

Optimizing the Use of Postapproval Pregnancy Safety Studies

Hybrid Public Workshop

National Press Club, Washington D.C.

September 18 – 19, 2023

Background

In the United States (U.S.), approximately 5.5 million pregnancies occur each year.¹ Half of individuals who are pregnant use at least one drug or biological product to treat chronic (e.g., diabetes, seizure disorders, or asthma), acute (e.g., infection) or serious medical conditions.² Typically at the time of initial market approval, there are limited to no human data on the safety of drug or biological products used during pregnancy. As a result, for most products, human pregnancy safety data are collected after a product is available on the market (i.e., postapproval).

In May 2019, FDA published a draft Guidance for Industry titled *Postapproval Pregnancy Safety Studies*,³ which discusses the strengths and limitations of postapproval study types including studies based on registry data and cohort studies using electronic health records or claims data. However, more research is needed to better understand the key considerations for determining the optimal postapproval study designs to obtain timely evidence to ensure the safe use of drug and biological products in pregnant individuals. The public workshop is a preliminary discussion with stakeholders to inform FDA's further development of a framework and also meets a performance goal under the FDA User Fee Reauthorization Act of 2022, in accordance with the Prescription Drug User Fee Act (PDUFA) Reauthorization Performance Goals and Procedures Fiscal Years 2023 Through 2027 letter.⁴ Specifically, the PDUFA VII Commitment Letter outlines the commitment of a public workshop to discuss postapproval pregnancy safety studies to facilitate determination of ideal study designs.

The Duke-Margolis Center for Health Policy, under a cooperative agreement with the U.S. FDA, is convening a two-day Public Workshop that will include discussion of designs of postapproval pregnancy safety studies for drug and biological products regulated by the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER). During this event, participants will hear FDA's considerations for constructing a framework describing how data from different types of postapproval pregnancy safety studies might optimally be used; stakeholders' perspectives on opportunities to optimize postapproval pregnancy safety study types and designs; design considerations and potential approaches to bridge knowledge gaps in developing the framework, including understanding how the Sentinel Initiative (i.e., Sentinel System and Biologics Effectiveness and Safety (BEST)) may address these gaps; and stakeholders' perspectives on considerations for FDA's proposed framework.

¹ U.S. Centers for Disease Control and Prevention, National Center for Health Statistics. U.S. Pregnancy Rates Drop During Last Decade [Press Release] Hyattsville (MD); 2023 April 12, Available from: https://www.cdc.gov/nchs/pressroom/nchs_press_releases/2023/20230412.htm.

² Mitchell AA, Gilboa SM, Werler MM, et al. Medication use during pregnancy, with particular focus on prescription drugs: 1976-2008. *Am J Obstet Gynecol* 2011;205:51.e1-8.

³ U.S. Food and Drug Administration. *Postapproval Pregnancy Safety Studies Guidance for Industry*. Silver Spring, (MD); 2019 May, Available from: <https://www.fda.gov/media/124746/download>.

⁴ Prescription Drug User Fee Act Reauthorization Performance Goals and Procedures Fiscal Years 2023 Through 2027 Commitment Letter, Available from <https://www.fda.gov/media/151712/download>.

Day 1

10:00 AM Welcome and Overview

Marianne Hamilton Lopez, Duke-Robert J. Margolis, MD, Center for Health Policy

10:10 AM FDA Opening Presentation: The Role of Postapproval Pregnancy Safety Studies

Objective: Provide a high-level overview of how work on postapproval pregnancy safety studies has progressed since the 2014 FDA public meeting (Study Approaches and Methods to Evaluate the Safety of Drugs & Biological Products During Pregnancy in the Postapproval Setting). This presentation will discuss the Postapproval Pregnancy Safety Studies draft Guidance, PDUFA VII commitments toward pregnancy safety, and set the overall stage for this convening.

Presenter: **Leyla Sahin**, CDER, U.S. Food and Drug Administration

10:30 AM Session 1: Stakeholder Perspectives on the Impact of Postapproval Pregnancy Safety Studies

Objectives: Stakeholders will discuss the impact of and considerations for pregnancy safety studies and identify potential opportunities to better meet stakeholder needs.

Moderator: **Megan Clowse**, Duke University School of Medicine

Panelists:

- **Mariah Leach**, Patient Representative
- **Keele Wurst**, GlaxoSmithKline
- **Katherine Wisner**, Asher Center, Feinberg School of Medicine, Northwestern University
- **Geeta Swamy**, Duke University School of Medicine

11:05 AM Break

11:20 PM Session 2: Stakeholder Perspectives on Challenges and Opportunities to Optimize Postapproval Pregnancy Safety Study Types and Designs

Objective: Stakeholders will share their thoughts on the key factors to enhance the generation of robust and timely drug/biologic safety data for pregnant individuals as part of the drug/biologic development process. Panelists will specifically focus on opportunities to optimize postapproval pregnancy study types and designs.

