NATIONAL ACADEMIES Sciences Engineering Medicine

Forum on DRUG DISCOVERY, DEVELOPMENT, and TRANSLATION

Inclusion of Pregnant and Lactating Persons in Clinical Trials – A Workshop

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June 16, 2022, 8:30 am – 5:00 pm (ET)

June 17, 2022, 8:30 am – 12:00 pm (ET)

Keck Center, Room 100
500 5th Street NW, Washington, DC 20001

PURPOSE

This workshop, convened by the National Academies of Sciences, Engineering, and Medicine's Forum on Drug Discovery, Development, and Translation, will provide a venue for stakeholders to examine the current state of evidence generation for drug* products used by pregnant and lactating persons, and discuss challenges and opportunities for including these populations in clinical trials.

The public workshop will feature invited presentations and discussions to:

- Highlight knowledge gaps on drug product use during pregnancy and lactation with consideration for the clinical, ethical, and public health impacts on patient health;
- Discuss the laws and regulations governing drug research and development for these populations;
- Consider the liability concerns of private and public stakeholders for conducting drug research and development that includes pregnant and lactating persons, liability concerns associated with the use of drug products in these populations, and other barriers to inclusion of pregnant and lactating persons in clinical trials;
- Discuss practical short- and long-term opportunities and/or actions to improve evidence generation on the risks and benefits of drug products for pregnant and lactating persons and increase their inclusion in clinical trials.

** A substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease. For more information, see https://www.fda.gov/industry/regulated-products/human-drugs#drug (accessed March 17, 2022)*

DAY 1: THURSDAY, JUNE 16, 2022

8:30 am WELCOME AND OPENING REMARKS

RUTH R. FADEN, *Workshop Co-chair*
Founder, Johns Hopkins Berman Institute of Bioethics
Philip Franklin Wagley Professor
Johns Hopkins University

SHIRLEY SYLVESTER, *Workshop Co-chair*
Senior Medical Director, Women's Health
Johnson and Johnson

8:50 am SESSION I – MAKING THE CASE: THE NEED FOR EVIDENCE GENERATION TO SUPPORT SAFETY AND EFFICACY OF DRUGS USED DURING PREGNANCY AND LACTATION

Purpose:

- Highlight knowledge gaps on drug product use during pregnancy and lactation;
- Consider the clinical, ethical, public health, and personal implications of excluding pregnant and lactating persons from participation in clinical trials or otherwise failing to collect data on safety and efficacy in pregnancy and lactation; and
- Discuss outputs from the Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC).

Discussion Questions:

- How has the exclusion of pregnant and lactating persons from clinical trials and the general lack of evidence for these population groups affected maternal health on an individual and societal level?
- How does the lack of evidence for treating pregnant and lactating persons with drug therapies and vaccines affect decision making for patients, clinicians, and public health authorities?
- What are the potential trade-offs of not taking a prescribed drug during pregnancy and lactation versus taking a prescribed drug during pregnancy and lactation, when there is no or limited evidence for safety and efficacy?
- What information about the relative absence of evidence specific to these populations should be shared with pregnant and lactating persons and their care providers in order to make informed decisions? What information *should* they have?

8:50 am **Fireside Chat**

MAGGIE LITTLE, *Keynote speaker*
Senior Research Scholar, Professor of Philosophy, and Director of Ethics Lab
Georgetown University Kennedy Institute of Ethics

LEYLA SAHIN, *Moderator*
Acting Deputy Director for Safety
Division of Pediatrics and Maternal Health
FDA

9:20 am **Panel Discussion**

LEYLA SAHIN, *Moderator*
Acting Deputy Director for Safety
Division of Pediatrics and Maternal Health
FDA

Physiological Differences in Response to Drugs during Pregnancy & Lactation
THOMAS HALE
University Distinguished Professor of Pediatrics and Associate Dean of Research
Texas Tech University

Pregnant & Lactating Person Perspective
SARAH MANCOLL
Mother and Advocate

Gaps in Evidence for Clinical Care of Persons Prescribed Drugs during Pregnancy & Lactation
DAVID HAAS
Robert A. Munsick Professor of Obstetrics and Gynecology
Indiana University

