1 PURPOSE

1.1 This guidance establishes the process for obtaining child assent and consent, obtaining parental or guardian permission, waiving child assent, and waiving parental permission. It also addresses consent in special circumstances: parents or guardians are unavailable, children who are wards, restrictions on guardian authority, and minors who may consent as adults.

1.2 This guidance begins when the investigator plans to submit a research study to the Sharp HealthCare (SHC) Institutional Review Board (IRB) that includes children as subjects.

1.3 This guidance ends when the investigator has notified the SHC IRB that the study has closed.

2 REVISIONS FROM PREVIOUS VERSION

2.1 If applicable, previous versions are available in Human Research Protection Program Change Log.

3 POLICY STATEMENT

3.1 The investigator or designee is knowledgeable of the following definitions as it relates to complying with consent regulations and this guidance: Assent, Children, Guardian, Ward. *See GUIDANCE: Definitions (HRP-001)*.

3.2 The IRB will follow Subpart D of the DHHS or FDA regulations or equivalent laws or regulations to approve an appropriate assent process for children and consent process for parents or guardians.

3.3 Prior to issuance of approval, the IRB will determine and document that the proposed process for the following is/are adequate and compliant with applicable federal and state regulations, laws, or statutes:

3.3.1 Obtaining child assent and consent, obtaining parental or guardian permission, waiving child assent, and waiving parental permission

3.3.2 Consent in special circumstances; for example, when parents or guardians are unavailable, for children who are wards, restrictions on guardian authority, and minors who may consent as adults.

4 RESPONSIBILITIES

4.1 The investigator or designee is responsible for carrying out these procedures.

5 PROCEDURE

5.1 Obtaining Child Assent and Consent.

5.1.1 Federal regulations require that investigators wishing to conduct clinical trials in children should seek the permission of both parents and subject (child). However, it does not specify an exact age at which informed assent must be obtained. It places the responsibility for this determination with the Institutional Review Board (IRB).

5.1.2 The investigator or designee must inform the IRB of the manner in which assent will be obtained and documented via *FORM: Initial IRB Review Application (HRP-211)* and (for investigator initiated research) via *TEMPLATE: Research Protocol (HRP-500)*. The IRB must determine and document whether the investigator's or designee's proposed process is adequate via *CHECKLIST: Research Involving Children (HRP-416)* and via *TEMPLATE: Agenda / Minutes (HRP-501)* or *TEMPLATE: Notification of Non-Committee Reviews (HRP-501b)*. The IRB's determination will include whether assent is a requirement of:

5.1.2.1 All children;

5.1.2.2 Some children; or

5.1.2.3 None of the children.

5.1.3 In California, an investigator or designee for an experimental drug study must normally obtain the assent of any child participant 7 years or older. For studies involving children 7 to 17 years, the IRB recommends that investigators or designees document the child's willingness to participate with a signed assent document. A child capacity to assent must be evaluated on an individual basis.

5.1.4 Assent Document:

5.1.4.1 For children under 7 years of age: In certain cases, the investigator may deem a child in this age range is capable of being involved in the assent process. If so, make sure the child is given a simple verbal explanation of what will happen to him or her or what he or she will be asked to do. Document this discussion on the parental permission form or in the study records.

5.1.4.2 For children 7-12 years of age: Create two documents: a simplified child assent form *TEMPLATE: Child Assent (Ages 7 - 12) (HRP-503)* (see option A and option B below) and a separate parental permission based on *TEMPLATE: Parent Permission with California Bill of Rights (HRP-505*). The assent form should be brief and study specific, with clear and concise subheadings or numerical paragraphs, and contain language that is both appropriate to the child's development and age. The assent form should have a simple format that is easy to read and when possible, limited to one page. The use of larger type, simple schema, and pictures will facilitate the child's understanding of the text.

5.1.4.3 A signature is not required on the child assent form but is encouraged when possible. Regardless of whether a signature was obtained on the child assent form, investigators are required to document that child assent has been obtained either on the parental permission form or retained separately within the study records.

