Department:	**UAMS Institutional Review Board**
Policy Number:	**17.1**
Section:	**Special Populations**
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SUBJECT: Children in Research

POLICY

Special ethical and regulatory considerations apply when reviewing research involving children, to protect the minor subjects' interests and to protect children from harm. The IRB may approve research involving children only if special provisions are met in addition to the other criteria required for approval. The IRB must classify research involving children into one of four defined risk categories and document its discussions of the risks and benefits of the research study.

The definition of Pediatric Risk Category IV is provided in this policy for reference only. As indicated in the UAMS Human Research Protection Program Plan (HRPP), research that falls into pediatric risk category IV may not be conducted under the UAMS HRPP.

DEFINITIONS

A. **Assent**. A child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent. Assent is generally sought beginning at age 7. Assent is a process, not a form. However, assent can be documented either on a separate assent form specifically tailored to children (especially adolescents) or on the same document used to obtain parental permission. Only the child's signature (or hand-printed name) is required to fulfill the assent document requirement.

B. **Children**. In Arkansas, "children" includes all those who have not yet reached their 18th birthday and have not been legally emancipated. Emancipation may be obtained through judicial decree. Certain events, such as marriage or incarceration do not result in automatic emancipation, but they do allow minors to provide consent for their own health care. Investigators should seek guidance if the issue arises.

C. **Guardian**. An individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care. [See Policy 17.13, Legally Authorized Representatives (LARs) for definitions.] Court-appointed guardians must petition and receive express permission from the court in order to provide consent authorizing experimental medical procedures.

D. **Parent**. Federal Regulations define this as a child's biological or adoptive parent. Arkansas law allows a parent to grant permission for his/her biological or adopted child for any care, treatment, service, or procedure to maintain, diagnose, treat, or otherwise affect an individuals' physical or mental condition. Note however that there are restrictions on who can consent on behalf of foster children (a.k.a. "wards") for the purpose of research. See the detailed information and Special Instructions Section below for more information.

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

F. **Wards**: Children who are considered to be in the custody of the state. Foster children are in the custody of the Arkansas Department of Human Services (DHS) and therefore are wards of the state. As such, only DHS may provide consent for their participation in research. Specifically, since foster care is under the Division of Children and Family Services (DCFS), the Director of that division will review all requests for research projects. Foster parents cannot provide permission for a foster child to participate in research.

PROCEDURES

A. Categories of pediatric research

1. **Pediatric Risk Category I**: Research Not Involving More Than Minimal Risk. When the IRB finds that no greater than minimal risk to children is present, the IRB may approve the proposed research only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth below.

2. **Pediatric Risk Category II**: Research Involving Greater than Minimal Risk but Presenting the Prospect of Direct Benefit to the Individual Subjects. If the IRB finds that more than minimal risk to children is present by an intervention or procedure but that the intervention or procedure holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, the IRB may approve the research only if the IRB finds that:
   a. The risk is justified by the anticipated benefit to the subjects;
   b. The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and
   c. Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth below

3. **Pediatric Risk Category III**: Research Involving Greater than Minimal Risk and No Prospect of Direct Benefit to Individual Subjects, but Likely to Yield Generalizable Knowledge about the Subject's Disorder or Condition. If the IRB finds that more than minimal risk to children is 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 wellbeing of the subject, the IRB may approve the research only if the IRB finds that:
   a. The risk represents a minor increase over minimal risk;
   b. The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
   c. The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and
   d. Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians, as set forth below.

4. **Pediatric Risk Category IV:** Research Not Otherwise Approvable Which Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Children. If the IRB does not believe the research proposal meets any of the requirements set forth above, it may still approve the protocol but only if:
   a. The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and
   b. The Secretary of the Department of Health and Human Services or The Commissioner of Food and Drugs, as applicable, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, has determined either that the research in fact meets one of the categories set forth above, or all of the following:
      i. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
      ii. The research will be conducted in accordance with sound ethical principles; and
      iii. Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth below.

B. Investigators proposing research involving children are required to:
   1. Design research projects involving children in accordance with this policy, making provisions to obtain the assent of all children age 7 or older. If the study population is such that the children will not be able to provide assent at the age of 7 or at all, the Investigator should specify this in the assent provisions of the application.
   2. Upload permission and/or assent documents or request appropriate waivers thereof.

