Assent of Children and Parental Permission

Definitions:

Assent: A child's or other individual's affirmative agreement to participate in research where the child or individual is not eligible by age or impaired decision making ability to provide consent. Mere failure to object by the child or individual should not be construed as assent.

Child: a person under eighteen years of age who has not been judicially emancipated under Civil Code Article 366, emancipated by marriage under Civil Code Article 367, or limitedly emancipated by authentic act per Civil Code Article 368.

FDA and HHS regulations at 45 CFR 46.402(a) 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." This provision means that the law of the site of the research will determine the legal age of consent of the participant.

Guardian: an individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care (45 CFR 46.402(e)). The role of a guardian in the context of research involving a child who is a ward is to provide permission, in lieu of a child's biological or adoptive parents, for the ward to participate in the research (45 CFR 46.402(c)).

Any person designated by court order as the minor's legal guardian or as a person who can otherwise make medical decisions on behalf of the minor. The term 'guardianship' means the judicial placement of a child under the care of a person who will have the duty and authority of a guardian to make decisions in matters having a permanent effect on the life and development of the child, as set forth in article 719. 'Legal custody' means the right to have physical custody of the child and to determine where and with whom the child shall reside; to exercise the rights and duty to protect, train, and discipline the child; the authority to consent to major medical, psychiatric, and surgical treatment; and to provide the child with food, shelter, education, and ordinary medical care, all subject to any residual rights possessed by the child's parents. Citation: Ch. Code Art. 116.

Minor: a person who has not attained the age of eighteen years.

Newborn: a child who is not more than thirty days old, as determined within a reasonable degree of medical certainty by an examining physician.

Parent: any living person who is presumed to be a parent under the Civil Code or a biological or adoptive mother or father of a child.

Tutor: one other than a parent who has qualified for the office and has been confirmed or appointed by a court.

Ward: Any child who has been adjudged dependent by a court and who is under the control of a public official, agency, or tutor.

Parental Permission

Since a child cannot consent for him/herself, the IRB must determine that adequate provisions have been made for soliciting the permission of each child's parent or legal guardian, as documented in the consent.

For research conducted in jurisdictions other than Louisiana, the research must comply with the laws regarding the legal age of consent in all relevant jurisdictions.

Parents or legal guardians must be provided with the basic elements of consent and any additional elements the IRB deems necessary, as described the policy Informed Consent Elements and Requirements. In addition to the requirements under Louisiana law, the IRB may find that the permission of one parent is sufficient for research to be conducted under FDA categories CFR 21.51 or 50.52 45, or under HHS categories CFR 46.404 or 45 CFR 46.405.

Permission from both parents is required for research to be conducted under categories CFR 21. 50.52 or 50.52, or under HHS categories 45 CFR 46.406 or 45 CFR 46.407 unless:

- One parent is deceased, unknown, incompetent, or not reasonably available; or
- When only one parent has legal responsibility for the care and custody of the child.

Determining who can provide permission

Consent should be sought from the child's parents or adoptive foster parents. Generally speaking, if the child was born within wedlock, and there is disagreement between the parents about the child's participation in research, the father's decision will prevail per La. C.C. art. 216. If the parents were unmarried at the time of the child's birth, and the father has not been judicially acknowledged as the father or has not established paternity of the child as outlined in La. C.C. art. 198, the mother is of right the tutrix of the child, per La. C.C. art. 256, and will have the sole authority to consent to the child's participation in the research. Alternatively, consent could be obtained from another adult if the child's parents had granted power of attorney to that adult. Additionally, should the child have a court recognized tutor, consent may be obtained from this tutor or from another adult to whom the child's court recognized tutor gave power of attorney according to LA Rev Stat § 9:951.

Investigators designing a protocol with the aim to include children who may be under guardianship/tutorship or in foster care should include a description of how the guardian's legal authority to authorize research participation for the child will be documented. It is recommended

that the court order granting guardianship be filed with the consent form for the minor participant.

Waiver of Parental Permission

For research not covered by FDA regulations, the IRB may waive the requirement for obtaining permission from a parent or legal guardian if:

- the research meets the provisions for waiver of consent (as outlined in the policy Waiver of Consent and Waiver of Documentation of Consent) or

- the IRB determines that the research protocol is designed for conditions or a subject population for which parental or legal guardian permission is not a reasonable requirement to protect the subjects (e.g., neglected or abused children), provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and that the waiver is not inconsistent with federal, state or local laws. 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 research subjects, and their age, maturity, status, and condition.

Research on Public Benefit or Service Programs

The IRB can waive or alter the requirements for parental permission for non-exempt research examining state or local public benefit or service programs or certain features of those programs if all of the following criteria are met:

- The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine public benefit or service programs, procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs
- The research could not practicably be carried out without the waiver or alteration
- The research is not FDA-regulated.

