Testimony of

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Before the U.S. House of Representatives, Energy and Commerce Committee Subcommittee on Health

Hearing on "FDA USER FEE REAUTHORIZATION: ENSURING SAFE AND EFFECTIVE DRUGS AND BIOLOGICS"

February 3, 2022

Good afternoon, Chairwoman Eshoo, Ranking Member Guthrie, and the Members of the Subcommittee:

My name is Lucy Vereshchagina, Vice President, Science and Regulatory Advocacy at the Pharmaceutical Research and Manufacturers of America (PhRMA). PhRMA represents the country's leading innovative biopharmaceutical research companies, which are devoted to discovering and developing medicines that enable patients to live longer, healthier, and more productive lives. Over the past 20 years, PhRMA member companies have invested more than $1 trillion in the search for new treatments and cures, including an estimated $91.1 billion in 2020 alone.[i]

I am pleased to appear before you to provide PhRMA's perspective on the importance of the Prescription Drug User Fee Act (PDUFA) and the Biosimilar User Fee Act (BsUFA) and their timely reauthorization. As you know, PhRMA served as one of Industry's principal negotiators with FDA and fully supports both the PDUFA VII and BsUFA III technical agreements.

Today, I will briefly speak to PhRMA's perspective on the successes of the two user fee programs and key elements of each agreement.

Perspectives on the Success of the PDUFA Program

For nearly 30 years, PDUFA has helped the FDA fulfill its central mission – to help protect and promote the public health – by allowing the Agency to stay abreast of ever-evolving science and have the resources to keep pace with the innovative drugs and biologics entering the review pipeline.

In large part because of PDUFA, the United States now leads the world in the introduction of new medicines,[ii] and the FDA's human drug review program is the global gold standard for regulatory review and approval. Over the years, the PDUFA program has produced positive and tangible results that matter to patients. Since 1992 when the program was first enacted, PDUFA has provided more timely patient access to more than 1,700 new drugs and biologics including treatments for cancer, rare diseases, cardiovascular, neurological, and infectious diseases.

The uncertainty of the global pandemic has highlighted the paramount importance of the economic competitiveness of our nation and the need for continued advancement of innovation-based industries. PDUFA VII will build on the Program's past successes to bolster critical capabilities, improve efficiencies in drug review, and encourage the significant R&D investments made by biopharmaceutical companies in the United States.

PDUFA plays a critical role in the FDA's ability to review human drug applications. Consequently, the Program also provides biopharmaceutical companies with greater regulatory predictability, which fosters continued investment in research and development. This has been illustrated by the significant number of approvals occurring during the COVID-19 pandemic, which is a testament to the Agency's commitment to the public health and the dedication of biopharmaceutical companies to drive medical advancements despite the ongoing challenges of COVID-19.

PDUFA VII will strengthen regulatory review fundamentals while enhancing accountability, transparency, and resource management at FDA. The overarching PDUFA VII efforts build on successes of the previous cycles and are aimed at modernizing the US regulatory and drug development paradigm and addressing new areas such as digital health technologies, cell and gene therapies, and manufacturing.

PDUFA VII also includes commitments that advance emerging COVID-19 lessons learned. FDA and the biopharmaceutical industry are utilizing novel approaches to clinical trials and facility inspections to support continued innovation and operations during the pandemic and to inform efficient regulatory decision-making to address COVID-19. The PDUFA VII provisions leverage lessons learned in adapting to and meeting the challenges presented by the COVID-19 pandemic, enhancing our future preparedness and ability to keep pace with scientific advancements.[iii]

Through the targeted improvements outlined in the draft PDUFA VII commitment letter, the PDUFA VII agreement will have a lasting and meaningful impact on the biopharmaceutical industry's ability to develop innovative, safe, and effective medicines for patients in a timely manner. Specifically, PDUFA VII will:

- strengthen scientific dialogue and advance innovation;
- enhance patient-centric drug review and support safety monitoring;
- support the next wave of advanced biological therapies;
- modernize regulatory evidence generation and drug development tools;
- advance digital technologies and IT infrastructure;
- enhance innovation in manufacturing and product quality reviews; and
- build on PDUFA VI efforts to modernize FDA financial and staff resource management.

