

# Advancing Clinical Research with Pregnant and Lactating Populations: Overcoming Real and Perceived Liability Risks

## Role of the National Institutes of Health

Congress requested that a committee of the National Academies of Sciences, Engineering, and Medicine undertake a comprehensive overview of the real and perceived liability around research conducted with pregnant and lactating women. This included a review of the legal landscape of tort liability for injuries related to pregnant and lactating populations' participation in clinical trials and use of products regulated by the Food and Drug Administration (FDA).

The committee found limited liability risk related to the use of medical products in clinical trials for both pregnant and lactating populations. The committee found evidence of potential liability relating to pregnant women's use of approved medical products on the market and that aspects of this liability may be prevented by conducting clinical trials with pregnant women. Despite this, perceptions and fear of liability remain.

Action is needed from federal agencies, including the National Institutes of Health (NIH), to improve the responsible and ethical inclusion of pregnant and lactating women in clinical research while mitigating the risk of legal liability. As the largest supporter of biomedical research, NIH has a responsibility to encourage and stimulate such research. NIH has already adopted several promising initiatives, but more

can be done to increase funding and support. NIH can also provide liability protections to NIH-funded investigators and research participants. The following recommendations address additional actions involving NIH.

### RECOMMENDATIONS

**NIH should develop an action plan to prioritize research that includes pregnant and lactating women across its institutes and centers.**

The committee recommends that, as a funder of biomedical research, NIH prioritize research with pregnant and lactating women. There is a need to increase basic knowledge of how pregnancy and lactation affect how the body handles and responds to drugs to guide and support future research and to fund and facilitate research that includes pregnant and lactating women when appropriate. NIH could play a particularly important role in funding research for off-patent products, given the lack of incentives for sponsors. NIH sets the clinical research agenda. Therefore, without leadership, emphasis, and prioritization from NIH, research with pregnant and lactating women will not be prioritized and the dearth of knowledge about the effects of most drugs on these populations will remain unchanged.

The committee recommends NIH create a new program with the NIH Common Fund to study the pharmacokinetics, pharmacodynamics, and dosage determination of on-market drugs in pregnant and lactating women. The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development should expand and sustain its network of institutions with expertise in conducting research with these populations.

**NIH and other federal agencies that fund clinical research should cover the cost of clinical trial insurance on clinical trial grants that include pregnant and lactating women for research that is conducted domestically.**

Given the challenges of the American tort system, it may be difficult for research participants who are harmed in clinical research to obtain any compensation. A clinical trial insurance plan purchased by an investigator, research institution, or sponsor could be a solution to provide modest compensation for research-related injuries. The insurance would also provide liability protections for the investigators and institutions, which will likely make these stakeholders more willing to conduct research with pregnant and lactating populations.

Because acquiring clinical trial insurance imposes an additional cost to the study, it would be appropriate for NIH to cover that cost for NIH-funded research involving pregnant and lactating women, which is within its authority. While the cost of policies for studies including pregnant and lactating women may be expensive at first, owing to scant actuarial data for these populations, the committee found that the cost of coverage is likely to moderate over time as the uncertainty of insurance underwriters decreases.

**If research being conducted with pregnant individuals, or individuals who may become pregnant over the course of the study, is not already covered by a certificate of confidentiality issued by NIH or other federal agency, the principal investigator of the study should apply to NIH for a certificate of confidentiality (COC).**

CoCs provide an opportunity to protect against the potential for legal liability—especially following the U.S. Supreme Court decision in *Dobbs v. Jackson Women’s Health Organization*—should law enforcement attempt to breach the privacy of research participants. A CoC can help achieve the research objectives and promote participation in studies by safeguarding the confidentiality of subject information and by protecting researchers and institutions from being compelled to disclose information that would identify research subjects. CoCs help reassure participants that their data are safe and protected from disclosure or use in legal proceedings. Such protection may be particularly necessary in states with laws that could criminalize or hold liable a pregnant individual should their fetus be harmed during clinical research.

**The U.S. Department of Health and Human Services (HHS) should form an interagency task force, including FDA, NIH, Centers for Disease Control and Prevention, Health Resources and Services Administration, Office of the National Coordinator for Health Information Technology, and National Library of Medicine to create and maintain infrastructure and guidelines for the conduct of postmarketing pregnancy and lactation safety studies that would use safety information, annual status reports from existing pregnancy and lactation exposure registries, and data generated through database studies.**

Real-world data collected through observational studies are important for detecting rare adverse events and understanding the long-term safety profile of medical products. However, the current system of real-world data capture and analysis needs substantial improvement before it can play a major role in increasing knowledge about the effects of medical products in pregnant and lactating women.

Although FDA maintains a list of pregnancy exposure registries on its website, that list has limited search capabilities and is not complete. A central repository of interoperable pregnancy exposure registries could facilitate enrollment by making registries more accessible for pregnant individuals, clinicians, and researchers. Including the results of complementary

database studies in the central repository would also be a useful mechanism to provide stakeholders with information regarding the safety of medical products during pregnancy and lactation. An important first step in designing such a repository would be to make it an interoperable, searchable resource for clinicians, investigators, or potential participants.

**Congress should pass legislation modeled on the Best Pharmaceuticals for Children Act (BPCA) to encourage and incentivize additional studies to provide more information in labeling on the safety and efficacy of approved medical products for pregnant and lactating women.**

The committee found that despite the limited liability present in research involving pregnant and lactating women, sponsors are largely unwilling to conduct studies that might indicate future risks once a drug is already

on the market. Furthermore, there is little financial incentive for sponsors to conduct this research and no requirements outside of occasional post-marketing requirements imposed by FDA if there are reported safety concerns. Therefore, for on-market products, the committee recommends that Congress increases public funding for clinical studies in pregnant and lactating women for marketed medical products.

The committee recommends that, similar to the BPCA, NIH publish an annual prioritization list of both on-patent and off-patent approved medical products for which additional studies are needed to assess dosage, safety, and effectiveness in pregnant and lactating women. Furthermore, the committee recommends that HHS award contracts to conduct clinical studies for products that are no longer subject to relevant patent or exclusivity protections that are identified as a priority by the published list.

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