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I. PURPOSE

The purpose of this SOP is to describe the special regulatory requirements that the researcher and the IRB must take into consideration when a proposed research study involves children, a vulnerable population, to provide additional protection for children involved in research.

II. POLICY STATEMENT

When reviewing research with children as subjects, in addition to ensuring adherence to the general regulatory requirements of 45 CFR part 46 (§46), Subpart A or 21 CFR 50 and 56 (§50 or §56), the IRB must determine which of four categories of research apply to that study, based on the degree of risk and benefit to the individual subjects (pursuant to Subpart D of §46 or §50 [Subpart D]). The IRB must also determine that there are adequate provisions for soliciting the assent of the children (if appropriate) and the permission of their parents or guardians. Special protections apply if children who are wards are to be included in the research.

III. SCOPE

These operating procedures apply to all IRB staff, IRB members, and researchers and their staff who propose and conduct research involving children.


IV. DEFINITIONS

Assent: A child's or other individual's affirmative agreement to participate in research where the child or individual is not eligible by age or impaired decision making abilities to provide consent. Mere failure to object by the child or individual should not be construed as assent.

Children: 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 Pennsylvania, persons age 18 years or older can consent to their own medical, dental and health care. Pennsylvania law also allows persons under the age of 18 years to consent to a wide variety of medical testing and treatment and health care services. [See, CHOP "Patient Care Manual: No. RI-5-01, Consent and **IRB SOP 505**].

Guardian: Any person designated by Court Order as the Minor's legal guardian or as a person who can otherwise make medical decisions on behalf of the Minor.

Minimal Risk: Defined as "...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

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examinations or tests...." (§46.102(i)). The IRB interprets “minimal risk” to be calibrated to the life of normal, healthy children and “daily life” to be those activities to which most children are exposed. The IRB may determine that procedures that are considered minimal risk for normal healthy children constitute greater than minimal risk for populations that are vulnerable by virtue of their condition or circumstances.

Minor: A person who has not yet reached the age of majority in the state where the research is conducted.

Parent: A child’s biological or adoptive parent.

Parental Permission: The agreement of parent(s) or guardian to the participation of their child or ward in research.


Ward: Any child who has been adjudged dependent by a court and who is under the control of a public official or agency, including Foster children, or any child under the control of DHS in Philadelphia or a County Children and Youth Agency in another county in Pennsylvania; also, children in penal custody or otherwise detained within the criminal justice system.

V. PROCEDURES

A. Categories of Research:

During initial review the IRB determines and documents which of four categories of research, (below) applies to the particular study, based on the degree of risk and benefit to individual subjects. At the time of continuing review, amendment review or new information review the IRB may determine that the category has changed.

1. Research not involving greater than minimal risk (§46.404/§50.51): The IRB may approve research where adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.
2. Research involving greater than minimal risk but presenting the prospect of direct benefit to the children (§46.405/§50.52): 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 guardians.


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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 (§46.406/§50.53). The IRB may approve the research only if the IRB finds that:

- (a) the risk presents no more than 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 parents (both), or guardians.

4. Research that does not fall into one of the three categories above, and is therefore not otherwise approvable, which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (§46.407/§50.54). Research in this category requires a special level of HHS review beyond that provided by the IRB, and requires the IRB to make certain findings and refer the proposed research activity to the Secretary of HHS for further review and approval. If 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, this research can be conducted only if the DHHS Secretary or the FDA Commissioner, after consultation with a panel of experts in pertinent disciplines and following opportunity for public review and comment, has determined either


- (a) that the research in fact satisfies the conditions of §46.404 (§50.51), §46.405 (§50.52), or §46.406 (§50.53), as applicable; *or*
- (b) the following conditions are met: (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; (iii) adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians.

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B. Wards of State

1. Children who are Wards of state may be included in research under sections §46.404 (§50.51) or §46.405 (§50.52) of Subpart D.
2. Children who are Wards may be included in research under sections §46.406 (§50.53) or §46.407 (§50.54) of Subpart D only if the IRB determines and documents that such research is:
 - (a) Related to their status as wards; *or*
 - (b) Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as participants are not Wards.

