



DEPARTMENT OF HEALTH & HUMAN SERVICES

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INTRODUCTION

Mr. Chairman and Members of the Committee, I am Theresa Mullin, Assistant Commissioner for Planning at the Food and Drug Administration (FDA or the Agency).

I am pleased to be here today, to talk about the Prescription Drug User Fee Act, or PDUFA. As the FDA Director of Planning, I've played a lead role in coordinating implementation of PDUFA III initiatives, and the on-going analysis of PDUFA performance and resource requirements. Most recently, I served as FDA's lead in the discussions with industry related to the reauthorization of PDUFA.

I'd like to begin by discussing FDA's success in implementing PDUFA and describe some challenges that we have tried to address in our recommendations for reauthorization. I will also summarize highlights of our proposal for PDUFA IV.

Before proceeding, however, I would like to emphasize the importance of timely reauthorization of this law. The Agency and the staff charged with implementing PDUFA III need to be confident that reauthorization will occur by the end of September.

BACKGROUND

FDA considers careful and timely review of the safety and effectiveness of new drug applications (NDAs) and biologics license applications (BLAs) to be a central part of FDA's mission to protect and promote the public health.

Before PDUFA, FDA's drug review process was not very predictable, and it was relatively slow. At the same time, regulators in other countries were able to review products faster. Access to new medicines for U.S. patients lagged behind. In 1992 Congress enacted

PDUFA, which provided the added funds through user fees that enabled FDA to hire additional reviewers and support staff and upgrade its information technology systems. At the same time, FDA committed to complete reviews in a predictable timeframe. These changes enabled FDA to speed the application review process for new drugs and biologics without compromising FDA's high standards for approval. PDUFA has since been reauthorized twice. In the most recent reauthorization, Congress directed FDA to consult with key stakeholders in developing recommendations for PDUFA reauthorization. This includes the House Committee on Energy and Commerce and the Senate Committee on Health, Education, Labor, and Pensions, as well as appropriate scientific and academic experts, health care professionals, patient representatives, consumer advocacy groups, and the regulated industry. We have complied with these requirements in preparing our PDUFA IV proposal.

PDUFA ACHIEVEMENTS

PDUFA has produced significant benefits for public health, including providing the public faster access to over 1200 new drugs and biologics since enactment in 1992. During the PDUFA era, FDA has approved many hundreds of important new medicines including treatments for cancer, infectious disease, neurological and psychiatric disorders, and cardiovascular diseases.

PDUFA implementation efforts have reduced product review times and eliminated the earlier lag in availability of new drugs to U.S. patients. The median approval time for priority drug and biologics applications has been reduced from 14 months in fiscal year (FY) 1993 to a median of six months in FY 2006. Priority applications are those for new drugs offering a

significant advance over existing treatments. Applications for drugs similar to those already marketed are designated “standard”. For standard NDAs, the median approval time was 22 months in FY 1993. By FY 2006, the median approval time had declined to 16 months for standard NDAs.

Along with these successes, the drug review program also has faced challenges. Program costs, including payroll and rent-related costs, and review workload continue to grow as more companies seek FDA advice during drug development, requesting meetings and special protocols assessments from FDA. This increased workload has not been reflected in the current fee adjustments.

The volume of post-market safety reports also has grown and has put a strain on our post-market capacity. For example, the number of reports of serious and unexpected adverse events has jumped by more than 65 percent in 3 years, from 129,000 reports in 2002, to 214,000 in 2005. PDUFA currently allows for fee-supported post-market activities, but that support is restricted to the first three years after marketing approval and it applies only to drugs approved after October 1, 2002. A recent analysis of safety-related labeling changes has found that the majority of those changes occur after the product has been on the market for three years.

FDA RECOMMENDATIONS FOR PDUFA IV

We have developed our recommendations in a manner designed to solicit broad and repeated public input. We began to seek public comment on PDUFA reauthorization at a public meeting in November 2005. We also had follow-up meetings with patient groups, consumer groups and healthcare professionals during 2006. Some participants expressed concern about

reliance on user fees. Almost all expressed support for more FDA resources to keep the review process strong and adequately staffed. And virtually all expressed the view that PDUFA should provide increased funding for post-market safety. Many of the public stakeholders who talked to us also expressed the view that FDA should expand its capacity to review direct-to-consumer (DTC) advertisements.

During 2006, we also held discussions with representatives from the pharmaceutical and biotechnology industries. In those discussions, we raised the concerns we heard in our meetings with other stakeholders, as well as our own concerns. The proposed changes we are recommending respond to many of those concerns and address FDA's goals for PDUFA IV.

