UNIVERSITY OF Cincinnati

Human Research Protection Program Institutional Review Board Procedure

INSTITUTIONAL REVIEW BOARD REVIEW OF RESEARCH INVOLVING MINORS

DESCRIPTION

Minors are vulnerable to undue pressure to participate in research and to harm that may be different or more severe than those experienced by adults. They also are not able to give legally effective consent to participate in research. Therefore the University of Cincinnati (UC) Institutional Review Board (IRB) will ensure that appropriate additional protections are provided so the rights and welfare of this population are maintained.

MINORS

- Includes individuals who have not attained the legal age for consent to the treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. In Ohio, the legal age for consent is 18 years.
- Includes viable neonates beginning at the time of delivery.
- Exemptions at 45CFR46.101(b)(1) and (b)(3) through (b)(6) are applicable to research involving minors.
- The exemption at 45CFR46.101(b)(2) regarding educational tests is applicable to research involving minors.
- The exemption at 45CFR46.101(b)(2) for research involving survey or interview procedures or observations of public behavior does not apply to research involving minors, except for research involving observation of public behavior when the investigator does not participate in the activities being observed.

RESPONSIBILITY

The IRB Chair or designee shall determine whether or not minors will be recruited as participants in a research study and, if so, shall ensure that review processes described in Human Research Protection Program (HRPP) Policy V.01 *Protecting Vulnerable Populations in Human Subjects Research* are followed.

HRPP staff shall ensure that required documentation is maintained in the IRB's study records and meeting minutes.

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PROCESS

DEFINITIONS

Assent**:** The agreement of a minor to participate in research. It is usually obtained in conjunction with permission from the child's parents or guardian. Mere failure to object should not be construed as assent.

Child or Minor**:** An individual who, under the applicable law of the jurisdiction in which the research will be conducted, has not attained the legal age for consent to treatments or procedures involved in the research..

Guardian: A person who is legally authorized to consent on behalf of a minor.

- 21 CFR 50.3 defines "Guardian" as "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. For purposes of subpart D of this part, a guardian also means an individual who is authorized to consent on behalf of a child to participate in research."

- 45 CFR 46.402 defines "Guardian" as "an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care."

- Under Ohio law, consent may be obtained by a legal guardian appointed by the probate court under Ohio Revised Code §2111.02.

- In order to satisfy federal requirements, the UC Office of General Counsel will determine guardianship requirements for research conducted in states outside Ohio, in accordance with HRPP Policy VII.06 *Research Conducted in Jurisdictions Outside Ohio.*

Legally Authorized Representative (LAR): An individual, judicial, or other body authorized under applicable law to grant permission on behalf of a prospective participant for their participation in research activities.

Minimal Risk: The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in

daily life or during the performance of routine physical or psychological examinations or tests.

Minor or Pediatric Representative: An individual who has expertise in working with children. For research involving medical or surgical tests or interventions, the representative must have appropriate medical expertise.

Parent: A minor's biological or adoptive parent.

Permission: The agreement of parent(s) or guardian(s) to the participation of their child or ward in research.

CONSIDERATIONS

1. Is inclusion of this vulnerable population in the research study appropriate?

2. Does the scientific or scholarly design of the study support inclusion of this vulnerable population?

3. Based on the age range of participants, is it likely that some participants may become adults during their study participation? If so, are appropriate procedures included to obtain adult consent from those participants?

4. Are there risks of coercion or harm to the study's participants that are related to being a minor?

5. Are participants able to give documented assent, using an age-appropriate Assent form?

6. Will the vulnerable population receive direct benefit from participating in the research?

7. Are the population-specific risks reasonable in relation to the anticipated benefits?

8. Are protections adequate to avoid coercion during recruitment and consenting of this vulnerable population?

9. Are parent(s) or guardian(s) appropriately included in the recruitment and consenting processes?

10. Are these vulnerable participants able to withdraw from the study without penalty, undue influence to remain in the study, or loss of benefits they would otherwise have?

