Cornell University
Office of Research Integrity and Assurance
Human Research Participant Protection Program

SOP 11: INFORMED CONSENT, ENROLLMENT, AND OTHER CONSIDERATIONS FOR RESEARCH INVOLVING CHILDREN

1. Subject of Policy & Procedure

This document sets forth the requirements for obtaining (a) IRB approval of research involving children; and (b) informed consent and enrollment of children in human research.

Under the federal regulations, children are "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." For research in New York State, individuals under the age of 18 are considered to meet the DHHS and FDA definitions of "children." This includes not only viable neonates, but also college and university students under the age of 18, unless a waiver is approved by the IRB. New York State does not recognize the concept of an "emancipated minor" for the purposes of research. If investigators are recruiting children outside of New York State, the Protocol PI must report this category of participant in the protocol and state the definitions of child, parent, and legal guardian in that jurisdiction.

Children are a "vulnerable population," because they are considered easily susceptible to coercion and undue influence and incapable of completely understanding the risks and benefits in making the decision to participate in research. The respect for persons elaborated in the Belmont Report requires that the decision to participate in research be wholly informed and voluntary. The IRB recognizes the importance of conducting scientifically sound research and ethically designed studies in this population. Excluding them from participating in the research is not an answer. Instead special precautions should be incorporated into the design of the study to protect the rights and welfare of child participants.

When children are involved, the IRB gives special consideration to recruitment methods, oversight of the consent/assent processes, and the completeness of information provided to the child's decision-maker. The extent of protection of the child's rights and welfare considered by the IRB depends on the risk of harm and the likelihood, the degree of the benefit to the child from involvement in the study, and the age range of the children who are being asked to participate. This policy discusses these special considerations and protections.

Moreover, in order to safeguard their interests and to protect them from harm, federally-mandated considerations are in place for reviewing research involving children. Adding to the protection provided under the Common Rule (45 CFR 46), federal regulations (45 CFR 46, Subpart D) provide protections for children involved in research such as obtaining assent from the child and obtaining the permission of the parents/legal guardians for the child to be enrolled in the research protocol. More specific provisions are based on the degree of risk involved in the proposed research and the nature and degree of anticipated benefits. While these regulations apply only to research supported by the Department of Human Health and Services (DHHS), Cornell University's institutional policy concerning the Human Research Protection Program extends the same protection to all research participants regardless of the source of financial support or funding.

Finally, certain children may be members of another vulnerable population (*e.g.*, children from economically or educationally disadvantaged families, children under the control of the court system, pregnant minors, mentally disabled children). In these instances, the Protocol PI and the IRB should carefully apply, as appropriate, not only this SOP, but also the SOPs pertaining to the second vulnerable population of which the child is a member. The IRB should give special attention to these groups of children who, while they need special protections, should not be denied the opportunity to participate in research, especially research which may benefit them.

2. Scope of Policy & Procedure

This Policy & Procedure applies to all on-going and future human participant research projects conducted by Cornell University faculty, staff, or students or by anyone conducting a research activity supported by Cornell University or where Cornell is considered to be engaged in the research.

3. Terms and Definitions

All parties to whom this policy applies (*e.g.*, faculty, students, staff, IRB members) should consult the IRB Glossary.

4. See Also

Affected researchers and employees should also consult:

1. Cornell University Federalwide Assurance Registration
2. Sample Parental Permission Form
3. Sample Child Assent Form
4. OHRP Guidance: Special Protections for Children as Research Subjects

5. Regulations Applicable to Informed Consent

5.1. The Belmont Report

5.2. 45 CFR 46.109(b), (c), & (e): IRB Review of Research, stating that (1) "[a]n IRB shall require that information given to subjects as part of informed consent is in accordance with §46.116. The IRB may require that information, in addition to that specifically mentioned in §46.116, be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects;" (2) "[a]n IRB shall require documentation of informed consent or may waive documentation in accordance with §46.117;" and (3) "[a]n IRB shall have the authority to observe or have a third party observe the consent process and the research."

5.3. 45 CFR 46.111(a)(4), (a)(5), & (b): Criteria for IRB approval of research, mandating that (1) informed consent "will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by §46.116," and "appropriately documented, in accordance with, and to the extent required by §46.117;" and (2) "[w]hen some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects."

5.4. 45 CFR 46.116: General requirements for informed consent

5.5. 45 CFR 46.117: Documentation of informed consent
5.6. 45 CFR 46, Subpart D, addressing additional protections for children involved as participants in research

6. Categories of Permissible Research Involving Children & Associated Parental Permission/Child Assent Requirements

The Protocol PI should involve children only in research protocols that meet the requirements of one of the three categories described below. He or she should state in the protocol why the research meets a certain category (*e.g.*, discuss the risk/benefit ratio, *etc.*). The Protocol PI should also meet the consent/assent requirements for each category. Finally, the Protocol PI should examine Sections 6.3 and 6.4, setting forth the IRB's considerations, in order to address those issues in the protocol.