The eIRB application requests that investigators indicate whether or not Wards of the state will be recruited and permitted to be included in the research.
3. If Wards are to be included in research under §46.406 (§50.53) or §46.407 (§50.54) of Subpart D, the IRB requires appointment of an advocate for each child who is a ward.
 - (a) The advocate serves in addition to any other individual acting on behalf of the child as guardian or in loco parentis;
 - (b) One individual may serve as advocate for more than one child;
 - (c) The advocate must 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;
 - (d) The advocate must not be 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.
 - (e) If children who are Wards are to be included, the investigator provides the IRB with detailed information about the proposed permission/assent process, as well as the identity and authority of the individuals who will provide permission for the Ward subjects.
4. Pennsylvania regulations regarding Wards distinguish between routine and non-routine medical treatment for purposes of consent. Experimental procedures or treatment are considered non-routine. In all cases of non-routine treatment, the child's parent or guardian must give prior permission. A foster parent can never give valid permission for a Ward. If the parent/guardian cannot be located, the

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county children and youth agency, the private foster care agency, or the residential facility with physical custody of the child must obtain a court order authorizing treatment. If a county agency has custody of a child for whom a decree of termination of parental rights has been entered, the agency can consent to all routine and non-routine treatment.


5. After approval, investigators must monitor the status of research subjects.
 - (a) For the Ward to continue participation in the research, the subject's consent (if not waived) must remain valid.
 - (1) The investigator determines whether the parent(s) or legal guardian(s) who consented to the child's participation continues to retain the legal authority to provide consent.
 - (2) If they do not retain this authority, then consent must be obtained from the person(s) who now hold this authority.
 - (b) If a research subject who is a child becomes a Ward during the course of the research approved under sections §46.406 (§50.53) or §46.407 (§50.54) of Subpart D, the investigator must promptly notify the IRB.
 - (c) When the research has been approved under sections §46.406 (§50.53) or §46.407 (§50.54) of Subpart D, an advocate must be assigned and must consent to the continued participation in accordance with the procedures outlined in Section B.2.c.

C. Parental/Guardian Permission and Assent of the Child

1. The IRB must find that there are adequate provisions for soliciting the permission of parents or guardians for the children involved in a research study. In Pennsylvania, a guardian is defined as: a party appointed as guardian of a minor by (a) action of a court of competent jurisdiction or (b) action of a legally qualified designator, including a parent, legal custodian or legal guardian. See **IRB SOP 702** for additional requirements related to parental permission.
2. The IRB must find that adequate provisions are made for soliciting the assent of children when, in the judgment of the IRB, the children are capable of providing assent. See **IRB SOP 702** for additional assent requirements.

D. Additional Protections

1. The IRB determines and documents any additional protections for research involving children. These may include recommendations regarding protocol-

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specific findings related to research involving children, assent requirements, permission requirements, and requirements related to research involving Wards.

2. The meeting minutes and approval letters document the IRB's protocol-specific findings related to research involving children, assent requirements, permission requirements, and requirements related to research involving Wards.

VI. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46, Subpart D

21 CFR 50, Subpart D

VII. REFERENCES TO OTHER APPLICABLE SOPS


SOP 702: Assent and Parental Permission

SOP 505: Minors Who Are Not Children in the Research Context

VIII. RESPONSIBILITIES

Title	Responsibility
Investigator	Responsible for providing sufficient information to allow the IRB to make a risk – benefit determination as required under Subpart D.
IRB Reviewer	Responsible for reviewing the submitted materials including the protocol and application and to document their findings.

IX. ATTACHMENTS

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X. REVISIONS:

- 9-26-2006: To incorporate investigator responsibilities for continuous monitoring of research subjects.
- 6-10-2010: Revised for clarity and formatting
- 9-25-2018 Revised to update definitions and minor edits.

 Director, Human Subjects Research

 Date

 Chair, Committees for the Protection of Human Subjects

 Date