5.1.4.4 For adolescents 13-17 years of age:

- Option A (usually preferred): Write one consent form for both the adolescent subject and the parents or guardians. Use clear, straightforward language written below 8th grade reading level. Base the form on the *TEMPLATE: Parent Permission with California Bill of Rights (HRP-505).* Address the form to the adolescent with the signature lines for assent and parental permission. The adolescent should be asked to sign first. Precede the signature line for parents with the wording above.
- Option B: Reserved 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 eight-grade level. A simplified assent form is written for adolescents. A separate more detailed permission form is written for the parents or guardians. Base the forms on the T*EMPLATE: Adolescent Assent (Ages 13-17) (HRP-504)* and *TEMPLATE: Parent Permission with California Bill of Rights (HRP-505)*. Only the adolescent is asked to sign the assent form. Precede the signature line for parents with the wording above.

5.2 Obtaining Parental or Guardian Permission.

5.2.1 Adequate provisions must also be made for soliciting the permission of each child's parent(s) or legally authorized representative or guardian, as noted below. At a minimum, the federal requirements for consent indicated below must be met. However, the investigator or designee or the IRB may determine that more stringent requirements are appropriate.

	Regulatory Category of Permitted Research with Children	Requirements for Permission by Parents or Guardians
1.	Minimal Risk (45 CFR 46.404, 21 CFR 50.51)	One parent/legal guardian may be sufficient

	Regulatory Category of Permitted Research with Children	Requirements for Permission by Parents or Guardians
2.	Greater than Minimal Risk, Direct Benefit to Subject (45 CFR 46.405, 21 CFR 50.52)	One parent/legal guardian may be sufficient but IRB must determine whether one or two is required
3.	Greater than Minimal Risk, No Direct Benefit to Subject, but Likely to Yield Generalizable Knowledge about Subject's Condition (45 CFR 46.406, 21 CFR 50.53	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.
4.	Greater than Minimal Risk, No Direct Benefit to Subject, but Results May Alleviate Serious Problems of Children's Health or Welfare (45 CFR 46.407, 21 CFR 50.54)	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.

5.2.2 When Parental Permission is Sufficient.

5.2.2.1 For research that falls into risk-benefit Category 1 or 2, the IRB may determine that permission from only 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 or 4 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.

5.2.2.2 Important Note: When there is only one living parent or guardian or one parent has sole custody after a divorce, the investigator may determine that single-parent or single-guardian permission is sufficient.

5.2.2.3 When Parents Disagree.

5.2.2.4 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.

5.3 Waiver of Child Assent

5.3.1 At the request of the investigator or designee, the IRB may determine no assent is required in one or more of the following circumstances (including FDA regulated protocols):

5.3.1.1 Children are not capable of assenting, after taking into account the ages, maturity, and psychological state of the children involved, either for all the children or for each child.

5.3.1.2 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.

5.3.1.3 Customary conditions for waiver or alteration of consent are satisfied [45 CFR 116(f)(3)(i-v), 21 CFR 50.55(d)].

5.4 Child's Dissent

5.4.1 A child's dissent should normally be respected. However, the dissent may be overruled by the child's parents. This possibility should be thoroughly explained in the

TEMPLATE: Protocol (HRP-500) and will be considered by the Committee. When research involves the provision of experimental therapies for life-threatening diseases such as cancer, however, investigators or designees should be sensitive to the fact that parents may wish to go to extremes, even when the likelihood of success is marginal and the probability of extreme discomfort is high. Should the child not wish to undertake such experimental therapy, and if, for example, the child is a mature adolescent and death is imminent, the child's wishes should be respected.

5.5 Waiver of Parental Permission

5.5.1 For FDA-Regulated Studies: FDA regulations (Subpart 21 CFR 50) lack the provision for waiver of parental permission. Investigators or designees who believe it appropriate to include minors in FDA regulated studies should consult with the IRB and consider the Minors Who May Consent as Adults below.

5.5.2 For Non-FDA-Regulated Studies: The IRB may waive parental/guardian 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 law (45 CFR 46.408). In such cases, the investigator may propose a waiver of parental consent/permission under 45 CFR 46.408(c) or 45 CFR 46.116 in the Sharp Initial IRB application. Investigators should address all such consent concerns for research with minors, including arguments for waiver of standard consent procedures in the Sharp Initial IRB application.

