THE UNIVERSITY OF ARIZONA Research & Partnerships

Research Involving Children

When does Human Research involve Children?

A study is considered to include children when a person who is under the age of 18 (in the state of Arizona) participates in a human research study through interaction or intervention with the research team, or collection of a child's identifiable data.

Requirements for Inclusion of Children in Human Research

Investigators must provide protocol specific justification to the Institutional Review Board (IRB) upon a request to include children, so that the IRB may determine that the enrollment of children in the research is justified.

Definitions (45 CFR §46.402)

- *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.
- *Assent* means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.
- *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.
- *Guardian* means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.
- *Homeless minor* is defined as "an individual under the age of eighteen years living apart from his parents and who lacks a fixed and regular nighttime residence or whose primary residence is either a supervised shelter designed to provide temporary accommodations, a halfway house or a place not designed for or ordinarily used for sleeping by humans" (A.R.S. §44-132(C)).

Categories of Research Involving Children

There are four (4) categories of research with children permissible under both the Office for Human Research (OHRP) and the Food and Drug Administration (FDA).

1. No greater than minimal risk to children is presented (45 CFR §46.404/21 CFR §50.51).
2. The research involves greater than minimal risk to subjects with prospect of direct benefit to the individual subjects (45 CFR §46.405/21 CFR §50.52).
3. The research involves greater than minimal risk to children presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual subject, or by a monitoring procedure which is not likely to contribute to the well-being of the subject (45 CFR §46.406/21 CFR §50.53).
4. The research does not meet the requirements of any of the above categories, and the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children (45 CFR §46.407/21 CFR §50.54). Projects that fall into this category require review by the federal agency, after consultation with a panel of experts in pertinent disciplines (e.g., science, medicine, education, ethics, law) and following opportunity for public review and comment.

The IRB will decide whether the proposed human research activities fit within the regulatory categories when the project is reviewed using the justification provided by the investigator.

Requirements for Obtaining Minor Assent and Parental Permission (45 CFR §46.408)

Minors are not able to consent to research activities for themselves. Therefore, the parent/legal guardian must give permission to participate in the research and the minor may give assent to participate. The investigator must provide an explanation of how parental permission and minor assent will be obtained. A statement of the proposed method of obtaining parental permission and minor assent along with protocol-specific discussions of the justification of the process must be included for complete IRB review.

Minor Assent

Assent of a minor participating in research is required; however, depending on the age, level of maturity, physical ability, psychological state, etc. of each child participating in the study, different consent/assent permissions may be approved by the IRB. ***The IRB does not require the signature of the minor to be obtained.*** In general, the IRB follows these standards:

- For children under 8 years of age (0-7 years): Formal assent of the child is not a necessary condition for participating in a research protocol.
- For children 8 - 13 years of age: Many children have limited capacity to understand what participation in a research protocol means. Nonetheless, the IRB expects that investigators provide children in this age range with developmentally appropriate information about the study.
- For children 14 years of age or older: Formal assent is required for participating in a research study.

Assent Best Practices

Chronological age is not a reliable method to determine youth language skills. Vocabulary develops at different rates and is influenced by many personal, biological, social, and environmental factors. Researchers should use simplistic language to help ensure that minors truly understand what they're agreeing to.

Language can be simplified by:

- Selecting simple words and phrases. *Example: "choose" instead of "decide" or "what it was like for you" instead of "your experience".*
- Using simple sentences. *Example: "Research helps us learn."*
- Avoiding sentences that contain more than one idea or require remembering one idea to understand the other. *Example: "To understand COVID-19, we want to ask you questions."*
- Keeping the subject consistent in each section. *Example: "You are the only person who knows about your experiences. We want to learn from you. You are the only person who can teach us about you."*

Providing instructional support enhances learning. Engaging learners in this way promotes understanding so minors can make appropriate decisions about participating in research. You can engage learners by:

- Presenting information in segments rather than all in one long paragraph.
- Adding images to the assent form.
- Asking questions to learn what needs to be clarified. *Example: "How can this study hurt you?"*

- Providing feedback that matches the knowledge that was demonstrated by the learner. *Example: Scaffold up (add) or down (simplify)*
- Encouraging participants to teach-back what they learned using their own words. *Example: "Tell me about the study."*

Parental Permission

Parental permission can be obtained through various mechanisms. Ideally, written parental permission is obtained; however, the IRB may waive the signature requirement or waive parental permission entirely. The investigator is responsible for providing the IRB with appropriate protocol specific justification for the proposed method.

