

**Institutional Review Board (IRB)**

**GUIDELINES FOR RESEARCH INVOLVING PREGNANT WOMEN AND FETUSES**

**1. Introduction**

Federal regulations (45 CFR 46.201, also “Subpart B”) require additional safeguards when approving research involving pregnant women and fetuses. The purpose of these guidelines is to assist investigators conducting research with pregnant women and fetuses by outlining the special considerations for such research.

**2. Definitions**

**Subpart B** refers to regulations that apply to research involving pregnant women and fetuses as subjects. Subpart B is found in 45 CFR 46 (DHHS).

**Pregnancy** encompasses the period of time from the implantation of the embryo within the uterus to delivery.

**Delivery** is the process of giving birth; complete separation of the fetus from the woman by any means.

**Fetus** refers to an unborn child; the product of conception, from implantation to delivery.

**Minimal Risk** is when the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. [45 CFR 46.102 (I)].

**3. Additional Protections for the Inclusion of Pregnant Women and Fetuses in Research**

To approve research involving pregnant women or fetuses, the IRB must determine that the research provides the additional protections described in 45 CFR 46 Subpart B in addition to meeting the regulatory criteria for approval of research involving non-pregnant participants.

The IRB must consider the degree of risk and discomfort involved in the research in relation to the direct benefits it offers to the pregnant woman for fetus, in order to determine whether the study is approvable under federal regulations. The standard of review is conducted consistently, regardless of full board or expedited review.

Risks that may be considered minimal when dealing with normal adults may be more risky when applied to pregnant women and fetuses. Efforts should be made to minimize any potential harm. There may also be unforeseeable risks to an embryo or fetus for a particular treatment or procedure. The possibility of unforeseeable risks must also be taken into consideration.

The IRB can approve studies involving pregnant women and/or fetuses only if the research fits into either category one or two below and meets all (1-6) of the following considerations:[[1]](#footnote-1)

**Category One:**

The research holds the prospect of direct benefit for the woman or the fetus. Any risk to the fetus is caused solely by interventions or procedures that hold the prospect of direct benefit for the woman or fetus.

**-Or-**

**Category Two:**

The research holds no prospect of direct benefit to the woman or fetus and the risk to the fetus is not greater than minimal (e.g. ultrasound, changes in maternal diet, etc.). The purpose of the research is to develop important knowledge[[2]](#footnote-2) which cannot be obtained by other means.

**Additional Considerations (1-6):**

1. Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies on non-pregnant women have been conducted and provide data for assessing potential risks to pregnant women and fetuses.
2. The risks to pregnant women and fetuses have been minimized, while still allowing the objectives of the research to be achieved.
3. The individual(s) providing consent will be fully informed regarding the reasonable foreseeable impact of the research on the fetus.
4. The individuals conducting the research are prohibited from offering inducements, monetary or otherwise, to terminate a pregnancy.
5. The individuals conducting the research are prohibited from taking part in the decisions as to the timing, method, or procedures used to terminate a pregnancy.
6. The individuals conducting the research are prohibited from determining the viability of the neonate.

**4. Obtaining Consent for Research Involving Pregnant Women or Fetuses**

Informed consent must be obtained from the necessary individuals as described below, unless the study meets the criteria to waive informed consent.

If the research falls into Category One (research holds the prospect of direct benefit for the woman or the fetus), the IRB will make a decision based on the risk-benefit ratio, as to which consent process method is appropriate for the study. The methods are as follows:

* If the research holds the prospect of direct benefit to the **pregnant woman and fetus**, consent must be obtained from the pregnant woman.
* If the research holds the prospect of direct benefit to the **pregnant woman only**, consent must be obtained from the pregnant woman.
* If the research holds the prospect of direct benefit to the **fetus only**, consent must be obtained from the pregnant woman and the father of the fetus.
	+ The father’s consent does not need to be obtained if he is unable to consent because of unavailability, incompetence, temporary incapacity, or if the pregnancy resulted from rape or incest.

If the research falls into Category Two (research holds no prospect of direct benefit to the woman or fetus and the risk to the fetus is not greater than minimal), consent from the pregnant woman only is required.

**5. Obtaining Consent from Women in Labor and Delivery**

Whenever practical and feasible, information about research conducted in the Labor and Delivery suite should be made available to patients prior to labor.

Investigators should acknowledge and be sensitive to the vulnerability of patients providing informed consent while in labor. It may be inappropriate to approach patients at certain times during the labor and delivery process, but it is inappropriate to arbitrarily deny all pregnant patients the opportunity to participate in research during the labor and delivery process simply because they are experiencing labor.

Investigators are responsible for ensuring that cooperation is obtained from those involved in the labor process (such as family and/or primary care providers). Investigators who plan on approaching a patient in the labor room should first consult with the patient’s obstetric care providers and/or family regarding the appropriateness of such an approach. If the patient’s obstetric care providers or family feel that a particular patient is not in a position to comprehend a research protocol and give informed consent, then that patient may not be approached for research participation until the circumstances have changed.

Many laboring women are competent to consent to research and other procedures after the administration of neuraxial (spinal or epidural) local anesthesia since the doses commonly used have little to no sedative effect, and the decrease in pain may make patients more able to consider and discuss options in their care. If feasible for the particular research study, it may be preferable to delay approaching pregnant patients for research participation until after the placement of epidural analgesia, if such analgesia is desired by the patient. Patients who’ve received systemic opioids or sedative medications may need a delay before being approached.

Written evidence of informed consent must be obtained in all cases unless a waiver of consent was granted or applies. In select cases, depending on the degree of perceived vulnerability of the patient, the IRB may require that the consent be co-signed by an independent witness, such as the patient’s physician, nurse or family member.

**6. Research on Dead Fetuses or Fetal Material (after delivery)**

A fetus that does not exhibit a heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, or pulsation of the umbilical cord will be considered a dead fetus. Research involving dead fetuses or fetal material obtained after delivery must be conducted in accord with any applicable federal, state, or local laws and regulations regarding such activities. For example, if identifiers are recorded, HIPAA may apply. If information is recorded in such a way that living individuals can be identified through the research, the activity may constitute human subjects research. As such, the IRB Office should be contacted for further guidance.

**7. Research involving Pregnant Women and Fetuses that does not meet the Protections found in Subpart B**

Research involving pregnant women and fetuses that does not meet the conditions for approval described by the federal regulations may be conducted only if all of the following conditions are met:

* The IRB finds that the research presents a reasonable opportunity to further in pertinent understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women or fetuses;
* The Secretary (DHHS), after consultation with a panel of experts in pertinent disciplines (e.g. science, medicine, ethics, law, etc.) and following opportunity for public review and comment (including a public meeting announced in the *Federal Register*), has determined either of the following:
	+ The research satisfies the regulatory conditions for approval
	+ 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 or fetuses; the research will be conducted consistent with sound ethical principles; and informed consent will be obtained in accordance with the regulatory requirements pertaining to pregnant women and fetuses.

**8. References**

45 CFR 46.201 (Subpart B)

Columbia University IRB: “Clinical Research Involving Pregnant Women”

AAHRPP, Inc. Elements II.3.F, II.4.A

1. 45 CFR 46.204 [↑](#footnote-ref-1)
2. In federally funded research, knowledge must be biomedical. [↑](#footnote-ref-2)