



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

STATEMENT OF

JOSHUA M. SHARFSTEIN, M.D.

PRINCIPAL DEPUTY COMMISSIONER

FOOD AND DRUG ADMINISTRATION

DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE

SUBCOMMITTEE ON HEALTH

COMMITTEE ON ENERGY AND COMMERCE

U.S. HOUSE OF REPRESENTATIVES

MARCH 10, 2010

FOR RELEASE ONLY UPON DELIVERY

INTRODUCTION

Mr. Chairman and Members of the Subcommittee, I am Dr. Joshua M. Sharfstein, Principal Deputy Commissioner at the Food and Drug Administration (FDA or the Agency) in the Department of Health and Human Services (HHS). Thank you for the opportunity to discuss the safety of the American drug supply.

Protecting Americans from unsafe or contaminated drugs is not just an important responsibility of FDA—it is our core charge. Drug safety was the primary reason for the passage of our guiding statute. In 1937, more than 100 people, including many children, died from ingesting Elixir Sulfanilamide, which contained the deadly poison diethylene glycol. Congress then passed, and President Franklin D. Roosevelt signed, the Federal Food, Drug, and Cosmetic Act (FD&C Act) to prevent future catastrophes.

And yet, as you know, the threat remains.

I would like to thank the Subcommittee for its leadership on this issue. Numerous hearings in this chamber have helped the public understand the challenge of regulating a global marketplace. Members of this Subcommittee, along with the Chairman of the full Committee and the Chairman Emeritus, were key architects of the Food and Drug Administration Amendments Act of 2007 (FDAAA), which gave the Agency significant new authorities and resources to address postmarket safety.

In this testimony, I will address two important issues: import safety and the implementation of the drug safety authorities in FDAAA.

IMPORTS

As the Subcommittee's work has documented, globalization has created new risks and challenges for the safety of the drug supply.

Where Americans once used drugs that were mostly manufactured domestically, now up to 40 percent of the drugs we take are imported, and up to 80 percent of the active pharmaceutical ingredients in the drugs we use are from foreign sources. In addition to the growth in the sheer volume of imports and foreign facilities, there has been an increase in the variety and complexity of imported products, and a large expansion in the number of countries involved in producing these products—including many with less sophisticated regulatory systems than our own. Simultaneously, the supply chain from raw material to consumer has become more and more complex, involving a web of repackagers and redistributors in a variety of locations. This makes oversight significantly more difficult and leaves weaknesses through which counterfeit, adulterated, and misbranded products might infiltrate the legitimate supply chain.

A few examples:

- In 2007 and 2008, contaminated heparin (a blood-thinning drug) came from China and was linked to deaths and a number of serious allergic-type reactions here at home.
- Counterfeit Tamiflu (oseltamivir phosphate) was discovered during the novel H1N1 outbreak.

- In 2007, Xenical (orlistat) capsules ordered over the Internet were found to be composed only of talc and starch.
- In January 2010, counterfeit Alli (orlistat) was discovered, which did not contain the active ingredient but instead contained varying amounts of the stimulant sibutramine, which can lead to serious toxicity if used by people with certain cardiac diseases.

These episodes and others were not random mistakes. They share a common feature—an economic incentive. In the case of heparin, it appears that a contaminant was introduced to increase the profit of the raw material suppliers. In the case of counterfeit drugs, criminals can make millions by pretending their dangerous or ineffective products are safe and effective. These are despicable acts that seek profit by putting lives at risk.

These are global problems. Contamination and counterfeit drugs represent a much greater threat in the developing world, where the systems of laws and regulatory oversight do not afford much protection. And these problems can pose a risk to us at home, when, for example, patients do not get fully treated for infection abroad because of ineffective drugs ... and as a result, drug resistance intensifies.

When the modern FDA was created in 1938, imports were a tiny part of the products used in our country. Our focus was on stopping harmful products at the border through inspections of imported goods. This approach is adequate to the challenge when the volume is small. But it fails when an estimated 20 million shipments of FDA-regulated imports come into the country each year.

