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STATEMENT OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

PRESCRIPTION DRUG USER FEES ACT

FOOD AND DRUG ADMINISTRATION STAKEHOLDER MEETING

PANEL I – PUBLIC HEALTH MISSION

DECEMBER 7, 2001

Good morning. Thank you for the opportunity to present the views of the nation's pharmacists on the Prescription Drug User Fee Act (PDUFA) program. I am Susan C. Winckler, RPh, JD, Group Director of Policy and Advocacy for the American Pharmaceutical Association, the national professional society of pharmacists. APhA represents more than 50,000 pharmacists, pharmaceutical scientists, pharmacy students, and pharmacy technicians. As the health professionals who work closely with patients and their medications (including prescription and over-the-counter medications and dietary supplements) every day, pharmacists rely on a credible drug review and approval process by the Food and Drug Administration (FDA).

My comments will focus on the questions posed by the Agency for today's discussion. Specifically, I will address whether or not the PDUFA program has supported the Agency's mission to promote and protect the public health, and how PDUFA could be enhanced if the program's focus was expanded to fund other Agency activities that ensure medications in the American marketplace are safe and effective.

Support of the FDA Mission

As part of its mission, the FDA is responsible for promoting the public health by promptly and efficiently reviewing clinical research and taking appropriate action on the marketing of regulated products in a timely manner. Through the new drug approval process, the Agency reviews and approves new, beneficial therapies. Prescription drugs are a valuable tool in the prevention and management of chronic illness and disease. The FDA and the drug approval process serve as a vital safety component in the development and marketing

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of new pharmaceuticals. Pharmacists, physicians, and patients look to the FDA to ensure that new medications are only brought to the market upon completion of a comprehensive, high-quality review.

Revenue generated by the PDUFA program has allowed the Agency to increase staffing levels and enhance the resources allocated to the application process for human drug and biologic products. Within the first five years of PDUFA's enactment, the Agency was able to increase its review staff by 60%. Financial resources for the Agency's review activities also experienced a nearly three-fold increase—rising from $120 million in 1992 to an estimated $329 million in fiscal year 2002.

The increased level of resources has clearly had an affect on the time required for Agency decision. Under PDUFA, the average approval time for standard new drugs and biologics applications has dropped from 23 months to 15 months; and the average approval time for priority new drug applications has dropped from 1 year to 6 months. However, the Association understands that due to an increase in the number of new drug applications, the increasingly stringent annual review goals required by PDUFA, and funding levels that were lower than anticipated, it has been increasingly difficult for the Agency to sustain the improvement achieved in prompt review of new drugs.

According to the *Federal Register* notice for this meeting, approval times for applications have begun to increase. In 1999, 35 new molecular entities were approved by the Agency. However by 2000, the number had decreased to 27 and continues to decrease in 2001. The reason behind the increase in approval time appears to be increased workload generated by the rising number of applications submitted to the Agency and the shorter time periods for required Agency action.

It is evident that the amount of revenue generated by PDUFA fees is not adequate for the Agency to maintain its shortened review times and meet increasingly stringent performance goals. Overall funding for the drug application review process—from fees

and appropriations—must be increased to keep pace with the expected expansion of new molecular entities and the emergence of pharmacogenomics. It is unacceptable that funding for a program as important as our drug review process was insufficient to keep pace with mandatory across-the-board pay increases. Additional appropriations must be provided to the Agency to properly fund vital public health programs.

While the PDUFA program has helped the Agency meet its mission to promptly and efficiently review clinical applications, it appears that current levels of funding are not adequate for the FDA to sustain these gains and continue to approve drugs efficiently without compromising review quality and safety.

Expansion of PDUFA Funding for Other Activities

The Agency's responsibilities do not end when the drug applications are approved. The Agency is also responsible for monitoring drug performance after approval. The PDUFA program could be enhanced if it was expanded to fund other activities related to the overview of direct-to-consumer advertising (DTC) and post-marketing surveillance. Both activities are crucial to the Agency's mission to protect the public health by ensuring that drugs are safe and effective.

Direct-to-Consumer Advertising

The PDUFA program does not currently provide funding for the review of DTC advertising. Oversight of direct-to-consumer (DTC) advertising activities should be added to the scope of PDUFA-funded activities. The prevalence of DTC-advertising is obvious to any of us watching television or reading magazines—a recent survey by the Kaiser Family Foundation found that 91% of all Americans have seen or heard a DTC advertisement for a prescription drug[1]—but the benefits and potential risks of this expansion are not so readily observable. It is unclear if consumers retain adequate information from a DTC ad, including a clear understanding of the drug's risks and benefits. Are DTC ads increasing consumer and health professional dialogue? Has

[1] Kaiser Family Foundation. "Understanding the Effects of Direct-to-Consumer Prescription Drug

the explosion of DTC advertising yielded an improvement in medication use, either through improved compliance or by stimulating consumers to seek medical care for untreated conditions? Or, by contrast, has the DTC explosion yielded an increase in the "casualness" with which our society perceives medication—that there is a tablet to treat everything, and all I must do is ask my doctor to get it? These questions must be answered.

