Alan Goldhammer, PhD
Deputy Vice President,
US Regulatory Affairs

PhRMA

February 23, 2007

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: FDA Proposal for Reauthorization of the Prescription Drug User Fee Act; 72 Fed. Reg. 1743 (January 16, 2007), Docket No. 2007N-0005

Dear Sir or Madam:

The Pharmaceutical Research and Manufacturers of America ("PhRMA") is pleased to submit these comments on the Food and Drug Administration's ("FDA's") proposed recommendations for the reauthorization of the Prescription Drug User Fee Act ("PDUFA") program for fiscal years ("FY") 2008 to 2012. PhRMA is a voluntary, non-profit trade association that represents the country's leading research-based pharmaceutical and biotechnology companies, which are devoted to inventing medicines that allow patients to lead longer and more productive lives. Investing almost $40 billion annually in discovering and developing new medicines, PhRMA companies are leading the way in the search for cures.

PhRMA is pleased to support the FDA's proposal for the reauthorization of PDUFA, which includes important new provisions and resources to enhance and modernize the drug safety system; increase FDA's oversight of direct-to-consumer advertising; and facilitate the timely review of innovative medications. While PhRMA and its member companies would rather see FDA's review functions funded primarily through general appropriations rather than user fees, we recognize that longstanding federal budget constraints in this area currently require that FDA be adequately funded in other ways to perform its critical functions of expediting the development of life-saving medications while protecting the public health. PhRMA supports the FDA's current proposal even though it includes substantial increases in user fees because in the end these increases benefit patient access to medicines that save and improve their lives. PhRMA encourages FDA to work with Congress and all stakeholders over the next several years to explore options for reducing or eliminating the Agency's reliance on industry user fees by the time the PDUFA program is scheduled for reauthorization in 2012.

Importance of the PDUFA Program

Since its original passage in 1992, PDUFA has been a crucial program not only for FDA and the pharmaceutical industry, but also – and most importantly – for patients. Prior to passage of PDUFA-I in 1992, the average review time for a new drug application ("NDA") had increased to over 30 months, and there was a significant backlog of pending NDAs at the Agency. As a result, life-saving medications routinely were available to patients in Europe well before they were available to patients in the United States. With the increased funding provided under the PDUFA program, FDA was able to hire additional staff and quickly eliminated the backlog of pending NDAs. In addition, FDA made great strides to complete its reviews of new NDAs in a more timely manner, which not only added predictability to the drug review process but more

importantly benefited patients by providing quicker and more widespread access to life-saving medications, such as treatments for HIV infection.

The PDUFA program was reauthorized in 1997. In PDUFA-II, the program was enhanced by increasing FDA resources in return for improved interactions during the drug development process. In particular, PDUFA-II sought to improve the drug development process by facilitating meetings between FDA and drug sponsors and increasing opportunities to obtain FDA reviews of research protocols. In addition, funding was provided to improve the Agency's information technology ("IT") infrastructure, providing the basis for electronic regulatory submissions. Finally, the target for reviewing a standard NDA was enhanced from twelve months to ten months.

The PDUFA program was reauthorized again in 2002 with little controversy. PDUFA-III once again increased FDA's resources to address the need for the drug review program to remain on a sound financial footing. Importantly, the PDUFA-III agreement committed substantial new funding to enhance FDA's ability to ensure drug safety and to increase the staffing in FDA's Office of Drug Safety. As a result of this new funding, FDA was able to develop concepts relating to risk management for prescription drugs throughout a product's lifecycle.

It is important to stress that throughout the PDUFA programs of the past 15 years; the exacting standards by which FDA evaluates NDAs have been maintained and, as a result of increased funding for drug safety, even strengthened. With more resources provided by PDUFA, FDA has been able to complete its rigorous reviews more quickly and efficiently while maintaining its high standards for safety. That tradition continues with the latest FDA proposal for the reauthorization of the PDUFA program.

FDA's PDUFA-IV Proposal

The Agency's PDUFA-IV proposal contains important new provisions and resources to:

- enhance and modernize the FDA drug safety program,
- add a new user fee program to give FDA additional resources to review and provide advisory opinions on direct to consumer television advertisements,
- improve drug development, and
- provide more stable financing for the program.

