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

## Role of the U.S. Congress

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.

The committee concluded that many factors influence stakeholder decisions about whether to include pregnant and lactating women in clinical research. Some, such as financial incentives, can be a powerful counterbalance to the dissuasive factors that sponsors, researchers, research institutions, and other stakeholders weigh in their decisions concerning the inclusion of pregnant and lactating women. The committee also concluded that a legal requirement that sponsors conduct studies that include pregnant and lactating women would advance product labeling information on the safety, efficacy, and dosing of medical products for these populations. Although the report recommendations target diverse stakeholders, two specific actions for Congress are listed below.

### RECOMMENDATIONS

Legislation passed in the early 2000s has helped to overcome challenges in conducting research in pediatric populations that have similarities to the challenges faced by research with pregnant and lactating women. The models that spurred innovation in pediatric populations—the Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA)—serve incentive and requirement functions in increasing pediatric research. The BPCA provides the incentive through a patent extension or provision of public funds for research for products that are off-patent and the PREA provides the requirement by establishing a regulatory mandate for sponsors of new products to collect preclinical and clinical data in pediatric populations. The committee concludes that this coupling of incentives and accountability would likewise spur research in clinical studies on the dosage, efficacy, and safety of drugs, biologics, and vaccines, as well as the

efficacy and safety of devices for pregnant and lactating women.

**Congress should pass legislation modeled on the 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 discover safety 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 postmarketing requirements imposed by FDA if there are reported safety concerns. Therefore, for on-market products, the committee recommends that Congress create incentive programs, such as extended market exclusivity or tax breaks, for patent holders to complete studies with pregnant and lactating populations within a requested time frame. The committee recommends that this program be authorized for an initial 5-year period, with reauthorization based on experience with the program and a determination of whether continuation of the program is necessary.

As with the pediatric experience prior to the implementation of the BPCA, there is virtually no incentive for product sponsors to conduct additional research once a drug is off-patent, as their limited profits would not offset the costs of such research. Therefore, the BPCA serves as a model for providing public funds to aid and incentivize clinical researchers and their institutions to conduct studies with pregnant and lactating populations.

The committee recommends that, similar to the BPCA, Congress should direct the National Institutes of Health to publish an annual prioritization list of both on-patent and off-patent approved medical products for which additional studies are needed to assess the dosage, safety, and effectiveness of the use of the product in pregnant and lactating women. Furthermore, the committee recommends that Congress directs the U.S. Department of Health and Human Services to 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.

**Congress should pass legislation modeled on the PREA to authorize FDA to require research related to the use of drugs, biologics, vaccines, and medical devices in pregnant and lactating women.**

Given the success of the PREA, FDA authority could be expanded to compel the same requirements to conduct clinical studies with pregnant and lactating women, which already exist for pediatric populations under the PREA.

Therefore, the committee recommends that Congress grant authority to FDA to require that any entity that submits an application for a new drug, biologic, or vaccine—or submits an application for a new indication, new dosage form, new dosing regimen, or new route of administration—be required to submit data on the dosage, administration, safety, and effectiveness of its use in pregnant and lactating women.

The committee also recommends that Congress amend the Food, Drug, and Cosmetic Act to expand FDA's authority to require postmarketing studies and postmarketing clinical trials. Currently, FDA can require postmarketing studies and clinical trials if there is evidence of a safety concern. However, the committee recommends that FDA should be able to require postmarketing studies to identify and characterize risks in pregnant and lactating women and their offspring.

To ease the initial challenges of implementing these programs, the committee recommends that Congress create incentives such as extended market exclusivity or tax breaks, which could expire after several years, once sponsors have experience conducting studies that include pregnant and lactating women.

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