



UNIVERSITY OF  
SOUTH ALABAMA

**IRB SOP 703**  
**Informed Consent: Research Involving Children**

**Purpose**

This Standard Operating Procedure (SOP) document outlines ethical and regulatory considerations involving children involving in human subject's research. This SOP complements *SOP 702: Informed Consent Documentation*, which should be used in conjunction with this SOP.

**Scope**

This SOP applies to all research involving children, regardless of funding source under the auspices of the University of South Alabama.

**Applicability**

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. 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).

**Definitions**

**Assent:** Agreement by an individual not competent to give legally valid informed consent (e.g., a child or cognitively impaired person) to participate in research. An assent is typically paired with permission from a parent or guardian, and together they comprise the informed consent to participate.

**Child:** An individual who meets the federal definition of “children” based on state law that defines the legal age to consent to the treatments or procedures.

**Guardian:** Under federal law, "guardian" means an individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care.

**Legally authorized representative (LAR):** an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research.

**Minor:** Refers to individuals who under state law meet the state law definition of “minor”.

**Parent:** A child’s biological or adoptive parent.

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

## Policy

Children (minors) are considered a vulnerable research population and, as such, require additional protections when they are potential research participants. Subpart D of both 45 CFR 46 (DHHS) and 21 CFR 50 (FDA) require certain additional protections for children involved as participants in research. These regulations require that adequate provisions be made for soliciting the assent of all children involved in research, when the children are capable of providing assent, and obtaining parental/legally authorized representative/guardian’s permission, as applicable. In determining whether children are capable of assenting, the ages, maturity and psychological state of the children should be taken into account.

### 1.0 Permitted Categories for Research with Children

As per U.S. Federal regulations (45 CFR 46 and 21 CFR 50, Subpart D), permissible research involving children are limited to those activities that meet one of four categories, based on the level of risk and potential for benefit to the individual participant. These categories are:

1. Research not involving greater than minimal risk (§46.404 and §50.51);
2. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual participants (§46.405 and §50.52);
3. Research that involves more than minimal risk and presents the prospect of no direct benefit to individual participants, but generalizable knowledge (societal benefit) (§46.406 and §50.53); or
4. Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (§46.407 and §50.54)

<b>Risk Determination</b>	<b>Benefit Assessment</b>	<b>IRB Action</b>
Minimal risk	With/without direct benefit	Approvable
Greater than minimal risk	Potential benefit to child	Approvable
Greater than minimal risk*	No direct benefit to individual, but offers general knowledge about child's condition or disorder	Approvable case-by-case
Greater than minimal risk**	No direct benefit to child, but other potential to, "understand, prevent, or alleviate a serious problem affecting the health and welfare of children	Proposed research must be considered by appropriate federal agency.
	For research involving no direct benefit or otherwise not approvable	Children who are wards of State may only be included if the research is related to their status as wards. IRB shall appoint advocate for child who is independent of research.
<p><i>* Both parents or legally appointed guardian must give consent unless one parent or guardian is deceased, incompetent or <b>not reasonably available</b>. NOTE: A parent who is "not reasonably available" is one who cannot be contacted by phone, email, mail or fax. If a parent is at work, traveling, or caring for other children, or even lives in another city/state, it is the investigator's responsibility to attempt to obtain that parent's permission before enrolling the child in research.</i></p>		
<p><i>** If IRB finds reasonable benefit assessment, the research must be considered by the Secretary of DHHS and/or FDA in consultation with a panel of experts and the opportunity for public comment.</i></p>		

The IRB will also consider the extent to which research procedures would be a burden to any child, regardless of whether the child is accustomed to the proposed procedures.

## 2.0 Assent By Minors

Children (minors) are a vulnerable research population and, as such, require additional protections when they are potential research subjects. Subpart D of both 45 CFR 46 (DHHS), and 21 CFR 50 (FDA) require certain additional protections for children involved as subjects in research. The requirements of Subpart D apply to all non-exempt research involving children conducted under the auspices of University of South Alabama. The

regulations require that adequate provisions be made for soliciting the assent of all children involved in research, when the children are capable of providing assent.

