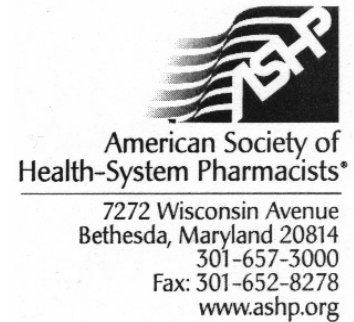


December 12, 2005

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



Docket No. 2005N-0410: Prescription Drug User Fee Act; Public Meeting

To Whom It May Concern:

The American Society of Health-System Pharmacists (ASHP) is pleased to respond to the Food and Drug Administration's (FDA's) notice in the October 18, 2005, *Federal Register* requesting comments on what changes the agency should propose for the next Prescription Drug User Fee Act (PDUFA) reauthorization. ASHP is the 30,000-member national professional association that represents pharmacists who practice in hospitals and other components of health care systems. ASHP members practice in hospitals and integrated health systems where they are involved in many phases of the medication-use process. Their goal is to help prescribers, their institutions and their patients make the best use of medicines. Given this mission, ASHP members are involved in the following activities:

- Establishing drug-use policy through the formulary system and by serving on pharmacy and therapeutics committees,
- Providing drug information to physicians and nurses,
- Managing drug product acquisition and inventory control,
- Preparing drug products for administration to patients (such as compounding intravenous admixtures) and managing drug product distribution,
- Providing frontline clinical pharmacy services, including reviewing medication orders before the first dose is administered, monitoring patients for response to therapy, and adjusting therapy as authorized by the prescriber, and
- Providing specialized clinical pharmacy services in areas such as intensive care, pediatrics, oncology, and emergency care.

In short, ASHP members play a major role in promoting public health by fostering safe and effective use of medicines in hospitals and health systems.

Fundamentally, ASHP believes that the FDA, as a major public health agency, should be appropriated ample funds by Congress to achieve the full scope of its mission. In this way, the American public as a whole would be supporting the vital work of the FDA, which benefits the entire population. However, we recognize that public policy has moved in another direction through the thirteen-year history of PDUFA, and this is unlikely to change in the foreseeable future.

Given this political reality, ASHP strongly encourages Congress to use the tool of user fees to make the necessary resources available to expand FDA's focus on drug safety issues. While ASHP is pleased that the PDUFA program continues to support the FDA's mission to protect and promote public health, and that the 2002 reauthorization for PDUFA III addressed some drug safety issues, we believe that the next reauthorization must go much further in this regard. As PDUFA has allowed faster drug approvals, manufacturers must bear some of the responsibility to provide support for drug safety initiatives.

What we noted in our comments on PDUFA reauthorization five years ago still holds true today -- 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. With many important new drugs entering the market each year, some of which have been fast-tracked through the approval process, FDA's ability to monitor safety has been questioned. Specifically Congress and the FDA should consider allocating significant PDUFA funds for a research program focusing on major drug safety issues with the following three goals:

1. Improve postmarketing safety regulation,
2. Answer important questions about the effect of certain FDA policies and drug manufacturer marketing practices, such as direct-to-consumer advertising, on medication-use safety, and
3. Develop models of patient care that bring actual medication use into better alignment with medication-safety information.

A recent article by Daniel Carpenter of Harvard University in *Health Affairs* in October ("A Proposal for Financing Postmarketing Drug Safety Studies by Augmenting FDA User Fees") notes that there is a "severe undersupply of information on long-term safety" of drug products.¹ Carpenter's solution is to increase user fees to fund new postmarketing safety initiatives. Some of Carpenter's ideas appeal to us, including his suggestion that an FDA advisory panel should be charged with identifying the most important drug-safety topics that merit research supported by user fees. ASHP does not believe, however, that the agency needs to create a new advisory committee to do this. The current Drug Safety and Risk Management Advisory Committee is composed of experts in the field of drug safety, can advise the agency on research topics.

