UNIVERSITY OF TENNESSEE GRADUATE SCHOOL OF MEDICINE INSTITUTIONAL REVIEW BOARD REVIEW OF RESEARCH – ADDITIONAL PROTECTIONS FOR VULNERABLE SUBJECTS – PREGNANT WOMEN, NEONATES & FETUSES

I. PURPOSE

To document the policy and procedures used by University of Tennessee Graduate School of Medicine Institutional Review Board (UTGSM IRB) regarding the review of clinical studies involving pregnant women and fetuses.

II. SCOPE

This SOP applies to the IRB administrative staff, IRB members and investigators.

Personnel Responsible:

UTGSM IRB administrative staff, IRB members, investigators

III. BACKGROUND

The IRB has the responsibility to assure that the rights and welfare of subjects are adequately protected. As research subjects, pregnant women, fetuses and neonates possess special vulnerabilities. These vulnerabilities relate to an increased susceptibility to harm associated with research procedures, as well as impediments to provision of adequate informed consent (e.g., women in labor) or the absence of the ability to provide informed consent (fetuses and neonates). Therefore, additional protections are afforded them as research subjects.

Research with pregnant women, fetuses and neonates must satisfy the regulatory requirements of 45CFR46, Subpart B, "Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research," as well as the general requirements of 45 CFR 46, Subpart A (the Common Rule). In addition to the requirements outlined in the SOP #03 (Review of Research), UTGSM IRB shall determine that research with pregnant women, fetuses, and neonates is conducted in accord with 45CFR46, Subpart B. Finally, if a neonate is viable, then it may be included in research only to the extent permitted by the requirements of 45 CFR 46, Subpart D, "Additional Protections for Children Involved as Subjects in Research," and the requirements of the UTGSM IRB as outlined in IRB SOP # 13.

In Accordance With:

45 CFR 46; OHRP Guidance on Written IRB Procedures, 7/11/02.

Additional information is also located at:
http://www.hhs.gov/ohrp/archive/irb/irb_guidebook.htm
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Compliance with this policy also requires compliance with state or local laws or regulations that provide additional protections for human subjects.

DEFINITIONS

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.

Fetus means the product of conception from implantation until delivery.

Neonate means a newborn.

Nonviable neonate means a neonate after delivery that, although living is not viable.

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.

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.

IV. PROCEDURES

A. Pregnant women or fetuses may be involved in research if all of the following conditions are met:
   1. Where scientifically appropriate, preclinical studies, including studies in 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;
   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;
   3. Any risk is the least possible for achieving the objectives of the research;
   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 45 CFR 46;

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 45 CFR 46, 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.
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;
7. For children, as defined in 45 CFR 46.402(a), who are pregnant, assent and permission are obtained in accord with the provisions of subpart D of this part;
8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
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; and
10. Individuals engaged in the research will have no part in determining the viability of a neonate

B. Special conditions must also be satisfied for IRB approval of research involving certain categories of neonates:
    1. Neonates of uncertain viability and nonviable neonates may be involved in research if 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. 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.
        c. Individuals engaged in the research will have no part in determining the viability of a neonate.
        d. The requirements of paragraph (b) or (c) of this section have been met as applicable.
    2. 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 subpart unless the following additional conditions have been met:
        a. The IRB determines that:
            i.) 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
            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 added risk to the neonate resulting from the research; and
        b. 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 45 CFR 46, except that the consent of the father or his legally authorized

representative need not be obtained if the pregnancy resulted from rape or incest.

3. Nonviable neonates. After delivery, a nonviable neonate may not be involved in research covered by this subpart unless all of the following additional conditions are met:
    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; and
    e.)The legally effective informed consent of both parents of the neonate is obtained in accord with subpart A of 45 CFR 46, except that the waiver and alteration provisions of 45 CFR 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).
4. Viable neonates. 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 45 CFR 46.

C. The IRB will approve research involving, after delivery, the placenta, the dead fetus or fetal material in accord with the following requirements:
    1. 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.
    2. 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 45CFR46 are applicable.

D. When research is not otherwise approvable under 45 CFR 46.204 or 45 CFR 46.205, but may present an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates, then the IRB will observe the following procedures:

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

    1. The IRB will determine whether 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. If the finding is positive, then the IRB will request that the Secretary of HHS convene an expert panel in accord with 45 CFR 46.207.

2. The IRB will approve such research if 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 Sec. 46.204, as applicable; or
   b. The following:
      i. 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;
      ii. The research will be conducted in accord with sound ethical principles; and
      iii. Informed consent will be obtained in accord with the informed consent provisions of subpart A and other applicable subparts of 45 CFR 46.