Department: UAMS Human Research Advisory Committee
Policy Number: 17.1
Section: Special Populations
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SUBJECT: Children in Research

The special vulnerability of children makes consideration of involving them as research subjects particularly important. To safeguard their interests and to protect them from harm, special ethical and regulatory considerations apply for reviewing research involving children. The HRAC may approve research involving children only if special provisions are met. Children include all those who have not yet reached their 18th birthday (e.g., 0 through 17 years old). The HRAC must classify research involving children into one of four categories and document their discussions of the risks and benefits of the research study.

Pediatric Risk Category I: Research Not Involving More Than Minimal Risk. When the HRAC finds that no greater than minimal risk to children is present, the HRAC may approve the proposed research only if the HRAC 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.

Pediatric Risk Category II: Research Involving Greater than Minimal Risk but Presenting the Prospect of Direct Benefit to the Individual Subjects.

If the HRAC 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 HRAC may approve the research only if the HRAC finds that:

1. The risk is justified by the anticipated benefit to the subjects

2. The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches

3. Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth below

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 HRAC 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 well being of the subject, the HRAC may approve the research only if the HRAC finds that:

1. The risk represents a minor increase over minimal risk;

2. 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;

3. 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

4. Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians, as set forth below.

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 HRAC does not believe the research proposal meets any of the requirements set forth above, it may still approve the protocol but only if:

1. The HRAC 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

2. The Secretary of the Department of Health and Human Services, 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 satisfies one of the conditions set forth above, or all of the following:

    a. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children

    b. The research will be conducted in accordance with sound ethical principles

    c. Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth below.

Requirements for Permission by Parents or Guardians and for Assent by Children.

1. **Waiver of Parental or Guardian Permission.** If the HRAC 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. 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.

2. **Adequate Provisions for Child's Assent.** The HRAC must find that adequate provisions are made for soliciting the assent of child subjects when in the judgment of the HRAC the children are capable of providing assent.

    a. **Assent Defined.** For purposes of this policy, "Assent" means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

    b. **In determining whether children are capable of assenting, the HRAC shall take into account the ages, maturity, and psychological state of the children involved**. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the HRAC deems appropriate. 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. **Waiver of Assent.** If the HRAC determines either of the following to be true, then the assent of the children is not a necessary

condition for proceeding with the research:

i. The capability of some or all of the children is so limited that they cannot reasonably be consulted; or

ii. 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.

iii. In circumstances where a child dissents, the child's parents, at the discretion of the HRAC, may overrule this. When research involves the provision of experimental therapies for life-threatening diseases such as cancer, however, the HRAC should be sensitive to the fact that parents may wish to try anything, even when the likelihood of success is marginal and the probability of extreme discomfort is high. Should the child not wish to undertake such experimental therapy, difficult decisions may have to be made. In general, if the child is a mature adolescent and death is imminent, the child's wishes should be respected.

iv. Finally, even where the HRAC determines that the child subjects are capable of assenting, the HRAC may still waive the assent requirement under circumstances in which consent may be waived for adults in accordance with Policy III.D regarding waiver or alteration of informed consent generally.

d. Adequate Provisions for Parents' or Guardian's Permission. The HRAC must find that adequate provisions are made for soliciting the permission of each child's parents or legally authorized representative.

i. Research not involving greater than minimal risk. Where parental permission is to be obtained, the HRAC may find that the permission of one parent is sufficient for research not involving greater than minimal risk when the provisions of section 2 above are met.

ii. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects. Where parental permission is to be obtained, the HRAC may find that 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 section 3 above are met.

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. When the research is approved under section 4 above, and permission is to be obtained from parents, 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.

iv. Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. When the research is approved under section 6 above and permission is to be obtained from parents, 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.

Wards of the State or Other Agency. Children who are wards of the state or any other agency, institution, or entity can be included in research approved under Paragraph 4 or Paragraph 5 only if the HRAC finds and documents that such research is: (1) related to their status as wards; or (2)

conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

If the research is approved, the HRAC 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 HRAC) with the research, the investigator(s), or the guardian organization.