

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

Role of the U.S. Department of Health and Human Services

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 populations, who are generally excluded from clinical studies. This exclusion leads to inadequate information on how best to care for women and their fetuses and children. Past studies have cited concerns about legal liability for the investigators and institutions that conduct and sponsor clinical research should research participants, or their fetuses or children, experience negative effects from the study intervention.

The committee found limited liability risk related to the use of medical products in clinical trials for both pregnant and lactating populations. Despite this, perceptions and fear of liability remain.

Action is needed from federal agencies, including the U.S. Department of Health and Human Services (HHS), to improve the responsible and ethical inclusion of pregnant and lactating women in clinical research while mitigating the risk of legal liability. Given its charge of enhancing the health and well-being of Americans, HHS has a crucial role to play in ensuring the health of pregnant and lactating women—and of their fetuses and children—is safeguarded through high-quality evidence

from clinical research. Specific report recommendations for HHS are listed below.

RECOMMENDATIONS

The Office for Human Research Protections (OHRP) within HHS should provide clarity on the inclusion of pregnant and lactating women as research subjects.

Institutional Review Boards (IRBs) are key in determining whether clinical research with human subjects can move forward; however, many IRBs are currently poorly equipped to assess the benefits and risks of clinical research that includes pregnant and lactating women. This dearth of relevant expertise is compounded by ambiguous human subject protection regulations, which result in interpretations by IRBs to exclude pregnant and lactating women from clinical trial participation.

OHRP should release guidance on the inclusion of pregnant and lactating women in clinical research to address current regulatory ambiguities and improve IRBs' understanding of regulatory requirements. OHRP should also develop additional resources, including frequently asked questions and training opportunities, to further contribute to IRB capacity to evaluate research protocols that include pregnant and lactating women. Furthermore, OHRP should engage the HHS Secretary's Advisory

Committee on Human Research Protections to develop recommendations on the safe and ethical inclusion of pregnant and lactating women in clinical research.

OHRP should work with the Food and Drug Administration (FDA) to harmonize applicable guidance pertinent to research with pregnant and lactating women.

Many federal departments and agencies have adopted the Federal Policy for the Protection of Human Subjects, or the “Common Rule,” including HHS. However, FDA has its own regulations for the protection of human subjects and IRBs and has not adopted the regulations used by HHS. FDA’s regulations for human subject protections and IRBs do not have specific considerations for pregnancy, other than to note that IRBs are to implement additional safeguards for clinical studies that include pregnant women and that IRBs might consider including among its membership individuals with relevant expertise if they regularly review protocols that include pregnant women. HHS’s regulations do not address whether additional protections for children apply when a lactating woman is enrolled in clinical research and continues to provide breastmilk to her child.

OHRP should work with FDA to harmonize guidance so that investigators and their institutions are following uniform guidelines and language for research involving pregnant and lactating women.

HHS should form an interagency task force, including FDA, National Institutes of Health, 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. Including additional information, such as adverse event data captured by the FDA Adverse Event Reporting System and Vaccine Adverse Event Reporting System, in one centralized location would be helpful. Improving the capacity to link the health records of pregnant and lactating women with those of their children is also needed to increase the informativeness of real-world data.

The interagency task force should develop a central repository for the collection of postmarketing safety data for medical products used by pregnant and lactating women. The task force should also develop guidelines on uniform data content and format to optimize analytic capabilities for the researchers and clinicians who will use the repository. To improve the ability to evaluate fetal and infant outcomes as a function of medical product exposure in utero or through breastmilk, the task force should adopt standards that require linkages of electronic health records of the pregnant or lactating women and their children. Finally, the interagency task force should evaluate the infrastructure, data elements, and resources that will be needed to develop a single national registry for postmarketing data on medical product use by pregnant and lactating women.

FOR MORE INFORMATION

To access the full report, visit nationalacademies.org/liability-study.

Health and Medicine Division

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