Specifically:

PDUFA VII Will Strengthen Scientific Dialogue and Advance Innovation

Effective interactions with FDA throughout development, from the pre-investigational new drug (IND) phase to the clinical development phase, can help minimize the risk of late-stage drug development failures, increase the probability that safety and efficacy data are available in a timely manner and mitigate issues that would delay patient access to approved treatments. PDUFA VII will help expand opportunities to incorporate FDA feedback throughout the drug development process, including through formalized Initial Targeted Engagement for Regulatory Advice on CDER/CBER Products (INTERACT) meetings for innovative products early in development. PDUFA VII will also provide for the creation of a new formal Type D meeting

with a shorter timeframe for focused discussion, including on innovative approaches, and enhanced processes and timelines for communicating and reviewing postmarketing requirements.

PDUFA VII proposed performance goals will also address regulation of combination products through new and enhanced procedures, timelines and guidance for human factor validation protocols and use-related risk analysis. In addition, PDUFA VII will support the development of treatments for rare diseases with the establishment of new pilot programs for supporting efficacy endpoint development and will establish a Split Real Time Application Review (STAR) to shorten the approval timeline for certain novel uses of approved therapies. Streamlined processes and prompt FDA feedback on sponsor questions and pressing development issues will help ensure regulatory efficiency and predictability for drug development programs involving innovative approaches.

PDUFA VII Will Enhance Patient-Centric Drug Review and Support Safety Monitoring

Through the Patient-Focused Drug Development (PFDD) Initiative established as part of PDUFA V[iv] and continued in PDUFA VI,[v] FDA has gained a better understanding of the disease, condition, and treatment elements that are of greatest importance to patients. PDUFA VI also provided significant resources to support the Agency's ability to review, track, and communicate important post-market safety information. This included an investment to expand the Sentinel System's capabilities and enhance the communication process with stakeholders on the use of Sentinel data.

PDUFA VII's proposed performance goals will build on initiatives from PDUFA V and VI and advance the incorporation of patient-centric data into drug development and regulatory reviews. Enabling further incorporation of the patient perspective, including through guidance on patient preference information, and expanded FDA staff training and outreach, will help enhance the patient-centric process by which the industry develops new medicines that address the needs of patients.

Implementation of the proposed PDUFA VII performance goals will also improve Risk Evaluation and Mitigation Strategies (REMS) assessments and advance Sentinel capabilities. PDUFA VII will establish new timelines for FDA review of methodological approaches and study protocols for REMS assessments. PDUFA VII will also advance the Sentinel analytical capabilities to support the use of Sentinel to address questions of product safety and address how real-world evidence (RWE) can be used for studying a drug's effectiveness.

Recognizing the importance of understanding and improving safety for all patients, PDUFA VII includes new Sentinel demonstration projects for assessing drug safety in pregnancy and the outcomes of pregnancies in women exposed to drugs and biological products. These activities will support implementation of a standardized process for determining necessity and type of pregnancy postmarketing studies,

PDUFA VII Will Support the Next Wave of Advanced Biological Therapies

A significant area of focus in modern drug development is the field of cell and gene therapies, which aim to treat, prevent, or cure disease by targeting the underlying cause through delivery of targeted cells or genetic material. Cell and gene therapy research holds tremendous promise in leading to the possible development of specialized treatments for patients with a variety of conditions, including genetic diseases, cancer, and infectious diseases.

Implementation of the proposed PDUFA VII performance goals will help ensure the efficient review of applications and timely patient access to innovative biological therapies regulated by FDA's Center for Biologics Evaluation and Research (CBER), including cell and gene therapies. FDA will provide further guidance to support the use of expedited programs for regenerative medicines, improve communication best practices, facilitate review of manufacturing information for products with accelerated clinical development, and advance PFDD activities. PDUFA VII also includes a public process to inform ways cell and gene therapy manufacturers can appropriately leverage a sponsor's internal prior knowledge and public knowledge across therapeutic areas to facilitate development and review of cell and gene therapies.

