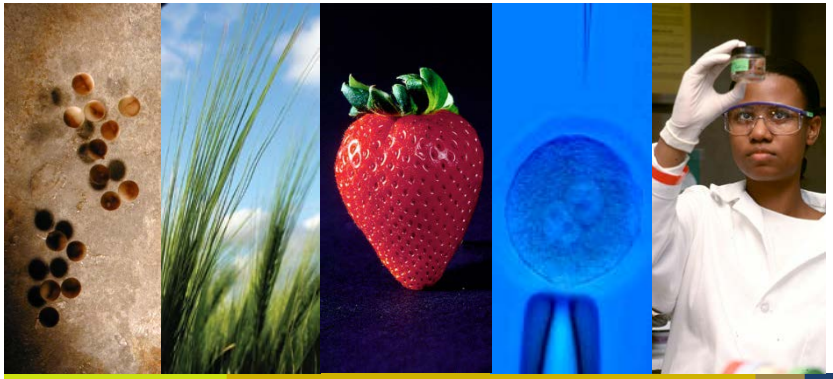

UC DAVIS OFFICE OF RESEARCH

AAHRPP Preparation
UC Davis Human Research
Part VII – Vulnerable Populations

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Background

Increased scrutiny for vulnerable individuals is based on the basic premises of the Belmont Report – *respect for persons* and *justice*

Respect for persons: two basic ethical convictions:

- Individuals should be treated as autonomous agents,
- "persons with diminished autonomy and thus in need of protection are entitled to such protections." National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

Justice:

- Distribution of scares benefits fits with distribution of burden – fair sharing of burdens (risks) and benefits.

Who is vulnerable?

- Pregnant Women
- Human Fetuses
- Neonates
- Prisoners
- Children
- Persons who are:
  - physically handicapped
  - cognitively impaired
  - economically disadvantaged
  - educationally disadvantaged
- Racial minorities
- Very Sick
- Students
- Patients
- Staff

Safeguards 46.111(b)

When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

Current Regulations

- 45 CFR 46 & 21 CFR 56
  - Subpart B – women, fetuses and neonates
  - Subpart C – prisoners
  - Subpart D – children

Subpart D is applicable to Both FDA and DHHS research. Subparts B&C are applicable to only federally funded research.

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Research Involving Pregnant Women, Fetuses, and Neonates

(45 CFR 46 Subpart B & 21 CFR 56)

Key Definitions

- **Dead fetus:** A fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord
- **Delivery:** A complete separation of the fetus from the woman by expulsion or extraction or any other means
- **Fetus:** The product of conception from implantation until delivery.
- **Neonate:** A newborn
- **Nonviable neonate:** A neonate after delivery that, although living, is not viable
- **Pregnancy:** The period of time from implantation until delivery. A woman is assumed to be pregnant if she exhibits any of the pertinent 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 available medical therapy) to the point of independently maintaining a heartbeat and respiration

Subgroups of Studies identified by the IRB

- Studies in which pregnancy is coincidental to subject selection
- Research involving pregnant women or fetuses
- Research involving neonates
- Research involving, after delivery, the placenta, the dead fetus or fetal material

Studies in Which Pregnancy is Coincidental to Subject Selection

- When the research population may include women of child bearing potential, the possibility exists for the inadvertent inclusion of pregnant women
- However, the IRB may take the following factors into account:
  - Is it appropriate to highlight potential risk to pregnancy in the informed consent?
  - Does the mother's involvement pose any risk to the fetus or nursing infant?
  - Should non-pregnant participants be advised to avoid pregnancy or nursing during the study period?
  - Is there a need to advise participant to immediately contact the investigator should they become pregnant?