1. ENSURE SOUND FINANCIAL FOOTING

Our first recommendation is to put the new drug review program on a sound financial footing. User fees have provided substantial resources to FDA, but these resources have not kept up with the increasing costs of the program due to inflation and the expanding review workload. The PDUFA III provisions for annually adjusting fees for inflation and workload have not adequately accounted for actual growth in costs and workload. Therefore, we are proposing changes to the PDUFA financial provisions to correct for these shortcomings.

In terms of payroll costs, PDUFA currently allows for adjustments for federal pay increases, but not full payroll cost increases, which would include the cost of employee health benefits, retirement benefits and other payroll compensation costs. While federal pay increases have grown at an average of 4.2 percent over the past 5 years, total payroll costs for FDA have grown at an average annual rate of 5.8 percent. In PDUFA IV we recommend changing the calculation of inflation adjustment to include the actual FDA rate of increase in total payroll

costs –including salary and benefits per full-time equivalent (FTE)--over the most recent 5-year period.

Rent and rent-related costs have also been increasing. Between fiscal year 2001 and 2005 rent and rent-related costs have gone up over 21 percent per FTE and these cost are expected to increase as we continue to move to the White Oak facility. Part of this cost reflects the increased building security requirements during recent years. We did not account for this cost growth in our current annual fee adjustments.

In addition, fee adjustments for workload should more accurately reflect the full scope of FDA review activities. For example, since FY 2000, meetings scheduled at the request of drug sponsors grew by 72 percent, up to 2,288 meetings in FY 2006. This figure translates to more than nine formal meetings per business day. But the current workload adjuster does not account for this dramatic increase. We recommend that the PDUFA IV workload adjuster be refined to include adjustments for growth in the number of meetings and special protocol assessments for investigational new drugs, and growth in the volume of labeling supplements and annual reports submitted for FDA review.

To pay for these proposals for sound financial footing, as well as for enhancements to pre-market and post-market review, that will be discussed shortly, we are recommending that PDUFA fees be increased by \$87.4 million per year. This increase yields a total of \$392.8 million in user fees in FY 2008. However, I note that this total is calculated based on the PDUFA workload through June of 2006. We expect that the final total would be higher once we have the workload data through June of 2007. We've estimated that with that 2007 data, the total fee funding during the first year of PDUFA IV would be on the order of \$437.8

million. This amount would be adjusted in later years based on measured changes in inflation and workload.

The recommended increase of \$87.4 million would include \$17.7 million to pay for salary and benefit increases; \$11.7 million to pay increased rents and rent-related costs like security, and a share of the costs of FDA's move to the new White Oak facility in Silver Spring, Md. The proposed increase also includes \$20 million to cover significant increases in the drug review workload that were incurred but not compensated for under PDUFA III. These costs could be supported under PDUFA IV, and these costs are expected to continue.

The recommended increase of \$87.4 million also includes \$37.9 million in enhancements to the drug review program. These would be in two basic areas: First, proposed enhancements to the pre-market review process. Second, proposed modernization of the post-market safety system. I'll next describe proposed enhancements to the drug review program, covering these two basic areas. Then I will turn to a proposed new program to assess user fees for advisory reviews of DTC television ads.

2. ENHANCE PROCESS FOR PRE-MARKET REVIEW

For PDUFA IV, FDA recommends enhancements in two areas for the pre-market review process: 1) expanding the implementation of Good Review Management Practices (GRMPs) developed under PDUFA III and 2) undertaking some additional initiatives designed to help expedite drug development. In the area of GRMPs, we propose to further implement the principles and goals for enhancing the efficiency and effectiveness of our review process that were outlined in our 2005 guidance document, *Guidance for Review Staff and Industry on Good Review Management Principles and Practices for Prescription Drug User Fee Act*

Products. We would expand the implementation of GRMPs by developing a planned timeline for the review of the application with particular attention to elements such as 1) discussion of labeling and post-marketing study commitments; 2) decision-making; and 3) documentation of such decisions in the administrative record by the signatory authority. By providing such a timeline, applicants will better understand FDA's review plan and when to expect feedback from the Agency on important issues such as application deficiencies, labeling, and post-marketing study commitments.

The PDUFA IV proposal also includes an increase of \$4.6 million in user fees to fund additional staff to further enhance the science base of our review processes and to develop guidance documents to assist in clinical drug development, including several guidances related to clinical trial design. Clarifying FDA's expectations on important topics such as clinical trial design will enable the industry to focus their efforts on useful trials and decrease less useful experimentation. Increased resources also would free up reviewer time for greater participation in scientific training and research collaborations that will ultimately help clarify regulatory pathways for development of promising future therapies.

