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 and SOP 901: Research Involving Children*, which should be used in conjecture 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: A child's affirmative agreement to participant in research. Mere failure to object should not, absent affirmative agreement, be construed as assent. An assent is typically paired with permission from a parent or guardian, and together they comprise the informed consent to participate.

Child: Persons who have not attained the legal age for consent to treatments or procedures involved in research and clinical investigations under the applicable law of the jurisdiction in which the research will be conducted. Children are a vulnerable population [45 CFR §46.602 (a)] [21 CFR§50.3]

Guardian: is an individual who is authorized under applicable state or local law to exercise the powers and responsibilities of a parent regarding the minor's health, support, education, or maintenance and to consent to the general medical care of the minor.

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: The legal age for consent is termed the age of majority and is a function of state law, not federal law. Individuals who have not attained the age of majority are termed ***minors***. Under Alabama law, a minor is a person younger than 18 years old, unless such a person has been emancipated.

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 Process of Consent/Assent

Children cannot legally give consent on their own behalf. The consent (permission) of one or both of their parent(s) or legal guardian(s) is, therefore, required before they can participate in any *non-exempt* (and some *exempt)* research projects unless waived by the IRB under the provisions of Health and Human Services regulations at 45 CFR §46.116(d).

1.1 The IRB will make a determination whether permission of one or both parents is required for research approvable under 45 CFR §46.404 or §46.405.

1.1.1 If the research involves activities that are *no more than minimal risk,* consent of only one parent must be obtained.

1.1.2 If the research involves *greater than minimal risk but presents the prospect of direct benefit* to the individual participants, consent of only one parent may be obtained.

1.1.3 If the research involves *greater than minimal risk and no prospect of direct benefit to individual participants,* consent of both parents must be obtained unless one parent is deceased, unknown, incompetent, or not reasonably available. Consent of both parents is not required, however, when only one parent has the legal responsibility for the care and custody of the child.

2.0 Consent of a Mature Minor

A minor may, with IRB approval, legally consent on his/her own behalf when he/she does not meet the DHHS definition of "child." In Alabama, if a participant over the age of 18 is legally declared emancipated, he/she may consent to participate in research because the individual no longer meets the DHHS definition of a child; therefore, Subpart D does not apply.

3.0 Assent of Children

In addition to obtaining of parental/legal guardian consent (permission), the investigator must also solicit assent of minor participant age 7 years or older, unless the participant displays intellectual or emotional development below that of the average 7-year-old child.

Obtainment of assent shows respect for a child's developing autonomy. In most circumstances (non-therapeutic research), a child's deliberate objection should be regarded as a veto to his/her involvement in the research.

For research conducted in educational settings the IRB may approve a waiver of consent for children as old as 12 years old.

Assent may be waived if its pursuit may require comprehension of fine distinctions between the required behaviors. For example, data is collected in the classroom. The behavior/work/participation is required and assent is being sought to use the data above and beyond its original purpose (for research not just for as an educational practice). The waiver is associated with a protocol that involves no more than minimal risk

Assent serves to provide information to the child and to allow the child to dissent. With these purposes in mind, the following points should be considered when writing the *Assent Form.* In deciding whether to seek assent, the minor's age is an important

criterion, but intellectual and emotional development also need be considered. The child must be able to identify the benefits and risks of the research, and to be able to reason about the consequences of participation as well as a typical 7 year old. A valuable function of seeking assent from the minor is to provide information that the minor and his/her parents may use in their decisions concerning the research.

In seeking assent, undue advantage should not be taken of the child's developmental limitations related to his/her voluntariness (acquiescence to authority figures and any lack of ability to express his/her rights).

4.0 Dissent of Children

Dissent from participation or withdrawal from research is always to be honored unless the protocol affords access to a therapeutic intervention that is not otherwise available. In that case, parental consent for therapeutic intervention may override a child's dissent. However, that information must be provided to the child prior to the intervention procedure.

5.0 Waiver of Assent

Parents or guardians may, with IRB approval, override a young child's objections to interventions that hold the prospect of direct benefit to the child in accordance with 45 CFR §46.408(a). Assent may also be waived by the IRB under 45 CFR §46.116(d).

6.0 Wards

Health and Human Services regulations at 45 CFR §46.408 set specific requirements for children who have been declared wards of the state or any other agency, institution, or entity.

1. Wards can participate in research approved under §46.406 or § 46.407 if:
    a) The research is related to their status as a ward.
    b) The research is conducted in schools, camps, hospitals, institutions, or similar settings where the majority of children involved in research are not wards.

2. The IRB will require appointment of an advocate for each child who is a ward.
    a) The advocate serves in addition to any other individual acting on behalf of the child as a guardian or in the absence of the parent(s).
    b) The advocate may represent more than one child.
    c) The advocate must have the background and experience to act in the best interest of the child for the duration of the child's participation in research.
    d) The advocate must not be associated in any way with the research, the investigator(s), or the guardian organization. The federal regulations do not

specifically exclude IRB members from serving as a child advocate if the other conditions are met.

7.0 Re-consent of participants reaching the age of majority

All minor participants actively participating in an IRB-approved study must be consented using the adult IRB-approved informed consent document *at the first visit after reaching the legal age of majority.* If the minor participated in a study that is completed, except for data analysis, re- consent is not required.

The now adult participant has the right to refuse to continue participation in the study. This is to be respected and undue pressure or coercion to continue may not be applied. While new data may not be collected on participants refusing participation, existing prior data collected under the assent/proxy consent process can be used.

If, upon reaching the age of majority, the now adult participant is found decisionally impaired or is of diminished capacity, the participant remains vulnerable and the proxy/parental consent remains in effect. This must be documented in the study records and the **IRB** must be notified.

8.0 Consent and Assent Documents

8.1 Parental/Guardian Consent Form

If the participant is under the age of 7 years, only a *Parental/Guardian Consent Form* is required. The *Parental/Guardian Consent Form* should include all relevant elements of informed consent as outlined previously and be written in a *proxy* consent style that indicates it is the parent or legal representative, who is consenting to allow the minor to participate in the study. The standard statements must be modified for the Parent Consent form *(e.g., all references to "you" must be changed to "your child").*

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

8.2 Youth Assent Form

If the participant is 7-18 years of age, a combined parental/youth informed consent document may be used or a separate Assent Form based on the adult consent form. If an *Assent Form* is used is should meet the cognitive and educational level of an average youth. The *Assent Form* must contain *simple* language written at the appropriate educational level of the youngest prospective participant in the youth age range. In some research projects, it may be necessary to utilize two assent forms written to accommodate participants at either end of the age range. The *Assent Form* must contain all of the required elements of consent. See sections 1.3.2, 1.3.3 and 1.3.4 below for explicit details.

8.3 Child Assent Form

If the participant is under the age of 7 years, only a *Parental/Guardian Consent Form* is required. However, verbal assent should be obtained as appropriate. The oral assent script should be conversational and stated in such a way that is understandable and age-appropriate. See sections 1.3.2, 1.3.3 and 1.3.4 below for explicit details.

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 CRF 50 Subpart D

University Related Documents:

SOP 701: Informed Consent
SOP 702: Consent Documentation
SOP 901: Research Involving Children

Related Forms:

Investigator Checklist for Research Involving Children

History:

Effective Date: January 2019
Revisions: November 2021

Responsible Office:

Office of Research Compliance and Assurance