July 15, 2015

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2010-N-0128: Prescription Drug User Fee Act; Public Meeting; Request for Comments

Dear Sir/Madam:

On behalf of the Biotechnology Industry Organization (BIO), thank you for the opportunity to provide our comments on the success of the PDUFA program and recommendations to enhance the program through the user fee reauthorization process.

BIO is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers, and related organizations across the United States and in more than 30 other nations. BIO members are involved in the research and development of innovative healthcare, agricultural, industrial, and environmental biotechnology products.

BIO fully supports timely reauthorization of PDUFA 6. We look forward to working closely with FDA, Congress, and other stakeholders to enhance the program further: to integrate the patient voice into the drug development and evaluation processes most effectively, support FDA's scientific capacity and infrastructure, and ensure the long term stability of the program.

A. PDUFA has been successful

Since 1992, the PDUFA program has been widely credited as one that has helped facilitate earlier patient access to more than 1,200 modern medicines, while preserving FDA's rigorous standards for safety and efficacy. The PDUFA program has provided FDA with resources to hire medical reviewers, scientists, and statisticians to review new drug and biologics applications, while introducing greater transparency into the review process through clear and predictable timelines for FDA action on pending applications.

We stand on the cusp of a new generation of precision medicines that will leverage recent scientific advancements in genomics and molecular biology. Modern scientific advancements are increasingly being translated into new, targeted therapies, diagnostics, and combination products that are transforming the practice of medicine and patient care. However, drug

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development continues to be a long and costly endeavor, often requiring more than $2.5 billion dollars per drug or biologic, with clinical development often lasting 10 to 15 years.[1]

To secure the necessary capital and investment to support the development of new therapies, including costly clinical trials, entrepreneurial biotechnology companies require a clear, reliable, and predictable regulatory environment. By providing funds for review enhancements that enhance clarity and predictability, PDUFA helps foster biomedical innovation so patients can benefit from novel therapies without unnecessary delay.

Three years ago, PDUFA 5 (enacted as part of the *Food and Drug Administration Safety and Innovation Act of 2012* (FDASIA)) made meaningful improvements to the human drug review program, and PDUFA 6 should build upon that record of continual process enhancement. For example, the New Molecular Entity (NME) Review program has stabilized review times and achieved historic first cycle approval rates. PDUFA 5 also took the first steps toward a new and critically important patient-focused drug development paradigm, intended to help understand patient views of disease and incorporate those perspectives into the regulatory process through a structured benefit/risk framework. Under PDUFA 5, FDA also committed to a philosophy of timely, interactive scientific communication during drug development and to the identification of and training in best communication practices.

The successes under PDUFA 5 are substantial, but there also have been challenges. For example, a portion of industry-funded user fees were unavailable to the Agency during the government-wide sequestration in the first year of PDUFA 5. This and other obstacles prevented FDA from meeting its hiring goals to bring new scientists and managers into the agency to support a number of the PDUFA 5 programs. In particular, to date, the Agency has been unable to meet fully regulatory science goals that had been suggested by FDA, patient organizations, and industry, and that are supported by industry. This seems principally to be because of an inability to hire essential scientific and technical experts. Enhancement in the Agency's expertise related to use of patient-reported outcomes (PROs), biomarkers as surrogate endpoints, innovative clinical trial designs, and pharmacogenomic data will have long-term positive impact for patient-centered drug development and regulatory decision-making. The inability to achieve this enhancement is concerning, and as the PDUFA 6 process moves forward, FDA and stakeholders need to work together to define the causes, understand them clearly, and try to address them.

B. Principles for PDUFA 6

The PDUFA program must continue to evolve to the benefit of patients. To this end, under PDUFA 6, the biopharmaceutical industry will be guided by the following principles:

To facilitate more efficient development of safe and effective innovative medicines for patients, in PDUFA 6, industry will advance and support policies to:

1. Better integrate the **patient perspective** in drug development and regulatory decision-making;

2. Enhance the **scientific expertise**, processes, and tools FDA uses to regulate increasingly complex medical products and public health issues; and

[1] Tufts Center for the Study of Drug Development, *Cost to Develop and Win Marketing Approval for a New Drug is $2.6 billion, November 18, 2014,* http://csdd.tufts.edu/news/complete_story/pr_tufts_csdd_2014_cost_study

3. Promote the **long-term stability** of the PDUFA program by improving its financial transparency, efficiency, and accountability and ensuring FDA can recruit, hire, and retain a highly skilled workforce to advance its public health mission.