¹ D. Carpenter, "A proposal for Financing Postmarketing Drug Safety Studies by Augmenting FDA User Fees," *Health Affairs* 18 October 2005, <http://content.healthaffairs.org/cgi/reprint/24/6/1571.pdf.w5.469>.

As stated by Carpenter, there are several ways that such research funds could be allocated. These include randomized controlled trials of widely used medications for chronic conditions, studies of the effectiveness of premarket risk assessment, epidemiologic studies of postmarketing safety, research to improve the FDA surveillance infrastructure, studies of the safety implications of direct-to-consumer advertising, methods of improving risk communication strategies, and studies relating to innovations in health care practice that affect safe use of drugs. The results of these studies would be of immense value to ASHP members and other healthcare professionals in their efforts to foster the best use of medicines.

Clinical Trials

This past June, ASHP members in our House of Delegates approved a policy position calling for an expansion of comparative clinical studies on the effectiveness and safety of marketed medications. Pharmacists, other members of the health care team, patients, and private and public payers need objective, authoritative, and reliable evidence in order to make the best treatment decisions. PDUFA reauthorization should support independent research comparing the effects of a particular medication with other medications, or with medical devices, or with procedures to treat a particular disease. A research fund derived from user fees and administered by the FDA could be drawn upon to support these studies, provide oversight to safeguard the integrity of the research process, and disseminate the findings. Such a research program would complement similar work being done by the Agency for Healthcare Research and Quality (AHRQ) as required by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003.

Premarket Risk Assessment

The FDA's goals under the last PDUFA reauthorization included new provisions to develop guidance for industry on good risk assessment, risk management, and pharmacovigilance practices. ASHP is not convinced, however, that drug manufacturers completely understand what should be involved in this process. ASHP has stressed to the FDA over and over again the need for manufacturers to consult with pharmacists when the agency and the manufacturer determines that there is a need to develop a restricted drug distribution system in order to obtain FDA approval for a high-risk drug.

Restricted distribution systems have been designed primarily with retail pharmacy settings in mind. However, thoughtful consideration needs to be given to the fact that some of these medications may be initiated or continued for hospitalized patients.

Hospital pharmacies may not be able to acquire these medications in a timely manner within the procedures of a restricted distribution system. This has an adverse effect on patient care and cost. Restricted distribution systems make it difficult for hospital pharmacies to acquire these drugs through their normal supplier channels. This pulls resources from hospital systems that are already stressed. Colored “sticker” systems that have been put into place for some high-risk drugs (e.g., Accutane and Lotronex) were not designed with hospital systems in mind. The manufacturer of Accutane acknowledged as much in conversations with ASHP. Because of the variety of procedures and ordering systems used in hospitals by physicians to enter orders and the different procedures and systems for transmitting orders to the pharmacy, the sticker system designed for affixing to the single handwritten prescription blank for ambulatory patients just won't work in hospitals.

In the years since restricted distribution systems have come into play, only one manufacturer has consulted with ASHP to determine how such a system would function under the supervision of hospital pharmacists. This is certainly not a satisfactory response to the agency's goal. We suggest that PDUFA funds be used to conduct research on how well existing and new restricted drug distribution systems are doing in achieving their goals. New PDUFA reauthorization legislation should mandate that drug manufacturers and the FDA partner with professional organizations in conducting this research

Postmarketing Surveillance

ASHP has long and consistently advocated for better postmarketing surveillance systems. As early as 1996, our House of Delegates approved a policy encouraging research to identify human factors causes of medication errors and opportunities for their prevention. We believe that pharmacists are especially positioned to provide leadership in medical error reporting programs.

The FDA needs sufficient resources to fully implement the depth of programs necessary to prevent injury and save lives. Congress needs to fund the financial needs of the FDA to meet its responsibility of protecting the American public from a potentially dangerous drug supply by implementing programs to further evaluate drug products once they are approved for marketing. The FDA's ability to measure the ultimate safety of a drug once it has entered the market is limited by the fact that the FDA cannot conduct independent clinical trials and by ambiguity about whether the FDA can require manufacturers to conduct such studies. For the FDA to fully understand the adverse effects that may not have surfaced in the limited pre-market test group for an approved drug, it is essential that the FDA be able to require these studies. As an initial step, PDUFA funds could be

used for research on best practices for identifying adverse drug events in the real-world medication-use system..

