

VULNERABLE POPULATIONS IN RESEARCH

October 2015 IRB Forum

Overview

- ❑ Defining vulnerable populations in research
- ❑ Pregnant Women, Fetuses and Neonates
- ❑ Children
- ❑ Prisoners
- ❑ Other populations

Limited autonomy = vulnerable populations

- ❑ Vulnerable populations are so-named because:
 - ❑ They are vulnerable to undue influence or coercion
 - ❑ Undue Influence = “...an offer of an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance”
 - ❑ Coercion = “...an overt threat of harm is intentionally presented by one person to another in order to obtain compliance.”
 - ❑ They have limited comprehension and understanding (i.e., children)
- ❑ The following groups are defined as vulnerable in the federal regulations:
 - ❑ Pregnant women, fetuses, and neonates
 - ❑ Children
 - ❑ Prisoners

Pregnant Women, Fetuses and Neonates

History of Women in Research

- ❑ Historically, women of childbearing potential (WOCBP) have been excluded (read: protected) from research;
- ❑ Same thinking has been applied to pregnant women, but this group continues to often be excluded from research;
- ❑ Guidance from the NIH and the FDA in the early 1990s put pressure on investigators to include WOCBP to increase our understanding of gender-related differences in research;
- ❑ The current presumption is that WOCBP should be included in research unless there is scientific and safety evidence that suggests otherwise;
- ❑ When working with these populations, the NIH and FDA require that:
 - ❑ Consent Form and Investigator's Brochure (IB) should describe any risks of fetal toxicity to the extent known

Common Myths...

- ❑ An exempt research study cannot involve pregnant women;
- ❑ Research with pregnant women always requires full board review;
- ❑ Pregnant women should be excluded from all types of research;
- ❑ Pregnant minors are emancipated and can consent for any type of research.

Research with Pregnant Women & Fetuses

- ❑ When the IRB reviews research involving pregnant women and fetuses, it must evaluate the following:
 - ❑ Preclinical studies to assess potential risks (i.e., low birth weight, deformities, reduced survival, etc.);
 - ❑ The prospect of direct benefit for the woman or the fetus. If no benefit, then the risk to the fetus is minimal and the knowledge cannot be obtained by any other means;
 - ❑ Any risk is the least possible;
 - ❑ Consent of pregnant woman only: If direct benefit to the pregnant woman and/or the fetus, or if minimal risk, no benefit for the woman nor the fetus;
 - ❑ Consent of father AND pregnant woman if direct benefit solely to fetus. Consent need not be obtained from the father if he is unavailable, incompetent, temporarily incapacitated, or the pregnancy resulted from incest or rape.

Research with Pregnant Women & Fetuses

- ❑ When the IRB reviews research with pregnant women and fetuses, it must evaluate the following:
 - ❑ No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
 - ❑ Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
 - ❑ Individuals engaged in the research will have no part in determining the viability of a neonate.

Research involving Neonates

- Neonates of *uncertain viability* and *nonviable neonates* may be involved in research if all of the following conditions are met:
 - Preclinical and clinical studies have been conducted and provide data for assessing potential risks;
 - Each individual providing consent...is fully informed regarding the reasonably foreseeable impact of the research;
 - Individuals engaged in the research will have no part in determining the viability of a neonate.

Neonates of Uncertain Viability

- Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research...unless the following additional conditions have been met:
 - The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective; or
 - The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and
 - The legally effective informed consent of either parent of the neonate or...the legally effective informed consent of either parent's legally authorized representative is obtained.

Nonviable neonates

- After delivery nonviable neonate may not be involved in research...unless all of the following additional conditions are met:
 - Vital functions of the neonate will not be artificially maintained;
 - The research will not terminate the heartbeat or respiration of the neonate;
 - There will be no added risk to the neonate resulting from the research;
 - The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
 - The legally effective informed consent of both parents of the neonate except that the waiver and alteration provisions of §46.116(c) and (d) do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice.
 - The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements.

Viabile Neonates

- A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of subparts A and D.

Minimizing undue influence or coercion with pregnant women

- It is important to provide truly voluntary methods for patient participation.
- For example:
 - ▣ Have someone other than the treating physician obtain informed consent;
 - ▣ Do not present research information or try to obtain consent during stressful periods;
 - ▣ Provide them time to think about their participation and discuss the study with family members or friends.
- Minimize ≠ eliminate

Children

45 CFR 46 Subpart D

Children

- ❑ Additional protections for children as research subjects are codified under subpart D in the HHS regulations;
- ❑ Children received additional protections as this group has been historically misused as research subjects;
- ❑ Orphans or wards of the state were used for early medical studies, as this population was easily available and parental consent did not need to be sought.

Regulatory Definition of Children

- ❑ Regulations define children as individuals who have not reached the legal age of consent for procedures involved in research;
- ❑ Legal age of consent (or age of majority) is dependent on jurisdiction and funding source. EXAMPLE: NIH considers anyone under age 21 a minor;
- ❑ In international research, age of majority may be dependent on culture (whether or not individual is considered an adult in their community) and local laws;
- ❑ Some minors may be considered “emancipated” minors, and therefore seeking parental permission would not be appropriate;
 - ❑ Definition of “emancipated” depends on state law
- ❑ May also be dependent on marital status, military status, etc.

Requirements for IRB approval

- In minimal risk research, the IRB must find that:
 - The benefits of the research justify the risks;
 - Appropriate provisions for obtaining assent and parental permission are included.
- In greater than minimal risk research, the IRB must find that:
 - Research procedures are similar to those expected in the children's daily lives (medical, educational, social settings);
 - Intervention likely to generate valuable results about child's condition or treatment of that condition;
 - Appropriate provisions for obtaining assent and parental permission are included.

