4.2 Research Involving Pregnant Women, Human Fetuses, and Neonates (Nonviable or of Uncertain Viability)

Last Revised: 9/25/2024

1.0 Purpose

The purpose of this policy is to describe the Organization's requirements for IRB review and approval of research involving pregnant women, fetuses, and neonates (nonviable or of uncertain viability).

2.0 Policy

It is the policy of the Organization that:

- 2.1. Federally funded non-exempt research involving pregnant women, fetuses, and neonates (nonviable or of uncertain viability) will be reviewed and approved in accordance with the requirements of HHS regulations at 45 CFR 46 Subpart B, and applicable state law.
- 2.2. Other non-exempt research involving pregnant women, fetuses, and neonates (nonviable or of uncertain viability) will be reviewed and approved in accordance with equivalent protections. These protections will be based upon the ethical principles in the Belmont Report. In addition, the requirements in 45 CFR 46 Subpart B will be applied as appropriate in consideration of the nature of the research.
- 2.3. Research involving fetuses and neonates (nonviable or of uncertain viability) will be reviewed and conducted in accordance with applicable state law.
- 2.4. Women who are pregnant should not be routinely excluded from participating in research unless there are sound medical and/or scientific reasons not to include them. However, if pregnant women are justifiably excluded, the protocol must include a valid way to screen for pregnancy in accordance with HRPP policy 3.10 (Pregnancy Testing).

3.0 Definitions

- 3.1. 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.
- 3.2. Fetus means the product of conception from implantation until delivery.
- 3.3. Viable neonate means a neonate, after delivery, which can survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration. (A viable neonate is covered by HHS regulations at 45 CFR 46, Subparts A and D).
- 3.4. Nonviable neonate is a neonate after delivery that, although living, is not viable.

4.0 IRB Review

In addition to review of research under HHS regulations at 45 CFR 46 (Subpart A) and FDA regulations at 21 CFR 50, 56 as applicable, the IRB must assure additional protections are in place for pregnant women, fetuses and/or neonates involved in research in accordance with the following:

- 4.1. Research involving pregnant women or fetuses
  - 4.1.1. For research which is subject to HHS regulations at 45 CFR 46 subpart B pregnant women may be involved in research if all of the following conditions are met.
    - 4.1.1.1. Where scientifically appropriate, preclinical studies, including studies on pregnant animals and clinical studies involving non-pregnant women, have been conducted and provide data for assessing potential risks for the enrollment of pregnant women and fetuses.
    - 4.1.1.2. Any risk to the fetus is caused solely by interventions that offer direct benefit for the woman or fetus, OR if there is no prospect of direct benefit, the risk to the fetus must not be greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means.
    - 4.1.1.3. Any risk to the pregnant woman or the fetus is the least possible to achieve the research objectives.
    - 4.1.1.4. The consent of the pregnant woman alone is obtained when the research holds out (1) the prospect of direct benefit to the pregnant woman, (2) the prospect of a direct benefit both to the pregnant woman and the fetus, or (3) 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.
    - 4.1.1.5. The consent of both the pregnant woman and the father is obtained when the research holds out the prospect of direct benefit solely to the fetus. 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

        - 4.1.1.6. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate.
        - 4.1.1.7. For children who are pregnant assent of the pregnant minor and permission of the pregnant minor's parent(s) are obtained in accordance with HHS regulations 45 CFR 46, Subpart D and HRPP policy 4.4 (Research Involving Children).
        - 4.1.1.8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy.
        - 4.1.1.9. Individuals engaged in research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy.
        - 4.1.1.10. Individuals engaged in research will have no part in determining the viability of a neonate.
    - 4.1.2. For research which is not subject to HHS regulations at 45 CFR 46 subpart B pregnant women may be involved in research if all of the conditions in section 4.1.1 are met, with the following exceptions:
        - 4.1.2.1. The IRB may decide that preclinical studies on pregnant animals and clinical studies involving non-pregnant women are not reasonable requirements to protect subjects. For example, this requirement would likely be of limited value in social and behavioral science research, or minimal risk biomedical research.
        - 4.1.2.2. The IRB may decide that the purpose of the research need only be the development of knowledge which has sufficient value which justifies the enrollment of pregnant women.
        - 4.1.2.3. The IRB may decide that the consent of the father is not a requirement for research which holds out the prospect of direct benefit solely to the fetus.
- 4.2. Research Involving Neonates of Uncertain Viability
    - 4.2.1. Neonates of uncertain viability may only be involved in research if:
        - 4.2.1.1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
        - 4.2.1.2. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.
        - 4.2.1.3. Individuals involved in the research will have no part in determining the viability of the neonate.
        - 4.2.1.4. 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 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.
        - 4.2.1.5. 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 is obtained, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.
    - 4.2.2. If a neonate of uncertain viability is determined, after delivery, to be viable, that neonate may be included in research only to the extent permitted by and in accord with the requirements of HHS regulations 45 CFR 46, Subpart D and HRPP policy 4.4 (Research Involving Children).
- 4.3. Research Involving Nonviable Neonates

