

Policies and Procedures

SECTION: Human Research Protection program	NUMBER: 116	
CHAPTER: Institutional Review Board	ISSUED: 9/2004	REVISED/REVIEWED: 6/2006; 7/2009; 7/2010; 11/2010; 11/2013
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1. PURPOSE

The purpose of this policy is to describe additional protections for vulnerable populations. The regulations specify additional protections for certain classes of human research involving children [45 CFR 46.401 et. seq (DHHS), 21 CFR 50.50. and 56.101 (FDA)], pregnant women, human fetuses, human *in vitro* fertilization [45 CFR 46.201 (DHHS)], and prisoners. [45 CFR 46.301 (DHHS) and 21 CFR 56.107(a) (FDA)]. In addition, other vulnerable populations, such as members of Native American tribes, other racial and ethnic minorities, persons who are cognitively impaired or mentally ill, and Creighton University students and employees, may require special protections and procedures as set forth in this policy or as required by the IRB.

2. RESEARCH INVOLVING CHILDREN (ANYONE UNDER THE AGE OF 19 PER NEBRASKA LAW; FOLLOWS STATE OR LOCAL LAWS IN ALL OTHER JURISDICTIONS)

2.1. Categories of Research

There are four basic categories of research that may be conducted on children. In all cases, adequate provisions must be made for soliciting the assent of children and the permission of their parents or guardians. The four categories of research are based on the level of risk and benefit, as follows:

- 2.1.1. Research involving minimal risk.
- 2.1.2. Research involving greater than minimal risk that presents the prospect of direct benefit to individual research subjects who are children. The IRB may approve such research only if both of the following conditions are met:
 - 2.1.2.1. The risk is justified by the anticipated benefit.
 - 2.1.2.2. The relation of the anticipated benefit to the risk is at least as favorable to the subjects who are children as that presented by available alternative approaches.
- 2.1.3. Research involving greater than minimal risk with no prospect of direct benefit to subjects who are children, but likely to yield generalizable

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knowledge about the subject's disorder or condition. The IRB may approve such research only if all of the following conditions are met:

- 2.1.3.1. The risk represents a slight increase over minimal risk.
- 2.1.3.2. The intervention or procedure presents experiences to the subjects who are children that are reasonably commensurate with those inherent in their actual or expected plan of care and/or social conditions.
- 2.1.3.3. The intervention or procedure is likely to yield generalizable knowledge about the child's disorder or condition that is of vital importance for the understanding or amelioration of the child's disorder or condition.
- 2.1.4. Research not otherwise approvable by the IRB that the IRB determines presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. The IRB may approve such research only if the Secretary of the DHHS (or the FDA Commissioner for FDA-regulated research), after consultation with a panel of experts, determines that the research meets defined criteria. [45 CFR 46.407(b) (DHHS)]
- 2.1.5. When planning a research project that will involve children as subjects, the Principal Investigator shall make the initial determination regarding which of the above categories applies to his/her research. The IRB shall make the final determination regarding the category of research prior to approval of the project.

3. RESEARCH INVOLVING CHILDREN WHO ARE STUDENTS (SECTION APPLICABLE TO RESEARCH CONDUCTED IN A SCHOOL RECEIVING DEPARTMENT OF EDUCATION FUNDING OR RESEARCH THAT IS FUNDED BY THE U.S. DEPARTMENT OF EDUCATION)

The U.S. Department of Education issued guidelines under the Protection of Pupil Rights Amendment regarding research involving students who are children. The Amendment defines *children* as persons who are enrolled in research not above the elementary or secondary education level, who have not reached the age of majority, as determined under state law. It also defines *research* as any program or project in any research that is

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designed to explore or develop new or unproven teaching methods or techniques. The amendment applies to programs that receive funding from the U.S. Department of Education or that are conducted in schools that receive funding from the U.S. Department of Education, and it is intended to protect the rights of parents and students in the following:

