

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) to review, approve, and provide guidance on the special ethical and regulatory considerations concerning all 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.

II. Authority

- A. Chapter 381.86, Florida Statutes, Institutional Review Board

III. Supportive Data

- A. 45 CFR 46 Subpart B
- B. OHRP Guidance Document: "Fetal Tissue Transplantation", February 2003.
- C. 42 USC 289g and Sections 498 and 498A

IV. Definitions

- A. **Dead Fetus:** A fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord (if still attached).
- 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. **Human Fetal Tissue:** Tissue or cells obtained from a dead human embryo or dead fetus after a spontaneous or induced abortion, or after a stillbirth.
- E. **Neonate:** A newborn.
- F. **Nonviable Neonate:** A neonate after delivery that, although living, is not viable.
- G. **Pregnancy:** Encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the presumptive signs of pregnancy, such as a missed menses, until the results of a pregnancy test are negative or until delivery.
- H. **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.

V. Procedures**A. IRB Review and Approval of Research Involving Pregnant Women**

Research involving women who are or may become pregnant shall 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 shall 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 and because of the need to prevent harm or injury to future members of society. Procedural protections beyond the basic requirements for protecting human participants are prescribed in the Federal regulations for research involving pregnant women.

B. 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:

1. 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; and
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; and
3. Any risk is the least possible for achieving the objectives of the research; and
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, the woman's consent is obtained in accord with the informed consent provisions of 45 CFR 46 Subpart A; and
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 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

6. 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
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 45 CFR 46 Subpart D (See IRB Policy, "Special Categories of Research: Children"); and
8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy; and
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.

C. 46.205: Research Involving 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; and
 - 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; and
 - c. Individuals engaged in the research will have no part in determining the viability of the neonate; and
 - 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 policy unless the following additional conditions have been met:

- a. The IRB must determine that:
 - (1) 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

(2) 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 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.

3. 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:

a. Vital functions of the neonate will not be artificially maintained; and

b. The research will not terminate the heartbeat or respiration of the neonate; and

c. There will be no added risk to the neonate resulting from the research; and

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 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.

4. Viable neonates

If a neonate is judged viable (i.e. being able, after delivery, to survive, given the benefit of available medical therapy, to the point of independently maintaining heartbeat and respiration) 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.

- D. 46.206: Research Involving, After Delivery, the Placenta, the Dead Fetus, or Fetal Material.
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 1 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 the regulations are applicable.
- E. 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

Per Federal Regulations, 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:

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. Per Federal Regulations, the Secretary of DHHS, 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 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; and

- (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 45 CFR 46 Subpart A and other applicable subparts of 45 CFR 46.

3. **Modification or Waiver of Specific Requirements.** Per Federal Regulations, 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.

F. Studies in Which Pregnancy is Coincidental to Subject Selection.

1. 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.
 - a. 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 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.

G. 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).

H. Research on Transplantation of Fetal Tissue

The IRB must assure that the following provisions have been met before approving such research activities:

1. Research involving the transplantation of human fetal tissue for therapeutic purposes may be conducted only if the woman providing the tissue makes a statement, in writing and signed by the woman, declaring that:
 - a. The woman donates the fetal tissue for research; and
 - b. The donation is made without any restriction regarding the identity of individuals who may be the recipients of transplantations of the tissue; and
 - c. The woman has not been informed of the identity of any such individuals.
2. Research involving the transplantation of human fetal tissue for therapeutic purposes may be conducted only if the attending physician with respect to obtaining the tissue from the woman involved makes a statement, in writing and signed by the attending physician, declaring that:
 - a. In the case of tissue obtained pursuant to an induced abortion:
 - (1) The consent of the woman for the abortion was obtained prior to requesting or obtaining consent for a donation of the tissue for use in such research; and
 - (2) No alteration of the timing, method, or procedures used to terminate the pregnancy was made solely for the purposes of obtaining the tissue; and
 - (3) The abortion was performed in accordance with applicable State law; and
 - b. The tissue has been donated by the woman in accordance with paragraph A of this section; and
 - c. Full disclosure has been provided to the woman with regard to:
 - (1) Such physicians interest, if any, in the research to be conducted with the tissue; and
 - (2) Any known medical risks to the woman or risks to her privacy that might be associated with the donation of the tissue and that are in addition to risks of such type that are

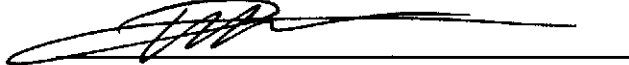
associated with the woman's medical care.

3. Research involving transplantation of human fetal tissue for therapeutic purposes may be conducted only if the Principal Investigator (PI) makes a statement in writing and signed by the PI, declaring that the PI:
 - a. Is aware that:
 - (1) The tissue is human fetal tissue; and
 - (2) The tissue may have been obtained pursuant to a spontaneous or induced abortion or pursuant to a stillbirth; and
 - (3) The tissue was donated for research purposes; and
4. The PI has provided such information to other individuals with responsibilities regarding the research; and
 - a. The PI will require, prior to obtaining the consent of an individual to be a recipient of a transplantation of the tissue, written acknowledgment of receipt of such information by such recipient; and
 - b. The PI has had no part in any decisions as to the timing, method, or procedures used to terminate the pregnancy made solely for the purpose of the research.
5. Research involving transplantation of human fetal tissue for therapeutic purposes may be conducted only if the head of the agency or other entity conducting the research involved certifies to the Secretary of the Department of Human Services (DHHS) that the statements required under paragraphs B and C of this section will be available for audit by the Secretary of DHHS.
6. Research involving transplantation of human fetal tissue for therapeutic purposes may be conducted only if it is conducted in accordance with applicable Federal, State and local laws and institutional policies and procedures.

VI. History Notes

This is a new policy. The Office of Statewide Research, Ethics and Human Research Protections Program are responsible for this policy.

VII. Signature Block with Effective Date



John O. Agwunobi, M.D., M.B.A., M.P.H.
Secretary, Department of Health

06/29/05
Date