4.1 Additional Protections for Vulnerable Persons

Last Revised: 4/16/2025

1.0 Purpose

The purpose of this policy is to describe the Organization’s requirements for additional protections for vulnerable persons.

2.0 Policy

It is the policy of the Organization that

- 2.1. Vulnerable persons will be afforded additional protections, in accordance with the ethical principles described in the Belmont Report, and the requirements of 45 CFR 46.111(b) and 21 CFR 56.111(b).
- 2.2. The requirements for special protections specified under HHS regulations at 45 CFR 46 Subpart B (pregnant women, human fetuses and neonates of uncertain viability or non-viable), Subpart C (prisoners), and Subpart D (children) will be applied for research funded by any of the Common Rule agencies or departments.
- 2.3. Equivalent protections will be provided for the specific vulnerable populations described above who are participating in research not funded or conducted by any of the Common Rule agencies or departments. Equivalent protections will be based upon the ethical principles in the Belmont Report, and the requirements in 45 CFR 46, Subpart B, C, and D will be applied to the greatest extent possible in consideration of the nature of the research.
- 2.4. Additional safeguards for children in clinical investigations subject to FDA regulations at 21 CFR 50 Subpart D will be applied for research regulated by the FDA.
- 2.5. Additional protections will be provided for other vulnerable persons including, but not limited to persons who are decisionally-impaired, terminally ill, or economically or educationally disadvantaged. In these situations, the IRB, in consultation with the PI, will determine the appropriate methods to protect the rights and welfare of the individuals in consideration of the principles of the Belmont Report, the nature of the research, and other factors determining vulnerability.

3.0 Definition

- 3.1. Vulnerable Persons are defined as individuals or groups of individuals “with diminished autonomy” (National Commission, 1979) or as individuals or groups of individuals who “have difficulty providing voluntary, informed consent arising from limitations in decision-making capacity … or situational circumstances …, or because they are especially at risk for exploitation” (National Bioethics Advisory Committee, 2001). Within any group of vulnerable subjects, individuals may have different levels of vulnerability based on the level of capacity, circumstance, or condition. In addition, “vulnerability is sensitive to context, and individuals may be vulnerable in one situation but not in another” (National Bioethics Advisory Committee, 2001).

4.0 Categories of Vulnerability

- 4.1. Broadly, vulnerabilities in the context of research may be considered to fall into one or more of the following types:
  - 4.1.1. Cognitive or Communicative: diminished capacity to understand or communicate.
  - 4.1.2. Institutional: subject to the formal authority of others.
  - 4.1.3. Deferential: informal subordination to others (gender, race or class inequalities; inequalities of power and knowledge).
  - 4.1.4. Medical: serious health conditions.
  - 4.1.5. Economic and/or Social - disadvantaged in the distribution of social goods and services, or belonging to an undervalued group.
- 4.2. Vulnerable persons may also be considered as belonging to certain groups or populations. Though useful, categorization in this manner needs to consider context and situation. Groups which may experience specific vulnerabilities include, but are not limited to:
  - 4.2.1. Pregnant women (Subpart B) (see HRPP policy 4.2).
  - 4.2.2. Fetuses and neonates (Subpart B) (see HRPP policy 4.2).
  - 4.2.3. Prisoners (Subpart C) (see HRPP policy 4.3).
  - 4.2.4. Children (Subpart D) (see HRPP policy 4.4).
  - 4.2.5. Decisionally impaired persons (see HRPP policy 4.6).
  - 4.2.6. Critically ill persons
  - 4.2.7. Terminally ill persons
  - 4.2.8. Blind or deaf persons, or persons with other disabilities
  - 4.2.9. Economically or socially disadvantaged persons
  - 4.2.10. Educationally disadvantaged persons
  - 4.2.11. Employees and students (see HRPP policy 4.7).
  - 4.2.12. Non-English speaking persons

> Note: Persons or populations may be “vulnerable” without belonging to one or more of the above groups, nor is it important to which particular

> group above a vulnerable population belongs (except as reflecting the necessity for specific regulatory or other protections). However, the groups may be convenient in that common themes may dictate additional protections. Vulnerable persons may be described as belonging to several groups, or to none of the above, as long as additional protections for that person are adequate.

5.0 Additional Protections for Vulnerable Populations

- 5.1. Investigators must consider to what extent subjects to be enrolled in their research might be vulnerable, and if so, what additional protections might be appropriate to minimize that vulnerability. In making these determinations, investigators should consider:
  - 5.1.1. Is inclusion of the vulnerable person or population necessary? That is, could the aims of the research be accomplished by enrolling persons or a population that is not (or is less) vulnerable?

> Note: Investigators should be aware that there are competing ethical imperatives related to enrollment of vulnerable persons. The Belmont principle of Respect for Persons requires that investigators protect those with limited autonomy (even to the extent of excluding them from the research); however, the principles of Beneficence and Justice require that researchers provide the benefit of research, and distribute those benefits fairly.