Direct-to-Consumer Advertising

Some of the resources of a user-fee research fund should be devoted to evaluation of the medication use safety implications of certain FDA policies and industry marketing practices. For example, consider the case of direct-to-consumer (DTC) advertising of prescription medicines. DTC advertising has more than doubled over the last five years. Despite this dramatic expansion in advertising, data on the impact that DTC ads have on the appropriateness of medication use is still negligible. ASHP members have discussed the implications of a delay in DTC promotion until postmarketing data are collected and assessed. ASHP suggests that in combination with this delay, it would be consistent with the FDA's public health mission for the agency to commission research on this topic, and the funding could come from user fees that are allocated to research.

Effective Risk Communication Strategies

While expanded FDA authority to broaden research on clinical trials premarket risk assessment, and postmarketing surveillance is an important start to building a stronger drug monitoring system, it will have limited impact if this information is not made available to the FDA and the public in some way. Disclosure is essential to creating a system of transparency and accountability necessary to promote consumer confidence. The current MedWatch and other existing adverse event reporting systems do not effectively provide the information that health professionals need.

A lot more is known today about the best methods to communicate risk to diverse populations, but the FDA seems not to have focused much attention on developing a more active system. The agency will be holding a public hearing on risk communication strategies later this month, and ASHP will be providing comments in response to the *Federal Register* notice announcing that hearing. In terms of PDUFA reauthorization, however, the agency could benefit from a research program examining methods and mechanisms for effective risk communication by health professionals, including looking

at who -- pharmacists, physicians, industry, etc. -- and where -- in the pharmacy, by telephone, via DTC -- such communication is most effective.

Innovations in Health Care Practice

Finally, ASHP believes that a portion of these research funds should be devoted to studying innovations in health care practice that may improve the safety of medication use. One of the big problems in health care is that insufficient attention is given to evidence about how to use a medication safely. The health policy community has largely ignored the prospect that the profession of pharmacy could play a larger role in addressing this problem.

Consider the situation in which it is well established that a certain laboratory test must be performed periodically to ensure that the patient is not experiencing an adverse effect from a medication. It is easy to contemplate a system, using today's information technology, in which the pharmacy is a final check on whether that laboratory test has been performed. If the test has not been done, a computer-assisted decision tree could guide the pharmacist through a number of options, ranging from a dialogue with the prescriber to a decision by the pharmacist to dispense only a few days' supply of medication until the necessary laboratory work has been completed and analyzed. It would be consistent with the FDA's public health mission to stimulate demonstration projects, in collaboration with AHRQ and possibly the Centers for Medicare & Medicaid Services, on practice innovations that foster safe use of medications, and the funding could come from user fees that are allocated to research.

Conclusion

The reauthorization of PDUFA is an important opportunity for the United States to marshal resources to expand our knowledge about medication safety. Hospital and health-system pharmacists urge the FDA and Congress, in considering reauthorization legislation, to expand the program in this direction. Doing so will give pharmacists firmer ground on which to pursue their efforts to help patients, prescribers, and health care institutions make the best use of medicines.

Division of Dockets Management
Food and Drug Administration
December 12, 2005
Page 7

ASHP appreciates this opportunity to present its comments on PDUFA reauthorization to the FDA. Feel free to contact me if you have any questions regarding our comments. I can be reached by telephone at 301-664-8702, or by e-mail at gstein@ashp.org

Sincerely,

A handwritten signature in black ink, appearing to read "Gary C. Stein". The signature is fluid and cursive, with a long horizontal stroke extending to the right at the end.

Gary C. Stein, Ph.D.
Director of Federal Regulatory Affairs