Minimal Risk Research

The IRB can waive or alter the requirements for parental permission for non-exempt research that meets all of the following criteria:

- The research involves no more than minimal risk to subjects
- The waiver or alteration will not adversely affect the rights and welfare of subjects

- The research could not practicably be carried out without the waiver or alteration
- Whenever appropriate, subjects will be provided with additional pertinent information after participation
- The research is not FDA-regulated

Research Designed to Study Conditions in Children

The IRB can waive or alter the requirements for parental permission for non-exempt research designed to study conditions in children or a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (e.g., neglected or abused children) when the following additional criteria are also met:

- An appropriate mechanism is in place to protect the children
- The waiver is not inconsistent with federal, state, or local law
- The research is not FDA-regulated.

Note: IRBs may waive the requirement for obtaining parental or guardian permission as described above even if the research involves greater than minimal risk to the participants.

Assent

Assent is an agreement by a child not competent to give legally valid informed consent to participate in research. When potential human subjects are not competent to give legally valid informed consent, respect for personal autonomy mandates that, when possible, the investigator obtain their voluntary assent to participate in addition to obtaining the informed consent from a parent or other legal representative. Mere failure to object should not, absent affirmative agreement, be construed as assent.

Assent is generally required whenever subjects will be children between the ages of 7 through 17, unless emancipated. If possible, subjects should attest to their willingness to participate by signing an assent form. When the IRB finds that no greater than minimal risk to children is presented, the IRB may approve the proposal only if the IRB finds that adequate provisions are made for obtaining the assent of the children and the permission of their parents or guardians.

No Requirement of Assent / Waiver of Assent

Assent for children under the age of seven is generally not required. When a child is under the age of seven and assent is not possible due to age or maturity, a parent or guardian may provide permission for the child to participate in research.

If the IRB determines either of the following to be true, then the assent of the children is not a necessary condition for proceeding with the research:

a. The capability of some or all of the children is so limited that they cannot reasonably be consulted; **OR**

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.

Additionally, in such circumstances as a child's dissent, which should normally be respected, may be overruled by the child's parents, at the IRB's discretion after consulting legal counsel. Even if the IRB determines that the children are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived for adults.

If some of the children age seven and above would not be able to provide meaningful assent, the IRB will determine and document whether their selection is justified. The requirement for assent of the child participant also may be waived under the circumstances in which consent may be waived under 45 CFR 46.116. For FDA regulated research, the requirement for assent of the child participant may be waived according to 21 CFR 50.55(d).

Suggested language for the signature page of the consent form for parental permission and waiver of assent:

Your signature below indicates that you have read (or been read) the information provided above and agree to have your child participate in this study. You will receive a copy of this signed consent form.

Your signature below indicates that you have read (or been read) the information provided above and agree to participate in this study. You will receive a copy of this signed consent form.

_____
Name of Proband Child (printed)

_____
Signature of Parent or Legally Authorized Representative Date

_____ _____ ____
Name of Parent Participant (printed) Relationship

_____
Signature of Parent Participant Date

_____
Signature of Person Obtaining Consent Date

In this research study, one consent form may be used to waive assent for the child and to document informed consent of one or both parents; however, a separate HIPAA Authorization form will be completed for each participant.

Waiver of Assent
The assent of _____ (name of child/minor) was waived because of:
Age _____ Maturity _____ Psychological state of the child _____

For the Common Rule, there are criteria for waiver of any or all of the elements of informed consent. The same criteria apply to waivers of parental permission and also to child assent (when assent is deemed applicable to the research). Refer to the Waiver of Consent and Waiver of Documentation of Consent policy for more information.

Obtaining Assent

The assent process for obtaining assent of children in research should be explained in the protocol. The format, style, and content of the assent form are essentially the same as for a consent form, except that the language should be appropriate for the age and capacity of the subjects. For example, "Assent Form" should be at the top of the page, an explanation about why the subject has been asked to participate, the purpose of the research, a description of the procedures to be performed, the anticipated time to complete the procedures, the potential risks and benefits, and that there is voluntary participation and withdrawal without penalty. The assent form for a child may be somewhat simplified and written with language appropriate for the intended age range of the subject.

The IRB must approve and affix a stamp of approval on all assent forms. Once the assent form has been approved by the IRB, the investigator must use that version of the form. The IRB must approve any proposed changes to the assent form prior to implementation.

Emancipated Minors

For emancipated minors, full judicial emancipation confers all effects of majority on the person emancipated unless otherwise provided by law; therefore, emancipated minors are able to consent for themselves for research purposes. A pregnant female over the age of 16 (age $\geq$ 16 years old) is emancipated (colloquially referred to as a mature minor rule) to make her own decisions about medical care related to the pregnancy.

