

OFFICE OF DRUG SAFETY (ODS)

Desired Outcome

Reduce preventable deaths and injuries associated with the use of medical products by increasing and enhancing the Office of Drug Safety's (ODS) review and analysis of both pre-marketing and post-marketing safety information on all products regulated by the Center for Drug Evaluation and Research (CDER).

Program Objectives

CDER has a central public health role to ensure that drug and biological therapeutic products are demonstrated safe and effective prior to marketing, and that these products continue to be safely used once approved and marketed.

Although products are required to be safe, safety does not mean zero risk. A safe product is one that has reasonable risks, given the magnitude of the benefit expected and the alternatives available. All participants in the product development and delivery system have a role to play in maintaining this benefit-risk balance by making sure that products are developed, tested, manufactured, labeled, prescribed, dispensed, and used in a way that maximizes benefit and minimizes risk.

Ensuring drug product safety is a mission-critical function of CDER. Drug safety analysis and decision-making is the result of collaborative efforts among offices across the Center.

ODS is one such office involved in the overall drug safety function, by playing the following roles in drug safety:

- Collaborating with CDER's Office of New Drugs (OND) in pre-market risk management analysis to:
 - Learn about and understand new drugs and its safety issues;
 - Make recommendations about potential additional population studies to be pursued after a drug is approved; and
 - Participate in advisory committee meetings
- Collaborating with OND to play a key role in safety signal (potential safety issue) identification and epidemiological analysis by:
 - Collecting and analyzing adverse event reports after a drug has been marketed; and
 - Performing epidemiological analysis to determine what a signal may mean using data from internal and external databases.
- Helping prevent medication errors and monitor previously identified errors by consulting on drug name and labeling issues; and,
- Acting as CDER's resource for epidemiological expertise for various analyses and population studies.

This initiative focuses on bolstering the drug safety functions within ODS by:

- increasing the professional staff in ODS who manage and lead safety reviews;
- increasing the number of staff with expertise in critical areas such as risk management, risk communication, and epidemiology; and,

- applying funding to increase access to a wide range of clinical, pharmacy and administrative databases.

Why is FDA's Contribution so Important?

FDA’s contribution, as laid out in the Federal Food, Drug, and Cosmetic Act, is devoted largely to pre- and post-marketing drug risk assessment. The approval/nonapproval decision is the Agency’s central risk management action. FDA must ensure that beneficial medical products are available and labeled with adequate information on their risks and benefits while protecting the public from unsafe products or false claims.

FDA approves a product when it judges that the benefits of using a product outweighs its risks for the intended population and use. A major goal of the pre-marketing review is to ensure that products are truthfully and adequately labeled for the population and use. Labeling is given considerable emphasis because it is the chief tool the Agency uses to communicate risk and benefit to the healthcare community and patients. Once medical products are on the market, however, ensuring safety is principally the responsibility of healthcare providers and patients, who make risk decisions on an individual, rather than a population, basis. They are expected to use the labeling information to select and use products wisely, thereby minimizing adverse events.

FDA has assumed a significant watchdog role regarding post-market surveillance. When FDA approves drugs and other medical products, it takes every precaution to ensure these products are safe when they are marketed. However, product safety continues throughout the product's lifetime.

Because the clinical trials that help gauge product safety are conducted on relatively small groups of patients--usually ranging from a few hundred to several thousand--problems can remain hidden, only to be revealed after hundreds of thousands or even millions of people use the product over a prolonged period. For these reasons and more, FDA relies on MedWatch and MedSun to provide a significant amount of data on post-marketing surveillance of medical products to identify safety concerns and take necessary action. These programs depend on doctors, dentists, nurses, pharmacists, and other health professionals to provide FDA details of serious adverse reactions and medical product problems.