5.5.3 Examples where parental permission may be waived:

5.5.3.1 Research on child abuse or neglect, or research that is reasonably likely to elicit information identifying child abuse or neglect, where there is serious doubt as to whether the parent's interests reflect the child's interests. [45 CFR 46.408(c)]. This type of study is difficult to pursue and thus rarely comes before the IRB. Since the federal regulations specifically refer to "research on neglected or abused children" as an instance where "parental or guardian permission is not a reasonable requirement to protect the subjects," the IRB would be likely to waive parental permission in such a case, provided the other requirements of the regulations 45 CFR 46.408 (c) are met.

5.5.3.2 Research on people under 18 who are in circumstances where they are clearly outside of parental influence or control. The IRB would evaluate each study carefully to determine whether parental permission is not a reasonable requirement to protect the subjects.

5.5.3.3 Investigators or designees also should be aware that some people under 18 who are living independently may not fit the federal definition of "children" and are able to consent for themselves without a waiver of parental permission. See Minors Who May Consent As Adults below.

5.6 Special Circumstances

5.6.1 Parents and Guardian are unavailable: Generally, an investigator or designee may not involve a child in research if the parent(s) or guardian is not available to provide permission and the IRB has not waived parental or guardian permission.

5.6.2 In California, an investigator or designee may be able to involve children for research involving treatment:

5.6.2.1 Where (i) the child is residing with a non-parent relative, (ii) the care of the child has been entrusted by a parent or guardian to an adult, or (iii) the child is in the custody of foster parents, a juvenile court, a social worker or probation officer, and

5.6.2.2 When certain conditions are satisfied, e.g. completion of a "Caregiver's Authorization Affidavit," or the issuance of a court order.

5.6.3 Children Who are Wards: Laws limit research with children who are "wards" of the state or other agency, institution or entity. The IRB may approve a protocol that involves

wards and research involving greater than minimal risk with no prospect of direct benefit to participants (under 45 CFR 46.406 or 21 CFR 50.53) or not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (under 45 CFR 46.407 or 21 CFR 50.54) only if the study is:

5.6.3.1 Related to their status as wards, or

5.6.3.2 Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of the participating children are not wards.

5.6.3.3 If research is approved under the above conditions, the IRB shall 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 may serve as advocate for more than one child in a study.

5.6.3.4 NOTE: The above does not apply for research approved under 45 CFR 46.404 and 46.405, or 21 CFR 50.51 and 50.52.

5.6.3.5 Who May Be An Advocate? An advocate: i) has the background and experience to act in (and agrees to act in) the best interest of the child for the duration of the research, and ii) is not associated in any way with the research (except as an advocate, or member of the IRB), the investigators or designees or any guardian association.

5.6.3.6 Investigators or designees are responsible for i) informing the IRB when the study intends to include children who are wards; and ii) compliance with any relevant requirements of the competent court, agency, institution, or entity of which the child is a ward.

5.6.3.7 For research involving medical care for wards of a court, an order from the judge is often required, in addition to permission from the person charged with the care of the child.

5.6.4 Guardians – Restrictions on Authority

5.6.4.1 Medical Care With No Research Involved: In California, a guardian normally has the same authority with respect to the child as a parent having legal custody, except as may be limited by statute or court order (e.g. the legal document establishing the guardianship).

5.6.4.2 Research Involving Medical Care: A guardian's authority to consent is restricted in the following circumstances (in the absence of an affirmative court order):

5.6.4.3 By the terms of any letters of guardianship issued by a court (a certified copy of which should be obtained and placed in the medical record);

5.6.4.4 Surgery on a child 14 years or older, unless (i) the child also consents, (ii) the guardian obtains a court order, or (iii) the guardian has determined based on medical advice that an emergency exists in which the child faces loss of life or serious bodily injury if the surgery is not performed;

5.6.4.5 Administering an "experimental drug" (e.g., FDA investigational drug), unless a 7 years or older child also consents and the drug is related to maintaining or improving health or obtaining information about a pathological condition of the child;

