

**University of South Alabama
Institutional Review Board
GUIDELINES FOR RESEARCH INVOLVING CHILDREN**

General Information:

Children are considered a vulnerable research population as their emotional and intellectual capacities are limited and they are legally incompetent to give valid consent. Therefore, special additional protections are required by the federal regulations for the review of research studies involving children. The Department of Health and Human Services and FDA have regulations governing the conduct of research involving children. These regulations are cited as DHHS 45 CFR 46 Subpart D and FDA 21 CFR Part 50 Subpart D, respectively.

If a proposed research study involves minors, the principal investigator should first consider four issues:

- What is the rationale for including minors? This information should be incorporated in the IRB protocol application in the section entitled “Relevant Background and Rationale for the Research”. (e.g., what unique outcomes/benefits/risks will come from studying minors?)
- Determine the study risk level by identifying what permissible category of research your study meets in order to approve the research. Permissible categories of approval are directly derived from the Subpart D regulations.
- How are study procedures different from standard of care for the subjects?
- What are consent (e.g., parental permission and assent) requirements for the study?

Age of Majority:

Under Alabama law (Ala. [Code 26-1-1](#)), a minor is a person younger than 19 years old, unless such a person has been emancipated. A person who is 18 years old and is either married or widowed is automatically emancipated. Further, Alabama law permits a person who is 18 years of age or older to consent to participate in research conducted by a college or university that is accredited by a federally recognized accrediting agency if the research has been approved by the Institutional Review Board of the institution. While Alabama law permits adolescents to consent to “medical” treatment, if they are (1) 14 years of age or older; (2) have graduated from high school; (3) are married or divorced; or (4) are pregnant, there is no statute addressing their capacity to consent to procedures purely for research purposes (i.e., where no “treatment” is involved).

Submission Requirements:

The IRB protocol application should provide sufficient detail in the research plan so that the IRB can make the determinations as outlined in Subpart D of the regulations. In addition, applications submitted to the IRB involving minors should include the application supplement entitled “Investigator Checklist for Research Involving Children”.

IRB Review of Research Involving Children – Determinations:

Federal regulations classify permissible research involving minors into four categories, based on degree of risk and type of prospective benefit. These categories are described in relation to “minimal risk.”

Minimal risk is defined as “the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves from those ordinarily encountered in daily life of during the performance of routine physical or psychological examination or tests.

Greater than minimal risk is a term used in defining Category 2 [45 CFR 46.405] and Category 3 [35 CFR 46.406]. The regulations do not provide any further definition or clarification of this term except for specifying “a minor increase over minimal risk” in regards to Category 3 only. Therefore, the protocol application should clearly describe the study risks so the IRB, in consultation with the investigator’s assessment, make an appropriate determination for category of approval.

** Permitted Categories for Research with Minors, including Conditions **

Research Category 1: Not greater than minimal risk
(46.404 and 50.51)

Requires: 1. Permission from ONE parent/legal guardian
 2. Assent of minor (if child is 7 years of age or older)
Type of Review: Expedited review by IRB

Research Category 2: Greater than minimal risk, but prospect of direct benefit to subject
(46.405 and 50.52)

Requires: 1. Permission of ONE parent/legal guardian
 2. Assent of minor (if child is 7 years of age or older)
 3. Risk be justified by anticipated benefit
 4. Relation of the benefit to the risk is at least favorable to the subjects as that
 presented by available alternative approaches
Type of Review: Full Board

Research Category 3: Greater than minimal risk, no prospect of direct benefit to subject, but likely to
(46.406 and 50.53) yield generalizable knowledge about the subjects disorder or condition

Requires: 1. Permission of BOTH parents/legal guardian, unless one parent is deceased,
 unknown, incompetent, not reasonably available, or done not have legal
 responsibility for the custody of the minor
 2. Assent of minor (if child is 7 years of age or older)
 3. Risk represents a minor increase over minimal risk
 4. The intervention or procedure experiences to the subjects that are reasonably
 commensurate with those inherent to their actual or expected situations
 5. The procedure is likely yield generalizable knowledge about the subject’s
 disorder or condition which is of vital importance for understanding the
 subject’s disorder
Review Type: Full Board

Research Category 4: Research not otherwise approvable which presents an opportunity to
understand, prevent or
(46.407 and 50.54) alleviate a serious problem affecting the health or welfare of children

Requires: 1. IRB finds the research presents a reasonable opportunity to further the

- understanding, prevention, or
alleviation of a serious problem
- 2. Review by the DHSS Secretary and FDA Commission after consultation with a panel of experts and public comment

IRB review of research with Wards of the State

1. May children who are in foster care or “court custody” participate in research?

Federal regulations and institutional policies do not prohibit children who are “wards of the state or any other agency, institution, or entity” from research participation. However, permission must be obtained from the legal guardian which is usually the agency or court, not a foster parent. In most cases, an agency supervisor or court officer, not a caseworker, must sign the permission/assent form.

