

PREGNANT WOMEN, FETUSES, AND NEONATES IN RESEARCH

This guidance document is intended for researchers planning to involve pregnant women, fetuses, and/or neonates as research subjects. Should you need additional assistance, please contact OPHS at 510-642-7461 or ophs@berkeley.edu.

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A. General Information:

Pregnant women as a population are considered vulnerable primarily because of the involvement of a third party (the fetus) that may be affected by the research and cannot give consent. Likewise, neonates (newborns) are not able to provide consent and are particularly vulnerable because of their often unknown health standing. Because of these vulnerabilities, federal regulations at [45 CFR 46 Subpart B](#) detail a number of specific requirements regarding research with pregnant women, fetuses, and neonates. Researchers must pay special attention and take these requirements into account when designing research involving these subject populations.

B. Definitions:

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.

Fetus means the product of conception from implantation until delivery.

Dead fetus means a fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord.

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

Neonate means a newborn.

Legally authorized representative means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

Minimal Risk means that 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.

C. Pregnant Women and Fetuses:

1. Approval Criteria:

As set forth in federal regulations at [45 CFR 46 Subpart B](#), the Committee for Protection of Human Subjects (CPHS) may approve research involving pregnant women and fetuses if all of the criteria below 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. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
- e. For children who are pregnant, assent and permission are obtained in accord with CPHS child assent and parent permission guidelines;
- f. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
- g. 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
- h. Individuals engaged in the research will have no part in determining the viability of a neonate.
- i. 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 [CPHS informed consent guidelines](#);
- j. 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 [CPHS informed consent guidelines](#), 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.*

Consent Decision Chart for Pregnant Women and Fetuses

	Direct benefit to mother only	Direct benefit to mother and fetus	Direct benefit to fetus only	No direct benefit or societal benefits only
Risk is more than minimal	Mother's consent	Mother's consent	Mother and father's consent	N/A- Not approvable
Risk is no more than minimal	Mother's consent	Mother's consent	Mother and father's consent	Mother's Consent

2. 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. Department of Health and Human Services (DHHS) 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 CPHS must judge whether the mother's participation would pose any risk to the fetus or nursing infant. In some studies, the CPHS may need to ensure that non-pregnant 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.

For example, because the risks to a fetus from magnetic resonance imaging (MRI) are unknown at this time, it is the policy of the CPHS that for all studies involving MRI or fMRI, women of childbearing potential must be excluded from the study if a pregnancy test is positive or if the subject or her parent thinks that she might be pregnant. Please see CPHS guidance on MRI research for detailed instruction (<http://cphs.berkeley.edu/mri.pdf>).

Note: National Institute of Health (NIH) policy requires the inclusion of women in research study populations so that research findings can be of benefit to all persons at risk of the disease, disorder, or condition under study. As such, women must not be excluded from research simply because of their child-bearing potential.

3. Studies Directed Primarily Toward the Mother's Health:

A number of women enter pregnancy with health problems or develop new ones during pregnancy. Some problems are affected positively or negatively by pregnancy; others are unaffected. A considerable amount of research is conducted on health problems that affect women during pregnancy (e.g., arthritis, hypertension, diabetes); despite standard therapy, deterioration of maternal health may also necessitate experimental treatment. In research undertaken to address the health problems of a pregnant woman, her needs generally take precedence over those of the fetus, except where the health benefit to the woman is minimal and risk to the fetus is high.

For example, if an experimental drug were considered necessary to improve a pregnant woman's condition, her consent alone would be sufficient to authorize its administration – even though it might have unknown or greater than minimal risk for the fetus.

4. Research in Anticipation of Abortion:

Only those research procedures that would be acceptable for a fetus going to term may be performed in anticipation of abortion. If the CPHS determines that the risk is acceptable for fetuses that will be carried to term, it is acceptable to select only fetuses to be aborted as subjects. By limiting the risk to what is acceptable for the fetus to be carried to term, the right of the mother to change her mind about abortion is protected; by selecting only those fetuses destined for abortion as subjects, risk to fetuses carried to term is minimized. In practical terms, research procedures that take place at the same time and during the same process as the abortion itself must fully meet these conditions (e.g., a fetoscopic procedure initiated after administering drugs to initiate abortion).

