

Policy Number: 36

Title: Children

Date of Last Revision: 6/16/08, 11/20/10, 05/01/16, 09/16/22

Policy:

It is the policy of UC Irvine (UCI) 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 based on the Federal regulations at 45 CFR 46 Subpart D and in addition to those imposed under other IRB policies, procedures, and other applicable Federal, State, and local laws.

I. Definitions:

- A. **Children:** 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 California, the legal age is 18.
- B. **Minors:** In California, individuals under the age of 18 years old are considered minors. Because in California some people under 18 years of age can consent for themselves to some research procedures, not all “minors” meet the federal criteria for being “children.”

II. IRB Review and Approval of Research Involving Children

The special vulnerability of children 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. Both the Office for Human Research Protections (OHRP) and the Food and Drug Administration (FDA) afford additional protections for children in research. The IRB may approve research involving children only if those special provisions, as applicable, 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 the degree of risk and benefit to individual subjects.

III. Categories of Research Involving Children

- A. Research Not Involving Greater than Minimal Risk to Children (45 CFR 46.404, 21 CFR 50.51). 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 legal guardians, as set forth below in Section III.
- B. Research Involving Greater than Minimal Risk but Presenting the Prospect of Direct Benefit to the Individual Child (45 CFR 46.405, 21 CFR 50.52). 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 by 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:
 - 1. The risk is justified by the anticipated benefit to the children;

2. 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
 3. Adequate provisions are made for soliciting the assent of the children and permission of their parents or legal guardians, as set forth below in Section III.
- C. 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, 21 CFR 50.53). 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 by 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:
1. *The risk represents a minor increase over minimal risk;*
 2. 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;
 3. 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
 4. Adequate provisions are made for soliciting assent of the children and permission of their parents or legal guardians, as set forth below in Section III.
- D. 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, 21 CFR 50.54). 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:
1. 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
 2. 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 an opportunity for public review and comment, has determined either:
 - a) That the research in fact satisfies the conditions of categories 46.404, 46.405, or 46.406; or
 - b) The following:
 - (1) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
 - (2) The research will be conducted in accordance with sound ethical principles; and
 - (3) Adequate provisions are made for soliciting the assent of children and the permission of their parents or legal guardians, as set forth below in Section III.
 - c) The research can not begin until the IRB has received approval for the research from OHRP and grants final approval.

3. For non-Federally funded research meeting 45 CFR 46.407, see IRB Procedure # 36.B.

IV. **Requirements for Permission by Parents or Legal Guardians and for Assent by Children**

- A. 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.
 1. 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, for some children, 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.
 2. 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:
 - 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.
 - (1) 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.
 - (2) 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.
 - (3) 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 # 32 regarding waiver or alteration of informed consent.
- B. Adequate Provisions for Parents' or Legal Guardians' 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 (45 CFR 46.404, 21 CFR 50.51, 21 CFR 50.55). Where parental permission is to be obtained, the IRB must determine whether the permission of one parent is sufficient even if the other parent was alive, known,

competent, reasonably available, and shared legal responsibility for the care and custody of the child; or the permissions of both parents is required unless one parent was deceased, unknown, incompetent, or not reasonably available, or when only one parent had legal responsibility for the care and custody of the child.

2. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual child (45 CFR 46.405, 21 CFR 50.52, 21 CFR 50.55). Where parental permission is to be obtained, the IRB must determine whether the permission of one parent is sufficient even if the other parent was alive, known, competent, reasonably available, and shared legal responsibility for the care and custody of the child; or the permissions of both parents is required unless one parent was deceased, unknown, incompetent, or not reasonably available, or when only one parent had legal responsibility for the care and custody of the child.
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, 21 CFR 50.53, 21 CFR 50.55). When the research is approved under Section III.C. 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 (45 CFR 46.407, 21 CFR 50.54, 21 CFR 50.55). When the research is approved under Section III.D. 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.

