Chapter 16

IRB Review of Research Involving Adults as Vulnerable Participants

DHHS regulations at 45 CFR 46.111(b), FDA regulation at 21 CFR 56.11(b), and Common Rule require IRBs to give special consideration to protection the welfare of particularly vulnerable subject, such as prisoners, pregnant women, individuals with mental health impairment, economically or educationally disadvantaged persons.

The IRB is required to consider potential vulnerability in all research populations and take required steps to assure their protection as participants in research.

1. Considerations in Reviewing Research Involving Vulnerable Participants

a. The IRB Chair, HRPP Director, and IRB Coordinators will ensure adequate discussion at IRB meetings of issues related to vulnerable populations. For DHHS-funded research, the HRPP Director certifies to OHRP the duties of the IRB have been fulfilled.
b. The IRB coordinators, during initial administrative review of all new protocol submissions, will assess the needs of any study that may include vulnerable populations that may require support of one of the IRB consultants to support review of the proposed population and proposed study interventions.
c. Critical issues to be included in review include:
    i. Selection and recruitment
    ii. Informed consent(s)
    iii. Voluntarism
    iv. Potential for coercion and undue influence, and
    v. Confidentiality
d. The IRB committee members, particularly assigned primary and secondary reviewers, will carefully consider group characteristics such as economic, social, physical, and environmental conditions to that the research incorporates additional safeguards that may be required to protect participants.
e. As it determined necessary, the IRB will seek to obtain information regarding any laws and science that bear on decision-making capacity of the potentially vulnerable populations to be involved in research.
f. In certain instances, it may be possible for researchers to enhance understanding for potentially vulnerable participants. Examples include:
    i. Inclusion of a consent monitor
    ii. Requiring a participant advocate
    iii. Translated consent forms
    iv. Reading the consent to the participants to gauge understanding
g. The IRB will consider any study population as vulnerable as their situation renders them especially vulnerable to coercion or influence.

2. Pregnant Women, Human Fetuses and Neonates

a. DHHS regulations at 45 CFR 46 Part 46, Subpart B detail special protections for research involving pregnant women, human fetuses, and neonates. Under these regulations the IRB is required to document specific findings to minimize the potential for risk or harm to the fetus, and additional attention must be given to conditions for obtaining informed consent. Subpart B requires that research involving pregnant women and fetuses should involve the least possible risk.
b. Also, to be considered, unilateral exclusions of non-pregnant women of reproductive potential from research for the purposes of avoiding a risk cannot be permitted by the IRB. Exclusion requires compelling scientific justification. Where such justification exists, it may also be appropriate to exclude men of reproductive potential.

3. Summary of Requirements for Research involving Pregnant Women, Fetuses and Neonates

a. Pregnant Women or Fetuses:
   i. Where appropriate, preclinical data identify potential risks.
   ii. Direct benefit for a pregnant woman or fetus, or risk to fetus is not greater than minimal risk.
   iii. Any risk is least possible for achieving research objectives.
   iv. Persons consenting are fully informed.
   v. Consent of pregnant woman if direct benefit to her or risk to fetus is not greater than minimal risk.
   vi. Consent of pregnant woman and father (if reasonably available) if research offers direct benefit solely to fetus.
   vii. For pregnant children assent and permissions per Subpart D and state consent law.
   viii. No inducements to terminate pregnancy.
   ix. Researchers have no part in decisions to terminate a pregnancy.
   x. Researchers have no part in determining viability.

b. Neonate of Uncertain Viability:
   i. Where appropriate, preclinical data identify potential risks.
   ii. Persons consenting are fully informed.
   iii. Researchers have no part in determining viability.
   iv. Enhance probability of survival and risks is least possible **or no added risk to** neonate and important medical knowledge will result.
   v. Informed consent of one parent or legally authorized representative.

c. Nonviable Neonates:
   i. **NOTE: The Prisma Health IRB cannot support research on Nonviable Neonates. Prior to considering such research, please contact the IRB Chair or HRPP Director**

d. IRB determinations regarding the applicable category and protocol specific findings relative to the specific requirements of the relevant category will be clearly documented in IRB meeting minutes and/or other IRB records.

4. DHHS regulations at 45 CFR 46, Subpart B provide the following §46.204 Research involving pregnant women or fetuses. Pregnant women or fetuses may be involved in research is all 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 assessment potential risks to pregnant women and fetuses.
b. The risk to the fetus is caused solely interventions or procedures that hole out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit the risk to 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 objects of the research.
d. If the research holds out the prospect of direct benefit to the pregnant women, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the 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, her consent is obtained with the informed consent provisions of subpart A of this part.
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 accordance with the informed consent provisions of subpart A of this part, 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 paragraph (d) or (e) of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate.
g. For children as defined in §46.402(a) who are pregnant, assent and permission are obtained in accordance with the provisions of subpart D of this part.
h. No inducements, monetary or otherwise, will be offered to terminate a pregnancy.
i. Individuals engaged in the research will have no part in any decisions, as to timing, method, or procedures used to terminate a pregnancy.
j. Individuals engaged in the research will have no part in determining the viability of a neonate.

5. § **46.205 Research involving neonates: Neonates of uncertain viability and nonviable neonates may be involved in research if all 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 (d)(5) of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonates.
c. Individuals engaged in the research will have no part in determining the viability of a neonate.
d. Neonates of uncertain viability: Until is have been ascertained whether or not a neonate is viable, a neonate may not be in involved in research covered by this subpart unless the following conditions have been met:
    i. The IRB determines 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 not added risk to the neonate resulting from the research
    ii. 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 this part, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

6. **Prisoners:** Prisma Health does not engage in review of research that involves prisoners. The IRB Chair or the HRPP Director should be consulted prior to consideration of engaging in research that involves prisoners as the subject.

7. **Research Involving Decisionally Impaired Participants.**
   The IRB evaluates each submission to determine whether the research involves participants who have diminished capacity and if so, provide additional safeguards to ensure an appropriate consent process.

   a. Decisionally-impaired persons are individuals who have a diminished capacity for judgement and reasoning due to a psychiatric, organic, developmental, or other disorder that affects cognitive or emotional functions. Other individuals who may be considered decisionally impaired, with limited decision-making ability are individuals under the influence of or dependent on drugs or alcohol, those suffering from degenerative disease affecting the brain, terminally ill patients, and persons with severely disabling physical handicaps.
   b. In cases where research involving cognitively impaired individuals is approved, the IRB will consider additional safeguards as part of the research plan to protect participants.
   c. When investigators are likely to approach adults who lack the ability to consent, the IRB evaluates whether:
      i. The proposed plan for the assessment of the capacity to consent is adequate,
      ii. Assent of the subjects is a requirement, and if so, whether the plan for assent is adequate.

8. **Research Involving Other Potentially Vulnerable Adult Participants:** The IRB will generally consider the following groups of participants to be potentially vulnerable and will carefully consider the context of the research in determining appropriate protections for them:
   i. Individuals participating in research in combination with treatment.
   ii. Members of potentially vulnerable minority groups.
   iii. Educationally disadvantaged persons.
   iv. Economically disadvantaged persons.
   v. Homeless persons.
   vi. Institution's employees, students, and trainees.

9. **Research Involving Deceased Persons:** Research involving deceased persons is not covered by FDA or DHHS human subjects regulations, or the Common Rule.