If consent for a child to participate in research is obtained from an individual other than biological or adoptive parents, the individual providing such permission must provide written documentation of the legal ability to consent to the child's medical care. A copy of this documentation is to be kept with the consent document in the research records.

If by law a child can consent to treatment without parental permission, can they also consent to participate in research related to that treatment?

U.S. Department of Health and Human Services (HHS) regulations at 45 CFR 46.402(a) define "children" as "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."

If research on a specific treatment involves solely treatments or procedures for which minors can give consent outside the research context (under applicable state and local laws, for example, research on sexually transmitted diseases or pregnancy), such individuals would not meet the definition of children as defined at 45 CFR 46.402(a). Thus, subpart D would not apply to the research and parental permission (or waiver thereof) is not a consideration for these minors. Under these circumstances, minors may provide their own informed consent. See Human Subjects Protection Program (HSPP) *Arizona State Law* guidance.

Additional References:

- **Adequate provisions are made for soliciting the permission of parents or guardians**: see 45 CFR §46.408, 45 CFR §46.116(c), or 45 CFR §46.116(d).
- **Adequate provisions are made for soliciting the assent of the children:** see 45 CFR §46.408(a), 45 CFR §46.116(c), or 45 CFR §46.116(d).
- **Research with Children FAQs:** https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/children-research/index.html

What if One Parent is Not Available?

When a study involves children and the research poses greater than minimal risk with no potential for direct benefit (45 CFR §46.406/21 CFR §50.53 or 45 CFR §46.407/21 CFR §50.54), "both parents must give their permission 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". The federal regulations do not provide specific guidance about what constitutes "not reasonably available".

Meeting These Requirements

If the parent who is present can provide documented proof that s/he has sole legal responsibility for the child, permission from that parent is sufficient. Such proof would include a copy of the court order granting sole custody and legal decision-making authority to the parent who is present, including sole legal authority to make medical decisions for the child or a copy of the birth certificate listing "unknown" for the other parent.

"Not reasonably available" does not refer to a situation in which one parent is simply not present during the consenting process. A parent who is "not reasonably available" is one who cannot be contacted by phone, email, mail or fax. Some examples of not reasonably available include:

- The other parent is on active military duty
- The other parent is incarcerated
- The whereabouts of the other parent are unknown

If the other parent is "not available" simply because they are at work, traveling, or caring for other children, or even if they live in another city or state, it is the investigator's responsibility to attempt to obtain that parent's permission before enrolling the child in the research.

If the signature of both parents is required, the parent who is present should be asked to provide the other parent's contact information, including address, home and work phone and fax numbers, email address, etc., and a concerted effort should be made to contact the absent parent by phone. Once contacted, a research investigator or other research staff who is eligible to obtain parental permission based on the eIRB *Local Study Team Members* SmartForm must be available to provide them with all the information required to make a fully informed decision about whether to permit the child's participation.

Since written informed consent is required, the approved consent document should be mailed and/or faxed, along with a cover letter or note from the investigator explaining the circumstances. The executed consent can be returned via mail, email, or fax. In the event of a time sensitive consent, the IRB will also permit the parent to take a picture of the signature page with a smart phone and send it via text messaging.

If the absent parent cannot be reached by telephone, email or fax after repeated attempts and no other contact information is available, the investigator may determine that the parent is "not reasonably available." Note that it is very important to retain dated copies of any letters, faxes or emails sent to the absent parent, and a log of all phone calls –attempted and answered – should be kept and documentation entered into the research record. **IMPORTANT NOTE**: If the second parent subsequently responds and refuses to provide permission, the child's participation must end.

