DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

STATEMENT OF

STEVEN K. GALSON, M.D., M.P.H.

DIRECTOR, CENTER FOR DRUG EVALUATION AND RESEARCH

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INTRODUCTION

Mr. Chairman and Members of the Committee, I am Rear Admiral Steven Galson, Director of the Center for Drug Evaluation and Research (CDER or the Center) at the Food and Drug Administration (FDA or the Agency). I am pleased to be here today to talk about FDA's drug safety program, and to emphasize our commitment to drug safety as part of our primary mission to protect and promote the public health. We have many initiatives already underway to strengthen the science of drug regulation, improve our internal operations, and enhance our communications with the public, health care professionals, and industry.

MODERNIZING DRUG SAFETY

As the Director of CDER, I play a significant role in helping to ensure the safety of drugs regulated by FDA. Drug safety has always been a key focus of my commitment to protect and promote the public health. In the past few years, the Center has reassessed many of its drug safety programs because of rapid advances in science and technology that have resulted in increasingly complex medical products. We take very seriously our response to safety-related issues raised by consumer advocates, health professionals, academic researchers, and Members of Congress.

For this reason, the Agency requested that the Institute of Medicine (IOM) convene an expert panel to assess the U.S. drug safety system and to make recommendations to improve risk assessment, surveillance, and the safe use of drugs. In addition to commissioning the IOM study in 2005, we initiated our own assessment of the drug safety program that continues

today. As part of that assessment, we received extensive input from external stakeholders and launched a number of initiatives that will enhance our abilities to review, monitor, and communicate about safety issues.

FDA has a strong safety record and remains the world's gold standard for drug approval and safety. We have maintained this record by taking actions to see what transformations are necessary to maintain and improve upon this standard. It is important to remember that no drug is absolutely safe. FDA approves drugs only after it is demonstrated that their benefits outweigh their risks for a specific population and a specific use, and that the drug meets the statutory standard for safety and efficacy. In other words, when we talk about drug safety, we are really talking about working to ensure a favorable benefit-to-risk balance for the drug when used by patients and to ensure that health care providers and patients have access to up-to-date information about the benefits and risks of a drug on which they can base their individual treatment decisions.

As the IOM report recognizes, resources are critical to improving our drug safety program. Both the President's fiscal year (FY) 2008 budget proposal and the Prescription Drug User Fee Act (PDUFA IV) proposal, include significant additional funding to modernize FDA's processes for ensuring drug safety. With the funds requested, FDA expects to strengthen the science and tools that support the product safety system at all stages of the product life-cycle from pre-market testing and development through post-market surveillance and risk management. FDA also expects to improve communication and information flow among all stakeholders. The FY 2008 Budget request and PDUFA IV funds would support FDA's

ability to effectively detect, communicate about, and act on important safety issues thereby improving patient safety and public confidence in FDA drug safety efforts.

FDA RESPONSE TO THE INSTITUTE OF MEDICINE REPORT

On September 22, 2006, IOM released its report *The Future of Drug Safety – Promoting and Protecting the Health of the Public*. The IOM report both recognizes specific progress and reform already initiated by the Agency and makes substantive recommendations about additional steps FDA can take to improve our drug safety program. In January 2007, FDA's comprehensive response to the IOM report described the Agency's commitment to strengthening our drug safety program as rapidly and efficiently as available resources allow. One of the driving forces for change is our ability to use the potential of emerging science and technology to develop useful tools to improve our drug safety programs. FDA is committed to a creating a comprehensive, systematic approach to improving the "drug safety system."

Our commitment has three interconnected themes: (1) strengthening the science that supports our medical product safety system, (2) improving communication and information flow among key stakeholders, and (3) improving operations and management to strengthen the "drug safety system." As Director of CDER, I have taken the lead in an aggressive effort to address and implement our response to the IOM's recommendations. We have made and will continue to make changes to our structure, policies, and processes to improve drug safety. I will discuss our IOM report response by highlighting the three themes of science, communications, and operations. In addition, I will discuss some of the significant changes and projects we are working on to improve drug safety in those areas.

1. Strengthening the Science

First, FDA is committed to strengthening the science that supports our medical product safety system at every stage of the product life cycle, from pre-market testing and development through post-market surveillance and risk management. We will focus our resources on three areas of scientific activity: (1) those relating to improving benefit and risk analysis and risk management, (2) surveillance methods and tools, and (3) incorporating new scientific approaches into FDA's understanding of adverse events.

One of our core functions is to continuously review post-marketing safety. Routine activities include reviewing many categories of information including adverse event reports, periodic safety reports, epidemiologic data, post-marketing clinical trial data, medical literature, information on other members of a class of drugs, and information from other sources to identify potential safety concerns. With the rapidly increasing number of adverse event reports that the Agency receives annually (fewer than 200,000 in 1996 and more than 470,000 in 2006), we are focusing on making our review processes more effective and efficient, using techniques such as data mining.