- 3.1. It seeks to ensure that schools and contractors make instructional materials available for inspection by parents if those materials will be used as part of the educational curriculum or in connection with a U.S. Department of Education-funded survey, analysis, or evaluation in which their children participate.
- 3.2. It seeks to ensure that schools and contractors obtain prior written parental informed permission (for adults and emancipated minors, see section 2.1 of IRB Policy 118, “Informed Consent (Including Permission/Assent)”) before students who are children are required to participate in any U.S. Department of Education-funded survey, analysis, or evaluation that reveals information concerning:
 - 3.2.1. Political affiliations or beliefs of the student or the student’s parent
 - 3.2.2. Mental and psychological problems potentially embarrassing to the student or his/her family
 - 3.2.3. Sexual behavior and attitudes
 - 3.2.4. Illegal, anti-social, self-incriminating, and demeaning behavior
 - 3.2.5. Critical appraisals of other individuals with whom the respondents have close family relationships
 - 3.2.6. Legally recognized privileged or analogous relationships, such as those of lawyers, physicians, and ministers
 - 3.2.7. Religious practices, affiliations, or beliefs of the student or student’s parents
 - 3.2.8. Income (other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under such programs)

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3.3. Investigators who are conducting research that requires any of the information listed in Section 3.2 of this policy, and the research is not directly funded by the U.S. Department of Education but it is conducted in a school that receives funding from the U.S. Department of Education, shall verify the school's compliance with the Pupil Rights Amendment. The investigator shall ask the school administrators to include verification in their agreement letter that the school is compliant with the Pupil Rights Amendment.

4. ADDITIONAL PROTECTIONS FOR RESEARCH INVOLVING CHILDREN WHO ARE WARDS OF THE STATE

- 4.1. Wards of the state are defined as children who are under the care of a governmental agency either directly or through placement in an individual or institutional foster care setting.
- 4.2. In addition to the specific protections set forth in Section 2 and 3 of this policy regarding research involving children as human subjects, the following additional protections also shall be followed for research protocols that include as human subjects children who are wards of the state:
- 4.2.1. The governmental agency that has control of the child provides written documentation evidencing its legal authority to give permission for the child's participation in the research protocol, authorizing a named agency representative to sign appropriate permission and HIPAA Authorization forms on behalf of the child; and
- 4.2.2. If the research protocol either
- 4.2.2.1. involves greater than minimal risk with no prospect of direct benefit to individual subjects but is likely to yield generalizable knowledge about the subjects' disorder or condition; or
- 4.2.2.2. must be approved under 45 CFR Section 46.406 or .407, or 21 CFR Section 50.53 or .54, then for wards of the state to be considered for enrollment, the IRB shall:
- 4.2.2.2.1. Determine that the research protocol is related to the subjects' status as wards of the state; or it shall be

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conducted in schools, camps, hospitals, institutions or similar setting in which the majority of children involved as subjects are not wards of the state;

4.2.2.2.2. Appoint an advocate for each child who is a ward of the state, and the advocate shall meet the following qualifications and have the following responsibilities:

4.2.2.2.2.1. The advocate shall serve in addition to any other individual acting on behalf of the child as legal guardian.

4.2.2.2.2.2. A single person may serve as advocate for more than one child;

4.2.2.2.2.3. The advocate shall be an individual who has the background and experience to act in and agrees to act in the best interest of the child for the duration of the child's participation in the research protocol.

4.2.2.2.2.4. The advocate shall not be associated in any way with the clinical investigation, the investigators, or the guardian's organization.

5. RESEARCH INVOLVING PREGNANT WOMEN, FETUSES, OR NEONATES

The DHHS has established certain criteria that must be met before pregnant women, fetuses, or neonates can be involved as subjects in research. According to the DHHS criteria, *fetus* and *neonate* are defined as follows: *fetus* means the product of conception from implantation until delivery, and *neonate* means a newborn.

