

The Christ Hospital IRB

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Reviewed By: Michael Jennings, MD/Steve Roberts, MD

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Approved By: Steve Roberts, MD

(II.4.A)

STANDARD OPERATING PROCEDURE

Additional Safeguards for Pregnant Women and Fetuses and Neonates in Research

POLICY:

The Christ Hospital requires that research will include additional safeguards to protect the rights and welfare of subjects when some or all of the subjects are pregnant women or fetuses or neonates. In addition to its other prescribed responsibilities, the IRB will review research involving pregnant women or human fetuses or neonates and approve only research which satisfies the applicable conditions as set out below. All research involving pregnant women, fetuses or neonates, regardless of funding source, will be reviewed and approved in accordance with 45 CFR Part 46, Subpart B, as applicable. This standard for review and approval also applies to research involving post-delivery placentas, dead fetuses, or fetal material.

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: Complete separation of the fetus from the woman by expulsion or extraction or any other means.

Fetus: The product of conception from implantation until delivery.

Neonate: A newborn.

Nonviable Neonate: A neonate after delivery that, although living, is not viable.

Pregnancy: 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.

Viable: As it pertains to the neonate, the ability, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration.

Studies in Which Pregnancy is Coincidental to Participant Selection: When potential participants are recruited from a population that includes women of child bearing potential, the IRB will determine when it is appropriate to inform participants that risks of participation to the

embryo, fetus or nursing infant are currently unforeseeable. In addition, the IRB will determine whether:

- a) The subject should be advised to avoid pregnancy or nursing during or following participation in the research or to notify the PI immediately should the subject become pregnant; or
- b) The participant should avoid causing a pregnancy during or following participation in the research or to notify the PI immediately should the participant cause a pregnancy;
- c) The PI should specifically exclude pregnant women from the research or require specified methods of contraception during or following participation in the research.

I. Research involving Pregnant Women or Fetuses (45 CFR 46.204)

Pregnant women or fetuses may be involved in research if all the conditions listed in 45 CFR 46.204 are satisfied:

- a) Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical sites, 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) 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 process (SOP 2.02 Informed Consent);
- 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 SOP 2.02, Informed Consent, 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;
- f) Each individual providing consent under (d) or (e) above, if fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
- g) No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
- h) Individuals engaged in the research will have no part in any decisions as to the timing, method or procedures used to terminate a pregnancy.
- i) Individuals engaged in the research will have no part in determining the viability of a neonate.

II. Research Involving Neonates (45 CFR 46.205)

- a. Neonates of uncertain viability and nonviable neonates may be involved in research only if all the conditions of are met:
1. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates;
 2. Each individual providing consent under b) 2) or c) 5) of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonate;
 3. Individuals engaged in the research will have no part in determining the viability of the neonate.
 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:
 - 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
 - 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.
 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 SOP 2.02 Informed Consent, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy results 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;
 2. The research will not terminate the heartbeat or respiration of the neonate;
 3. There will be no added risk to the neonate resulting from the research;
 4. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means;
 5. The legally effective informed consent of both parents of the neonate is obtained in accord with SOP 2.02 Informed Consent, except that the waiver and alteration provisions of informed consent 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 this requirement.

- d. Viable Neonates: If a neonate is judged viable, it is then called an infant and should be treated as a minor for purpose of research participation. All requirements of human subjects' research, including special protections for minors, will apply.

III. Research involving, after delivery, the placenta; dead fetus; macerated fetal material (45 CFR 46.206)

- a. Research involving, after delivery, the placenta; dead fetus; macerated fetal material; or cells, tissues or organs excised from a dead fetus may be conducted only in accord with any applicable Federal, State, or local laws and regulations regarding such activities. Ohio Revised Code 2919.14 makes it a misdemeanor of the first degree to "experiment upon or sell the product of human conception which is aborted." Autopsies are specifically excluded.
- b. If information associated with any of the above human materials is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals will be research subjects and all relevant human subjects research protections will apply.

IV. 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.

For HHS-funded research, if the IRB believes the research does not meet the review requirements or conditions of 45 CFR 46.204 or 45 CFR 46.205, but 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, then the research will be referred to OHRP in accordance with 45 CFR 46.207. For non-HHS-funded research, the IRB may approve the research if it finds that the research will be conducted in accordance with sound ethical principles and informed consent will be obtained in accordance with the informed consent provisions of 45 CFR 46, including all applicable subparts.