6.1. Three Categories of Permissible Research Involving Children: Federal regulations require the IRB to classify research involving children into one of three categories and to document the discussions of the risks and benefits of the research study. The IRB Minutes should document how the research protocol meets its assigned category. These are the three categories of permissible research, based on the degree of risk and benefit to the child:

1. *Category 1*: Research not involving greater than minimal risk (§46.404)

   Children can be approved for these studies only when the IRB finds that adequate provisions have been made for soliciting the assent of the children and the permission of their parents or legal guardians to participate in the research study.

   Permission from one parent/guardian is sufficient for Category 1 research, unless this is contradictory to the regulations of the U.S. or foreign jurisdiction in which the research is being conducted. *See, e.g.,* SOP 14: International Human Research.

2. *Category 2*: Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual participants (§46.405)

   Children can be approved for these studies only when the IRB finds that: (1) the risk is justified by the anticipated benefit to the participants; (2) the relation of the anticipated benefit to the risk is at least as favorable to the participants as that presented by available alternative approaches; and (3) adequate provisions are made for soliciting the assent of the children and permission of their parents or legal guardians to participate in the research study.

   Permission from one parent/guardian is sufficient for Category 2, unless this is contradictory to the regulations of the U.S. or foreign jurisdiction in which the research is being conducted. *See, e.g.,* SOP 14: International Human Research.

3. *Category 3*: Research involving greater than minimal risk and no prospect of direct benefit to individual participants, but likely to yield generalizable knowledge about the participants' disorder or condition (§46.406)

Children can be approved for these studies only when the IRB finds that: (1) the risk represents a minor increase over minimal risk; (2) 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; (3) 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 (4) adequate provisions are made for soliciting assent of the children and permission of their parents or legal guardians to participate in the research study.

For Category 3, both parents must give parental permission. When there is disagreement between both parents, the child may not be enrolled in the research study. However, only one signature of a parent is required when the second parent is deceased, unknown, incompetent, or not reasonably available (*e.g.*, no contact with child, serving in war, in solitary confinement or otherwise hard to reach in prison), or if one parent has the legal responsibility for the care and custody of the child, as long as this comports with the regulations of the U.S. or foreign jurisdiction in which the research is being conducted. *See*, *e.g.*, SOP 14: International Human Research. The reason for the allowance of only one parental signature should be documented in the research records.

6.2. Wards of the State: The special protections for children set forth in 45 CFR 46, Subpart D, addressing children, include additional limitations on some research involving children who are wards of the state or any other agency, institution, or entity. When the research involves greater than minimal risk to the participants with no prospect of direct benefit to individual participants (Category 3), the research must either relate to their status as wards or else be conducted in schools, camps, hospitals, institutions, or similar settings where the majority of participating children are not wards. The IRB requires for each ward the appointment of an advocate in addition to any other individual acting on behalf of the child as a parent, legal guardian, or other legally authorized representative. In addition, where required, the PI must obtain the approval of other implicated IRBs, such as the state department of health IRB or an IRB affiliated with the research site. Where this is required, the Cornell IRB's approval should be contingent on the approval of the non-Cornell IRB—in short, there must be agreement between the IRBs.

6.3. Determination by IRB of Probable Risks and Associated Discomforts:

In short, the IRB is required to consider the following when reviewing research involving children: (1) probable risks; (2) associated discomforts; and (3) potential benefits.

Procedures that usually present no more than minimal risk to a healthy child include: urinalyses, obtaining small blood samples, EEGs, allergy scratch tests, minor changes in diet or daily routine, and/or the use of standard psychological and educational tests.

The assessment of the probability and magnitude of the risk, however, may be different in sick children and vary depending on the diseases or conditions afflicting the participant. For example, obtaining a small blood sample from a hemophiliac child may present more than minimal risk to him or her. The IRB must also consider the extent to which research procedures would burden any child, regardless of whether the child is accustomed to the proposed procedures.

Procedures that exceed the limits of minimal risk may be difficult to define in the abstract, but should not be too difficult to identify on a case-by-case basis. For example, behavioral interventions may, in some circumstances, exceed minimal risk.

6.4. Determination by IRB of Potential Benefits:

In assessing the potential benefits of a research intervention, the IRB, again, should consider the variability in health statuses among the potential participants. For example, a potential participant might be a normal, healthy child, or a child who has been exposed to a disease or a toxin (*e.g.*, lead) or some psychological upset or trauma. A child may also suffer from a medical condition. The IRB must take into account the current health status (mental and physical) of a child and the likelihood of progression to a worsened state without (or with) the research intervention.

