

Policy Number 38:

Title: Pregnant Women, Human Fetuses, Neonates, and Fetal Tissue

Date of Last Revision: 10/12/07, 10/23/10, 08/22/2017

Policy:

It is the policy of the UC Irvine (UCI) Institutional Review Board (IRB) to review and approve research involving pregnant women, human fetuses, and neonates of uncertain viability or nonviable neonates based on the Federal regulations at 45 CFR 46 Subpart B and in addition to those imposed under other IRB policies, procedures, and other applicable Federal, State, and local laws.

- I. Research involving women who are or may become pregnant should receive special attention from the IRB 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, the IRB must determine when informed consent of the father is required for research. Special attention is justified because of the involvement of a third party (the fetus) who may be affected but cannot give consent. Procedural protections beyond the basic requirements for protecting human participants are prescribed in the Federal regulations (Subpart B) for research involving pregnant women.

- II. **§46.204: Research Involving Pregnant Women or Fetuses** - 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 nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses; and
 - 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; and
 - C. Any risk is the least possible for achieving the objectives of the research; and
 - 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 45 CFR 46 Subpart A; and
 - 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 accord with the informed consent provisions of 45 CFR 46 Subpart A, 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; and
 - F. Each individual providing consent under (D) or (E) above, is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate; and
 - G. For children as defined in 45 CFR 46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of 45 CFR 46 Subpart D (See IRB Policy 36); and
 - H. No inducements, monetary or otherwise, will be offered to terminate a pregnancy; and

- 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; and
- J. Individuals engaged in the research will have no part in determining the viability of a neonate.

III. **§46.205: Research Involving Neonates**

- A. 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; and
 - 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; and
 - 3. Individuals engaged in the research will have no part in determining the viability of the neonate; and
 - 4. The requirements of paragraph B or C of this section have been met as applicable.
- B. Neonates of uncertain viability. Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by this policy 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 45 CFR 46 Subpart A, 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. After delivery a nonviable neonate may not be involved in research covered by this policy unless all of the following additional conditions are met:
 - 1. Vital functions of the neonate will not be artificially maintained; and
 - 2. The research will not terminate the heartbeat or respiration of the neonate; and
 - 3. There will be no added risk to the neonate resulting from the research; and
 - 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 45 CFR 46 Subpart A, except that the waiver 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, 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.
- D. Viable neonates. If a neonate is judged viable (i.e. likely to survive to the point of sustaining life independently, given the benefit of available medical therapy), it is then called an infant and should be treated as a child for purpose of research participation. 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 Subparts A and D.

- IV. **§46.206: 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.
1. For example, the California Protection of Human Subjects in Medical Experimentation Act makes it unlawful for any person or entity to engage in medical experiments or research without the prior knowledge and consent of the mother.
 2. Additionally, no person or entity may offer or accept money or anything of value for an aborted fetus. Violations of these provisions are punishable as a Class E felony.
- V. **§46.207: 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 of the Department of Health and Human Services (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:
- 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 (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:
1. That the research, in fact, satisfies the conditions of §46.204, as applicable; or
 2. 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; and
 - 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 45 CFR 46 Subpart A and other applicable subparts of 45 CFR 46.
- VI. **Modification or Waiver of Specific Requirements** - Upon the request of the Investigator (with the approval of the IRB), the Secretary of the Department of Health and Human Services may modify or waive any of the above requirements of this policy.
- VII. **Studies in Which Pregnancy is Coincidental to Subject Selection**
- A. 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.
1. The IRB must judge whether the mother's participation would pose any risk to the fetus or nursing infant. In some studies, the IRB may need to assure 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.

