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HOW INNOVATION HELPS PATIENTS AND JOBS”
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Chairman Pitts, Ranking Member Pallone, Members of the Subcommittee, good afternoon. 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 reauthorization of the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA).

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 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.

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.

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.

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 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.

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.

Reauthorization of the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research and Equity Act (PREA)

Prior to passage of the pediatric exclusivity provisions in the Food and Drug Modernization Act (FDAMA) of 1997, there were significant disincentives for biopharmaceutical companies to conduct clinical trials for pediatric use - generally speaking, in patients under the age of 18 - for medicines developed primarily for adults. At the same time, there were concerns that many FDA-approved drugs had not been clinically tested in children. For example, at that time about 70 percent of medicines used in children had been dispensed without adequate pediatric dosing information.²

Growing recognition of the need for pediatric-specific information prompted action by Congress and the FDA. Congress responded by establishing BPCA to provide incentives to encourage manufacturers to conduct pediatric studies of medicines with the potential for use in children as part of FDAMA. The legislation included a provision that granted pharmaceutical companies an additional six-month period of exclusivity, known as pediatric exclusivity, upon the completion and submission of pediatric studies that meet the terms of a written request from FDA.

In addition to BPCA, the Pediatric Research and Equity Act (PREA) gave FDA the authority to require manufacturers to conduct pediatric studies for certain new drugs and biologics approved for use in adults where the indication for use in children would be comparable to that for adults and produce formulations appropriate for children, *e.g.* liquid or chewable tablets.

Although FDAMA included a sunset provision effective January 1, 2002, Congress subsequently reauthorized these provisions in BPCA and PREA in 2002, and again in 2007 as part of the Food and Drug Administration Amendments Act (FDAAA). Similarly, there are provisions in the Biologics Price Competition and Innovation Act of 2009 (BPCIA) to provide pediatric exclusivity for biologics if the

² U.S. Pediatric Studies Incentive Led to New Labeling for Nearly 100 Drugs, Impact Report, Tufts Center for the Study of Drug Development, Vol. 7, No. 4, July/August 2005.

sponsor submits pediatric studies in accordance with a written request from FDA. BPCA and PREA both sunset on September 30, 2012, unless reauthorized or made permanent.

BPCA and PREA have been extraordinarily successful in improving medical care for children by driving research to create innovative medicines for use in pediatric patients. According to the FDA, the current pediatric exclusivity program has done more to spur research and generate critical information about the use of medicines in pediatric patients than any other government initiative.³ As of 2008, an estimated 50 to 60 percent of prescription drugs used to treat children have been studied in some part of the pediatric population.⁴ Since 1998, BPCA and PREA have resulted in 426 pediatric labeling changes⁵ and a GAO report released in May 2011 states that pediatric studies conducted in the past five years represent 16 different therapeutic areas including oncology, endocrinology, hematology, cardiovascular disease, infectious disease, and neurology.

A recent issue of the NIH's *NIH MedlinePlus* magazine notes the importance of pediatric clinical trials and cites several examples of how clinical trial knowledge has improved the lives of children. The article states that, among other examples of great progress in innovative pediatric drug development, "as a result of repeated clinical trials in children with cancer, most children who develop leukemia survive" compared to 50 years ago when "acute leukemia was almost universally fatal in young children". Additionally, clinical trials in young children "showed that surfactant - a substance that keeps air sacs in the lungs inflated - helps premature infants breathe" and with this knowledge "the lives of thousands of babies who would otherwise die of respiratory failure are saved each year".⁶

Permanent Reauthorization of BPCA and PREA is Key to Ensuring Innovation in Pediatric Research. Ensuring that the pediatric exclusivity incentive is preserved is key to continued innovation and improvement in pediatric medical care in the face of rising research costs. Since its initial enactment and subsequent reauthorizations, the pediatric exclusivity incentive and PREA have been subject to a "sunset clause" under which their provisions expire after five years unless reauthorized by Congress. To build upon the tremendous success of BPCA and PREA in improving medical care for children over the past fifteen years, Congress should permanently reauthorize BPCA and PREA.

³ Pediatric Study Costs Increased 8-Fold Since 2000 as Complexity Level Grew, Impact Report, Tufts Center for the Study of Drug Development, Vol. 9, No. 2, March/April 2007.

⁴ FDA, "Giving Medication to Children: Q&A With Dianne Murphy, MD." June 2009.

⁵ FDA, <http://www.fda.gov/downloads/ScienceResearch/SpecialTopics/PediatricTherapeuticsResearch/UCM163159.pdf>

⁶ NIH Medline Plus, "Developing Safe and Effective Medicines for Children," Winter 2012. <
http://www.nlm.nih.gov/Program_MLP/MLP_intro.html>

Permanent reauthorization of these provisions would provide greater certainty to companies by allowing a more predictable regulatory path and would help spur increased pediatric research, a fact also highlighted in the recently released Institute of Medicine (IOM) report entitled, “Safe and Effective Medicines for Children”⁷. Pediatric product development would also benefit from updated regulatory guidance to assist both industry and FDA review staff in achieving a common understanding of the requirements under the Federal Food, Drug, and Cosmetic Act (FDCA). Because of the five-year BPCA/PREA sunset and reauthorization cycle, no such current guidance exists, since every reauthorization has brought new changes to the law. The lack of current FDA guidance creates additional challenges for sponsors involved in pediatric product development to incorporate any differences into its plans due to changes in statutory requirements. If Congress were to reauthorize BPCA and PREA permanently, it would enable the FDA to publish and maintain up-to-date regulatory guidance for companies that seek to develop pediatric treatments.

Further, making BPCA and PREA permanent would allow sponsors to build upon the existing pediatric research infrastructure and expand their capacity to conduct clinical studies. Uncertainty about whether incentives will continue could deter this vital investment. A similar pediatric incentive was successfully introduced in the European Union in 2007, and while the regulation is subject to review, the EU’s pediatric incentive is permanent. The permanent incentive in the EU has enabled the European Medicines Agency (EMA) to publish clear guidelines for industry and regulators making the process more efficient, transparent, and predictable.

Given the undisputed success of BPCA and PREA, we urge Congress to permanently reauthorize BPCA and PREA in its current form to allow pediatric research to thrive and create more options for our most vulnerable population, children. Additionally, 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. PhRMA therefore urges Congress to reauthorize PDUFA in a timely manner based on the negotiated PDUFA-V agreement.

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

⁷ IOM (Institute of Medicine). 2012. *Safe and Effective Medicines for Children: Pediatric Studies Conducted Under the Best Pharmaceuticals for Children Act and the Pediatric Research Equity Act*. Washington, DC: The National Academies Press.