C. Waiver of Parental or Legal Guardian Permission - If the IRB determines that a research protocol is designed for conditions or a participant population in 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.
3. Waiver of Parental Permission may be considered when the:
 - a. Research involves procedures for which adolescents have the legal right to consent on their own behalf, such as prevention, diagnosis and/or treatment of mental health disorders; pregnancy; venereal disease or other infectious or sexually transmitted diseases; alcohol or drug abuse; rape or sexual assault (California Family Code 6920-6929). (See Policy # 29.)
 - b. Research involves self-sufficient minors. (See Policy # 29.)
 - c. Research involves legally emancipated minors. (See Policy # 29.)

- D. Documentation
 - 1. Permission by parents or legal guardians shall be documented in the same manner as required for participants under IRB Policy # 31.
 - 2. When the IRB determines that assent of a child is required, it shall also determine whether and how assent must be documented.
 - E. 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 Section III.C. (45 CFR 46.406) and Section III.D. (45 CFR 46.407) 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.
 - F. If the research is approved under 45 CFR 46.408(a), 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 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 should:
 - 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 a non-voting consultant to assist in the review of issues which require expertise beyond, or in addition to, that available among voting IRB members. If expertise is not available, the IRB will defer review to another meeting.
 - 3. When reviewing research funded by the National Institute on Disability and Rehabilitation Research, should the research purposefully include children with disabilities as research participants, the IRB must include at least one person primarily concerned with the welfare of these research participants.
- V. **California Requirements Involving Children**
- A. Consent for Themselves: (California Family Code, Sections 6920-6929): Describes when minors (children) may consent for themselves.
 - B. California Requirements for Human Subject Research – Consent of a Minor: Additional Guidance and Requirements:
 - 1. Children - For subjects < 18 years of age, their parents or legal guardians are the legally authorized representatives who may grant permission for their participation in research.
 - 2. Parents - Only the parents may grant permission for their child's participation in research. Assent is to be sought from the child, only after permission has been obtained from the parents. Grandparents and other relatives or caregivers may not grant permission unless they have been granted formal custody of the child by a court. In such cases, the LR must obtain a copy of the court order as evidence of that person's authority to grant permission for participation in research

on the child's behalf.

3. Children in State Custody - According to the California Department of Children's Services' (DCS) applicable policies by virtue of the court order granting DCS legal custody of certain children (e.g., foster children) that Department is the agency that is authorized to grant permission for participation in research for children in their custody. The decision of whether to grant permission for research is made on a case-by-case basis by DCS. In such cases, the LR must obtain a copy of the court order from DCS.
4. Mature Minors or Emancipated Minors - In certain limited circumstances, it may be appropriate to allow a mature minor to consent to participation in a research study in the absence of the permission of a parent or legal guardian if the minor has the sufficient capacity to consent to the procedures involved in the research study.
5. The IRB will determine whether the inclusion of mature minors or emancipated minors in research activities in the absence of the permission of a parent or legal is appropriate. Further, each situation is judged on a case-by-case basis. *For clinical investigations, UCIMC Hospital Administration should be consulted before initiating any research activity including screening.* Documentation of those decisions must be included in the research file.
6. The following information provides examples of circumstances under which California law combined with federal regulations permits individuals under 18 to enroll in research without permission from parent(s) or guardian(s):
 - (1) Minors may consent for themselves to medical care related to the prevention or treatment of pregnancy, but not necessarily to sterilization or abortion [California Family Code Section 6925; Health and Safety Code Section 123450 for abortion].¹
 - (2) Minors 12 years of age or older have the legal right to consent on their own behalf, for:
 - a) Mental health treatment or counseling on an outpatient basis or residential shelter services (in limited circumstances) [California Family Code Section 6924].
 - b) Medical care related to the diagnosis or treatment of infectious, contagious, or communicable diseases that are required to be reported to the local health officer or a related sexually transmitted disease [California Family Code Section 6926].
 - c) Medical care related to the diagnosis or treatment of the condition and collection of medical evidence about alleged rape or sexual assault [California Family Code Section 6927].
 - d) Medical care and counseling related to the diagnosis and treatment of an alcohol or drug-related problem [California Family Code Section 6929].
 - (3) Self-sufficient minors who are:
 - a) 15 years of age or older;
 - b) living separately from their parents/guardians; and

¹ (highlighting remains intentionally): American Academy of Pediatrics v. Lungren (1997) 16 Cal.4th 307. **A minor may consent to an abortion without parental consent and without court permission.** California Health and Safety Code remains unchanged.