REQUIREMENTS OF IRB REVIEW

- When reviewing research that involves minors, the IRB chair or designee will ensure that a minor representative is included in the review of the research.

- If a research study requires review at a convened meeting, the IRB Chair or designee will ensure that a minor representative is present at the meeting where the research is being reviewed.

- If the necessary expertise is not available among the membership, the IRB will use consultants to review the research and advise it, in accordance with HRPP Policy III.01 *Review of Human Subjects Research by the Institutional Review Board.*

REQUIREMENTS OF RESEARCH WITH MINORS CONDUCTED AT CVAMC

Research involving minors may not be conducted by Veterans Administration medical Center (VAMC) investigators while on official duty or at the VAMC unless a waiver has been granted by the Chief Research and Development Officer (CRADO) and criteria stipulated by the VAMC have been met.

In cases involving VAMC funded research, the UC IRB will certify to the VAMC facility CRADO that the review of research involving prisoners as research subjects has been conducted in accordance with these requirements. The research may not be conducted without the approval of the CRADO.

Further guidance may be found in the Veterans Health Administration (VHA) Handbook 1200.5, Appendix D.

DETERMINATIONS REQUIRING DOCUMENTATION

The IRB must determine that the research meets the criteria of one of the following categories of research. If it does not, the research cannot be approved.

- 45 CFR 46.404 *Research Not Involving Greater than Minimal Risk to Children*: The IRB shall determine that appropriate provisions are made for soliciting assent of the minors and permission of their parents or guardians, as set forth in §46.408.

  45 CFR 46.405 *Research Involving Greater than Minimal Risk but Presenting the Prospect of Direct Benefit to the Minor*: If the research presents greater than minimal risk to participants but has the prospect of direct benefit for the minor, the IRB may approve the research only if all of the following conditions are true.

  1. The risk is justified by the anticipated benefit to the minor.

  2. The relation of the anticipated benefit to the risk is at least as favorable to the children as that presented by available alternative approaches.

  3. The IRB shall determine that appropriate provisions are made for soliciting assent of the minors and permission of their parents or guardians, as set forth in §46.408.

  45 CFR 46.406 *Research Involving Greater than Minimal Risk and No Prospect of Direct Benefit to the Individual Child, but Likely to Yield Generalizable Knowledge about the Child's Disorder or Condition*: If the research presents greater than minimal risk to participants and does not hold out the prospect of direct benefit for the minor, the IRB may approve the research only if the IRB finds that all of the following conditions are true:

  1. The risk represents a minor increase over minimal risk;

  2. The intervention or procedure is reasonably commensurate with actual medical, dental, psychological, social, or educational situations;

  3. The intervention or procedure is likely to yield generalizable knowledge about the minors' disorder or condition which is of vital importance for the understanding or amelioration of the disorder or condition; and

  4. The IRB shall determine that appropriate provisions are made for soliciting assent of the minors and permission of their parents or guardians, as set forth in 45CFR46.408.

  45 CFR 46.407 *Research Not Otherwise Approvable, which Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Children*: When the research does not meet the requirements set forth in

the categories described above, the IRB may approve the research only if all of the following conditions are true.

1. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children.

2. If the research is federally funded, the IRB shall obtain documentation that the Secretary of the Department of Health and Human Services (HHS) has determined that the research satisfies the conditions of categories 45CFR 46.404, 45CFR46.405, or 45CFR 46.406 cited above or all of the following are true, and minors may participate in the research.

    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.

    b. The research will be conducted in accordance with sound ethical principles.

    c. The IRB shall determine that appropriate provisions are made for soliciting assent of the minors and permission of their parents or guardians, as set forth in 45CFR 46.408.

The IRB must determine the appropriate parental permission and child assent requirements for the research.

- 45CFR46.408 *Permission by Parents or Guardians and Assent by Children*

    1. Assent by Children

        The IRB shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent.

        In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate.

The assent of the children is not a necessary condition for proceeding with the research if the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that 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 children and is available only in the context of the research,.

Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accord with 45CFR46.116.

2. Permission by Parents or Guardians

   The IRB shall determine that adequate provisions are made for soliciting the permission of each child's parents or guardian. The IRB may determine that waiver of the permission requirement is appropriate under circumstances in which consent may be waived in accord with 45CFR 46.116.

   Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted under 45CFR 46.404 or 45CFR 46.405. Where research is covered by 45CFR 46.406 or 45CFR 46.407 and permission is to be obtained from parents, both parents must give their permission 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.

3. Waiver of Permission by Parents or Guardians

   If the IRB determines that parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), the IRB may determine that waiver of the permission requirement is appropriate under circumstances in which consent may be waived in accord with 45CFR 46.116. If the IRB determines that parental or guardian permission is not a reasonable requirement to protect minor subjects, the IRB shall ensure that an appropriate mechanism for protecting child participants is provided. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

The IRB shall not approve a waiver of parental or guardian permission that is inconsistent with federal, state, or local law. The IRB shall not approve a waiver of parental or guardian permission if the research is regulated by the Food and Drug Administration (FDA).

4. Documentation of Permission by Parents or Guardians

   Permission by parents or guardians shall be documented in accordance with 45CFR46.117 and HRPP Procedure 201 *Writing an Informed Consent Document for Human Subject Research*.

5. Documentation of Assent by Children

   The IRB shall determine and document that assent is a requirement for all children, some children, or no children. The IRB shall determine whether and how assent must be documented.
   Minors who are five to ten years old are usually expected by the IRB to be able to provide oral assent. A very simplified assent document may be used to guide that discussion. The IRB may require documentation of assent for some or all children in this age group.
   Minors who are eleven to seventeen years old are usually expected by the IRB to provide documented assent. A simplified version of a standard consent document may be used with children in this age group. It must be consistent with HRPP Procedure 201 *Writing an Informed Consent Document for Human Subjects Research.*

   When the IRB determines that assent is not a requirement of some children, the IRB will determine and document which children are not required to assent.

   When the IRB determines that assent is a requirement, the IRB determines whether assent will be documented and the process to document assent.

   When the IRB determines that assent is not a requirement for some or all children, the IRB determines and documents one or more of the following:
   - 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 reasonably be 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.

45CFR46.409 *Wards of the State:* The IRB must determine if minors who are wards of the state are included as research participants. The following additional protections apply to these children.

1. Children who are wards of the state can be included in research approved under 45CFR46.404 or 45CFR 46.405 without additional special protections.

2. Children who are wards of the state can be included in research approved under 45CFR46.406 or 45CFR 46.407 only if the research meets either of the following conditions.

    1. The research is related to their status as wards.

    2. The research is conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

3. If wards will be included in research approved under 45CFR46.406 or 45CFR 46.407 the IRB shall require 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. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in the best interests of the child and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

Applicable Regulations:
21 CFR 50, Subpart D
45 CFR 46.101
45 CFR 46.116
45 CFR 46.117
45 CFR 46 Subpart D

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Checklist for Principal Investigators to Complete Regarding Research Involving Children
Ohio Revised Code §2111.02
VHA Handbook 1200.5, Appendix D
HRPP Policy V.01 *Protecting Vulnerable Populations in Human Subject Research*
HRPP Policy VII.06 *Research Conducted in Jurisdictions Outside Ohio*.
HRPP Procedure 201 *Writing an Informed Consent Document for Human Subject Research*

Adoption Date:	Created by:	Date of Revision:	Revised By:	Summary of Revision:
4/2014	C. Norman			New Procedure to replace Policy V.04 (Minors) and include excerpted language from Procedure 308 regarding minors, including revisions to wording and formatting for clarity and to be consistent with other Procedures.
		09/2014	A.Braggs-Brown	Revised to reflect AAHRPP recommendations
3/2015		3/2015	J. Strasser	Revisions for clarification

Date Adopted **March 2015** **Signature** **signed copy on file**