Assent

- Before taking part in a research study, minors are asked for their assent. Assent means that they agree to take part. They may also dissent, which means they do not agree;
 - ▣ *Mere absence of dissent does not imply assent*
- To take part in the assent process, children must be mature enough to understand the study and what they are expected to do;
- As with the informed consent process, the assent process is meant to be an ongoing conversation between the child and research team;
- At GW, it is generally required that children 7-17 be assented for research participation.

Assent

- How much information should be included in the child assent?
- Depends on the age:
 - Toddlers/Pre-K/Kindergarten: “Do you want to play blocks with me?”
 - Elementary school age: At least the basics: what is involved, for how long, voluntary, etc.
- Middle school – High school: Varies, getting closer to adult consent form content.

Parental Permission

- ❑ Parental permission is required unless the IRB specifically waives the requirement;
- ❑ Generally, parental permission may be waived if the IRB finds:
 - ❑ It is minimal risk research;
 - ❑ It is not possible to carry out the research if parental permission is required;
 - ❑ Waiving consent does not adversely affect the subjects' welfare;
 - ❑ And when appropriate, parents should be provided with information after the study.

Parental Permissions

Category			
45CFR46.404 Research not involving greater than minimal risk	45CFR46.405 Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.	45CFR46.406 Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.	45CFR46.407 Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.
Permission			
<u>At least one parent</u> The IRB may find that permission of one parent is sufficient.	<u>At least one parent</u> The IRB may find that permission of one parent is sufficient.	<u>Both Parents</u> Requires permission to be obtained from both parents, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.	<u>Both Parents</u> Requires permission to be obtained from both parents, unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

Children and Exempt Research

- Generally, children may only participate in the following categories of exempt research:
 - (1) Research conducted in established or commonly accepted educational settings, involving normal educational practices;
 - (2)*Observation of public behavior* when the investigator(s) do not participate in the activities being observed;
 - (4) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

Prisoners

Definition of Prisoner [45 CFR 46.303(c)]

- “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 a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.”

Prisoners

Prisoner

- Individuals who are detained in a residential facility for court-ordered substance abuse treatment as a form of sentencing or alternative to incarceration;
- Individuals with psychiatric illnesses who have been committed involuntarily to an institution as an alternative to a criminal prosecution or incarceration;
- Parolees who are detained in a treatment center as a condition of parole are prisoners.

Not Prisoner

- Individuals living in a residential treatment facility community and the treatment is not court-ordered;
- Individuals in a psychiatric facility whose commitment has been voluntary or through civil procedures;
- Persons living in the community and sentenced to community-supervised monitoring, including parolees (IRB will consult with legal counsel on a case-by-case basis);
- Probationers and individuals wearing monitoring devices (IRB will consult with legal counsel on a case-by-case basis).

Research with Prisoners

- If you (or the study team) will be interacting or intervening with individuals who meet the prisoner definition OR viewing private identifiable information from individuals who meet the prisoner definition, then you are engaged in prisoner research;
- ***Prisoner research cannot be exempt.*** It may be expedited, but requires initial full board review at GW;
- Each of the institutions involved in research involving prisoners must perform their own Subpart C review.

Considerations

- For studies receiving federal funds (e.g., HHS, DoE, CDC, etc.), there is an additional requirement beyond the IRB;
- The IRB/institution is responsible for making a certification to the federal agency, which is subject to the agency's review and approval;
- Consider your timelines...certain types of research require convening additional panels of experts outside of the agency.

Other Vulnerable Populations

Other Populations to Consider

- The following populations do not have specific requirements via federal regulations but are still considered vulnerable:
 - Students
 - Employees
 - Patients
 - Educationally/Economically Disadvantaged
 - Impaired decision making (mentally ill/
dementia/traumatic brain injury)
 - Illiterate or low fluency in language of study

How to Minimize Risk and Ensure Informed Consent in These Populations

- Students, Employees, Patients:
 - Do not present research during stressful period (exam, review, right before surgery);
 - Have someone other than person “in charge” provide consent and collect data. EXAMPLE: A department manager who is also collecting data for her dissertation should pursue another company or division in which to obtain information;
 - Ensure that the subject may refuse to participate and can withdraw at any time without losing any benefits to which s/he is entitled.

How to Minimize Risk and Ensure Informed Consent in These Populations

- Educationally/ Economically Disadvantaged:
 - Avoid coercive inducements. EXAMPLE: A 15 minute survey should not offer \$100 for participation;
 - Ensure study related materials are presented in a manner which can be understood by target populations;
 - Use alternative means of consent such as videos that describe the study and the consent document in addition to obtaining a signature;
 - Use a study quiz to gauge comprehension.

How to Minimize Risk and Ensure Informed Consent in These Populations

- Impaired Decision Making:
 - Explore use of Legally Authorized Representative;
 - Have an unaffiliated witness observe consent process and if necessary, data collection;
 - Use a study quiz to gauge comprehension;
 - If available, have friend or family member involved in all research activities as observer.

How to Minimize Risk and Ensure Informed Consent in These Populations

- Low Literacy or Fluency in Language of Study:
 - ▣ Always use translated documents in language of target population;
 - ▣ If not fluent in language, use interpreter;
 - ▣ Explore appropriateness of study related procedures and consent process (cultural).

Questions?



Office of Human Research

202-994-2715

ohrirb@gwu.edu

Humanresearch.gwu.edu