

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In May 2019, FDA published a draft Guidance for Industry titled *Postapproval Pregnancy Safety Studies*,³ which discusses the strengths and limitations of postapproval study types including studies based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 (PDUFA VII Commitment Letter), which is available at <https://www.fda.gov/media/151712/download>. 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 gather stakeholder input on how to optimize the design and type of postapproval pregnancy safety studies of drugs and biologics 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 how postapproval studies have informed the FDA's regulatory decisions and labeling; stakeholder experiences with implementing pregnancy safety studies; the current and preliminary thinking from the FDA on considerations for a pregnancy safety framework on optimizing selection of pregnancy safety study types at time of approval; opportunities to fill the known gaps with additional research of electronic data sources, including use of Sentinel and Biologics Effectiveness and Safety System (BEST); and potential next steps in optimizing the use of postapproval pregnancy safety studies.

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>.

Day 1:

10:00 Welcome and Overview

10:10 FDA Opening Presentation: The Role of Postapproval Pregnancy Safety Studies in Drug Development for Pregnant Individuals

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.

10:30 Session 1: Stakeholder Perspectives on the Impact of Postapproval Pregnancy Safety Study Types and Designs

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

Moderated discussion and Q&A (15 minutes): The moderator will guide panelists in a discussion about their opening remarks and perspectives using the prepared discussion questions. Selected questions submitted by the in-person and virtual audience via Slido will also be integrated into the discussion.

11:00 Break

11:20 Session 2: Stakeholder Perspectives on Challenges and Opportunities to Optimize Postapproval Pregnancy Safety Study Types and Designs (1 hour, 25 min)

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.

12:45 Lunch Break

01:45 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, and use of drug utilization data that have helped form their key considerations for the construction of a pregnancy safety study framework.

Moderated Q&A (25 minutes): Led by the Moderator addressing selected questions submitted by the in-person and virtual audience via Slido

3:10 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

Moderated panel discussion and clarifying questions and answers (25 minutes): The moderator will guide panelists in a discussion about their opening remarks and perspectives using the prepared discussion questions. Selected questions submitted by the in-person and virtual audience via Slido will also be integrated into the discussion.

03:55 Wrap-Up Day 1 – Brief Closing Remarks

04:05 Adjourn Day 1

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Day 2:

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

10:15 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.

10:45 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.

Moderated panel discussion and Q&A (25 minutes): The moderator will guide panelists in a discussion about their opening remarks and perspectives using the prepared discussion questions. Selected questions submitted by the in-person and virtual audience via Slido will also be integrated into the discussion.

11:55 Lunch

12:55 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.

Panelists (each will provide 5 minutes of opening remarks except for FDA followed by panel discussion)

Moderated discussion (60 minutes): The moderator will guide panelists in a discussion about their opening remarks and perspectives using the prepared discussion questions. Selected questions submitted by the in-person and virtual audience via Slido will also be integrated into the discussion.

02:15 Wrap-up and Closing Remarks

02:25 Adjourn

This public workshop is supported by the Food and Drug Administration (FDA) of the U.S. Department of Health and Human Services (HHS) as part of a financial assistance award [U19FD006602] totaling \$4,241,714 with 100 percent funded by FDA/HHS.

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