Research Involving Children (HRPP 4.4) (*45 CFR 46 Subpart D*)

Description:

This policy describes UNMC's requirements for research involving children.

Definitions:

Assent: a child's affirmative agreement to participate in research.

Commensurate: the requirement that children are familiar with procedures that are reasonably similar in nature and risk proportional to those the child has experienced.

Dissent: a child's affirmative decision to decline participation in research.

General Considerations:

- Age of majority in Nebraska: 19 years and older
- Minors in Nebraska: all persons under 19 years old
- If the subject is Native American and living on federal tribal lands, the age of majority is 18 regardless of any state or federal laws.

Research Involving Children:

Research involving children **must be approvable under 1 or more of the following categories**:

- §404 - The research is minimal risk.
- §405 - The research is greater than minimal risk but presents the prospect of direct benefit to the subject.
    - The risk is justified by the anticipated benefit.
    - The benefit to risk ratio is at least as favorable as alternative approaches.

- §406 - The research is greater than minimal risk and there is no prospect of direct benefit to the subject, but it's likely to yield generalizable knowledge.
    - The risk is a minor increase over minimal risk.
    - The intervention/procedure presents experiences to subjects that are reasonable with regards to their actual medical experiences/situations.
    - The intervention/procedure is likely to yield generalizable knowledge which is of vital importance to the subject's disorder or condition.
- §407 - The research, not otherwise approvable, presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.
    - The IRB will submit this category of research to a panel of experts at HHS and/or FDA for approval, if the research is funded by HHS or is FDA regulated.
    - If the research is not HHS-funded or subject to FDA regulations, the ORA will, at the IRB's discretion, convene an equivalent Local 407 Panel, as per HRPP policy 4.5 (Local 407 Panel Review of Pediatric Research).

Research Involving Wards:

Wards may participate in research **if ALL the following conditions are met:**

- Wards may participate in research classified as 45 CFR 404 or 405 and 21 CFR 50.51 or 50.52 providing all of the requirements under Subpart D are met, and NE DHHS approval for including wards has been received.
- Wards may participate in research classified as 45 CFR 406 or 407 and 21 CFR 50.53 or 50.54 only if all of the following additional conditions are met:
    1. The research is related to their status as wards or will be conducted in a setting which the majority of children involved are not wards.
    2. An advocate will be appointed to each child who is a ward. The advocate must:
        i. Serve in addition to any other individual acting as the child's guardian.
        ii. Have appropriate education and training.
        iii. Not be associated with the research, investigator, or organization except as an advocate or member of the IRB.
        iv. Promptly notify the investigator and IRB of any concerns about the child's participation.
    3. The investigator must provide justification for including this vulnerable population.

4. (In the state of Nebraska) the ward must receive direct treatment/therapy that might benefit them, and approval to include wards must be received from NE DHHS.
5. If a child becomes a ward during research, the IRB must be promptly notified, and a Request for Change must be submitted justifying the inclusion.

Obtaining Consent/Assent:

- Children 7-12 years old: given verbal assent and the study team documents
- Children 13-18 years old: sign the consent form to provide assent

Assent may be waived if:

- The capacity of some, or all, of the children is so limited that they cannot be reasonably consulted.
- The intervention/procedure holds direct benefit to the child and is available only in the context of research.
- The research meets the requirements for a waiver of assent.

Research **no more than minimal risk**	Research **greater than minimal risk** and **has direct benefit**	Research **greater than minimal risk** and **no direct benefit**
• 1 parent signature • Child assent	• 1 parent signature • Child assent	• 2 parent signatures • Child assent

Exceptions to 2 parent signatures:

- Parent deceased
- Parent unknown
- Parent incompetent
- Parent not reasonably available
- Only 1 parent has legal responsibility for care and custody of the child

Parent/guardian permission MAY be waived if:

- Parent/guardian permission is not reasonable to protect the subjects (ex. Neglected or abused children)
- Waiver not consistent with federal, state, or local laws

If a Child Reaches 19 During Research:

- The subject must give their consent (as the subject) to continue participation at the **first visit after reaching 19.**
- If the research interventions are over and the study only involves data analysis, re-consent is NOT required.
- If the now adult subject is unable to give informed consent, the parent/guardian consent remains in effect (this should be documented in the study records).
- If the now adult refuses to give consent, no additional research interventions may be performed and no additional data may be collected, but existing data may still be used.

If a Child Reaches 13 During Research:

- The subject must give their “written” assent to continue participation at the **first visit after reaching 13.**
- If the research interventions are over and the study only involves data analysis, written assent is NOT required.
- If the subject is unable to give written assent, the parent/guardian consent remains in effect (this should be documented in the study records).
- If the subject refuses to give written assent, no additional research interventions may be performed and no additional data may be collected, but existing data may still be used.