
Yale University Institutional Review Boards

IRB Policy 310 Participation of Children in Research

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Scope

This policy defines the standards for the participation of children in research studies conducted at or by Yale University. Children participating in research constitute a special class of subjects for which special protections apply.

Policy Statement

All children considered for enrollment in, or enrolled as subjects in research must be treated in a manner commensurate with their special status as minors. Such research must be designed to ensure the appropriate enrollment of children and employ additional safeguards as described in this policy to ensure and protect their rights and welfare.

Reason for the Policy

The University has an ethical responsibility to protect the rights and welfare of human research subjects and ensure that research does not endanger their safety or undermine the public confidence in the conduct of research. The special vulnerability of children makes review of their involvement particularly important and charges the researcher and the IRB with ensuring that such research is not contrary to the rights and welfare of the child subjects.¹

Special ethical and regulatory standards have been defined for reviewing research involving children. The participation of children in research is only permissible if it incorporates additional protections which reflect the anticipated risks to the child subjects in relation to the expected benefits to the child. As the study risks increase, there must also be an increased likelihood of benefit to the child subject or importance of the knowledge to be gained about the child's disorder or condition. The standards for research involving children have been codified into federal regulations found at Subpart D of 45 CFR 46 (Department of Health and Human Services regulations). It is important to note that clinical trials that involve children as research subjects are also subject to specific regulations defined by the U.S. Food and Drug Administration found at Subpart D of 21 CFR 50 (U.S. Food and Drug Administration regulations).

¹ DHHS, Institutional Review Board Guidebook, Chapter VI, Special Classes of Subjects, Children and Minors

Definitions

Adolescent Assent Form

An Assent Form generally written for children 13-17 years of age in a format appropriate for their cognition and understanding. An Adolescent Assent Form differs from the Assent Form noted below in that it may use more sophisticated language and format than one written for younger children, often following the format provided for adult consent.

Assent

A child's affirmative agreement to participate in research. This should be sought in addition to the consent of a legally authorized representative or surrogate when the individual is sufficiently cognitively capable of understanding the nature of his or her participation in a research study. Mere failure to object should not, absent affirmative agreement, be construed as assent.

Assent Form

A document written in language that is appropriate to the child subject's maturity and cognitive level and used as part of the assent process to 1) describe the research study, including the research procedures, risks and benefits, and 2) obtain the child's written agreement to participate in the study. (See <http://info.med.yale.edu/hic/forms/index.html>)

Child/Children

For purposes of this policy, a child is any individual who at the time of enrollment in a research study has not yet reached the legal age of majority under the law in the jurisdiction in which the research will take place. In the State of Connecticut, the age of majority is 18. Investigators working in locations outside Connecticut should confirm the local age of majority to determine at what age an individual is considered to be an adult.

Emancipated Minor

A minor who is to be treated as an adult for purposes of this policy. An emancipation order allows a minor to consent to "medical, dental or psychiatric care, without parental consent, knowledge or liability." In Connecticut, minors above age sixteen or their parents may petition the Superior Court for Juvenile Matters or the Probate Court for emancipation orders. The court may declare the minor emancipated if (1) the minor has been married, (2) the minor actively serves in the U.S. armed forces, (3) the minor willingly lives away from home and manages his or her own finances, or (4) the court determines "for good cause" that emancipation is in the "best interest" of the minor. A minor may also be considered emancipated under common law under similar circumstances.

Guardian

An individual who is judicially appointed parental rights for a child including (A) the obligation of care and control; and (B) the authority to make major decisions affecting the child's education and welfare, including, but not limited to, consent determinations regarding marriage, enlistment in the armed forces and major medical, psychiatric or surgical treatment.

Minimal Risk

The probability and magnitude of harm or discomfort anticipated in the research is not greater in and of itself than that ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Parent

A child's biological or adoptive parent.

Parental Permission Form

A document used to obtain the written permission of a child subject's parent or guardian allowing that child to participate in research. The parental permission form must be written in a language understandable by the parent/guardian and must contain all elements of informed consent, including a description of the research study, the research procedures, risks and benefits. (See <http://info.med.yale.edu/hic/forms/index.html>)

Permission

The agreement of parents or guardians to the participation of their child or ward in research.

Ward

For the purpose of this policy, a ward is a child under the care of a guardian, or other non-parental custody arrangement. For example, children under the protection of a court, child protective services, or under the care of a non-parental relative would be considered to be wards.

Policy Sections

310.1 Research Risk Categories

The IRB will only approve research involving children as subjects if the research satisfies the federal requirements for the participation of children, the research can be characterized into one of the research categories defined below and the IRB finds sufficient safeguards in place for protecting the rights and welfare of the child subjects. In addition, all clinical trials involving children must satisfy the FDA requirements found at Subpart D of 21 CFR 50.

