Statement PhRMA

TESTIMONY OF DAVID E. WHEADON, M.D.
SENIOR VICE PRESIDENT, SCIENTIFIC AND REGULATORY AFFAIRS
PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA
SENATE COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS
HEARING ON "FDA USER FEE AGREEMENTS: STRENGTHENING FDA AND THE MEDICAL PRODUCTS INDUSTRY FOR THE BENEFIT OF PATIENTS"
MARCH 29, 2012

Chairman Harkin, Ranking Member Enzi, Members of the Committee, good morning. I am David Wheadon, Senior Vice President, Scientific and Regulatory Affairs at the Pharmaceutical Research and Manufacturers of America (PhRMA). PhRMA appreciates this opportunity to testify today and share our views on the fifth reauthorization of the Prescription Drug User Fee Act (PDUFA) and the authorization of the Biosimilars User Fee Act (BsUFA).

Reauthorization of the Prescription Drug User Fee Act (PDUFA-V)

PDUFA has been a great success for patients – the tens of millions of Americans who rely on innovative drugs and biologics to treat disease and to extend and improve the quality of their lives. The PDUFA user fee program has provided FDA with additional staffing and resources it needed to significantly reduce the timeframe for review of new medicines, while protecting public health by assuring the safety of these products. Furthermore, PDUFA has helped to improve America's competitiveness around the world. Since the passage of the original Prescription Drug User Fee Act in 1992, the U.S. has become the word leader in bringing new medicines to patients first.

The PDUFA-V performance goals letter is the result of extensive negotiations between the U.S. Food and Drug Administration (FDA) and the innovative biopharmaceutical industry and is intended to improve FDA's ability to conduct thorough and efficient reviews of new medicines for patients. FDA's process for negotiating these performance goals included unprecedented

Pharmaceutical Research and Manufacturers of America
*950 F Street, NW * Washington, DC 20004 * (202) 835-3400*

transparency and input from all stakeholders, including patient advocates, healthcare professionals, consumers and academia.

PhRMA and its members, the country's leading pharmaceutical research and biotechnology companies, strongly support the original goals of PDUFA, namely - to provide patients with faster access to innovative medicines, to preserve and strengthen FDA's high standards for safety, efficacy and quality, and to advance the scientific basis for the Agency's regulatory oversight.

PhRMA strongly endorses the recommendations of the PDUFA-V performance goals letter. This agreement will provide FDA with the resources and tools required to further enhance the timeliness, completeness, and efficiency of the drug review process. Failure to reauthorize PDUFA in a timely manner would have catastrophic effects on the FDA's ability to carry out its important role in bringing new medicines to patients suffering from debilitating diseases.

The Role of PDUFA in Encouraging Innovation and Economic Growth. Ensuring that the U.S. maintains a policy and regulatory environment that encourages an efficient, consistent and predictable drug review process is key to keeping America competitive in today's global economy. A 2011 report by *Battelle*[1] found that the U.S. biopharmaceutical industry "is well recognized as a dynamic and innovative business sector generating high quality jobs and powering economic output and exports for the U.S. economy." According to the report, nationwide the sector supported a total of 4 million jobs in 2009, including 674,192 direct jobs. The total economic output from the sector's direct, indirect, and induced impacts was $918 billion. Because PDUFA has injected greater consistency, transparency and predictability into the FDA's drug review process, its reauthorization is an important factor in ensuring that biopharmaceutical companies maintain this level of job creation and economic growth. Failure to reauthorize PDUFA in a timely manner would not only have an extraordinarily disruptive effect on the Agency and impede patients' access to new and innovative treatments, but such a failure would also endanger biopharmaceutical innovation.

[1] Battelle Technology Partnership Practice. The U.S. Biopharmaceuticals Sector: Economic Contribution of the Nation. July 2011. Battelle Memorial Institute. Prepared for the Pharmaceutical Research and Manufacturers of America.

Pharmaceutical Research and Manufacturers of America

950 F Street, NW * Washington, DC 20004 * (202) 835-3400

There are a number of important new commitments in the carefully negotiated PDUFA-V performance goals letter, including provisions to make the regulatory review of new medicines more efficient and timely, to advance regulatory science and modernize drug development, to improve benefit/risk decision-making, and to further strengthen FDA's focus on patient safety.

Below I discuss these significant enhancements of the PDUFA-V performance goals letter.

