



## RESEARCH INVOLVING CHILDREN

### 1. Overview

Federal regulations require additional protections for children involved in research. These requirements include, among other things, IRB review for some research activities involving children that would be exempt if the participants were adults, use of parental permission and child assent instead of informed consent for participation, and conditions for IRB approval of proposed research depending on the level of risk.

The purpose of this policy is to describe the additional protections that must be provided to children involved in research.

### 2. Definitions

**Assent:** Agreement to participate in research expressed by an individual (e.g., a child) who cannot provide legally effective informed consent to participate on his/her own behalf.

*Note: Failure to object does not constitute assent.*

**Child/Children:** Person(s) 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. For purposes of HRPP policy, individuals under 18 years of age are considered children in Ohio unless they meet the definition of emancipated minors.

**Emancipated Minors:** For purposes of HRPP policy, the following persons under the legal age of 18, who because of their unique circumstance have the legal rights of adults, including the right to consent to treatments or procedures involved in research:

- Persons under the age of 18 on active duty in the military
- Married persons under 18 years of age.

*Note: Pregnancy or childbirth outside of marriage does not emancipate a minor in Ohio.*

**Guardian:** An individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care. In Ohio, a guardian may be a grandparent, other family member, or other person, association, or agency other than the biological or adoptive parents who has been formally appointed as a guardian or legal representative by a court to care for a child, including to consent on behalf of a child to general medical care. *Note: Grandparents or other family members who are not formally appointed as guardians or legal representatives by a court generally do not have the authority to provide consent on behalf of a child without consent by the child's parents.*

**Parent:** A child's biological or adoptive mother or biological or adoptive father.

**Permission:** The agreement of a parent(s) or legal guardian to the participation of his/her child or ward in research.



### 3. General Information

- A. To approve research involving children, the IRB must determine that the proposed research provides the special protections for children specified by federal regulations and this policy, in addition to meeting the criteria for approval of all human subjects research described by HRPP policy [[Review of Research by the Convened IRB](#)].
- B. One or both parents (or a guardian) must provide and document permission for a child to participate in research, unless these requirements are waived by the IRB. In most cases, children capable of assent must also express their willingness to participate. For more information on the requirements for permission of parents (or guardians) and assent of children, see HRPP policy [[Assent and Parental Permission](#)].
- C. The exemption in DHHS regulations for research involving survey or interview procedures or observation of public behavior (Category 2) does not apply to research with children, except for research involving educational tests or observations of public behavior when the investigator does not participate in the activities being observed. For more information on exempt research, see HRPP policy [[Exempt Research](#)].
- D. If the research involves incarcerated and/or pregnant children, the requirements for research involving prisoners and/or pregnant women, respectively, must be met in addition to the requirements for research involving children. For more information, see HRPP policies [[Research Involving Prisoners](#)] and [[Research Involving Pregnant Women, Fetuses, or Neonates](#)].
- E. When a child who was enrolled in research with parental or guardian permission reaches the legal age of consent, he/she must provide informed consent (unless waived) to continue study participation. For more information, see HRPP policy [[Assent and Parental Permission](#)].
- F. In certain situations, children under 18 years of age may legally provide informed consent for some or all of the activities involved in research (e.g., to release information from education records). For more information on special circumstances involving assent and parental permission, see HRPP policy [[Assent and Parental Permission](#)].

### 4. Permissible Categories of Research

- A. Three categories of research involving children may be approved by the IRB. These categories differ according to the level of risk involved, prospect of direct benefit to participants, and anticipated research findings. For all categories, the proposed research must satisfy the requirements for parental or guardian permission and child assent described by HRPP policy [[Assent and Parental Permission](#)].
- B. The following are the categories of research that may involve children and any additional conditions that must be met for approval:
  - 1. Research involving not greater than minimal risk
  - 2. Research involving greater than minimal risk, but presenting the prospect of direct benefit
    - The risk is justified by the anticipated benefit to the child



- Comparison of the risk to the anticipated benefit is at least as favorable as that presented by available alternative approaches
3. Research involving greater than minimal risk without the prospect of direct benefit, but likely to yield generalizable knowledge about the child's disorder or condition
- The risk presents no more than a minor increase over minimal risk
  - The research involves experiences that are reasonably equivalent to those in the child's actual (or expected) medical, dental, psychological, social, or educational situations
  - The research is likely to yield generalizable knowledge about the child's disorder or condition that is of critical importance for the understanding or improvement of the disorder/condition
- C. Research that does not fall into one of the three categories above, but presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children requires additional review, as described below.
- 5. Research Subject to DHHS Regulations Requiring Additional Review ("407 Review")**
- A. Additional requirements apply for research involving children that is conducted or supported by DHHS and that does not fall into one of the three categories of approvable research described above. The research may be conducted only under all of the following conditions:
- The IRB finds and documents that 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 is reviewed by OHRP (on behalf of DHHS), in consultation with a panel of experts in pertinent disciplines (e.g., science, medicine, education, ethics, law, etc.) and relevant child advocates
  - An opportunity is provided for public review and comment (including a public meeting announced in the *Federal Register*)
  - The Assistant Secretary for Health (on behalf of the Secretary) will determine either:
    - The research satisfies the regulatory conditions for approval
    - The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; will be conducted in accordance with sound ethical principles; and that adequate provisions will be made for soliciting the assent of children and the permission of their parents or guardians
- B. Upon IRB approval, ORRP staff will forward the "407 review request" to OHRP. The following information should be included:
- Institution name and OHRP Federal-wide Assurance (FWA) number
  - IRB name and registration number