- A. Research not involving greater than minimal risk to the children (45 CFR 46.404, 20 CFR 50.51)**
To approve this category of research, the IRB must make the following determinations:
- the research presents no greater than minimal risk to the children; **and**
 - adequate provisions are made for soliciting the assent of the children and the permission of one or both of their parents or guardians.
- B. Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual child subjects involved in the research (45 CFR 46.405, 20 CFR 50.52).**
To approve research in this category, the IRB must make the following determinations:
- the risk is justified by the anticipated benefits to the subjects;
 - the relation of the anticipated benefit to the risk presented by the study is at least as favorable to the subjects as that provided by available alternative approaches; **and**
 - adequate provisions are made for soliciting the assent of the children and the permission of one or both of their parents or guardians.
- C. Research involving greater than minimal risk and no prospect of direct benefit to the individual child subjects involved in the research, but likely to yield generalizable knowledge about the subject's disorder or condition (45 CFR 46.406, 20 CFR 50.53).**
In order to approve research in this category, the IRB must make the following determinations:
- the risk of the research represents a minor increase over minimal risk;
 - the intervention or procedure presents experiences to the child subjects that are reasonably commensurate with those inherent in their actual, or expected medical, dental, psychological, social, or educational situations;
 - the intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital importance for the understanding or amelioration of the disorder or condition; **and**

- adequate provisions are made for soliciting the assent of the children and the permission of both parents or guardians, unless one parent is deceased, unknown, incompetent, or not reasonably available or when one parent has legal responsibility for the care and custody of the child subject.

D. Research that the IRB believes does not meet the conditions of 45 CFR 46.404, 46.405, or 46.406, but 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 (45 CFR 46.407, 20 CFR 50.54).

Research that falls into this category cannot be approved under any of the other three research categories. However, 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, it may refer the protocol to the federal Department of Health and Human Services (DHHS) for review. The research may proceed only if DHHS determines either that (a) the research does, in fact, fall into one of the permissible research categories or (b) it makes the following determinations:

- the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
- the research will be conducted in accordance with sound ethical principles; **and**
- adequate provisions are made for soliciting the assent of the children and the permission of both parents or guardians, unless one parent is deceased, unknown, incompetent, or not reasonably available or when one parent has legal responsibility for the care and custody of the child subject.

310.2 Consent and Assent Requirements

A. Requirements for Permission from Parents or Guardians

Permission from one or both parents or guardians is required for children to participate in research unless one of the exceptions described in section 0000.3 applies. The IRB will determine the number of parents or guardians that must provide permission for a child to participate in research based upon an assessment of the risks and benefits as described in section 0000.1. Parental or guardian permission must meet the requirements for informed consent and documentation of consent found in the IRB Policy on Informed Consent.

B. Requirements for Assent from the Child Subject

Adequate provisions to obtain assent from the child must be sought in addition to parental permission unless the IRB determines that the children are not capable of assenting, the IRB determines that the research holds out a prospect of direct benefit that is important to the health or well-being of the child which is only available in the context of the research, or the requirements of section 0000.3 are met for waiver of child assent. The assent procedures must be approved by the IRB, which may include obtaining oral assent from the child or written assent through the use of an assent form signed by the child. In determining whether children are capable of assenting, the IRB shall take into account the age, 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. If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds 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, the assent of the children is not a necessary condition for proceeding with the research.

When assent is required, assent must be documented either through the child signing an assent form or through documentation in the study record of verbal agreement in cases of verbal assent.

Assent forms may be used with children of appropriate maturity and cognition and must be tailored to the subject's age, maturity level and psychological state.

Verbal assent may be approved when the research involves young children, children with poor literacy, or children undergoing treatment for an illness which may impact their ability to provide written assent. If appropriate for the child's cognition level, an information sheet can be used to inform subjects about the research, or to solicit a verbal agreement to participate. If no form or information sheet is to be used, a script of the information to be presented verbally must be approved by the IRB in accordance with the IRB Policy on Informed Consent.

Assent forms and parental permission forms must be consistent in guaranteed elements of privacy and confidentiality. Any limits to the child's privacy, or the confidentiality of his or her data, must be clearly stated in both forms.

C. Consent Requirements for Studies in Which Children Reach the Age of Majority During the Study

Once a child subject reaches the age of majority, he or she no longer qualifies as a child, and parental permission is no longer valid. Child subjects enrolled in a study who reach the age of majority while the study is on-going must provide consent to continue participation in the research in accordance with the IRB Policy on Informed Consent.

D. Emancipated Minors

A participant who has been granted status as an emancipated minor is considered to be able to consent on his/her own behalf and is treated as an adult for the purposes of this policy.

