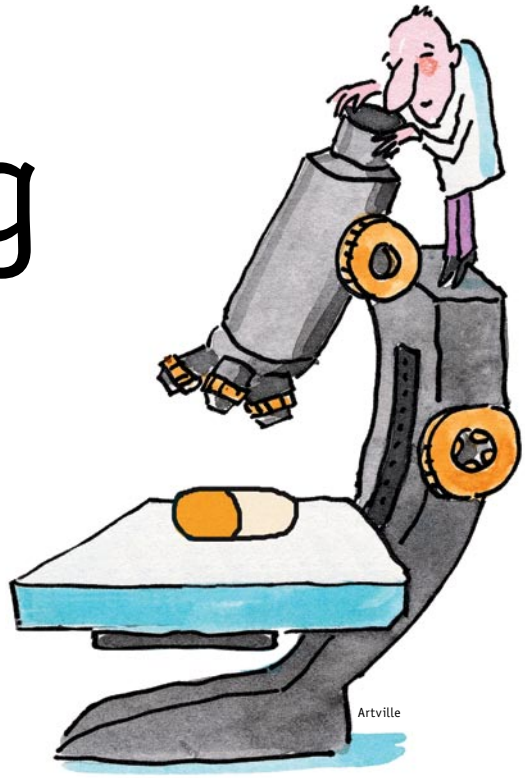
Strengthening Drug Safety



In any given week, half of U.S. adults will use prescription medicines and 10 percent will take at least 5 different ones, according to a 2004 survey conducted by the Slone Epidemiology Center at Boston University. Over-the-counter drugs are also used frequently in American households.

Under the law, FDA must make sure that these treatments are safe and that for most people the drugs will not cause harm. But almost all drugs can cause harm to some people. FDA deems a drug "safe" when its benefits outweigh its risks for the people the drug is intended to treat and for its intended use.

"What we need to do is make drugs as safe as possible," says FDA Deputy Commissioner and Chief Medical Officer Janet Woodcock, M.D. "And we need to make sure we recognize the harm they can do so that prescribers and patients can make informed decisions about using them and watching for problems."

And that's what FDA is doing.

On Jan. 30, 2007, FDA announced 41 initiatives it is undertaking in its ongoing commitment to drug safety, as well as the safety of medical devices and biologics such as vaccines, blood products, and gene therapies.

Many of the initiatives respond directly to recommendations made by the National Academy of Sciences' Institute of Medicine (IOM), the nation's foremost body for independent, science-based advice on issues that affect health. In early 2005, FDA had asked the IOM to examine the U.S. drug safety system in detail and recommend ways to improve it. In September 2006, the IOM released the results of its study and made substantive recommendations in its report, "The Future of Drug Safety: Promoting and Protecting the Health of the Public."

After careful consideration of the IOM recommendations, along with advice from other experts, FDA came up with its drug safety initiatives, organized around three key themes:

- Strengthening the science that supports FDA's medical product safety system
- Improving communication so that health care providers and patients can get the information needed to make informed decisions about treatments
- Improving FDA's operations and management supporting drug safety.

STRENGTHENING THE SCIENCE

Genetic research is just one example of how FDA is employing science to help improve drug safety.

More than 700,000 people make a trip to U.S. emergency rooms each year because of bad drug reactions, according to a study authored by researchers at the Centers for Disease Control and Prevention, FDA, and the Consumer Product Safety Commission. The study was published in the *Journal of the American Medical Association*, Oct. 18, 2006.

One of the most common drugs implicated in emergency room visits for unexpected medical problems (adverse events) is warfarin, a blood-thinner used by roughly 2 million Americans annually. The optimal dose of warfarin varies from one patient to another. If the dose is too high, serious bleeding may occur. If the dose is too low, a stroke may result.