To fulfill our public health mission in a global age, FDA must adopt a new approach—one that addresses product safety by preventing problems at every point along the global supply chain, from the raw ingredient through production and distribution, all the way to U.S. consumers.

We are moving from an approach based on reacting to problems to one that proactively prevents such problems from ever occurring.

In the food arena, this approach to prevention is embodied in legislation passed by this Committee and the full House of Representatives, and which is now awaiting action in the Senate. This bill would for the first time allow FDA to establish basic preventive controls throughout the food production process and give the Agency strong enforcement authorities and resources to meet these obligations.

In the arena of drugs and other medical products we are taking a number of steps to begin making this shift within our current authorities.

First, we are seeking better controls at the point of production, wherever that may be.

We now have permanent FDA offices in Beijing, Shanghai, and Guangzhou, China, in New Delhi and Mumbai, India, in San Jose, Costa Rica, Mexico City, Santiago, Chile, and soon, Amman, Jordan. These offices enable us to have a regional presence around the world, a home base from which to undertake a range of important activities, including building regulatory capacity.

We now have more than 30 agreements with foreign counterparts to share inspection reports and other nonpublic information that can help us make better decisions about the safety of foreign

products. So if a shipment of contaminated drugs shows up in a port in Italy, we will hear about it swiftly and be on the lookout for products from the same shipper.

Second, we are working with industry to help them strengthen the safety of their supply chains. In this day and age, companies should be able to effectively demonstrate that safety, quality, and compliance with international and U.S. standards are built into every component of every product and every step of the production process.

Some companies already do a terrific job at this, tracking where and how their products and their components are made and the path taken to reach our shores. In fact, I have met with some companies that react with incredible swiftness to questions about the integrity of their supply chain. Obviously they have a vital interest in ensuring confidence in the safety and quality of their products and their brand. These best practices need to become standard practice throughout industry.

There is much more to be done. As Secretary of Health and Human Services Kathleen Sebelius noted when she appeared before this Committee on February 4, 2010, FDA needs additional tools to move our oversight capabilities into the 21st century. FDA needs to access regulatory information quickly, hold all parties responsible for the quality of products in the supply chain, and have reasonable and reliable options for enforcement.

DRUG SAFETY AUTHORITIES IN FDAAA

I will now turn to the drug safety authorities in FDAAA, a milestone legislative achievement that has helped the Agency protect the public health in many different ways.

Because no amount of premarket study can provide the full information about what the benefits and risks of a new drug will be when it is used by the general population, FDAAA provided important new authorities to enhance our ability to monitor approved drugs after they are marketed and to take definitive action when needed.

Under FDAAA, FDA can require drug sponsors to conduct postmarketing studies and clinical trials, make certain safety-related labeling changes, and develop and put into place risk evaluation and mitigation strategies (REMS)—all with the goal of better identifying and managing the risks of drugs on the U.S. market.

Here are some details.

Between the passage of FDAAA and March 8, 2010, FDA has required that sponsors conduct around 200 postmarketing studies or trials. FDA is tracking the conduct of these studies and will take enforcement action if studies are not conducted in a timely manner without good cause.

With respect to label changes, as of February 28, 2009, FDA had used its new authorities to require safety label changes in individual or classes of drugs 32 times since March 25, 2008. For example, FDA required safety label changes to add the risk of a life-threatening neurological disorder to the prescribing information for certain antidepressants, and changes to the prescribing information of a class of antibiotics to warn about the risk of tendon rupture.

With respect to risk management, if FDA determines that a REMS is necessary to ensure that the benefits of a drug outweigh the risks of the drug, FDA can require manufacturers to have a REMS in place when a drug comes on the market, or implement one later if FDA becomes aware of new safety data. The authority to require REMS provides FDA a very useful set of tools that can be used to reduce the risks of marketed products, while allowing patients to benefit from lifesaving and other beneficial treatments that could not be safely marketed without a risk management program.

In the design of REMS with elements to ensure safe use (the most comprehensive REMS programs), FDA is mindful of the provisions in FDAAA stating that the elements to ensure safe use must be, among other things, commensurate with the specific serious risk listed in the FDA-approved labeling of the drug, not be unduly burdensome on patient access to the drug, and be designed to be compatible with established distribution, procurement, and dispensing systems for drugs.

