Protecting Vulnerable Populations in Research

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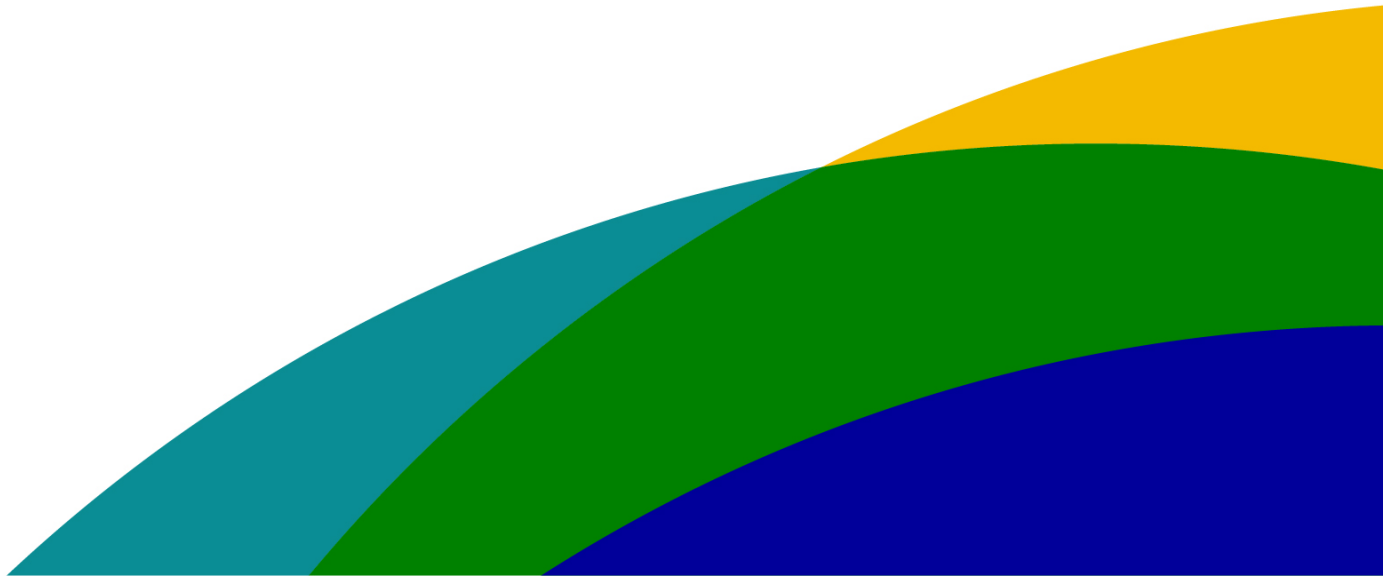
Overview

- Vulnerable Subjects in Research
- Research Involving Pregnant Women, Human Fetuses, and Neonates
- Research Involving Children
- Research Involving Other Potentially Vulnerable Groups

Vulnerable Subjects in Research



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What Does it Mean to Be Vulnerable?

Types of Vulnerability

- Cognitive or communicative vulnerability
- Institutional vulnerability
- Deferential vulnerability
- Medical vulnerability
- Economic vulnerability
- Social vulnerability

An individual may experience more than one type of vulnerability.

NBAC (2001), *Ethical and Policy Issues in Research Involving Human Participants*

What Does it Mean to Be Vulnerable?

Characteristics of Being Vulnerable

- Reduced capacity to make autonomous decisions
- Susceptibility to coercion or undue influence
- Susceptibility to potential harms
- General ease of availability/susceptibility to being taken advantage of

Consider relevant factors, such as:

- Homelessness
- Poverty
- Substance abuse
- Mental illness
- Co-occurring disorders
- Others …

What Does the Common Rule Say About Vulnerable Subjects?

When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, **additional safeguards have been included in the study to protect the rights and welfare of these subjects**.

§ 46.111(b)

… vulnerable to coercion or undue influence …

Vulnerable to Coercion or Undue Influence

Coercion occurs when an overt threat of harm is intentionally presented by one person to another in order to obtain compliance

Undue influence occurs through an offer of an excessive, unwarranted, inappropriate, or improper reward or other overture in order to obtain compliance

Protections for Vulnerable Populations

Certain populations have additional protections written into the regulations

- Subpart B – Pregnant women, fetuses, and neonates
- Subpart C – Prisoners
- Subpart D – Children

Do the regulations identify other vulnerable populations?