- VIII. **Exemption from Review** - Note that with the revision of Subpart B on November 13, 2001, the exemptions from IRB review listed at 45 CFR 46.101(b) may now be applied to research involving pregnant women, human fetuses, and neonates in accordance with 45 CFR 46.201(b).
- IX. **Environmental Protection Agency Requirements When Involving Pregnant or Nursing Women in Research**
- A. The EPA prohibits research involving the intentional exposure of pregnant or nursing women to any substance.
 - B. The EPA requires application of 40 CFR 26 Subpart B to provide additional protections to pregnant women as participants in observational research, i.e., research that does not involve intentional exposure to any substance.
 - C. EPA policy requires submission of IRB determinations and approval to the EPA Human Subjects Research Review official for final review and approval before the research can begin.
 - D. Research not conducted or supported by any federal agency that has regulations for protecting human research participants and for which the intention of the research is submission to the EPA, the EPA regulations protecting human research participants apply, including:
 - 1. The EPA extends the provisions of the 40 CFR 26 to human research involving the intentional exposure of non-pregnant, non-nursing adults to any substance.
 - 2. The EPA prohibits the intentional exposure of pregnant women or nursing women to any substance.
- X. **Research Involving Specimens from the Placenta After Delivery or Postmortem Fetal Tissue**
- A. The University of California (UC) is compliant with California law that permits research using fetal remains, which is defined as a lifeless product of conception regardless of the duration of pregnancy (CA Health and Safety Code 123440).
 - B. If identifying data are associated with the material in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and IRB review and approval is required before such materials are collected or used.
 - C. Research involving the transplantation of human fetal tissue for therapeutic purposes must be conducted in accord with applicable State law and the Secretary may not provide support for such research unless the applicant for assistance agrees to conduct the research. The conduct of such research by the Secretary must be in accord with applicable state and local law. Additional guidance on fetal tissue transplantation research is available on the OHRP website.
 - D. The provisions of section 498B of the Public Health Service Act (42 U.S.C. 298g-2), added by Public Law 103-43, the NIH Revitalization Act of 1993 are summarized as follows:
 - 1. It shall be unlawful for any person to knowingly acquire, receive, or otherwise transfer any human fetal tissue for valuable consideration if the transfer affects interstate commerce.
 - a) Valuable consideration does not include reasonable payment associated with the transportation, implantation, processing, preservation, quality control, or storage of human fetal tissue.
 - 2. It shall be unlawful for any person to solicit or knowingly acquire, receive, or accept a donation of human fetal tissue for the purposes of transplantation of such tissue into

another person if:

- a) The donation effects interstate commerce;
- b) The tissue will be obtained pursuant to an induced abortion; and:
 - (1) The donation will be or is made pursuant to a promise to the donating individual that the donated tissue will be transplanted into a recipient specified by such individual;
 - (2) The donated tissue will be transplanted into a relative of the donating individual; or
 - (3) The person who solicits or knowingly acquires, receives, or accepts the donation has provided valuable consideration for the costs associated with such abortion.
 - (a) Valuable consideration does not include reasonable payments associated with the transplantation, implantation, processing, preservation, quality control or storage of human fetal tissue.)

XI. Research Involving Dried Blood Spots Obtained Through Newborn Screening

- A. NIH funded research using newborn dried blood spots collected on or after March 18, 2015, will be considered to be non-exempt human subjects research, and therefore, must follow the HHS protection of human subjects regulations at 45 CFR part 46.
- B. Grant applications and R&D contract proposals submitted to NIH that will use such materials in research should be designated as non-exempt human subjects research and include a complete human subjects section per relevant NIH instructions including plans for inclusion on the basis of sex/gender, race, ethnicity, and age per the NIH Policies on the Inclusion of Women, Minorities, and Children.
- C. Such applications and proposals that are funded by NIH must comply with all the relevant federal regulatory and NIH policy requirements for human subjects research including the requirement that the awardee institution (and all engaged institutions) have a Federalwide Assurance (FWA) from OHRP and certification of IRB approval of the proposed research.
- D. Parental permission must have been obtained in order to use newborn dried blood spots **collected on or after March 18, 2015**, in NIH-funded research. Waiver of parental permission for such research is not permitted under this legislation.
- E. Continuing NIH awards that are conducting research with newborn dried blood spots collected on or after March 18, 2015, will also have to comply with these new requirements. Awardee institutions will need to meet all NIH requirements for human subjects research, including IRB approval, prior to starting such research.
- F. NIH will add a specific term and condition to all new and continuing awards conducting applicable newborn dried blood spot research to ensure compliance with the new legislation.
- G. Non-identifiable newborn dried blood spots collected prior to March 18, 2015, may continue to be used in NIH-funded research without parental permission, and this activity would continue to be considered research that does not involve human subjects under the current human subjects regulations.