- c) managing their own financial affairs have the legal right to consent on their own behalf to medical or dental care [California Family Code 6922].
 - (4) Emancipated minors, those who are:
 - a) married or divorced
 - b) on active duty in the U.S. armed forces **or** emancipated by the court; and
 - c) have the legal right to consent on their own behalf to medical, dental, or mental health treatment. They also have extensive other rights to enter into legal and business arrangements, and so can consent to be included in other research (e.g., interviews, surveys) [California Family Code 7000-7143].
 - (5) Capacity to consent depends upon:
 - a) The age, ability, experience, education, training, and degree of maturity and judgment of the minor. A minor between the ages of fourteen (14) and eighteen (18) may have such capacity, but a minor under the age of fourteen (14) would rarely have such capacity;
 - b) The conduct and demeanor at the time consent is to be given;
 - c) The totality of the circumstances;
 - d) The nature of the proposed research procedures and their risks, probable consequences, benefits, and alternatives to the treatment; and
 - e) The minor's ability to appreciate the nature, risks, consequences, benefits, and alternatives of the proposed research procedures.
- C. **Emancipated Minors** (California Family Code, Sections 7000-7002; 7050-7052; 7120-7123): Further defines an emancipated minor and rights of emancipated minors.
- D. **Experimental Use of Drugs and Consent for Minors Provision** (California Health and Safety Code, Sections 111515– 111545): Minor consent is required prior to administering an experimental drug. Parental or legal guardian consent (permission) is required and minor consent (assent) is required for children 7 years of age or older.
- E. **Mandatory Reporting of Child Abuse or Neglect** (California Penal Code, Section 11164 -11174.3) Identifies who is a “mandated reporter” required to report known or reasonably suspected child abuse or neglect.
- F. **Parental Consent for Children to Participate in Research** (California Education Code, Section 51513): For K-12 students - tests, questionnaires, surveys, or examinations containing any questions about the pupil's or the pupil's family's personal beliefs or practices in sex, family life, morality, and religion require written parental consent (permission).

VI. **Department of Education Requirements When Involving Minors in Research**

- A. The Family Educational Rights and Privacy Act (FERPA) (20 U.S.C. § 1232g; 34 CFR Part 99) is a Federal law that protects the privacy of student education records. The law applies to all schools that receive funds under an applicable program of the U.S. Department of Education.
- B. The Protection of Pupil Rights Amendment (PPRA) (20 U.S.C. § 1232h; 34 CFR Part 98) applies to programs that receive funding from the U.S. Department of Education (ED). PPRA is intended to protect the rights of parents and students.
- C. *Children* are persons enrolled in research not above the elementary or secondary education level, who have not reached the age or majority as determined under state law.
- D. No student shall be required, as part of any program specified in 98.1 (a) or (b), to submit without *prior consent* to psychiatric examination, testing, or treatment, or psychological examination, testing, or treatment, in which the primary purpose is to reveal information concerning one or more of the following:
 - a. Political affiliations or beliefs of the student or the student's parent;
 - b. Mental and psychological problems potentially embarrassing to the student or his or her family;
 - c. Sex behavior and attitudes;
 - d. Illegal, anti-social, self-incriminating and demeaning behavior;
 - e. Critical appraisals of other individuals with whom the student has close family relationships;
 - f. Legally recognized privileged and analogous relationships, such as those of lawyers, physicians, and ministers;
 - g. Religious practices, affiliations, or beliefs of the student or student's parent or;
 - h. Income, other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under a program.
- E. Prior Consent means:
 - a. Prior consent of the student, if the student is an adult or emancipated minor; or
 - b. Prior written consent of the parent or guardian, if the student is an unemancipated minor.
- F. For certain types of research projects not directly funded by the United States (U.S.) Department of Education and conducted in a school that receives funding from the U.S. Department of Education, the IRB will ensure compliance with U.S. Department of Education regulations that schools are required to develop and adopt policies in conjunction with parents regarding the following:
 - a. The right of a parent of a student to inspect, upon the request of the parent, a survey created by a third party before the survey is administered or distributed by a school to a student.
 - b. A procedure for granting a request by a parent for reasonable access to such survey within a reasonable period of time after the request is received.
- G. Arrangements to protect study privacy that are provided by the agency in the event of the administration or distribution of a survey to a student containing one or more of the following items (including the right of a parent of a student to inspect, upon the request of the parent, any survey containing one or more of such items);

