August 22, 2011

The Honorable Kathleen Sebelius
Secretary
U.S. Department of Health & Human Services
200 Independence Avenue, SW
Washington, DC 20201

Re: Proposed Recommendations for PDUFA V

Dear Secretary Sebelius,

As members of the Patient, Consumer, and Public Health Coalition, which includes nonprofit organizations and individuals that represent patients, consumers, scientists, and researchers, we want to express our concerns and recommendations regarding the results of the Prescription Drug User Fee Act (PDUFA V) negotiations between the FDA and pharmaceutical industry. We appreciate that the FDA shared with us the High-Level of Proposed Recommendations for PDUFA V upon conclusion of their negotiations with regulated industry. After reviewing the recommendations, we offer our comments on the agreement as it stands at this stage of the reauthorization process.

Our main concern is that most of the recommendations are aimed at industry perceived barriers to new drug approvals, rather than concerns about protecting and promoting the health of

patients and consumers by ensuring timely access to safe and effective drugs. We recognize that some of the recommendations have the potential to benefit patients by speeding up the approval process and improving the chances that drugs will be available when they are needed. There is too little emphasis, however, on performance goals aimed at improving the safety and efficacy of drugs. The focus must be on a process that provides timely access to safe and effective drugs while reducing exposure to harmful drugs that pose undue risks. Drugs must only be approved with adequate evidence to support their safety and effectiveness and a robust post-market surveillance system must be in place to ensure that drugs found to be dangerous are removed from the market as quickly as possible.

Summarized below are key drug safety proposals that we would like included in the PDUFA V reauthorization, as well as information about the FDA/Industry negotiated proposals that we support.

Issues Not Discussed during Negotiations

While we appreciate the FDA's efforts to keep stakeholders informed about its negotiations with industry and to solicit our input on the proposals under discussion, we were not present during the negotiations, and as a result, several patient safety and consumer protection initiatives that we put forward were never discussed in the formal dialogue with industry. The constituencies we represent have identified the need for reforms to improve the regulation of direct-to-consumer (DTC) advertising, the adverse event reporting system, and the safety of drugs prescribed off-label (OL). We briefly recap our recommendations here. We believe that HHS should not accept the negotiated settlement without adding these essential provisions.

- **Expand capacity for monitoring of DTC advertising**. There continues to be a dangerous imbalance between the volume of DTC advertising and the resources available for monitoring and reviewing these drug promotion campaigns in a timely manner, particularly in light of the growth of Internet and social media advertising of prescription drugs. The FDA has yet to issue a guidance document to help shape industry practices and protect consumers from inaccurate or inappropriate marketing on websites and through social media tools. Given the growing burden of monitoring drug promotion efforts, it is essential that the FDA be provided with funds to support the staff and resources necessary to ensure that consumers receive a balanced understanding of the drug advertised to them.[1]

- **Improvements to the MedWatch safety information and adverse event reporting program**. Adverse event reports from consumers and clinicians may be the first indication of safety problems that a drug's clinical trial, with its carefully screened population, did not identify. The MedWatch system, however, is cumbersome to use and largely unfamiliar to the public. We support FDA's ongoing process to solicit consumer input on a new MedWatch form but that will not address the most important problem – complaints entered into the MedWatch system are rarely used because of shortcomings in IT capabilities at FDA. More resources are needed to improve the overall MedWatch system, so that this program will fulfill its intended purpose - to serve as an important

[1] Heavey S, *et al*. (2010). Special Report: Outgunned FDA Tries to Get Tough on Drug Ads, *Reuters*, 2.

early warning function in the successful operation of a larger post market safety surveillance system.

- **Evaluate the safety and effectiveness of Off Label (OL) drug uses**. While OL drug use is legal and sometimes beneficial, 73 percent of drugs prescribed for OL use have no valid scientific evidence in support of such prescribing.[2] The FDA should determine where OL drug use is occurring and conduct low-cost, observational research to determine whether the OL use is generally safe and effective. The results of the research could then be used to guide regulatory action and, if the results of the research were made public, prescribers and patients could make more informed choices. This proposal does not in any way prohibit a physician's freedom to prescribe.

