MCW IRB Committee Procedures

RESEARCH INVOLVING CHILDREN

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

Applies to: Institutional Review Board Committees

PURPOSE:
To outline criteria the IRB Committee should apply when reviewing studies that seek to enroll or that may enroll children. Children require additional safeguards in the context of participation in research.

The IRB will include one or more individuals who are knowledgeable about or experienced in working with children when reviewing research that involves individuals from this population.

DEFINITIONS:
Children (also known 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 interests 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. It is the policy of MCW IRB to require adherence to the federal regulations regarding the additional responsibilities assigned to the IRB under HHS 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.

2. These regulations protect children who are the subjects of research. The IRB must review projects covered by Subpart D and approve only projects that satisfy the conditions of all applicable sections of Subpart D. This is documented via the *IRB Member Form: Research involving Minors (subpart D) Checklist.*
    a. This includes identification of the applicable categories of risk
        i. Category 46.404 / 50.51
        ii. Category 46.405 / 50.52
        iii. Category 46.406 / 50.53
        iv. Category 46.407 / 50.54
    b. IRB will also document how the research will obtain assent and parental permission in accordance with 45 CFR 46.408 and/or 21 CFR 50.55.
3. When a 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*.
4. According to Wisconsin State Law, minors are persons under the age of eighteen. The general rule is that a person may consent for their own medical care at the age of eighteen. Therefore, the MCW IRB generally defines children as individuals under eighteen years of age.
5. As 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.
6. 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:
    a. An emancipated minor
    b. A minor who is married, widowed or divorced
    c. A minor who is a parent
    d. 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")
    e. A minor seeking care for drug addiction, sexually transmitted diseases, emotional disorders, or abortion or mental health treatment

    For Department of Defense projects only, active-duty service members and reserve component members are considered to be adults even if they are under the age of eighteen.

Parental permission and assent of minors

1. Whenever Subpart D applies, the IRB must determine that permission will be obtained from each child’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, the IRB will consider the ages, maturity, and psychological state of the children involved. The IRB will

determine if assent is required of some or all children to be enrolled in the research project and will document one or more of the following:
   a. The children are not capable of providing assent based on the age, maturity, or psychological state.
   b. The capability of the children is so limited that they cannot be reasonably consulted.
   c. 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.
   d. Assent can be waived using the criteria for waiver of the consent process.
3. When the IRB determines that assent is a requirement, the IRB determines 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. For research where parental permission is required, the IRB expectation is for two parents to provide permission; however, under certain circumstances permission from one parent is sufficient.
5. The above determinations will be documented in the *IRB Member Form: Research involving Minors (subpart D) Checklist* and within the IRB meeting minutes.

Consent and children who reach the legal age of consent while enrolled in 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, the subject's participation in the ongoing 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, the Investigator is expected to seek and obtain the legally effective informed consent, as described in 45 CFR 46.116 and 21 CFR 50.20 and .25, for the now-adult subject for any ongoing interactions or interventions with the subjects. However, the IRB could approve a waiver of informed consent under 45 CFR 46.116(d), if the research is not FDA-regulated and the IRB finds and documents that the required conditions are met.
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. The IRB may consider, if appropriate and if the research is not FDA-regulated, a waiver under 45 CFR 46.116(d) of the requirements for obtaining informed consent for the subjects to continue their participation in the research.

Waiver of parental permission

1. The IRB may waive or alter the elements of parental permission if it finds that criteria at 45 CFR 46.116(d) are met.
2. 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:
        a. Public health or serve programs
        b. Procedures for obtaining benefits or services under those programs
        c. Possible changes in or alternatives to those programs or procedures
        d. Possible changes in methods or level of payment for benefits or services under those programs.
    c. The research cannot be practicably carried out without the waiver or alteration.
    d. The research is not FDA-regulated.

The above determinations will be documented within the *IRB Member Form: Research involving Minors (subpart D) Checklist and* IRB meeting minutes.

Other Federal Agency Requirements:

1. For research intended for submission to the Environmental Protection Agency (EPA), any research involving the intentional exposure of children to any substance is prohibited and will not be approved by the IRB.
    a. For observational research (research which does not involve intentional exposure to substances) which is being conducted for or supported by the EPA, the IRB must also consider and apply 40 CFR 26 subparts C and/or D in providing additional protections to children.
2. For EPA supported observational research projects that involve children, and which are no greater than minimal risk, the IRB must find that adequate protections are made for soliciting the assent of children and permission of parents or guardians in accordance with 26.406.
3. For EPA supported observational research projects that involve children, and which are greater than minimal risk but present the prospect of direct benefit to individual subjects, the IRB must find and document:
    a. The intervention or procedure holds out the project of direct benefit to the individual subjects or is likely to contribute to the subject's well-being.
    b. The risk is justified by the anticipated benefits to subjects.
    c. The relation of the anticipated benefit to the risk is at least as favorable to subjects as that presented by available alternative approaches.
    d. Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians in accordance with 26.406.
4. Any additional federal agency requirements are documented via the *IRB Member Form: Additional Federal Agency Requirements Checklist*

IRB Committee Review

1. The IRB shall include representation, either as members or ad hoc consultants, individual(s) interested in or who have experience with the vulnerable populations involved in a project.
    a. For projects which involve children, a pediatric reviewer will be assigned as a reviewer.
2. The IRB will review Investigators' justifications for including vulnerable populations in the research project to assess appropriateness of the proposal.

3. The IRB must ensure that appropriate safeguards have been included in each research project at the time of initial review to protect the rights and welfare of vulnerable subjects.
4. The IRB shall continue to review the research project at intervals appropriate to the degree of risk and determine whether the proposed project continues to fulfill criteria for approval. Information reviewed should include the number of vulnerable subjects.
5. The IRB will assess the adequacy of additional protections for vulnerable populations provided by the Investigator.

Documentation of IRB Review

1. An IRB Committee member who is designated as a pediatric representative is assigned as a reviewer of the eBridge submission and will complete the appropriate reviewer checklist.
2. Documentation of that member's review will be uploaded to the workspace within eBridge. The pediatric representative will structure and focus their review of the project around meeting the requirements of Subpart D.
3. The pediatric representative will indicate which of the categories under Subpart D is met for any project involving minors.
    a. When the project involves wards of state or other agency, the pediatric representative will also review and indicate if the research is related to the ward's status as a ward, or if it will be conducted in schools, camps, hospitals, institutions, or similar settings in which a majority of children involved as subjects are not wards.
4. The pediatric representative must be present at the convened IRB meeting. The recommendations will be discussed, and a final decision made by the IRB Committee.

REFERENCES:

Wisconsin Legislature: s. 48.02 (8)
45 CFR 46.116
45 CFR 46 Subpart D
45 CFR 46.404-407
45 CFR 46.408
21 CRF 50.50 Subpart D
21 CFR 50.20 and .25
21 CFR 50.55
40 CFR 26 Subparts C and D
40 CFR 26.406

SUPPORTING DOCUMENTS:

IRB Member Form: Research involving Minors (subpart D) Checklist
IRB Member Form: Additional Federal Agency Requirements Checklist

Effective Date:	11/01/2023
Version number:	6.0
Previous Version/date:	5.0, 07/01/2023
Responsible Office:	HRPP Office
Approval Date:	10/27/2023

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