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August 21, 2020

Submitted electronically to: <https://www.regulations.gov>

Lowell Schiller, JD
Principal Associate Commissioner for Policy
Food and Drug Administration
Room 4300, White Oak Building One
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: FDA-2010-N-0128: Reauthorization of the Prescription
Drug User Fee Act; Public Meeting; Request for Comments

Dear Mr. Schiller:

The Society for Women's Health Research (SWHR) is pleased to offer comments as a follow-up to the U.S. Food and Drug Administration (FDA) public meeting regarding the proposed recommendations for the reauthorization of the Prescription Drug User Fee Act (PDUFA) for fiscal years (FYs) 2023 through 2027. We write specifically in response to Docket No. FDA-2010-N-0128 for "Reauthorization of the Prescription Drug User Fee Act; Public Meeting; Request for Comments."

SWHR is a 30-year-old national education and advocacy nonprofit dedicated to promoting research on biological sex differences in disease and improving women's health through science, policy, and education. Working collaboratively with the FDA is part of SWHR's legacy.

SWHR championed the framework for the scientific discipline of sex-based biology, which encourages the inclusion of female subjects in clinical trials and analyzes the differences between women and men in relation to disease. Through the systematic collection and reporting of more accurate, sex-specific drug and device information and labeling, the FDA has been able to better serve both women and men.

In advance of PDUFA VI's expiration in September 2022, SWHR offers several recommendations, detailed below, that represent priorities for the millions of women nationally who rely on prescription medications.



1. Apply lessons learned from the COVID-19 pandemic to strengthen the agency's approach to decentralizing clinical trials and making research participation more available to an increasingly diverse range of patients.

Women are frequently the health care decision-makers for both themselves and for family members, and they are often unduly burdened by in-person health care visits. Frequently, caregiving obligations make it difficult for women to participate in clinical research. Traditional clinical trial models typically involve frequent, and at times lengthy, site visits to receive a therapeutic or to engage in routine patient monitoring. Low participation in clinical trials may be in large part due to difficulties accessing in-person clinical sites.¹

COVID-19 has had significant effects on health care in the U.S. In the midst of a global pandemic, decentralized and siteless trials seem more appealing than ever and may have the added benefit of increasing participation and improving diversity within research. Decentralized trials can improve patient comfort and increase convenience for research participants.² SWHR encourages the FDA to view the current environment as an opportunity to reconsider the conventional trial model. Virtual, siteless, and direct-to-patient trials, as well as hybrid approaches, should all be considered. The FDA can play a major role in shepherding this transition and providing guidance to relevant stakeholders on best practices for moving from traditional to more innovative clinical trials models.

We commend the FDA for quickly releasing guidance on changes to trials during the current pandemic.³ SWHR encourages the FDA to incorporate lessons learned during the time of COVID-19 to further evolve clinical trials, and we encourage the consideration of a shift to innovative trials models within upcoming PDUFA legislation.

2. Coordinate the FDA approach to digital health technologies in order to support the decentralization of clinical trials and to increase participation of diverse patient groups within research.

The use of digital health technologies (e.g., mHealth, health information technology, wearable devices, telehealth, etc.) can improve remote monitoring of patients and provide for real-time data capture within clinical trials. These technologies may be a means of increasing patient access to clinical trials and improving participation of women, people of color, and other underrepresented populations across the lifespan. Data gathered through the use of digital technologies may also help researchers learn about the real-world effects of medications. Additionally, mobile apps may be a potential avenue for allowing researchers not only to gather data, but also to consent and enroll participants in studies.⁴

¹ Spears, PA. (2020). Patient barriers to participation in breast cancer clinical trials. *Breast Cancer Management*, 9(1). doi: 10.2217/bmt-2020-0004

