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August 23, 2020

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

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

Dear Sir or Madam:

The Pharmaceutical Research and Manufacturers of America ("PhRMA") is pleased to submit these comments on the Food and Drug Administration's (FDA or the Agency) Reauthorization of the Prescription Drug User Fee Act (PDUFA). PhRMA commends FDA for holding the virtual meeting to hear stakeholder views on PDUFA as the Agency considers the features to propose, update, and discontinue in PDUFA VII.

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. Since 2000, PhRMA member companies have invested more than $900 billion in the search for new treatments and cures, including an estimated $79.6 billion in 2018 alone.[1]

Discovery, development, and delivery of safe and effective innovative medicines to patients is the core mission of our members. With more than 8,000 medicines in development around the world,[2] 74 percent of which are potentially first-in class,[3] the pipeline of biopharmaceutical promise is extraordinary. New developments in medical and fundamental science – including immunotherapies and cell and gene therapies – hold the promise of treating debilitating diseases such as Alzheimer's, cancer, diabetes, and many rare disorders. Fulfilling this promise depends on a modern regulatory paradigm that is able to serve patients by providing timely, science-based regulatory decisions.

That is why PhRMA and our member companies support a strong and science-based U.S. FDA staffed appropriately and resourced through a combination of appropriated funds and user fees from the regulated industry. 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 keep pace with the rapid increase in the number and complexity of innovative drugs and biologics entering the review pipeline.

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[1] PhRMA, "PhRMA 2019 Annual Membership Survey," (2019), https://www.phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/P-R/PhRMA_2019_membership_survey_Final.pdf.

[2] Adis R&D Insight Database (May 2019).

[3] *See* Analysis Group, "The Biopharmaceutical Pipeline: Innovative Therapies in Clinical Development," (July 2017), at 5, https://www.phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/A-C/Biopharmaceutical-Pipeline-Full-Report.pdf.

PhRMA has been a strong supporter of, and participant in, PDUFA since its inception in 1992. We appreciate the opportunity to provide the following comments on the reauthorization of the PDUFA program.[4]

I. PDUFA HAS BEEN A SUCCESS FOR FDA, INDUSTRY, AND PATIENTS

PDUFA was created to augment the staffing and funding for the review of new drug applications and meet urgent patient demands for more timely approvals of life-saving medicines. PDUFA has played a critical role in strengthening the FDA's ability to regulate safe and effective medicines for patients. The Program for Enhanced Review Transparency and Communication for NME NDAs and Original BLAs ("the Program") established under PDUFA V[5] continues to meet its goals of increasing the efficiency and effectiveness of the first review cycle and decreasing the number of review cycles necessary for approval, so that patients have timely access to safe, effective, and high-quality new drugs and biologics.

PDUFA has enabled significant improvements in the average review and approval times for new drug applications and biologics license applications. In 2019, FDA approved 48 New Molecular Entities,[6] including 21 orphan drugs.[7] Last year, FDA met 100% of their PDUFA review goals for new molecular entities and biologics license applications, and 90% of these drugs were approved in the first review cycle.[8]

II. COVID-19 RESPONSE AND LESSONS LEARNED

This year, FDA is also at the forefront of the response to the COVID-19 pandemic, while continuing to perform PDUFA VI review activities.[9] FDA has acknowledged impacts of the current public health emergency on formal meetings and user fee applications in guidance[10] on these topics. The Agency has been working with the biopharmaceutical companies to facilitate their efforts to accelerate the development of safe and effective COVID-19 therapeutics and vaccines. Specifically, FDA has provided timely recommendations, regulatory guidance, and technical assistance to developers of potential treatments and vaccines for COVID-19. More broadly, FDA has also provided clarity to biopharmaceutical sponsors on how to continue to advance drug and biologic development during the current pandemic.

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[4] Reauthorization of the Prescription Drug User Fee Act; Public Meeting; 85 Fed. Reg. 35096-35099 (June 8, 2020).

[5] *See* U.S. Food and Drug Administration [hereinafter FDA], "PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2013 Through 2017," at 5, https://www.fda.gov/media/81306/download [hereinafter PDUFA V Commitment Letter].

[6] *See* FDA, Center for Drug Evaluation and Research, "Advancing Health Through Innovation: New Drug Therapy Approvals 2019," (January 2020), at 10, https://www.fda.gov/media/134493/download [hereinafter CDER 2019 New Drug Therapy Approvals Report].

[7] *Id.* at 13.

[8] *Id.* at 23, 24.