7. Procedures for Obtaining Permission from Parent(s) and Assent from the Child

The Protocol PI generally should obtain permission from parents *before* approaching a child. In most cases, after parental permission has been obtained and documented, the assent of the child is required. Enrollment of children in a research protocol requires the Protocol PI's consideration of the steps set forth in this Section for obtaining permission from the parent(s) and the assent from the child.

"Assent" in research involving children means a child's affirmative agreement to participate in the research. Mere failure to object cannot be construed as assent. "Permission" in research involving children means the agreement of the parent(s) or legal guardian to the participation of their child or ward in the research. "Parent" means a child's biological or adoptive parent. "Legal Guardian" means an individual who is authorized under applicable New York State law to consent on behalf of a child to general medical care.

A child may be under the care of a family member who serves as the child's primary caregiver. While such primary caregivers may be eligible to provide permission for more clinical type activity, they are not legally authorized to enroll their minor charges in a research project, regardless of whether it meets Categories 1, 2, or 3 set forth in Section 6.1 of this policy, *unless* a court has appointed them as the child's legal guardian.

7.1. Permission of the Parent(s)/Guardian(s):

1. If children are eligible to be enrolled in a research protocol, parental permission is generally required for each of the three categories of permissible research set forth in Section 6, *before* the child is approached for his or her assent. Permission by parents or guardians shall be documented in accordance with and to the extent required by SOP 10: Informed Consent Options, Processes, and Documentation, Section 9 and, if applicable, Section 11 (obtaining consent from non-English speakers).

2. However, the IRB has the authority to waive the requirement for parental permission (a) under the same conditions that it can waive informed consent (*see* SOP 10, Section 7.6), and (b) if it determines that a research protocol is designed for conditions or for a participant population for which parental or guardian permission is not a reasonable

requirement to protect the participants (*e.g.,* neglected or abused children are participants or research protocol poses minimal risk and parental/guardian permission would provide no additional protection from risks), provided an appropriate mechanism for protecting children who will participate in the research is substituted, if appropriate, and the waiver is not inconsistent with federal, state, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the participating children, and the children's age, maturity, status, and condition.

3. If the child has a legal guardian, the Protocol PI should maintain in the child participant's file legal documentation showing the decision-maker's status as the child's legal guardian.

4. In certain types of research with children, investigators often use the term "passive consent." The term is not defined in federal regulations. Instead investigators should request the IRB to waive parental permission with the assent being obtained from the child. For example, a notice may have been sent to the parents that their child would be asked to participate in a research project conducted at school unless the parent calls a certain number or returns a post card. The investigator then assumes that because he or she did not hear from the parent, the parent has given permission (*i.e.,* waived consent) for the child to participate in the research activity. Protocol PIs who wish to utilize this concept should (1) request a waiver of parental permission, with an IRB-approved written statement of information about the study sent to the home by first class or overnight mail; and (2) obtain assent from the child.

   However, the IRB's authority to grant a waiver differs for Research Categories 1, 2, and 3 in Section 6.1, as follows:

   Category 1 (Research not involving greater than minimal risk): The IRB may exercise the option to approve a waiver of parental permission, as long as the child's assent is obtained.

   Category 2 (Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual participants): The IRB may exercise the option to approve a waiver of parental permission, as long as consent has been obtained from an advocate for the child. The advocate should be knowledgeable about children and issues affecting children, as well as independent of the research project. Examples of suitable advocates would be principals, teachers, or guidance counselors for the child.

   Category 3 (Research involving greater than minimal risk and no prospect of direct benefit to individual participants, but likely to yield generalizable knowledge about the participants' disorder or condition): The IRB does not have the authority to waive parental permission for this category of research.

5. Regarding the involvement of minor college students (under the age of 18), in research the IRB determines to be no greater than minimal risk, the IRB may waive parental permission, if parental permission offers no additional protection to the participant. The IRB makes this determination on a case-by-case basis. An investigator who wishes to obtain a waiver of parental permission to enroll minor college student participants in his or her study should make this request to the IRB in the protocol application.

7.2. Assent of the Child:

1. Children cannot consent to participate in research themselves. Therefore, parental permission and the assent of the child must be obtained. There are no regulatory standards for assent outside of the statement in 45 CFR 46.408, requiring the IRB to "determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. In determining whether children are capable of assenting, the IRB shall take into account the ages, 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."

