



MCW Office of Research Standard Operating Procedure

RESEARCH INVOLVING CHILDREN

Unit: Human Research Protections Program (HRPP), Office of Research

Applies to: Faculty and Staff involved in human research

PURPOSE:

Children are a population that require additional safeguards in the context of their participation in research projects.

If the IRB reviews research that focuses on categories of subjects vulnerable to coercion or undue influence, the review process will include one or more individuals who are knowledgeable about or experienced in working with these subjects.

DEFINITIONS:

Children (also referred to as minors): 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.

Advocate: 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. An Advocate is not associated in any way (except in their role as advocate or member of the IRB) with the research, the investigators, or the guardian.

Guardian: an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.

- In Wisconsin a "Guardian" of a minor means having the duty and authority to act in the best interests of the minor, subject to residual parental rights and responsibilities, to make important decisions in matters having a permanent effect on the life and development of the minor and to be concerned with his or her general welfare. (s. 48.02 (8)).
- Under DHHS regulations "guardian" means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.
- Under FDA regulations "guardian" means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care when general medical care includes participation in research; a guardian also means an individual who is authorized to consent on behalf of a child to participate in research. A guardian may grant permission for a child to participate in research.

PROCEDURE:

Children

1. Investigators who wish to conduct research which will involve children/minors as subjects should be aware of the federal regulations and institutional policies governing this research. Investigators should indicate the inclusion of children in

their eBridge PRO Smartform and submit the project in accordance with *IRB SOP: Submitting New Projects*

2. MCW IRB adheres and applies the federal regulations regarding the additional responsibilities assigned to the IRB under DHHS regulations (45 CFR 46 Subpart D) and FDA regulations (21 CFR 50 Subpart D), as applicable.
 - a. For Department of Defense supported research, research which involves minors cannot be determined to be exempt.
 - b. For projects following EPA regulations, research involving intentional exposure of pregnant women or children to any substance is prohibited and not approved by the IRB.
3. These regulations protect children who are the subjects of research. The IRB must review research covered by Subpart D and approve only research that satisfies the conditions of all applicable sections of Subpart D.
 - a. Category 46.404/50.51:
 - i. No greater than minimal risk to children is presented and adequate provisions are made for soliciting assent of the children and permission of their parents or guardians in accordance with 46.408/50.55.
 - b. Category 46.405/50.52:
 - ii. More than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, and the IRB finds that:
 - a) The risk is justified by the anticipated benefit to the subjects;
 - b) The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and
 - c) Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians in accordance with 46.408/50.55
 - c. Category 46.406/50.53:
 - iii. More than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure which is not likely to contribute to the well-being of the subject, and the IRB finds that:
 - a) The risk represents a minor increase over minimal risk;
 - b) The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
 - c) The intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital importance for the understanding or amelioration of the subject's disorder or condition; and
 - d) Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians, as set forth in 46.408/50.55.
 - d. Category 46.407/50.54:
 - iv. Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children, and the IRB finds that:
 - a) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and

- b) The Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, has determined either:
 - That the research in fact satisfies the conditions of 46.404/50.51, 46.405/50.52, or 46.406/50.53; or
 - The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; the research will be conducted in accordance with sound ethical principles; and adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians in accordance with 46.408/50.55.
- 4. When a research project involves wards of state or any other agency:
 - a. the IRB will determine and document that the research (a) is related to their status as wards, or (b) will be conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of the children involved as subjects are not wards.
 - b. For research which falls under 46.406/50.53 or 46.407/50.54, the IRB will require the appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or *in loco parentis*.

Wisconsin State Law:

1. According to Wisconsin State Law, minors are persons under the age of eighteen. The general rule is that a person may consent for his or her own medical care at the age of eighteen. Therefore, the MCW IRB generally defines children as persons under eighteen years of age. Because Wisconsin law does not specifically address consent of children with majority status to research, the MCW IRB will review issues of consent related to enrollment of these children in research on a case-by-case basis.
2. Certain statutes and case law provide minors with "majority" status in some circumstances, giving them the right to consent to their own medical care. Wisconsin Law defines individuals less than 18 years of age to be minors, and children as defined in federal regulations, and Subpart D applies to such individuals unless:
 - an emancipated minor
 - a minor who is married, widowed or divorced
 - a minor who is a parent
 - a mature minor (Wisconsin law recognizes that some minors may be sufficiently "mature" to give consent to medical treatment, even though they do not qualify as "emancipated")
 - a minor seeking care for drug addiction, sexually transmitted diseases, emotional disorders, or abortion or mental health treatment.

