STATEMENT OF THE ACADEMY OF MANAGED CARE PHARMACY

PUBLIC MEETING

ON

PRESCRIPTION DRUG USER FEE ACT

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PANEL ON POSTMARKET SURVEILLANCE

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DECEMBER 7, 2001

Good morning. Thank you for the opportunity to present the views of the Academy of Managed Care Pharmacy on the Prescription Drug User Fee Act (PDUFA). I am Judith A. Cahill, Executive Director of AMCP. The Academy is a professional organization of pharmacists and associates who practice in managed health care systems. Our members serve patients and the public through the promotion of wellness and rational drug therapy through the application of managed care principles. The Academy has more than 4,800 members nationally who provide comprehensive coverage and services to the millions of Americans served by managed care.

AMCP believes extending the PDUFA user fee program is a necessity. The program has made a significant contribution in securing the financial resources to expedite the Food and Drug Administration's (FDA) drug and biologic review and approvals.

My comments today will focus on whether PDUFA should also allow the use of user fees for the purpose of monitoring safety after a new drug or biologic has been approved.

My observations arise from the Academy's members who have the responsibility of designing and implementing pharmacy benefit management for over 170 million Americans. They are employed by health plans, pharmacy benefit management companies, integrated health care delivery systems, third party administrators and retail pharmacy. Their views are reflective of what the profession of pharmacy encounters in the ambulatory setting.

The fundamental goal of the FDA is to promote and protect the public health by determining in a timely manner a drug or biologic's safety and effectiveness based on clinical research and taking appropriate action on the marketing of these products.

FDA approval does not mean that medications are risk-free. First, approved medications are generally safe and effective and then only when used appropriately. Second, even when used appropriately, there are potential side effects, with health care professionals and the patient making the judgment as to whether the benefits outweigh the adverse secondary effects. Third, problems associated with drugs are sometimes identified either only after a drug has

been on the market and available to a broader population than was tested during the approval process or only after the passage of a certain period of time.

The Academy believes the objective of FDA's postmarket surveillance program must be the ongoing collection and review of data related to problems associated with a drug's use in order to determine if that drug should continue to be marketed to the public (1) under the original approval or (2) under modified marketing requirements (labeling, restricted distribution, etc.) or (3) be withdrawn either permanently or until further studies are conducted. The Agency has the further responsibility of disseminating information regarding any determination that it makes.

Consequently, we consider postmarket surveillance to be an essential programmatic function for the FDA if the agency is to fulfill its mission of promoting and protecting public health.

Pharmacists in the ambulatory setting depend on the FDA to perform its postmarket surveillance responsibility for four principal reasons:

1. The Agency is in the unique position to be able to aggregate data on drugs in the marketplace. The data encompasses a wide range of matters including such items as patient compliance, effectiveness, off-label use, etc., the most important of which is whether there are problems, either minor or serious, associated with the use of a drug.

2. Postmarket surveillance provides expanded data on a drug's performance not available through pre-approval clinical trials. The more we know how a drug functions in the general population, or a segment of the population, the more confidently we can use that information to enhance the care provided to our patients.

3. The dissemination of patient safety information acquired through postmarket surveillance allows health care professionals to minimize risk to the patient, thus improving their ability to achieve the desired therapeutic outcome.

4. The information obtained through postmarket surveillance enhances the ability of health care professionals to assure the appropriate use of a drug and avoid the adverse drug event and the concomitant expenses for treatment that otherwise would have resulted.

Now let us look at each of these points.

First, the Agency's ability to aggregate data. In the inpatient setting, there is the institutional structure that provides a mechanism to collect data on drug use in a systemic way. This is not the case in the ambulatory environment. The highly fragmented nature of health care delivery in this country defies systematic aggregation of adverse drug

events. Only in the most highly integrated health care organizations are there structures and processes in place to allow reporting, collecting, storing, and analyzing of adverse event data that arise from an organization's covered population. These highly integrated health care organizations have the opportunity and capability to perform their own postmarket surveillance for drug safety, but they are not typical.
Notwithstanding what integrated organizations may be able to do, the reality is that most health care organizations look to the FDA to provide vital postmarket surveillance data. Even integrated delivery systems must rely on FDA data to validate the observations that arise out of their own patient populations. Less sophisticated organizations – which are the majority – rely on FDA postmarket surveillance alerts to protect patients.

Second, the data collected after approval is arguably more important than that collected during the drug approval process. The information gained from clinical trials in pre-approval is limited. Studies are conducted in small populations under strictly controlled parameters. The clinical trial data is reviewed and analyzed and the results extrapolated to the population-at-large. It is only when a drug is used in the general population or after the passage of a certain period of time that the real attributes, weaknesses, limitations and/or problems of the product are revealed. The information gained on drugs after approval and in the marketplace is critical to establish guidelines and protocols that will ensure patient safety.

Third, postmarket surveillance data are a vital source of information that health care professionals use to enhance patient care. Nowhere is this more evident than within the integrated delivery system environment.