5.1. Pregnant Women or Fetuses

The DHHS has established the following criteria [45 CFR 46.201 et. seq. (66 FR 56775, November 13, 2001)] that must be met prior to conducting research activities that involve pregnant women or fetuses as research subjects:

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- 5.1.1. When scientifically appropriate, preclinical studies (including studies on pregnant animals) and clinical studies (including studies on non-pregnant women) have been conducted and provide data for assessing potential risks to pregnant women and fetuses.
- 5.1.2. Risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that can not be obtained by any other means.
- 5.1.3. Any risk is the least possible for achieving the objectives of the research.
- 5.1.4. The woman's consent or the consent of her legally authorized representative is obtained in accord with the informed consent provisions, unless altered or waived by the IRB as allowed under the regulations. A legally authorized representative is defined as a person assigned by the courts to represent a person with diminished decision-making capability. If the research holds out the prospect of direct benefit solely to the fetus, the consent of the pregnant woman and the father must be obtained in accord with the informed consent provisions, unless the father is unable to consent because of unavailability, incompetence, or temporary incapacity, or the pregnancy resulted from rape or incest.
- 5.1.5. Individuals providing consent are fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate.
- 5.1.6. For pregnant children, assent and permission are obtained in accord with the provisions for assent of children (see IRB Policy 118, "[Informed Consent \(Including Permission/Assent\)](#)").
- 5.1.7. No inducements, monetary or otherwise, will be offered to terminate a pregnancy.
- 5.1.8. Individuals engaged in the research will have no part in 1) any decisions as to the timing, method, or procedures used to terminate a pregnancy, or 2) determining the viability of a neonate.

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5.2. Neonates

The DHHS has established the following criteria [45 CFR 46.201 et. seq. (66 FR 56775, November 13, 2001)] that must be met prior to conducting research activities that involve neonates:

5.2.1. Neonates of uncertain viability and nonviable neonates may be involved in research if **ALL** of the following conditions are met:

- 5.2.1.1. When scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
- 5.2.1.2. Individuals providing consent are fully informed regarding the reasonably foreseeable impact of the research on the neonate.
- 5.2.1.3. Individuals engaged in the research will have no part in determining the viability of a neonate.
- 5.2.1.4. The requirements set forth below have been met as applicable.

5.2.2. Neonates of uncertain viability may not be involved in research unless the following additional conditions are met:

- 5.2.2.1. The research must hold 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
- 5.2.2.2. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means, and there will be no added risk to the neonate resulting from the research; and
- 5.2.2.3. Informed consent of either parent or either parent's legally authorized representative is obtained, unless altered or waived by the IRB as allowed under the regulations, or unless the pregnancy resulted from rape or incest.

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5.2.3. Nonviable neonates may not be involved in research unless the following additional conditions are met:

- 5.2.3.1. Vital functions of the neonate will not be artificially maintained;
- 5.2.3.2. The research will not terminate the heartbeat or respiration of the neonate;
- 5.2.3.3. There will be no added risk to the neonate resulting from the research;
- 5.2.3.4. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
- 5.2.3.5. Informed consent of both parents is obtained, unless one parent is unable to consent because of unavailability, incompetence, or temporary incapacity, in which case the consent of one parent is sufficient, or unless the pregnancy resulted from rape or incest. The consent of a legally authorized representative cannot be substituted for parental consent and informed consent cannot be waived or altered.

5.2.4. Viable neonates may be included in research only to the extent permitted by and in accord with informed consent requirements, IRB regulations, and requirements for research involving children (see section 2, "Research Involving Children," of this policy).

6. RESEARCH INVOLVING, AFTER DELIVERY, THE PLACENTA, THE DEAD FETUS, OR FETAL MATERIAL

If information associated with the placenta, the dead fetus, or fetal material is recorded for research purposes in a manner such that living individuals can be identified, those individuals are research subjects and all pertinent consents and IRB approval requirements apply. As part of a Catholic institution, the Creighton IRB will not review or approve the use of fetal materials obtained by induced abortions in any research or study.

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6.1. Research Not Otherwise Approvable by the IRB

If the IRB determines that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates, the IRB may approve the research only if the Secretary of the DHHS, in consultation with experts, determines that certain criteria [[45 CFR 46.207\(b\)](#)] are met.

7. RESEARCH INVOLVING PRISONERS

A policy on research involving prisoners can be found in IRB Policy 117, "[Prisoners in Research](#)."

8. RESEARCH INVOLVING OTHER VULNERABLE POPULATIONS

8.1. Members of Native American Tribes

Prior to submitting the protocol to the IRB for review and approval, the Principal Investigator shall obtain approval from the appropriate tribal council(s) for research involving members of Native American tribes.