References:

40 CFR 26
40 CFR 26.Subpart B
45 CFR 46

45 CFR 46 Subpart B

Office for Human Research Protections Guidance for Investigators and Institutional Review Boards
Regarding Research OHRP IRB Guidebook, Chapter 6, "Special Classes of Subjects"

OHRP Guidance Document: "Fetal Tissue Transplantation", February 2003.

The NIH Revitalization Act of 1993 (Public Law 103-43) Section 498B of the Public Health Service Act (42 U.S.C. 298g-1).

Procedure Number: 38.A

Title: Procedure for Review of Research Involving Pregnant Women, Human Fetuses, Neonates, and Fetal Tissue

Procedure:

The purpose of this procedure is to provide guidance on the requirements for review and approval for pregnant women, human fetuses, neonates, and fetal tissue activities in human subjects research under the UC Irvine (UCI) Institutional Review Board (IRB) jurisdiction.

I. Lead Researcher (LR) Responsibilities

- A. The LR will submit the "Vulnerable Populations - Pregnant Women, Human Fetuses, or Neonates" (Appendix B) with a new study submission in which the target population for research includes pregnant women, fetuses, or neonates.
- B. The LR will contact the hSCRO Administrator to obtain the necessary documentation to submit with a new IRB Application when the research involves the collection of fetal tissue to derive stem cells.
- C. Once the full IRB Committee approves the study, the LR will obtain informed consent from the mother and father as outlined in IRB Policy Section 30.

II. IRB Committee Responsibilities

- A. The IRB Committee must review the proposed research taking into consideration all applicable IRB policies and the requirements for involvement of pregnant women, fetuses, neonates, and fetal tissue transplantation activities in research.
- B. The IRB Committee will review and approve research in accordance with the Federal regulations at 45 CFR 46 Subpart A.
- C. When reviewing research involving pregnant women, the IRB Committee will include in its composition one or more individuals who are knowledgeable about and experienced in working with pregnant women.
- D. The IRB will discuss the additional protections necessary for this population as outlined in the "Vulnerable Populations: Pregnant Women, Human Fetuses, or Neonates" (Appendix B). The Primary and Secondary Reviewers will be responsible for documenting these added protections with the completion of the "Supplemental Reviewer's Checklist for Pregnant Women, Human Fetuses, & Neonates."
- E. The IRB must review the proposed research involving fetal tissue to ensure that all federal and state requirements outlined in IRB Policy 38 are met.
- F. The IRB Committee will review observational research involving pregnant women and fetuses using 40 CFR 26 and 45 CFR 46 Subpart B.
- G. For research following Environmental Protection Agency (EPA) regulations and guidance;
 - 1. When research is conducted or supported by the EPA or when research is intended for submission to the EPA, research involving intentional exposure of pregnant or nursing women, or children to any substance is prohibited.

III. IRB Administrator Responsibilities

- A. The Administrator will verify that the "Vulnerable Populations: Pregnant Women, Human Fetuses, or Neonates" (Appendix B) is completed as part of the initial study documents.
- B. The Administrator will verify if necessary hSCRO documentation has been completed or needs completion as part of the initial study documents and will inform the Human Stem Cell Oversight Committee (hSCRO) Administrator that the new application requires hSCRO review.
- C. The Administrator will conduct a pre-review and will take into consideration the additional

requirements under Subpart B for research activities involving pregnant women, fetuses, neonates, or research involving transplantation of fetal tissue.

- D. E-mails recommending pre-review changes to the informed consent documents are to be sent to the LR by the Administrator.
- E. Once the pre-review revisions are received from the LR, the Administrator will forward the revised informed consent documents to the assigned Reviewers with appropriate expertise in pregnant women or children, as applicable, and prepare the Reviewer and Committee packets.

References:

IRB Policy 38, "Vulnerable Populations: Pregnant Women, Human Fetuses, Neonates and Fetal Tissue"