Statement at the Senate Health Education Labor and Pension Committee Hearing on the Prescription Drug User Fee Act and Drug Safety

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Thank you, Mr. Chairman and Members of the Committee. I bring to the hearing today a broad perspective on the Prescription Drug User Fee Act (PDUFA). Prior to joining Wyeth I spent more than 17 years at the Food and Drug Administration (FDA) where I had responsibilities in the Biologics and Drug Centers. I was the acting Deputy Center Director for Medical Affairs when PDUFA was enacted in 1992. I finished my career at FDA by serving for 6 years as the Director of the Medical Device and Radiological Health Center during the period when Congress enacted the Food and Drug Modernization Act (FDAMA).

At Wyeth, I serve as the Executive Vice President for Business Practices and Compliance. I have had overall responsibility for regulatory submissions to the FDA, including New Drug Applications (NDAs) and Biologic License Applications (BLAs). I also was responsible for manufacturing quality assurance, drug safety and FDA compliance.

Wyeth is a member of the Pharmaceutical Research and Manufacturers of America (PhRMA), the trade organization which represents the research-based pharmaceutical and biotechnology industries. During the past year, I served as Chairperson of PhRMA's PDUFA reauthorization team, which met with FDA representatives to develop improvements to PDUFA. The outcome of those nine months of intense discussions, the FDA's PDUFA IV proposal, will be the principle focus of my testimony today. I will also comment on drug safety proposals currently before Congress.

Reauthorization of PDUFA is one of the most important legislative issues facing Congress this year. By virtually any measure, PDUFA has been a resounding success. Since its enactment in 1992, PDUFA has delivered tangible and important benefits to patients, the FDA, and the pharmaceutical industry. PDUFA provides the FDA with critical additional resources to conduct rigorous reviews of new drug applications. As a direct result of PDUFA, important new medicines are now available to patients much more quickly.

In 1997, Congress built upon the early success of PDUFA when it adopted PDUFA II by passing FDAMA. PDUFA II further increased FDA's resources and provided improved interactions during the drug development process, which enhanced the drug approval process. In 2002, PDUFA III addressed FDA's need for a sound financial footing and provided additional resources for drug safety initiatives. PDUFA II and III also directed funding toward information technology so that the FDA, industry, and, most importantly, patients could realize the significant efficiencies of electronic regulatory submissions.

Congress must continue to build on the success of PDUFA by passing PDUFA IV reauthorization legislation in a timely manner this year.

Throughout the 15 years of PDUFA's existence, the exacting standards by which FDA evaluates New Drug Applications have not been compromised or diluted. Indeed, user fees provide indispensable additional funds to FDA so that it can be more rigorous, and yet expeditious, in discharging its critical function of reviewing safety and effectiveness of potentially life-saving medications.

The level of evidence of safety and effectiveness needed for the approval of a new medication have not been reduced in any way. In fact, the extent of clinical studies and safety information in applications has increased markedly since PDUFA's inception. For instance, instead of assessing the general safety data base to address the chance that a drug might cause changes in heart rhythms, as was done in 1992, the drug industry now routinely submits additional studies of new drugs given at higher doses than therapeutic levels to specifically address this concern. When the FDA studies new applications, the outcome of its review is not affected in any way by PDUFA funding. The decision to approve or disapprove an application is predicated exclusively on the FDA's analysis of the science and the evidentiary data in the application.

Each successive reauthorization of PDUFA has focused on issues critical to the FDA's mission. Enhancements to PDUFA have always been carefully structured to be responsive to the needs of both the agency and the public.

The FDA's PDUFA-IV proposal is carefully crafted and contains important new provisions and resources to:

- Enhance and modernize the FDA drug safety program;
- Add a new user fee program to give FDA additional resources to review and provide advisory opinions on direct to consumer (DTC) television advertisements;
- Improve drug development; and
- Provide more stable financing for the program.

There can be no doubt that patients will be well-served by the improvements contained in the PDUFA IV agreement.

The substantial new funding provided to enhance and modernize the FDA drug safety system – nearly $150 million dollars plus additional information technology (IT) support – will continue to assure that FDA's pre- and post-market safety assessment system is the world's best. In addition, the PDUFA IV proposal incorporates many of the recommendations made by the Institute of Medicine in its report on the U.S. drug safety system which it issued last year.

The additional resources under the PDUFA IV agreement for post-marketing surveillance will allow the FDA to augment its reliance on the spontaneous reporting of adverse events through modernized techniques and resources, such as epidemiology studies and large medical databases, to identify risks more quickly and accurately. The FDA will be able to use new IT systems, secure access to electronic health records, employ new algorithms for detecting drug safety signals, and use new approaches to

validate drug safety signals. The PDUFA IV agreement provides the funding for these initiatives.