- a. Political affiliations or beliefs of the student or the student's parent;
 - b. Mental and psychological problems potentially embarrassing to the student or his or her family;
 - c. Sex behavior and attitudes;
 - d. Illegal, anti-social, self-incriminating and demeaning behavior;
 - e. Critical appraisals of other individuals with whom the student has close family relationships;
 - f. Legally recognized privileged and analogous relationships, such as those of lawyers, physicians, and ministers;
 - g. Religious practices, affiliations, or beliefs of the student or student's parent or;
 - h. Income, other than that required by law to determine eligibility for participation in a program or for receiving financial assistance under a program.
- H. The right of a parent of a student to inspect, upon the request of the parent or guardian, any instructional material to be used as part of the educational curriculum for the student. Instructional material may include teacher's manuals, films, tapes or other supplementary instructional material, which will be used in connection with any research or experimentation program or project.
- 1. Research or experimentation program or project means any program or project in any research that is designed to explore or develop new or unproven teaching methods or techniques.
 - a. Any applicable procedures for granting a request by a parent for reasonable access to instructional material received.
- I. The administration of physical examinations or screenings that the school or agency may administer to a student.
- J. The collection, disclosure or use of personal information collected from students for the purpose of marketing or for selling that information (or otherwise providing that information to others for that purpose), including arrangements to protect student privacy that are provided by the agency in the event of such collection, disclosure or use.
- a. The right of a parent of a student to inspect, upon the request of the parent, any instrument used in the collection of personal information before the instrument is administered or distributed to a student and
 - b. Any procedure for granting a request by a parent for reasonable access to such instrument within a reasonable period of time after the request is received.
- VII. **Environmental Protection Agency Requirements When Involving Minors in Research**
- A. Research requirements when supported by the EPA:
 - 1. The EPA prohibits research involving the intentional exposure of children to any substance.
 - 2. The EPA requires application of 40 CFR 26 Subpart D to provide additional protections to children as participants in observational research, i.e., research that does not involve intentional exposure to any substance.
 - B. EPA policy requires submission of IRB determinations and approval to the EPA Human Subjects Research Review official for final review and approval before the research can begin.
 - C. Research not supported by any federal agency that has regulations for protecting human research participants and for which the intention of the

research is submission to the EPA, the EPA regulations protecting human research participants apply, including the prohibition of the intentional exposure of children to any substance.

References:

21 CFR 50 Subpart D

40 CFR 26 Subpart D

45 CFR 46 Subpart D

Department of Education 34 CFR 356.3, 34 CFR 98.4

The Protection of Pupil Rights Amendment (PPRA) (20 U.S.C. § 1232h; 34 CFR Part 98)

The Family Educational Rights and Privacy Act (FERPA) (20 U.S.C. § 1232g; 34 CFR Part 99)

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

California Family Code 6920-6929

California Family Code 7000-7143

California Health and Safety Code 111530

HRP Policy # 29

Procedure Number: 36.A**Title: Procedure for Review of Research Involving Children****Procedure:**

This procedure provides guidance on the special ethical and regulatory considerations of children involved in human subjects research under the jurisdiction of the UC Irvine (UCI) Institutional Review Board (IRB).

