

IRB Guidelines on Research with Children for Consent, Permission, and Assent

Special ethical and regulatory considerations apply when research involves children as participants. Only people who are “children” under the federal IRB regulations are covered by the additional protections described in Subpart D of 45 CFR 46 (HHS regulations) and 21 CFR 50 (FDA regulations).

This guidance discusses who is considered a child for research purposes, and provisions for obtaining assent from children and permission from the parent(s) or guardian.

Definitions

Children: The federal IRB regulations define children as “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.” 45 CFR 46.402; 21 CFR 50.3. Thus, who is a “child” for research purposes rests on the applicable law in the jurisdiction(s) where the research will occur. If research on a specific treatment or procedure involves solely treatments or procedures for which minors can give consent outside the research context (under applicable state and local laws, for example, research on sexually transmitted diseases or pregnancy), such individuals would not meet the definition of children in the IRB regulations and can consent to their own research participation.

Assent: a child’s affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

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

Parent: a child’s biological or adoptive parent.

Guardian: an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care.

Circumstances in Which Minors May Consent to Research Participation

In New York, the legal age for consent to medical treatment is usually 18 years old. Some exceptions apply under New York law that permit a minor to consent to medical treatment for him or herself, and these exceptions depend on the minor’s legal status (e.g., emancipated minor, pregnant or married minors, minors who are parents) or the medical condition or treatment received by the minor. A detailed discussion of the circumstances in which minors can consent to medical treatment under New York law is beyond the scope of this guidance document – if you need further assistance on this topic, contact the IRB to be directed to the appropriate offices for assistance.

A minor who understands the risks, benefits, and alternatives to certain health services may give informed consent (i.e., parental permission is not required) for research participation when the research involves solely treatments or procedures for which minors can give consent under the law of the jurisdiction where the research will take place – if some of the treatments or procedures encompassed by the research would require parental permission under applicable law, then parental permission is

required for all of the research procedures and treatments to be used in the study. The decision to allow minors to consent on their own behalf to research participation must be made by the IRB on a case-by-case basis after careful consideration of the nature of the research, anticipated benefits, and potential risks, and may also require consultation with MC's General Counsel.

For research involving children that will take place outside New York, the investigator is responsible for understanding local requirements regarding who qualifies as a "child" and whether local requirements provide any other unique protections to children.

Researchers working in other states or countries should consult with local collaborators, ethics committees, or other relevant sources about the applicable laws and regulations of that jurisdiction.

Assent

Because assent consists of affirmative agreement to participate in research, the child must actively show his/her willingness to participate in the research, rather than merely complying with directions to participate or not resisting in any way. The IRB determines and documents whether obtaining assent is a requirement for all, some, or none of the children who will participate in a research study.

In determining whether children are capable of assenting, the IRB will take into account the age, maturity, and psychological state of the potential child participants. This judgment may be made for all participants to be involved in a research study, or for each participant, as the IRB deems appropriate.

If a child is capable of assent and the IRB has required that assent be sought, assent must be obtained before the child participates in the research. If a child dissents from participating in research, even if the parents or guardian have granted permission, the child's decision prevails. However, as discussed below, the IRB can waive the assent requirement if the research intervention/procedure holds out the prospect of direct benefit that is important to the child's health or well-being and is available only in the context of the research.

Assent forms and scripts should be written at the appropriate educational and maturity level of the youngest prospective participant in the age range. Depending on the age range of the children to be enrolled, multiple assent forms or scripts may be required for different reading comprehension and cognitive/developmental stages. For older children, a combined parental permission/child assent document may be developed to serve as a joint assent/permission form, with signatures to be obtained from both the child and the parent(s) or guardian on the same document – see the table below for further guidance on documenting parental permission and child assent.

