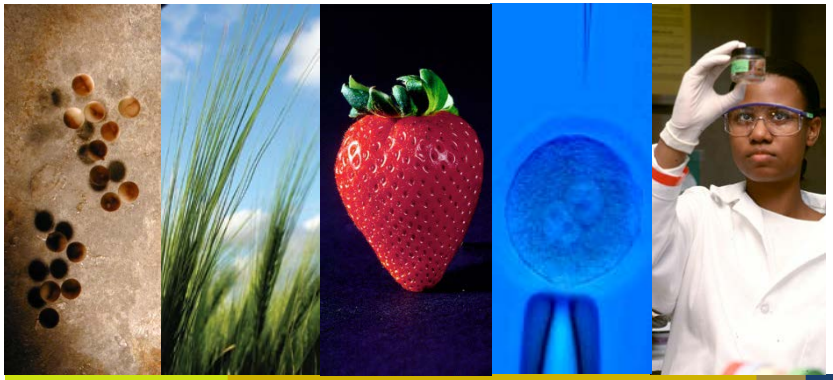

UC DAVIS OFFICE OF RESEARCH

AAHRPP Preparation
UC Davis Human Research
Part VIII – 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.

Research Involving Children

(45 CFR 46 & 21 CFR 56 Subpart D)

Key Definitions

- **Assent:** A child's affirmative agreement to participate in research
- **Child/children/minors:** An individual under the age of 18 years old
- **Foster child**: A ward of the state
- **Guardian:** An individual is authorized to consent on behalf of a child to general medical care

Classification

- In order to provide additional safeguards, children are classified into one of four categories based on the risk-benefit profile
- For each cohort in the study, the IRB should decide whether the subjects fit within an approvable category.
- For these categories, "minimal risk" means that 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.

Classification

- Category 1: Research not involving greater than minimal risk (one parent permission required)
- Category 2: Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual child (one parent permission required)
- Category 3: Research involving greater than minimal risk and no prospect of direct benefit to the individual child, but likely to yield generalizable knowledge about the child's disorder or condition (two parent permission required)
- Category 4: Research not otherwise approvable, which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (two parent permission required)

Other IRB Considerations

- When assent is required by the IRB, the decision of the child assenting is binding, provided parental or guardian permission, when necessary, has been obtained
- When the durations of the child's participation may continue beyond the age of majority, the investigator must include provisions for the now-adult's continued participation
- All potential geographical and jurisdictional IRB considerations must be accounted for.

Regulations

§ 46.204 – Subpart D

- IRB regularly reviewing research involving children and should include one or more individuals with knowledge and experienced in working with these subjects.
- Risks to subjects are:
  - Minimized and
  - Reasonable in relation to anticipated benefits
- Selection of subjects is equitable.
  - IRB should take into account
    - the purposes of the research,
    - the setting in which the research will be conducted,
    - special problems of research involving children

Obtaining Child Assent

- The IRB generally requires assent for children aged 7 years and older
- Is the child capable of providing assent?
  - Age?
  - Maturity?
  - Psychological state?
- The assent process should provide the child with an age-appropriate explanation of the proposed research procedures (explanation of activities, duration of research etc.)
- The IRB determines whether and how assent must be documented
- The IRB may waive child assent if the following criteria are met:
  - meets the criteria for waiver of consent
  - child incapable to consent
  - research possibly provides direct benefit only available in the research

Wards of the State

If the research falls under Category 3 or 4 may participate in research only when one of the following apply:

- Research is related to their status as wards
- Research is conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of the children involved as subjects are not wards

- An advocate will be appointed for each child that is a ward
  - Will act on behalf as guardian
  - Have experience to act in the best interest of the child
  - Not be associated with the research, investigator, or the guardian organization

- If the research involves wards of the California Youth Authority, the Prisoner Checklist also has been completed and prior approval has been secured from the California Department of Corrections and Rehabilitation

Circumstance When Minors Can Consent for Themselves

- Emancipated or Mature Minor
- Special situations
  - Married
  - Parent
  - Pregnant

Persons who are Decisionally and/or Cognitively Impaired Adults

Key Definitions

Cognitively impaired: Having either a psychiatric disorder, an organic impairment (e.g., dementia) or a developmental disorder (e.g., mental retardation) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished

Competence: Ability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice

Decisional capacity: The ability to understand and appreciate the nature and consequences of a decision regarding medical treatment and the ability to reach and communicate an informed decision in the matter

Incapacity/incompetent: Inability to understand information presented, to appreciate the consequences of acting (or not acting) that information and to on information, make a choice

IRB Approval

- Research with anticipated direct benefits to subjects, ***either*** must be true:
  - Subjects have a disease or condition for which the procedures involved in the research hold out a prospect of direct benefit to the individual subject that is unavailable outside the research context
  - Objective of the trial cannot be met by means of subjects who can give consent personally
- Research with **NO** anticipated direct benefits, ***both*** must be true:
  - Research involved should be relevant to subject's condition or circumstance
  - Objective of the trial cannot be met by means of subjects who can give consent personally
- Trial not prohibited by law
- PI must propose adequate procedures for evaluation of mental status
- Risk-Benefit consideration
- Close monitoring of the subjects
- Subjects withdrawn if they appeared unduly stressed

Role of the LAR

- In general, consent is provided by the subject's legally authorized representative (LAR). Assent is obtained from the subject.
- The IRB ensures the LAR is given a description of the study, and is well-informed of his or her obligation of protecting the interests of the subject
- In order to seek consent from the LAR, the PI should obtain a copy of documents certifying that the subject is unable to make decisions

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 IX of this continuing series!