[9] FDA, Coronavirus (COVID-19) Update: FDA Continues User-Fee Related Reviews Through COVID-19, (April 16, 2020), https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-continues-user-fee-related-reviews-through-covid-19.

[10] FDA Guidance for Industry: "Effects of the COVID-19 Public Health Emergency on Formal Meetings and User Fee Applications — Questions and Answers," (May 2020), https://www.fda.gov/media/138358/download.

In response to the COVID-19 pandemic, FDA and industry are utilizing novel approaches to clinical trials, facilities inspections, drug review, manufacturing, and supply chain security to support continued innovation and inform rapid regulatory decision-making. There is a pressing need for FDA and industry to identify actions taken during the COVID-19 pandemic and evaluate their effectiveness and applicability to innovative drug development beyond the public health emergency declaration. FDA has created streamlined approaches and updated processes as a result of the public health crisis. For example, FDA has primarily been teleworking and utilizing technology to continue to communicate with sponsors in lieu of in-person meetings by holding virtual sponsor and advisory committee meetings to maintain continuity of operations.

PDUFA VII can include provisions and commitments that help address lessons learned from FDA and sponsors developing COVID-19 drugs and vaccines. For example, industry and FDA could benefit from more predictable and timely engagement and better communication during drug development, additional clarity on innovative drug development and risk-based inspections and manufacturing approaches, and a strengthened infrastructure at the Agency.

III. PDUFA VII OFFERS THE OPPORTUNITY FOR FURTHER IMPROVEMENTS

It is important that all stakeholders work together to further build on the successes of previous PDUFAs, including initiatives on novel drug development tools and trial designs, use of patient perspectives in regulatory decision-making, and use of real-world evidence. PDUFA VII offers the opportunity to build upon the efforts started in PDUFA VI to advance the use of innovative drug development tools and approaches that have the potential to expedite patient access to new therapies.

1. PDUFA VII Can Enhance Patient-Centric Drug Review

As scientific advances lead to a better understanding of specific diseases or conditions, knowing which elements of the disease or of a potential treatment are most important to patients is increasingly important to researchers. Continuing to develop a science-based and systematic approach to gathering patient input robust enough to support FDA's regulatory decision making is necessary to realize the goal of a patient-centered approach to drug development and regulatory review. New and powerful tools – including complex innovative trial designs (CID), advanced statistical methods (including use and acceptability of alternative data analysis tools such as Bayesian statistical methods), digital health technologies, patient-reported outcomes, and real-world evidence – have the potential to expedite drug development and ultimately patient access to new therapies.

For industry, innovative trial designs can enable early assessment of treatment effect and reduce the risk of drug development failure, while also reducing investment in multiple, duplicative, or large clinical trials that may not provide additional safety and efficacy information. For patients, novel clinical trial designs (e.g., seamless phase 2/3 design) can minimize human exposure to investigational drugs, reduce the need for a placebo arm (e.g., by using a historical control) and bring needed medicines to patients faster and more efficiently.

2. PDUFA VII Can Advance Digital Health Technologies

Digital health technologies – such as digital health products, artificial intelligence and machine learning –are transforming nearly every aspect of the health care system, improving efficiency, expanding access to treatments and technologies, and enhancing development of personalized medicine. The use of digital health technologies has been a powerful tool for industry, regulators, health professionals, and patients in the response to the COVID-19 pandemic. Sponsors have incorporated telehealth into clinical trials, virtualizing study visits, and collecting data remotely. Digital health technologies present significant opportunities to support clinical trials and decentralized or virtual clinical trials. PDUFA VII can advance a flexible and scalable global framework for digital technology development and build upon the "lessons learned" during the COVID-19 pandemic (e.g., decentralized clinical trials, virtual study site visits, remote data collection) to further enable the use of digital health technologies throughout drug development.

3. PDUFA VII Can Modernize Regulatory Evidence Generation

Rapid advances in information technology and data science have enhanced the ability to use unprecedented volumes of data to generate timely insights on the use, benefits, and risks of medicines. PhRMA believes that real-world data and evidence may, in some circumstances, be adequate on their own to satisfy the substantial evidence criteria for demonstrating effectiveness, whereas in others, they may provide substantial evidence of effectiveness in combination with other data. Real-world evidence can enable more efficient drug development programs for additional uses of a drug, provide more robust information about the benefits and risks of new medicines after approval, and ultimately lead to more timely access to innovative, safe and effective medicines for patients.

