CAMT
Coalition to Advance Maternal Therapeutics

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September 26, 2024

The Honorable Robert M. Califf, MD
Commissioner
US Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

RE: FDA-2021-D-0789-0159 - Diversity Action Plans to Improve Enrollment of Participants from Underrepresented Populations in Clinical Studies; Guidance for Industry - Draft Guidance

Dear Commissioner Califf,

As members of the Steering Committee of the Coalition to Advance Maternal Therapeutics (CAMT), which represents medical and scientific societies, public health groups, patient advocacy organizations, and entities dedicated to the inclusion of pregnant and lactating populations in research, we thank you for the opportunity to provide comments on the recently released Food and Drug Administration (FDA) Draft Guidance on Diversity Action Plans to Improve Enrollment of Participants from Underrepresented Populations in Clinical Studies ("the Draft Guidance").

We applaud the FDA for pursuing guidance that advances our shared goal of increasing enrollment of historically underrepresented populations in clinical studies. As leaders of CAMT, we are particularly interested in promoting the inclusion of pregnant and lactating people in clinical trials to ensure medications and devices used by these populations are both safe and effective.

Historically, pregnant and lactating women have been excluded from clinical trials, leading to significant evidence gaps impacting the health outcomes of mothers and infants. Of the more than 3.5 million women in the United States who give birth each year, approximately 90 percent take at least one over-the-counter or prescription medication during their pregnancy.[1] Despite the high rates of usage, 70 percent of medications approved by the FDA have no human pregnancy data, and 98 percent have insufficient data to determine risk to the infant.[2] For women who live with chronic conditions, such as diabetes, narcolepsy, epilepsy, lupus, mental health conditions, and hypertension, this lack of data creates serious challenges for management of their conditions during pregnancy, putting both mothers and infants at risk. Further, failure to conduct studies in these populations has led to limited innovations in how to care for pregnancy-induced conditions, such as preeclampsia.

[1] Ke, A. B., Greupink, R., & Abduljalil, K. (2018). Drug Dosing in Pregnant Women: Challenges and Opportunities in Using Physiologically Based Pharmacokinetic Modeling and Simulations. CPT: pharmacometrics & systems pharmacology, 7(2), 103–110. https://doi.org/10.1002/psp4.12274.
[2] Ibid.

We appreciate steps the FDA has taken to ameliorate this evidence gap, including hosting workshops, issuing guidance documents, educating clinicians, conducting research and more. However, the data indicates that more must be done. In the six years since the United States Department of Health and Human Services (HHS) Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC) provided recommendations to Congress and HHS on how to increase the inclusion of these populations in research, there have been no improvements in participation of pregnant or lactating people in clinical trials.[3] We provide the following recommendations for the Draft Guidance to promote the inclusion of these populations.

1. Retain language in the Draft Guidance encouraging sponsors to include pregnant and lactating populations in their Diversity Action Plans.
We appreciate that the FDA notes in the draft guidance that, "a sponsor developing a Diversity Action Plan that specifies enrollment goals disaggregated or tabulated by race, ethnicity, sex, and age group, should also consider the potential that pregnant or lactating individuals with the condition or disease may use the medical product." Specifically calling out pregnant and lactating populations is critical to raising the visibility of these populations with sponsors. We call on the FDA to retain this language in final guidance.

2. Require sponsors to provide the estimated prevalence or incidence of a disease or condition in the U.S. pregnant and lactating populations.
We contend that calling out pregnant and lactating populations in guidance is not enough. While the long-term goal of CAMT is to require sponsors to specifically justify exclusion of pregnant and lactating populations in study design, as recommended by the PRGLAC[4], we recognize that is beyond the scope of this Draft Guidance. However, Congress did give FDA the authority to use this Draft Guidance to require sponsors to provide rationale for their clinical trial enrollment goals.

As currently drafted, the Draft Guidance requires sponsors to provide "1) the sponsor's goals for enrollment in the clinical study, disaggregated by race, ethnicity, sex, and age group of clinically relevant study populations, 2) the sponsor's rationale for such goals, and 3) the sponsor's explanation of how the sponsor intends to meet such goals."

We encourage include an additional requirement that sponsors provide an estimated prevalence or incidence of the disease or condition for which the medical product is being studied in the U.S. pregnant population and lactating population. Estimates should be provided regardless of whether the sponsor is setting a specific enrollment goal for these populations. Further, these estimates should be included in the annual report to Congress summarizing in the aggregate the Diversity Action Plans and made publicly available of the FDA website.

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[3] Thiele, L, Thompson, J, Pruszynski, J, Spong, CY, et al. Gaps in evidence-based medicine: underrepresented populations still excluded from research trials following 2018 recommendations from the Health and Human Services Task Force on Research Specific to Pregnant Women and Lactating Women. American Journal of Obstetrics & Gynecology, Volume 227, Issue 6, 908 – 909. Available at https://www.ajog.org/article/S0002-9378(22)00548-8/fulltext.

[4] Recommendation 10. Task Force on Research Specific to Pregnant Women and Lactating Women. Report Implementation Plan. August 2020. Available from: https://www.nichd.nih.gov/sites/default/files/inline-files/PRGLAC_Implement_Plan_083120.pdf. Accessed September 25, 2024.

Requiring sponsors to provide these estimates, regardless of whether setting an enrollment goal, will serve to elevate these populations in the minds and plans of sponsors. Further, they will provide stakeholders with valuable data to further advocate for the inclusion of pregnant and lactating people in clinical trials.

Such a requirement is squarely within the authority provided by the Food and Drug Omnibus Reform Act of 2022 (PL 117-328), which states that Diversity Action Plans may include "rationale for the sponsor's enrollment goals, which may include – [...] any other data or information relevant to selecting appropriate enrollment goals, disaggregated by demographic subgroup, such as the inclusion of pregnant and lactating women [...]" Requiring plan sponsors to provide a rationale for populations *not* selected for enrollment goals is just as important – if not more – than for those they do select as targets. Requiring sponsors to include this data will help FDA and other stakeholders assess whether sponsors are adequately recruiting trial participants that reflect those that will be using the medical product when it comes to market.

Again, thank you for the opportunity to provide comments. We look forward to continuing to work with you on advancing the inclusion of pregnant and lactating populations in clinical trials. Please direct any questions to CAMT Chair Rebecca Abbott (rabbott@smfm.org).

Sincerely,
American College of Obstetricians and Gynecologists
Elizabeth Glaser Pediatric AIDS Foundation
Epilepsy Foundation of America
March of Dimes
Preeclampsia Foundation
Society for Maternal-Fetal Medicine
Society for Women's Health Research