IRB Interpretation of 45 CFR 46 Subpart B

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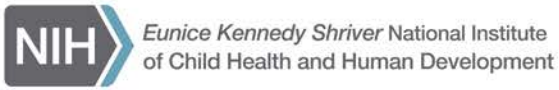

Task Force on Research Specific to Pregnant Women and Lactating Women
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Disclosure Statement

- No conflicts of interest to disclose
- No financial relationships with proprietary entities that produce health care goods and services
- Uncompensated academic appointments
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- ***Disclaimer:*** The opinions expressed in this presentation are those of the speaker and do not necessarily reflect the official views or policies of the FDA, NIH, or DHHS.

General Considerations

- IRBs must be independent and must have knowledge of ethical principles and expertise in relevant areas of science and medicine
- IRBs must concurrently consider the interests and well-being of both the mother and fetus, which are highly interdependent
- While exercising caution regarding exposures during pregnancy is justified, IRBs must recognize that withholding potentially beneficial medical treatments during pregnancy could itself adversely affect the health of mother and fetus

General Considerations

- The IRB must also consider if enrollment of pregnant women in a clinical trial can offer the prospect of direct benefit to the woman and/or fetus that otherwise may not be available outside of the research setting
- Study risks and benefits must be carefully interpreted in the context of the specific condition under study and all available data of relevance
- IRBs may vary in their interpretation of regulations governing clinical research and even in their assessment of research-related risks and benefits

Potential Barriers to IRB Approval

- Lack of awareness regarding the gaps in knowledge in this patient population
- General concerns regarding potential harm to the mother and fetus
- Conservative and risk-averse research oversight
- Current regulations which classify women as a “vulnerable” population

Vulnerable Populations

- The regulatory definition of “vulnerable” pertains to susceptibility to coercion or undue influence (i.e., someone incapable of protecting their own interests)
- Do women become “vulnerable” based on their pregnancy alone?
- Will changing the “vulnerable” designation mitigate some of the perceived barriers to inclusion in research?
- Ultimately, advocacy, education, and increased awareness about specific considerations for research in pregnant women may be the key to overcoming some of the barriers

Specific IRB Considerations

- The IRB must have access to certain data to assess the level of risk to the pregnant woman and fetus
- The IRB must consider the potential risks and benefits to the woman and the fetus:
  - If the research holds the promise of directly benefiting the woman or fetus, a greater than minimal risk to the fetus is acceptable.
  - If the research does not hold the prospect of directly benefiting the woman or fetus, the research is allowed only if the risk to the fetus is not greater than minimal risk.

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Research involving pregnant women or fetuses can be approved if the following conditions are satisfied:

- Preclinical studies have been conducted, including studies on pregnant animals; clinical studies, that include nonpregnant women and provide data for assessing potential risks to pregnant women and fetuses
- Risk to fetus is caused solely by interventions or procedures that hold prospect of direct benefit for the woman or the fetus or,
- If no benefit, risk to the fetus is not greater than minimal and the research develops important biomedical knowledge not obtainable by any other means.

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- Any risk assumed is the least possible for achieving the objectives of the research.
- Individuals engaged in the research will have no part in (1) any decisions as to the timing, method, or procedures used to terminate a pregnancy, and (2) determining the viability of the fetus at the termination of the pregnancy; and
- No inducements, monetary or otherwise, will be offered to terminate the pregnancy.

Challenges of Interpreting Subpart B

- Complex risk/benefit calculus because of limitations of the data and the interdependence of maternal and fetal health and welfare
- Risks of the study intervention are often unknown and cannot be adequately assessed using other means
- Assessment of risk is particularly challenging when the research involves investigational products with limited human exposure
- Extrapolation from existing data in other species or populations or from data obtained through other study designs or methods may not reliably predict the effects that may observed in pregnant women or in the developing fetus

Conclusions

- The protections afforded to pregnant women in Subpart B are in place not because pregnant women are “vulnerable” to coercion or undue influence and incapable of protecting their own interests, but rather because of the complex nature of research in this specific population
- Regardless of how pregnant women may be classified under the Common Rule, IRBs will continue to adhere to the existing protections, all of which remain intact under Subpart B.

Conclusions

- As with any population, the IRB must consider the research risks and benefits and carefully balance the ethical and scientific considerations for including or excluding pregnant women as study participants.
- The IRB has a clinical and ethical imperative to safeguard and protect the interests of research participants from overzealous investigators and occasionally even from research participants themselves
- The IRB also has a clinical and ethical imperative to ensure the responsible inclusion of pregnant women in clinical research and prevent their unjustified exclusion