> ***…category of subjects that is vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.***

Research Involving Pregnant women, Human Fetuses, and Neonates

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General Points

- Focus is on protecting the fetus or neonate
- Requires prior preclinical and clinical studies, where scientifically appropriate
- Minimal risk or prospect of direct benefit if more than minimal risk
- Additional informed consent requirements
- Researchers cannot be part of termination or viability decisions
- Additional limitations for research with neonates of uncertain viability and nonviable neonates
- Viable neonates are protected under subpart D

Subpart B: Protections for Pregnant Women, Fetuses, and Neonates

Pregnant women generally may consent to research involving self or fetus

- She (alone) can consent if the prospect of direct benefit is to her *or* to both her and the fetus
  - If no prospect of direct benefit, then the research must present no more than minimal risk to the fetus and the purpose of the research must be to develop important biomedical knowledge that cannot be obtained by other means
- Consent also obtained from father if sole prospect of direct benefit is to the fetus*
- Information provided must include reasonably foreseeable impact on fetus

Research with neonates

- Consent of one parent generally required for neonates of uncertain viability (additional conditions required)
- Consent of both parents required for nonviable neonate (additional conditions required)*
- For research with viable neonates, subpart D protections apply

*exceptions to paternal consent requirement in case of incapacity, rape, or incest

Research Involving Children

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Definition of Children

Persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted

§46.402(a)

Subpart D: Protections for Research Involving Children

Approval categories for research under Subpart D:

- **§46.404**: Minimal risk research
- **§46.405**: Greater than minimal risk, prospect of direct benefit
- **§46.406**: Greater than minimal risk (minor increase over minimal risk) with no prospect of direct benefit, but likely to yield generalizable knowledge about subjects' disorder or condition
- **§46.407**: Not otherwise approvable, but presents opportunity to further understand, prevent, or alleviate a serious problem affecting health and welfare of children (HHS Secretary)

Subpart D: Parental Permission

- Must be **documented** according to §46.117
- Some research requires permission from only **one parent** (§46.404, §46.405)
- Certain research requires permission from **both parents***:
  - Greater than minimal risk with no prospect of direct benefit but likely to yield generalizable knowledge (§46.406)
  - Research not otherwise approvable but which presents a reasonable opportunity to further understand a serious problem (§46.407)

§46.408(b)

*unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the child

Subpart D: Child Assent

- Adequate provisions to seek **assent** of children to participate
  - IRB determines whether children are capable of providing assent
    - ✓ Can determine for all children or for each child
    - ✓ Account for age, maturity, psychological state of children involved

§46.408(a)

  - When IRB determines that assent is required
    - ✓ IRB shall determine whether and how assent must be documented

§46.408(e)

Subpart D: Waiver of Permission or Assent

- IRB can waive requirement for parental permission
  - According to provisions for waiver of informed consent in §46.116, or
  - If protocol designed such that parental permission is not a reasonable requirement to protect subjects (e.g., neglected or abused children), and an appropriate mechanism is substituted to protect children and is consistent with federal, state, local law
- IRB can waive requirement for child assent
  - If some or all children are not capable of providing assent, or
  - Intervention/procedure in the research holds out a prospect of direct benefit important to the health or well being of the children and is available only in the context of the research, or
  - In accordance with §46.116 waiver of informed consent

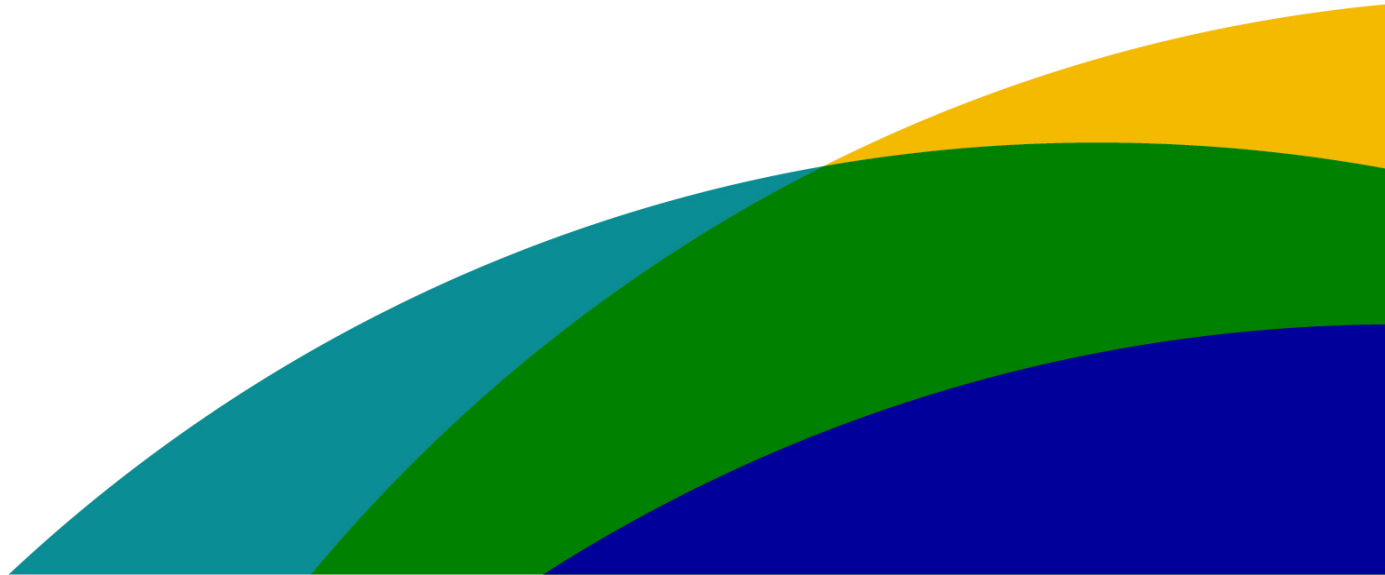
§46.408(a)