V. Research on the Transplantation of Human Fetal Tissue

Research on the transplantation of human fetal tissue will be conducted in accordance with FDA regulations, as applicable. When funded or conducted by HHS, such research will also be conducted in accordance with federal laws at 42 U.S.C. 289g-1 and 289g-2, including obtaining informed consent from the donor and donee, as well as written statements from the attending physician and researcher. "Human fetal tissue" refers to tissue or cells obtained from a dead human embryo or fetus after a spontaneous or induced abortion. The IRB will approve only research that meet the requirements of 289g-1 and 298g-2, when applicable.

PROCEDURE

Investigator:

- Completes protocol submission forms, indicating pregnant women, fetuses, neonates will be target population for the research activities.
- Addresses obtaining informed consent process and selection of participants with particular attention to preventing undue influence or coercion.

IRB Chair:

- Assesses whether the protocol meets the criteria for research involving after delivery, the placenta, dead fetus or fetal material and whether it represents human subjects research requiring IRB review, or appears to meet the criteria for Not Human Subjects Research designation.
- Reviews the protocol to ensure the following:
 - All required materials were submitted (See SOP 2.01, Guidelines for Protocol Submission) for Subpart A, using the IRB Review Checklist A.
 - The additional required information is provided to satisfy Subpart B for research activities involving pregnant women, fetuses, neonates.
 - For HHS-funded research, reviews to see if criteria under 42 U.S.C. Secs. 289g (fetal research), 289g-1 (research on transplantation of fetal tissue), and 289g-2 (prohibitions regarding human fetal tissue) are met.
- Contacts investigator and/or study coordinator with questions or needed clarification/documentation regarding the vulnerable population.
- Assures that the IRB discusses and makes the required determinations under 45 CFR 46.204 or 46.205, when applicable.
- For HHS-funded research that the IRB believes is not approvable under 45 CFR 46.204 or 46.205, but presents an opportunity to understand, prevent or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses or neonates:
 - Refers to the HHS Secretary through OHRP for determination on the conduct and/or funding of the research under 45 CFR 46.207.
- Verifies that discussion and determinations of the IRB are reflected in the minutes.
- Reviews the IRB minutes, including the IRB's protocol-specific findings justifying waiver of the consent process or waiver of documentation of consent.
- Issues approval only after all criteria in subparts A and B are satisfied.

IRB Staff:

- Assists IRB Chair in preparing the letter of determination to the investigator.
- Documents discussion and required determinations of the IRB in the minutes.
- Mails approval and informed consent documents.

IRB Members:

For convened IRB review, each member:

- Reviews the protocol at the time of initial or continuing review.
- Reviews the research outline assuring additional protections for pregnant women, fetuses, neonates/nonviable neonates are included.

- Reviews the proposed research, informed consent process and other applicable documents to determine whether the study meets criteria at 45 CFR 46.111, and 21 CFR 56.111 if applicable, for approval by the convened IRB.
- Discusses the proposed research, taking into consideration additional requirements for pregnant women, fetuses, neonates and nonviable neonates to participate in research described in 45 CFR 46, Subpart B, including whether:
 - The protocol meets the criteria for pregnant women or fetuses under 45 CFR 46.204, or
 - The protocol meets the criteria for neonates of uncertain viability and nonviable neonates under 45 CFR 46.205, and
 - If the protocol is funded by HHS and involves fetal research, the criteria of 45 U.S.C. Sec. 289g are satisfied, or
 - The protocol meets the criteria for research involving, after delivery, the placenta, the dead fetus or fetal material, and
 - If the protocol is funded by HHS and involves transplantation of human fetal tissue, the criteria of 42 U.S.C. Secs 289g-1 and 289g-2 are satisfied, or
 - The IRB believes the protocol is not approvable under the criteria above, but finds the research presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses or neonates, and
 - If the research is funded by HHS, refers the protocol to OHRP for a determination under 45 CFR 46.207(b); defers further action until a response is received from OHRP; reviews any changes proposed by OHRP through the response review process, and takes final action on the protocol at that time,
 - If the research is not funded by HHS, approves the research only if it determines the following are satisfied: 1) the research is conducted in accordance with sound ethical principles, and 2) informed consent will be obtained in accordance with 45 CFR 45 Subpart A and all applicable additional subparts.
 - Issues approval only when all applicable sections of 45 CFR Part 46 Subparts A and B are satisfied.

REVISION HISTORY:

Date Revised	Reason For Change	Revised By