Gaps in Evidence for Public Health Policy Affecting Pregnant & Lactating Persons
AJOKE SOBANJO-TER MEULEN
Vice President, Medical Affairs & Policy, Icosavax
Affiliate Associate Professor in Global Health, University of Washington

9:50 am **Q&A/Audience Discussion**

10:10 am **COFFEE BREAK (*30 minutes*)**

10:40 am SESSION II – PRACTICAL CHALLENGES AND OPPORTUNITIES FOR INCLUDING PREGNANT AND LACTATING PERSONS IN CLINICAL TRIALS

Purpose:

- Explore the social and cultural contexts for conducting clinical trials that include pregnant and lactating persons;
- Consider the barriers to and opportunities afforded by participation in clinical trials for pregnant and lactating persons; and
- Discuss practical short- and long-term opportunities and/or actions to improve access to clinical trials for pregnant and lactating persons.

Discussion Questions:

- What are the challenges that you or your institution face when considering including pregnant and lactating persons in clinical trials? How should these challenges be addressed to ultimately improve inclusion of these populations in clinical trials?
- What are specific challenges and opportunities to ensuring diversity in research participants and equity in science dissemination in regards to research involving pregnant and lactating persons?
- What should clinicians and researchers know about recruiting pregnant and lactating persons for participation in clinical research?
- What approaches can be used to decrease the burden on clinical trial participants who are pregnant or lactating?

10:40 am **Panel Discussion**

EBONY BOYCE CARTER, *Moderator*
Chief of Clinical Research in Obstetrics and Gynecology
Washington University School of Medicine in St. Louis

Advocating for Pregnant & Lactating Persons in Clinical Trials
ZSAKEBA HENDERSON
Senior Vice President of Maternal Child Health Impact and Interim Chief Medical Officer
March of Dimes

Equity and Diversity Considerations for Including Pregnant & Lactating Persons in Clinical Trials
VERONICA GILLISPIE-BELL
Associate Professor, Senior Site Lead and Section Head of Obstetrics and Gynecology, and Director of Quality for Women's Services, Ochsner Health System
Medical Director, Louisiana Department of Health

Recruitment and Retention of Pregnant & Lactating Persons in Chronic Disease Trials
BRITTANY BETTENDORF
Clinical Assistant Professor
University of Iowa

11:10 am **Q&A/Audience Discussion**

11:45 am **LUNCH BREAK (*1 hour*)**

12:45 pm SESSION III – LEGAL CONSIDERATIONS: REGULATORY PATHWAYS

Purpose:

- Discuss the laws and regulations governing drug research and development for pregnant and lactating persons, including human subject regulation, institutional review boards, and drug approval; and
- Discuss practical short- and long-term opportunities and/or actions to make regulatory pathways more supportive of including pregnant and lactating persons in clinical trials.

Discussion Questions:

- What are the most easily addressable legal and regulatory barriers that have prevented the inclusion of pregnant and lactating persons in clinical trials for both therapeutics and preventatives? How can these barriers be addressed?
- What are the more persistent legal and regulatory barriers to inclusion, and how could government, industry, patients, clinicians, and researchers collaborate to address them? What might that look like?
- How can researchers and institutional review boards address barriers to the inclusion of pregnant and lactating persons in clinical trials?

12:45 pm **Presentation**

Legal Landscape
LESLIE MELTZER HENRY, *Moderator*
Professor of Law
University of Maryland

1:05 pm **Panel Discussion**

Human Subjects Research Regulation Perspective
ANNA MASTROIANNI
Charles I. Stone Professor of Law
University of Washington

FDA Perspective
CATHERINE SEWELL
Acting Deputy Director and Deputy Director for Safety
Division of Urology, Obstetrics, and Gynecology
FDA

Vaccine Regulation Perspective
JEFF ROBERTS
Associate Vice President, Vaccine Clinical Development
Merck Research Laboratories

1:30 pm SESSION IV – ADDRESSING REAL AND PERCEIVED LIABILITY CONCERNS

Purpose:

- Discuss real and perceived liability concerns with including pregnant and lactating persons in drug research and development on the part of private and public sponsors of clinical trials;
- Discuss the real and perceived liability concerns associated with the use of drug products and vaccines in these populations on the part of practicing clinicians, researchers, and other key stakeholders; and
- Discuss practical short- and long-term opportunities and/or actions to address liability concerns.