Research Involving Pregnant Women or Fetuses

- **2 primary considerations of the IRB**
  - Whether the research is directed to the mothers' or fetus' health
  - The risk to the woman and the fetus
- **The following conditions must be met for pregnant women or fetuses to be involved with research:**
  - Animal and non-pregnant studies have indicated safety
  - Favorable risk-benefit profile
  - No inducements, monetary or otherwise, will be offered to terminate pregnancy
  - Individuals engaged in research will have no part in the decision making of terminating pregnancy or determining viability
  - Any risk is the least possible for achieving the research objectives

Regulations

§ 46.204 – Subpart B

- Preclinical data identifying risks required where appropriate
- Least possible risk to achieve research objective(s)
- Fully informed participants
- No inducements to terminate pregnancy
- Researchers have no part in:
  - Decisions to terminate pregnancy
  - Determining viability

Consent Issues

- Consent of pregnant woman if *direct* or *no direct* benefit to her or to both her and the fetus and is *not* greater than minimal risk
- Consent of pregnant woman **AND** father if research offers direct benefit solely to fetus
- Pregnant children – assent and permission per Subpart D

Research Involving Neonates

- Differ by degree of viability
  - Neonates of uncertain viability
  - Nonviable neonates
  - Viable neonates
- Generally, IRB restrictions increase as prospect for survival decreases

Research Involving Prisoners

(45 CFR 46 Subpart C & 21 CFR 56)

Key Definitions

- **Prisoner:** Any individual involuntarily confined or detained in a penal system institution
  - Individuals in prison, jail, or juvenile offender facility
  - Individuals detained in a residential facility for court-ordered substance abuse treatment
  - Individuals committed involuntarily due to psychiatric illness as an alternative to criminal incarceration
  - Parolees who are detained in a treatment center as a condition of their parole

Key Definitions

- **Minimal risk** is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.

Limitations of Intervention

Biomedical research involving prisoners are prohibited for research to be conducted within the California Department of Corrections and Rehabilitation

To Obtain IRB Approval

- Any possible advantages accruing to the prisoner for participation should not be great enough to impair his or her judgment
- The risks involved in the research are commensurate with the risks that would be accepted by non-prisoner volunteers
- Procedures for the selection of participants are fair to all prisoners, unless the investigator provides justification for the enrollment of a specified prison sub-group
- The information is presented in a language which is understandable to the participants
- Assurance that participation in the study will in no way influence a parolees status
- Adequate provisions have been made for a prisoner's incarceration status at follow-up

Categories of Approvable Prisoner Research

- Studies of the possible causes, effects, and processes of incarceration
- Study of prisons as institutional structures or of prisoners as incarcerated persons
- Research on conditions particularly affecting prisoners as a class (requires OHRP approval)
- Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health and well-being of the participant
- Epidemiologic research

Measures if a Current Subject Becomes a Prisoner

- The investigator is responsible for reporting the event in writing to the IRB within 5 business days
- If the subject continues participation, an amendment must submitted to the IRB
- Until these measures are taken, interactions/interventions and the obtaining of identifiable private information must cease

Regulations

§ 46.204 – Subpart C

- At least one member of the Board shall be a prisoner, or a prisoner representative
- No coercion
- No imbalance in the risk/benefit
- Participant selection is fair
- Research is directly related to prison environment

Consent Issues

- Terminology must be understandable to the individual subject
- No special treatment for study participation
- Parole board cannot consider study participation when determining parole

UCD Reviewer Tools

Compliance Issues

- “we were unable to identify records indicating that the IRB made the seven additional findings required under HHS regulations at 45 CFR 46.305(a)” ~ Brown University 2011

- “45 CFR 46.111(b)…. we determine that the protocol did not include additional safeguards for subjects who have recently lost a loved one, and therefore may have been vulnerable to coercion or undue influence” ~ University of Arizona 2008

- “HHS regulations require specific findings on the part of the IRB, such as (a) approving a procedure which waives the requirement for obtaining a signed consent form …; (b) approving research involving pregnant women, human fetuses, or neonates …; (c) approving research involving prisoners …; or (d) approving research involving children …, the IRB should document such findings. OHRP recommends that for research approved by the convened IRB, all required findings be fully documented in the minutes of the IRB meeting, including protocol-specific information justifying each IRB finding” ~ University of Washington 2005

Checklist

- HRP-412 - Pregnant Women
- HRP-413 - Non-Viable Neonates
- HRP-414 - Neonates of Uncertain Viability
- HRP-415 - Prisoners
- HRP-416 - Children
- HRP-417 - Cognitively Impaired Adults

Thank you – Don’t miss Part VIII of this continuing series!