5. 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 extracted from a dead fetus, shall be conducted only in accord with any applicable federal, state, or local laws and regulations regarding such activities. If investigators are accessing Protected Health Information (PHI) they must adhere to rules set forth by the Health Insurance Portability and Accountability Act (HIPAA).
- 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 investigators must adhere to applicable regulations as set forth in [45 CFR 46](#).

D. Neonates:

- 1. Viable neonate** means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration. 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](#). Investigators should pay special attention to additional protections for children involved as subjects in research as detailed in subpart [D](#). Please see [CPHS Guidelines on Children](#) in Research for further information.
- 2. Neonates of uncertain viability:** Researchers planning to include neonates of uncertain viability should be aware of the following requirements:

Protocol Considerations:

- a. Where scientifically appropriate, the protocol should include information regarding preclinical and clinical studies that have been conducted and provide data for assessing potential risks to neonates.
- b. The protocol should make it clear that study personnel or others engaged in the research will have no part in determining the viability of a neonate.

Consent Process:

- a. The legally effective informed consent of either parent of the neonate should be obtained, 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 must be obtained in accord with [CPHS Guidelines on Informed Consent](#), except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.*
- b. Each individual providing consent must be fully informed regarding the reasonably foreseeable impact of the research on the neonate.

Additional IRB Findings:

When approving research involving neonates of uncertain viability, the CPHS 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.
- 3. Nonviable neonate** means a neonate after delivery that, although living, is not viable. After delivery a nonviable neonate may not be involved in research unless all of the following additional conditions are met:

Protocol Considerations:

- 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 the neonate.

Consent Process:

- a. The legally effective informed consent of both parents of the neonate is obtained. *When nonviable neonates are included in research, the consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice. In addition, alterations and waivers of informed consent do not apply.* 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.*
- b. Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate.

Consent Decision Chart for Neonates of Uncertain Viability and Nonviable Neonates

	Consent Requirements	Legally Authorized Representative	Consent Waivers and Alterations
Neonates of Uncertain Viability	Mother or father's consent	Y	Y
Nonviable Neonates	Mother AND father's consent	N	N

Additional IRB Findings:

When approving research involving neonates of uncertain viability, the CPHS must determine that:

- 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.

E. Research Not Otherwise Approvable:

Secretary means the Secretary of the Department of Health and Human Services (DHHS) and any other officer or employee of DHHS to whom authority has been delegated.

The Secretary of DHHS will conduct or fund research that the CPHS does not believe meets approval requirements described above only if:

1. The CPHS 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 (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:
 - a. That the research in fact satisfies the conditions describe above; 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.

F. Levels of Review:

- 1. Exempt review:** Exempt review is acceptable for research with pregnant women when the research presents no greater than minimal risk to both the mother and the fetus and the research fits within one or more exempt categories. Please see the CPHS exempt guidelines for further information: <http://cphs.berkeley.edu/exempt.pdf>.
- 2. Expedited review:** Expedited review is acceptable for pregnant women, fetuses and/or neonates when the research presents no more than minimal risk to subjects and the involvement of human subjects falls into one or more expedited categories provided under [45 CFR 46.110](#).
- 3. Full Committee review:** Full Committee review is required for research with pregnant women, fetuses and/or neonates when the research presents greater than minimal risk to subjects or does not fit into an exempt or expedited category.

G. Additional Information: For additional information on research involving pregnant women, fetuses, or neonates, please visit the links below and/or contact the Office for the Protection of Human Subjects.

<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#subpartb>

http://www.hhs.gov/ohrp/irb/irb_chapter6.htm

*Note: The CPHS will generally not accept a consent process that involves obtaining consent from the father when the pregnancy resulted from rape or incest.