

**Testimony of
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INTRODUCTION

Good morning Mr. Chairman and Members of the Subcommittee. I am Michael Mangano, Principal Deputy Inspector General for the Department of Health and Human Services. I appreciate the opportunity to be part of today's hearing on consumer safety and weight-loss supplements and to share with you the results of our work on the effectiveness of the Food and Drug Administration's (FDA) adverse event reporting system for dietary supplements. Millions of consumers take supplements every day without any apparent problems and receive health benefits. However, risks do exist, and it is important that consumers are protected. FDA does not have the authority to require supplements to undergo premarket approval for safety and efficacy. Instead, it relies mostly on its adverse event reporting system to identify safety problems.

Mr. Chairman, our review of the adverse event reporting system for dietary supplements disclosed that it is an inadequate safeguard to protect consumers. FDA lacks much of the information to effectively analyze adverse events. Specifically, the system has three major shortcomings. First, the system detects relatively few adverse event reports. Second, the system has difficulty generating signals of possible public health problems due to incomplete reports and difficulty in conducting follow-up. Third, FDA lacks the information necessary to adequately assess those signals to determine if action is necessary to protect the public's safety.

Many of these shortcomings are due to the limited tools available to FDA regarding dietary supplements.

BACKGROUND

In 1993, FDA created a system to collect and review adverse event reports on dietary supplements. An adverse event is an incident of illness or injury that may be associated with a product or ingredient. Reported events range in severity from nausea and dizziness to cardiac arrest or death.

Reporting adverse events associated with dietary supplements to FDA is entirely voluntary. FDA receives adverse event reports from consumers, health professionals and manufacturers through various reporting mechanisms. These mechanisms include State health departments, Poison Control Centers, direct communication with FDA and through FDA's Medwatch program, a web-based reporting system used to monitor FDA-regulated products.

FDA's adverse event reporting system for dietary supplements is an important consumer safeguard. Unlike new prescription drugs and some over-the-counter medicines, dietary supplements are not subject to premarket approval. In addition, FDA is still developing good manufacturing practices for supplement manufacturers. Instead, FDA relies largely on its adverse event reporting system to help generate signals of possible public health concerns.

We analyzed FDA's database for adverse event reports for dietary supplements received between 1994-1999. Our analysis included over 2,000 such reports. Specifically, we checked the completeness of each report in the FDA data fields. We also reviewed relevant FDA laws, regulations, policies and procedures and interviewed various FDA officials and stakeholders, including consumer and industry representatives. We conducted our review during 2000 and issued the final report in April 2001.

RESULTS OF THE REVIEW

FDA's adverse event reporting system detects relatively few adverse events.

Adverse event reporting systems typically detect only a small proportion of events that actually occur. They are passive systems that depend on someone linking an adverse event with the use of a product and then reporting the event. FDA's system for dietary supplements is no exception. A study commissioned by FDA in March 2000 estimated that the agency receives less than

1 percent of all adverse events associated with dietary supplements. Our study confirmed findings in the FDA commissioned report that few events are actually reported. In fact, FDA received only 2,547 adverse event reports related to supplements between 1994 and 1999 — a period when it is estimated that more than 100 million people were taking supplements. Of particular relevance for this hearing, according to FDA's analysis, is that between 1993 and March 2000, the agency received 1,173 adverse event reports associated with products

containing, or suspected to contain, ephedrine alkaloids, which are commonly used for losing weight and boosting energy.

We recognize that no clear standard exists on how many reports FDA should receive. While similar but not identical to FDA's system, Poison Control Centers, a network of sites, predominantly hospitals and academic health centers that respond to consumer calls about problems with products, appear to be receiving more reports. For the year 1999, we found that FDA received 460 reports compared to the estimated 13,000 reports that Poison Control Centers reported receiving nationwide relating to dietary supplements. Many factors may contribute to the under-reporting of adverse events for dietary supplements. First, many consumers presume supplements to be inherently safe and may fail to link an adverse event with the use of a product. Second, many consumers use these products without the supervision of a health professional who can help identify adverse events. Third, consumers may be unaware that FDA regulates dietary supplements. Fourth, FDA does not have the authority to require manufacturers to report the adverse events they receive. Finally, FDA does not conduct enough outreach to consumers, health professionals and manufacturers about the importance of reporting adverse events.