Discussion Questions:

- What are the most common sources of risks that are more perceived then real (e.g. knowledge deficits, incorrect information presented to stakeholders, augmented risk aversion based on perspective as a clinician, researcher, or industry, other)?
- What are ways that clinicians, researchers, and industry could partner or support each other in

addressing real liability concerns? Are these roles for other stakeholders in also addressing real liability concerns?
- In considering strategies to address liability concerns, is there a logical order in which the solutions should be pursued? Are there any that are low hanging fruit, and which will be the most challenging to address?
- Looking the next 3-5 years, is there a realistic path towards mitigation of actual or perceived liability risks? What is the best-case forecast for where the field could be at the end of 3-5 years?

1:30 pm **Panel Discussion**

WILLIAM COOPER, *Moderator*
Professor of Pediatrics and Health Policy
Vanderbilt University

Clinician Perspective
CARMEN ZORRILLA
Professor of Obstetrics and Gynecology
University of Puerto Rico

Industry Perspective
AVIVA WEIN
Assistant General Counsel
Johnson and Johnson

Research Perspective
JESSICA COHEN
Director, Office of Research Affairs
PATH

2:05 pm **Q&A/Audience Discussion**

2:40 pm **COFFEE BREAK (*30 minutes*)**

3:10 pm SESSION V – BREAKOUT GROUPS

Purpose:
- Discuss opportunities to address liability concerns in the inclusion of pregnant and lactating persons in clinical trials; and
- Consider strategies to advance evidence generation for the clinical care of pregnant and lactating persons.

3:10 pm **Charge to Breakout Groups**

RUTH R. FADEN, *Workshop Co-chair*
Founder, Johns Hopkins Berman Institute of Bioethics
Philip Franklin Wagley Professor
Johns Hopkins University

3:15 pm **Breakout Group Discussions**

Workshop participants can select one of the follow breakout group topics:

Group 1: Opportunities to address liability concerns on the part of clinical investigators

Group 2: Opportunities to address liability concerns on the part of trial sponsors

Group 3: Opportunities to improve evidence generation for persons during pregnancy

Group 4: Opportunities to improve evidence generation for persons during lactation

4:15 pm	**Breakout Group Report-outs**
5:00 pm	**ADJOURN WORKSHOP DAY 1**

DAY 2: FRIDAY, JUNE 17, 2022

8:30 am SESSION VI – FIRESIDE CHAT: PROGRESS TOWARDS INCLUDING PREGNANT AND LACTATING PERSONS IN TRIALS

Purpose:

- Discuss progress towards implementing the PRGLAC recommendations and improving the inclusion of pregnant and lactating persons in clinical trials; and
- Consider next step opportunities to improve the inclusion of pregnant and lactating persons in clinical trials.

Discussion Questions:

- How are the finding and recommendations of PRGLAC advancing the inclusion of pregnant and lactating persons in clinical trials?
- What are the short- and long-term opportunities to execute the PRGLAC recommendations?
- Following the publication of the PRGLAC recommendations, are there any success stories from their implementation that can inform ongoing efforts to improve the inclusion of pregnant lactating persons in clinical trials?
- Are there areas that PRGLAC did not address that still require additional study? What opportunities exist to better understand and begin to resolve these issues?

DIANA BIANCHI, *Keynote speaker*
Director
Eunice Kennedy Shriver National Institute of Child Health and Human Development, NIH

SHIRLEY SYLVESTER, *Workshop Co-chair, Moderator*
Senior Medical Director, Women's Health
Johnson and Johnson

9:00 am SESSION VII – CASE STUDIES: LESSONS LEARNED IN TRIALS IN MENTAL HEALTH AND COVID-19

Purpose:

- Examine lessons learned from case studies for improving the inclusion of pregnant and lactating persons; and
- Consider opportunities to apply and/or scale-up approaches for including pregnant and lactating persons in clinical trials across therapeutic areas.

Discussion Questions:

- How can the lessons from research with pregnant and lactating persons in the cases of mental health and COVID-19 inform future clinical trials in other therapeutic and public health areas?
- How can stakeholders in this area continue to share lessons learned from clinical trials that include pregnant and lactating persons to build on previous successes?
- What are the opportunities for researchers, trial sponsors, and regulators to expand access to clinical trials to pregnant and lactating persons?
- Are there ways to prioritize clinical research in different therapeutic and public health areas that would provide the greatest benefit to pregnant and lactating persons?