I. Lead Researcher (LR) Responsibilities

- A. The LR will address specific questions related to the inclusion of children with any new study submission in which children will be a target population for research activities.
- B. When the research is funded by the United States (U.S.) Department of Education or the research is conducted in a school that receives funding from the U.S. Department of Education, the LR will comply with requirements of the FERPA and the PPRA.
- C. For certain types of research projects not directly funded by the United States (U.S.) Department of Education and conducted in a school that receives funding from the U.S. Department of Education, the investigator will obtain a permission letter from an authority of the school (e.g., school principal) or school district that the school complies with requirements of the FERPA and the PPRA and that these requirements are followed in the conduct of the research.
- D. The LR should describe in the protocol narrative if and how assent will be obtained and documented for IRB review and approval.
 1. An LR must take into account the ages, maturity, and psychological state of the children involved when planning methods to obtain and document assent.
 2. In some cases, the IRB may require additional techniques such as the use of larger type, simple schema, and pictures to help boost a child's comprehension of the text.
 3. The UCI IRB recommends the following documentation:
 - a) Parental permission utilizing an informed consent document;
 - b) Ages less than 7 years: An oral script in very simple language appropriate for children less than 7 years of age;
 - c) Ages 7 to 12 years: An assent form written simply and at a comprehension level appropriate for a child 7 years of age; and
 - d) Ages 13 to 17 years: A combination assent/parental permission consent form which may be in the same language as the adult consent document.
 4. The LR should not solicit a child's assent without intending to take his or her wishes seriously. In situations where the potential benefits of the study are such that the physicians and parents will enroll the child regardless of the child's wishes, the child should simply be told what is planned and should not be deceived. In such cases, the LR should request a waiver for assent from the IRB.
 5. Once a waiver of assent has been approved, the Investigator will obtain parental permission unless waiver from parental permission has been granted (See IRB Policy # 32)
 6. The LR may not approach the child to assent to the research study until the parents or legal guardians have given written permission.

II. IRB Committee Responsibilities

- A. The IRB Committee must review the proposed research taking into consideration all applicable UCI policies, as well as the degree of risk and discomfort involved in the research in relation to the direct benefits it offers to the child before it can determine whether or not the IRB has authority to approve the study.
- B. When determining whether children are capable of assenting, the IRB shall take into account the age, maturity, and psychological state of the children targeted for the study population. This determination may apply to all children involved in the study, some of the children, none of the children, or on a case-by-case basis, as deemed necessary by the IRB. When the IRB decides that assent is not a requirement of some children, the IRB will determine and document which children are not required to provide assent.
- C. The IRB must determine the appropriate ages for assent and the method of documentation of assent.
- D. The IRB must assure that special protections afforded to children found in 45 CFR 46, Subpart D have been met for this population.
- E. The Committee may not review or make a determination regarding studies involving children, as a target population, unless it has sufficient expertise in pediatric ethical, clinical, and psychosocial issues. Therefore, a Committee member with expertise must be in attendance at the convened meeting or experts who have this knowledge must be consulted by the IRB. When the IRB Committee renders its determination, it will include:
 1. The children's category and corresponding rationale under which the proposed research qualifies (e.g., 45 CFR 46.404-46.407); and
 2. Adequate provisions for obtaining assent from the children and how such assent will be documented. If assent is waived by the Committee, the rationale for such determination must be provided.
 3. Federally-funded studies determined by the IRB Committee to meet 45 CFR 46.407 for children, will be given a "pending approval" status until a determination by the Secretary of the Department of Health and Human Services (DHHS) is received. The Director of Human Research Protections or designee will be promptly notified when the IRB determines a study meets 45 CFR 46.407. Documentation sent to the Secretary includes:
 - a) IRB minutes from the convened meeting documenting the IRB findings;
 - b) The complete IRB application and informed consent documents;
 - c) The relevant protocol and/or grant application; and
 - d) Any supporting material including the Investigator's Brochure, if applicable.
 4. If OHRP grants approval under Category 46.407, then the IRB may grant final approval.
 5. If OHRP requires changes in the process of approval, or any other changes are made after the IRB "approved pending" revisions, an amendment request must be submitted for review and approved by the IRB Chairperson or his or her designee, unless the IRB Chairperson determines the changes submitted are significant, which require IRB Committee review (See IRB Procedure # 18.A).