Important FDA Proposals That Were Not Included in the Recommendations

We also strongly support a proposal put forward by the FDA, but which is not included in the proposed recommendations because of industry opposition: a proposal to safeguard human subject protection by improving clinical trial oversight. Clinical trials are a critical part of the drug approval process, and ensuring the safety of trial participants is essential to maintaining the international reputation and public health mission of the FDA. We supported the agency's original proposal to build quality systems into trial oversight, and we also believe there is a significant need for increased inspection of trial sites. Ideally, the number of foreign and domestic sites inspected should be at least 10 percent, but assuming that is not affordable, the number should be increased to at least 2 percent.

We recognize and appreciate that the FDA officials involved in negotiations with industry advocated for the inclusion of this important proposal but that industry was unwilling to support it. We ask that you urge Congress to include these additional patient safety proposals.

Drug Safety System Proposals

We are pleased that the recommendations include proposals to improve the Sentinel and REMS systems. We are concerned, however, that they do not adequately describe the reforms that will be needed to implement the necessary changes successfully.

- We commend the agency's progress in developing the Sentinel Initiative. Broader use of an active risk identification and analysis system such as this has the potential to fundamentally transform post-market safety surveillance and dramatically improve the safety of prescription drug use in the United States. We are very disappointed, however, that this proposal does not explicitly commit the agency to scaling up from Sentinel's successful pilot stage to the full and robust system that will enable the FDA to realize this potential. In addition, we are concerned about the focus on expected risks, rather than a broader approach that would enable the Sentinel Initiative to provide preliminary data on unexpected adverse reactions. Lives will be saved if those improvements are made.

[2] Radley, et al. (2006) Off-label Prescribing Among Office-Based Physicians, *Archives of Internal Medicine*, 166: 1021-1026.

- We support the agency's goal of making REMS easier and less expensive for pharmacies and others to comply with – but are concerned that standardization efforts could take away needed flexibility or potentially compromise patient safety. As you know, when it comes to managing the risks of prescription drugs "one size does not fit all." Unique features should be permitted in a REMS to deal with unique situations. We appreciate that the proposal includes mechanisms for public participation in the development of strategies to standardize REMS so that we will have the opportunity to raise these issues as the process goes forward.

Regulatory Science Proposals

We strongly support the "methods for meta-analysis" and "use of patient-reported outcomes (PROs)" proposals and appreciate the planned opportunities for public participation and input during implementation of these proposals.

- We urge the FDA to ensure that its guidance document on meta-analyses be consistent with the best practices set forth in the recent IOM study on this topic, *Finding What Works in Health Care: Standards for Systematic Reviews*.

- We agree there is a need for the FDA to enhance capacity to address submissions involving PRO's and look forward to the public meeting to discuss qualification standards for members of the PRO Consortium, aimed at ensuring strong protections against conflicts of interest.

Finally, a word about the FDA budget overall. For years, the agency has been under-resourced and has struggled to manage expanded demand with inadequate appropriations. The user fee program was designed to provide supplemental funding to the agency for specific services and outcomes, but it was never intended to supplant public funding to meet FDA's mission and statutory responsibilities. Many consumer groups object to these fees because under current law they tend to give priority to industry interests. Regardless, to ensure that the agency has the resources it needs to carry out its critical mission of protecting and promoting the public health, we will continue to advocate with the Congress for increased appropriations funding for the FDA.

In conclusion, we believe that the proposed recommendations must do more to ensure the safety of patients and consumers and the scientific integrity of the drug review process. We appreciate the efforts of the agency to work toward those ends, but as long as patients and consumers are excluded from the PDUFA negotiations, the concerns and priorities of these principal stakeholders will get less attention than they deserve. We ask the Obama Administration to stand up for these excluded interests and improve the PDUFA V proposals by supporting the proposals discussed in this letter and by ensuring that the agency is provided with sufficient resources to carry out these initiatives.

Sincerely,

Annie Appleseed Project
Breast Cancer Action
Center for Medical Consumers
Consumer Federation of America
Consumers Union
Institute for Ethics and Emerging Technologies
National Consumers League
National Research Center for Women & Families/Cancer Prevention and Treatment Fund
National Women's Health Network
Our Bodies Ourselves
Reproductive Health Technologies Project
The TMJ Association, Ltd.
Truth in Medicine, Inc.
Union of Concerned Scientists, Scientific Integrity Program
US PIRG
Woody Matters

Cc: Margaret A. Hamburg, M.D., Commissioner, Food and Drug Administration