9:00 am **Case Study 1: Lessons Learned from Drug Trials for Mood Disorders**
KATHERINE WISNER
Norman and Helen Asher Professor of Psychiatry and Behavioral Sciences, and Obstetrics and Gynecology
Director, Asher Center for Research and Treatment of Depressive Disorders
Northwestern University Feinberg School of Medicine

9:15 am **Case Study 2: Lessons Learned from COVID-19 Vaccine Trials**
RUTH KARRON
Professor of International Health
Johns Hopkins University Bloomberg School of Public Health

9:30 am **Panel Discussion: Opportunities to Scale-up Evidence Generation across Health Concerns**
KAVITA SHAH ARORA, *Moderator*
Associate Professor and Division Director of General Obstetrics and Gynecology
University of North Carolina at Chapel Hill

Research Perspective
GEETA SWAMY
Associate Vice President for Research and Vice Dean for Scientific Integrity
Professor of Obstetrics and Gynecology
Duke University

Industry Perspective
IONA MUNJAL
Director, Clinical Research and Development, Pfizer Vaccines
Assistant Professor of Pediatrics, Albert Einstein College of Medicine and Montefiore Medical Center

Regulatory Perspective
LYNNE YAO
Director, Division of Pediatric and Maternal Health
FDA

Advocating for Pregnant & Lactating Persons in Clinical Trials
KATHRYN SCHUBERT
President and CEO
Society for Women's Health Research

10:05 am **Q&A/Audience Discussion**

10:30 am **COFFEE BREAK (*30 minutes*)**

11:00 am **SESSION VIII – NEW APPROACHES TO GENERATE EVIDENCE FOR TREATING PREGNANT AND LACTATING PERSONS**

Purpose:
- Consider different approaches to generate evidence on the safety and effectiveness of drug products for pregnant and lactating persons, in addition to randomized control trials; and
- Discuss practical short- and long-term opportunities and/or actions to increase the use of these approaches to evidence generation in both product development and oversight, and clinical and public health practice.

Discussion Questions:

- What methods and approaches are most amenable to generating quality evidence on the short- and long-term safety as well as effectiveness of drugs for use in pregnant and lactating persons?
- What are opportunities for pregnant and lactating persons to be better engaged in designing clinical trials?
- How can evidence generated outside of randomized control trials best inform drug research and development for pregnant and lactating persons?
- For what kinds of questions and for what kinds of drugs can new approaches approximate the quality of evidence generated in RCTs or be an appropriate source of adequate data?
- What are the short- and long-term opportunities to advance the use of new approaches for evidence generation on the safety and effectiveness of drugs for use in pregnant and lactating persons?

11:00 am **Panel Discussion**

STEVEN KERN, *Moderator*
Deputy Director, Quantitative Sciences
Bill and Melinda Gates Foundation

Real World Evidence Perspective
CHRISTINA CHAMBERS
Professor of Pediatrics
University of California, San Diego School of Medicine

Pharmacology Perspective
RAMAN VENKATARAMANAN
Professor of Pharmaceutical Sciences and Pathology
University of Pittsburgh

Novel Approaches to Engage Pregnant & Lactating Persons in Real World Evidence Studies
TOLÚWALÀṢÉ AJAYI
Director of Clinical Research and Diversity Initiatives, Scripps Research Translational Institute
Assistant Professor, Scripps Research

Regulatory Perspective
WEI HUA
Acting Deputy Director, Division of Epidemiology
Office of Surveillance and Epidemiology
FDA

11:30 am **Q&A/Audience Discussion**

11:50 am **WRAP UP DISCUSSION AND CLOSING REMARKS**

RUTH R. FADEN, *Workshop Co-chair*
Founder, Johns Hopkins Berman Institute of Bioethics
Philip Franklin Wagley Professor
Johns Hopkins University

SHIRLEY SYLVESTER, *Workshop Co-chair*
Senior Medical Director, Women's Health
Johnson and Johnson

12:00 pm **ADJOURN DAY 2**