The IRB must find that the research meets the following stipulations:

1. That the research is related to their status as wards - OR –
2. That the research is conducted in schools, hospitals, or similar settings in which majority of children involved are NOT wards

Additional protections: An Advocate must be appointed for each child.

Advocate:

1. Serves in addition to guardian
2. May serve for more than one child
3. Must have background and expertise and serve throughout the study
4. Must be independent of the research, investigator or organization

Parental Permission/Assent from Children:

The American Academy of Pediatrics indicates that a child with the cognitive age of seven is capable of assenting to research. The USA IRB has adopted this as our institutional guideline as well. In circumstances where there is a disparity between cognitive age and chronological age, the investigator must document in the medical record his or her rationale for obtaining or not obtaining child assent. Notation may also be made on the permission/assent form. The USA IRB guidelines for obtaining research permission/assent from minors are specified below:

1. In most cases, parental consent must be obtained if the research involves minors under the age of 18. The requirement for parental consent may be inappropriate in some cases such as research on child abuse.
2. Minors 6 years of age or younger, verbal or written assent is typically not required. Consent is based on the permission of the parent(s)/guardian(s) and no assent is required. A brief verbal explanation of the research procedure should be explained to the child.
3. Minors 7 years or older should be involved in the decision to participate in a research projects unless: a) the subject is not capable or mentally/emotionally, of being consulted, b) the IRB specifically waives the requirement.
4. It is highly encouraged that a separate written assent form be used for children age 7 -12 years

old to document assent. In general, it should briefly explain in basic terms:

- they are being asked to participate in a research study;
 - the purpose of the study;
 - an estimate of how much time is involved in participating;
 - what will happen to them if they agree to participate (e.g., ‘draw some blood’);
 - foreseeable risks/discomfort and any benefits they may experience;
 - they should ask their parents and doctor/researcher any questions they have about participation;
 - participation is voluntary and they can withdraw at any time
5. Typically, adolescents 13-18 years old should be fully informed about a study and give assent to their own participation in the research. In the instance, both the adolescent and the parents(s)/guardian(s) sign the form, with a signature line for the adolescent first. The signature line for parental consent/permission should follow.
6. NOTE: Assent expires when a child becomes an adult. At that time the participant must sign the IRB approved adult consent for the research study.

Federal regulations do not provide specific information on parental permission/child assent. However, they do provide parental permission requirements. In addition, they also charge 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 taking into account the ages, maturity, and psychological state of the children involved” [45 CFR 46.408]

Request for Waiver of Assent (45 CFR 46.408 and 46.116, Subpart A)

There are three circumstances in which the IRB may waive assent for children to be enrolled in a research study. This judgment may be made for all children participating in the study, or for each child, as the IRB deems appropriate. **The investigator must request and justify a waiver of assent. This can be achieved by completing the Investigator Checklist for Research Involving Children.**

- When the ability of a child to understand some or all of the study is so limited that he or she cannot reasonably comprehend it because of age, maturity, or mental state.
- When it is evident that the intervention/procedure involved in the research shows 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.
- When the intervention/procedure involved in the research shows a prospect of direct benefit to the child and the protocol has a risk level similar to standard treatment.

If enrolling children in studies in which assent has been waived by the IRB, an information sheet written at the age appropriate level for the child, may be useful in informing the child about the study. The information sheet needs to be approved by the IRB.

Waiver of assent for research protocols are documented in the IRB minutes and listed on the IRB approval.

Safety Monitoring

The American Academy of Pediatrics emphasizes ethical responsibilities regarding the conduct of drug trials with children. A safety plan should be implemented phase 1 and 2 drug trials without a Data Safety Monitoring Committee (DSMC). For phase 3 drug trials a DSMC is recommended if not required by the FDA. Data monitoring mechanisms helps to ensure studies can be rapidly terminated if an unexpected hazard is identified.

Further Information:

For additional information contact the Office of Research Compliance and Assurance at (251) 460-6225 or email dlayton@southalabama.edu