    - 4.3.1. Nonviable neonates may only be involved in research if:
        - 4.3.1.1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
        - 4.3.1.2. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.
        - 4.3.1.3. Individuals involved in the research will have no part in determining the viability of the neonate.
        - 4.3.1.4. The vital functions of the neonate will not be artificially maintained.
        - 4.3.1.5. The research will not terminate the heartbeat or respiration of the neonate.
        - 4.3.1.6. There is no additional risk to the neonate resulting from the research.
        - 4.3.1.7. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means.
        - 4.3.1.8. The legally effective informed consent of both parents of the neonate is required. 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.
            - 4.3.1.8.1. The waiver and alteration provisions at 45 CFR 46.116(e) and 45 CFR 46.116(f) do not apply.
            - 4.3.1.8.2. The consent of the father is not required where the pregnancy resulted from rape or incest.
            - 4.3.1.8.3. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate is not permitted.
- 4.4. Research involving placenta, dead fetus(s) or fetal material
    - 4.4.1. Research involving the placenta, dead fetus, or fetal material after delivery does not constitute human subject research under 45 CFR 46 (unless any information associated with the material used in the research can be linked in any way to a living person). Research involving the placenta may occur if all federal, state, or local laws and regulations are met. Research involving dead fetus, or fetal material, is prohibited under University of Nebraska Board of Regents policies.
- 4.5. Research not otherwise approvable
    - 4.5.1. Research which is subject to HHS regulations at 45 CFR 46 subpart B but which does not satisfy the requirements of 45 CFR 46 subpart B, and which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates, may be conducted only if the additional requirements of 45 CFR 46.207 are met.

5.0. Non-pregnant subjects who become pregnant during research

- 5.1. If a subject becomes pregnant while actively participating in a research protocol, all research activities and interventions for the pregnant subject must stop until the protocol is reviewed under the requirements of this policy, except where the PI has determined that it is in the best interest of the pregnant subject to continue participating in the study and has provided justification to the IRB Chair who is authorized to make the final determination.
    - 5.1.1. If the investigator or the IRB chair determines that it is not in the best interest of the pregnant subject to remain in the study, participation will be terminated and the PI must make provisions for the continuation of any necessary treatment of the

subject as appropriate.
    - 5.1.2. If the investigator and the IRB chair determines that it is in the best interest of the pregnant subject to continue participating, research activities may continue but the study must be re-reviewed by the full IRB, as soon possible, in consideration of this policy.

6.0 Documentation of Compliance with Subpart B

- 6.1. For research reviewed by the convened IRB, compliance with Subpart B (or with the equivalent protections described in this policy) will be documented in the letter to the investigator which is part of the meeting minutes.
- 6.2. For research reviewed through the expedited mechanism, compliance with Subpart B (or with the equivalent protections described in this policy) will be documented in the letter to the investigator which is available for review by the IRB in RSS.

DOCUMENT HISTORY:

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? Revised: 12/22/2022 – clarified exceptions to requirements under subpart B for research not subject to subpart B (section 4.1.2); deleted specific language related to 45 CFR 46.207 (section 4.5); stylistic changes for clarity.

? Revised: 9/25/2024 – added that research involving fetuses and neonates (nonviable or of uncertain viability) will be reviewed and conducted in accordance with applicable state law (section 2.3).

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