



MCW Office of Research Standard Operating Procedure

RESEARCH INVOLVING PREGNANT WOMEN AND FETUSES

Unit: Human Research Protections Program (HRPP), Office of Research

Applies to: Faculty and Staff involved in human research

PURPOSE:

Pregnant women are populations that require additional safeguards in the context of participation.

If the IRB reviews research that focuses on categories of subjects vulnerable to coercion or undue influence, the review process will include one or more individuals who are knowledgeable about or experienced in working with these subjects. For example, the IRB will include one or more individuals who are knowledgeable about or experienced in working with pregnant women and/or children, when reviewing projects that involves individuals from these populations.

For Department of Defense supported research only, the applicability of Subpart B and requirements described in this procedure is limited to research involving pregnant women as participants in research that is more than minimal risk and included interventions or invasive procedures to the woman or the fetus or involving fetuses or neonates as participants.

For projects following EPA regulations, research involving intentional exposure of pregnant women or children to any substance is prohibited and will not be approved by the IRB.

DEFINITIONS:

Pregnancy: 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.

Delivery: complete separation of the fetus from the woman by expulsion or extraction or any other means

Fetus: the product of conception from implantation until delivery

Deceased fetus: a fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord

Neonate: a newborn

Viable: as it pertains to the neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration. If a neonate is viable then it may be included in research only

to the extent permitted and in accordance with the requirements of Subparts A and D of 45 CFR 46.

PROCEDURE:

Pregnant Women

1. Investigators when submitting a new research project via eBridge should identify the potential for enrolling pregnant women, fetuses and/or neonates (nonviable or uncertain viability) in their research.
2. Pregnant women or fetuses may be involved in projects only if the IRB finds that all of the following ten (10) elements are met for federally funded projects. The same ten (10) elements should be evaluated for all other projects, but are not binding.
3. The Investigator should address all 10 elements in their eBridge SmartForm application to allow the IRB to evaluate and document the protocol-specific findings supporting that conclusion for each condition:
 - a. Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant 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 or generalizable knowledge for DoD supported research 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 45 CFR 46.116 and 117;
 - 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 45 CFR 46.116 and 117, 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 items d or e of this policy is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
 - g. For children as defined in 45 CFR 46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of 45 CFR 46 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; and
 - j. Individuals engaged in the research will have no part in determining the viability of a neonate.

Research Involving Neonates of Uncertain Viability

1. Neonates of uncertain viability and nonviable neonates may be involved in research only if the IRB finds that all four (4) of the following elements are met for federally funded projects. The same four (4) elements should be evaluated for all other projects, but are not binding.

2. The Investigator should address the four (4) elements in their eBridge SmartForm application to allow the IRB to evaluate and document the protocol-specific findings supporting that conclusion for each condition:
 - a. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
 - b. Each individual providing consent under paragraph 45 CFR 46.205(b)(2) or (c)(5) of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonate.
 - c. Individuals engaged in the research will have no part in determining the viability of a neonate.
 - d. The requirements of paragraph 45 CFR 46.205(b) or (c) of this section have been met as applicable.

Neonates of uncertain viability

1. Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research unless the IRB finds that the following two (2) additional elements are met for federally funded projects. The same two (2) additional elements should be evaluated for all other projects, but are not binding.
2. The Investigator should address the two (2) additional elements in their eBridge SmartForm application to allow the IRB to document the protocol-specific findings supporting that conclusion for each condition:
 - a. The IRB determines that:
 - i. The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or
 - ii. The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and
 - b. The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative (LAR) is obtained in accord with 45 CFR 46 subpart A of, except that the consent of the father or the father's LAR need not be obtained if the pregnancy resulted from rape or incest.

Nonviable neonates

1. After delivery, a nonviable neonate may not be involved in research unless the IRB finds that all of the following five (5) additional conditions are met for federally funded projects. The same five (5) additional elements should be evaluated for all other projects, but are not binding.
2. The Investigator should address the five (5) additional elements in their eBridge SmartForm application to allow the IRB to document the protocol-specific findings supporting that conclusion for each condition:
 - a. Vital functions of the neonate will not be artificially maintained;
 - b. The research will not terminate the heartbeat or respiration of the neonate;
 - c. There will be no added risk to the neonate resulting from the research;
 - d. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
 - e. The legally effective informed consent of both parents of the neonate is obtained in accord with 45 CFR 46 subpart A,
 - o The waiver and alteration provisions of 45 CFR 46.116(c) and (d) do not apply in these circumstances.
3. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a

nonviable neonate will suffice to meet the requirements of this paragraph 45 CFR 46.205 (c)(5), except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest.

