Current Regulatory Landscape and Efforts to Advance Pharmacokinetic Studies in Pregnancy

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Disclaimer

- I do not have any financial disclosures to report
- This presentation represents the views of the speaker, and not the official position of the FDA

Current Regulatory Landscape

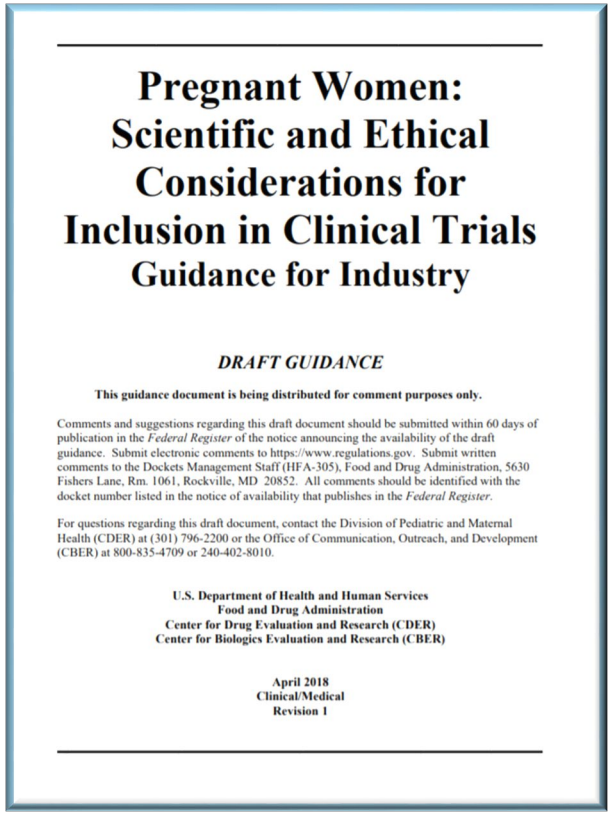
- There are approximately 3.6 million births in the U.S./year
- Pregnant people are often left out of drug development
  - Currently no requirements to study drugs in pregnancy
  - Data are needed to inform dosing recommendations and safety in drug labeling and clinical care
- COVID-19 pandemic clearly illustrated the need for early planning and consideration for inclusion of pregnant people
- Regulatory advances
  - Common Rule: has removed reference to pregnant people as "vulnerable"
  - FDA is working to harmonize its regulations with the Common Rule

FDA Efforts to Advance the Conduct of Pharmacokinetic (PK) Studies in Pregnancy

Guidances to Advance Drug Development and PK Data Collection in Pregnant People

- Pregnant people are an important segment of the population that need to be studied
- Early and thoughtful consideration are needed to avoid delays

Guidances that Discuss Pregnancy PK Data Collection



Pregnant Women: Scientific and Ethical Considerations for Inclusion in Clinical Trials
Guidance for Industry

DRAFT GUIDANCE

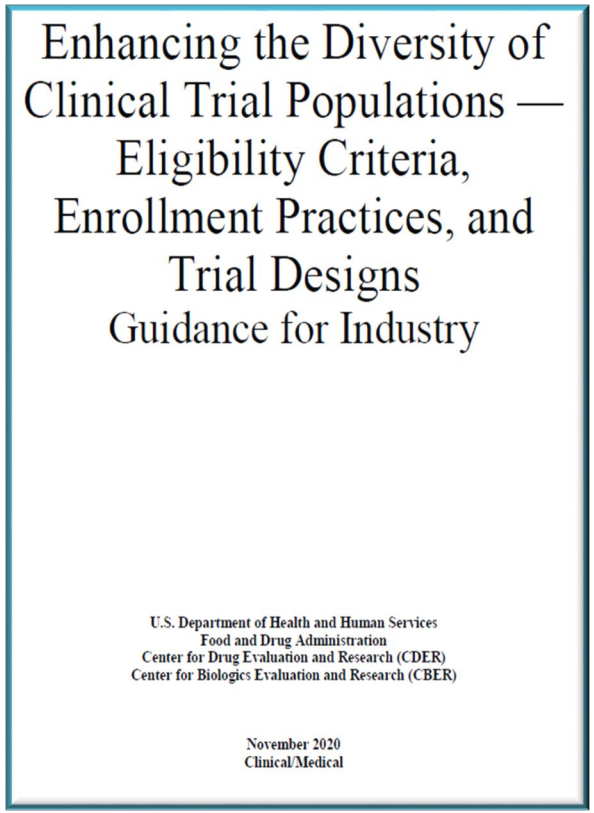
This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact the Division of Pediatric and Maternal Health (CDER) at (301) 796-2200 or the Office of Communication, Outreach, and Development (CBER) at 800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

