INSTITUTIONAL POLICY & PROCEDURE
Date of Original P&P: 11/20/2013
Revision No.: 1
Effective Date 05/18/2015

TITLE: Institutional Review Board Functions and Operations
SC 503 Pregnant Women, Fetuses and Neonates as Research Participants

ORIGINATOR: Institutional Official

APPROVAL: Institutional Official

POLICY STATEMENT: The purpose of this policy is to outline the requirements for Institutional Review Board (IRB) review and approval of research involving pregnant women, fetuses or neonates as research participants. Pregnant women, fetuses and neonates are considered to be vulnerable populations, and therefore must be treated with special consideration. In addition to federal regulations, all research conducted at Mercy Health regional sites complies with the CHE Trinity Health (add new name when we have it) Mission, Core Values, and Catholic moral/ethical principles, as delineated in the "Ethical and Religious Directives for Catholic Health Care Services." In this regard, IRB review and decision making gives special consideration for research participants' cultural, racial, social, religious, and economic circumstances.

GENERAL PROVISIONS:
The IRB must ascertain that inclusion of a vulnerable population such as a pregnant woman, fetus or neonate is adequately justified and that safeguards are implemented to minimize risks unique to that population.

The following moral/ethical principles from the Catholic Church’s “Ethical and Religious Directives for Catholic Health Care” (ERD's) serve as fundamental principles for all research related to pregnant women and fetuses.

ERD #4 A Catholic health care institution, especially a teaching hospital, will promote medical research consistent with its mission of providing health care and with concern for the responsible stewardship of health care resources. Such medical research must adhere to Catholic moral principles.

ERD #23 The inherent dignity of the human person must be respected and protected, regardless of the nature of the person's health problem or social status. The respect for human dignity extends to all persons who are served by Catholic Health Care

ERD #31 No one should be the subject of medical or genetic experimentation even if it is therapeutic, unless the person or surrogate first has given free and informed consent. In instances of non-therapeutic experimentation, the surrogate can give this consent only if the experiment entails no significant risk to the person's well-being. Moreover, the greater the persons incompetency and vulnerability, the greater the reasons must be to perform any medical experimentation, especially nontherapeutic.

When the IRB reviews research that focuses on categories of subjects vulnerable to coercion or undue influence, the review process will include one or more individuals who are knowledgeable about or experienced in working with these subjects. For example, the IRB will include one or more individuals who are knowledgeable about or experienced in working with pregnant women, fetuses and neonates, when reviewing projects that involves individuals from these populations. As a Catholic healthcare organization, an expert in Catholic healthcare directives will also be included when reviewing projects that involve these individuals.
Pregnant women may be involved in several categories of research. IRB duties differ in each category, but the primary objectives are assessing: (1) whether the research holds out the prospect of direct benefit for the mother’s health or for the fetus; and (2) the risks to the woman and to the fetus or infant. These requirements do not apply when the enrollment of pregnant women is entirely coincidental and bears no relation to the research (e.g., a minimal risk survey of 1000 individuals and 1 happens to be pregnant). The IRB may approve a project involving pregnant women, fetuses, or neonates as subjects only if the following requirements, intended to provide equivalent protections to those in the federal regulations, are met:

**CRITERIA FOR APPROVAL.**
Research involving pregnant women, fetuses or neonates qualifies for Exemptions at 45 CFR 46.101(b)(1) through (6). The provisions of 45 CFR 46.101(c) through (i) also apply. If the study does not qualify for an exemption, it will automatically be sent to full board for review. The following criteria from 45 CFR 46 Subpart B must be met.

**PREGNANT WOMEN OR FETUSES**
Catholic Religious Directives provide moral guidance in the utilization of pregnant women or fetuses as participants in research.

ERD directive #51: “Nontherapeutic experiments on living embryo or fetus are not permitted, even with the consent of the parents. Therapeutic experiments are permitted for a proportionate reason with the free and informed consent of the parents (or at least of the mother, if the father cannot be located). Medical research that will not harm the life or physical integrity of the unborn child is permitted with parental consent.”

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 risk, 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. The pregnant woman’s consent is obtained in accord with the informed consent provisions of subpart A if the research holds out the prospect of direct benefit to her and/or to the fetus. Consent is also obtained when no prospect of benefit for the pregnant woman or 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;
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 subpart A. The father’s consent is not necessary if he is incapable to consent because of unavailability, incompetence or temporary incapacity, or if the pregnancy resulted from rape or incest, as stated in 45 CFR 46.204(c);
F. Each individual providing consent is fully informed regarding the reasonably foreseeable impact to the fetus or neonate from the research;
G. For children who are pregnant, assent and permission are obtained in accord with the provisions of subpart D;
H. No incentives, monetary or otherwise, will be offered to terminate a pregnancy;
I. Individuals involved in the research will have no part in any decisions relating to the timing, method or procedures used to terminate a pregnancy; and
J. Individuals involved in the research will have no part in determining the viability of a neonate.

**RESEARCH INVOLVING NEONATES**
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 as describe in subpart B (b)(2) or (c)(5) is fully informed regarding the reasonably foreseeable impact to the neonate from the research.
C. Individuals involved in the research will have no part in determining the viability of a neonate.
D. The following requirements of paragraph E or F of this section have been met as applicable.
E. Neonates of uncertain viability: Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research unless the following additional conditions have been met as determined by the IRB:
- The research has allowed the opportunity for increased attempts for the survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or
Institutional Policy & Procedure

- The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means. There will also be no added risk to the neonate resulting from the research; and
- The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of provisions listed in 45 CFR 46.204(e).