5.6.4.6 Authorizing electro-convulsive treatment;

5.6.4.7 Admitting the child to a "mental health treatment facility" without the child's consent;

5.6.4.8 Authorizing antipsychotic drugs except under certain circumstances;

5.6.4.9 Authorizing an elective procedure performed primarily for the purpose of rendering the child sterile (this prohibition does not include treatment which secondarily results in sterilization);

5.6.4.10 Authorizing psychosurgery under any circumstances.

5.6.5 Minors Who May Consent as Adults

5.6.5.1 NOTE: These laws are complex: Contact the Sharp HealthCare General Counsel for guidance.

5.6.5.2 In California, minors may consent to participation in research without parental or guardian permission if legally Emancipated, Self-Sufficient and in certain treatment circumstances. An “Emancipated” minor and “Self-Sufficient” minor may consent to participation in any type of research.

5.6.5.3 “Emancipated” Minor is any minor who:

- Has entered into a valid marriage, whether or not the marriage has been dissolved;
- Is on active duty with the armed forces of the United States; or
- Has received a declaration of emancipation pursuant to Section 7122 of the California Family Code.
- “Self-Sufficient” Minor is:
- A minor 15 years of age or older;
- Who is living separate and apart from the minor’s parents or guardian, whether with or without the consent of a parent or guardian and regardless of the duration of the separate residence; and
- Is managing her/his own financial affairs, regardless of the source of the minor’s income.

5.6.5.4 In addition, certain un-emancipated minors may consent to research involving specific types of medical treatment, including:

- Outpatient mental health treatment for a minor 12 years or older when certain criteria are met;
- Hospital, medical, or surgical care related to prevention or treatment of pregnancy for minors (any age);
- Medical care related to diagnosis/treatment of a communicable reportable disease or condition;
- Hospital, medical, or surgical care related to rape for a minor 12 years or older;
- Hospital, medical, or surgical care related to sexual assault, but must attempt to contact parent/guardian unless reasonably believe involved;
- Care for alcohol or drug abuse.

6 MATERIALS

6.1 GUIDANCE: Definitions (HRP-001).
6.2 FORM: Initial IRB Review Application (HRP-211)
6.3 CHECKLIST: Research Involving Children (HRP-416)
6.4 TEMPLATE: Research Protocol (HRP-500)
6.5 TEMPLATE: Agenda – Minutes (HRP-501)
6.6 TEMPLATE: Notification of Non-Committee Reviews (HRP-501b)
6.7 TEMPLATE: Child Assent (Ages 7 – 12) (HRP-503)
6.8 TEMPLATE: Adolescent Assent (Ages 13-17) (HRP-504)
6.9 TEMPLATE: Parent Permission with California Bill of Rights (HRP-505)

7 REFERENCES

7.1 DHHS Regulations and Guidance

7.1.1 45 CFR 46, Subpart D: Additional Protections for Children Involved as Subjects in Research

7.1.2 45 CFR 46.408(c): Requirements for Permission by Parents or Guardians and For Assent by Children

7.1.3 45 CFR 46.116(d): General Requirements for Informed Consent

7.1.4 45 CFR 46.117: Documentation of Informed Consent
7.1.5 OHRP, Protecting Human Research Subjects Guidebook (1993) Chapter 6, Section C, "Children and Minors."
7.1.6 OHRP Children's Special Issues Page
7.1.7 OHRP Research with Children – FAQs

7.2 FDA Regulations and Guidance
7.2.1 21 CFR 50, Subpart D: Additional Safeguards for Children in Clinical Investigations
7.2.2 FDA Guidance for Clinical Investigators, Institutional Review Boards and Sponsors: Process for Handling Referrals to FDA under 21 CFR 50.54 – December 2006

7.3 California Statutes and Guidance
7.3.1 California Minor Consent Laws. National Center for Youth Law, 2003
7.3.2 California: Minor Consent Rules for Adolescent Care
7.3.3 Understanding Confidentiality and Minor Consent in California: An Adolescent Provider toolkit

This document is available on www.sharp.com/research, IRBANA, or by contacting research@sharp.com.