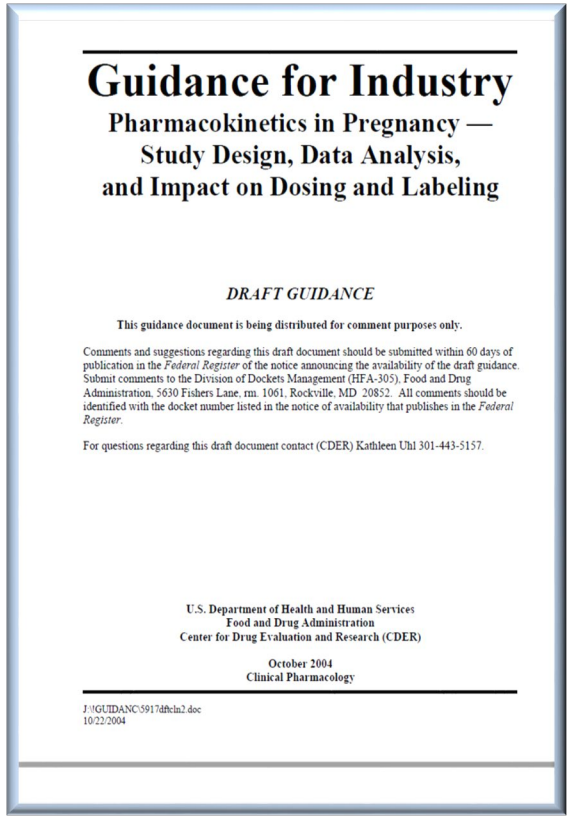
April 2018
Clinical/Medical
Revision 1



Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs
Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

November 2020
Clinical/Medical



Guidance for Industry
Pharmacokinetics in Pregnancy — Study Design, Data Analysis, and Impact on Dosing and Labeling

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For questions regarding this draft document contact (CDER) Kathleen Uhl 301-443-5157.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

October 2004
Clinical Pharmacology

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10/22/2004

Regulatory Considerations for the Conduct of PK Studies in Pregnancy

- Have the regulatory requirements of 45 CFR 46 Subpart B been met ?* (nonclinical studies complete; preliminary studies in nonpregnant women to inform risk, etc.)
- What are the benefit-risk considerations?
  - Pre-marketing vs. post-marketing setting
  - Trial (administration of a study drug) vs opportunistic study

* Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research; Applies to research conducted or supported by HHS; however, recommended by FDA

Task Force on Research Specific to Pregnant and Lactating Women (PRGLAC)

- Required under the 21st Century Cures Act of 2016
- Objectives: Identify and address gaps in knowledge and research regarding safe and effective therapies for pregnant women and lactating women
- Prepare a report and recommendations to the Secretary of the Department of Health and Human Services (first report completed September 2018; Implementation Report published October 2020)

PRGLAC Recommendations Relevant to PK Studies

- Increase the quantity, quality, and timeliness of research involving therapeutic products used by pregnant people
- Implement a proactive approach to protocol development and study design
- Develop a systematic plan for timely collection of data, including PK data, in pregnant people
- Strengthen the infrastructure for conducting PK/Pharmacodynamic (PD) studies
- Develop new research tools for PK and PD

