CHAPMAN UNIVERSITY | INSTITUTIONAL REVIEW BOARD

# Guidelines for IRB Review of Research Involving Children

The federal Department of Health and Human Services (HHS) and the FDA 21 have regulations governing the conduct of research involving children. The IRB must review research/clinical investigations involving children as subjects covered by Subpart D and approve only those protocols that satisfy the criteria and conditions described below.

Children are considered a vulnerable research population because their intellectual and emotional capacities are limited. They are legally incompetent to give valid informed consent.

Investigators interested in enrolling children are required to complete the associated questions in the Cayuse IRB submission and approval for Subpart D must be documented in the IRB approval letter.

Research involving minors can be approved by the IRB if it satisfies the following requirements:

- When reviewing research involving minors as subjects, the IRB considers the risks and discomforts inherent in the proposed research and assesses their justifications in light of the expected benefits to the child-subject or to society as a whole;
- Federal regulations regarding "children" (both 45 CFR 46 and 21 CFR 50) state "Children are persons who have not attained the legal age to consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted." Thus, who qualifies as a "child" depends on the local laws for consent. In California, 18 is the usual age when people can consent to treatments or procedures, but there are important exceptions, such as when seeking medical care related to the prevention or treatment of pregnancy (see below for further clarification).

**Permitted Categories for Research with Children**

Federal regulations classify permissible research involving children into four categories based on degree of risk and type of individual subject. These categories are described in relation to "minimal risk."

**Research not involving greater than minimal risk (45 CFR 46.404 and 21 CFR 50.51) requires:**

- Permission from at least one parent/guardian*
- Assent of the child (if child is 7 or older)
- Expedited level of review

**Research involving greater than minimal risk, but presenting the prospect of direct benefit to the individual subject, (45 CFR 46.405 and 21 CFR 50.52) requires:**

- That the risks are justified by the anticipated benefits; and the risk-to-benefit ratio must be at least as favorable as the alternative treatments or approaches.
- Permission from at least one parent/guardian*
- Assent of the child (if child is 7 or older)
- Full committee review

**Research that involves more than minimal risk and presents the prospect of no direct benefit to the individual subjects, but generalizable knowledge (societal benefits) are expected (45 CFR 46.406 and 21 CFR 50.53) requires:**

- That the risks represent a small increase over minimal risk, and the interventions or procedures are commensurate with those associated with the subject's actual or expected medical, dental, psychological, social or educational situations; and
- the interventions or procedures are likely to yield generalizable information about the subjects' disorder, condition or situation, which is of vital importance to understand or ameliorate
- Permission from both parents/guardians
- Assent of the child (if child is 7 or older)
- Full committee review

**Research not otherwise approvable that presents an opportunity to understand, prevent or alleviate a serious problem affecting the health or welfare of children (45 CFR 46.407 and 21 CFR 50.54) requires:**

- Permission of both parents/guardians*
- Assent of the child (if child is 7 or older)
- Full committee review

**Note**: This type of study is rarely approved.

**Also note**: If it is approved, this type of research requires submission to the secretary of the U.S. Department of Health and Human Services who, after consultation with a panel of experts and an opportunity for public review and comment, must approve or deny the study.

**Parental Permission**

Because a child cannot legally provide consent for research on his or her own behalf, permission by at least one parent or legal guardian is required before a minor is enrolled research study.

- Research involving **no more than minimal risk** requires permission from at least **one parent/guardian**.
- Research that involves **more than minimal risk,** but presents the prospect of **direct benefit to individual subjects,** requires permission from at least **one parent/guardian**.*
- Research that involves **more than minimal risk** and presents the prospect of **no direct benefit to individual subjects**, but generalizable knowledge, requires permission from **both parents.***
- Research that presents an opportunity to understand, prevent or alleviate a serious problem affecting the health or welfare of children, but does **not provide direct benefit to the subject or societal benefit,** requires permission from **both parents**.

**Note**: If there are two parents available to give permission but they disagree about allowing their child to participate in the study, the child should not be enrolled unless that disagreement can be resolved. This policy applies to all permissible categories of research involving children.

*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. If these circumstances are present, the research should document this in the record.

**Waiver of Parental Permission**

For some expedited research studies, the IRB might waive the requirement to obtain written parental permission.

In certain cases, research may be designed for conditions or for a subject population for which parental permission for inclusion is not a reasonable requirement to protect the subjects (e.g., neglected or abused children).

- For non-FDA-regulated studies, the IRB may waive the requirement to obtain parent(s)/guardian(s) permission provided "an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with federal, state or local laws."

- For FDA-regulated studies, parent(s)/guardian(s) permission cannot be waived for FDA-regulated clinical investigations; FDA regulations lack the provision for wavier of parental permission.

**Child Assent**

Federal regulation and state statute require that minors assent to participate in research.

- Assent is defined as a **minor's affirmative agreement** to participate in research.
- In most cases, this must be **documented in writing** if the subjects are at least **7 years old**.
- The IRB has authority to require assent from **children younger than 7** if they are likely to comprehend and appreciate what it would mean to volunteer to participate in a given protocol.

**Written Assent Requirements**

Assent forms should be written at the appropriate educational and maturity level of the youngest prospective subject in the age range.

- Techniques such as the use of larger type, simple schema and pictures may help boost a child's understanding of the text.
- Depending on the age range of the minors to be involved, the lead researcher might be required to develop two different assent forms at different reading comprehension levels (e.g., one assent form written for young children ages 7-12 years old, and one assent form written for minors ages 13-17 years old).
- Alternatively, for children 13-17 years of age, the researcher may develop a joint assent/permission consent form and obtain the signatures of the minor and parent(s) or guardian(s) on one document.

**Assent Elements**

An assent form should contain date and signature lines for the child, a witness and an investigator. The assent form should cover the following points:

- what the study is about;
- why the child is eligible to participate for the study;
- what procedures will be performed;
- potential risks and discomforts to the child;
- potential benefits to the child and society;

- for non-therapeutic research, a statement that the child can choose whether to participate and may withdraw at any time without negative consequences, an invitation to ask questions any time; and
- names and phone numbers of whom to contact with questions

A sample **Assent Form** is available. The sample is not a template. Assent forms must be tailored to the reading and comprehension level(s) of the subject populations to be enrolled and will vary widely from study to study.

**Waiver of Assent**

Assent of the child is not a necessary condition for proceeding with the research under the following conditions:

- If the capability of some or all of the children is so limited that they cannot reasonably be consulted; or
- if the IRB determines that the intervention or procedure involved in the research holds a prospect of direct benefit that is important to the health or wellbeing of the children and is available only in the context of the research.

Under such circumstances, a child's dissent, which should normally be respected, may be overruled by the child's parents at the IRB's discretion.

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 45 CFR 46.116(d) regarding waiver or alteration of informed consent.

REFERENCES

Department of Health and Human Services (HHS) 45 CFR Part 46 Subpart D
Food and Drug Administration (FDA) 21 CFR Part 50 Subpart D