PRGLAC Implementation Working Group of the National Advisory Child Health and Human Development (NACCHD) Council

Report on PRGLAC Implementation Progress

June 3, 2024

Background

- 90% of people take a medication while pregnant or lactating but have traditionally excluded from clinical trials and research.
- Pregnant people and their clinicians make clinical decisions without adequate scientific evidence.
- There is an urgent public health need to increase scientific evidence around medication use during pregnancy and lactation.

Background

We need to shift to protecting pregnant and lactating people *through* research, instead of from research

Historical Context

- **2016: Congress established PRGLAC** via the 21st Century Cures Act to identify and address gaps in knowledge regarding safe and effective therapies and vaccines for pregnant and lactating women.
- **Representation from all sectors**: multiple NIH institutes, CDC, FDA, AHRQ, HRSA, HHS, VA, professional societies, industry, academia, non-profit organizations. NICHD as lead.
- 2018: PRGLAC Report to Congress included **15 recommendations** to promote the inclusion of pregnant and lactating women in clinical trials.
- HHS Secretary extended PRGLAC charter, requesting guidance on implementation.
- 2020: PRGLAC issued an **Implementation Plan.**

- 2021: PRGLAC's charter expired

PRGLAC Recommendations

1. Integrate pregnant women and lactating women in the clinical research agenda
2. Increase the quantity, quality, and timeliness of research on safety and efficacy of therapeutic products used by pregnant women and lactating women
3. Expand the workforce of clinicians and research investigators with expertise in obste and lactation pharmacology and therapeutics
4. Remove regulatory barriers to research in pregnant women
5. Create a public awareness campaign to engage the public and health care providers in research on pregnant women and lactating women
6. Develop and implement evidence-based communication strategies with health care provi on information relevant to research on pregnant and lactating women
7. Reduce liability to facilitate an evidence base for new therapeutic products that may be used women who are, or may become, pregnant and by lactating women

8. Develop separate programs to study therapeutic products used off-patent in pregnant women and lactating women using the NIH BPCA as a model
9. Develop programs to drive discovery and development of therapeutics and new therapeutic products for conditions specific to pregnant women and lactating women
10. Implement a proactive approach to protocol development and study design to include pregnant women and lactating women in clinical research
11. Leverage established and support new infrastructures/collaborations to perform research in pregnant women and lactating women
12. Utilize and improve existing resources for data to inform the evidence and provide a foundation for research on pregnant women and lactating women
13. Optimize registries for pregnancy and lactation
14. The HHS Secretary should consider exercising the authority provided in law to extend the PRGLAC Task Force when its charter expires in March 2019 (extended to Mar 13, 2021)
15. Establish an Advisory Cmte to monitor and report on implementation of recommendations, updating regulations, and guidance, as applicable, regarding the inclusion of pregnant women and lactating women in clinical research

Congressional Language

Report Language from Consolidated Appropriations Act of 2023 (P.L. 117-328).

The Committee includes $200,000 for the creation of an Advisory Committee to monitor and report on the implementation of the recommendations from the Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC). PRGLAC's 2020 Implementation Plan called for the creation of an Advisory Committee to monitor and report on implementing recommendations, updating regulations, and guidance, as applicable, regarding the inclusion of pregnant women and lactating women in clinical trials. Additionally, the Committee directs the Secretary to submit a report to Congress within 180 days of the date of enactment of this Act outlining the Department's progress on implementing each of PRGLAC's 15 recommendations from the Implementation Plan it submitted to the Secretary in August 2020 (H. Report: 117-403).

The Working Group of Council and Objectives

- Recommended in the Implementation Plan (Recommendation #15)
- The Working Group will:
- Review publicly available materials pertaining to implementation progress
- Invite speakers from relevant Federal agencies or non-federal entities to discuss progress to-date on PRGLAC implementation plan, including possible barriers
- Report their findings to NICHD Council and submit the report to Congress
  - Implementation progress
  - Provide recommendations to facilitate implementation, where necessary
  - Advise reconsideration, as relevant

Review of Implementation Progress by Cluster

Cluster A: Conduct clinical research and trials

Cluster B: Education, outreach, training, and career development

Cluster C: Policy, regulatory, and liability

Cluster D: Registries and real-world data

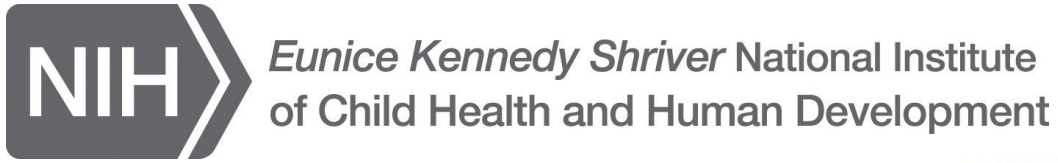
Cluster E: Novel drug discovery and development