The FDA's PDUFA proposal provides funds to develop guidance on best epidemiology practices that will serve as a base for agency, academia, and industry use. The guidance is intended to serve the public's interest by assuring that studies reporting drug-associated signals of risk do so based on defined scientific standards. It also provides funds necessary to identify which risk management and risk communication tools are effective. Moreover, the drug industry will benefit by having an array of risk management tools that work, simplifying the development of drug-specific risk management plans.

FDA will also conduct research during PDUFA-IV to determine the best way to maximize the public health benefit associated with collecting and reporting adverse events. This will lead to a better deployment of drug safety resources.

A key patient safety initiative in PDUFA IV is effectively addressing the potential for medication errors arising from confusion in drug names. The FDA proposal allocates a portion of the user fee funding to improving the trade name review process. Trade names are reviewed by the FDA to help ensure that new trade names are unlikely to be confused with existing trade names in an effort to reduce possible medication errors. FDA will now have additional resources to review trade names during drug development and provide industry with guidance on "good naming practices."

The FDA's PDUFA proposal also includes a new user fee for direct-to-consumer (DTC) television advertisements. In 2005, PhRMA issued a set of voluntary guiding principles regarding DTC advertising. In those guiding principles, PhRMA member companies committed to submit all new DTC TV ads to FDA prior to public dissemination to ensure that FDA's suggestions could be addressed before the advertisement is seen widely by the public. The PhRMA principles are working but they will be enhanced by a strong and fully funded FDA drug advertising review program. The proposed new user fee will allow FDA to hire 27 additional employees in the Division of Drug Marketing, Advertising and Communications (DDMAC) and elsewhere to oversee drug promotional activities and to ensure that TV advertisements voluntarily submitted in accordance with the PhRMA principles are reviewed in a thorough and timely manner. This will benefit patients and the public health by permitting the free flow of important medical information that is accurate, balanced and useful.

The PDUFA IV agreement also enables the FDA to fully implement the good review management principles that were developed and piloted during PDUFA-III. FDA will communicate to sponsors a timeline for discussing labeling and post-market commitments in advance of the action date. This will improve the predictability of the drug review process and lead to post-market studies that are more meaningful and appropriate for the new drug.

Under the agreement, funding is allocated for the purpose of advancing how FDA can expedite drug development under the agency's Critical Path Initiative. This will permit FDA staff to be directly involved in external activities such as partnerships and consortia that generate data and information that will be used to create new paradigms for drug development. FDA has also committed to developing draft guidance in areas related to safety assessment, clinical trial design, and the use of biomarkers. In addition, FDA will

participate in workshops and other public meetings to explore new approaches to a structured model for benefit/risk assessment. The results of these interactions will be used to assess whether pilot(s) of such new approaches can be conducted during PDUFA-IV.

Finally, it is important that we continue to assure that FDA is appropriately funded through a combination of appropriations and user fees so that the drug review program can address America's public health needs with the development of new medicines. During our discussions with the agency, a considerable amount of time was spent examining the increased workload within FDA, how it is measured, and how an appropriate workload adjuster can be constructed. The increases in funding to the program from the end of PDUFA III together with the new approach to workload adjustment will provide the sound financial footing needed to continue keeping FDA's drug and biological review program strong throughout the PDUFA IV years.

PDUFA is vital to ensuring that FDA has the necessary resources to perform its critical functions of fostering drug development and innovation and protecting the public health. The PDUFA IV proposal will provide FDA with substantial new funding and resources to enhance its oversight over drug safety and DTC advertising while ensuring that the drug review program is as robust and efficient as possible.

S. 484, "Enhancing Drug Safety and Innovation Act"

Wyeth believes the Kennedy-Enzi bill presents a thoughtful effort to maintain the important balance of providing safe drugs while not unduly delaying patient access to new therapies. The Risk Evaluation and Mitigation Strategy (REMS) system would bring FDA closer to the risk management approach taken by the European Union, a desirable goal.

To this end, a statutory construct that is somewhat less prescriptive and instead lays out principles and creates a framework to guide FDA in developing specific criteria for applying risk mitigation tools, through regulations, would be a preferable approach. Under such a system, FDA would be afforded the flexibility to develop varied programs for medications with differing levels of risk and to adapt to evolving technologies for post marketing risk evaluation. Because the bill envisions broad latitude in developing REMS plans that may have far-reaching impact, it is important that these decisions be approved at the highest levels of the agency.

Additionally, the funding mechanism proposed in S. 484 conflicts with the PDUFA agreement so that matter would need to be reconciled before proceeding.