Although the industry-funded part of the drug review process will increase during the PDUFA-IV years, patients will be well served by a more predictable drug review process and assurance that the excellent drug safety office within the Agency will be enhanced and modernized.

PhRMA believes that the substantial new funding provided to enhance and modernize the FDA drug safety system– nearly $150 million dollars over the next five years – will continue to assure that FDA's pre- and post-market safety assessment system is the world's gold standard. PhRMA believes that this PDUFA agreement substantively addresses all relevant recommendations of the IOM Drug Safety report.

As the IOM Report recommends, the PDUFA-IV proposal will provide additional resources to reduce FDA's reliance on the spontaneous reporting of adverse events and increase use of modernized techniques and resources, such as epidemiology studies and large medical

databases, to identify risks more quickly and accurately. The FDA's PDUFA proposal also provides funds to allow FDA to develop guidance on best epidemiology practices that will serve as a base for agency, academia, and industry use. This guidance is intended to serve the public's interest by assuring that studies reporting drug-associated signals of risk do so based on defined minimum scientific standards. FDA and industry also need a process to identify risk management and risk communication tools that are effective. Industry will benefit by having a list of risk management tools that work, simplifying the development of drug-specific risk management plans. This PDUFA agreement provides resources to accomplish this.

Significant resources are spent by companies late in a drug's life cycle monitoring for adverse events. It is rare that significant new safety issues are identified this late and such resources could be better allocated to other drug safety activities. FDA will also conduct research during PDUFA-IV to determine the best way to maximize the public health benefit associated with collecting and reporting adverse events.

A key patient safety initiative is the allocation of a portion of this funding to improving the trade name review process. Trade names are reviewed within FDA's drug safety office to help ensure that new trade names cannot be confused with existing trade names in an effort to reduce possible medication errors. FDA will now have additional resources to review trade names during drug development and provide industry with guidance on "good naming practices." This will improve the predictability of the trade name review process.

The FDA's PDUFA proposal also includes a new user fee for direct-to-consumer television advertisements. In 2005, PhRMA issued a set of voluntary guiding principles regarding direct to consumer advertising. In those guiding principles, PhRMA member companies committed to submit all new direct-to-consumer ("DTC") television advertisements to FDA prior to public dissemination to ensure that FDA's suggestions could be addressed before the advertisement was seen widely by the public. The proposed new user fee would ensure that FDA has the necessary resources to review pre-submitted DTC television advertisements in a timely and predictable manner prior to public dissemination. This, in turn, will create incentives for companies to voluntarily submit advertisements prior to public dissemination, consistent with PhRMA's Guiding Principles. PhRMA thus supports the proposed new user fee for DTC television advertisements.

The PDUFA-IV proposal also continues forward with suggested improvements to the drug review process. FDA will implement the good review management principles that were formulated during PDUFA-III. FDA will communicate to sponsors a timeline for discussing labeling and post-market commitments in advance of the action date. This will improve the predictability of the drug review process and lead to more meaningful post-market studies that are appropriate for the new drug.

Funding is also allocated for the purpose of expediting drug development. This will permit FDA staff to be directly involved in external activities such as partnerships and consortia that are generating data and information that will create new paradigms for drug development. In return, FDA commits to developing draft guidance in areas related to safety assessment, clinical trial design, and the use of biomarkers. In addition, FDA will participate in workshops and other public meetings to explore new approaches to a structured model for benefit/risk assessment. The results of these interactions will be used to assess whether pilot(s) of such new approaches

can be conducted during PDUFA-IV. Collectively, this will lead to new paradigms for drug development leading to earlier patient access of important therapies.

Finally, there are a number of proposed technical adjustments for financing the PDUFA program over the next five years. It is PhRMA's hope that collectively these will provide the sound financial footing needed to continue keeping FDA's drug and biological review program strong.

In conclusion, PhRMA supports the FDA's PDUFA-IV proposal. The PDUFA program is vital to ensuring that FDA has the necessary resources to perform its critical functions of fostering drug development and innovation and protecting the public health. The PDUFA-IV proposal in particular will provide FDA with substantial new funding to enhance its oversight over drug safety and DTC advertising while ensuring that the drug review program is as robust and efficient as possible so that patients are not left waiting for needed cures.

Sincerely,