The proposed PDUFA VII performance goals will also help enable broader use of novel clinical trial designs and approaches for small patient populations and evaluate their application to more common diseases. CBER will be provided dedicated resources to facilitate necessary hiring and training reviewers for these transformative therapies.

PDUFA VII Will Modernize Regulatory Evidence Generation and Drug Development Tools

PDUFA VII will build on successful initiatives from previous PDUFA cycles and authorities in the 21st Century Cures Act to further modernize regulatory evidence generation and drug development tools, including advancing the appropriate use of real-world evidence (RWE) and real-world data (RWD) in regulatory decision-making. Delivering new medicines to patients through biomedical innovation requires advancing the development and application of the latest regulatory science approaches to drug development. New and powerful tools emphasize individual patient characteristics and include complex innovative clinical trial designs, the use of RWE, patient-reported outcomes, and advanced statistical methods. PDUFA VII initiatives will help advance regulatory evidence generation and the use of innovative clinical trial approaches and statistical models as well as increase transparency and promote stakeholder learning around acceptable uses of innovative approaches for regulatory decision-making. These initiatives include the establishment of a new pilot program to advance the use of RWE for regulatory decision-making, including for approval of new indications or to satisfy postmarketing study requirements, holding public workshops, and issuing guidance documents on the use of RWE.

PDUFA VII will also facilitate greater use of innovative clinical trial designs by advancing the use of complex adaptive and other novel clinical trial designs, including guidance on Bayesian approaches, and continuing the complex innovative trial design pilot put in place as part of the PDUFA VI commitments. PDUFA VII will also further advance consistency and predictability around the use of modeling and simulations, including model-informed drug development (MIDD) approaches, in regulatory decision-making.

PDUFA VII Will Advance Digital Health Technologies and Information Technology (IT) Infrastructure

PDUFA VII will help usher in the future of innovative biopharmaceutical R&D and regulatory review by advancing the use of digital health technologies (DHTs). DHTs – such as digital health products, artificial intelligence, and machine learning – present significant opportunities to support clinical trials and enable remote or decentralized clinical trials. Importantly, decentralized clinical trials have the potential to increase enrollment opportunities and provide access to more diverse patient populations.

PDUFA VII will establish a robust and efficient framework to facilitate the adoption of innovative digital health products, as well as promote coordination and utilization of DHTs in regulatory decision-making across FDA.

PDUFA VII initiatives will also help facilitate a modernized technology infrastructure to underpin and support the FDA's regulatory review process. FDA's data and IT capabilities will be enhanced during PDUFA VII, including, improved support for the review of DHT-generated data, and increased bioinformatics and computational biology capacity to enable review of complex biological data, such as Next Generation Sequencing. PDUFA VII will also help resource the cloud-based modernization of the Electronic Submissions Gateway (ESG) with an improved architecture that supports expanding data submission bandwidth and storage. FDA will also enhance accountability and transparency for the Agency's IT modernization plans by establishing a strategy on data-driven regulatory initiatives that will build on FDA's ongoing efforts as outlined in the Agency's Technology Modernization Action Plan (TMAP) and Data Modernization Action Plan (DMAP).

PDUFA VII Will Enhance Manufacturing and Product Quality Reviews

For the first time in the history of PDUFA, manufacturing and product quality reviews will be addressed through provisions in PDUFA VII. Manufacturing and quality play a vital role in the drug development process and ensuring timely patient access to innovative medicines. In each reauthorization of PDUFA, FDA and industry have further defined the review process for marketing applications to help ensure that the Agency's review remains on track and allows applicants visibility into FDA's review for purposes of increasing first cycle approvals for those applications that are approved by FDA. PDUFA VII will help promote a more efficient review process, advance the use of innovative manufacturing technologies across product platforms and manufacturing sites, and establish a new pilot to facilitate Chemistry, Manufacturing and Controls (CMC) readiness for products with accelerated clinical development timelines. PDUFA VII also includes a commitment for FDA to issue guidance on the use of alternative tools to assess manufacturing facilities named in pending applications, including incorporation of best practices from the use of such tools during the COVID-19 pandemic.

