

Docket Management

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Commentor	Dr. Gary Stein	Date/Time	2002-01-25 08:47:48
Organization	American Society of Health-System Pharmacists		
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Questions			
1. General Comments	<p>The American Society of Health-System Pharmacists (ASHP) is pleased to provide comments on the Food and Drug Administration's (FDA) November 19, 2001, Federal Register notice soliciting stakeholder comments to assist the FDA in evaluating the current PDUFA provisions. ASHP is the 31,000-member national professional association that represents pharmacists who practice in hospitals (including outpatient services), health maintenance organizations, long-term care facilities, home care agencies, and other components of health care systems. The FDA asked three questions in its Federal Register notice: 1. Has PDUFA supported FDA's mission to protect and promote public health? What should be retained or changed to enhance the program? 2. Should PDUFA allow the use of user fee funding to monitor safety after new drug or biologic approval? 3. How can FDA ensure that PDUFA goals are met if there continues to be a funding shortfall? If the funding shortfall persists, should FDA, in order to best protect and promote the public health, set review priorities and, if so, how? Should there be flexibility in setting user fees to cover the increased cost of the program? Public Health and the FDA's Mission The first question that the FDA asked in its November 19, 2001, Federal Register notice is whether PDUFA has supported the FDA's mission to protect and promote public health, and what parts of the PDUFA program should be retained or changed. ? Support? may be too strong a word. ASHP believes that by reducing the amount of time that new products spend in the drug approval process, resources generated by PDUFA have, indeed, supplemented the resources the FDA has available to meet its public health mission. Many life-saving therapies have been reviewed for approval in less time than comparable drugs prior to the original enactment of PDUFA in 1992. Earlier access to safe and effective new medicines has expanded the options available to health care professionals in providing care to their patients. However, PDUFA funds have not, nor were they meant to, support FDA's public health mission. They are additional funds for FDA's use in improving the agency's review of new drug products. If any changes are</p>		

needed in PDUFA reauthorization legislation, they must be changes that include funding for the consumer safety aspect of the FDA's public health mission. In reauthorizing PDUFA, Congress must consider the impact that faster drug reviews have on consumers' health care providers and patients' and fund FDA programs, such as postmarketing surveillance and monitoring Direct-to-Consumer advertising, that relate to the safe use of medications. Monitoring Safety In its second question, the FDA asked whether user fees should be used to fund safety monitoring after a new drug or biologic is approved. ASHP believes that the PDUFA performance goals need to appropriately reflect all FDA functions related to a drug's appearance in the marketplace -- from pre-approval review, through postmarketing surveillance and advertising. The most consistent message ASHP hears from its members is that the FDA should be doing more to assure that drugs are safe for patients, and Congress must evaluate and appropriately fund the increasing financial needs of the FDA to meet its responsibility of protecting the American public from a potentially dangerous drug supply. The extensive amount of time and effort Congress has expended focusing on the implications of the 1999 Institute of Medicine report, *To Err is Human -- Building a Safer Health System* should be matched by Congress's recognition that it will take appropriate funding for the FDA to implement the programs the agency intends to put in place to meet its portion of the recommendations of that report. Funding for FDA core functions could be in the form of direct appropriations to the agency for those functions, or through redefining PDUFA to allow those functions to be funded by user fees. Pre-approval safety review Monitoring for drug safety is appropriate during FDA's review of New Drug Applications. In particular, there needs to be a better balance of the risk/benefit of drugs before approval. Safety issues must be anticipated through premarket evaluation. Perhaps one specific, new performance goal that should be considered is for the FDA to engage pharmacists, physicians, nurses, and human factors experts in documented failure-mode-and-effects analyses of prospective product nomenclature and labeling to minimize the opportunities for sound-alike names and look-alike packaging for causing medication errors. Later this year, the FDA will issue a proposed regulation requiring bar-codes on human drug and biological products. The bar code would contain information about the product that will help reduce the number of medication errors. ASHP believes that user fees should be used in a pre-approval program to ensure that appropriate bar-coding appears on the appropriate dosage forms of drug products. Increased reliance on restricted drug distribution systems for new, high-risk drugs is a growing concern. These systems often exclude individual hospital as well as community pharmacies from distributing medications and use other means of distribution to deliver medications directly to patients, either

