another 10 years beyond the date contained in the enabling legislation, extending it from 1962 to 1972. This has had the effect of increasing the number of products on the market that have not gone through the NDA process or met the requirements of a final monograph.

I used the phrase "undetermined number of products" purposely. We found that FDA does not know, and is unable to determine, the number of nonprescription products currently being marketed in the United States. You may ask, how could such a situation exist? We found that, although FDA requires manufacturing firms to notify it of the products they market, it was not until recently that FDA made the maintenance of nonprescription product listing files a priority issue.

Now let me turn briefly to the other two aspects of FDA's approval and monitoring system for nonprescription drugs--quality assurance in manufacturing and postmarketing surveillance. I think we can all agree that it is impossible to identify all the possible problems that could occur with a product <u>before</u> it is marketed. However, it is incumbent upon an agency mandated with protecting the public health to have a system in place that will quickly identify and remedy postmarketing problems.

FDA has acted to remove some specific ingredients and problem products from the market. As recently as November 1990, the agency published final rules in the <u>Federal Register</u> eliminating more than 200 unsafe or ineffective active ingredients from the nonprescription market. It should be noted that this recent action by the agency was based on the recommendations of the FDA nonprescription drug advisory panels, which concluded their deliberations nearly 10 years ago. FDA had also removed some nonprescription products from the market when it had evidence of a potential problem. However, "when it has evidence" is the operative phrase here because our research has shown that the agency may be handicapped in its efforts to discover the existence of problems and to act quickly on this knowledge.

The fundamental problem here is lack of information. This in turn often places the agency in a reactive rather than a proactive posture. For example, during the regular inspection of manufacturers' quality assurance programs, FDA does not have statutory authority to inspect the records of nonprescription

drug manufacturers. The agency is dependent upon the largess of the manufacturer when attempting to review complaint and other manufacturing-related files. And, it is those complaint files that may contain early indications of problems associated with a particular product or its active ingredients, including adverse effects caused by drug interactions or associated with specific population subgroups (such as the elderly). Clearly, without full access to these types of files, the agency cannot fully evaluate the effectiveness of the manufacturer's efforts to analyze complaints, remedy problems, and generally produce a safe and effective product. Moreover, this lack of full access may limit FDA's ability to have an "early warning" of a problem that may be generic rather than product or manufacturer specific.

Furthermore, lack of access to critical information derived from manufacturers' postmarketing surveillance of nonprescription monograph drugs may hinder the agency in fully carrying out its mandate. While FDA does receive adverse drug reaction reports about products that enter the market through the NDA process, these are a relatively small proportion of the nonprescription drugs available to the public. Conversely, monograph-controlled nonprescription drugs represent the vast majority of all nonprescription drugs, yet they are the category for which FDA's postmarketing surveillance system provides the least amount of information. Currently, the agency is largely dependent upon voluntary reports on monograph-controlled products from manufacturers, health providers, and consumers for postmarketing problem information.

Our study did not evaluate the adequacy of this voluntary system. However, in a 1989 study of medical device problem-reporting systems, when we compared a voluntary system with the mandatory system that replaced it, we found the number of problems reported increased seven-fold with the mandatory system within 3 years. Yet prior to mandatory reporting, medical devices were thought to have relatively few unknown problems, and it was assumed that the industry would police itself. Both beliefs have proven false. A similar consensus of opinion exists today with respect to nonprescription drugs--that is, that these products have been on the market a long time with few or no known adverse effects associated with them. With this untested assumption in mind, and in view of both the changes in nonprescription drugs and the changing demographics of nonprescription drug use, we are pleased to learn that FDA believes it is time to reevaluate the adequacy of its existing adverse-event reporting system for nonprescription products.

In summary, our research has identified several gaps and potential vulnerabilities in the current system for approving and monitoring nonprescription drugs. First, FDA has been slow to develop monographs for nonprescription drugs. As a result, those

manufacturers whose products are marketed without benefit of final monographs have not been required to measure their product against generally accepted standards of safety and effectiveness. Second, FDA currently lacks the authority to require manufacturers to provide certain critical records, such as complaint files. As a consequence, FDA may not even know of adverse reactions experienced by consumers. Third, because the number of nonprescription drug products is unknown, FDA is unable to determine the magnitude of those problems of which it is made aware. In view of the gaps and potential vulnerabilities identified in our review, we are not confident that the public is adequately protected from unsafe and ineffective nonprescription drugs.

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

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