Re: Docket No. FDA-2010-N-0128

The Academy of Managed Care Pharmacy (AMCP) is pleased to provide comments to the Food and Drug Administration (FDA) on the proposed recommendations for the Congressional reauthorization of the Prescription Drug User Fee Act (PDUFA) for fiscal years 2013 to 2017. This letter is in response to information presented at the FDA public meeting on PDUFA reauthorization held October 24, 2011.

AMCP is a national professional association of pharmacists and other health care practitioners who serve society by the application of sound medication management principles and strategies to improve health care for all. The Academy's more than 6,000 members develop and provide a diversified range of clinical, educational and business management services and strategies on behalf of the more than 200 million Americans covered by a managed care pharmacy benefit.

The fundamental goal of the FDA is to promote and protect public health both by determining in a timely manner a drug or biologic’s safety and efficacy based on clinical research, and, based on that determination, to approve or disapprove the marketing of these products. An FDA approval does not, of course, mean a medication is risk-free. First, approved medications are generally safe and efficacious only when used appropriately. Second, even when used appropriately, prescription medications have potential side effects. Third, problems associated with drugs may only become apparent after a drug has been on the market and has been used by a broader population for a longer period than was tested during the approval process.

In order to help fund FDA activities, Congress passed PDUFA in 1992 authorizing the agency for a five-year period to collect user fees from drug manufacturers seeking FDA approval of their drugs for marketing. PDUFA was subsequently renewed in 1997, 2002 and 2007. Congress must decide whether to pass another renewal by September 2012.
User fees have been pooled to provide FDA with the funding necessary to hire additional reviewers and to monitor the safety of new drug products post-approval. If the collection of user fees is not reauthorized, Congress will have to establish alternative source(s) of funding for necessary agency activities.

As a member of the Alliance for a Strong FDA, AMCP believes funding the FDA at a dollar level sufficient so it may fulfill its obligation to ensure medication safety is absolutely necessary. The Alliance for a Stronger FDA works to ensure annual appropriations that will adequately fund the FDA’s essential missions. The Academy’s preference is for this funding to be provided in total by the federal government. However, the federal government gives the FDA about $8 per year for each American (an appropriation of $2.457 billion for FY 2011). Absent more adequate funding by the federal government, the Academy supports PDUFA reauthorization.

The Academy’s comments in this letter focus on the areas of postmarket risk management, specifically risk evaluation and mitigation strategies (REMS) and the Sentinel Initiative, and direct-to-consumer (DTC) advertising. The Academy is pleased that postmarket risk management is addressed in the proposed PDUFA reauthorization performance goals and procedure document. The Academy is concerned that DTC advertising was not addressed.

**Postmarket Risk Management**

Although FDA is responsible for evaluating not only a drug’s efficacy but its safety as well, the reality is the drug review process emphasizes "approval" so patients are able to have access to new drugs as soon as possible. The process imposes limitations because of the comparatively limited timeframes and parameters of clinical trials and the relatively small population of subjects tested. Only after a drug has been on the market and available to a broader population can a determination be made as to whether a drug is effective in treating medical conditions and whether there are any safety problems associated with its use. This is the reason postmarket surveillance constitutes a patient safety imperative.

AMCP believes the FDA’s responsibility for medications extends over the life span of the medication. The FDA must stand behind its assurance of the safety of medications not just after initial drug approval but for the life span of the drug. This includes working to ensure that medications are safe throughout their longevity and may occur through fee-supported post-market activities. PDUFA IV initiated this change in the Agency’s recognition of its responsibilities by eliminating time limits on support of post-market risk management. This action is critical to increasing safety of medications after their initial approval. In a presentation on PDUFA IV in 2007, it was demonstrated that the extent of adverse events is not fully realized until more than five years after a medication is approved.

**Standardizing REMS:**

A risk evaluation and mitigation strategy (REMS) is a strategy to manage a known or potential serious risk associated with a drug or biological product. A REMS will be required if FDA finds that a REMS is necessary to ensure that the benefits of the drug or biological product outweigh the risks of the product, and FDA notifies the sponsor. A REMS can include a medication guide, patient package insert, a communication plan, elements

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1 Alliance for a Stronger FDA. [www.strengthenfda.org](http://www.strengthenfda.org) (accessed October 24, 2011)
to assure safe use, and an implementation system, and must include a timetable for assessment of the REMS.\textsuperscript{4} The Food and Drug Administration Amendments Act of 2007 (FDAAA) authorizes FDA to require pharmaceutical manufacturers to submit a proposed REMS as part of an application if the FDA determines that a REMS is necessary to ensure that the benefits of a drug outweigh the risks of the drug. FDA is also authorized to require pharmaceutical manufacturers to submit a proposed REMS if the FDA becomes aware of new safety information and determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks of the drug.\textsuperscript{5}

The Academy supports the concept of risk evaluation and mitigation strategies (REMS) when and as necessary to protect patients from a medication’s risks. With increasingly complex medications in the pipeline, the need to use REMS programs will become more common, and it is therefore important that REMS programs are designed to be manageable for all the concerned stakeholders, including patients, prescribers and dispensing pharmacies.