² National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Health Sciences Policy; Forum on Drug Discovery, Development, and Translation; Shore C, Khandekar E, Alper J, editors (2019).. *Virtual Clinical Trials: Challenges and Opportunities: Proceedings of a Workshop*. Washington (DC): National Academies Press (US). 2, Opportunities to Improve Clinical Trials. Available from: <https://www.ncbi.nlm.nih.gov/sites/books/NBK548971/>

³ FDA guidance on conduct of clinical trials of medical products during COVID-19 public health emergency (2020). Available from: <https://www.fda.gov/media/136238/download>

⁴ Klonoff, DC, King, F, Kerr, D. (2019). New opportunities for digital health to thrive. *Journal of Diabetes Science and Technology*, 13(2), 159-163.



Per Cox, Lane & Volchenboum's 2018 review articles⁵ on digital health technology, the "[n]ext steps for establishing mHealth methods and tools as legitimate and accepted measures in oncology clinical trials include continuation of regulatory definition by the FDA; establishment of security standards and protocols; refinement and implementation of methods to establish and document data accuracy; and finally, creation of feedback loops wherein regulators receive updates from researchers with better and more timely data, which should decrease trial times and lessen drug development costs."

SWHR encourages the FDA to build upon its ongoing work in the digital health technology field in order to coordinate the use of digital technology within clinical trials. The FDA should consider how researchers may use various alternative approaches of collecting information within clinical trials and include potential examples of less burdensome (potentially digital health-based) approaches in order to improve research participation.

3. Better integrate real-world data (RWD) and real-world evidence (RWE) within agency drug approval and decision-making initiatives.

SWHR has been pleased to follow the FDA's work to include RWE and RWD within its regulatory framework. RWE, derived from data collected during routine health care practice (such as electronic health records, claims and billing activities, and product and disease registries), can help to capture the impact of a potential treatment on patient quality of life or reflect differences in treatment outcomes based on heterogeneity.

This type of data can enable more efficient drug development programs and provide information that clinical trials alone may not be able to capture. When generated and used appropriately, RWE is an incredibly valuable resource to patients, researchers, and regulators.

We commend the FDA for its previous guidance, "Framework for Real-World Evidence Program," as well as its draft guidance on "Submitting Documents Utilizing Real-World Data and Real-World Evidence to FDA for Drugs and Biologics."^{6,7} SWHR requests that the FDA include further RWE commitments within PDUFA VII and continue incorporating these types of data within drug approval and decision-making initiatives. We urge the FDA to continue to provide guidance on when RWE might be satisfactory in meeting the "substantial evidence" standard and to build a foundation for all uses of RWE across the drug development and approval processes.

4. Continue efforts to gather patient input on drug development and to prioritize diverse patient voices to the greatest extent possible.

SWHR has been outspoken in the need to include the unique perspectives of women as patients, caregivers, and family decision-makers within the drug development process, as

⁵ Cox, SM, Lane, A., Volchenboum (2018). Use of wearable, mobile, and sensor technology in cancer clinical trials. *JCO Clinical Cancer Informatics*. Accessed from: <https://ascopubs.org/doi/pdfdirect/10.1200/CCI.17.00147>

⁶ Framework for FDA's real-world evidence program (2018). Accessed from: <https://www.fda.gov/media/120060/download>

⁷ Submitting documents using real-world data and real-world evidence to FDA for drugs and biologics: Guidance for industry (draft; 2019). Accessed from: <https://www.fda.gov/media/124795/download>



exemplified in SWHR's "Policy Principles: Patient-Focused Drug Development."⁸ Obtaining meaningful input from historically marginalized populations of women across the lifespan is particularly crucial. Greater diversity in the patient population increases the potential of learning more about how different subgroups might respond to a new medication.

SWHR supports the continued work of the FDA within its Patient-Focused Drug Development (PFDD) program. We were pleased to see the release of the first of four PFDD guidance documents⁹ providing recommendations for how researchers can collect and submit patient experience data and other relevant information. We look forward to further efforts from the FDA on how drug developers may be able to best capture patient-centered outcomes (PCOs) to obtain information on variables that matter most to women. Engaging diverse populations and encouraging contributions from women will help researchers ensure they are obtaining information that matters to patients.