FDA's adverse event reporting system has difficulty generating signals of possible public health concerns.

FDA's database not only didn't contain many reports of adverse events, those reports lacked sufficient information to analyze and generate signals of public health concern. We found that FDA attempted to follow-up and obtain much needed information, such as consumer medical records, product ingredients and identity of the manufacturer to help evaluate reported events.

However, the agency frequently could not obtain this necessary information. To be more specific:

Limited medical information. Without medical information, it is difficult for FDA to determine if the event was related to the use of the supplement. We found that FDA could not obtain medical records for 58 percent of the reports for which the agency requested. To obtain medical records, FDA first must receive permission from the alleged injured party. However, FDA told us they often have difficulty locating or reaching consumers. And even when they do reach them, consumers sometimes refuse to release medical records out of concern for their privacy. At least half of the adverse event reports that FDA receives come from consumers. Given that supplements are generally self-care products, it is not surprising that the majority of reports come from consumers. However, consumers generally are not able to provide as much medical information as health professionals. Only 27 percent of the reports come from health professionals, who are in a better position to provide important medical information and to determine if there is a relationship between the product and the event.

Limited product information. For 32 percent of the products mentioned in the adverse event reports, FDA was unable to determine the ingredients. FDA lacks a quick and easy reference for the name and ingredients of all products. FDA must rely on the report itself or conduct its own investigation, which can be resource intensive. In addition, because dietary supplement manufacturers are not required to prove the safety of their products prior to marketing them, FDA generally has relatively little information about the safety of particular products.

For 77 percent of the products mentioned in the adverse event reports, FDA lacked the product label. FDA often depends on the product label to determine the ingredients in a particular dietary supplement. FDA officials emphasized the importance of obtaining the actual label from the product because some dietary supplements sold under the same name vary in the amount and type of ingredients they contain. FDA also lacked a sample for 69 percent of the products for which it requested one. Samples are sometimes necessary for further testing regarding contamination and other issues. FDA finds that it is not only difficult to locate supplement consumers, but that consumers cannot or will not provide a product sample or label. Consumers may have discarded the remaining product, may want to hold on to it pending legal action, or may have sent it back to the manufacturer for a refund.

Limited manufacturer information. We found that FDA could not identify the manufacturers for 32 percent of the products in its reports. Of the manufacturers in its database, FDA lacked the location for 71 percent. Manufacturers may have additional information that would be helpful to FDA. However, until recently, FDA lacked the authority to require manufacturers to register with the agency. Again, FDA does not have authority to require manufacturers to report the adverse events they receive. FDA officials estimated that it has received less than 10 such reports from manufacturers. Unfortunately, we cannot confirm this, because FDA does not track this in its database. This is in contrast to the adverse event reporting system for prescription drugs and biologics, where about 90 percent of the 280,000 reports in 1999 came from manufacturers. (Prescription drug manufacturers are legally required to report adverse event reports.)

Limited contact information on the alleged injured party. FDA could not follow up on 27 percent of the reports it tagged for follow-up, primarily because the reports lacked enough contact information for the alleged injured party, who may be reluctant to provide such information because of privacy concerns.

Limited ability to analyze trends. It is difficult for FDA to conduct rigorous statistical analysis, because the agency receives relatively few reports and many are of such poor quality. Furthermore, FDA's database for analyzing adverse event reports is inadequate. The database was designed for administrative purposes rather than for trend analysis. For example, it is difficult to query the database for all reports associated with one ingredient, because all the ingredients for one product are entered into the same data field. The database also lacks automatic data edits to prevent common data entry errors, such as misspellings or illogical entries that make it difficult to perform accurate queries.