- Institutional contact's name, title, telephone and fax numbers, mailing address, and email address
  - IRB documentation that the proposed research does not meet the regulatory requirements for approval but presents a reasonable opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children
  - Title of protocol and name of principal investigator
  - Most current version of protocol reviewed by the IRB (modified by the principal investigator if required by the IRB)
  - DHHS application number and name of funding agency
  - Relevant grant application or proposal
  - Most current version of parental permission/assent documents reviewed by the IRB (modified by the principal investigator if required by the IRB)
  - Relevant IRB minutes and correspondence
- C. When FDA regulations also apply to the research, OHRP delegates its authority to FDA to convene a panel of experts (i.e., FDA Pediatric Advisory Committee, Pediatrics Ethics Subcommittee) to review the research, solicit public comment, and advise the Secretary (DHHS).
- D. For more information on the 407 review process, see [OHRP Guidance on the DHHS 45 CFR 46.407 \("407"\) Review Process](#).

## 6. Research Not Subject to DHHS Regulations Requiring Additional Review

Research involving children that does not fall into one of the three categories of approvable research described above (see "Permissible Categories of Research") and that is not subject to DHHS regulations may be conducted under all of the following conditions:

- The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children
- Consultation is obtained, as necessary, from expert(s) in pertinent disciplines (e.g., science, medicine, education, ethics, law, etc.) and relevant child advocates
- An opportunity is provided for review and comment by the local community where the research is to be conducted
- The Institutional Official, in consultation with the above groups, determines that the research is consistent with sound ethical principles and the requirements of HRPP policy regarding assent and parental permission and may proceed

The principal investigator and any consultants assisting with the review will be invited to attend the IRB meeting at which the research is discussed.

## 7. Wards

As described below, specific protections are required for children who are also wards of the state or any other agency, institution, or entity.



- A.** Children who are wards may be included in research involving greater than minimal risk without the prospect of direct benefit but likely to yield generalizable knowledge about the child's disorder or condition if the research is either:
- Related to their status as wards
  - Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as participants are not wards
- B.** When wards are included in the research described above, an advocate must be appointed for each child who is a ward to protect the child, to the extent possible, from exploitation, coercion, or undue influence. The following requirements apply to individuals serving as advocates:
- The advocate will serve in addition to any other individual acting on behalf of the child as a guardian or *in loco parentis*
  - An individual may serve as an advocate for more than one child
  - The advocate must be an individual who has the background/experience and agrees to act in the best interests of the child throughout the child's participation in the research
    - This includes helping to ensure that the child understands what will be required of him/her during the research, and if capable, that the child provides assent to participate
    - Acting in the best interests of the child could also include evaluating the ongoing effect(s) of the research on the child
  - The advocate must not be associated in any way (except in the role as an advocate or IRB member) with the research, investigator(s), or guardian organization
- C.** Examples of individuals who might serve as advocates are IRB members, patient advocates, caseworkers, social workers, or counselors knowledgeable about children's rights and welfare. An advocate's appointment should be made by a group or individual with no interest in or affiliation with the research being conducted. The IRB should review and approve the process for appointing advocates.

## 8. Documentation

Protocol-specific findings related to the additional protections required for research involving children will be documented according to the HRPP policies [\[IRB Recordkeeping\]](#) and [\[Expedited Review Procedures\]](#).

## 9. Additional Information on Inclusion of Children in Research

- A.** For more information on NIH requirements for inclusion of children in research, see [NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects](#) and [NIH Inclusion of Children Policy Implementation](#).
- B.** For more information on the "407 review process" for DHHS-conducted or supported research involving children, see [OHRP Guidance on the DHHS 45 CFR 46.407 \("407"\) Review Process](#).

**10. Applicable Regulations/Guidance**

21 CFR 50.50, 21 CFR 50.51, 21 CFR 50.52, 21 CFR 50.53, 21 CFR 50.54, 21 CFR 50.55, 21 CFR 50.56, 45 CFR 46.401, 45 CFR 46.402, 45 CFR 46.403, 45 CFR 46.404, 45 CFR 46.405, 45 CFR 46.406, 45 CFR 46.407, 45 CFR 46.408, 45 CFR 46.409, NIH "Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects" (03/06/98, updated 10/13/15), OHRP "Research With Children FAQs," OHRP "Special Protections for Children as Research Subjects: Children Involved as Subjects in Research: Guidance on the HHS 45 CFR 46.407 ("407") Review Process" (05/26/05)

**11. History**

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