



UNIVERSITY OF
SOUTH ALABAMA

IRB SOP 901
Research Involving Children

Purpose

The purpose of this policy and procedure is to outline the requirements for research involving children. It is the policy of the Institutional Review Board to review all research proposals involving participation of children in accordance with Health and Human Services regulations at 45 CFR 46 Subpart D, 21 CFR 50 Subpart D and applicable state law.

Scope

This SOP applies to all research involving children, regardless of funding source.

Applicability

This policy applies to all human subjects' research conducted under the auspices of University of South Alabama involving children as subjects.

Definitions

Assent: A child's affirmative agreement to participate 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.

Children: 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.

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 19 years old, unless such a person has been emancipated.

Emancipated person: A person who is 18 years old and is either married or widowed is emancipated by operation of law without the need for any formal action before a court or other authority. A person under the age of 19 years but over the age of 18 years may be emancipated, or "relieved of the disability of nonage," by order of a juvenile court when such relief is in the best interest of the minor.

Policy

The University of South Alabama IRBs' membership shall include persons who can serve as advocates for research involving children.

The IRB shall review research involving children in accordance with federal and state regulations, principles of sound design, and consideration of children's special needs within the context of each application.

1.0 Research involving children requires the IRB to consider the following within a pediatric population:

1.1 Determination of probable risks and associated discomforts

- Procedures that usually present no more than minimal risk to a healthy child include urinalysis, obtaining small blood samples, EEG's, allergy scratch tests, minor changes in diet or daily routine, and/or the use of standard psychological or educational tests.
- The assessment of the probability and magnitude of the risk, however, may be different in sick children, and may vary depending upon the diseases or conditions the participants have. For example, obtaining blood samples from a hemophiliac child may present more than minimal risk to the child. On the other hand, the IRB may consider that children suffering from chronic illnesses, who are accustomed to invasive procedures, are placed at minimal risk by their involvement in similar research procedures, in contrast to those children who have not had such experiences. The IRB must also consider the extent to which research procedures would burden any child, regardless of whether the child is accustomed to the proposed procedure.
- Procedures that exceed the limits of minimal risk may be difficult to define in the abstract, but should not be too difficult to identify on a case-by-case basis.

Riskier procedures might include the biopsy of internal organs, spinal taps or the use of drugs whose risks to children have not yet been established. Behavioral interventions likely to cause psychological stress or directed at groups at risk of violent or self-destructive behaviors may also exceed minimal risk levels.

-

1.2 Determination of Possible Benefits

- When assessing potential benefits of research intervention, the IRB considers the differences in health status among potential participants. For example, a potential participant might be a normal, healthy child, or a child who has been exposed to a disease or a toxin (e.g., meningococcus or lead) where it is known that a percentage of the children exposed will actually experience untoward consequences. A child may also be in an early stage of disease, e.g., an HIV-infected child, or may actually suffer from disease or other significant medical condition. Thus, the IRB must take into account the current health status of a child and the likelihood of progression to a worsened state without research intervention.

1.3 Wards of the State

- The special protections for children set forth in Subpart D include additional limitations on some research involving children who are wards of the state or any other agency, institution or entity.
- Where the research involves greater than minimal risk to the participants with no prospect of direct benefit to individual participants (45 CFR 46.406), or requires HHS Secretarial approval (45 CFR 46.407), the research must be either related to their status as wards, or else be conducted in schools, camps, hospitals, institutions or similar settings in which the majority of children involved as participants are not wards (45 CFR 46.409).
- The IRB requires the appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as a guardian.
 - The advocate will serve in addition to any other individual acting on behalf of the child as guardian or in loco parentis.
 - One individual may serve as advocate for more than one child.
 - The advocate must be an individual who has the background and experience to act in the best interest of the child for the duration of the child's participation in the clinical investigation.
 - The advocate must not be associated in any way (other than the role as advocate or member of the IRB) with the clinical investigation, the investigator(s), or the guardian.

2.0 Classification of Risk

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.

- 2.1 Research not involving greater than minimal risk (§46.404 and §50.51);
- 2.2 Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual participants (§46.405 and §50.52);
- 2.3 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
- 2.4 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)

| Risk Determination | Benefit Assessment | IRB Action |
|-----------------------------|---|--|
| 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. |

** Both parents or legally appointed guardian must give consent unless one parent or guardian is deceased, incompetent or **not reasonably available**. 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.*

*** 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.*

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.