The HHS regulations do not specify the order in which parental permission and child assent should be sought. In general, parental permission should be sought before seeking the assent of a child, particularly in more than minimal risk research, unless the requirement for obtaining parental permission can be waived. There might be some cases, however, involving minimal risk research, where it would be reasonable to seek child assent prior to seeking parental permission. For example, a school-based study of minimal risk (e.g., investigating children's responses to music), could be posed to children in the school setting. Children could be asked if they wanted to participate and if so, sent home with a request for parental permission. In all cases, except when the requirement for obtaining parental permission has been waived by the IRB, parental permission is required before the child can be enrolled in the study, even if parental permission is sought after child assent is provided.

Assent and Parental Permission Guidelines for Children by Age:

Age of Minor Participant	Assent Form/Script	Separate Parental Permission Form
Infant-6 years old	No	Yes
7-11 years old	Yes	Yes
12-17 years old (Option A)	Yes	No. Create a single document addressed to the adolescent with signature lines for assent and parental permission.
12-17 years old (Option B)	Yes. See adolescent assent form template	Yes

Assent Guidelines: Signature and Documentation Requirements

For children under 7 years old: Only parental permission is required. Simple verbal explanation of research procedures should be provided to the child.

- Although a formal assent process is not required for use with children less than 7 years old, each child should still be given a simple verbal explanation of what will happen to him or her, or what he or she will be asked to do.
- Use the parental permission form template on the NU IRB website. Within the parental permission form, refer to the participant throughout as “your child” or “your infant.”
- If parents will also participate in the study, one consent/permission form may be used to describe the study procedures for the child and the parent(s).

For children 7 to 11 years old: In most cases, children this age will be able to participate in the assent process, using a simplified assent script/form. A separate, more detailed permission form will be needed for the parents or guardians.

- Create two documents: a simplified child assent script or form and a separate parental permission, using the MC IRB templates. The investigator can choose whether to seek signed assent or verbal assent from children in this age range. Verbal assent is acceptable for children ages 7 to 11 years old, but if children will not be signing an assent form, the IRB still must review and approve the assent script to be used with children in this age range.
- The assent form or script should contain language that is appropriate to the child’s development and age, use a simple format that is easy to read and, when possible, be limited to one page. The use of larger type, simple schema, and pictures will facilitate the child’s understanding of the information.
- If parents are also part of the study, a consent/permission form may be used to describe the study procedures for both the child as well as the parent(s), although the child would also have a separate assent form/script.

For children 12 - 17 years old: Two options are available in these circumstances.

Option A (usually preferred):

- Using the MC IRB template, write one consent form for the adolescent participant and the parents or guardians.
- Use clear, straightforward language written at a 7th to 8th grade reading level.
- Address the form to the adolescent with signature lines for assent and parental permission. The adolescent should be asked to sign first.

Option B (for studies where Option A is not feasible or appropriate).

- This option can be used for studies with a very complex protocol and/or involving adolescent subjects whose medical condition demands a simpler form than the adult's form, even when the adult's form is written at an eighth-grade level.
- A simplified assent form is written for the adolescents. A separate more detailed permission form is written for the parents or guardians.
- Only the adolescent is asked to sign the assent form.

Waiver of Assent

The IRB can determine that assent is not a requirement for some or all children to be enrolled in a study if the IRB finds that one or more of these criteria for a waiver of assent are met:

- The capability of some or all of the participants is so limited that they cannot reasonably be consulted; OR
- 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 participant and is available only in the context of the research; OR
- The research meets the conditions for waiver or alteration of informed consent that apply to research involving adults, as specified in the regulations at either 45 CFR 46.116(e) or 45 CFR 46.116(f)

Children who become adults during the research study

When a participant who was enrolled in research with parent permission reaches the age of consent, the provisions for parent permission no longer apply to that participant. Unless the IRB determines that the requirements for obtaining informed consent can be waived, the research team should obtain informed consent for the now-adult participant for any ongoing interactions and interventions with the participant – this is because the prior parent permission and child assent are not equivalent to legally effective informed consent for the now-adult participant. If the research does not involve any ongoing interactions or interventions with the participants, but continues to meet the regulatory definition of human subjects research (e.g., involves continued analysis of identifiable data or specimens), the research team must obtain informed consent from the now-adult participants. The IRB can consider, if appropriate, waiving informed consent in cases in which the now-adult participant's ongoing participation is no more than minimal risk and meets all the requirements for a waiver of consent, including that the research could not practically be carried out without the waiver.