F. Nonviable neonates: After delivery nonviable neonate may not be involved in research unless all of the following additional conditions are met:
- Vital functions of the neonate will not be artificially maintained;
- The research will not terminate the heartbeat or respiration of the neonate;
- There will be no added risk to the neonate resulting from the research;
- The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
- The legally effective informed consent of both parents of the neonate is obtained in accord with subpart A, 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 the provisions listed in 45 CFR 46.204(e), the consent of one parent of a nonviable neonate will suffice; however, the consent of a legally authorized representative of either or both of the parents of a nonviable neonate is not an equal substitute.

G. 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.

RESEARCH INVOLVING AFTER DELIVERY- PLACENTA, A DEAD FETUS OR FETAL MATERIAL
Research involving post-delivery placenta; the dead fetus (or cells, tissue, or organs excised from a dead fetus) or macerated fetal material shall be conducted only in accord with any applicable federal, state, or local laws and regulations regarding such activities.

If information associated with material described in the above paragraph 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 this part are applicable.

EXCEPTIONS
If research is not approvable by the Federal Regulations contained in this document but presents an opportunity to understand, prevent or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses or neonates, it may be approved by special standards. The Secretary will conduct or fund research that the IRB does not believe meets the requirements of 45 CFR 46.204 or 46.205 only if:

A. The IRB finds 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:
   - The research does satisfy the conditions of 45 CFR 46.204, as applicable; or
   - 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

The research will be conducted in accord with sound ethical principles and informed consent will be obtained in accord with the informed consent provisions of subpart A and other applicable subparts.

DEFINITIONS: The following definitions are found as stated in 45 CFR 46.202

Expired Fetus: A fetus not exhibiting heartbeat, spontaneous respiratory activity, and spontaneous movement of voluntary muscles or pulsation of the umbilical cord.

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

Fetus: The product of conception, from implantation until delivery.

Neonate: Newborn. A neonate will be classified as a child and reviewed according to 45 CFR 46 subpart D, Additional Protections for Children Involved as Subjects in Research

Nonviable Neonate: A neonate after delivery that is not viable even though he or she is living.

Neonate of Uncertain Viability: A newborn with uncertain viability

Viable: Refers to a neonate’s likelihood of survival post-delivery, given the benefit of available medical therapy, to the point of independently maintaining heartbeat and respiration. The Secretary may from time to time, taking into
account medical advances, publish in the federal register guidelines to assist in determining whether a neonate is viable for purposes of this subpart. If a neonate is viable then it may be included in research only to the extent permitted and in accordance with the requirements of 45 CFR 46 subparts A and D and Ethical and Religious Directives for Catholic Health Care.

**Pregnancy:** Refers to the period of time from implantation until delivery. A woman is assumed to be pregnant if she exhibits any of the pertinent signs of pregnancy, specifically missed menstrual cycles, until the results of a pregnancy test are negative or until delivery.

**REFERENCE:**
45 CFR 46 Subpart B
45 CFR 46.116
45 CFR 46 Subpart D
45 CFR 46.402-407
45 CFR 46.408-409
21 CFR 50.50-56
Ethical and Religious Directives for Catholic Health Care Services, Fifth Edition

**ATTACHMENTS:**
SC 503-A Worksheet for Review of Research Involving Pregnant Women and Fetuses
SC 503-B Worksheet for Review of Research Involving Non-Viable Neonates
SC 503-C Worksheet for Review of Research Involving Neonates of Uncertain Viability

**PROCEDURE:**

<table>
<thead>
<tr>
<th>Responsibility</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>IRB Specialist/IRB Coordinator</td>
<td>1. Verifies the protocol submission documents are complete and contain sufficient information on the inclusion of pregnant women, fetuses and neonates as participants for the IRB to review.</td>
</tr>
<tr>
<td></td>
<td>2. Reviews, specifically, informed consent documents for consent permission as applicable.</td>
</tr>
<tr>
<td></td>
<td>3. Ensures the minutes reflect the deliberations of the IRB regarding any decisions rendered.</td>
</tr>
<tr>
<td></td>
<td>4. Ensures the IRB letter includes the proper language referencing the findings and directives of the IRB.</td>
</tr>
<tr>
<td>IRB Chairperson (or designee)</td>
<td>1. Reviews protocol at time of initial and continuing review, and review of modifications.</td>
</tr>
<tr>
<td></td>
<td>2. Using appropriate IRB Review Worksheet as a guide, reviews additional protections for the inclusion of pregnant women, fetuses and neonates as study participants.</td>
</tr>
<tr>
<td></td>
<td>3. Reviews the completed IRB review worksheets and shares reviewer concerns with committee.</td>
</tr>
</tbody>
</table>

For Expedited Review:
1. Takes into account the inclusion of the proposed population.
2. Utilizes the appropriate review worksheet.
3. Determines that adequate provisions for obtaining consent from the participant are addressed and also how documentation of consent will be noted.
4. Reviews and determines if the method of screening potential participants and controls...
and the factors that will be the basis for excluding potential participants from the study are adequate.
5. May recommend additional safeguards for the participants in order to secure approval of the research.
6. If unable to approve the research, forwards for convened IRB committee for review.

1. Referring to the appropriate IRB Review Worksheet, reviews the submission documents in accordance with criteria for approval with 45 CFR 46.111 and 21 CFR 56.111 if applicable, and other applicable regulations.
2. When additional expertise is required, appoints a consultant to assist with review for additional safeguards in protecting pregnant women, fetuses and neonates as participants.
3. Makes the specific findings and determinations necessary to approve research that includes pregnant women, neonates or fetuses as appropriate.
4. Determines and documents that the informed consent process for consent minimizes possibility of undue influence and coercion.
5. May determine that it is not appropriate to include pregnant women, neonates and fetuses as participants in the study.

CONCURRENT CONSENTS:
Institutional Official