The IRB may approve research involving children only if special provisions are met. In general, children should be given developmentally appropriate information about a research study in a language and manner that is understandable to them, given their age, maturity, and cognitive abilities.

The IRB must classify research involving children into one of four categories and document their discussions of the risks and benefits of the research study. The four categories of research involving children that may be approved by the IRB are based on degree of risk and benefit to individual participants.

The USA IRB approves research involving children by following the *“Investigator Checklist for Research Involving Children”*.

### **3.0 Parental Permission**

Unless otherwise provided by state law, or unless this requirement is waived by the IRB pursuant to 45 CFR 46.408(c), the permission of the parent or legal guardian is required in order for minors to participate in research. Where research is covered by 45 CFR 46.406 and 46.407, permission is to be obtained from both parents 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.

Per 45 CFR 46.408(c), in addition to the normal waiver requirements, the IRB may waive the parental permission requirement if it determines that a research protocol designed for conditions or a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects. This waiver might apply to studies involving neglected or abused children, or older adolescents presenting in medical situations wherein a parental consent requirement might deter the child from seeking needed care (e.g., seeking care at an STD clinic). The IRB will not waive the requirement to obtain parent or guardian permission based on the above-stated criterion if the research study is subject to FDA regulations (21 CFR Parts 50 and 56) governing human subject protections (i.e., the research study involves an evaluation of any article regulated by the FDA).

If parental permission is waived, the IRB must be sure that an appropriate mechanism for protecting the children is substituted. The choice of an appropriate mechanism would depend on the nature and purpose of activities in the protocol, the risk and benefit to the subject, and their age, maturity, status, and condition.

#### 4.0 Children Who Reach the Legal Age of Consent While Enrolled in a Study

Informed consent is an ongoing process throughout the duration of a research study. When a child who was enrolled in research with parental/LAR/guardian permission reaches the legal age of consent, the participant's participation no longer requires parental/LAR/guardian permission. Informed consent must then be obtained from the now-adult participant to continue research participation, unless the IRB determines that the requirements for obtaining informed consent can be waived.

#### 5.0 Parent Signature Requirements

Parental, guardian, or Legally Authorized Representative signature is required for any study in which a minor is the subject population unless otherwise stated by the IRB. The requirement for one versus two parental signatures is determined by the IRB.

When your study is...	Then this is required...
Minimal Risk	One parent/legal guardian may be sufficient
Greater than Minimal Risk, Direct Benefit to participant	One parent/legal guardian may be sufficient but the IRB must determine whether one or two is required
Greater than Minimal Risk, No Direct Benefit to participate, but likely to yield generalizable knowledge about the participant's condition	Both parents/legal guardians, unless one parent is deceased, unknown, incompetent, not reasonably available, or does not have legal responsibility for the custody of the child
Greater than Minimal Risk, No Direct Benefit to participant, but results may alleviate serious problems of children's health or welfare	Both parents/legal guardians, unless one parent is deceased, unknown, incompetent, not reasonably available, or does not have legal responsibility for the custody of the child

### Procedures

#### 1.0 Investigator Responsibilities

- 1.1 The Investigator submits an initial IRB application including the explanation for including children in the selection of participant section.
- 1.2 Plans should be described regarding if and how assent will be obtained and documented for IRB review and approval.
- 1.3 An Investigator must take into account the ages, maturity, and psychological state of the children involved when planning methods to obtain and document assent. The USA IRB recommends the following:

- 1.3.1 Parental permission utilizing an informed consent document;
- 1.3.2 **Ages less than 7 years**: An oral script in very simple language appropriate for children less than 7 years of age. The oral assent script should be conversational and stated in such a way that is understandable and age-appropriate.
- 1.3.3 **Ages 7 to 11 years**: This age group should be fully informed about the research, using language appropriate to their age and maturity, and assent should be obtained from those deemed capable of making a meaningful decision; and
- 1.3.4 **Ages 12 to 18 years**: Children in this age group should be fully informed about the research and documented assent should be obtained. The child may either sign his/her own Assent Form or may verbally assent to participate in the study, but in either case, the information provided to the subject should be appropriate to the individual's age, maturity and developmental abilities. An assent form which may be in the same language as the adult consent document. 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.