PDUFA VII Will Build on PDUFA VI Efforts to Modernize FDA Financial and Resource Management

Transparency into and accountability for the use of user fee resources is a core pillar of the Program and of utmost importance to the biopharmaceutical industry. PDUFA VI included improvements to the financial structure of the PDUFA program[vi] aimed to help ensure financial stability and appropriate staffing for the FDA to meet negotiated goals, with implementation and maturation of these reforms expected to continue into PDUFA VII. PDUFA VI also included improvements to the hiring process and set goals for the hiring of new staff that was needed to fulfill the human drug review program mission. PDUFA VII will build further on the foundational work started in PDUFA VI to help improve accountability and transparency and modernize financial and staff resource management. PDUFA VII includes hiring goals and improvements to recruitment, hiring, retention and training to help ensure that FDA has adequate staffing and can fulfill the commitments outlined in PDUFA VII.

Perspectives on the Success of the BsUFA Program

Biosimilars are playing an increasingly critical role in bringing new treatment options to patients and increasing competition. BsUFA has been essential to strengthening the FDA's ability to implement a regulatory review approach for biosimilar products that is consistent with the Agency's high standards, and the Program has resulted in 33 FDA-approved biosimilar products to date, including two interchangeable biosimilars.

The BsUFA III initiatives will build on the success of the Program and enhance FDA's biosimilar review process while ensuring stability and continued maturation of the Program. In helping provide FDA with the resources needed to enhance the development and review of biosimilars, BsUFA III will, in turn, help increase competition in the marketplace to the benefit of patients. Specifically, BsUFA III will:

- enable timely sponsor interactions with FDA for biosimilars development and review;
- establish timelines for review of certain application supplements, including those seeking to update safety labeling to reflect changes to the reference product labeling;
- advance development of interchangeable biosimilar products and pilot a regulatory science program;
- enhance manufacturing inspection-related communications and modernize facility assessment approaches;
- modernize FDA's IT infrastructure and support adoption of cloud-based technologies; and
- build on BsUFA II efforts to modernize FDA financial and staff resource management.

Specifically,

BsUFA III Will Enable Timely Sponsor Interactions with FDA for Biosimilars Development and Review

BsUFA III will enable timely interactions between sponsors and FDA during biosimilar development and review. Specifically, BsUFA III includes modifications to existing meeting types such as modification of the current Biosimilar Initial Advisory (BIA) meeting to provide flexibility for discussion of biosimilarity prior to the availability of preliminary comparative analytical data and establishment of a new meeting type for rapid, targeted feedback to assist sponsors during biosimilar product development.

BsUFA III Will Establish Timelines for Review of Certain Application Supplements, Including Those Seeking to Update Safety Labeling to Reflect Changes to the Reference Product Labeling

BsUFA III will enhance consistency and predictability of the biosimilars review process by establishing specific timelines for review of certain application supplements, including those seeking to update safety labeling to reflect changes to the reference product labeling.

BsUFA III Will Advance Development of Interchangeable Biosimilar Products and Pilot a Regulatory Science Program

BsUFA III will provide information and guidance to sponsors for development of biosimilar and interchangeable biosimilar products. FDA will issue guidance and hold a corresponding public workshop on topics foundational for the development of interchangeable biosimilar products. FDA will also pilot a regulatory science program with demonstration projects and deliverables focused on advancing the development of interchangeable biosimilar products and improving the efficiency of biosimilar product development. Informed by the pilot program, FDA will develop and publish a comprehensive strategy outlining specific actions the Agency will take to facilitate the development of biosimilar and interchangeable biosimilar products.

