

Chapter 15

SPECIAL POPULATIONS AS SUBJECTS OF RESEARCH

When subjects in a study may be vulnerable to injury, coercion or undue influence, the study must include additional safeguards to protect their rights and welfare.

Special populations requiring additional safeguards are:

- children
- persons who are intellectually or emotionally impaired
- the elderly
- pregnant women and fetuses
- prisoners
- persons who are illiterate or whose primary language is not English
- students or trainees
- employees of institutions associated with the study
- employees or subordinates of investigator(s)

A. Children

1. Policy:

Children are defined in the HHS regulations as “persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.: 45 CFR 46.402(a).

Children must be included in all human subjects research, conducted or supported by federal funds, unless there are scientific and ethical reasons not to include them. This policy applies to research that would otherwise be exempted from the DHHS Policy for Protection of Human Research Subjects. Examples of such research include surveys, evaluation of educational interventions, and studies of existing data or specimens that should include children as participants.

The inclusion of children will be in compliance with all applicable subparts of 45 CFR 46 as well as with other pertinent federal laws and regulations whether or not the research is otherwise exempted from 45 CFR 46. **Therefore, proposals for research involving human subjects that are federally initiated or being submitted for federal funding, must include a description of plans for including children. If children will be excluded from the research, the proposal must present an acceptable justification for the exclusion.**

2. Background:

This policy was developed because medical treatments applied to children are often based upon testing conducted only in adults, and scientifically evaluated treatments are less available to children due to barriers to their inclusion in research studies.

The goal of this policy is to increase the participation of children in research so that adequate data will be developed to support the treatment modalities for disorders and conditions that affect adults and may also affect children.

3. Definition:

For purposes of this policy, a child is an individual under the age of 21 years. This policy and definition do not affect the human subject protection regulations for research on children (45 CFR 46) and their provisions for assent, permission, and consent

4. Research Proposal:

The research proposal must provide either a description of the plans to include children and a rationale for selecting or excluding a specific age range of child, or an explanation of the reason(s) for excluding children as participants in the research. When children are included, the plan must also include a description of the expertise of the investigative team for dealing with children at the ages included, of the appropriateness of the available facilities to accommodate the children, and the inclusion of a sufficient number of children to contribute to a meaningful analysis relative to the purpose of the study.

5. Justifications for Exclusion:

- a. The research topic to be studied is irrelevant to children.
- b. There are laws or regulations barring the inclusion of children in the research. For example, the regulations for protection of human subjects allow consenting adults to accept a higher level of risk than are permitted for children.
- c. The knowledge being sought in the research is already available for children or will be obtained from another ongoing study. Documentation of other studies justifying the exclusions should be provided.
- d. A separate, age-specific study in children is warranted and preferable.
 - i. The relative rarity of the condition in children, as compared to adults.
 - ii. The number of children is limited because the majority are already accessed by a nationwide pediatric disease research network.
 - iii. Issues of study design preclude direct applicability of hypotheses and/or interventions to both adults and children (including different cognitive, developmental, or disease stages or different age-related metabolic processes). While this situation may represent a justification for excluding children in some instances, consideration should be given to taking these differences into account in the study design and expanding the hypotheses tested or the interventions to allow children to be included rather than excluding them.
- e. Insufficient data are available in adults to judge potential risk in children (in which case one of the research objectives could be to obtain sufficient adult data to make this judgement).
- f. Study designs aimed at collecting additional data on pre-enrolled adult study participants (e.g., longitudinal follow-up studies that did not include data on children).

g. Other special cases justified by the investigator.

6. Roles and Responsibilities:

a. Principal Investigator:

The principal investigator should address the policy in the application, providing the required information on participation of children in research projects, and required justifications for any exceptions allowed under the policy in the research plan.

b. Institutional Review Board (IRB)

The IRB must address the appropriateness of the population studied in terms of the aims of the research and ethical standards. The IRB has the responsibility to examine the ethical issues, including equitable selection of research participants in accordance with Federal Regulations (45 CFR 46). The participation of children in research, including children of both genders and children from minority groups, is important to assure that they receive a share of the benefits of research. The IRB may approve research involving children only if the special review requirements (45 CFR 46, Subpart D, Sec. 401-409) have been met.

c. Institutional Scientific Review Board (ISRB)

In conducting a review for scientific merit, the ISRB will evaluate the proposed plan for inclusion or exclusion of children as acceptable or unacceptable. Therefore, this Board must include the appropriate expertise in research involving children to make the evaluation.