Lastly, the PDUFA IV proposal includes a \$4 million increase in funding to further improve the information technology (IT) infrastructure for human drug review, to move FDA toward an all-electronic drug review system.

3. MODERNIZE AND TRANSFORM THE POST-MARKET DRUG SAFETY SYSTEM

FDA would also use the proposed PDUFA IV funds to 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 would include \$29.3 million and hiring 82 additional staff for post-market safety activities. This would triple the amount of user fee funding available to improve the post-market drug safety system. We also propose to eliminate the current statutory time limit that restricts user fee funding of 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 limitation will provide enhanced funding for the assessments of drug products over time, to adequately manage drug risks, regardless of a drug's approval date. Among other initiatives described below, FDA would use the increased funds to further enhance and improve communication and coordination between FDA pre-market and post-market review staff, a key recommendation made by the Institute of Medicine in their September 2006 Report.

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 procure external 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. Such studies would attempt to answer central questions related to: 1) the number and types of safety concerns that are discovered by various types of adverse event collection; 2) the age of the medical products at the time such safety concerns are detected; and 3) the types of actions that are subsequently taken and their ultimate effect on patient safety.

The proposed funds also would be used by FDA 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 obtaining access to additional drug safety information beyond that discovered through spontaneous adverse event reports, including population-based epidemiological data and other types of observational data resources. In addition, fees would support additional training for our current staff, and hiring additional epidemiologists, safety evaluators, and programmers who can best use the existing and new adverse event information.

PDUFA IV also would allow us to develop a plan to evaluate current risk management plans and tools. We would hold a public workshop to obtain input from academia, industry and other stakeholders regarding the prioritization of the plans and tools to be evaluated. The evaluation would include assessments of the effectiveness of identified Risk Minimization Action Plans (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.

We would also 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 a safety workflow tracking system, to support access to and analyses of externally linked databases, and to enhance FDA's AERS and surveillance tools.

4. REVIEW OF DIRECT-TO-CONSUMER (DTC) ADVERTISING

We also are proposing a new program to assess fees for advisory reviews of DTC television advertisements. Research has shown benefits associated with DTC prescription drug television advertising, such as informing patients about the availability of new treatment options and encouraging patients to see a physician about an undiagnosed illness. However, some have expressed concerns that DTC advertisements may overstate benefits or fail to fairly convey risks.

Currently, companies have the option of submitting their planned advertisements to FDA for advisory review before public dissemination. This approach provides the benefit of FDA input on whether or not the advertisements are accurate, balanced, and adequately supported, enabling advertisements to be changed, if necessary, before they are shown to the public.

Companies recognize the benefits this advisory review mechanism offers. However, though FDA's DTC advisory review workload has been steadily increasing, our staffing for this activity has remained relatively level.

Therefore, we propose creating a separate program to assess, collect, and use fees for the advisory review of prescription drug television advertisements. These user fees would not be funded by application, product, or establishment fees assessed under PDUFA. Instead, these

new fees would be assessed separately and collected only from those companies that intend to seek FDA advisory reviews of DTC television advertisements. This program would provide for increased FDA resources to allow for the timely review of DTC television advertisement advisory submissions and ensure FDA input on whether or not the advertisements are accurate, balanced, and adequately supported.

To ensure stable funding for the program in case the number of advisory submissions fluctuates widely from year to year, the program would assess a one-time participation fee to be placed in an operating reserve. The program would then charge fees each year for each advisory review requested. These new fees would provide sufficient resources for FDA to hire additional staff to review DTC television advertising submissions in a predictable, timely manner. FDA anticipates collecting \$6.25 million in annual fees during the first year of the program (and a similar amount to go into an operating reserve fund) to support 27 additional staff to review DTC television advertising. Advisory review fee amounts would be adjusted annually for inflation and to take into account increases in workload. As part of this program, FDA is proposing to commit to certain performance goals including review of a certain number of original advisory review submissions in 45 days and resubmissions in 30 days. The goals would be phased in over the 5 years of the program to allow for the recruitment and training of staff.

CONCLUSION

PDUFA III expires on September 30, 2007 and I want to re-emphasize the importance of achieving a timely reauthorization of this law. FDA is ready to work with you to accomplish this goal. If we are to sustain our record of accomplishment under PDUFA III, it is critical

that the reauthorization occur seamlessly without any gap between the expiration of the old law and the enactment of PDUFA IV. Any delay in the reauthorization of this program could trigger erosion in our work force, particularly among senior reviewers whose skills are in very high demand. The repercussions of such a loss would be with us for years to come.

Thank you for your commitment to the continued success of PDUFA and to the mission of FDA. I am happy to answer questions you may have.