6. At any time the Chairperson may refer the study to the IRB Committee for further review.
 7. The research can not begin until the IRB has received approval for the research from OHRP and grants final approval.
- F. Non-Federally funded studies determined by the IRB Committee to meet 45 CFR 46.407 for children and meet all criteria for approval under 45 CFR 46.111, will be given a “pending approval” status until the research proposal is reviewed by both an expert panel and a community panel, for recommendations (See IRB Procedure # 36.B).
- G. When children as wards of the State are involved in research under 45 CFR 46.406 and 45 CFR 46.407, the required additional individual acting on behalf of the child as guardian or *in loco parentis* 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 interest of the child for the duration of the child’s participation in the research and who is not associated in any way with the Investigators, or the guardian organization (e.g., CASA Volunteer).
- H. For research following Environmental Protection Agency (EPA) regulations and guidance;
1. When research is conducted or supported by the EPA or when research is intended for submission to the EPA, research involving intentional exposure of pregnant women or children to any substance is prohibited.
 2. The IRB may review and approve observational research involving children that does not involve greater than minimal risk 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 in §26.406
 3. The IRB may review and approve observational research involving children that involves greater than minimal risk but presenting the prospect of direct benefit to the individual participants if the IRB finds and documents that:
 - a. The intervention or procedure holds out the prospect of direct benefit to the individual subject or is likely to contribute to the subject’s well-being;
 - b. The risk is justified by the anticipated benefit to the subjects;
 - c. 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
 - d. Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in §26.406.

III. IRB Analyst or Higher Responsibilities

- A. The Analyst will verify that all documentation related to the enrollment of children is complete as part of the initial study documents.
- B. When the research is funded by the U.S. Department of Education or the research is conducted in a school that receives funding from the U.S. Department of Education, the Analyst will confirm that the LR obtained permission from the school to conduct research at the school and the school has verified that it complies with requirements of FERPA and the PPRA and that these requirements are followed in the conduct of the research.

- C. For certain types of research projects not directly funded by the U.S. Department of Education and conducted in a school that receives funding from the U.S. Department of Education the Analyst will confirm that the LR obtained permission from the school to conduct research at the school and the school has verified that it complies with requirements of the FERPA and the PPRA and that these requirements are followed in the conduct of the research.
- D. The Analyst will conduct a pre-review and take into consideration the type of research and verify the appropriate category of research under Subpart D.
- E. The Analyst takes into consideration the age, maturity, and psychological state of the children targeted in the proposed research when pre-reviewing the assent and informed consent documents.
- F. E-mails recommending pre-review changes to the informed consent documents are to be sent to the LR by the Analyst.
- G. Once the pre-review revisions are received from the LR, the Analyst will forward the revised informed consent documents to the assigned Reviewers with appropriate expertise in children and prepare the Reviewer and Committee packets.

References:

45 CFR 46.116

45 CFR 46 Subpart D

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

IRB Guidebook, Chapter 6, Section C, Children and Minors

IRB Procedure 18.A, "Procedure for Modifications to Previously Approved Applications or Claims for Exemption"

IRB Policy 30, "Legally Effective and Prospectively Obtained Informed Consent"

IRB Policy 32, "Waiver of Informed Consent for Human Subjects Research or Exception of Informed Consent Requirements for Emergency Research"

IRB Procedure 36.B, "Review of Non-Federally Funded Research Meeting 45 CFR 46.407"

40 CFR 26.404-.406

Procedure Number: 36.B**Title: Procedure for Review of Non-Federally Funded Research Meeting 45 CFR 46.407****Procedure:**

This procedure outlines the process for reviewing non-federally funded research which meets 45 CFR 46.407 for the protection of children as a vulnerable population.