The amount of time and effort that investigators should devote to contacting an absent parent will vary depending on the individual circumstances and the constraints posed by the research protocol. However, investigators must have standard operating procedures in place for contacting the absent parent, and all such efforts must be documented in the research record.

Re-consent of Participants Enrolled as Children Upon Reaching the Age of Majority

When a minor participant turns the age of majority (18 in Arizona), this changes their legal status. They are no longer a "child" under the regulations and can provide legally effective consent on their own. Therefore, parental permission and prior assent are no longer sufficient to continue participation.

If study procedures are ongoing when a child turns 18 years old, then the participant must be re-consented to continue participation in the study as an adult. Ongoing study procedures include active participation (e.g., study visits, interventions, surveys, etc.), continued collection or analysis of identifiable private information/specimens, and continued use of identifiable data/specimens collected prior to the participant's 18th birthday (including future use and repository collections). If the investigator plans to only retain de-identified data, then reconsent is not required.

Investigators are responsible for tracking when a participant turns the age of majority and obtaining consent as close to the participants' birthday as possible. The IRB expects a prospective plan in the protocol that explains:

- How participants who turn 18 will be identified
- How and when they will be contacted
- What consent materials will be used and the reconsent process
- What happens if the participant cannot be reached or declines participation

Ideally, this information should be included in the initial IRB application; however, a modification can be submitted in eIRB to add or update the plan.

Investigators should pause continuing research procedures after age 18 until informed consent is obtained from the participant.

Expansion of Categories Involving Children

The University of Arizona (UA) has adopted flexible procedures for projects that are not federally funded, supported, or otherwise subject to the federal rules. Projects that meet the requirements of the HSPP Guidance, *Flexible Review,* may be eligible for increased research categories with children than defined in the federal regulations.

- Requirements for assent and parental permission may be altered or waived for reasons other than those outlined in 45 CFR 46.408. For example, passive parental permission may be appropriate if the school district generally uses this process for normal school activities.
- Research that would otherwise be subject to the requirements at 45 CFR 46.407 may be handled locally, not through the Secretary of HHS.
- Online surveys, in-person focus groups, and/or interviews involving minors, as long as the information is minimal risk may be considered exempt.

Inclusion of Wards in Research (45 CFR §46.409)

Wards are minors who are in the custody of the State. They can be included in minimal risk research (45 CFR §46.404) and research with direct benefit (45 CFR §46.405) with no special requirements.

If wards will be included in research that is greater than minimal risk with no direct benefit (45 CFR §46.406) or research not otherwise approvable (45 CFR §46.407) then the research must be:

- Related to their status as wards; or
- Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards (45 CFR §46.409).

The IRB requires appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as an 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 interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research.

Pregnancy Test Results

Researchers are not required to inform the parents of the results of a minor's pregnancy test conducted in the context of research **unless**:

- The research consent form signed by the parents includes an expectation on the part of the researcher to do so, OR
- The researcher is also the minor's medical provider.
  - The researcher will need the parent's consent for further medical care provided to the minor.

In all cases, the consent form should include whether, to what extent, and when the research record will be available to the parent/minor.

Mandatory Reporters

An investigator who knows of, or reasonably suspects, neglect or abuse of a child while engaged in university approved research may need to report the information, per Arizona law. These laws outline various categories of individuals who are considered mandatory reporters. If a reportable observation or revelation of suspected harm to a child is **likely** to occur during the research, the IRB may require that the parental permission form and/or assent form include a warning of the limits to research confidentiality and advise subjects of the investigator's duty to report known or suspected incidents of abuse or neglect to appropriate authorities. See HSPP Guidance on *Mandatory Reporting* for more information.

Providing Information about Health Care Services

A UA researcher may be able to provide this information depending upon the scope of the research project and the extent to which the parent consented to the child's participation. If the parents did not consent to the researcher providing that information to the minor (i.e., it is not part of the research project), doing so falls outside of the scope of acceptable communication with the minor. The researchers could provide that information to the parents, or to the minor **if** the consent form signed by the parent includes the parent's agreement for such information to be disseminated.