University of Toledo
Social, Behavioral and Educational IRB
Information for Research Involving Children as Research Subjects[1]

There are special requirements for research involving children that are found in Subpart D of the HHS regulations for the protection of human subjects in research. These regulations provide additional protection for research participants who are under 18 years of age. All University of Toledo Related Research[2] that involves individuals less than 18 years of age must apply these protections. If a research participant reaches 18 years of age while the research is ongoing (including data analysis), the participant must be re-consented under the standard adult informed consent process. The purpose of this document is to highlight the requirements of Subpart D.

Definitions – Federal Regulations 45 CFR 46.402

"Assent" means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

"Children" are 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. In Ohio, legal age for consent is eighteen years old.

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

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

"Parent" means a child's biological or adoptive parent.

Investigator Responsibilities When Conducting Human Research Involving Children

Investigators involving children in research must comply with the requirements in Subpart D, as well as the Common Rule/Subpart A, other applicable subparts (e.g. Subpart B for pregnant participants and Subpart C for incarcerated participants), and University of Toledo DHRP Policies and Procedures.

- Obtain permission of one or both parents, based on federal requirements. Permission must be documented with the parent(s) signature on a written permission form that contains all elements of the standard adult informed consent form.
- Obtain the assent of the child. Document the assent, and obtain written signed assent when required by the IRB (generally a signature is required for older children).
- Understand the categories of research involving children that an IRB may approve.

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[1] Biomedical research involving children is reviewed by the St. Vincent Mercy Medical Center's Pediatric IRB pursuant to a written IRB agreement. The Pediatric IRB has the required expertise to review biomedical research involving children. A representative from UT serves as a community member on the Pediatric IRB.

[2] Defined in the UT DHRP Policies and Procedures – ***UT Related Research*** means research carried out on- or off-campus (including other states or countries) by UT faculty, students, or other employees, and any studies conducted by any investigator using UT facilities and/or UTMC patients as subjects, including patient records, biological samples, or surveys.

Institutional Review Board Responsibilities

In addition to other responsibilities assigned to the IRB under federal regulations and University policies, the IRB shall only approve research that satisfies the additional protections for child research participants. **[§ 46.403 IRB duties; UT DHRP Policy]**

- Requiring IRB review of some research activities involving children that would be exempt if research subjects were adults (e.g. observation with investigator participation, surveys or interviews).
- Require parental permission and child assent [46.408] instead of the usual informed consent process used for adults.
- 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. The IRB shall take into account the ages, maturity, and psychological state of the children involved.
- Consider whether written, signed assent only oral assent is appropriate considering the age and characteristics of the proposed participants.
- Understand and apply the conditions for IRB approval of proposed research involving children, utilizing the three categories of approvable research depending on the level of risk and other specified features of the research.
- Apply additional conditions to children who are wards of the State or any other agency. These conditions limit the kind of research activities in which children who are wards can participate, and require the appointment of an advocate to act in the best interests of the child.

Categories of Research Involving Children That May Be Approved By The IRB

1. The IRB finds that the risks of the research are ***no more than minimal***.
2. The IRB finds that:
    - ***more than minimal risk*** to children is presented:
        a. by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or
        b. by a monitoring procedure that is likely to contribute to the subject's well-being;
    - the risk is justified by the anticipated benefit to the subjects; and,
    - the relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches.
3. The IRB finds that:
    - more than minimal risk to children is presented:
        a. by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or
        b. by a monitoring procedure that is not likely to contribute to the well being of the child;
    - the risk represents ***a minor increase over minimal risk***;
    - 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; and,
    - the intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition.

Parental Permission In The Context of Research Involving Children

By definition, children are unable to provide informed consent to participate in research, although they might be able to give their assent. The IRB should determine that unless parental permission can be waived adequate provisions are made for soliciting the permission of the parent(s) or legal guardian(s). The regulations define "permission" at 46.402(c) as the "agreement of parent(s) or guardian to the participation of their child or ward in research." The term "parent" means a "child's biological or adoptive parent." The term "guardian" means "an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care."

Waiver of Parental Permission – Limited Circumstances

The Institutional Review Board (IRB) may waive the requirements for obtaining parental or guardian permission if it makes and documents the findings under either 45 CFR 46.116(c) or (d).

In addition to the provisions for waiver contained in 46.116(c) and (d), if the IRB determines that a research protocol is designed to study conditions in children or a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the parental permission requirements provided that an appropriate mechanism is in place to protect the children, and provided that the waiver is not inconsistent with federal, state, or local law (45 CFR 46.408(c)). The choice of an appropriate substitute mechanism (for example, appointing a child advocate or an assent monitor) for protecting children participating in research would depend on the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and the child's age, maturity, status, and condition (45 CFR 46.408(c)).

Additional Guidance

The Office for Human Research Protections provides guidance on its regulations related to research involving children. Please go to the OHRP website for the most up to date guidance:

1. Frequently Asked Questions – Research Involving Children: http://www.hhs.gov/ohrp/researchfaq.html

2. Special Protections for Children as Research Subjects: http://www.hhs.gov/ohrp/children

University of Toledo researchers, research staff, IRB members, IRB staff and research participants may contact the Director of Regulatory Compliance at 419-383-6903 for additional questions related to research involving children.