IRB Tip Sheet: Inclusion of Pregnant Subjects in Clinical Research

Research that enrolls pregnant subjects, fetuses or neonates must satisfy all of the requirements of **Subpart B: Protections for Pregnant Women, Human Fetuses, and Neonates Involved in Research at 45 CFR 46**.

Regulatory Definition of Pregnancy: *Pregnancy encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery.*

Note: *Pregnant Partners of Research Subjects* are considered research subjects in the NIH IRP. To collect pregnancy outcome data, the pregnant partner must be enrolled on a protocol such as the *NIH IRP Pregnancy Registry* (IRB 000268).

IRB Responsibilities: The IRB must determine and document that applicable regulatory protections from both Subpart A and Subpart B are satisfied during its review and approval of the proposed research.

Pregnant subjects are included in the protocol being reviewed:

- The justification for the inclusion of pregnant subjects needs to be provided by the PI in the written protocol.

FDA Regulated Studies:

- Generally, pregnant subjects are excluded from drug development trials; though there are times where it may be scientifically and ethically appropriate to include them.
- Examples of possible circumstances are included the **Draft** Guidance for Industry: Pregnant Women: Scientific and Ethical Considerations for Inclusion in Clinical Trials.

Pregnant subjects are neither included nor excluded in the protocol being reviewed:

- If the study does not intentionally enroll or exclude pregnant subjects, but it is possible for a participant to become pregnant while on study, and the researcher intends to keep the participant on the study during the pregnancy, then the protocol must provide sufficient justification for their continued inclusion in the research.
- If the study is minimal risk, the researcher may choose to not specifically address the issue in the protocol inclusion if not scientifically relevant. However, if the protocol contains research procedures that in the context of standard medical care require a negative pregnancy test, the protocol needs to include this test and state it must be negative.

Pregnant subjects are excluded in the protocol being reviewed:

- In studies that explicitly exclude pregnant subjects, if a participant becomes pregnant while on study and the researcher wishes the to keep the participant on study, then an amendment must be submitted to provide the justification for continued participation of the pregnant subject on the research.
- Because the potential benefits of research participation may extend to pregnant subjects, the rationale for excluding pregnant subjects from a specific protocol should be explicitly stated. This justification for exclusion should include an assessment of both the potential risks posed by study interventions above the standard of care with the condition being studied, and the potential effects of pregnancy on the scientific validity of the study. This could include a known or unknown potential risk specific to a pregnant subject or the fetus.

Additional Information to be included in the Written Protocol:

- Definition of subject who can become pregnant or person of childbearing potential
- Any protocol that includes pregnant subjects should be clear as to which procedures will be performed on the pregnant subjects. This is important since a different level of risk may be acceptable for the pregnant subjects, and they may have to be excluded from certain procedures.
- Details on required pregnancy testing in studies when pregnant subjects are included or when they are excluded.
  - Note: While an MRI without contrast is generally considered minimal risk and does not require a pregnancy test for standard of care evaluations, when this imaging is performed for the *purposes of research*, a pregnancy test is required prior to performing the test. This is due to lack of data related to the risk to the fetus when performing in an MRI with a field strength higher than 1.5 T such as the ones used at the NIH Clinical Center.
- See NIH IRP Guideline for Inclusion/Exclusion of Pregnant People and Information About Pregnancy Testing on the IRBO website under Policy 400 for more details.

Additional Information to be included in the Written Consent:

- A brief statement describing known, suspected, or unknown risks to a developing fetus or breastfeeding infant, or, if pregnancy is being excluded for scientific reasons, a brief explanation why should be provided.
- Pregnancy testing does not need to be included in the consent if it is standard practice to perform this before a study intervention such as a CT scan. A description does need to be included if the timing or method of pregnancy testing differs from standard of care.

Summary of Conditions of Approval from Subpart B: Protections for Pregnant Women, Human Fetuses, and Neonates Involved in Research at 45 CFR 46

Pregnant Subjects or Fetuses	*Inclusion approved under 45 CFR 46.204: Research involving pregnant women or fetuses* Conditions that must be meet for the approval of the inclusion of pregnant subjects: a) Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses. b) The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means. c) Any risk is the least possible for achieving the objectives of the research. d) If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions of subpart A. e) If the research holds out the prospect of direct benefit solely to the fetus, then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of subpart A of this part, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest. f) Each individual providing consent under paragraph (d) or (e) of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate. g) For children who are pregnant, assent and permission are obtained in accord with the provisions of subpart D. h) No inducements, monetary or otherwise, will be offered to terminate a pregnancy. i) Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy. j) Individuals engaged in the research will have no part in determining the viability of a neonate.
Neonates (Newborns)	*Inclusion approved under 45 CFR 46.205: Research involving neonates*
Placenta/Fetal Material	*Inclusion approved under 46 CFR 46.206: Research involving, after delivery, the placenta, the dead fetus or fetal material*
HHS Secretarial Review for the Inclusion of Pregnant Subjects/Neonate/ Fetuses	*Inclusion approved after secretarial review under 45 CFR 46.207: Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates* • Prior to review by the Secretary HHS, the IRB must determine and document in the minutes that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, human fetuses, or neonates. • NIH OHSRP will than forward the research protocol and other relevant documents such as the IRB minutes, to the HHS Office for Human Research Protections (OHRP) for review by the HHS Secretary after a consultation with a panel of experts. • *NIH HRPP Policy 400: Research Involving Pregnant Women, Human Fetuses, and Neonates*