- a. The consent of a LAR either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph 45 CFR 46.205 (c)(5).
4. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

Viable neonates

A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of 45 CFR 46 subparts A and D. See *IRB SOP: Research Involving Children*

Projects Involving the Placenta, a deceased Fetus or Fetal Material after Delivery

1. Projects involving the following items after delivery, shall be conducted only in accord with any applicable Federal, State, or local laws and regulations regarding such activities:
 - a. The placenta
 - b. A deceased fetus
 - c. Macerated fetal material
 - d. Cells, tissue, or organs excised from a dead fetus
2. If information associated with material described in paragraph (a) of this section is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are subjects and the provisions of 45 CFR 46, subparts A and D, must be met as applicable.
3. Investigators should also review *IRB SOP: Use of Human Fetal Tissue in Research* for any additional requirements.

Other Federal Agency Requirements:

EPA: For research intended for submission to the EPA or being conducted in accordance with EPA regulations, any research involving the intentional exposure of pregnant women or children to any substance is prohibited and will not be approved by the IRB.

1. For observational research (research which does not involve intentional exposure to substances) which is being conducted for or supported by the EPA, the Investigator must also comply with 40 CFR 26 subparts C and/or D in providing additional protections to pregnant women and/or children.
 - a. The IRB must review observational research involving pregnant women and fetuses using 40 CFR 26 and 45 CFR 46 Subpart B
 - b. The IRB must review and approve observational research involving children that does not involve greater than minimal risk only if the IRB finds that adequate provision is made for soliciting the assent of the children and the permission of their parents or guardians as set for in 26.406.
 - c. The IRB may only approve observational research involving children that involves greater than minimal risk but presenting the prospect of direct benefit to the individual subjects if the IRB finds and documents that:
 - i. The intervention or procedure holds out the prospect of direct benefit to the individual subject or is likely to contribute to the subject's well-being.
 - ii. The risk is justified by the anticipated benefits to the subjects.
 - iii. The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches.

- iv. Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in 26.406.

DoD: For Department of Defense supported research projects, research which involves fetuses or fetal tissue must comply with the US Code Title 42, Chapter 6A (Public Health Service), Subchapter III (National Research Institutes), Part H, 289g which state the following:

- a. Restrictions:

The Secretary may not conduct or support any research or experimentation, in the United States or in any other country, on a nonviable living human fetus ex utero or a living human fetus ex utero for whom viability has not been ascertained unless the research or experimentation—

 - i. may enhance the well-being or meet the health needs of the fetus or enhance the probability of its survival to viability; or
 - ii. will pose no added risk of suffering, injury, or death to the fetus and the purpose of the research or experimentation is the development of important biomedical knowledge which cannot be obtained by other means.
- b. Risk standard for fetuses intended to be aborted and fetuses intended to be carried to term to be same. In administering the regulations for the protection of human research subjects which—
 - i. apply to research conducted or supported by the Secretary;
 - ii. involve living human fetuses in utero; and
 - iii. are published in section 46.208 of part 46 of title 45 of the Code of Federal Regulations; or any successor to such regulations, the Secretary shall require that the risk standard (published in section 46.102(g) of such part 46 or any successor to such regulations) be the same for fetuses which are intended to be aborted and fetuses which are intended to be carried to term.

In addition, Investigators must comply with 289g1 and 289g2 which covers research on transplantation of fetal tissue and the prohibitions regarding human fetal tissue

REFERENCES:

45 CFR 46 Subparts A, B, D
45 CFR 46.102
45 CFR 46.116, 116(c)
45 CFR 46.117
45 CFR 46.205 (b), (c)
45 CFR 46.208
45 CFR 46.402 (a)
40 CFR 26 Subparts C, D
42 U.S.C. 289g

SUPPORTING DOCUMENTS:

IRB SOP: Research Involving Children

IRB SOP: Use of Human Fetal Tissue in Research

Effective Date: 11/01/2023
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