2. However, there are three exceptions to the need to obtain the assent of the child:

   a. The IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted.
   b. 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 children and is available only in the context of the research.
   c. The IRB determines that the child participants are capable of assenting, but the situation presents circumstances in which the IRB may waive the consent requirement, as set forth in SOP 10, Section 7.6 or otherwise. However, for some types of research where documentation of informed consent would normally be waived (such as surveys), the IRB may require documentation for children.

3. Assent is documented depending on the age, maturity, and psychological state of the child. All of the forms/documents referenced in Section 7.2(3) should be submitted by the Protocol PI as part of the protocol application for IRB review and approval.

   a. *Age under 7 years*, assent is waived or oral assent is obtained, as determined by the IRB
   b. *Age 7-12 years*, oral assent is recommended; but a written statement of information can be used to provide information about the study to the child when appropriate; a copy of the oral assent script should be submitted with the protocol; parental permission forms should have a line for documenting oral assent and should be signed by the person obtaining assent.
   c. *Age 13-17 years*, written assent should be obtained by a document that is written at an appropriate reading level. If the parental permission form is written at a grade level that is understandable for children ages 13-17, the Protocol PI may add a line for child assent and use the form for documenting both the child's assent and parental permission. However, separate assent and consent forms may be required if the language in the consent form is so complex that the child may not be able to understand it.

   The IRB may waive the documentation requirement where the assent document would be the only link between the participant and the research and would pose a confidentiality risk.

4. Participants who were enrolled in research studies when they were minors must be re-consented when they turn 18 years old if they are still participating actively in the study. The Protocol PI should follow the procedures for re-consenting participants set forth in SOP 10, Sections 9.5 (Consent Form Revisions) and 9.6 (Re-Consenting Participants).

5. In general, a child's dissent should be respected. However, a child's assent cannot override a "no" from a parent, unless the IRB has waived the requirement for parental permission. Ordinarily, a disagreement between parent(s) and child may arise because the child is depressed, the parents have unrealistic hopes, the child has different goals and outcomes than the parent(s), or the risk/benefit ratio has been misunderstood. Every effort should be made to reach consensus between the parent(s) and child. However, when the research offers the child the possibility of direct benefit important to his/her own health and may be available only through research (Category 2), the parent(s)' wishes generally prevail over the child's dissent.

8. Special Considerations for IRB Review and Approval of Research Involving Children

8.1. Most of the exemptions from IRB review applicable to research in adults (*see* SOP 2: Requirements for Submission of Research Protocols for a Determination by ORIA of Exemption from IRB Review, Section 6), also apply to children. However, children cannot be enrolled in a research project exempt from IRB review and approval under category 6.1.2 in SOP 2 (*i.e.*, surveys, interview procedures, or observation of public behavior), unless the research involves the observation of public behavior where the investigator(s) does not participate in the activities being observed (*see* SOP 2, Section 6.2.1).

8.2. The Protocol PI must submit as part of the protocol application all parental permission forms, child assent forms, written statements of information, and oral consent scripts. A submission omitting any of these consent/assent documents will result in having the protocol tabled because of the IRB's inability to assess the risk/benefit ratio of the protocol.

8.3. Submitted protocol applications are reviewed in accordance with SOP 3: Initial and Continuing Review by the IRB: Requirements for Submission of Applications, Approval Criteria, and Expedited and Convened Committee Review Procedures.

The inclusion of children does not, in and of itself, necessitate a convened committee review. The level of risk involved must be considered in making this determination. For example, research involving children which poses minimal risk may be expedited under 45 CFR 46.404. *See* SOP 3: Initial and Continuing Review by the IRB, Section 8.3.

8.4. The IRB may invite members or consultants with special expertise and competency related to the protocol involving children to participate in the protocol review.

8.5. When IRB-requested changes are returned by the Protocol PI, ORIA will confirm that all the changes have been made and will, as applicable, present them to the Expedited Reviewer/IRB Chair for review and approval or place them on the agenda of the next available meeting of the convened IRB.

8.6. The IRB Administrator or other ORIA member will document clearly in the minutes the outcome of any IRB discussion related to the enrollment of children in the protocol, including but not limited to:

1. Federally required considerations per 45 CFR 46, Subpart D
2. Consent/Assent process

3. Re-consent timing and procedures, if any

8.7. Protocols that include children may be reviewed for Continuation by the IRB more often than every 12 months per the determination of the IRB.

8.8. As stated above in Section 7.2(4), participants who were enrolled in research studies when they were minors must be re-consented when they turn 18 years old if they are still participating actively in the study. The Protocol PI should follow the procedures for re-consenting participants set forth in SOP 10, Sections 9.5 (Consent Form Revisions) and 9.6 (Re-Consenting Participants).