

When subjects are likely to be vulnerable to coercion or undue influence, additional safeguards must be included to protect their rights and welfare. In addition to children and prisoners, other vulnerable populations may include: pregnant women, fetuses and neonates, cognitively impaired individuals, and educationally or economically disadvantaged individuals.

1.0 Cognitively impaired persons.

Cognitively impaired persons are considered vulnerable because they may have insufficient decision-making capacity to provide their own consent for participation in research. The impairment may be due to a psychiatric disorder, physical disease or condition, substance abuse or extreme stress, and may be permanent, temporary or transitory.

1.1 Justification for use of vulnerable population.

Investigators must provide sufficient justification for selectively targeting cognitively impaired persons for research participation. Research that relates directly to their condition or circumstances would be considered an adequate justification for use of this vulnerable group.

1.2 Assessment of competency to consent to research participation.

When some or all prospective participants are likely to include persons with some level of cognitive impairment, an assessment of their competency to consent may be necessary. A potential participant may be considered competent if able to understand information presented on the research project, make their own decision, and appreciate the consequences of that decision. When a participant's cognitive capacity is diminishing or fluctuating, periodic assessments may be needed to maintain legally effective consent for ongoing research participation. Investigators should describe in the protocol use of any assessments that will be performed. The IRB may require assessments for all or some participants where necessary to protect their rights and welfare.

1.3 Informed consent.

Participants determined competent may provide their own legally effective informed consent. It may be necessary to include additional educational measures to enhance understanding for this population.

Those determined not competent will require consent from either a legally authorized representative, or if none is available, a next-of-kin, to participate in research. However, a participant's obvious objections to research participation should always be respected. Some participants with only limited impairment may also be asked to provide their assent for research, similar to the child assent process. Refer to *9.4 Children as Research Participants* for a description of the assent process that could be adapted for adults with impaired cognitive capacity.

Investigators should describe in the protocol any process for locating and obtaining consent from legally authorized representatives, as well as the process for obtaining participants' assent, if applicable. The IRB may require an assent process for some or all participants where beneficial for protecting their rights and welfare.

1.4 IRB review.

When reviewing research that will involve cognitively impaired individuals, the IRB must include a member or consultant familiar with the concerns of the population being studied.

2.0 Pregnant women, human fetuses and neonates.

Pregnant women, human fetuses or neonates are considered a vulnerable population, and require additional safeguards to protect their rights, safety and welfare.

2.1 Justification for use of vulnerable population.

Investigators must provide adequate justification for selectively recruiting pregnant women, human fetuses or neonates for research. Research that relates directly to their condition or circumstances would be considered an adequate justification for use of this vulnerable group.

2.2 Pregnant women or fetuses.

Pregnant women or fetuses may be involved in research if all the following conditions are met:

- Where appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
- 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 that cannot be obtained by other means;
- Any risk is the least possible for achieving the objectives of the research;
- 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;
- 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, 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.
- Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
- For children who are pregnant, assent and parent or guardian permission are obtained;
- No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
- 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
- Individuals engaged in the research will have no part in determining the viability of a neonate.

2.3 Neonates.

2.3.1 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:

- The IRB determines 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
 - (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

- 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. The consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.

2.3.2 Nonviable neonates.

After delivery nonviable neonates may not be involved in research covered by this subpart 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, except that consent cannot be waived or altered (Refer to 1.2 in SOP 9.3 *Waiver or Alteration of Informed Consent Requirements*). 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, 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.

2.3.3 Viable neonates.

A neonate, after delivery, that has been determined to be viable is considered a child. They may be included in research under the requirements described in *10.1 Vulnerable Groups: Children*.

2.4 Research not otherwise approvable.

Research involving pregnant women, fetuses or neonates that does not meet the requirements under 2.2 or 2.3 above, may only be approved if:

- 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
- The Secretary of DHHS, after consultation with a panel of experts in pertinent disciplines (i.e., science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the Federal Register, has determined either:
 - That the research satisfies the conditions under 2.2 or 2.3 above, or all of the following:
 - 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 accordance with other requirements

2.4 IRB review.

The IRB reviews research involving pregnant women, fetuses or neonates at a convened meeting, and must ensure that all applicable conditions above are satisfied to safeguards their rights, safety and welfare.

3.0 Economically or educationally disadvantaged persons.

Economically or educationally disadvantaged individuals are considered vulnerable to coercion and undue influence, and require additional safeguards to protect their rights, safety and welfare.

3.1 Justification for use of vulnerable group.

Investigators must provide adequate justification for selectively recruiting economically or educationally disadvantaged persons for research. Research that relates directly to their condition or circumstances would be considered an adequate justification for use of these vulnerable groups.

3.2 Compensation.

Economically disadvantaged individuals may be more influenced than the general population by the level of compensation offered for research participation. The level of compensation offered should not be such that it would cause participants to overlook risks, or accept risks they would not normally accept without compensation.

3.3 Informed Consent.

Educationally disadvantaged individuals may have difficulty comprehending information. Consent documents should contain simplistic language and terms and additional explanations. Extra time may be needed to answer questions and ensure their understanding prior to agreeing to participate in research.

3.4 IRB review.

When reviewing research involving economically or educationally disadvantaged individuals, the IRB should include a member or consultant familiar with the concerns of the population being studied.

DEFINITIONS:

Competence: capacity to act on one's own behalf; the ability to understand information presented, appreciate the consequences of acting on the information, and to make a choice.

Fetus: the product of conception from implantation until delivery.

Legally authorized representative: an individual authorized by a judicial body or other appropriate body to give consent on behalf of a prospective subject to the subject's participation in research. This may include a health care agent (named as a durable power for health care decision maker while the subject had competency), or a court-appointed guardian.

Neonate: a newborn.

Pregnancy: encompasses the period of time from implantation until delivery. A woman shall be assumed 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 medical therapy) to the point of independently maintaining heartbeat and respiration.

Minimal risk: the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Next-of-kin: in the following order: spouse, adult child (18 yrs of age or older), parent, adult sibling, grandparent, or adult grandchild.

REFERENCES:

OHRP Guidebook, Special Classes of Subjects: [Cognitively Impaired Persons](#)
NIH, [Research Involving Individuals with Questionable Capacity to Consent: Points to Consider 45 CFR 46 Subpart B](#) Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research
ND Century Code Chapter 14-02.2 [Fetal Experimentation 45 CFR 46.111](#) and [21 CFR 56.111](#) Criteria for IRB approval of Research
OHRP FAQs: [Informed Consent](#)

RELATED FORMS:

IRB Protocol Form

Informed Consent Waiver Request Attachment form

RELATED HRPP SECTIONS:

9.3 Waiver or Alteration of Informed Consent Requirements

9.4 Children as Research Participants

10.1 Vulnerable Groups: Children