1.3.4.1 Assent form should include:

- why the research is being conducted;
- what will happen and for how long or how often;
- that it's the child's decision to participate and that it's okay to say no;
- explanation if it will hurt and if so for how long and how often;
- what the child's other choices are;
- description of any good things that might happen;
- whether there is any compensation for participating; and
- ask for questions.

- 1.4 An Investigator should not solicit a child's assent without intending to take his or her wishes seriously. In situations where the potential benefits of the study are such that the physicians and parents will enroll the child regardless of the child's wishes, the child should simply be told what is planned and should not be deceived. In such cases, the Investigator should request a waiver for assent from the IRB before enrolling the child.
- 1.5 Assent expires when a child becomes an adult. At that time, the subject must sign the IRB approved adult consent for the research study.

## 2.0 IRB Responsibilities

The IRB shall take care in approving research where the child is suffering from a life-threatening illness with little real chance of therapeutic benefit from the research. The IRB shall be cautious in allowing the parents to overrule the child's dissent where experimental therapy has little or no reasonable expectation of benefit.

- 2.1 The IRB reviews the degree of risk and discomfort involved in the research in relation to the direct benefits it offers to the child before it can determine whether or not the IRB will approve the study.
- 2.2 When determining whether children are capable of assenting, the IRB shall take into account the age, maturity, and psychological state of the children targeted for the study population. This determination may apply to all children involved in the study, or on a case-by-case basis, as deemed necessary by the IRB.
- 2.3 The IRB determines the appropriate ages for assent and the method of documentation of assent.
- 2.4 The IRB must assure that special protections afforded to children found in 45 CFR 46, Subpart D have been met for this subject population. The IRB documents this review on the IRB Reviewer Form completed by the designated IRB member.
  - 2.4.1 Although the IRB may determine that subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accord with 45 CFR 46.116
- 2.5 The IRB membership includes experts in pediatrics or field of profession involving work with children. When the IRB renders its determination, it will include:
  - 2.5.1 The children's category and corresponding rationale under which the proposed research qualifies (e.g., 45 CFR 46.404-46.407); and
  - 2.5.2 Adequate provisions for obtaining assent and dissent from the children and how such assent and dissent will be documented. If assent and dissent is waived by the IRB, the rationale for such determination must be provided.
  - 2.5.3 Federally-funded studies determined by the IRB to meet 45 CFR 46.407 for children, will be given a "pending approval" status until a determination by the Secretary of the Department of Health and Human Services (DHHS) is received. The Office of Research Compliance will be notified when the IRB determines a study is determined to meet 45 CFR 46.407. Documentation sent to the Secretary include:

- IRB minutes from the convened meeting documenting the IRB findings;
- The complete IRB application and informed consent documents;
- The relevant protocol and/or grant application; and
- Any supporting material including the Investigator's Brochure, if applicable.

2.5.4 If DHHS Office of Research Protections (OHRP) grants approval under Category 46.407, then the IRB may grant final approval.

2.5.5 If OHRP requires changes in the process of approval, or any other changes are made after the IRB "approved pending" modifications, an amendment must be submitted for review and approved by the IRB Chair or his or her designee, unless the IRB Chair determines the changes submitted are major, which require IRB at a convened meeting.

2.6 When children as wards of the State are involved in research under 45 CFR 46.407, the required additional individual acting on behalf of the child as guardian or *in loco parentis* may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interest of the child for the duration of the child's participation in the research and who is not associated in any way with the Investigators, or the guardian organization.

### **Regulated Documents:**

45 CFR 46.116  
45 CFR 46 Subpart D  
45 CFR 46.404-46.407  
21 CFR

### **University Related Documents:**

[SOP 701: Informed Consent](#)  
[SOP 702: Consent Documentation](#)

### **Related Forms:**

[Investigator Checklist for Research Involving Children](#)

### **History:**

Effective Date: January 2019  
Revisions:

### **Responsible Office:**

Office of Research Compliance and Assurance