FDA Update Recommendation 10

Lynne Yao, M.D.
Director, Division of Pediatrics and Maternal Health
Office of Rare Diseases, Pediatrics, Urology and Reproductive Medicine
Office of New Drugs
Center for Drug Evaluation and Research
U.S. FDA

Background

- Recommendation 10: Implement a proactive approach to protocol development and study design to include pregnant women and lactating women in clinical research
  - 10A: Investigators/sponsors must specifically justify exclusion in study design
  - 10B: Ensure studies are designed to capture the time dependency of physiologic changes in pregnancy and lactation
  - 10C: Develop a systematic plan on how data for pregnant women and lactating women will be obtained in a timely fashion to include pharmacokinetics/pharmacodynamics and safety
  - 10D: Develop guidance for institutional review boards and investigators about the inclusion of pregnant women and lactating women in research
  - 10E: Develop a systematic plan for if a woman becomes pregnant in a study to include whether product should continue, if un-blinding is necessary, how to capture opportunistic information on pharmacology, clinical data, and pregnancy outcome information

FDA Guidance

- FDA draft guidance issued April 2018: Pregnant Women: Scientific and Ethical Considerations for Inclusion in Clinical Trials
  - Specifically discusses considerations for inclusion of pregnant individuals in clinical trials (recommendation 10D)
  - Does not specifically indicate a requirement to justify exclusion (recommendation 10A)
  - Specifically discusses collection of PK data during pregnancy (recommendation 10B)
  - Specifically discusses women who become pregnant while enrolled in a clinical trial including unblinding, and pregnancy outcome data; does not discuss collection of opportunistic data (recommendation 10E)
  - Undergoing review and revision

FDA Guidance, continued

- FDA draft guidance published 2004: Pharmacokinetics in Pregnancy — Study Design, Data Analysis, and Impact on Dosing and Labeling
  - Specifically discusses study designs to capture PK information pre-pregnancy, during all three trimesters, and post-partum (recommendation 10B)
  - Undergoing substantial revision

FDA Guidance, continued

- Draft guidance published May 2019: Clinical Lactation Studies: Considerations for Study Design
  - Specifically discusses types of lactation studies and collection of PK data based on stages of lactation (recommendation 10B)
  - Specifically describes situations in which lactation studies should be considered (recommendation 10D)
  - Undergoing review and revision

FDA Guidance, continued

- Draft guidance published May 2019: Postapproval Pregnancy Safety Studies
  - Specifically discusses the types of studies that can be considered to collect post-approval safety data (recommendation 10C)
  - Does not discuss specifics related to “timeliness” but FDA framework under PDUFA VII focuses optimizing use of Postapproval pregnancy safety studies (recommendation 10C)

Summary of FDA Update

PRGLAC Recommendation	FDA Guidances and/or Framework	Comment
10A	No	Does not include justification for exclusion at this time but includes reasons for inclusion
10B	Yes	Guidances for both pregnancy and lactation
10C	Yes	PDUFA VII Framework focuses on safety, not PK/PD
10D	Yes	FDA Guidance can be used by IRB and investigators
10E	Yes	Does not include recommendations on opportunistic collection of safety/PK data

Gaps

- PRGLAC recommendations 10A states, "*authorize the FDA to require drug developers to provide a "PRGLAC Study Plan" and "PRGLAC Assessment" during drug development"* (repeated in recommendation 10C)
  - There is currently no explicit statutory or regulatory requirement that sponsors must submit a PRGLAC Study Plan
- Cannot speak for academia, industry, or other governmental agencies