3.0 Parental Permission

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. The federal regulations state that permission from both parents is required but empowers IRBs to consider investigator requests to obtain consent from only one parent. The IRB determines whether the permission of both parents is necessary, and the conditions under which one parent may be considered not reasonably available.

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 Assent of Minors

The IRB determines 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 (21 CFR 50.55).

Children 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”*.

5.0 Waiver of Assent

The assent of the child is not always a necessary condition for proceeding with the clinical investigation. The IRB may determine that assent is not necessary.

6.0 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.

7.0 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 Screening and Educational Guidance

- The principal investigator submits the IRB application stating that the research will involve the use and participation of children and FORM: *Investigator Checklist for Research Involving Children*, which focuses on ethical and regulatory issues pertaining to the conduct of research involving children.
- If the research sponsor has special requirements for protection of children, the investigator describes how those requirements will be met.
- Upon receipt of the IRB review application, IRB staff will conduct a preliminary screening to determine whether the proposed research study involves the use of children as study participants. Subsequently, the IRB staff will provide (as necessary or requested) appropriate regulatory or educational materials applicable to children as vulnerable subjects for guidance during the IRB review.
- The IRB staff will verify that a member with expertise in research on children as a vulnerable population will be present at the convened IRB meeting or will submit comments in writing in advance of the IRB meeting.

2.0 Review Process

- The IRB will review the application and determine whether the study protocol includes the enrollment and participation of children and whether appropriate safeguards have been considered and are in place.
- As applicable and in addition to application elements required for all full board reviews, the IRB will consider and/or acquire information for special consideration of the following elements when reviewing research involving vulnerable children:
 - Inclusion/Exclusion criteria
 - Over-selection or exclusion of certain groups based upon perceived limitations
 - Recruitment and incentive strategies, including any possibly coercive inducements to children or parents/guardians
 - Degree of risk, risk minimization, and risk-benefit balance

- Whether the children’s assent is desirable and if so, the adequacy of the assent plan (developmentally appropriate, includes elements of consent, obtained at an appropriate time in the consent process and in appropriate setting).
 - Specific laws governing the State of Alabama application to children which may have a bearing on the final approval of the research protocol (emancipated individuals, legally authorized representatives, age of majority for research consent, etc.)
 - Conformity to any special sponsor requirements for the protection of children.
 - Special requirements of federal funding agencies for studies conducted with their support
 - The IRB will follow all relevant federal/state regulations or guidelines and internal IRB policies regarding vulnerable populations, in reviewing and approving research with children, because the involvement of children may involve other vulnerable populations (e.g., the children’s mothers are prisoners or the children are mentally disabled). These regulations and policies include: Pregnant Women, Fetuses, and Human In-Vitro Fertilizations (45 CFR 46, Subpart B); Research Involving Prisoners (45 CFR 46, Subpart C); Research Involving Children (45 CFR 46, Subpart D; 21 CFR 50, Subpart D; and US Department of Education, Subpart D)
 - Research Involving Mentally Disabled Individuals
 - Research Involving University of South Alabama Students
- Whether approval for one year is adequate or whether the project should be approved for less than one year, based on the nature of the research and the level of risk involved.
 - Whether the study should be flagged for routine post-approval monitoring based on the nature of the research and the level of risk involved.
 - The IRB will consider and deliberate each response indicated on the IRB application form applicable to research involving vulnerable subjects and the Form: *Investigator Checklist for Research Involving Children*. IRB approval will also document whether the IRB members acknowledge and agree with the description of all safeguards and risk assessments contained within the protocol as submitted by the Principal Investigator or what changes are required.
 - IRB staff will document all discussions of controverted issues within IRB convened meetings in the minutes.
 - IRB staff will document in the minutes, specific findings or IRB determinations in accordance with IRB policy. The IRB does not need to reconsider pre-determined subjects during continuing reviews, unless changes to the protocol dictate otherwise.

Regulated Documents

[45 CFR Part 46: Subparts A, B, C, D](#)

[45 CFR 46: 101, 46.115\(b\), 46.116, 46.122](#)

[21 CFR 50: Subpart D](#)

University Related Documents

[SOP 703: Informed Consent: Research Involving Children](#)

Related Forms

Investigator Checklist for Research Involving Children (located in IRBNet forms/templates)

References

[Guidelines: Requirements for Research Involving Children](#)

[OHRP Guidance on Special Protections for Children as Research Subjects](#)

[OHRP Research with Children FAQs](#)

HISTORY

Effective Date:

Revisions: November 2021

Responsible Office:

Office of Research Compliance and Assurance