Integrated delivery systems share postmarket surveillance data with the prescribers who treat their patient populations. Advisories on observed adverse drug events alert health care professionals to concerns associated with the use of a given drug and permit the adjustments of health plan practice guidelines designed to enhance patient care.

Additionally, pharmacy and therapeutics committees employ postmarket surveillance data as one factor in determining whether a drug should be included on the organization's formulary for recommended use by its patient population. FDA reports on experiences with the product gleaned from postmarket observations allow the committees to validate patient reaction within their own populations, weigh the potential harm of a drug versus its potential benefit, make informed decisions about inclusion on the formulary, and identify high risk patients using the drug who warrant close scrutiny. Patients who fall within the high-risk category identified by postmarket surveillance can be targeted for case management to forestall the occurrence of untoward effects of a drug.

Fourth, problems associated with a drug's use - ranging from minor side effects to serious to potentially life-threatening safety problems - directly impact the overall costs of providing health care. Numerous studies in recent years have demonstrated that many physician office visits, emergency room visits, hospital and nursing home admissions, laboratory tests etc. are directly related to adverse drug events and that the resulting costs to the health care system, both in terms of dollars and lost productivity, are substantial –

in the billions of dollars. Clearly, a postmarket surveillance program that identifies the safety problems associated with drug use and effectively disseminates that information to health care professionals not only enhances patient care, but helps avoid adverse drug events and can thus save our health care system significant dollars in unnecessary expenditures.

Where does the responsibility for postmarket surveillance rest?

The federal government, drug manufacturers and prescribers all have responsibility and obligations regarding postmarket surveillance. Until relatively recently, the programs of the FDA were almost entirely focused on the drug approval process. To some extent that has changed and we do believe the Agency recognizes that its role must extend well beyond the approval process if it is to fulfill its mission. On the other hand, legitimate questions can be raised as to whether the Agency has been able to implement and coordinate an effective post-approval monitoring program. Clearly, the overwhelming majority of the resources of the FDA are still devoted to the drug approval process.

Similarly, drug manufacturers must recognize their obligations to assure – throughout the life cycle of their products - the safety of all of their products and that they must be accountable to both the public and regulators in providing those assurances. It is absolutely clear that resources that drug manufacturers devote to postmarket surveillance are miniscule when compared with expenditures associated with pre-market research, securing drug approval and marketing of their products. That must change.

Prescribers are in the most critical position for assessing the problems associated with drug use because of their direct interaction with patients and because of their overall responsibility for monitoring and directing patient care. They need to better understand their responsibility for reporting drug safety problems. Unless the prescriber becomes far more engaged in the postmarket surveillance process, it's potential for success will be limited. The FDA must use its resources to encourage far greater reporting by the prescriber.

FDA, manufacturers and prescribers must be far more proactive in the gathering, evaluating and disseminating of information about drug safety after market approval than they have been.

The Academy of Managed Care Pharmacy makes the following recommendations:

1. FDA's current postmarket surveillance system for identifying previously unknown adverse effects of drugs suffers from a lack of resources – manpower and financial – to collect, analyze and respond to reports received by the Agency. A new user fee imposed on manufacturers should be added under PDUFA and should be designated for an improved and coordinated postmarket surveillance program. Such an earmarked fee is appropriate given the manufacturer's responsibility to provide a drug that is both safe and effective throughout its lifecycle. The funds collected from user fees should be of an amount sufficient to

recognize that postmarket surveillance is as important as the drug approval process and a part of the primary mission of the Agency.

2. Prescribers, pharmacists, manufacturers and health plans are remiss in reporting adverse drug events and other problems associated with a drug's use. The FDA should initiate an aggressive educational campaign targeted at patients and health professionals stressing the importance of and encouraging the reporting of adverse drug events and related problems to the Agency.

3. The FDA should undertake an audit of the notification mechanisms it uses to inform the public and health care professionals of actual and potential safety problems associated with the use of a drug to ascertain if all parties with a need to know are being informed. This assessment should determine whether the communications process has been effective in timely informing those who need to know by providing sufficient and detailed information and appropriate opportunity for feedback and inquiries. We believe there are significant gaps in the system and would point to the pharmacy director at health plans who too often fail to receive appropriate notification from the FDA.

4. Fourth, we suggest policy makers consider the alternative of creating an independent organization responsible for postmarket surveillance, separate from the FDA. The public agency would collect, analyze, and disseminate information about the safety and efficacy of drugs in use in the marketplace. The arrangement would be similar to the one that exists between the Federal Aviation Administration and the National Transportation Safety Board. Both the FDA and the postmarket surveillance agency would serve the public in assuring that safe and effective drugs were available to the public. A separate agency would provide significantly higher visibility to postmarket safety issues and be independent of the decision-making process that originally approved a drug for marketing to the public. The separation of pre and post approval functions would enable distinct, independent assessment of the critical issue of product safety.

The Academy of Managed Care Pharmacy supports changes that would result in a significantly improved and comprehensive program for identifying problems associated with the use of drugs by patients following market approval. We look forward to working with the Agency and other public health authorities to protect patient health by assuring an effective postmarket surveillance system.