The Academy supports the provisions proposed by the FDA to measure the effectiveness of REMS and to standardize and better integrate REMS into the health care system. Specifically, AMCP was pleased to see the following provisions:

- By the end of FY 2013, FDA will issue guidance on how to apply statutory criteria to determine whether a REMS is necessary to ensure that benefits outweigh risks
- By the end of FY 2013, FDA will hold public meetings to explore strategies to standardize REMS, where appropriate, with the goal of reducing burden
- By the end of FY 2013, FDA will initiate one or more public workshops on methodologies for assessing the effectiveness and impact of REMS

The efforts listed above will guide important improvements in the operation of REMS programs and the Academy supports these measures.

\textit{Using the Sentinel Initiative to Evaluate Drug Safety:}

With the passage of FDAAA, the FDA was directed to establish the Sentinel System, a network of external entities that would develop electronic databases of health information utilized for surveillance and safety signal evaluation for drugs and other marketed medical products.\textsuperscript{6} FDA’s Sentinel pilot program is now enabling scientists to evaluate safety questions far more rapidly than using traditional channels. The current Sentinel database includes 17 data partners across the U.S., with the majority being managed care organizations, and encompasses the data of nearly 100 million patients.\textsuperscript{7}

One of the concerns with a large-scale sentinel system is the privacy and security of protected health information to be used in a clear and meaningful method only for specified purposes.\textsuperscript{8} The current Sentinel


\textsuperscript{6} U.S. Government Accountability Office. \textit{FDA Has Begun Efforts to Enhance Postmarket Safety, but Additional Actions are Needed}, GAO report Number GAO-10-68, November 2009.


System has proven that the FDA can accomplish active postmarketing surveillance without the establishment of a large centralized database, thereby maintaining the security of protected health information. Through this system, nearly all confidential personal health data can remain with the clinicians or original data holders.9

The ability to capture postmarketing data in real time under the Sentinel System will provide a foundation for the monitoring and communication of adverse events. In order to protect patient safety, the FDA must communicate postmarketing surveillance results in a timely, transparent and appropriate manner to a range of audiences. Priorities for communication with patients should include finding ways of placing information about risks in the context of information about benefits, specifying the degree of certainty in particular findings, and identifying next steps for developing and communicating information that is more definitive. AMCP applauds the FDA’s commitment to create a more transparent and efficient postmarketing surveillance system so stakeholders receive information that is more meaningful.

Managing and monitoring of direct-to-consumer (DTC) advertising of prescription products

In a letter dated May 12, 2010, the Academy strongly encouraged the FDA to include provisions related to DTC advertising under PDUFA V. AMCP is deeply concerned that the FDA has indicated that it will not include provisions related to DTC advertising in PDUFA V. Without such a recommendation, companies continue to have the option of only submitting their proposed advertisements on a voluntary basis to FDA for advisory review before publicly disseminating them. The Academy strongly recommends that the DTC advertising reviews should be required and the requirement should include precise language to provide an extension to all modes of DTC advertising, including media other than television.

The Academy discourages the use of direct-to-consumer advertising that promotes specific prescription drug products, but supports advertisements that educate the public about disease symptoms and available treatment options. Advertising that increases public awareness about disease symptoms, informs consumers about available treatment options and diagnostic procedures that may be of benefit, stimulates discussions between prescribers and patients, and encourages individuals to pursue healthier lifestyles can improve the health status of patients. It does this by encouraging consumers to become more proactive about their health in general, and by fostering constructive dialogue between patients and their providers regarding their care.

AMCP strongly discourages advertising aimed at consumers that promotes the use of specific prescription drug products. In general, such advertisements aim to increase a product's market share or create a new market for the product. Whether or not a prescription item is medically indicated for a given patient, direct-to-consumer advertising of the product can create unwarranted patient demand. The advertisements can often be misleading, failing to sufficiently warn consumers about the potential risks of using the product and about alternative treatment options.

AMCP appreciates the opportunity to comment on the PDUFA reauthorization performance goals and procedure document. If you have any questions, please contact me at (703) 683-8416 or at jcahill@amcp.org.

Sincerely,

Judith A. Cahill
Chief Executive Officer