We have created a pilot program to look at selected New Molecular Entities after they have been on the market for a period of time (e.g., 18 months) to examine whether we can more rapidly and predictably detect problems in newly approved drugs. We are examining the analyses needed, the most efficient approaches to communicating and discussing the data, and how this systematic look compares to the review processes already in place. The results of

our experience with at least four drugs will be studied initially. Then the Agency will assess the pilot program for possible wider implementation.

In addition, we are implementing an electronic post-marketing safety tracking system to track and help manage safety issues. This system is already helping some CDER reviewers and managers to prioritize their work on safety issues and, when fully implemented, this system will replace multiple office and division specific systems.

We are working to strengthen surveillance methods and tools. We are in the process of upgrading the electronic Adverse Event Reporting System (AERS) by incorporating the latest tools, such as signal detection and tracking, and integrating medication error evaluation functions. This upgrade will make data more readily accessible to other public health agencies, research organizations, and the general public. We also are increasing safety database resources. Access to valuable data housed in large public and private databases will help us understand how the products we regulate are used by patients. Having these data available to our scientists will enhance their ability to detect and evaluate drug safety problems and medication errors.

In support of these functions, we are improving our data accuracy and completeness through measures including a renewed focus on registration of drug establishments and listing of their marketed products. This information is essential to identify drugs on the market and those who make them. It likewise allows us to link specific drug products to their approvals, labeling, and other critical information. We have proposed revisions to Title 21, *Code of*

Federal Regulations Part 207 (Registration of Producers of Drugs and Listing of Drugs in Commercial Distribution) that will mandate electronic registration and listing.

2. Improving Communications

FDA is committed to improving communication and information flow among all stakeholders to further strengthen the drug safety system. Open and transparent communication including rapid and effective dissemination of new information regarding safety issues among FDA, patients, and health care providers is key to promoting the safe use of medical products.

We plan to establish a new advisory committee to obtain input on how to improve the Agency's communication policies and practices, and to advise FDA on implementing communication strategies consistent with the best available and evolving evidence. We intend to include patients and consumers on the committee as well as experts in risk and crisis communication and social and cognitive sciences. The IOM report recommends legislation to establish this advisory committee, but we intend to implement this recommendation more expeditiously through administrative procedures.

We plan to conduct assessments of the effectiveness of identified risk minimization action plans (RiskMAPS) and current risk management and communications tools and to conduct public discussions on these issues. On June 25-26, 2007, we will co-host a public workshop with the Agency for Healthcare Research and Quality to seek input from outside experts from medical and pharmacy professional organizations, patient advocacy organizations, and others

to discuss how risk management plans are working to enhance patient safety. This meeting is another step towards that safety enhancement goal.

In March 2007, we issued final guidance that describes FDA's current approach to communicating drug safety information, including emerging safety information, to the public. The guidance affirms the Agency's commitment to communicate important drug safety information in a timely manner, including in some situations when the Agency is still evaluating whether to take any regulatory action. FDA's final guidance about the communication of drug safety information is available on FDA's website. We also plan to regularly publish a newsletter on FDA's website containing: (1) summaries of results of FDA post-marketing reviews, (2) information on emerging safety issues, and (3) information on recently approved products to inform providers and encourage reporting of adverse events to FDA. This newsletter will not include any confidential commercial or pre-decisional information.

3. Improving Operations and Management

FDA is committed to improving operations and management to ensure implementation of the review, analysis, consultation, and communication processes needed to enhance drug safety. It may be noted that approximately one-half of our daily work is safety related, and includes such diverse areas as assuring drug manufacturing quality over the product's lifecycle and human subject protection. Consistent with the IOM recommendations, we are implementing several reforms that, together, will improve the culture of safety at FDA.

CDER has initiated a series of changes designed to effect a true culture change that will strengthen operations and management. I have charged the members of my senior leadership team to lead the Center in an integrated manner that crosses organizational lines and they have taken steps to achieve this better integration.

CDER has reorganized in part to enhance our drug safety focus and to strengthen the integration of drug safety into regulatory decision making at all stages of the medical product life cycle. We have elevated the Office of Surveillance and Epidemiology (OSE) to report directly to me. In addition, I have established an Associate Center Director for Safety Policy and Communication to focus on the development and implementation of broad drug safety and communication policies. The person in this position serves as Chair of the Drug Safety Oversight Board and oversees that staff and the Medwatch staff. This position also reports directly to me.

In addition to CDER's own reorganization steps to enhance the drug safety focus of the Center, we have enlisted the help of external experts in organizational improvement. These external management consultants will help CDER develop a comprehensive strategy for improving CDER/FDA's organizational culture.

CDER has employed process improvement teams comprising staff in various organizations including OSE and the Office of New Drugs (OND) to recommend improvements in the drug safety program. The Center has implemented their recommendations to (1) establish an Associate Director for Safety and a Safety Regulatory Project Manager in each OND review

division within CDER and (2) conduct regular safety meetings between OSE and all the OND review divisions. We are committed to providing the necessary management attention and support to effect sustained culture change in our drug safety program.