8.2. Persons with Cognitive Disabilities or Severe Mental Illness

8.2.1. Involvement of persons who have cognitive disabilities or severe mental illness in research requires additional safeguards, because these individuals may, because of their conditions, be susceptible to undue influence during the enrollment process or may be unable to understand the informed consent process. The IRB shall review each case individually when research may involve cognitively impaired or severely mentally ill and may require additional safeguards to protect these vulnerable segments of the population.

8.2.2. When the IRB reviews research funded by the National Institute on Disability and Rehabilitation Research that purposefully requires inclusion of children with disabilities or individuals with mental disabilities as research participants, the IRB shall ensure that an IRB member primarily concerned with the welfare of these research participants reviews the protocol.

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8.2.3. All research studies that enroll persons who are unable to give direct consent shall require the consent of a surrogate or legally authorized representative.

8.2.4. It is acceptable to include these persons if the following conditions are fulfilled:

8.2.4.1. The objectives of the clinical trial cannot be met by means of a trial in participants who can give consent personally.

8.2.4.2. The foreseeable risks to the participants are low.

8.2.4.3. The negative impact on the participants' well-being is minimized and low.

8.2.4.4. The participant has a disease or condition for which the investigational product is intended.

8.2.4.5. The clinical trial is not prohibited by law.

8.2.4.6. The IRB approves inclusion of such participants and includes this permission in the approval letter. The investigator shall be advised of the need for close monitoring of these participants, and participants should be withdrawn if they appear to be unduly distressed.

8.3. Other Vulnerable Populations

Commonly cited examples of vulnerable populations include racial and ethnic minorities, the rural and urban poor, undocumented immigrants, and people with disabilities or multiple chronic conditions. The primary concern here is the equitable selection of subjects and their fair treatment, including protection from risks or undue burdens.

8.4. Creighton University Employees and Students

It is the policy of the IRB that recruitment of employees or students in the laboratory, office, clinic, or class of an investigator is generally discouraged, particularly in

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research involving more than minimal risk to the participant. This participant population is considered potentially vulnerable because of the subordinate position of the employee/student and the potential for coercion or undue pressure. However, research conducted with Creighton University employees or students shall follow the same guidelines as research with other participants and shall be reviewed by the IRB if it is intended to be generalizable.

If course requirements or extra credit options involve research participation, alternative activities shall be available to students to ensure that they do not feel coerced into research participation.

8.4.1. Requirements

If an investigator wishes to recruit employee/student participants from within his/her clinic, laboratory, office or class, the IRB application shall clearly address:

- 8.4.1.1. The nature of the professional relationship between the investigator and the prospective participants
- 8.4.1.2. Justification of the need to recruit participants from the investigator's clinic, laboratory, office, or class; this justification must be particularly strong for any study that involves greater than minimal risk procedures.
- 8.4.1.3. Description of the method of participant recruitment and how situational coercion will be minimized to the greatest extent possible. **Note:** the investigator should consider use of general advertising or bulletin board posting and not engage in one-on-one solicitation and use of an individual to obtain consent who does NOT have any supervisory or instructional role relative to the prospective participant.

9. RESEARCH SPONSORED BY THE U.S. ENVIRONMENTAL PROTECTION AGENCY (EPA)

- 9.1. The EPA prohibits research involving the intentional exposure of pregnant women, nursing women, or children to any substance.

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- 9.2. The EPA requires application of 40 CFR 26 Subparts C and D to provide additional protections to pregnant women and children as participants in observational research (i.e., any research that does not involve intentional exposure to any substance).
- 9.3. EPA policy requires submission of IRB determinations and approval to the EPA Human Subjects Research Review official for final review and approval before the research can begin.
- 9.4. For research not conducted or supported by any federal agency that has regulations for protecting human research participants and for which the intention of the research is submission to the EPA, the EPA regulations protecting human research participants apply, including:
 - 9.4.1. The EPA extends the provisions of 40 CFR 26 to human research involving the intentional exposure of non-pregnant, non-nursing adults to any substance.