I. Lead Researcher (LR) Responsibilities

- A. The LR is responsible for providing a written rationale for use of this vulnerable population, including supporting documentation (e.g., literature search) of study design, safety monitoring, and risk/benefit ratio justification.
- B. The LR will provide additional documentation or materials as requested by the IRB in order to support the justification for research under category 45 CFR 46.407.
- C. The LR will, as requested, assist the IRB in preparation for Panel and Committee review by providing any additional materials and documentation required for adequate review.
- D. The LR will be available and may be required to present the proposed study to the Expert Panel.
- E. The LR cannot initiate the research, including screening and recruitment, until all reviews are complete and all requested revisions or recommendations are satisfied and final approval has been granted by the IRB.

II. IRB Committee Responsibilities

- A. The IRB Committee will review the proposed research according to IRB Policy # 36 and determine that the research involving children does not meet the requirements for approval under 45 CFR 46.404 (research not involving greater than minimal risk), 46.405 (research involving greater than minimal risk but presenting the prospect of direct benefit to individual subjects), or 46.406 (research involving greater than minimal risk and no prospect of direct benefit to the individual subjects but likely to yield generalizable knowledge about the subject's disorder or condition), but that the research, not otherwise approvable, presents a reasonable opportunity to further the understanding, prevention or alleviation of a serious problem affecting the health or welfare of children.
 1. The IRB Committee will provide the rationale and documentation that the research does not meet 45 CFR 46.404, 46.405, or 46.406 for the protection of this vulnerable population.
 2. The IRB Committee will provide rationale and documentation that the research would be approvable under 45 CFR 46.407.
- B. The IRB will consult with experts at DHHS, experts in relevant disciplines, and representatives of the community in which the research will be conducted to provide the opportunity for review and comment, before determining whether the proposed research may be conducted under 45 CFR 46.407.
- C. The IRB Committee will determine the composition for both the Expert Review Panel and the Community Review Panel.
 1. Expert Review Panel Membership:
 - a) IRB or other neutral Facilitator;
 - b) Between 10 and 15 Members;

- c) IRB Committee Child Representative/Expert;
 - d) Additional IRB Representatives with clinical knowledge;
 - e) Non-affiliated Experts in the field specific to the proposed research;
 - f) Ethicists;
 - g) Community Pediatricians (not involved in research, but appropriate to the study population);
 - h) Pharmacy representatives (if applicable);
 - i) Other applicable Experts (e.g., pediatric social worker, child psychologist, etc.); and
 - j) No person which may be perceived as having a conflict of interest (to avoid possible coercion).
2. Community Review Panel Membership:
 - a) Between 10 and 15 Members;
 - b) IRB Committee Community Member;
 - c) Additional IRB Representatives with clinical knowledge and ability to answer questions in lay language;
 - d) Community Representatives that work regularly with the involved population; and/or
 - e) Parent representatives of the target population.
- D. The IRB Committee will identify questions for each panel to address and discuss, utilizing the Reviewer Checklist.
- E. The IRB Committee will determine the information to be provided to each panel for review. Information that may be included in the packet:
1. Expert Review Panel (to meet before the Community Review Panel):
 - a) Cover letter from IRB;
 - b) Reviewer Checklist;
 - c) Belmont Report;
 - d) Regulations, including Subpart D;
 - e) IRB Committee Minutes;
 - f) Complete IRB Application for Human Research including informed consent and assent documents, and the study protocol;
 - g) Ad hoc reviewer comments (if applicable); and/or
 - h) Summary of background information including articles, literature search, and supporting materials.
 2. Community Review Panel:
 - a) Cover letter from IRB;
 - b) Reviewer Comment Form;
 - c) Lay Summary of Belmont Report;
 - d) Regulations, including Subpart D and a lay summary;
 - e) Complete IRB Application for Human Research including informed consent and assent documents, and the study protocol;
 - f) Ad hoc reviewer comments (if applicable);
 - g) Summary of background information including articles, literature search, and supporting materials; and/or
 - h) Summary from the Expert Review Panel meeting.
 3. The IRB Committee will identify a deadline for completion of the panel reviews.
 4. Following completion of both panel reviews, the IRB Committee will review recommendations from the panel meetings and make a determination regarding approval of the research, including any additional study revisions identified by the Expert Review Panel and Community Review Panel.

