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Public Workshop on the Seventh Reauthorization of
the Prescription Drug User Fee Act

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Introduction

Good morning. Thank you to the U.S. Food and Drug Administration (FDA) for the opportunity to share some insights on the importance of the prescription drug user fee program in advancing personalized medicine.

My name is Cynthia Bens and I serve as Senior Vice President of Public Policy at the Personalized Medicine Coalition (PMC). PMC is an education and advocacy organization that has more than 200 members from across the health care spectrum. We are working together to advance personalized medicine in ways that benefit patients.

We define personalized medicine as an evolving field that uses diagnostic tools to identify specific biological characteristics to help determine which medical treatments and procedures will be best for each patient. By combining this information with an individual's medical history, circumstances, and values, personalized medicine allows doctors and patients to develop targeted treatment or prevention plans.

The prescription drug user fee program is a critical source of funding that ensures the timeliness of drug reviews, encourages innovation in drug development, and promotes FDA initiatives that leverage the best science. Having a well-resourced, focused, and flexible FDA is essential to achieving PMC's mission of bringing personalized medicine closer to all patients.

PMC has documented that personalized medicines account for more than 20 percent of the FDA's new drug approvals each year. These approvals have increased sharply since the Coalition first started looking at approval trends in 2005. At that time personalized medicines only accounted for 5 percent of newly approved therapies. There have been notable regulatory approvals since the last *Prescription Drug User Fee Act (PDUFA)* reauthorization. These include the approval of cell and gene therapies, N-of-1 therapies, and tissue-agnostic therapies. Activities undertaken by the FDA in recent years have fostered a favorable environment for innovations like these, and we believe this progress will continue.

Our analyses have also shown that recent successes in personalized medicine product development have increased outside of oncology. There are lessons learned from targeted treatment in oncology that are being applied in drug development for an increasing number of diseases. We believe enhancements included in the seventh *PDUFA* reauthorization that advance the future of personalized medicine will yield benefits for a wide range of patients, including patient populations with unmet medical needs.

There are three main areas that should be addressed in discussions leading up to the *PDUFA VII* agreement. These areas are targeted staffing needs to support drug review, additional considerations for advancing the use of real-world evidence (RWE) and real-world data (RWD), and the use of digital health tools to support personalized medicine.

Addressing Targeted Staffing Needs

To help the FDA fulfill its mission to protect public health while meeting the challenges posed by the increasingly complex regulatory landscape, *PDUFA VI* and the *21st Century Cures Act (Cures Act)* included provisions supporting the agency's efforts to maintain a capable and well trained staff. The FDA has made progress addressing staffing needs but we understand that challenges remain in attracting and retaining expert staff. *PDUFA VII* should focus on addressing areas where there are still staffing gaps. PMC supports adequate staffing of FDA's Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) as part of *PDUFA VII*.

For as long as medical researchers have been discovering genes that contribute to particular diseases, there has been interest in developing ways to repair abnormal genes or introduce new genetic material directly into cells to treat or prevent disease. Gene and cell-based therapies are designed to either "knock out" or replace a mutated gene that causes illness or introduce a new or healthy copy of a gene to help treat a disease. Since 2012, 10 cell-based or direct gene therapies have been approved by the FDA to target a variety of diseases ranging from metabolic and rare neuromuscular disorders to more common cancers. FDA finalized a suite of guidances for the development and assessment of gene therapies earlier this year and anticipates that by 2025 it will be reviewing and approving between 10 and 20 cell and gene therapies annually.

Cell and gene-based therapies have the potential to yield unprecedented improvements in clinical outcomes for patients with some diseases, and it continues to be an important area for personalized medicine. PMC is concerned by the size of the workload facing CBER resulting from the need to evaluate increasing numbers of new cell and gene therapies. We have called on Congress to provide the FDA with the budget authority appropriations necessary to deal with this issue, but meeting FDA's staffing needs for work on cell and gene therapies will take funding outside of the appropriations process. In order to continue much of the exciting progress we have seen in this area, attention should be paid in *PDUFA VII* to increasing CBER's staffing.

Advancing Real-World Evidence and Real-World Data

Real-world evidence, or data acquired in everyday clinical practice, can provide valuable insights about an individual's lifestyle, disease biology and treatment outcomes. Thanks to new technologies and data science approaches, this information can be harnessed as a powerful complement to traditional clinical trials. Real-world data applications can provide new ways to track disease, allow for optimization of treatment approaches, and capture insights about patient populations to accelerate clinical development. We believe the use of real-world evidence can help transform the future of personalized medicine if this information can be combined and aggregated in ways that inform answers to questions

that meet patient needs. *PDUFA VI* made some initial improvements at the agency to enhance the use of real-world evidence and real-world data. PMC commends the FDA for recognizing real-world evidence and real-world data as a strategic priority, and for its 2018 framework for real-world evidence.