Investigators should also be cognizant of the risks of not including certain persons and populations in research. For example, considering children as research subjects, the National commission noted “The argument in favor of conducting research involving children rests on … the consequences of not conducting research involving children in those instances. Such consequences might include the perpetuation of harmful practices, the introduction of untested practices, and the failure to develop new treatments …” (National Commission: Research Involving Children. Report and Recommendations, 1977; page 21).

- 5.1.2. If inclusion of the vulnerable person or population is appropriate, then are protections afforded to subjects adequate?
  - 5.1.2.1. Do prospective subjects have difficulty providing voluntary, informed consent? Are the conditions for informed consent satisfied? Specifically, is information presented in an understandable manner? Do subjects comprehend the details of the research and their rights as research subjects? Is the process of consent conducive to true voluntariness?
  - 5.1.2.2. Are prospective subjects at risk for exploitation?

- 5.2. Specific additional protections that might be considered include (but are not limited to):
  - 5.2.1. The use of an extended consent process.
  - 5.2.2. The use of a consent monitor.
  - 5.2.3. Appointment of a subject advocate.
  - 5.2.4. Involvement of the prospective subject's family and/or friends.
  - 5.2.5. The requirement for re-consenting of subjects/LARs.
  - 5.2.6. Limits placed on risk (for example, through more rigorous inclusion or exclusion criteria).
  - 5.2.7. Increased monitoring of the research (for example, through use of a Data and Safety Monitoring Board or other mechanisms).
  - 5.2.8. More stringent withdrawal criteria.
  - 5.2.9. Exclusion of certain persons or populations from participating in the research.

6.0. Investigator Responsibilities

- 6.1. The investigator must identify whether research will include any population which is directly subject to the additional protections in 45 CFR 46 subpart B, C or D, or 21 CFR 56 subpart D
- 6.2. The investigator must identify (1) whether subject eligibility criteria will specifically target other potentially vulnerable populations, or (2) whether there is a high likelihood that a sizable number of subjects will come from a vulnerable population.

> Note: the intent here is to identify research proposals for which it would be reasonable to have additional protections in place prior to enrollment. The intent is not to identify situations when a vulnerable person would incidentally be enrolled. In the latter case, it is expected that the investigator would identify that person and take appropriate actions.

  As noted above, the particular group which might be used to describe a vulnerable person is not important per se (except as reflecting the necessity for specific regulatory or other protections). However, the groups may be convenient in that common themes may dictate additional protections.
- 6.3. The investigator must specifically describe additional protections for persons or populations identified above under "Categories of Vulnerability."
- 6.4. If a person, after enrollment, becomes vulnerable (for example, by being incarcerated, or becoming pregnant or homeless), or now would be subject to one of the applicable subparts to the Common Rule or the FDA regulations, the PI must:
  - 6.4.1. consider whether additional protections are needed for that subject, and must notify the IRB as appropriate; and
  - 6.4.2. consider whether changes to the protocol are needed for all enrolled or prospective subjects, and revise the IRB application as appropriate; and
  - 6.4.3. in discussion with the IRB, consider whether the subject must be withdrawn unless their continued participation is in compliance with that Subpart.

7.0 IRB Responsibilities

- 7.1. The IRB will consider whether inclusion of vulnerable subjects or populations is appropriate, and whether the additional protections proposed as adequate, as required in HRPP policy 2.5 (Criteria for Approval).
- 7.2. The IRB will consider whether the inclusion of vulnerable subjects satisfies the requirements of 45 CFR 46 subpart B, C or D, or 21 CFR 56 subpart D, and of HRPP policies 4.2 (Research Involving Pregnant Women, Human Fetuses, and Neonates – Nonviable or of Uncertain Viability), 4.3 (Research Involving Prisoners), 4.4 (Research Involving Children), 4.6 (Research Involving Subjects with Impaired Decision Making Capacity) and/or 4.7 (Research Involving Employees and Students).
- 7.3. The IRB determinations regarding inclusion of pregnant women, prisoners, and children will be documented in accordance with HRPP policies 2.2 (Full IRB Review), 2.3 (Expedited IRB Review), 4.2 (Research Involving Pregnant Women, Human Fetuses, and Neonates-Nonviable or of Uncertain Viability), 4.3 (Research Involving Prisoners), and/or 4.4 (Research Involving Children).
- 7.4. The IRB determinations regarding inclusion of other vulnerable populations will documented in accordance with HRPP policies 2.2 (Full IRB Review) and 2.3 (Expedited Review).

DOCUMENT HISTORY:

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? Revised 4/16/2025 – changed “populations” to “person” throughout; added note (section 4.2) to clarify that “Persons or populations may be ‘vulnerable’ without belonging to one or more of the above groups, nor is it important to which particular group above a vulnerable population belongs”; restructured policy to focus on responsibilities of investigators and IRB/ORA; deleted description of processes more appropriate for SOPs; stylistic changes

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