Enhanced NME Review Program. PDUFA-V will improve the review process for new molecular entity (NME) drug and biologic applications which will be particularly significant for patients, because NMEs are novel compounds that have the potential to address unmet medical needs and advance patient care. The enhanced NME review model addresses the increasing complexity of reviewing new drug applications (NDAs) and biologic license applications (BLAs), and provides for increased communication between FDA and drug sponsors prior to and during the drug review process. A validation period will help FDA plan activities such as inspections and advisory committee meetings, and will accommodate iterative interactions between sponsors and the Agency. As a result, the NME review program is expected to improve the efficiency of the review process and reduce the overall time until new medicines become available to patients. Specifically, it is anticipated that earlier and more comprehensive communication between the Agency and drug sponsors will improve the rate of "on-time, first-cycle" successes – that is, the number of new medicines that are fully reviewed and for which definitive regulatory action is taken within the target timeframe following initial submission. The success of the new review program and of the Agency's ability to achieve its drug review goals will be independently assessed and publicly reported in 2015 and 2017.

Advancements in Regulatory Science. Several new provisions in the PDUFA-V performance goals letter will afford FDA with appropriate staffing and resources to develop, through public input, new tools and methods to integrate emerging scientific data and techniques into the drug development and review process. These advancements in regulatory science will rely on

Pharmaceutical Research and Manufacturers of America

950 F Street, NW * Washington, DC 20004 * (202) 835-3400

engagement with industry, academia and other stakeholders to identify best practices so the Agency can provide appropriate guidance to stakeholders involved in drug development.

Provisions to enhance FDA's regulatory review capabilities include:

- The use of pharmacogenomics and biomarkers to decrease drug development time by helping demonstrate therapeutic benefits more rapidly, and identifying patients who are likely to benefit from treatment, as well as those at increased risk for serious adverse events.
- Avenues for accelerating drug development for rare and orphan diseases and provide FDA with the necessary regulatory flexibility to encourage and advance research into novel treatments for patients with significant unmet needs today.
- Standards for and validation of patient-reported outcomes and other assessment tools that may assist regulators in evaluating treatment benefits and potential risks from the patient's point of view.
- And the evaluation of the use of meta-analyses in regulatory review and decision-making, highlighting best practice and potential limitations.

Systematic Approach to Benefit-Risk Assessment. A key provision in the PDUFA-V performance goals letter recognizes that the drug review process could be improved by a more systematic and consistent approach to benefit-risk assessment that fairly considers disease severity and unmet medical needs. During PDUFA-V, the Agency will implement a structured benefit-risk framework, and hold public meetings to assess the application of such frameworks in the regulatory environment. In addition, over the course of PDUFA-V the Agency will hold a series of public meetings with the patient advocacy community to identify disease states that – from the patient perspective – have considerable unmet needs. Development and implementation of a patient-focused, structured framework for evaluating benefits and risks of new treatments will help inform the drug development process as well as ensure that regulatory decisions are consistent, appropriately balanced, and based on best science.

Pharmaceutical Research and Manufacturers of America

950 F Street, NW * Washington, DC 20004 * (202) 835-3400

Modernizing the U.S. Drug Safety System. Finally, further enhancement and modernization of the FDA drug safety system under PDUFA-V will ensure that patient safety remains paramount. The PDUFA-V performance goals letter provides for a public process to help standardize risk evaluation and mitigation strategies (REMS), with the intent to assess and reduce burden on healthcare providers and patients. Additionally, FDA will continue to evaluate the feasibility of using the Agency's Sentinel Initiative to actively evaluate post-marketing drug safety issues.

PDUFA has advanced public health by accelerating the availability of innovative medicines to patients while helping to ensure patient safety. The PDUFA program has strengthened the scientific basis of FDA's regulatory review process through the development and application of new tools, standards, and approaches that facilitate assessment of the safety and efficacy of innovative drugs and biologics. PDUFA-V will continue to provide FDA with the resources and tools that are essential to support patient safety and promote medical innovation through enhanced timeliness, completeness, and efficiency of the drug review process. PhRMA encourages Congress to reauthorize PDUFA in a timely manner based on the negotiated PDUFA-V performance goals, and to minimize the inclusion of additional provisions that may have the unintended consequence of distracting from the Act's original intent - to provide patients with faster access to innovative medicines, to preserve and strengthen FDA's high standards for safety, efficacy and quality, and to advance the scientific basis for the Agency's regulatory oversight.

