ILLINOIS
Office for the Protection of Research Subjects

Research Guidance Document

RESEARCH INVOLVING CHILDREN

Definitions

Subpart D: This term refers to the regulations which apply to research involving children as subjects. Subpart D is found in both 45 CFR 46 (DHHS) and 21 CFR 50 (FDA).

Children: By regulatory definition, "children" are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under applicable law of the jurisdiction in which the research will be conducted, according to DHHS and FDA regulations.

In Illinois, individuals under the age of 18 are considered children as defined in federal regulations unless one of the exceptions listed below applies. In Illinois, a person under the age of 18 is no longer considered a child as defined above and Subpart D of 45 CFR 46 and 21 CFR 50 does not apply if the individual meets one of the criteria below and has the capacity to protect their own interests and the research is related to the care for which they have consented:

- Married;
- "Emancipated," a finding typically made by a court;
- A parent
- Pregnant

Federal Research Regulations

Federal regulations require additional safeguards when approving research involving children. These special protections are found in Subpart D. The IRB may approve research involving children only if the research falls under one of the three categories found in Subpart D (see description of categories below) provided that the research also meets the general criteria for approval.

Description

The IRB must consider the general criteria for IRB approval for all studies, including those that involve children. In determining whether the general criteria for approval are met, the IRB may have additional considerations for the research that would generally not be of concern in an adult population.

Risks
Risks that may be considered minimal when dealing with adults (e.g., blood draw) may be riskier when applied to a child population. Efforts should be made to minimize any potential harm.

Equitable selection of subjects
Children may be particularly vulnerable to undue influence and coercion due to the significant influence that parents and other authority figures (e.g., teachers, doctors) have over this population. It is extremely challenging (if not impossible) to eliminate all the influential elements in a research study involving children; however, with special consideration to alternatives to participation, setting(s) of the research and other factors that have great importance to children, elements of coercion and undue influence can be alleviated. Children should be included in research only when their participation is necessary to answer the research question and not out of convenience.

Privacy
Efforts made to protect privacy may differ depending on whether research participants are children, adolescents, or adults. For example, a small child may prefer to have a parent present during a physical examination while adolescents may prefer to have no parent present during a physical examination.

Additional Protections for the Inclusion of Children in Research
The IRB must consider the degree of risk and discomfort involved in the research in relation to the direct benefits it offers to the child to determine whether the study is approvable under the federal regulations. The standard of review is conducted consistently, regardless of full board or expedited review. The IRB may approve studies involving children only if the research falls into one of the three following categories:

(1) Research involving no greater than minimal risk. [45 CFR 46.404; 21 CFR 50.51]

If the IRB determines the interventions or procedures present no more than minimal risk to the child, the research is approvable under this category regardless of whether there is a prospect of direct benefit to the child.

(2) Research involving interventions or procedures that present greater than minimal risk but offers the prospect of direct benefit or may contribute to the well-being of the individual child. [45 CFR 46.405; 21 CFR 50.52]

Most therapeutic medical trials that hold out the prospect of direct benefit to the child may be approvable under this category. Phase I trials and placebo-controlled trials often do not hold out the prospect for direct benefit to participants and may not be approvable under this category. Any submissions that include children in such research practices should include a thorough justification for the involvement of children.

(3) Research involving interventions or procedures that present a minor increase over minimal risk and no prospect of direct benefit to individual children, but likely to yield generalizable knowledge about the child's disorder or condition. [45 CFR 46.406; 21 CFR 50.53]

The risk involved with each procedure must represent minimal risk or a minor increase over minimal risk. It is up to the board to determine the risk level presented by each procedure associated with the study to determine if the research can be approved under this category.

If a proposal involving children cannot be adequately justified in one of these three categories, the IRB must either disapprove the research or refer it to the Secretary of the DHHS and/or the FDA Commissioner. This category of research is considered category (4). Before the IRB refers a project for federal review, the IRB must first find 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". [45 CFR 46.407; 21 CFR 50.54]

Permission from a parent or guardian and a child's assent is required. Requirements for parental permission are described in the Research Guidance Document: Parental Permission (see links at end of this document).

Additional Considerations

Wards of State: Special considerations and requirements are associated with the inclusion of wards in research. Requirements are outlined in the Research Guidance Document: Research Involving Wards of State.

Child Abuse and Neglect: In cases where the nature or procedures of the research may reveal cases of child abuse and/or neglect, researchers must inform participants and their parents whether their confidentiality in this regard is limited by State laws.

Sexual Activity of Adolescent Subjects: When the proposed participants are adolescents, additional sensitivity is required in discussions of the participant's sexual activity. If the consent, parental permission, and/or assent document stipulates that pregnant women must not participate in the research and must have a negative pregnancy test prior to participation in research, investigators must clarify who will receive the results of the pregnancy test.

Individuals Under 18 Who are Not Considered Children: As indicated in the Definitions section above, in certain circumstances Illinois law authorizes an individual under the age of 18 to function as an adult when seeking or receiving health care. In such circumstances, parental permission is not required as part of the research consent process. When an

individual under the age of 18 is authorized to consent for care or treatment because the care or treatment is connected to a sexually transmitted disease or pregnancy/childbirth, the individual may only consent for himself/herself in connection with that treatment or care and the individual may only provide full informed consent for research that is directly connected to that treatment or care.

Researchers are required to conduct a full consent process in a way that is understandable to the individual under 18. The IRB may require parental permission or other methods to ensure comprehension of the study prior to enrollment.

Points to Address

New Study Application:	1. **Participants Page**: a) Select "Less than 7 years old" and/or "7-17" years old, as applicable. b) Enter the exact age range of participants (e.g., 1-12 years old). 2. **Vulnerable Populations Page**: Please complete all the sections on this page as they apply to children as a vulnerable population. 3. **Study Information Page**: Be specific in this section as to how you will protect the confidentiality, privacy, and safety of the children included in the study. Describe why the study has direct benefit to the child participants, as applicable. Include justification for the use of placebo, as applicable. Address special considerations included in the study for the children, and any plans for addressing special risks experienced by this population.

References & Links

Additional Protections for the Inclusion of Children in Research (OHRP): 45 CFR 46, Subpart D	*http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartd*
Additional Protections for the Inclusion of Children in Research (FDA): 21 CFR 50	*http://www.ecfr.gov/cgi-bin/text-idx?SID=73aec6d4923eb29d3ef60696c0d1b662&mc=true&node=pt21.1.50&rgn=div5*
Research Guidance Document: Parental Permission	*To be updated*
Research Guidance Document: Assent	*https://oprs.research.illinois.edu/forms-templates/guidance/guidance-assent*
Research Guidance Document: Research Involving Wards of State	*To be updated*