

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) to review, approve and provide guidance on the special ethical and regulatory considerations when children are involved in human subjects research under 45 CFR 46, Subpart D, "Additional DHHS Protections for Children."

II. Authority

A. Chapter 381.86, Florida Statutes, Institutional Review Board

III. Supportive Data

A. 45 CFR 46.11645 CFR 46 Subpart D

B. 21 CFR 50, Subpart D

C. OHRP Report 98-03, NIH Policy Guidance on the Inclusion of Children in Research

D. OHRP Guidance, Children Involved as Subjects in Research: Guidance on the HHS 45 CFR 46.407 ("407") Review Process at:
http://www.hhs.gov/ohrp/children/guidance_407process.html

E. OHRP IRB Guidebook Online, Chapter 6, Section C, "Children and Minors" at:
http://www.hhs.gov/ohrp/irb/irb_guidebook.htm

F. DOH IRB Policy, "Legally Effective and Prospectively Obtained Informed Consent"

G. DOH IRB Policy, "Documentation of Informed Consent for Human Subjects Research"

IV. Definitions

A. Assent: An individual's affirmative agreement to participate in research obtained in conjunction with permission from the individual's parents or legally authorized representative. Mere failure to object should not, absent affirmative agreement, be construed as assent.

B. Children/Minors: According to Federal regulations, 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. In Florida, the legal age for consent is 18 years of age.

C. Dissent: An individual's negative expressions, verbal and/or non-verbal, that they object to participation in the research or research activities.

- D. **Greater than Minimal Risk:** The probability and magnitude of harm or discomfort anticipated in the research are greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.
- E. **Legally Authorized Representative:** An individual, judicial, or other body authorized under applicable law to grant permission on behalf of a prospective participant for their participation in research activities.
- F. **Minimal risk:** The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. An example of minimal risk is the risk of drawing a small amount of blood from a healthy individual for research purposes (because the risk of doing so is no greater than the risk of doing so as part of a routine physical examination).

V. Procedures

A. IRB Review and Approval of Research Involving Children

The special vulnerability of children and adolescents makes consideration of involving them as research participants particularly important. To safeguard their interests and to protect them from harm, special ethical and regulatory considerations apply for reviewing research involving children. The IRB may approve research involving children only if special provisions are met. 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 Committee are based on degree of risk and benefit to individual subjects.

B. Categories of Research Involving Children

1. **Research Not Involving Greater than Minimal Risk to Children (45 CFR 46.404).** When the IRB finds that no greater than minimal risk to children is presented, the IRB may approve the research only if the IRB finds that adequate provisions are made for soliciting the assent of the children and permission of their parents or legally authorized representatives, as set forth below.
2. **Research Involving Greater than Minimal Risk but Presenting the Prospect of Direct Benefit to the Individual Child (45 CFR 46.405).** If the IRB finds that more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual child, or involves a monitoring procedure that is likely to contribute to the child'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 children;

- b. The relation of the anticipated benefit to the risk is at least as favorable to the children 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 legally authorized representatives, as set forth below
 3. **Research Involving Greater than Minimal Risk and No Prospect of Direct Benefit to the Individual Child, but Likely to Yield Generalizable Knowledge about the Child's Disorder or Condition. (45 CFR 46.406).** 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 child, or involves a monitoring procedure which is not likely to contribute to the well-being of the child, 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 participants 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 participants' disorder or condition which is of vital importance for the understanding or amelioration of the participants' disorder or condition; and
 - d. Adequate provisions are made for soliciting assent of the children and permission of their parents or legally authorized representatives, as set forth below.
 4. **Research Not Otherwise Approvable, which Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Children (45 CFR 46.407).** If the IRB finds the research does not meet the requirements set forth in categories 46.404, 46.405 or 46.406 as described above, the IRB may approve the research 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. If Federally funded, the Secretary of the Department of Health and Human Services (DHHS), 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:

- (1) That the research in fact satisfies the conditions of categories 46.404, 46.405, or 46.406; or
- (2) 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; and
 - (c) Adequate provisions are made for soliciting the assent of children and the permission of their parents or legally authorized representatives, as set forth below in Section VII.C.1.

C. Requirements for Permission by Parents or Legally Authorized Representatives and for Assent by Children

1. Adequate Provisions for Child's Assent.

The IRB must find that adequate provisions are made for soliciting the assent of child participants when in the judgment of the IRB the children are capable of providing assent.

- a. In determining whether children are capable of assenting, the IRB 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 IRB 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.
- b. **Waiver of Assent**

If the IRB determines either of the following to be true, then the assent of the children is not a necessary condition for proceeding with the research:

- (1) The capability of some or all of the children is so limited that they cannot reasonably be consulted; or
- (2) 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.

- (a) Therefore, when the research offers the child the possibility of a direct benefit that is important to the health or well-being of the child and is available only in the context of the research, the IRB may determine that the assent of the child is not necessary.
- (b) Additionally, in such circumstances, a child's dissent which should normally be respected, may be overruled by the child's parents at the IRB's discretion. When research involves the provision of experimental therapies for life-threatening diseases such as cancer, however, the IRB 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.
- (c) Finally, even where the IRB determines that the child participants are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived for adults in accordance with IRB Policy regarding waiver or alteration of informed consent generally.

D. Adequate Provisions for Parents' or Legally Authorized Representative's Permission

The IRB must find that adequate provisions are made for soliciting the permission of each child's parents or legally authorized representative.

1. Research not involving greater than minimal risk to children. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research not involving greater than minimal risk.
2. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual child. Where parental permission is to be obtained, the IRB 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 participants when the provisions of VII.B.2 above are met.

3. Research involving greater than minimal risk and no prospect of direct benefit to the individual child, but likely to yield generalizable knowledge about the child's disorder or condition. When the research is approved under Section VII.B.3 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.
4. 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 VII.B.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.

E. Waiver of Parental or Legally Authorized Representative's Permission

If the IRB determines that a research protocol is designed for conditions or for a participant population for which parental or legally authorized representative permission is not a reasonable requirement to protect the participants (for example, neglected or abused children), it may waive the consent requirements described above, provided both:

1. An appropriate mechanism for protecting the children who will participate as subjects in the research is substituted; and
2. 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 participants, and their age, maturity, status, and condition.

F. 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 sections D (permission of legally authorized representative) or E (waiver of consent/assent) above only if the IRB 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 participants are not wards.
3. If the research is approved under 45 CFR 46.407, 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 representative, guardian or *in loco parentis*. 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 Investigators, or the guardian organization.

G. Pediatric Expertise on IRB Committee


An IRB Committee considering a protocol involving children as participants shall:

1. Assess its needs for pediatric expertise among the IRB voting membership to assure that it possesses the professional competence necessary to review the specific research activities; and
2. Include one or more individuals who are knowledgeable about and experienced in working with children. To fulfill this requirement, the IRB Committee may invite nonvoting individuals to assist in the review of issues which require expertise beyond, or in addition to, that available among voting IRB members.

VI. History Notes

This is a new policy. The Office of Statewide Research, Ethics and Human Research Protections Program are responsible for this policy.

VII. Signature Block with Effective Date


John O. Agwunobi, M.D., M.B.A., M.P.H.
Secretary, Department of Health

06/29/05
Date