5. The IRB Committee will recommend any additional compliance guidelines (e.g., increased review frequency, observation of consent and assent process, additional DSMB protections, etc.)

III. **IRB Administrator Responsibilities**

- A. The Administrator will prepare guidance to assist the IRB Committee in making a determination that proposed research meets 45 CFR 46.407 for the IRB Committee.
- B. The Administrator will notify the Director of Human Research Protections or designee of the 45 CFR 46.407 determination by the Committee.
- C. The Administrator will prepare guidance to assist the Expert Review Panel and the Community Review Panel in evaluating the proposed research for approval under 45 CFR 46.407.
- D. Following the determination that a non-federally funded research proposal meets 45 CFR 46.407, the Administrator with the assistance of the Director of Human Research Protections or designee will seek guidance from administration and/or OHRP in the continuation of review under this category.
- E. The Administrator will prepare or request that the LR provide a literature search for supporting documentation of study design, safety monitoring, and risk/benefit ratio justification.
- F. The Administrator with the assistance of others (i.e., IRB Chair, IRB Members, and Director of Human Research Protections or designee) will recruit and coordinate identified Experts for participation on the Expert Review Panel.
- G. The Administrator with the assistance of others (i.e., IRB Chair, IRB Members, and Director of Human Research Protections or designee) will recruit and coordinate identified Community Members for participation on the Community Review Panel.
- H. The Administrator will prepare and obtain confidentiality agreements (Consultant Agreement) from all Community and Expert Panel Members.
- I. The Administrator will prepare and distribute packets to Panel Members for review prior to panel meetings only after a signed and dated Confidentiality Agreement has been received.
- J. The Administrator will coordinate arrangements for Panel Meetings (e.g., location, time, notification of Panel members, etc.)
- K. The Administrator will attend each Panel meeting, documenting minutes from the meeting.
- L. The Administrator will write a summary of the Expert Review Panel meeting for distribution and review by the attendees.
- M. The Administrator will prepare Panel recommendations for IRB Committee review and final determination regarding the study.

IV. **Expert Review Panel and Community Review Panel Responsibilities**

- N. The Community Review Panel may meet for an initial orientation session prior to convening a meeting for formal review of the proposed research to allow for an overview of the research in general.
- O. The Expert Review Panel and the Community Review Panel will review the proposed research and make one of the following recommendations:
 1. The Expert and Community Panels will recommend that the proposed research be disapproved, as it does not meet 45 CFR 46.404, 46.405, 46.406, or 46.407 for the protection of children as a vulnerable population;

2. The Expert and Community Panels will recommend that the proposed research meets 45 CFR 46.404, 46.405, or 46.406 for the protection of children as a vulnerable population; or
3. The Expert and Community Panels will recommend that the proposed research be approved under 45 CFR 46.407, only if the panels determine that:
 - 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 legal guardians as set forth in 45 CFR 46.408; and
 - d) Any recommendations for revisions (e.g., added protections, etc.) for IRB Committee review and consideration.

V. **IRB Administration Responsibilities**

- A. IRB Administration will assist the IRB Committee members with identification of Panel Members.
- B. IRB Administration will assist with appointing a moderator or facilitator for the Expert and Community Panel Meetings.
- C. IRB Administration will assist with providing compliance support to ensure consistency among HRP teams, IRB Committees, and Panel Meetings and adherence to Federal regulations and institutional policies and procedures.
- D. IRB Administration will assist with oversight of proceedings and processes.

References:

45 CFR 46, Subpart D

21 CFR 50, Subpart D

IRB Policy 36, "Vulnerable Populations: Children"