

P&P: SC 501 Version No: 1.1 Effective Date: 10/1/2009	PREGNANT WOMEN, FETUSES AND NEONATES AS VULNERABLE POPULATIONS	Supercedes: CPHS Policies and Procedures 9/1/2007
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1. POLICY

The use of the term “vulnerable” in the context of human research protections does not refer to susceptibility of harm, but rather the inability or a threat to the ability of an individual to give voluntary informed consent. When some or all subjects are likely to be vulnerable to coercion or undue influence the IRB must ensure that additional safeguards have been included in the study to protect the rights and welfare of these subjects. Pregnant women as a population are considered vulnerable primarily because of the involvement of a third party with a unique and inextricable relationship to the mother (the fetus) that may be affected by the research and cannot give consent. Therefore, the IRB may only approve research involving pregnant women, fetuses and/or neonates which satisfies the applicable criteria below in addition to the requirements delineated in RR 401 – Initial Review.

Specific Policies

1.1 Important Definitions

- 1.1.1 **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.
- 1.1.2 **Fetus** means the product of conception from implantation until delivery.
- 1.1.3 **Dead fetus** means a fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord.
- 1.1.4 **Delivery** means complete separation of the fetus from the woman by expulsion or extraction or any other means.
- 1.1.5 **Neonate** means a newborn.
- 1.1.6 **Nonviable neonate** means a neonate after delivery that, although living, is not viable.
- 1.1.7 **Viable** means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration. The Secretary may from time to time, taking into account medical advances, publish in the **FEDERAL REGISTER** guidelines to assist in determining whether a neonate is viable for purposes of this subpart. If a neonate is viable then it may be included in research only to the extent permitted and in accordance with the requirements of SC501B – Vulnerable Populations: Children and RR401 – Initial Review
- 1.1.8 **Secretary** means the Secretary of Health and Human Services (DHHS) and any other officer or employee of the Department of Health and Human Services to whom authority has been delegated.
- 1.1.9 **Children** are persons who have not yet attained the legal age for consent to treatment or procedures involved the research, under the applicable law of jurisdiction in which the research is conducted (be it local, national, foreign or domestic).

1.2 Research Involving Pregnant Women or Fetuses

- 1.2.1 *Pregnant women or fetuses* may be involved in research if all of the following conditions are met:
- 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 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 IC701 – General Requirement and Documentation of Informed Consent.
 - 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 accordance with the informed consent provisions of IC701 – General Requirement and Documentation of Informed Consent, 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 above 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 SC503 – Children as a Vulnerable Population.
 - 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.

1.3 Research involving Neonates

- 1.3.1 *Viable Neonates*: a neonate that has been determined to be viable may be included in research only to the extent permitted by and in accordance with SC503 – Children as a Vulnerable Population, and RR401 – Initial Review.
- 1.3.2 *Neonates of uncertain viability* may not be involved in research until it has been ascertained whether or not a neonate is viable or the following conditions are met:
- A. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.

- B. Individuals engaged in the research will have no part in determining the viability of a neonate.
- C. The IRB determines that either of the following conditions has been met:
 - i. The research holds out the prospect of enhancing the probability of survival of the particular fetus to the point of viability, and any risk is the least possible for achieving the objectives of the research.
 - 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 risk to the fetus resulting from the research.
- D. The legally effective informed consent of either parent of the fetus 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 in accordance with IC701 – General Requirement and Documentation of Informed Consent, unless altered or waived in accordance with IC702 – Informed Consent Waivers.
- E. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

1.3.3 *Nonviable neonates*: a nonviable neonate may not be involved in research unless all of the following conditions are met:

- A. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
- B. Individuals engaged in the research will have no part in determining the viability of a neonate.
- C. Vital functions of the neonate will not be artificially maintained.
- D. The research will not terminate the heartbeat or respiration of the neonate.
- E. There will be no added risk to the neonate resulting from the research
- F. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means.
- G. The legally effective informed consent of both parents of the neonate is obtained in accordance with IC701; however, the waiver and alteration provisions of do not apply here. 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, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to replace the consent of the parent.
- H. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

1.4 Research involving after delivery, the placenta, the dead fetus, or fetal material.

- A. Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable federal, state, or local laws and regulations regarding such activities.

- B. If information associated with this material 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 research subjects and all pertinent regulations apply.

1.5 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.

The Secretary will conduct or fund research that the IRB does not believe meets the requirements of 1.2 or 1.3 (above) only if:

- A. The IRB finds 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, fetuses or neonates; and
- B. The Secretary, after consultation with a panel of experts in pertinent disciplines (e.g., science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the FEDERAL REGISTER, has determined either:
 - i. That the research in fact satisfies the conditions of 1.2 (above), as applicable; or
 - ii. The following:
 - a. 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, fetuses or neonates;
 - b. The research will be conducted in accord with sound ethical principles; and
 - c. Informed consent will be obtained in accord with the informed consent provisions of IC 701 and other applicable subparts of this part.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

The OPHS Director and/or IRB Manager is responsible for maintaining up-to-date review tools for review of research pertaining to vulnerable groups based on new and evolving applicable regulations and guidelines. The Director and Manager are also responsible for ensuring that the IRB members are apprised of new and evolving regulations and guidelines pertaining to vulnerable populations, for selecting primary reviewers with appropriate expertise to conduct the reviews of such research, and for securing appropriate consulting expertise as needed for selected reviews.

The IRB Chair/Designee is responsible for providing IRB members with ongoing guidance and leadership.

IRB Members are responsible for conducting appropriate review of research planned for vulnerable populations, including an assessment of potential for coercion, in consultation with any appropriate experts and resources.

4. PROCESS OVERVIEW

When proposed research involves vulnerable populations, the IRB must take special precautions to ensure research participants' rights, safety, and welfare. In all cases involving vulnerable populations, the IRB Chair(s) and members must be cognizant of the subjects' needs when evaluating the protocol and are responsible for determining any additional protective stipulations to be applied to the research.

When proposed research involves pregnant women and fetuses, OPHS staff, IRB Chair(s), and IRB members will ensure that the protocol contains the appropriate consent and/or assent processes.

5. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46 Subpart B

45 CFR 46.111

21 CFR 56.111

The Belmont Report

OHRP IRB Guidebook