Consent from Pregnant Minors

A minor may consent to medical care or the administration of medication by a hospital licensed to provide hospital services or by a physician licensed to practice medicine for the purpose of

alleviating or reducing pain, discomfort, or distress of and during labor and childbirth. [LA R.S. 40:1095(A) (2)]. This consent shall be valid and binding as if the minor had achieved her majority, and it shall not be subject to a later disaffirmance by reason of her minority. If research pertains to such permitted minor consent, then the minor may consent to the involved research. If not and the IRB has not waived the consent requirement, then assent from the minor is required, as well as parental permission.

Children who are Wards of the State

Children who are wards of the state or any other agency, institution, or entity can be included in research involving greater than minimal risk where there is no prospect of direct benefits to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition, only if such research is:

- Related to their 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.

If the research meets the condition(s) above, the IRB Chair will determine an advocate must be appointed by the IRB or institution for each child who is a ward (one individual may serve as advocate for more than one child), in addition to any other individual acting on behalf of the child as legal guardian or in loco parentis. The advocate must 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 the guardian organization. Regulations & Guidance: DHHS 45 CFR 46.409.

Child's Dissent

The IRB may request that the investigator include a description of behaviors that will be viewed as indicators that the child does not wish to participate in the research (such as crying, moving away from the investigator, or being unwilling to complete tasks). Therefore the investigator may not rely solely on the absence of verbalized objection as the basis for deciding that assent has been given. When the research offers the child the possibility of a direct benefit that is important to the health or well-being of the child and is available only in the context of the research, the IRB may determine that a child's dissent, which should normally be respected, may be overruled by the child's parents or legal guardian. Finally, even where the IRB determines that the children are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived for adults.

When a Previously Enrolled Child Turns 18

When a child who was enrolled in research with parental or guardian permission subsequently reaches age 18 years, the legal age of consent to the procedures involved in ongoing research, the subject's participation in the research is no longer regulated by the requirements of this policy or by 45 CFR 46.408 or 21 CFR 50.55 regarding parental or guardian permission and subject assent. Unless the IRB determines that the requirements for obtaining informed consent can be waived, the investigator is expected to seek and obtain the legally effective informed consent, as described in 45 CFR 46.116 and 21 CFR 50.20 and .25, for the now-adult subject for any ongoing interactions or interventions with the subjects.

However, the IRB could approve a waiver of informed consent under 45 CFR 46.116(d), if the research is not FDA-regulated and the IRB finds and documents that the required conditions are met. Similarly, if the research does not involve ongoing interactions or interventions with the subjects, but continues to meet the regulatory definition of "human subjects research" (for example, it involves the continued analysis of specimens or data for which the subject's identity is readily identifiable to the investigator), then it would be necessary for the investigator to seek and obtain the legally effective informed consent of the now-adult subjects. The IRB may consider, if appropriate and if the research is not FDA-regulated, a waiver under 45 CFR 46.116(d) of the requirements for obtaining informed consent in order for the subjects to continue their participation in the research.

Additional FDA Regulation of Placebos

FDA does not consider the administration of a placebo to a child to offer a prospect of direct benefit to the recipient. (Additional Safeguards for Children in Clinical Investigations of Food and Drug Administration-Regulated Products – Federal Register 78(38):12937-12951) Consequently, for a study of a drug or biologic (whether investigational or FDA-approved) versus a placebo, with no other therapy permitted (standard of care and/or known effective treatment is withheld), the placebo recipient would be viewed as having no prospect of direct benefit from participating in the study. In such a circumstance, the risks in the placebo control group should present no more than minimal risk or a minor increase over minimal risk. The placebo control arm of such a study must be approvable under either 21 CFR 50.51 or 21 CFR 50.53, or the clinical investigation must be referred for review under 21 CFR 50.54. Those in the arm that receive the investigational product often would be viewed as having the prospect of direct benefit, and that portion of the study could be approvable under 21 CFR 50.52. Each study arm requires a separate pediatric risk assessment. However, in a study where one study drug or study biologic is given in addition to standard therapy specified by the protocol (with drugs and doses delineated) compared with a placebo given in addition to standard therapy specified by the protocol (with drugs and doses delineated), the placebo recipient would be viewed as having the prospect of direct benefit from the standard therapy, and the study would be approvable under 21 CFR 50.52. Also those in the arm that receive the investigational product and the standard

therapy would be viewed as having the prospect of direct benefit, and that portion of the study could also be approvable under 21 CFR 50.52. With respect to the criteria that must be met for approval under 21 CFR 50.53, the inclusion of children without the disorder or condition under study would not meet the requirement of 21 CFR 50.53(c) that ‘‘the intervention or procedure is likely to yield generalizable knowledge about the subjects’ disorder or condition.’’