The *Cures Act* also acknowledged how real-world data could generate evidence and accelerate our understanding of which patients could benefit the most from new medicines. The *Cures Act* directed the Secretary of Health and Human Services to establish a program that evaluates the potential use of real-world evidence to support new indication approvals and satisfy post-approval study requirements. We understand there are organic activities going on within individual review divisions to increase reviewers' comfort level with this science and ways that real-world data can inform drug review. We encourage FDA to continue hosting workshops and facilitating FDA staff participation in other educational forums.

The agency noted in its 2018 framework that "There is more data available to inform medical decisions than ever before. But we (the agency) need to provide clear guidance on the appropriate collection and evaluation of this information." We agree with this statement and we have identified some areas that should be given additional attention. The future of personalized medicine will increasingly rely on the ability to continuously leverage high-quality, regulatory-grade data. To allow the FDA to make further transformations in the use and acceptance of real-world evidence beyond early phase trials and for purposes beyond demonstrating product safety, PMC would support additional staffing, resources and guidance development under *PDUFA VII*.

One issue to be mindful of is that the aggregation of large volumes of data over time is one of the most valuable characteristics of real-world databases. Real-world databases **cannot** be single use, as it would limit a dataset's full potential. There are multiple ways data can be used to support research, development, and regulatory approvals, including hypothesis generation (e.g., predictive treatment effect for a novel biomarker) or providing supplemental evidence to an existing companion diagnostic or label expansion. We would recommend that the FDA consider addressing the repeated use of real-world databases for regulatory submission as part of *PDUFA VII*. Clearer guidance on acceptable surrogate clinical endpoints and methods to establish equivalence to patient enrollment criteria and defining the clinical comparability between the real-world data and the intended use population are two areas where PMC would have interest.

Further, stakeholders could benefit from increased visibility into FDA's experience with real-world evidence and real-world data as the space continues to evolve. We would encourage the FDA to disseminate learnings from real-world data submissions while protecting sponsors' proprietary and confidential information. This type of transparency would allow manufacturers, researchers, and health data organizations to more efficiently leverage real-world datasets.

Finally, we know that FDA is committed to its *Technology Modernization Action Plan (TMAP)*. The initial phase involves updating agency computer hardware, software, data, and analytics. PMC knows that much of what we highlight as potential areas for improvement in this section will not be possible without the completion of fundamental steps like those laid out in the *TMAP*. *PDUFA VII* should provide resources to the FDA so that it can rapidly move beyond near-term

steps to full implementation actions in the plan, particularly those that focus on data and application solutions achieved through direct engagement with stakeholders and other government agencies.

Realizing the Potential of Digital Health Tools

The ubiquity of mobile information devices such as smart phones, advanced sensing technologies and self-management platforms have made them important tools for personalized medicine. A growing number of ongoing clinical trials feature the use of wearable and environmental sensors to learn how to deliver real-time care to patients. Digital health platforms like wearables and mobile apps can help us gather more information and also capture the patient experience, which is a critical perspective. People can report detailed information about their symptoms, treatment burden, quality of life and other experiences, actively and passively documenting their health in detail in ways that go far beyond standard testing performed episodically in a physician's office.

Digital health technologies hold the potential for enhancing trial efficiency, parallel to the delivery of real-world care, and provide personalized insights at the point of care. However, as the adoption of digital health technologies increases, evidence generation may need to evolve and incorporate approaches such as decentralized trials.

Decentralized trials utilize telemedicine, including remote patient visits and monitoring, to enhance recruitment, incorporate diverse patient populations within community settings, maintain the physician-patient relationship, and reduce trial timelines. Decentralized trials provide more patients with access to investigational therapies, while also generating more data to inform scientific understanding. Importantly, such an approach increases patient participation in research and can make it easier for diverse populations and patients in difficult geographic regions to access clinical trials.

Recognizing the cost, time, and complexity associated with the research and development of new medicines, the *Cures Act* called for the incorporation of novel clinical trial designs. The FDA signaled in the *PDUFA VI* reauthorization process that the agency appreciates the value of new approaches and technologies and their incorporation into trials. Shortly after releasing the FDA's most recent real-world evidence framework, then commissioner Scott Gottlieb stated that "Pragmatic and hybrid clinical trials, including decentralized trials that are conducted at the point of care—and incorporate real-world evidence—can help clinical trials become more agile and efficient by reducing administrative burdens on sponsors and those conducting trials, and can allow patients to receive treatments from community providers without compromising the quality of the trial or the integrity of the data that's being collected."

PMC believes that the FDA should accelerate the use of decentralized trials especially now since health care delivery has radically changed as a result of the COVID-19 pandemic. There is a growing acceptance and availability of telemedicine and remote patient visits that are important to this area. Guidance regarding digital technology issues, including the acceptance of decentralized trials, should be considered as part of *PDUFA VII*. Further, we would ask FDA to consider in any new guidance barriers that it can remove to allow for greater patient participation

in novel clinical trials and enable the collection of information on the off-label use of approved therapies.

Conclusion

Thank you again to the FDA for the opportunity to comment on behalf of PMC. My colleagues and I look forward to working with the agency over the next year as the *PDUFA VII* stakeholder consultation process begins.