Most of the REMS with elements to ensure safe use include educating prescribers about the risks and appropriate use of the drug as a condition of certification or enrollment in the REMS program. Other programs require enrollment by pharmacists and sometimes patients as well. Some programs require the prescriber to monitor the patient immediately following drug administration and for a period of time afterwards. Each of these programs is designed to provide critical information to clinicians without unduly restricting access to the drugs.

We have learned that designing and implementing the most comprehensive REMS requires a careful balancing of the need to adequately manage risks and also to maintain patient access to important medications. Since using this authority is a work in progress, FDA is committed to addressing the concerns we have heard from prescribers, pharmacists, distributors, and payers about their roles in implementing REMs and from patient groups about the effects of REMS on access to needed products, and are planning to hold a public meeting to hear from these and other stakeholders.

Additional implementation challenges include ensuring consistency in the handling of safety problems with all products, including over-the-counter (OTC) products and generic drugs; the lack of clarity in certain provisions of the law with respect to REMS; and burdens imposed on application holders and FDA that do not contribute significantly to drug safety. We would be very happy to discuss the lessons we have learned over the last two years with Congress and work together to fine tune the program so that it can be even more effective in improving public health.

Sentinel Initiative

FDAAA requires the HHS Secretary to develop methods to obtain access to disparate data sources and to establish a postmarket risk identification and analysis system to link and analyze health care data from multiple sources. On May 22, 2008, FDA launched the Sentinel Initiative with the ultimate goal of creating and implementing the Sentinel System—a national, integrated, electronic system for monitoring medical product safety. The Sentinel System, once up and running, will enable FDA to actively gather information about the postmarket safety and

performance of its regulated products—a significant step forward from our current, primarily passive safety surveillance systems. The law sets a goal of access to data from 25 million patients by July 1, 2010, and 100 million patients by July 1, 2012.

FDA has gathered public input on issues related to the creation and development of Sentinel, held numerous meetings and a public workshop, and established a working group consisting of representatives of numerous federal agencies to share information and discuss issues related to ongoing efforts that are complementary to Sentinel. FDA has awarded key contracts for a pilot project to gather information that will be essential to fully implementing the Sentinel System.

Track and Trace

FDAAA also required the development of standards for the identification, validation, authentication, and tracking and tracing of prescription drugs as a step towards further securing our nation's drug supply. Very shortly, FDA will issue a guidance establishing a standard for unique identification for prescription drug packages, which ultimately will help in identifying the whereabouts and authenticity of drug packages and distinguish them from counterfeits.

SAFE USE INITIATIVE

Before I close, I would like to briefly mention a new drug safety initiative at FDA called the Safe Use Initiative. Every approved drug has both benefits and risks. Underlying FDAAA is the principle that Congress wants to see the benefits maximized for patients and the risks minimized. We all want patients to get better on medication and avoid unnecessary injuries, even death, as a result of preventable medication errors or misuse.

In November 2009, we announced the launch of FDA's Safe Use Initiative. Through this initiative, FDA will identify, using a transparent and collaborative process, specific candidate cases (e.g., drugs, drug classes, and/or therapeutic situations) that are associated with significant amounts of preventable harm. FDA will then work with hospitals, doctors, nurses, patient groups and others to recognize and mitigate these risks. In a voluntary complement to the REMS program, we will use our understanding of drug risk as a tool to gather partners together and develop and implement strategies for progress.

CONCLUSION

Over the last seven decades, so much has changed in pharmaceutical science and drug regulation. Yet in 2007, when scores of patients died of contamination in Bangladesh, and in 2006 when children died in Panama, the culprit was familiar. It was diethylene glycol, or DEG—the very same poison that had led to the passage of the FD&C Act in 1938.

FDA's work is far from done. The scientists, doctors, nurses, inspectors, and other public health professionals who make up FDA thank you for your support and confidence in our mission.

Thank you very much for the opportunity to testify today. I welcome your ideas and your questions.