Global Efforts to Advance PK Studies in Pregnancy

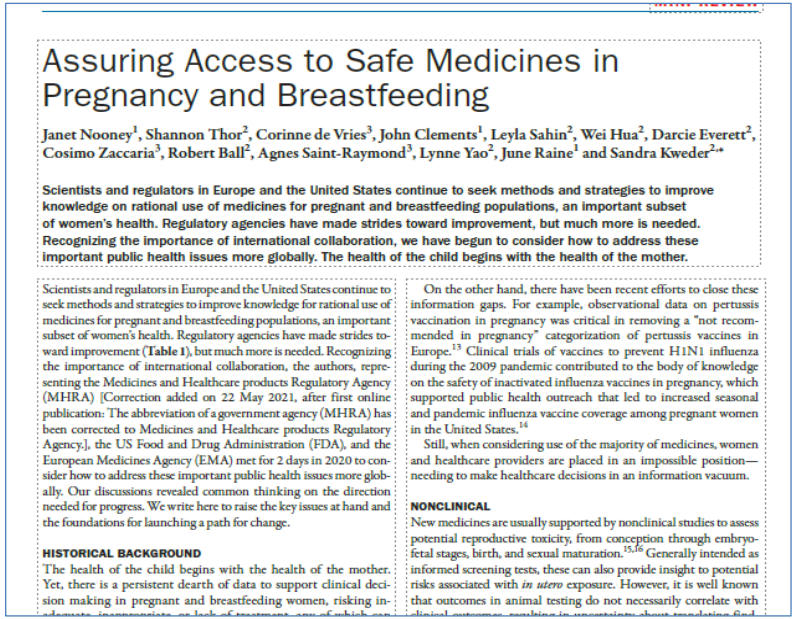
ICMRA
INTERNATIONAL COALITION OF MEDICINES REGULATORY AUTHORITIES

FDA

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

MHRA

Pregnancy and Lactation cluster



Assuring Access to Safe Medicines in Pregnancy and Breastfeeding

Janet Nooney[1], Shannon Thor[2], Corinne de Vries[3], John Clements[1], Leyla Sahin[2], Wei Hua[2], Darcie Everett[2], Cosimo Zaccaria[3], Robert Ball[2], Agnes Saint-Raymond[3], Lynne Yao[2], June Raine[1] and Sandra Kweder[2,*]

Scientists and regulators in Europe and the United States continue to seek methods and strategies to improve knowledge on rational use of medicines for pregnant and breastfeeding populations, an important subset of women's health. Regulatory agencies have made strides toward improvement, but much more is needed. Recognizing the importance of international collaboration, we have begun to consider how to address these important public health issues more globally. The health of the child begins with the health of the mother.

Scientists and regulators in Europe and the United States continue to seek methods and strategies to improve knowledge for rational use of medicines for pregnant and breastfeeding populations, an important subset of women's health. Regulatory agencies have made strides toward improvement (**Table 1**), but much more is needed. Recognizing the importance of international collaboration, the authors, representing the Medicines and Healthcare products Regulatory Agency (MHRA) [Correction added on 22 May 2021, after first online publication: The abbreviation of a government agency (MHRA) has been corrected to Medicines and Healthcare products Regulatory Agency.], the US Food and Drug Administration (FDA), and the European Medicines Agency (EMA) met for 2 days in 2020 to consider how to address these important public health issues more globally. Our discussions revealed common thinking on the direction needed for progress. We write here to raise the key issues at hand and the foundations for launching a path for change.

HISTORICAL BACKGROUND

The health of the child begins with the health of the mother. Yet, there is a persistent dearth of data to support clinical decision making in pregnant and breastfeeding women, risking in-

On the other hand, there have been recent efforts to close these information gaps. For example, observational data on pertussis vaccination in pregnancy was critical in removing a "not recommended in pregnancy" categorization of pertussis vaccines in Europe.[13] Clinical trials of vaccines to prevent H1N1 influenza during the 2009 pandemic contributed to the body of knowledge on the safety of inactivated influenza vaccines in pregnancy, which supported public health outreach that led to increased seasonal and pandemic influenza vaccine coverage among pregnant women in the United States.[14]

Still, when considering use of the majority of medicines, women and healthcare providers are placed in an impossible position—needing to make healthcare decisions in an information vacuum.

NONCLINICAL

New medicines are usually supported by nonclinical studies to assess potential reproductive toxicity, from conception through embryo-fetal stages, birth, and sexual maturation.[15,16] Generally intended as informed screening tests, these can also provide insight to potential risks associated with *in utero* exposure. However, it is well known that outcomes in animal testing do not necessarily correlate with

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Summary

- PK studies are part of FDA's commitment to advance data collection in pregnant people
- Growing recognition that pregnant people need to be included in clinical studies to optimize care
- Challenges and potential solutions will be discussed at this meeting
- Stakeholder collaboration is essential to move forward: federal agencies, industry, researchers, professional organizations, advocacy groups

Thank You