7. Criteria for Approval

The Board will approve research involving children only if it falls within one of the following categories:

a. The research involves no more than minimal risk.
(Requires the consent of one parent or guardian.)

b. The research involves more than minimal risk but presents the prospect of direct benefit to individual subjects, which is sufficient to justify the risk.
(Requires the consent of one parent or guardian.)

c. The research involves more than minimal risk and presents no direct benefit to subjects, but it is likely to yield important generalizable knowledge about the topic under study.
(Requires the consent of both parents-see below under 3.)

d. The research presents a reasonable opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.
(Requires the consent of both parents-see below under 3.)

B. Persons Who Are Intellectually or Emotionally Impaired

1. Definition

An "intellectually or emotionally impaired" person is one whose cognitive or emotional functions are affected or whose capacity for judgment and reasoning is significantly diminished, either by a psychiatric disorder (e.g., psychosis, neurosis, personality or behavior disorder), a developmental disorder (e.g., mental retardation), or a neurological disorder. These individuals may be vulnerable to coercion or may not be able to give legally valid informed consent.

2. Criteria for Approval

The Board will approve research that targets intellectually or emotionally impaired persons only if it falls within one of the following categories:

- a. The research involves no more than minimal risk.
- b. The research involves more than minimal risk but presents the prospect of direct benefit to individual subjects, which is sufficient to justify the risk.
- c. The research involves more than minimal risk and presents no direct benefit to subjects but is likely to yield generalizable knowledge about the subjects' condition.
- d. The research presents a reasonable opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of intellectually or emotionally impaired persons.

C. Elderly Subjects

1. Definition

"Elderly" subjects are those over the age of 65. Advancing age may entail a decline of some physical capabilities, making some elderly individuals more vulnerable to the risks posed by a research protocol. A decline of some mental capabilities may, in addition, make some elderly individuals vulnerable to coercion or incapable of giving legally valid informed consent.

2. Criteria for Approval

The Board will approve research that targets elderly persons only if it falls within one of the following categories:

- a. The research involves no more than minimal risk.
- b. The research involves more than minimal risk but presents the prospect of direct benefit to individual subjects, which is sufficient to justify the risk.
- c. The research involves more than minimal risk and presents no direct benefit to subjects but is likely to yield generalizable knowledge about the subjects' disorder or condition.

- d. The research presents a reasonable opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of older persons.

D. Pregnant Women and Fetuses

1. Definitions

"Pregnancy" encompasses the period of time from the confirmation of implantation until the expulsion or extraction of the fetus.

A "fetus" is the product of conception from the time of implantation until a determination is made, following expulsion or extraction, that it is visible.

"Viable" refers to the ability of the fetus, after either spontaneous or induced delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heart beat and respiration.)

"Nonviable fetus" means a fetus ex utero (outside the body) which, although living, is not viable.

"Dead fetus" means a fetus ex utero which exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movements of voluntary muscles, nor pulsation of the umbilical cord (if still attached).

"In vitro fertilization" means any fertilization of human ova which occurs outside the body of a female, either through admixture of donor human sperm and ova or by any other means.

2. Criteria for Approval

The IRB will approve research involving pregnant women and fetuses only if all of the following conditions are met:

- a. Appropriate studies on animals and nonpregnant subjects have been completed.
- b. The risk to the fetus is minimal, except where the purpose of the activity is to meet the health needs of the mother or the fetus.
- c. The risk to the fetus is the least possible risk for achieving the objectives of the research.
- d. Investigators involved in the study will have no role in any decisions regarding (i) the timing, method or procedure used to terminate the pregnancy, or (ii) the viability of the fetus.
- e. When termination of a pregnancy is involved, no changes from standard procedures which may cause more than minimal risk to the fetus or to the pregnant woman may be introduced solely for purposes of the research.
- f. No monetary or other inducements may be offered to terminate a pregnancy for purposes of the research.