C. Wards (foster children) in research require additional protections:
   1. Investigators considering a research project specifically targeting these children must contact the Director of the Arkansas Division of Children and Family Services before finalizing the protocol. The study must address special considerations. DCFS staff are to assist with efforts to protect this special population.

   2. If a child in foster care is found to qualify as a participant in research targeting a general population, a copy of the consent form and a cover letter describing the following must be faxed to the DCFS's Director's office prior to enrolling the child.
      a. The nature of the project,
      b. The Principal Investigator and Research Coordinator's contact information (telephone numbers email addresses) and
      c. The timeframe for completion of the consent process.

      DCFS contact information is:
      Phone: (501) 682-8770
      Fax: (501) 682-6968
      700 Main Street P.O. Box 1437, Slot S560
      Little Rock, AR 72203-1437

D. For minor participants who reach the age of majority while involved in on-going research: When a child who is enrolled in research with parental or guardian permission subsequently reaches the legal age of consent to the procedures involved in ongoing research, the subject's participation in the research is no longer regulated by regulatory requirements regarding parental or guardian permission and subject assent. In these cases:
   1. The investigator may request a waiver of the requirement to obtain the informed consent of the now-adult child. The request may only be approved if the IRB finds and documents the required waiver conditions are met OR
   2. The investigator must seek and obtain the legally effective informed consent, as described in IRB Policy 15.1, for the now-adult subject for any ongoing interactions or interventions or continued storage/use of the subject's data or specimens.

E. The IRB must make the following relevant determinations when reviewing research involving children, in addition to the standard determinations for approval.
   1. The IRB must determine and document the pediatric category under which the research can be approved.
   2. If the IRB determines one of the following conditions to be true, then the assent of the minor participants is not a necessary condition for proceeding with the research:
      a. The capability of some or all of the children is so limited that they cannot reasonably be consulted; or
      b. The intervention or procedure involved in the research holds out 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.
      c. The research meets the same conditions as those for waiver or alteration of informed consent in research involving adults, as specified in the regulations at either 45 CFR 46.116(c) or 45 CFR 46.116(d).

3. If the IRB determines assent is required and the minor participants are capable of providing assent, it must find that adequate provisions are made for soliciting that assent. When determining capacity to assent, the IRB shall consider the ages, maturity, and psychological state of the children involved.
    a. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate.
    b . The child should be given an explanation of the proposed research procedures in a language that is appropriate to the child's age, experience, maturity, and condition.
    c. The IRB must also determine the process for documenting the assent.
4. The IRB must consider the following when determining the extent to which parental permission is required:
    a. If the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or legally authorized representative permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements described above, provided both (i) an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and (ii) the waiver is not inconsistent with Federal, State, or local law.
    b. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.
5. If the IRB determines that parental permission is to be obtained, then there must be adequate provisions for soliciting parent or guardian permission(s) as follows:
    a. The IRB must consider if the permission of one parent is sufficient for research not involving greater than minimal risk when the provisions of Pediatric Risk Category I above are met. The IRB may require both parents' permission even in Category I research.
    b. The IRB must consider if the permission of one parent is sufficient for research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects when the provisions of Pediatric Risk Category II above are met. The IRB may require both parents' permission.
    c. When the research is approved under Pediatric Risk Category III above, 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.
    d. For studies not subject to Federal regulations or other requirements to obtain permission of both parents for research approved under Pediatric Risk Category III above, the IRB may consider, on a case-by-case basis, whether permission of one parent is sufficient.
6. If wards of the state or of another agency are to be involved in Pediatric Risk Category III research, the IRB can only approve the research if it finds and documents that such research is one of the following:
    a. Related to the participants' status as wards, OR
    b. Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.
7. To approve research involving wards described at No. 6 immediately above, the IRB must require 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. One individual 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 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, the investigator(s), or the guardian organization.

REFERENCES

45 CFR 46 Subpart D
21 CFR 50 Subpart D
FDA Guidance titled, *"IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More than Minimal Risk to Human Subjects"*
AAHRPP Elements I.1.G; II.3.G; II.4.A; II.4.B; III.1.C; III.1.F