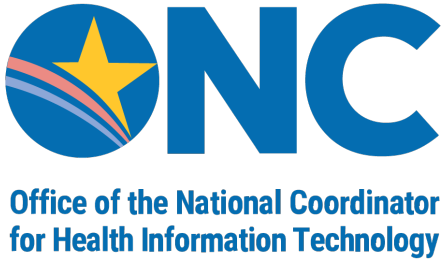
Working Group Work Plan

- **Meeting One (Nov 17, 2023)**:
  - Overview of PRGLAC 1.0, Cluster D (Registries and real-world data)
- **Meeting Two (Jan 19, 2024):**
  - Clusters A + E (Conduct clinical research and trials, Novel drug discovery and development)
  - Cluster C (Policy, regulatory, and liability)
- **Meeting Three (March 22, 2024, in person):**
  - Cluster B (Education, outreach, training, and career development)

Information gathering

- Invited speakers from relevant federal agencies, professional societies, and stakeholder groups.





Findings

Overarching Themes

1. Distinguishing between pregnancy and lactation
2. Assigning clear ownership
3. Engaging multiple, diverse stakeholders
4. Requiring additional resources and congressional action
5. Continuing assessment of implementation progress

Cluster A +E: Conduct clinical research and trials and novel drug discovery

IMPLEMENTED	2B. Utilize longer award periods by government funders (beyond the typical 5-year award), when needed, for study design and data collection
	8B. Develop separate prioritization processes for therapies and/or conditions in pregnant women and lactating women
	9A. Create separate prioritization processes for pregnant women and lactating women
IN PROGRESS	2A. Provide additional resources and funding for research to obtain clinically meaningful and relevant data for specific and co-existing conditions in pregnant women and lactating women
	2B. Broaden focus of ongoing research networks to include research on therapeutic products in pregnant women and lactating women
	11A. Provide financial support and incentives to established and develop new multicenter infrastructures
NOT IMPLEMENTED	8A. Provide specific funding
	9B. Consider a Biomedical Advanced Research and Development Authority (BARDA)-like model and the NIH vaccine model that takes clinical development up to phase II
	C. Encourage networks/collaborations to engage in public-private partnerships to facilitate research

Cluster B: Education, outreach, training, and career development

IN PROGRESS	3A. Develop and support training and career development opportunities in obstetric and lactation pharmacology and therapeutics for both clinical and basic science
	3B. Develop mentors in obstetric and lactation pharmacology and therapeutics for both clinical and basic science
	5A. Highlight the importance of research on therapeutic products in pregnant women and lactating women
	6A. Increase the knowledge of health care providers regarding obstetric and lactation therapeutics and research needs
	6B. Increase the engagement of health care providers to disseminate information from research findings to their patients
NOT IMPLEMENTED	3C. Increase the knowledge and engagement of health care providers regarding obstetric and lactation pharmacology and therapeutics
	5B. Engage stakeholders such HHS, professional societies, industry, advocacy groups, and public and global partners
	6C. Increase the engagement of health care providers to discuss participation in clinical trials, research, and registries
	6D. Develop appropriate strategies for sharing and interpreting research findings and risk

Cluster C: Policy, regulatory, and liability

IN PROGRESS	1A. Remove pregnant women as an example of a vulnerable population in the Common Rule
	1B. The Food and Drug Administration (FDA) should harmonize with the Common Rule and remove pregnant women as a vulnerable population
	7A. Implement a liability-mitigation strategy for conducting research and evaluating new therapeutic products in pregnant women and lactating women
	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
NOT IMPLEMENTED	1C. HHS should develop guidance to facilitate the conduct of research in pregnant women and lactating women
	4A. Modify Subpart B of the Common Rule
	7B. Consider implementing a targeted incentive program and/or strengthening FDA authority to require clinically relevant data) on pregnant women and lactating women
	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

Cluster D: Registries and Real-World Data (Pregnancy)

IN PROGRESS	12A. Design health record systems to link mother and infant records
	12B. Leverage large studies and databases
	12C. Use novel data resources
	12D. Use innovative methods of data analytics
	12E. Require common data elements to facilitate collaboration and use
	13B. Develop registry standards and common data elements that facilitate input of pertinent data in real time
NOT IMPLEMENTED	13A. Create a user-friendly website for registry listing
	13C. Facilitate access to data and transparency of information in registries
	13C. Develop disease/condition-focused registries

Cluster D: Registries and Real-World Data (Lactation)

NOT IMPLEMENTED	12A. Design health record systems to link mother and infant records
	12B. Leverage large studies and databases
	12C. Use novel data resources
	12D. Use innovative methods of data analytics
	12E. Require common data elements (CDEs) to facilitate collaboration and use
	13B. Develop registry standards and CDEs that facilitate input of pertinent data in real time
	13A. Create a user-friendly website for registry listing
	13C. Facilitate access to data and transparency of information in registries
	13C. Develop disease/condition-focused registries

Next Steps

Finalize report (mid-June)

Publish and disseminate report (End of July)

Federal agencies continue implementation activities

Questions and Feedback