Moderator: **Geeta Swamy**, Duke University School of Medicine

Presenters:

- **Christina Chambers**, University of California San Diego
- **Jessica Albano**, Syneos Health
- **Christine Olson**, Centers for Disease Control and Prevention
- **Elyse Kharbanda**, HealthPartners Institute

12:45 PM **Lunch Break**

02:00 PM **Session 3: FDA’s Considerations for Constructing a Pregnancy Safety Study Framework**

Objectives: FDA presenters will provide information on recent work, including a landscape analysis of postapproval pregnancy safety studies that informed FDA decision making, a review of postapproval pregnancy safety studies that informed the Pregnancy and Lactation Labeling Rule (PLLR), and use of drug utilization data that have helped form their key considerations for the construction of a pregnancy safety study framework.

Moderator: **Megan Clowse**, Duke University School of Medicine

Presenters:

- **Wei Hua**, CDER, U.S. Food and Drug Administration
- **Adebola Ajao**, CDER, U.S. Food and Drug Administration
- **Aida Kuzucan**, CDER, U.S. Food and Drug Administration
- **José J. Hernández-Muñoz**, CDER, U.S. Food and Drug Administration

03:15 PM **Break**

03:25 PM **Session 4: Design of the Pregnancy Safety Study Framework**

Objective: FDA presenters will describe important study characteristics and factors that will be essential to include in the framework, such as considerations to determine the size of potential exposure, timeliness of signal identification, and validation. In addition, the proposed decision schematic for the framework will be discussed.

Moderator: **Geeta Swamy**, Duke University School of Medicine

Presenter: **Wei Hua**, CDER, U.S. Food and Drug Administration

Panelists:

- **Wei Hua**, CDER, U.S. Food and Drug Administration
- **Clara Kim**, CDER, U.S. Food and Drug Administration
- **Leyla Sahin**, CDER, U.S. Food and Drug Administration
- **Sara Eggers**, CDER, U.S. Food and Drug Administration

04:25 PM **Wrap-Up Day 1 – Brief Closing Remarks**

Marianne Hamilton Lopez, Duke-Robert J. Margolis, MD, Center for Health Policy

04:30 PM **Adjourn Day 1**

Day 2

10:00 AM Welcome, Brief Recap, and Overview of Agenda for Day 2

Gerrit Hamre, Duke-Robert J. Margolis, MD, Center for Health Policy

10:10 AM Open Public Comment

Objective: Individuals who wish to provide oral public comments during this workshop will make a request prior to the meeting via the workshop website, then be slotted into a slot during this session. There will be no dialogue/responses – This will just be a listening session for the audience.

Moderator: **Gerrit Hamre**, Duke-Robert J. Margolis, MD, Center for Health Policy

10:40 AM Session 5: Filling the Known Gaps for a Comprehensive Pregnancy Safety Study Framework

Objective: FDA presenters will discuss plans, per the PDUFA VII commitment, to develop and conduct demonstration projects that will address identified knowledge gaps in the design and performance of different pregnancy safety study types to better inform the development of the framework. In addition, capabilities in the Sentinel and BEST system to improve study designs and conduct safety research will be discussed.

Moderator: **Evan Myers**, Duke University

Presenters:

- **Patricia Bright**, CDER, U.S. Food and Drug Administration
- **Judith Maro**, Harvard Pilgrim Health Care Institute and Harvard Medical School
- **Joann Gruber**, CBER, U.S. Food and Drug Administration

11:50 AM Lunch

01:05 PM Session 6: Stakeholder Perspectives on the FDA's Proposed Pregnancy Safety Study Framework

Objective: Stakeholders will provide feedback on the FDA's proposed framework and discuss additional potential opportunities to enhance the framework to ultimately optimize pregnancy safety studies.

Moderator: **Evan Myers**, Duke University

Panelists:

- **Marie Teil**, UCB BioPharma SRL
- **Lynne Yao**, CDER, U.S. Food and Drug Administration
- **Robert Ball**, CDER, U.S. Food and Drug Administration
- **Sonia Hernandez-Diaz**, Harvard TH Chan School of Public Health
- **Krista Huybrechts**, Brigham and Women's Hospital, Harvard Medical School
- **Janet R Hardy**, Independent Consultant

02:25 PM **Wrap-up and Closing Remarks**

Gerrit Hamre, Duke-Robert J. Margolis, MD, Center for Health Policy

02:30 PM **Adjourn**

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