Additional initiatives will be needed to provide even greater clarity to sponsors to help increase use and regulatory acceptance of these tools and approaches. PDUFA VII should be used to further modernize regulatory evidence generation and increase transparency and promote stakeholder learning around acceptable uses of innovative approaches for regulatory decision-making.

4. PDUFA VII Can Optimize FDA Infrastructure, Staffing, and Resources

For the Agency to keep up with the rapid pace of scientific advances, it must be able to deploy the most modern technologies and expertise to review cutting-edge scientific developments. PDUFA user fees help ensure that the FDA's human drug review program's staffing, resourcing, and infrastructure are robust and able to support efficient drug review and approval.

FDA has taken significant steps toward modernizing the financial structure of PDUFA and improving the forecasting and planning to better align the user fee resources to the workload needs of the review staff. PhRMA commends FDA for completing key financial deliverables from PDUFA VI,[11] including implementing staff time reporting and establishing a new capacity planning methodology[12] that will help better identify and align PDUFA resources

[11] *See* FDA, "PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2018 Through 2022," at 37-38, https://www.fda.gov/media/99140/download.

[12] FDA, "Resource Capacity Planning & Modernized Time Reporting Implementation Plan," (July 31, 2020), https://www.fda.gov/media/112562/download.

to programmatic needs. As these reforms continue to mature through the next few years, they will lead to even greater efficiency and sustainability for the human drug review program.

In June 2020, FDA released a third-party interim assessment of hiring and retention ("Hiring Assessment")[13] for public comment as per the PDUFA VI Goals Letter commitments.[14] The Hiring Assessment detailed ongoing issues related to the hiring capabilities at FDA and barriers to recruiting, hiring, and retention of staff, including limitations of the data management systems to properly track Agency progress against hiring initiatives.[15] The Hiring Assessment includes specific recommendations for FDA to take in order to address these challenges.[16] In order to fully realize the impact of the proposed improvements in PDUFA VII, these recommendations need to be addressed during PDUFA VI and completed prior to the start of PDUFA VII in October 2022. In PDUFA VII, FDA can adopt continued improvements to processes supporting hiring, recruitment, and retention of staff and key experts to fully support FDA's ability to fulfill its PDUFA commitments and public health mission.

5. PDUFA VII Can Improve FDA's Regulatory Information Technology Infrastructure

Information technology is another critical infrastructure component underpinning the success of the human drug review program. Modernizing and enhancing FDA's ongoing technological efforts is necessary to leverage recent advances in data science, analytics, predictive models in support of regulatory and clinical decisions, and the next generation of digital health products. PDUFA VII should build on ongoing efforts such as the Technology Modernization Action Plan (TMAP).[17] PhRMA strongly supports an Agency-wide, strategic data and technology approach that is transparent and promotes active collaboration with industry stakeholders to successfully ensure that necessary technology and innovation investments promote convergence in data compatibility, interoperability, and interpretability for current and future FDA data initiatives throughout the regulatory lifecycle. PhRMA strongly believes that the integration of cloud-based technologies as part of a comprehensive strategy for data modernization and regulatory processes is key to the Agency's ability to support the proposed multi-year strategic plan.

IV. CONCLUSION

By focusing on the key areas outlined above, PDUFA VII can play a critical role in continuing to advance an effective, science-based regulatory review program that helps ensure that biopharmaceutical companies continue to bring innovative medicines to patients in need.

The United States leads the world in the introduction of new medicines thanks in part to the FDA's human drug review program.[18] PDUFA VII will help ensure that the Agency keeps

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[13] Booz Allen Hamilton, "FDA Interim Hiring and Retention Assessment," (April 13, 2020), https://www.fda.gov/media/138662/download [hereinafter Hiring Assessment].

[14] *See* PDUFA VI Commitment Letter at 38-41.

[15] *See* Hiring Assessment at 59-64.

[16] *Id.* at 59.

[17] FDA, "FDA's Technology Modernization Action Plan," (September 18, 2019), https://www.fda.gov/media/130883/download.

[18] *See* CDER 2019 New Drug Therapy Approvals Report at 5.

pace with scientific discovery and helps bring the next generation of safe and effective new medicines and potential cures to patients.

PhRMA looks forward to working collaboratively with FDA, patient groups and other stakeholders to enhance the existing program and make improvements where appropriate in PDUFA VII. The timely reauthorization of the PDUFA program is important to maintain the high level of the human drug review program performance, while creating the predictable regulatory review framework needed to support future biopharmaceutical investment. PhRMA supports an efficient reauthorization process and expeditious approval in Congress to ensure there are no disruptions to the FDA activities.

Respectfully submitted,

_____/s/_____

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