

**Guidance and Procedures Number: 22**

**Title: Special Subject Populations: Pregnant Women, Human Fetuses, and Neonates**

**Date of Last Revision: July 5, 2007**

## **I. Introduction**

Research involving women who are or may become pregnant receives special attention from IRBs because of women's additional health concerns during pregnancy and because of the need to avoid unnecessary risk to the fetus. Further, in the case of a pregnant woman, IRBs must determine when the informed consent of the father to the research is required. Special attention is justified because of the involvement of a third party (the fetus) who may be affected but cannot give consent and because of the need to prevent harm or injury to future members of society. Procedural protections beyond the basic requirements for protecting human subjects are prescribed in federal regulations for research involving pregnant women (45 CFR 46, Subpart B).

## **II. Definitions**

The following definitions are taken from 45 CFR 46.202:

- A. **Dead fetus:** A fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord.
- B. **Delivery:** Complete separation of the fetus from the woman by expulsion or extraction or any other means.
- C. **Fetus:** The product of conception from implantation until delivery.
- D. **Neonate:** A newborn.
- E. **Nonviable neonate:** A neonate after delivery that, although living, is not viable.
- F. **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.
- G. **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.

### **III. Research Involving Pregnant Women or Fetuses**

Pregnant women may be involved in several categories of research. IRB duties differ in each category, but the primary objectives are assessing: (1) whether the research is directed toward the mother's health or toward the fetus; and (2) the risks to the woman and to the fetus or infant. Pregnant women or fetuses may be involved in research if the IRB determines that all of the following conditions are met:

1. 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; [45 CFR 46.204(a)]
2. 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; [45 CFR 46.204(b)]
3. Any risk is the least possible for achieving the objectives of the research; [45 CFR 46.204(c)]
4. 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 of this part; [45 CFR 46.204(d)]
5. 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. [45 CFR 46.204(e)]
6. 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; [45 CFR 46.204(f)]
7. For children as defined in §46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of subpart D of this part; [45 CFR 46.204(g)]
8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy; [45 CFR 46.204(h)]
9. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; [45 CFR 46.204(i)] and
10. Individuals engaged in the research will have no part in determining the viability of a neonate. [45 CFR 46.204(j)]

#### **IV. Research Involving Neonates [45 CFR 46.205]**

##### **A. Neonates of uncertain viability and nonviable neonates**

Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met:

1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
2. Each individual providing consent under paragraph (b)(2) or (c)(5) of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonate.
3. Individuals engaged in the research will have no part in determining the viability of a neonate.
4. The requirements of paragraph (b) or (c) of this section have been met as applicable.

##### **B. Neonates of uncertain viability [45 CFR 46.206(b)]**

Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by this subpart unless the following additional conditions have been met:

1. The IRB must determine that:
  - a. 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
  - b. 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
2. 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 in accord with subpart A of this part, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

##### **C. Nonviable neonates [45 CFR 46.205(c)]**

After delivery nonviable neonate may not be involved in research covered by this subpart unless all of the following additional conditions are met:

1. Vital functions of the neonate will not be artificially maintained;
2. The research will not terminate the heartbeat or respiration of the neonate;

3. There will be no added risk to the neonate resulting from the research;
4. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
5. The legally effective informed consent of both parents of the neonate is obtained in accord with subpart A of this part, except that the waiver and alteration provisions of §46.116(c) and (d) do not apply. 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 (c)(5), 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 meet the requirements of this paragraph (c)(5).

**D. Viable neonates [ 45 CFR 46.205(d)]**

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 subparts A and D of this part.

**V. Research involving, after delivery, the placenta, the dead fetus or fetal material [45 CFR 46.206]**

- 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 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 research subjects and all pertinent subparts of this part are applicable.

**VI. 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 [45 CFR 46.207]**

The Secretary of DHHS will conduct or fund research that the IRB does not believe meets the requirements of 45 CFR 46.204 or 45 CFR 46.205 only if:

1. 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
2. The Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the Federal Register, has determined either:

- a. That the research in fact satisfies the conditions of 45 CFR 46.204, as applicable; or
- b. The following:
  - (1) 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;
  - (2) The research will be conducted in accord with sound ethical principles; and
  - (3) Informed consent will be obtained in accord with the informed consent provisions of subpart A and other applicable subparts of this part.

**VII. Studies in Which Pregnancy is Coincidental to Subject Selection**

Any study in which women of childbearing potential are possible subjects may inadvertently include pregnant women. Federal regulations require that, when appropriate, subjects be provided a statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable as part of the informed consent process.

The IRB must judge whether the mother's participation would pose any risk to the fetus or nursing infant. In some studies, IRBs may need to ensure that nonpregnant subjects are advised to avoid pregnancy or nursing for a time during or following the research. Furthermore, where appropriate, subjects should be advised to notify the investigator immediately should they become pregnant. In some instances there may be potential risk sufficient to justify requiring that pregnant women either be specifically excluded from the research or studied separately.

**Regulations:**

45 CFR 46, Subpart B