Authorization of a User Fee Program for Biosimilar Biological Products Under the Biologics Price Competition and Innovation Act of 2009 (BsUFA)

An abbreviated approval pathway for biosimilar products and interchangeable biological products was established in the Biologics Price Competition and Innovation Act of 2009 (BPCIA) and PhRMA has been supportive of FDA's ongoing efforts to implement BPCIA in a manner that ensures patient safety and encourages biopharmaceutical innovation. PhRMA was a participant in the technical negotiations with the US Food and Drug Administration (FDA) that, together with input from patient and healthcare provider groups, resulted in the Biosimilars User Fee Act (BsUFA) performance goals letter.

The BsUFA FDA performance goals are consistent with Congressional intent to create a unique user fee program to meet the needs of biosimilar product applicants, and to provide FDA with the means necessary to build, essentially from scratch, its capacity for science-based review of biosimilar applications. PhRMA believes that the BsUFA performance goals will benefit patient safety and public health as biosimilar products will be required to meet FDA's high standards for safety, purity, and potency.

Several of PhRMA's member companies for many years have been actively engaged in the development of innovative biological products. In addition, some of PhRMA's member companies have expressed their intent to develop biosimilar products. PhRMA therefore supports the development of a robust user fee program for biosimilar products to provide FDA with the resources needed to review biosimilars without diverting resources from the review of innovative medicines. PhRMA is further supportive of the appropriation of Congressional funds for this purpose, a feature common to existing user fee programs, to ensure that user fees supplement, rather than replace, appropriations.

PhRMA believes that the review process for biosimilar and interchangeable biological products must be scientifically rigorous, timely, and above all, protective of patient safety. Achieving these objectives will require a clear and formalized regulatory pathway for biosimilar products, quality standards that meet standards for innovative products, and adequate preclinical and clinical testing to ensure that biosimilars are both safe and effective.

PhRMA recognizes that, for the purpose of this first authorization, the biosimilar user fee program must be structured differently from other user fee programs. It will be necessary, for example, to collect fees earlier in the biological product development process, until fees from licensing applications can provide sufficient ongoing revenues to support the Agency's activities. It must be understood, however, that the proposed user fee program for biosimilar products – and, in particular, the provision for payment of a portion of the application fee at the time of an

Pharmaceutical Research and Manufacturers of America

950 F Street, NW * Washington, DC 20004 * (202) 835-3400

Investigational New Drug (IND) submission and yearly thereafter – is a stop-gap measure, subject to review at the time of BsUFA reauthorization in 2017.

Among the key aspects of FDA's proposed BsUFA performance goals is the expectation for FDA, in FY 2013, to review and act on 70 percent of original biosimilar application submissions within 10 months of receipt and to review and act on 70 percent of resubmissions within 6 months of receipt. As the Agency's review capacity for biosimilar products develops, review performance goals will gradually increase.

The BsUFA performance goals further provide for specific FDA/sponsor meetings to facilitate the biosimilars development phase. This provision includes a special protocol assessment mechanism for clinical study protocols that are intended to establish biosimilarity and/or interchangeability with a reference biological product, to help ensure that the study design is adequate to meet scientific and regulatory requirements for approval.

The proposal also calls for FDA to issue guidance on procedures for meetings between the Agency and sponsor prior to submission of a biosimilar licensing application, and PhRMA urges the Agency to accelerate its guidance development in this area. Eventually, the biosimilar application process should be codified in regulations similar to all other approval pathways.

Additionally, user fees will be applied to enhance patient safety through implementation of measures to reduce medication errors related to similar sounding proprietary names, unclear labeling, and confusing package design.

PhRMA supports the proposed BsUFA performance goals agreement as a means of advancing public health by making adequate resources available to FDA to build a capacity for regulatory review of biosimilar products, consistent with the Agency's high standards for patient safety and scientific rigor.

Pharmaceutical Research and Manufacturers of America

950 F Street, NW * Washington, DC 20004 * (202) 835-3400

PhRMA and its member companies are committed to working closely with FDA, and all stakeholders, to insure the continued success of PDUFA in bringing safe, effective innovative medicines forward to address unmet medical needs for all patients. Additionally, PhRMA stands ready to work with the FDA and other stakeholders in establishing a science-based approach to the development and review of biosimilar and interchangeable biological products. PhRMA therefore urges Congress to reauthorize PDUFA in a timely manner based on the negotiated PDUFA-V agreement and to authorize BsUFA with Congressional appropriations allocated in support of this program for fiscal years 2013 through 2017.

Thank you for the opportunity to testify today and I welcome any questions you may have.

Pharmaceutical Research and Manufacturers of America

950 F Street, NW * Washington, DC 20004 * (202) 835-3400