BsUFA III Will Enhance Manufacturing Inspection-related Communications and Modernize Facility Assessment Approaches

As with PDUFA VII, the BsUFA III agreement includes dedicated initiatives to address manufacturing for the first time in the history of the Program. In response to the significant challenges presented by the COVID-19 pandemic to foreign and domestic inspections, FDA employed the use of alternative tools and a risk-based approach to ensure the safety and continuity of the global biopharmaceutical supply chain. BsUFA III will advance use of alternative inspection tools (e.g., requesting records and other information directly from facilities and other inspected entities, utilizing new or existing technology platforms to assess manufacturing facilities as appropriate) to apply COVID-19 lessons learned beyond the current public health emergency. FDA will develop guidance on the use of alternative tools to assess manufacturing facilities named in pending applications, including incorporation of best practices

from the use of such tools during the COVID-19 pandemic. In addition, BsUFA III will promote timely FDA communication with sponsors regarding manufacturing facility inspections.

BsUFA III Will Modernize FDA's IT Infrastructure and Support Adoption of Cloud-based Technologies

As with the PDUFA VII agreement, BsUFA III will also provide dedicated resources and includes corresponding initiatives related to enhancing the capabilities of FDA's IT and data infrastructure to support the regulatory review of drugs. BsUFA III will help support a modernized, cloud-based ESG and also help with the establishment of a strategy on data-driven regulatory initiatives that will leverage the Agency's current initiatives as detailed in the TMAP and DMAP.

BsUFA III Will Build on BsUFA II Efforts to Modernize FDA Financial and Staff Resource Management

BsUFA II included improvements to the financial structure of the BsUFA program[vii] aimed to help ensure financial stability and appropriate staffing for the FDA to meet negotiated goals, with implementation and maturation of these reforms expected to continue into BsUFA III. Implementation of the proposed BsUFA III performance goals will build on the foundational work started in BsUFA II to modernize financial and staff resource management, accountability, and transparency, including clear hiring goals and progress reporting.

Conclusion

America's biopharmaceutical research and development ecosystem is the best in the world. However, due to the ongoing COVID-19 pandemic and increased global competition, it is imperative that FDA is equipped to help us deliver new treatments and cures to meet patients' unmet medical needs. PDUFA VII and BsUFA III will help ensure that patients have timely access to lifesaving medicines, while maintaining the United States' global leadership in biopharmaceutical innovation.

PhRMA and its member companies are committed to working closely with FDA and all stakeholders to ensure the continued success of the PDUFA and BsUFA programs in bringing safe and effective medicines to patients. PhRMA therefore urges Congress to reauthorize PDUFA and BsUFA in a timely manner to ensure the new enhancements are implemented as planned and protect against any disruptions to these critical programs.

PhRMA applauds your continued commitment to ensuring the long-term stability of the FDA's human drug and biosimilar review programs and to continuing to strengthen the Agency's capabilities in areas critical to keeping pace with the latest scientific advances in drug development and regulation. We look forward to continuing to work with the Committee,

Members of Congress, and other stakeholders on these important issues. Thank you for the opportunity to provide this testimony. I would be happy to address any questions.

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[i] PhRMA, "PhRMA 2021 Annual Membership Survey," (2021), https://www.phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/M-O/PhRMA_membership-survey_2021.pdf

[ii] *See* U.S. Food and Drug Administration [hereinafter "FDA"], Center for Drug Evaluation and Research, "Advancing Health Through Innovation: New Drug Therapy Approvals 2021," (January 2022), at 21, https://www.fda.gov/media/155227/download.

[iii] *See* FDA, "PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2023 Through 2027," [hereinafter "PDUFA VII Commitment Letter"] at 28, 49-50, https://www.fda.gov/media/151712/download.

[iv] *See* FDA "PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2013 Through 2017," at 22, 24-25, https://www.fda.gov/media/81306/download.

[v] *See* FDA, "PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2018 Through 2022," [hereinafter "PDUFA VI Commitment Letter"] at 27-30, https://www.fda.gov/media/99140/download.

[vi] PDUFA VI Commitment Letter at 37-41.

[vii] See FDA, "BsUFA Reauthorization Performance Goals and Procedures Fiscal Years 2018 Through 2022," at 27-32, https://www.fda.gov/media/100573/download.