FDA has initiated the development of two pilot projects to evaluate ways to involve OSE staff in reviews of drug and biologic applications. These include having an OSE staff person participate in each new drug application or biologic license application review, and other models for OSE involvement in post-marketing decision making. The Agency is committed to ensuring that OSE staff has a strong voice in pre- and post-marketing safety decision making. Furthermore, the proposed performance goals under PDUFA IV include provisions for enhancing and improving communication and coordination between OSE and OND.

In addition, we are committed to improving our use of advisory committees. In March 2007, FDA issued new draft guidance that would implement a more stringent approach for considering potential conflicts of interest for its advisory committee members and for recommending eligibility for meeting participation. FDA is currently accepting public comments on the proposal. The draft guidance is designed to make the advisory committee process more rigorous and transparent so that the public has confidence in the integrity of the recommendations made by its advisory committees. In addition, we are in the process of creating standard operating procedures for presenting post-market safety issues to an advisory committee. Furthermore, we plan to increase epidemiology expertise on our advisory committees.

PDUFA IV INCLUDES DRUG SAFETY ENHANCEMENTS

FDA proposes to use funds in PDUFA IV to help modernize and transform the drug safety system, throughout the entire life cycle of drug products. Our proposed enhancements include the activities and investments identified as most critical by our post-market review staff.

The recommended $87.4 million increase in drug user fees for FY 08 would include $29.3 million to support hiring of 82 additional staff for post-market safety activities as well as resources to support other important post-marketing drug safety activities. This would triple the amount of user fee funding available for post-market drug safety monitoring activities. We also propose to eliminate the current statutory time limit that restricts the use of user fees for drug safety activities to the first three years that a drug is on the market. This would allow user fees to fund safety activities on a marketed product at any time in the drug's life-cycle. Eliminating the statutory time limit will provide enhanced funding for the assessments of drug products over time, to adequately manage drug risks, regardless of a drug's approval date. FDA also would use the increased funds to further enhance and improve communication and coordination between FDA pre-market and post-market review staff, a key IOM recommendation.

In addition, as part of the proposed enhancements, we would analyze and adopt new scientific approaches to improve our tools for detection, evaluation, prevention, and mitigation of adverse events associated with drugs and biological products. We would use these increased funds to conduct research to determine the best way to maximize the public health benefits

associated with the collection and reporting of adverse events throughout a product's life cycle.

FDA would also use the proposed funds to identify and document epidemiology best practices, through input from academia, industry, and others in the public. This would inform our development of a guidance document that addresses epidemiological best practices and principles for the conduct of scientifically sound observational studies using quality data sources.

Another critical part of the proposed drug safety modernization would be maximizing the utility of current tools for adverse event detection and risk assessment. We would do this by seeking access to more and better data, such as population-based epidemiological data and other types of observational data resources. In addition, fees would support additional training for our current staff, and allow us to increase the number of professional staff who can review and analyze this safety information.

PDUFA IV also would allow us to develop a plan to evaluate current risk management plans and tools. We will obtain input from academia, industry, other government agencies, and other stakeholders regarding the prioritization of the plans and tools to be evaluated. The evaluation would include assessments of the effectiveness of identified RiskMAPS and current risk management and risk communication tools. Based on those evaluations, FDA would conduct an annual systematic review and public discussion of the effectiveness of one or two risk management programs and one major risk management tool. By making such

information publicly available we would promote effective and consistent risk management and communication.

Our PDUFA IV proposal includes a $4 million increase in funding to improve the information technology (IT) infrastructure for human drug review, to move FDA toward an all-electronic drug review system. These infrastructure upgrades will allow us to implement a number of the IOM's recommendations to enhance drug safety. We would use the increased PDUFA IV funds to improve our post-market safety-related IT systems to ensure the best collection, evaluation, and management of the vast quantity of safety data received by FDA. We would use these funds to improve our IT infrastructure to support access to and analyses of externally linked databases, and to enhance FDA's AERS and surveillance tools.

In addition, FDA is proposing $6.25 million in new user fees for a voluntary program to review direct-to-consumer television advertisements for accuracy and balance prior to airing. This new program would support 27 additional staff with performance goals phased in over five years.

CONCLUSION

A core mission at FDA is to ensure that the American public has access to safe and effective medical products. We base decisions to approve a drug or to keep it on the market if new safety findings surface, on a careful balancing of risk and benefit, as well as consideration of the tools we have to help minimize the risks to patients from a drug's use. This multifaceted and complex decision process involves weighing both scientific and public health issues.

The recent initiatives we have announced will improve our current abilities to assess drug safety and to help assure that the drug products available to the American public are safe and effective. Moreover, we will continue to evaluate new approaches to advance drug safety. As always, we value input from Congress, the public, and the medical community as we develop and refine these drug safety initiatives.

Thank you for the opportunity to testify before the Committee today. I am happy to respond to questions.