Parental/Guardian Permission

By definition, children are unable to provide informed consent to participate in research, although they might be able to give their assent. The IRB will determine that, unless parental permission can be waived, adequate provisions are made for seeking the permission of the child participant's parent(s) or legal guardian(s). The IRB regulations define "parent" as a "child's biological or adoptive parent." The term "guardian" means "an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care."

Where parental permission is to be obtained, the IRB will require permission from one or both parents in accordance with specifications relating to the four categories of permissible research with children:

Regulatory Category of Permitted Research with Children	One Parent's or Both Parents' Permission Required?
Minimal Risk (<u>45 CFR 46.404; 21 CFR 50.51</u>)	One parent/legal guardian can be sufficient
Greater than Minimal Risk, Direct Benefit to Subject (<u>45 CFR 46.405; 21 CFR 50.52</u>)	One parent/legal guardian can be sufficient but IRB must determine whether one or two is required
Greater than Minimal Risk, No Direct Benefit to Subject, but Likely to Yield Generalizable Knowledge about Subject's Condition (<u>45 CFR 46.406; 21 CFR 50.53</u>)	Both parents/legal guardians, unless one parent is deceased, unknown, incompetent, not reasonably available, or does not have legal responsibility for the custody of the child.
Greater than Minimal Risk, No Direct Benefit to Subject, but Results May Alleviate Serious Problems of Children's Health or Welfare (<u>45 CFR 46.407; 21 CFR 50.54</u>)	Both parents/legal guardians, unless one parent is deceased, unknown, incompetent, not reasonably available, or does not have legal responsibility for the custody of the child.

For research that falls into risk-benefit Category 1 [45 CFR 46.404; 21 CFR 50.51] or Category 2 [45 CFR 46.405; 21 CFR 50.52], the IRB may determine that permission from only one parent is sufficient -- the IRB generally will find that permission of one parent is sufficient unless the nature of the study seems likely to provoke disagreements about participation among two parents, in which case permission from two parents may be required unless one parent is deceased, unknown, incompetent, not reasonably available, or does not have legal responsibility for the custody of the minor. Research that falls into Category 3 [45 CFR 46.406; 21 CFR 50.53] or Category 4 [45 CFR 46.407; 21 CFR 50.54] requires permission from both parents, unless one parent is deceased, unknown, incompetent, not reasonably available, or does not have legal responsibility for the custody of the child [45 CFR 46.406 or 407; 21 CFR 50.55(e)].

Generally, IRBs do not review the circumstances of whether a second parent is reasonably available for each enrolled participant -- this is a task for the investigator. The IRB determines the requirement for parental permission at the time of IRB review of the research, based on the regulatory category that is most appropriate to the nature of the research under review and with regard to the entire population of prospective participants. It is not until the investigator meets the parent (s) and child and discusses

the particulars of the research and enrollment that information about the availability of both parents becomes apparent. While the IRB may certainly be consulted by investigators for guidance on a particular situation, it is ultimately the responsibility of the investigator to adequately assess, document, and decide whether a parent is not reasonably available given the specific facts and circumstances of each situation, including the level of that second parent's participation in the life of the child.

When Parents Disagree

If there are two parents available to give permission but they disagree about allowing their child to participate in the study, the child may not be enrolled unless that disagreement can be resolved. This applies to all permissible categories--even if only one parent's signature is required, when both parents are involved in the decision, they must agree for the child to be enrolled. If a parent who was not involved or available for the original consent later becomes involved or available, the two parents must then agree.