Subpart D: Wards

- Children who are wards of the state or another agency can be involved in research approved under §46.406 or §46.407 ONLY if the research is:
  - Related to their status as wards, or
  - Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children in the research are not wards
- IRB shall require appointment of an advocate for each child in addition to others acting as guardian or in loco parentis
  - Advocate must have the background/experience to act in the child's best interests throughout the research
  - Advocate must not be associated with the research, investigators, or guardian organization aside from acting as the advocate or IRB member

§46.409

Research Involving Other Potentially Vulnerable Groups



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What About Other Vulnerable Subjects?

When some or all of the subjects are likely to be **vulnerable to coercion or undue influence**, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, **additional safeguards have been included in the study to protect the rights and welfare of these subjects**.

§ 46.111(b)

Additional Safeguards for Vulnerable Subjects Generally

IRB Membership*:*

consideration shall be given to the inclusion of one or more individuals who are ***knowledgeable about and experienced in working with these categories of subjects***

Equitable selection of subjects*:*

consideration of the purposes and setting of the research …the IRB should be ***particularly cognizant of the special problems of research*** *that involves a category of subjects who are* ***vulnerable to coercion or undue influence***

Review of recruitment procedures: Consider recruitment plans and materials

- Is the recruitment process unduly enticing?
- Is the research purpose making exaggerated or unfounded claims?
- Is the reimbursement appropriate given the catchment area?

Research Involving Subjects with Impaired Decision-making Capacity

- As a general rule, **all** adults, regardless of diagnosis/condition, should be considered competent to provide consent unless there is evidence of impaired capacity to consent.
  - Mental disability alone does not disqualify a person from consenting to participate in research.
- Conduct the informed consent process under circumstances that are not coercive and that allow subjects the opportunity and time to consider the information
- Whenever appropriate, include the presence of an LAR to support the informed consent process
- Note new definition of Legally Authorized Representative

Research Involving Subjects that Speak Another Language

- If subject population includes groups that do not speak English, informed consent materials should be translated
  - Informed Consent must be in language understandable to the subject
  - Remember focus on understandability

- If subject population primarily includes English-speakers, but non-English speaking subjects are included incidentally, can use short form

Research with Military Personnel Who May be Susceptible to Coercion

- The IRB could include members representative of the subject population
  - Majority of IRB members should not be from the same military structure
- IRBs could avoid coercion by ensuring:
  - Procedures for subject selection and recruitment are immune from arbitrary influence or intervention by military authorities
  - Adequate assurance that decision about participation will not have any negative impact or repercussions for the subjects
  - The process of informed consent supports voluntariness and informed decision-making

Research with Economically or Educationally Disadvantaged Populations

- Does the research pertain to the specific population? Are they included with good reason? To the exclusion of others?
- The IRB could include members representative of the subject population
- IRBs could avoid coercion by ensuring:
  - Recruitment procedures are fair and respectful
  - Adequate assurance that decision about participation will not have any negative impact or repercussions for the subjects (e.g., loss of benefits)
  - The process of informed consent supports voluntariness and informed decision-making
  - Incentives do not create undue influence

Balancing the Ethical Tension in Research is Vital to Promoting Public Trust in Research

Promote the common good derived from research

Protect the rights and welfare of individual participants

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Thank you!

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