FDA lacks the information to adequately assess signals of possible public health concerns generated by adverse event reports.

Adverse event reports in and of themselves typically cannot generate conclusive evidence about the safety of a product or ingredient. Rather, the system generates signals that FDA must assess to confirm if, in fact, a public health problem exists. In assessing signals, FDA can rely on a variety of sources, including clinical research, scientific literature, and/or laboratory testing. However, FDA lacks many of these key tools when it comes to dietary supplements.

Limited clinical information. One key tool that FDA lacks in assessing signals is adequate clinical information. This information can sometimes be obtained from large-scale clinical trials, small research studies and epidemiological studies. However, the current regulatory framework for dietary supplements does not require manufactures to conduct these types of studies prior to or after marketing a product. FDA lacks the resources to conduct this type of research itself. Although some manufacturers and independent researchers have conducted such studies, these studies by no means cover all dietary supplements or ingredients. FDA has some information on the history of use, since many of these products have been used for hundreds of years. However, this information can be difficult to interpret and verify.

Lack of information on consumer use. The size of the consumer population and the dosages taken by consumers help FDA estimate the size of the potential threat to public health. Unlike prescription drugs, self-care products, such as dietary supplements, lack a formal tracking system. When FDA evaluates adverse event reports that it receives, it is difficult for the agency to know the common denominator, and, thus, the incidence of adverse events relating to a particular product or ingredient remains unknown. Consequently, this makes it difficult for FDA to determine the magnitude of the safety concern.

With limited information to draw upon to generate signals, it is not surprising that FDA rarely reaches the point of knowing whether a safety action is warranted to protect consumers. We estimated that, based on this system, FDA has taken 32 actions between January 1994 and June

2000. The two most common types of actions were (1) requesting a voluntary product recall, and (2) issuing a warning to consumers. FDA also has disseminated letters to health professionals, required additional information on product labels, issued import alerts and seized products.

CONCLUSION

Mr. Chairman, our review of the adverse event reporting system for dietary supplements disclosed that it is an inadequate safeguard to protect consumers.

FDA is aware of these limitations and has taken steps along the lines we have called for in our report. Similarly, dietary supplement manufacturers, the General Accounting Office, and the White House Commission on Dietary Supplements have also called for reforms. We recognize that FDA faces legislative and financial barriers to implementing many of our recommendations. Therefore, we offer our recommendations as a blueprint for action that can be taken over time. We also recognize that dietary supplements are self-care products and that they are regulated as foods. However, without some additional regulatory mechanisms in place, FDA's system will continue to fall short of its potential.

Although we made many recommendations in our report, today I would like to highlight a few key ones. We recommended that FDA seek the authority to require manufacturers to report serious adverse events to FDA for certain products. Required reporting by manufacturers would help to increase the number and quality of reports that FDA receives. This requirement need not

apply to all dietary supplements, but FDA could determine the types of ingredients and products for which required reporting would be the most appropriate. We recommended that FDA receive Poison Control Centers reports. We also recommended that FDA seek the authority to require manufacturer and product registration for all dietary supplements. A manufacturer registry would enable FDA to more quickly identify and contact manufacturers for more information when necessary. And a product registry would allow FDA to have easy access to a list of all ingredients in a particular product. The final recommendation that I would like to highlight is for FDA to develop a new computer database to track and analyze adverse event reports for dietary supplements. A new system will allow the agency to analyze reports more rigorously and easily.

We are pleased that FDA has already taken important steps to address many of our recommendations, including the receipt of some Poison Control Centers reports and implementation of a registration system for manufacturers' facilities. In addition, FDA is currently improving its computer systems for analyzing adverse event reports.

Mr. Chairman, this concludes my testimony. I appreciate the opportunity to discuss our work regarding this important issue. We recognize that millions of consumers rely on dietary supplements. Therefore, we are committed to ensuring that FDA has the necessary tools to guarantee that the adverse event reporting system is effective in helping protect consumers.

I welcome your questions.

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