Parental Permission when the Parent is a Minor

A minor who is a parent may consent to research participation of his/her own child. The federal IRB regulations do not require that the parent have reached the age of majority. Because statutory provisions of New York law allow a minor parent to consent to medical treatment for his/her child, the minor parent is also able to provide informed consent for research participation.

Research with pregnant minors, their fetuses, and the children of minors requires special considerations and involves complicated ethical and regulatory issues. The decision to allow minors to consent to research on their own behalf and/or on behalf of their fetuses, neonates, and children must be made by the IRB on a case-by-case basis after careful consideration of the nature of the research, anticipated benefits, and potential risks.

Waiver of Parent/Guardian Permission

The IRB can waive the requirements for obtaining parental or guardian permission for research involving children if either:

- The criteria for a waiver of parental permission are met, as set out in the IRB regulations at 45 CFR 46.116(e) or 45 CFR 46.116(f); OR
- The IRB determines that the research is designed to study conditions in children or a participant population for which parental or guardian permission is not a reasonable requirement to protect the participants (e.g., neglected or abused children), and also finds that: (i) an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted; and (ii) the waiver is not inconsistent with federal, state, or local law. 45 CFR 46.408(c)

The choice of an appropriate substitute mechanism will depend on the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

Parents/Guardians as Research Participants

At times, research that primarily involves children as participants may also include procedures for the parents/guardians of participating children. Consent should be obtained and documented from the parent/guardian for that individual's own participation in the study, as well as permission for their child to participate in the study. If the parent/guardian's participation will include specimen collection, genetic testing, or access to protected health information about the parent/guardian, the separate adult consent template should be used and appropriate HIPAA authorization language included if PHI about the parent/guardian will be accessed.

Children who are Wards

The federal IRB regulations provide special protections for children enrolled in research who are wards of the state or any other agency, institution, or entity, if the research is approved under 45 CFR 46.406 or 45 CFR 46.407. Before children who are wards can be included in either of those two regulatory categories of research, the research must meet these conditions:

- the research must be either related to the children's status as wards; or conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards; and
- 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 can serve as advocate for more than one child, and must be an individual who has the background and expertise to act in the best interests of the child for the duration of the child's research participation. The advocate must not be associated in any way (except in the role of advocate or as an IRB member) with the research, investigators, or the organization.

Research in the School Setting

When doing research in the school setting, each K-12 site may have different procedures for approving external research. It is the expectation of the IRB that researchers will contact the schools/districts/administrators to get permission from the appropriate authority. Depending on the specific site, permission may be granted by a superintendent, principal, a committee at the school district, or other individual/entity in an appropriate position of authority.

School sites will often require proof of MC IRB review prior to their approval. If a school district has its own review process for research proposals, it is important to plan additional time for the review process since the study will be reviewed by both the MC IRB and the school's review process.

Student Educational Records and FERPA

The Family Educational Rights and Privacy Act (FERPA) is a federal law that protects the privacy of student education records maintained by schools. Educational records include class assignments, grades, GPA, attendance, disciplinary reports, individual student educational plans, etc. Parental consent is required for the release of FERPA-protected identifiable student records for minors, unless the release is covered by a FERPA exception. The IRB cannot waive parental permission for access to

student educational records as part of research in situations where FERPA requires parental consent. Many states also have their own laws on privacy of student educational records. Researchers who wish to access student education records will need to take into account the requirements of FERPA and any applicable state laws.

REGULATIONS AND GUIDELINES

45 CFR 46 Subpart D (HHS regulations)

21 CFR 50 Subpart D (FDA regulations)

HHS Office of Human Research Protections FAQs on Research with Children

(<https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/children-research/index.html>)

Parental Permission in Research Involving Children, Focusing on “Not Reasonably Available,” Recommendation of the HHS Secretary’s Advisory Committee on Human Research Protections, <https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-d-november-13-2018/index.html>