310.3 Waiver of Permission and/or Assent

A. Waiver of Permission of Parent or Guardian

Under certain limited conditions, the IRB may grant a waiver of parental/guardian permission in advance of a child subject's enrollment. A waiver of parental/guardian permission is acceptable only if:

1. The research involves a treatment for which a child's consent is permissible under law (i.e., outpatient mental health care, pregnancy, treatment for venereal disease, or treatment for alcohol or drug dependence); or
2. The subject is legally emancipated through the Superior Court or the Probate Court, after hearing, finding that: (1) The minor has entered into a valid marriage, whether or not that marriage has been terminated by dissolution; or (2) the minor is on active duty with any of the armed forces of the United States of America; or (3) the minor willingly lives separate and apart from his parents or guardian, with or without the consent of the parents or guardian, and that the minor is managing his/her own financial affairs, regardless of the source of any lawful income; or (4) for good cause shown, where it is in the best interest of the minor, any child of the minor, or the parents or guardian of the minor, the court may enter an order declaring that the minor is emancipated; or
3. Parental/guardian permission is not a reasonable requirement because it poses additional risk or may be at odds with the interests of the child subject (e.g., research concerning neglected or abused minors, reproductive health issues). In such cases, the research protocol must propose an alternative to parental/guardian permission appropriate to the nature and purpose of the research, the risk and anticipated benefit to the child subjects, as well as the child subjects' ages, maturities, statuses, and conditions; or

4. The study meets the requirements for waiver of consent as described in the IRB Policy on Informed Consent.

B. Waiver of Assent

The IRB may waive or modify the assent requirements when one of the following conditions is met:

- 1 The IRB finds that
 - i. the project could not practicably be carried out without the waiver or alteration and
 - ii. the project is subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under these programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs;

OR

- 2 The IRB finds that:
 - i. The research involves not more than minimal risks to the children;
 - ii. The waiver or alteration does not adversely affect the rights and welfare of the children;
 - iii. The research could not practicably be carried out without the waiver or alteration and
 - iv. information after participation.

310.4 Inclusion of Wards of the State or Any Other Agency, Institution, or Entity

Children who are wards of the state or any other agency can be included in research that is determined by the IRB to be minimal risk. They may also participate in research considered greater than minimal risk when the research has the potential to provide direct benefit to the ward. However, wards may not participate in research that is considered greater than minimal risk when there is no prospect of direct benefit to them unless the IRB determines 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 subjects are not wards.

In studies which are deemed by the IRB to be greater than minimal risk with no prospect of direct benefit to the ward, an advocate must be appointed 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 investigator(s), or be the child's guardian or foster parent.

Assent and permission from the child's legal guardian is required as described in section 0000.2 above.

All research protocols designed to enroll children who are wards of the State of Connecticut must obtain approval from the Connecticut Department of Children and Families (DCF) IRB. (See <http://www.ct.gov/dcf/cwp/view.asp?a=2555&q=314538>).

In studies which do not intentionally plan or expect to enroll wards of the state, if at any time during the course of research a research participant becomes a ward of the state, the PI must notify the IRB as soon as the investigators become aware of the change of status, and must seek approval from the Connecticut DCF IRB.

310.5 Other Institutional Approvals

Protocols involving children also may require review and approval by other University committees such as the Pediatric Protocol Review Committee (PPRC) or the Yale Cancer Center Protocol Review Committee (PRC) prior to approval by the IRB. Investigators should consult these offices for information on their submission requirements.

310.6 IRB Record Keeping Requirements

When reviewing a protocol including children, the IRB must classify the research into one of four categories (see section 0000.1). The minutes and/or reviewer checklist must document the category under which the protocol is approved, together with protocol specific findings that justify application of the category under which the protocol is approved as well as determination as to whether one or both parents/guardians must provide permission. The minutes and/or checklist will also document findings related to waiver of consent and/or inclusion of wards.

Related Information

Procedure 310 PR.1 Informed Consent in Research Involving Children

Procedure 310 PR.2 Submission of Protocols for Research Involving Children

Guide 310 GD.1 Research Conducted in Schools

Form: 310 FR 1 Assent Template

Checklist 310 CH 1 Children's Findings Worksheet

Contacts

Subject	Contact	Phone
Biomedical Studies involving Children	Human Investigation Committee	785.4688 ysmhc@yale.edu
Nursing Studies involving Children	Human Research Review Committee	203.737.2371
Social or Behavioral studies involving Children	Human Subjects Committee	436-3650 human.subjects@yale.edu
Scientific Review of Pediatric Research Proposals	Pediatric Protocol Review Committee (PPRC)	203-764-9199

Roles and Responsibilities

[Human Investigation Committee](#)

The HIC serves as Institutional Review Boards or IRBs for biomedical human research conducted at Yale University.

[Human Subjects Committee](#)

The HSC is responsible for the review and oversight of social and behavioral human research.

[Human Subjects Research Review Committee](#)

The HSRRC serves as the IRB for all human research that is conducted by faculty and students at the Yale School of Nursing.

[PPRC](#)

The Pediatric Protocol Review Committee (PPRC) reviews protocols involving minors. The Committee is sponsored by the Department of Pediatrics. The purpose of the PPRC is twofold: (1) to review the scientific validity of proposed studies in minors; and (2) to ensure that appropriate and systematic measures to minimize risk to participating subjects are incorporated into the protocols.

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