3. Special Considerations

a. The fetus in utero

The fetus in utero may be involved as a research subject only if the purpose of the research is to meet the health needs of the particular fetus, and the fetus will be placed at the minimum risk necessary to meet such ends or the risk to the fetus is minimal and the purpose of the research is to obtain important biomedical knowledge which cannot be obtained by other means.

b. The fetus ex utero

Until it has been ascertained whether or not a fetus is viable, a fetus ex utero may be involved as a research subject only if there will be no added risk to the fetus, and the purpose of the study is to develop important biomedical knowledge which cannot be obtained by other means; or the purpose of the research is to enhance the possibility of survival of the fetus to the point of viability.

c. The nonviable fetus

A nonviable fetus may be involved as a research subject only if vital functions will not be artificially maintained solely for purposes of the research, experimental procedures which would of themselves terminate heartbeat or respiration are not used, and the purpose of the research is to develop important biomedical knowledge which cannot be obtained by other means.

4. Consent for Research Involving Pregnant Women or Fetuses

The mother of the fetus must be legally competent and have given her informed consent for any research involving herself or the fetus. The mother's consent alone is sufficient if the purpose of the activity is to meet the health needs of the mother, the father's identity or whereabouts cannot be reasonably determined, the father is not reasonably available, or the pregnancy resulted from rape.

E. Prisoners

1. Definition

A "prisoner" is an individual involuntarily confined in a penal institution, including persons: (1) sentenced under a criminal or civil statute; (2) detained pending arraignment trial or sentencing; and (3) detained in other facilities (e.g., for drug detoxification or treatment of alcoholism) under statutes or commitment procedures providing such alternatives to criminal prosecution or incarceration in a penal institution.

2. Criteria for Approval

The Board will approve research targeting prisoners only if:

- a. The research is a study of possible causes, effects and processes of incarceration and of criminal behavior; a study of prisons as institutional structures or of prisoners as incarcerated persons; a study of conditions particularly affecting prisoners as a class; or concerns practices (both innovative and accepted) having the intent and reasonable probability of improving the health and well being of the subjects.

- b. Any possible advantages to the prisoner resulting from participation in the research must not be of such a magnitude that they impair the prisoner's ability to weigh the risks of the research against the value of such advantages in the prison environment.
- c. The risks involved in the research must be commensurate with risks that would be accepted by nonprisoner volunteers.
- d. Procedures for the selection of subjects within the prison must be fair to all prisoners.
- e. Adequate assurance exists that participation in the research will have no effect on the subject's parole, and the investigator must clearly inform each prisoner of this fact in advance.

F. Subjects Who Are Illiterate or Whose Primary Language Is Not English

1. Illiterate Subjects

If the research targets subjects who are illiterate, the protocol should use an oral consent process.

2. Subjects Whose Primary Language Is Not English

If the research targets subjects whose primary language is not English, your protocol must include a consent form written in the subject's primary language.

G. Students or Trainees

1. Students in General

The fact that a person is a student can affect that person's ability to make a voluntary and uncoerced decision about participating as a subject of research.

If prospective subjects are students at any institution associated with the study, the consent form must state that class standing or grades or status on an athletic team will not be affected by refusal to participate or by withdrawal from the study.

If students are to receive class credit, other opportunities must be available to earn credit, and the consent form must so indicate.

2. Students or Trainees of an Investigator

Except in special circumstances, the Board will approve a protocol involving the investigator's current students or trainees as subjects only if the study is designed to assure anonymity, including whether or not any particular individual elected to participate. (One method of assuring anonymity is for all contact with subjects to be made by persons other than the investigator.)

H. Employees or Subordinates

1. Employees of Institutions Associated with the Study

If prospective subjects are employees of CAMC, WVU or any institution associated with the study, the consent form must state that job standing will not be affected by refusal to participate or by withdrawal from the study.

2. Employees or Subordinates of an Investigator

Except in special circumstances, the Board will approve a protocol involving the investigator's current employees or subordinates as subjects only if the study is designed to assure anonymity, including whether or not any particular individual elected to participate. (One method of assuring anonymity is for all contact with human subjects to be made by persons other than the investigator).