Module: Research with Protected Populations–Vulnerable Subjects: An Overview (7–18–11)
Belmont Report

The *Belmont Report* identifies three basic ethical principles essential to the review of research:

- Respect for Persons, Beneficence, and Justice.
According to the *Belmont Report*,

- "Respect for Persons incorporates at least two ethical convictions: first, that individuals should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection."

- Vulnerable subjects are those subjects with diminished autonomy. It is useful to further analyze the components of autonomy in order to understand which subjects have diminished autonomy.
Autonomy is generally broken down into two general elements in the bioethics literature.

- Mental capacity, the ability to understand and process information.
- Voluntariness, freedom from the control or influence of others.
When a subject has limitations on either capacity or voluntariness, then the subject is vulnerable.
Vulnerability often does not apply uniformly to a given research population. Some of the variables in vulnerability are provided below:

1. Within any population of vulnerable subjects, **individuals will have different levels of vulnerability**.

2. The level of vulnerability of an individual may change due to changes in capacity or in conditions affecting voluntariness. For instance, a subject with diminished capacity due to pain control medication may have lucid periods. It is the researcher's responsibility to systematically assess capacity to consent prior to and during the research activity.

3. The IRB considers a hypothetical group of subjects, whereas the investigator interacts with actual subjects. Therefore, the investigator must take into account the actual vulnerability of a given subject and act accordingly in the consent process and in the conduct of the research.
Subjects who are vulnerable are more likely to have their rights abused in the following ways:

- Physical Control
- Coercion
- Undue Influence
- Manipulation
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<th>Determination of Vulnerable Subjects</th>
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DHHS and FDA regulations provide lists of potentially vulnerable subjects, and require the consideration of additional safeguards for vulnerable subjects, but do not provide a definition of vulnerability or an explanation of the causes of vulnerability.
Specific Classes of Vulnerable Subjects

There are several classes of vulnerable subjects, with varying degrees of potential vulnerability.

- Children
- Embryos and Fetuses
- Mentally Disabled Individuals
- Emergency Situations
- Hierarchical Social Structures
- Educationally Disadvantaged Subjects
- Economically Disadvantaged Subjects
- Marginalized Social Groups
- Individuals with Incurable or Fatal Diseases
Vulnerable Subjects

Special regulations exist in the common rule for:

- Pregnant women, fetuses, and neonates (subpart B)
- Prisoners (subpart C)
- Children (subpart D)
Subpart D includes:

- Restrictions on the applicability of the criteria for exemption when children are the subjects.

- Provisions for parental permission and child assent, including criteria for waivers.

- Hierarchy of four levels of risk and associated benefits, with specifications for parental permission and child assent requirements at each level.
According to federal regulations, children are persons who have not yet attained the legal age of consent under the applicable laws in the jurisdiction in which the research will be conducted.
According to Subpart D, exemptions may **not** be used for any of the following, which involve children:

- Research involving interviews.
- Research involving surveys.
- Observation in which the researcher participates in the activities observed.
All the regulations that apply to the informed consent process apply to the parental permission process. They are:

- Content
- Documentation
- Waivers
Assent is a child’s affirmative agreement to participate. The absence of dissent should not be construed as assent.

In determining whether children are capable of asserting the IRB should take into account:

- Age
- Maturity
- Psychological status
Waiver of Parental Permission and Assent

1. The risk involves no more than minimal risk to subjects.

2. The waiver will not adversely affect the rights and welfare of the subjects.

3. The research could not practically be carried out without the waiver.

4. Whenever appropriate, the subjects will be debriefed after the study.
Acceptable Categories of Research

- Research with no more than minimal risk.
- Research involving more than minimal risk but presenting the prospect of direct benefit to the children participating in the study.
- Research involving more than minimal risk but not presenting the prospect of direct benefit to the children participating in the study.
- Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.
The regulation impose strict limits on the use of prisoners as research subjects.

In essence, the only research that may be conducted with prisoners as subjects is that which is material to the lives of prisoners.

Prisoners may not be used as a population of convenience.
“A Prisoner means any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under criminal or civil statute, individuals detained in other facilities by virtue of the statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.”
Research Allowed
Under the Regulations

1. Studies of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects.

2. Studies of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects.
3. Research on conditions particularly affecting prisoners as a class.

4. Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the well-being of the subjects.
Required Composition of the IRB

- Majority of the IRB members (excluding prisoner members) must have no association with the prison(s) involved, apart from their membership on IRB.

- At least one member of the IRB must be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity.
1. The research under review falls into one of the categories of permitted research.

2. Any benefits to the prisoner which may result from being in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earning in the prison, do not impair his or her ability to weigh the risks of the research against the benefits in prison.
3. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers.

4. Procedures for the selection of subjects within the prison are fair to all prisoners, and control subjects must be selected randomly from the group of available prisoners.

5. The study information is presented in language which is understandable to the subject population.
6. Parole boards will not take into account a prisoner’s participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole.

7. Adequate provisions have been made for follow-up experimentation or care, taking into account the varying lengths or individual prisoners’ sentences, and for informing participants of this facet.
When Enrolled Subjects Become Prisoners

OHRP recommends that:

1. Investigators inform the IRB immediately upon learning that a subject has entered the prison system; and

2. The IRB review the protocol “at the earliest opportunity” to determine whether continued participation in the research is appropriate under the regulations.
Other Vulnerable Subjects

Subpart B provide additional protection for:

- Pregnant women
- Human fetuses
- Neonates
Conclusion

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