The Agency recently announced an initiative to survey physician and patient attitudes toward DTC promotion of prescription drugs. While APhA strongly recommends that the Agency expand the survey beyond physicians to include pharmacists and other members of the health care team, APhA appreciates the Agency's efforts to examine the effects of DTC advertising on both the public and health care practitioners. An assessment of the impact of DTC advertising on medication use, including prescribing, patient compliance, etc. is essential—and should be a component of PDUFA-funded activities. Such activity is important to support the Agency's mission to promote and protect public health.

Post-Marketing Surveillance

Post-market monitoring activities are also not funded by the PDUFA program. APhA supports the expansion of PDUFA-funded activity to include enhancements in post-marketing surveillance. Close monitoring of newly approved drug products is crucial to the Agency's mission to protect the public health. The reality is that some problems—and benefits—of products will not be discovered in pre-approval clinical trials. Medication use in "real life" is far different from the controlled environment of clinical trials, with concurrent use of other medications, OTC products and dietary supplements, as well as personal activities, impacting how medications actually work. Identifying the risks and benefits of medication use in "real life" will likely not benefit from a slower review time: only assessment of extensive use of the medication will identify some problems and benefits of therapy in actual consumer use.

Advertising, and Prescription Drug Trends—A Chartbook Update." November 2001.

Rigorous post-marketing surveillance and early detection of potential problems is particularly important as the number of new molecular entities introduced first in the U.S. has increased substantially since PDUFA was enacted. According to the Tufts University Center for the Study of Drug Development, 80% of new molecular entities received FDA approval within their first year of introduction on the world market during 1996-1998, compared to only 43% from 1991 to 1995. While the FDA approval of new molecular entities brings new drug therapies to the U.S. first, it also brings the Agency an added responsibility since significant adverse events will likely be first detected here.

Providing the Agency the resources to closely monitor newly approved drug products during the first few years the product is marketed could help identify potential problems before serious, widespread patient harm occurs. In the last 20 years, 14 drugs that had received FDA approval and were on the market were later withdrawn for safety reasons. For example, Propulsid® (cisapride) was approved in 1993 for treatment of severe nighttime heartburn in patients with GERD. Seven years later the drug was withdrawn after adverse event reports showed evidence that the drug caused an abnormal heart rhythm in many patients—some of which resulted in the patient's death. However, a majority of patients experiencing adverse events had identifiable risk factors such as pre-existing heart disease or were taking multiple medications. Also in 2000, the irritable bowel syndrome medication Lotronex® (alosetron hydrochloride) was taken off the market after adverse event reports showed evidence of ischemic colitis—intestinal damage resulting from reduced blood flow. Although the drug was only indicated for diarrhea-predominant IBS, many of the adverse events were found in patients with constipation-predominant IBS who should not have received the medication. In these situations, patients lost access to a number of valuable medications because the health care system failed to appropriately manage risk.

This reality creates an opportunity for pharmacists and the FDA to work together, focused on the profession's goal to help patients make medications work. There are two problems in the important function of post-marketing surveillance at the Agency. First, FDA does not receive a sufficient number of adverse drug reports; far fewer than expected compared to published reports regarding the amount of morbidity and mortality associated with drug use. The Agency needs to work with prescribers, pharmacists, and consumers to promote swift reporting of all adverse events to FDA.

Second, simply increasing reports does not fix the situation. The current adverse event reporting system is insufficient as a strategy to identify adverse effects and problems with appropriate prescribing and use of pharmaceuticals. FDA's current system for identifying unknown adverse effects of prescription drugs suffers from a lack of resources to analyze and respond to reports received by the Agency. Use of PDUFA funds to improve this activity is vital to maintain the integrity of our drug review system, a system that relies on surveillance to identify, analyze and communicate adverse effects of products in "real life". Pharmacists have demonstrated that their active participation in Phase IV studies produces valuable data about the safety and effectiveness of approved products. APhA would like to work with the Agency to use this promising mechanism more often when products are approved.

An additional component of post-marketing surveillance would be a new system for higher-risk prescription pharmaceuticals. Developing a standardized process to work with medicines or devices demanding special attention helps manage risks and optimize medication use. An enhanced risk management system should be developed through a cooperative effort among stakeholders including prescribers, manufacturers, pharmacists and patients. The system would involve a standardized process to work with products identified as drugs that demand special attention from clinicians and patients. Health professionals would know that a drug in the high-risk category bears special or unusual risks that require close monitoring—and a common system would allow pharmacists and prescribers to build these services into their practices. Such

programs might limit medication access to those pharmacists and other providers willing to meet legitimate use and monitoring requirements—but would not arbitrarily limit health care provider participation.

Thank you for the opportunity to prevent the views of the nation's pharmacists. Again, let me express our support for the PDUFA program and its ability to support the FDA's mission to promote and protect public health. I will close by underscoring our recommendations for increased funding for the review process. However, managing the risk of the powerful technology we call medications is not simply a function of the approval process—the risk must be managed when consumers use these products in real life. Pharmacists are essential to that management, and we look forward to continuing to work with the Agency, consumers and other health care professionals. Thank you.