Society for Women's Health Research

July 8, 2019

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

Amy Abernethy, MD, PhD
Principal Deputy Commissioner
U.S. Food and Drug Administration

Re: Docket No. FDA-2018-D-4525 for "Clinical Lactation Studies: Considerations for Study Design Guidance for Industry"

Dear Dr. Abernethy:

The Society for Women's Health Research (SWHR) commends the Food and Drug Administration (FDA) for issuing draft guidance regarding pre- or post-marketing lactation studies by drug sponsors and provides information to facilitate the conduct of them.

SWHR, an education and advocacy non-profit, is dedicated to promoting research on biological differences in disease and improving women's health through science, policy, and education. SWHR strongly supports the inclusion of lactating women in clinical research and is pleased to provide comments on this topic.

The lack of evidence for clinical decision-making concerning medication use by lactating women is an important public health issue that must be addressed.

By some estimates, more than 80% of new mothers in the United States breastfeed in the months following delivery.[1] More than 50% of women globally are estimated to take one or more medications during the postpartum period.[2] Despite these profound statistics, there is a paucity of human data on drug safety and efficacy in lactating women.

An analysis of LactMed — an online database that provides clinicians and patients with information on the effects of drugs and on their substance levels in breast milk and infant blood

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— found that just 2% (28 out of 1,408) products included recommendations based on strong lactation-specific data.[3] An FDA analysis of 575 prescription drug and biologic products with labeling approved from 2015 to 2017 found only 15% of products included human lactation data.[4] Consequently, when a lactating woman needs a therapeutic because of chronic disease, diagnosis of a new disease, or an accident, both she and her health care provider are largely blind as to the effect therapeutics could have on human milk, milk production, and the infant. In many instances, lactating women will disrupt or stop breastfeeding to take a medication for which evidence is lacking.

The rationale for considering the inclusion of breastfeeding women in clinical research is similar to considerations for pregnant women and should be stated in FDA guidance.

In April 2018, FDA issued draft industry guidance titled "Pregnant Women: Scientific and Ethical Considerations for Inclusion in Clinical Trials; Draft Guidance; Availability (Docket No. FDA-2018-D-1201). The rationale for considering the inclusion of lactating women in clinical research is similar to the following FDA stated reasons for considering the inclusion of pregnant women in clinical trials, all of which SWHR supports:

- *"Women need safe and effective treatment during pregnancy.*
- *Failure to establish the dose/dosing regimen, safety, and efficacy of treatments during pregnancy may compromise the health of women and their fetuses.*
- *In some settings, enrollment of pregnant women in clinical trials may offer the possibility of direct benefit to the woman and/or fetus that is unavailable outside the research setting.*
- *Development of accessible treatment options for the pregnant population is a significant public health issue."*[5]

SWHR suggests FDA include corollary text specific to lactating women in its final guidance.

CONSIDERATIONS FOR CLINICAL LACTATION STUDIES

SWHR commends FDA for issuing unique guidance to outline considerations for the conduct of lactation studies. Specifically, we support FDA encouragement of sponsor consideration to conduct a clinical lactation study whenever such study *would be appropriate*, even if the study is *not required* by the agency (lines 73-74).

Further, SWHR finds it informative that the draft guidance seeks to identify specific "situations when a sponsor may wish to consider whether conducting a clinical lactation study would be appropriate" (lines 74-77). SWHR agrees that each of the following situations should be considered (lines 78-87) on a case-by-case basis:

- *A drug under review for approval is expected to be used by women of reproductive age*
- *After approval, use of a drug in lactating women becomes evident (e.g., via report in the medical literature or lay press)*

- *A new indication is being sought for an approved drug and there is evidence of use or anticipated use of the drug by lactating women*
- *Marketed medications that are commonly used by women of reproductive age (e.g. anti-depressants, anti-hypertensives, anti-infectives, diabetic and pain medications)*

SWHR supports this draft guidance's identification and examination of proposed ethical considerations with respect to the following three populations of lactating women:

1. *Lactating women prescribed a drug that is subject of a lactation study as part of a standard clinical care (lines 100-101)*
2. *Women in a research setting being administered an investigational drug (line 111)*
3. *Women who are healthy volunteers and are administered an investigational drug for the purpose of clinical research (lines 127-128).*

SWHR finds the ethical considerations presented for each population plausible, and we look forward to hearing feedback from sponsors and lactation study design experts on this issue.

GENERAL COMMENTS

SWHR strongly supports HHS interagency collaboration to advance concurrent work to address gaps in research on medication use by lactating women.

Provisions of the 21st Century Cures Act sought to help address the significant gap in research on safe and effective therapies in pregnant women and lactating women by requiring the National Institutes of Health (NIH) to establish a Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC). Task Force membership consists of the heads of NIH and other national research agencies and institutes, the Office of the FDA Commissioner, and representatives from medical societies, industry, nonprofit organizations, and others with expertise on pregnant women, lactating women, or children. The Task Force was charged with providing recommendations that were submitted to the secretary of the Department of Health and Human Services (HHS) and Congress in a September 2018 report. In March 2019, HHS extended the term of the PRGLAC for two additional years to provide guidance to HHS on the implementation of the report's recommendations.

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Thank you for providing SWHR this opportunity to comment on FDA-2018-D-4525 and for consideration of the above comments. We look forward to serving as a resource on this and

other topics affecting women's health. If you have questions, please contact me or Sarah Wells Kocsis, Vice President of Public Policy, at 202.496.5003 or swellskocsis@swhr.org.

Sincerely,

Amy Miller, PhD
President and Chief Executive Officer
Society for Women's Health Research

[1] Centers for Disease Control and Prevention. Breastfeeding report card: United States, 2018.
[2] Saha, MR et al. Postpartum Women's Use of Medications and Breastfeeding Practices: A Systemic Review. International Breastfeeding Journal. 2015;10:28.
[3] Byrne, J and Spong, C. "Is it Safe?" — The Many Unanswered Questions about Medications and Breast-Feeding. Perspective. New England Journal of Medicine. 380:14. April 4, 2019.
[4] Ibid.
[5] US Food and Drug Administration. Pregnant Women: Scientific and Ethical Considerations for Inclusion in Clinical Trials; Draft Guidance for Industry; Availability. Docket No. FDA-2018-D-1201.