through a central mail-order pharmacy, a patient's physician, or through the manufacturer itself. Pharmacists are responsible for ensuring an ongoing supply of drug products for patients. Any restricted distribution or special handling procedure that disrupts that central oversight role of pharmacists represents an interruption in standard medication-use policies and procedures in the health-system setting. Disruptions and non-standardized distribution processes are not trivial matters; they create procedural confusion for pharmacy and other hospital staff and increase the potential for mistakes. If a manufacturer wants a restricted distribution of a drug product, the FDA should obligate the company to ensure the ongoing protections of a pharmacist of the patient's choice. ASHP also recommends that, if a restricted distribution system is being considered by the FDA as a condition for marketing approval, practicing pharmacists, professional pharmacist societies, and patients should be consulted before any restricted distribution requirements are imposed on the product. Open hearings, at which patients and pharmacists can express their views concerning the design of such a system and the impact those systems may have on the safety and effectiveness of patient care, may be one mechanism to accomplish this. PDUFA resources could be used for pre-approval evaluation of restricted drug distribution systems. ASHP believes that, rather than unique drug product distribution schemes, the FDA, in consultation with stakeholders including pharmacists, physicians, nurses, other health care professionals, and patients, should develop models for managing patients for whom any high-risk drug product might be indicated and prescribed. Manufacturers should be required to design distribution procedures and supporting patient care materials in conformance with these models. Drug-specific requirements for a model should be developed during pre-approval demonstrations and adjusted over time based on post marketing surveillance. Pre-approval demonstrations should focus on requirements for ensuring appropriate use and monitoring, such as patient work-up and selection, provider and patient education, and patient monitoring. Postmarketing Surveillance Postmarketing surveillance of drug products once they have been approved is an essential, critical program function of the FDA, and use of PDUFA funds is appropriate for this function. Shortened drug reviews have been a boon to the drug industry. However, adverse drug reactions which were undetectable during clinical trials often emerge only when drugs are taken by a much larger patient population. The pharmaceutical industry must take a greater responsibility for the safety of its products throughout a product's life cycle. This is particularly important because of public perception ? through media stories about problems associated with new drugs -- that new drugs are not as safe as older therapies because of faster approval. Congress must specifically authorize PDUFA funding for ongoing, proactive

postmarketing surveillance activities. ASHP does not believe that it was the intent of the manufacturers, the agency, consumers, or Congress to speed up the drug approval process at the expense of appropriate surveillance of adverse drug reactions, drug advertising, or other monitoring functions of the FDA. The fact that the drug approval process has been shortened may lead, in some cases, to discovery of problems with particular drugs that were not seen before the product was in widespread use. Rapid review and approval of new drugs must be predicated on a robust postmarketing surveillance system. Many new drugs need closer monitoring after approval, because of the increased numbers of drugs approved, increased drug utilization, and the increased risks posed by many new drugs. The FDA, however, lacks the resources necessary to analyze and respond to reports of problems relating to new drugs and disseminate that information to healthcare providers. User fees are an appropriate way to fund programs to encourage post-marketing reporting from healthcare providers and consumers and disseminate surveillance information back to prescribers and other healthcare practitioners in a timely and useful manner. ASHP believes that some of the following programs should be funded by User Fees and carried out by the FDA:

- Intense post-marketing surveillance for adverse events.
- In the case of direct-to-consumer advertising of drugs approved through use of PDUFA fees, more work needs to be done to determine if such advertising has improved medication use or has a negative effect on medication use. FDA monitoring has not kept pace with the vast increase in manufacturer spending for DTC advertising, and manufacturers must be held accountable for misleading advertising. User fees should be used to develop a program to foster proportionate communications to health professionals (including physician and other prescribers, pharmacists, and nurses) to ensure that appropriate information about the product's safe and effective use and adequate awareness of the potential for adverse events reach these professionals. In addition, there must be more prominent references to risks/benefits of new products in television, radio, and print advertising, as well as more prominent referrals to physicians and pharmacists in case of adverse events.
- Education of health care professionals on the safe and effective use of newly-approved drugs.
- There should be funding for adequate review of any restricted drug distribution mechanism that would deprive patients of the protections of a pharmacist or physician of the patient's choice during use of a manufacturer's product. This review should include a systematic and objective assessment of whether the restrictive distribution system is meeting its goals. In short, ASHP strongly encourages the FDA to develop a comprehensive, proactive system for postmarketing surveillance of new drugs that is not dependent on volunteer reporting. This program should include

appropriate health professional and consumer education based on findings from that postmarketing surveillance system, and it should be funded through user fees. PDUFA Funding The last question posed by the FDA in the agency's November 19, 2001, Federal Register notice relates to how the FDA can ensure that PDUFA goals are met if there continues to be a funding shortfall. The two most important features of FDA program funding that must be maintained are stability and flexibility. The agency must have stable, predictable resources to meet all of its program goals. PDUFA fees alone will not completely solve the problems in drug approval and review that are faced by the FDA. Lack of appropriate congressional funding for other FDA programs compromises both review quality and drug safety. To achieve the major component of its public health mission (aside from faster approval of drugs), PDUFA funding and congressional appropriations have to complement each other in order for the agency to carry out all of its public health functions. Above all, there should be appropriate funding for the agency's public health functions that have lagged behind in this era of faster drug reviews ? postmarketing surveillance of drug safety, adverse event reporting, and direct-to-consumer advertising. The FDA should also have more flexibility in the use of PDUFA funding. Meeting PDUFA goals should not inhibit the rest of the agency's public health mission. If necessary, PDUFA performance goals should be redefined in terms of all the agency's priorities. ASHP appreciates this opportunity present its comments on PDUFA to the FDA. Feel free to contact me if you have any questions regarding our comments.

EC -9