Parental permission and assent of minors

1. When subpart D applies, Investigators should identify and describe how permission will be obtained from each child subject's parents or guardian, except as provided by the regulations in addition to the child's assent (when applicable).
2. In determining whether children are capable of assenting, Investigators should take into account the ages, maturity, and psychological state of the children involved. Investigators should identify how assent will be obtained of some or all children to be enrolled in the research project and indicate if one or more of the following may apply:

- The children are not capable of providing assent based on the age, maturity, or psychological state;
 - The capability of the children is so limited that they cannot be reasonably consulted;
 - The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the child and is available only in the context of the research;
 - Assent can be waived using the criteria for waiver of the consent process.
3. Investigators should describe whether assent will be documented, and if so, the process for documentation such as the use of an assent form or consent/assent form.
 4. Investigators should indicate how parental permission will be obtained and documented. Investigators should use MCW Consent and Assent Templates which are available on the HRPP website.
 - a. For research that involves no more than minimal risk (46.404/50.51) or more than minimal risk with the prospect of direct benefit to the individual subject (46.405/50.52), Investigators may indicate that (a) permission of both parents is obtained 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, or (b) the permission of one parent is sufficient.
 - b. For research that involves more than minimal risk without prospect of direct benefit to the individual subjects (46.406/50.53 and 407/50.54), Investigators must obtain permission must be obtained from both parents unless one is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.
 5. The IRB will review the Investigator's proposed assent and parental permission process and documents to ensure it meets the federal regulatory requirements and institutional policies.

Consent and children who reach the legal age of consent while enrolled in a research project

1. When a child who was enrolled in research with parental or guardian permission subsequently reaches age 18 years, the legal age of consent to the procedures involved in ongoing research, the subject's participation in the research is no longer regulated by the requirements of this policy or by 45 CFR 46.408 or 21 CFR 50.55 regarding parental or guardian permission and subject assent.
2. Unless the IRB determines that the requirements for obtaining informed consent can be waived, Investigators are expected to seek and obtain the legally effective informed consent, as described in HHS and FDA regulations, for the now-adult subject for any ongoing interactions or interventions with the subjects.
 - a. Investigators may consider, if appropriate and if the research is not FDA-regulated, to request a waiver of consent under 45 CFR 46.116(d) of the requirements for obtaining informed consent in order for the subjects to continue their participation in the research.
 - b. The IRB will review these requests on a project by project basis.
3. Similarly, if the research does not involve any ongoing interactions or interventions with the subjects, but continues to meet the regulatory definition of "human subjects research" (for example, it involves the continued analysis of specimens or data for which the subject's identity is readily identifiable to the investigator), then it would be necessary for the investigator to seek and obtain the legally effective informed consent of the now-adult subjects.
 - a. Investigators may consider, if appropriate and if the research is not FDA-regulated, to request a waiver of consent under 45 CFR 46.116(d) of the requirements for obtaining informed consent in order for the subjects to continue their participation in the research.

- b. The IRB will review these requests on a project by project basis.

Waiver of parental permission

1. Investigators may request a waiver or alteration of the parental permission requirements given the design of the proposed research.
2. The IRB may waive or alter the elements of parental permission if it finds that criteria at 45 CFR 46.116(d) are met. When permission is not a reasonable requirement (for example, for neglected or abused children), the IRB may waive the consent process when the following are met:
 - a. The research is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects.
 - b. An appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, for example appointing a child advocate or an assent monitor.
 - c. The research is not FDA-regulated.
3. The IRB may waive parental permission for a public demonstration project when the following are met:
 - a. The research is conducted by or subject to the approval of state or local government officials.
 - b. The research or demonstration protocol is designed to study, evaluate, or otherwise examine:
 - v. Public health or serve programs
 - vi. Procedures for obtaining benefits or services under those programs
 - vii. Possible changes in or alternatives to those programs or procedures
 - viii. Possible changes in methods or level of payment for benefits or services under those programs.
 - c. The research cannot be practically carried out without the waiver or alteration
 - d. The research is not FDA-regulated
4. The IRB will review requests to waive or alter parental permission requirements on a project by project basis. All determinations will be documented and identified in the IRB determination letters in accordance with *IRB SOP: IRB Approval Documents*.

Other Federal Agency Requirements:

1. For research intended for submission to the Environmental Protection Agency (EPA), any research involving the intentional exposure of pregnant women or children to any substance is prohibited and will not be approved by the IRB.
 - a. For observational research involving pregnant women or children being conducted for or supported by the EPA, Investigator must also comply with 40 CFR 26 subparts C and/or D in providing additional protections to pregnant women and/or children.
 - b. The IRB will review and approval observational research involving children that does not involve greater than minimal risk only if the IRB finds that adequate provisions are made for soliciting the assent of the child and the permission of their parents or guardians as set forth in 40 CFR 26.406.
 - i. Investigators must include a description of the assent process and parental permission process within the eBridge SmartForm.
 - c. The IRB may only approve observational research involving children that involves great than minimal risk but presenting the prospect of direct benefit to the individuals subjects if the IRB finds and documents that:

- i. The intervention or procedure holds out the prospect of direct benefit to the individual subject or is likely to contribute to the subject's well-being.
- ii. The risk is justified by the anticipated benefit to the subjects
- iii. The relation of the anticipated benefit to the subjects is at least as favorable to the subjects as that presented by available alternative approaches
- iv. Adequate provision are made for soliciting the assent of the children and permission of the parents or guardians as set forth in 26.406

REFERENCES:

45 CFR 46 Subpart D
21 CFR 50 Subpart D
45 CFR 46.116
45 CFR 46.408
45 CFR 46.404-407
45 CFR 46.408
21 CFR 50.20, 50.25
21 CFR 50.55
40 CFR 26 Subparts C, D
Wisconsin Legislature: s. 48.02 (8)

SUPPORTING DOCUMENTS:

IRB SOP: IRB Approval Documents
IRB SOP: Submitting New Projects
MCW Consent and Assent Templates

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