1. Integrating Patient Perspectives into Drug Development

Integrating patients' perspectives into an efficient drug development and review process is a driving theme behind the 21st Century Cures Act in the House of Representatives, the Senate's Innovation for Healthier Americans initiative, and the upcoming PDUFA 6 reauthorization. By providing the patient perspective on issues such as disease burden and benefit/risk, elevating the patient voice will better inform FDA's regulatory decision-making and can lead to the development of new treatments that are most meaningful to patients.

As the science of patient preference assessment evolves and matures, it is essential for FDA and stakeholders to work together to drive the process forward: from an *ad hoc* and anecdote-driven approach to a robust, systematic, and data-driven process that occurs at each stage of drug development and review. To incorporate the patient voice more effectively throughout drug development, it is crucial that FDA and industry work together to evaluate and utilize appropriate scientific methodologies for assessing patient views and perspectives and to leverage FDA's structured benefit/risk framework throughout a therapy's life cycle. Clear guidance and established processes on patient preference assessment methodologies and data should translate patient feedback into new and effective drug development tools, such as qualified PROs and biomarkers.

2. Enhance FDA's scientific expertise, processes, and tools

PDUFA 5 made significant changes that helped to enhance the FDA review process. This is good news. However, it is equally important that PDUFA provide FDA with the tools and scientific capacity necessary to help streamline and modernize the clinical development process, which takes ten years or more before FDA even receives an NDA or BLA. The process must embrace new, modern research methodologies such as innovative clinical trial designs, new methods of statistical analysis, and the use of "big data" and real world evidence to inform both the pre-market and post-market phases of drug development and review. Building on the success of the NME review program, targeted review process enhancements can improve other aspects of review, such as the processes for evaluating combination products, timely determination of the most informative and appropriate label, and identification of post-market research commitments.

BIO has long advocated for enhancing communication between FDA and industry scientists during drug development. Robust scientific communication can lead to a better understanding of FDA's expectations, improve the ability to resolve issues, and address scientific questions that do not rise to the level of requiring a formal meeting with the Agency. It is undeniable that drug development fares better for both FDA and sponsors when there is productive communication. Such communication can improve efficiency by addressing key issues before they can manifest as significant disruptions or delays in clinical development.

With this in mind, over the last year BIO has conducted a survey designed to understand our member companies' experiences in interacting with the Agency during various stages of

drug development. Based on 324 clinical development programs representing 230 distinct survey participants, early results indicate that about half of the participants report that their interactions with FDA are very beneficial and productive, while half of the participants state that there is room for improvement. Additionally, the survey indicates that there is considerable variability in communication practices and timeliness of communication across review divisions. The survey identified several review divisions that excelled in communicating with sponsors interactively and productively. We continue to share these survey results with survey participants and with FDA so we can move forward together to identify best practices for communication that can be emulated across all FDA review divisions.

3. Long-term Stability of PDUFA

We must continue to support the sustainability of the PDUFA program to ensure that it will benefit future generations of patients and drug developers. Enhanced financial transparency and accountability will promote appropriate allocation of user fee funding to existing and emerging priorities. We also must ensure that FDA has the hiring flexibility and human resources processes necessary to recruit and retain world-class scientists and managers. Finally, we must work with Congress to guarantee once and for all that user fees are not subject to any future sequestration.

C. Conclusion

In conclusion, thank you for the opportunity to present BIO's views on the PDUFA program, which has been a win-win for patients, industry, and FDA. BIO looks forward to working with FDA, stakeholder groups, and Congress to ensure timely reauthorization of this program. We encourage all involved partners to work in collaboration to pass PDUFA no later than mid-2017 to avoid any disruptions to the human drug review program. Under PDUFA 6, we must seize the opportunity to realize fully a patient-centric, scientifically innovative, and sustainable process for translating new discoveries to cures.