In collaboration with the Critical Path Institute and the University of Utah, FDA is working to improve drug safety using pharmacogenomics—looking at how genetic differences in individuals affect the way they respond to drugs. The agency also is assisting researchers at the National Heart, Lung, and Blood Institute with a clinical study to

determine how factors such as age, gender, and weight might influence a person's response to warfarin.

The goal of these research projects is to develop a mathematical method, or algorithm, for doctors to use to help personalize dosing of warfarin so that an optimum dose can be given to individual patients based on their genetic makeup.

IMPROVING COMMUNICATION

In addition to labels on drug products, other communication tools FDA uses to give important drug safety information are posted on its Web site and include:

- public health advisories—information and advice on emerging drug safety issues or other important public health information
- patient information sheets—concise summaries, in plain language, with the most important information about a particular drug
- alerts on a patient information sheet—additional information on a drug, such as newly observed serious adverse events and how they might be prevented
- an index to drug-specific information—safety information on all drugs, while highlighting those drugs that are the subject of a public health advisory or an alert (*www.fda.gov/cder/drug/drugsafety/DrugIndex.htm*)
- podcasts—a series of Internet broadcasts of public health advisories. By subscribing, consumers can listen to podcasts on their computer or transfer them to a device like an iPod. Anyone can subscribe for free at *www.fda.gov/cder/drug/podcast/*

All of these methods are included in FDA's final guidance, released in March 2007, on its approach to communicating drug safety information to the public.

COMMUNICATIONS ADVISORY COMMITTEE

Just as FDA has created advisory committees made up of outside expert scientists to provide recommendations for medical products, FDA is creating an advisory committee to help improve communicating medical product risks to the public. The committee of outside experts in risk and crisis communication, social scientists, patients, and consumers will review FDA's current public communication tools and help the agency improve risk communications.

IMPROVING OPERATIONS AND MANAGEMENT

The IOM report recommended that the agency make changes to improve morale and retention of professional staff, strengthen transparency, restore credibility, and create a culture of safety.

Some of the actions FDA is taking to create a culture that will strengthen the drug safety system are:

- engaging external experts in organizational improvement to help identify and carry out changes to improve the organizational culture
- making specific organizational and management changes to increase communications among drug review and drug safety staff, and to involve drug safety staff more directly in the review of new drugs
- improving the use of FDA's advisory committees, including making the selection process of committee members more transparent to the public.

HEADLINES, HOOPLA, AND DRUG SAFETY

FDA has had an ongoing commitment to drug safety since 1938, when federal law required drugs to be shown safe before being allowed on the market. Yet, the popular press sometimes attributes recent FDA drug safety initiatives to problems with newer drugs, such as Vioxx.

Vioxx (rofecoxib) was approved in 1999 and withdrawn from the market in 2004 because of an increased risk of heart attacks and strokes.

"The safety of drugs and other medical products regulated by FDA has always been, and continues to be, a key focus of the agency's programs," says Steven Galson, M.D., Director of FDA's Center for Drug Evaluation and Research. "Our drug safety efforts are not tied to a specific drug or series of events."

Drug safety has been in the headlines for over 60 years, adds Woodcock. "Over time, there has been increased scrutiny of drugs, yet every decade has seen drug withdrawals and controversies over whether FDA's drug approval standards ensure adequate safety."

"Something seems scarier if it's new or unknown," she says. "New drugs that show harmful side effects seem to make the headlines most, but proportionately, the vast amount of harm from drugs is from those that have been on the market a long time." For example, fenfluramine, approved in 1973, was removed from the market in 1997. Fenfluramine, the "fen" half of the popular weight-loss combination known as "fen-phen," was linked with potentially fatal heart valve disease in some people.

Estrogen to relieve menopausal symptoms has been marketed since the 1940s, yet it wasn't until 2002 that cardiovascular risks were recognized in a landmark study, the Women's Health Initiative. On the basis of an evaluation of study data, FDA called for revised labeling and provided new safety advice to post-menopausal women and their health care providers concerning drug products that contained estrogen.

For more information, see *www.fda.gov/cder/drugSafety.htm*