5. Improve inclusion of pregnant and lactating women within clinical trials.

Each year in the United States, 6 million women are pregnant,¹⁰ nearly 4 million women give birth,¹¹ and more than 3 million women breastfeed.¹² Despite these profound statistics, there is a paucity of human data on safety and efficacy of therapeutics in pregnant and lactating women. Exclusion of pregnant and lactating women in research has led to significant, unacceptable gaps in women's health.

The Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC), established by the 21st Century Cures Act, released a report in 2018 recommending the inclusion of pregnant and lactating women in clinical research. We encourage the FDA to consider how best to improve the inclusion of pregnant and lactating women in the drug development and approval process, and recommend coordination with PRGLAC to remove regulatory barriers to research in pregnant and lactating women.

In line with PRGLAC's 2018 recommendations,¹³ SWHR encourages the FDA to ensure that the Common Rule is implemented to ensure that pregnant women are no longer classified as a vulnerable population, and to highlight the importance of research on therapeutic products in pregnant women and lactating women, including the effects of not taking medication during pregnancy and lactation as well as the impact of not breastfeeding on both mother and child. SWHR looks forward to PRGLAC's upcoming report that will detail implementation recommendations, and we are hopeful the FDA will take the full body of PRGLAC's important work into consideration for PDUFA VII.

⁸ SWHR principles addressing disparities in drug development (2019). Accessed from: https://swhr.org/swhr_resource/swhr-principles-addressing-disparities-in-drug-development/

⁹ Patient-focused drug development: Collecting comprehensive and representative input (2020). Accessed from: <https://www.fda.gov/media/139088/download>

¹⁰ Curtin, SC, Abma, JC, Ventura, SJ, Henshaw, SK (2013). Pregnancy rates for US women continue to drop. *National Center for Health Statistics Data Brief*, 138. Accessed at: <https://www.cdc.gov/nchs/data/databriefs/db136.pdf>

¹¹ Martin, JA, HaMilton, BE, Osterman, MJK, Driscoll, AK (2019). Births: Final data for 2018. *National Vital Statistics Reports*, 68(13). Accessed at: https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68_13-508.pdf

¹² Centers for Disease Control (2018). Breastfeeding report card, United States, 2018. Accessed at: <https://www.cdc.gov/breastfeeding/pdf/2018breastfeedingreportcard.pdf>

¹³ PRGLAC report to the HHS Secretary and Congress (2018). Accessed from: <https://www.nichd.nih.gov/about/advisory/PRGLAC/recommendations>



6. Continue FDA's focus on hiring and retaining experienced, highly qualified staff.

Finally, SWHR is supportive of previous PDUFA efforts to improve the hiring and retention of highly qualified staff to support the drug review and approvals processes. The recent Booz Allen Hamilton report, "FDA Interim Hiring and Retention Assessment," completed in response to PDUFA VI and BsUFA II commitment letters, provides specific information on the FDA's progress in this area, as well as areas for continued improvement.¹⁴ We urge the FDA to maintain its focus in this area within the next PDUFA cycle.

SWHR is grateful for the opportunity to provide feedback to the FDA on PDUFA VII, and we look forward to continued opportunities to collaborate with the FDA and other stakeholders over the coming months. If you have any questions, please do not hesitate to contact SWHR's Director of Science Policy, Melissa Laitner, PhD, MPH, at melissa@swhr.org.

Sincerely,

A handwritten signature in black ink that reads "Kathryn G. Schubert".

Kathryn G. Schubert, MPP
President and Chief Executive Officer
Society for Women's Health Research

¹⁴ FDA interim hiring and retention assessment. (2020). Accessed from: <https://www.fda.gov/media/138662/download>