**Requested Increases for FY 2006
(Dollars in \$000)**

Program	Center	Field	Total
Human Drugs	\$5,000	\$0	\$5,000
Total	\$5,000	\$0	\$5,000

With the \$5,000,000 increase, ODS will:

- Hire 6 FTE to:
 - Establish policies and processes regarding safety reviews and risk management;
 - Manage communications with the Office of New Drugs; and,
 - Support patient safety initiatives and external partnerships with CMS, AHRQ, and other HHS Agencies.
- Hire 10 FTE in the 3 operating divisions of ODS to:
 - Handle the increased workload of monitoring biologic therapeutics;
 - Increase communication and coordination of safety review activities within the divisions; and,
 - Increase focus on medical error signal detection and address current

backlog of unaddressed potential signals

- Hire 4 FTE to increase staff dedicated to evaluating and communicating drug safety risks to the healthcare community and the American Public; and,
- Apply funding to increase access to a wide range of clinical, pharmacy and administrative databases. Given the highly fragmented healthcare system in the U.S., there is no single healthcare database that the Agency can rely upon to widely monitor drug adverse events. As each drug has its own indication(s) that may result in its differential use in different populations, it is essential that the CDER have access to a wide range of databases to adequately assess drug safety.

Consequences of Not Achieving the Objectives

Recent drug safety issues have resulted in questions regarding the capability and credibility of FDA's drug safety program. Without additional resources to help achieve our stated objectives, FDA may continue to be perceived as unable to ensure the safety of marketed drugs.

How Are We Doing?

Learning about the relative safety of a drug product starts from the earliest development of a chemical entity and continues throughout the clinical development and review. Once a drug is approved for marketing in the U.S. and available for general distribution, there are two fundamental ways to continue the assessment of both the safety and safe use of a medicinal product. These two approaches include 1) monitoring of adverse drug events and medication errors as they occur in individual patients, and 2) formally

studying in populations the occurrence of such events.

The FDA currently relies primarily on the reporting and analysis of instances of adverse events. In 2003, we received over 370,000 such reports, a third of which (over 144,000) were serious in nature. The strengths and limitations of our Adverse Event Report System (AERS), which now contains over 2.5 million reports, are well known. We have made vast improvements in the way we manage and analyze this large data set over the last 7 years, using a variety of electronic and statistical tools that have increased our ability to get information to safety evaluators in a timely manner.

Improvements in drug safety must begin well before the drug is approved, while the product sponsor is evaluating the safety of candidate products and deciding which will be moved forward to each successive stage of testing. For example, FDA is collaborating with NIH to develop common data standards for electronic reporting of adverse event in clinical trials, to assist and facilitate rapid analysis of safety findings. FDA work to improve identification of safety issues early in drug development includes efforts to mine FDA data to create predictive software that uses structure-activity relationships to help identify compounds with potentially significant adverse properties, so they can be eliminated as lead compounds earlier in development.

FDA published the *Draft Guidance for Industry: Pharmacogenomic Data Submissions* to encourage drug and biologic developers to conduct pharmacogenomic tests during drug development. Among the many potential uses of this data is identification of early signals of product toxicity. FDA scientists developed a new technique to detect the presence of

contaminating virus in small pox vaccine products; this technique can be applied to other vaccine and cell-based products.

recommend measures to enhance the confidence of Americans in the safety and effectiveness of their drugs.

During FY 2005 and 2006, FDA plans a variety of activities focused on increasing and enhancing the review and analysis of both pre-marketing and post-marketing safety information on all products regulated by CDER. FDA's actions during this timeframe will focus on establishing a "drug safety net", a comprehensive effort that ultimately will require that FDA have:

In FY 2006, FDA anticipates it will expend \$22,900,000 on the Office of Drug Safety.

- Access to large clinical and drug use data sets for detecting adverse events and medication errors, and for conducting population-based safety studies;
- Linkage of these data sets to increase the "power" to detect problems;
- Development of strong analytic tools to rapidly identify "signals"; and,
- Timely, thoughtful and actionable communication of information to healthcare providers and consumers.

FDA will continue its efforts to improve the timeliness and availability of drug safety information and will be seeking alternative strategies for managing drug safety issues as well as increasing its use of external experts in evaluating post-marketing safety issues. FDA actions will be harmonized with the emerging results of an Institute of Medicine (IOM) Study of the drug safety system. In this study, IOM will evaluate the effectiveness of the U.S. drug safety system with emphasis on the post-market phase to assess what additional steps could be taken to learn more about the side effects of drugs. The committee will examine FDA's role within the health care delivery system and