REQUIRED ADDITIONAL PROTECTIONS FOR CHILDREN INVOLVED IN RESEARCH

REQUIRED DETERMINATION #1 – RESEARCH CATEGORIES

Federal regulations require the IRB to classify research involving children into one of four categories and to document discussion of the risks and benefits of the research study. Those four categories of research are as follows:

Category 1: Research not involving greater than minimal risk (45 CFR 46.404)

Category 2: Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects (45 CFR 46.405) For research to qualify for Category 2, all of the following- A, B, and C must be true:

A. One of the following is true:
   (1) More than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for each individual participant. OR
   (2) More than minimal risk to children is presented by a monitoring procedure that is likely to contribute to the participant’s well-being.

B. The risk is justified by the anticipated benefit to the participants.

C. The relation of the anticipated benefit to the risk is at least as favorable to the participants as that presented by available alternative approaches.

Category 3: Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition (45 CFR 46.406). For research to qualify for Category 3, all of the following- A through F must be true:

A. More than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual participant, or by a monitoring procedure which is not likely to contribute to the well-being of the participant.

B. The risk represents a minor increase over minimal risk.

C. 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;

D. The participants have a disorder or condition.
REQUIRED ADDITIONAL PROTECTIONS FOR CHILDREN INVOLVED IN RESEARCH

E. 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.

F. One of the following is true:
   (1) The research DOES NOT involve wards of the state or any other agency, institution, or entity. OR
   (2) The research meets the criteria for involvement of wards of the state or any other agency, institution, or entity. (See checklist for Review of Research Involving Children as Wards)

Category 4: Research not otherwise approvable which presents an opportunity research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children. For research to qualify for Category 4, all of the following- A through C - must be true:

A. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children.

B. Either of the following is true:
   (1) For DHHS regulated-research, all of the following are true (a and b):
      (a) The research is conducted, funded, or otherwise subject to regulation by DHHS.
      (b) The Secretary of DHHS, after consultation with a panel of experts in pertinent disciplines (for example, science, medicine, ethics, law) and following public opportunity for review and comment, has determined that either of the following is true:
         • The research in fact satisfies the conditions of 45 CFR 46.404, 45 CFR 46.405, 45 CFR 46.406 above. OR –
         • All of the following are true:
            o The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children.
            o The research will be conducted in accordance with sound ethical principles.
REQUIRED ADDITIONAL PROTECTIONS FOR CHILDREN INVOLVED IN RESEARCH

- Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians

(2) For FDA regulated-research, all of the following are true (a and b):

(a) The research is subject to FDA regulation.

(b) The Commissioner of Food and Drugs, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, has determined that either of the following is true:
   - The research in fact satisfies the conditions of 21 CFR 50.51, 21 CFR 50.52, 21 CFR 50.53 above. OR –
   - All of the following are true:
     - 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
     - Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians

C. One of the following is true:

(1) The research DOES NOT involve wards of the state or any other agency, institution, or entity. OR

(2) The research meets the criteria for involvement of wards of the state or any other agency, institution, or entity. (See checklist for Review of Research Involving Children as Wards)

REQUIRED DETERMINATION #2 - ASSENT

The research makes adequate provisions for soliciting the assent of the children. Regulations require that the IRB determine that adequate provisions are made for obtaining and documenting 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 assent, 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 the research under a particular protocol, or for each child, as the IRB deems appropriate.

- When the IRB determines that assent is required, it will also determine whether and how assent must be documented. One of the following (A,B,C,D, or E) is true

A. Assent is required for each child who is capable of providing assent based on age, maturity, and psychological state.

B. Assent is NOT required because the capability of some or all of the children is so limited that they cannot reasonably be consulted.

C. Assent is NOT required because both of the following are true:
   (1) 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.
   (2) The intervention or procedure involved in the research is available only in the context of the research.

D. The requirement for assent is waived or altered because all of the following are true:
   (1) The research or demonstration project is to be conducted by or subject to the approval of state or local government officials
   (2) The research or demonstration project is designed to study, evaluate, or otherwise examine one of the following:
      (a) public benefit or service program
      (b) procedures for obtaining benefits or services under those programs
      (c) possible changes in or alterations to those programs or procedures
      (d) possible changes in methods or levels of payments for benefits or services under those programs
   (3) The research could NOT practicably be carried out without the waiver or alteration.
   (4) The research is NOT subject to FDA regulations

E. The requirement for assent is waived or altered because all of the following are true:
   (1) The research involves no more than minimal risk to the participants.
REQUIRED ADDITIONAL PROTECTIONS FOR CHILDREN INVOLVED IN RESEARCH

(2) The waiver or alteration will NOT adversely affect the rights and welfare of the participants.
(3) The research could NOT practicably be carried out without the waiver or alteration.
(4) Whenever appropriate, the participants will be provided with additional pertinent information after participation.

REQUIRED DETERMINATION #3 – PARENTAL PERMISSION

The research makes adequate provisions for soliciting the permission of the children’s parents or guardians. One of the following (A, B, C, D, or E) is true.

A. The permission of each child’s parents or guardian will be obtained 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, and all of the following are true (1-4):

(1) Permission will be obtained appropriately (See Informed Consent Checklist).
(2) Either of the following is true:
   (a) Permission will be appropriately documented. (see checklist for documentation of IC)
   (b) Documentation of permission is waived (see checklist for waiver of documentation of IC)
(3) Both of the following are true:
   (a) The research is NOT subject to DHHS regulations (Complete checklist for Determining Whether a Proposed Activity is Human Research) AND
   (b) If permission is to be obtained from a guardian, the guardian will be an individual who is authorized under applicable State or local law to consent on behalf of the child to general medical care when general medical care includes participation in research, or be an individual who is authorized to consent on behalf of a child to participate in research
(4) Both of the following are true:
REQUIRED ADDITIONAL PROTECTIONS FOR CHILDREN INVOLVED IN RESEARCH

(a) The research is NOT subject to FDA regulations (Complete checklist for Determining Whether a Proposed Activity is Human Research) AND

(b) If permission is to be obtained from a guardian, the guardian will be an individual who is authorized under applicable State or local law to consent on behalf of the child to general medical care when general medical care

B. The permission of one parent is sufficient and all of the following are true (1 – 7)

(1) The permission of one parent is sufficient.

(2) Either of the following is true:

(a) The permission of one parent is consistent with state law.

(b) The activity is NOT subject to FDA regulations (see checklist for Determining Whether a Proposed Activity is Human Research)

(3) The research involves Categories 1 or 2 in the checklist for Review of Research Involving Children.

(4) Permission will be obtained appropriately (see checklist for Informed Consent)

(5) Either of the following is true:

(a) Permission will be appropriately documented. OR

(b) Documentation of permission is waived. (See checklist for Waiver of Documentation for Informed Consent)

(6) Both of the following are true:

(a) The research is NOT subject to DHHS regulations (Complete checklist for Determining Whether a Proposed Activity is Human Research) AND

(b) If permission is to be obtained from a guardian, the guardian will be an individual who is authorized under applicable State or local law to consent on behalf of the child to general medical care when general medical care includes participation in research, or be an individual who is authorized to consent on behalf of a child to participate in research

(7) Both of the following are true:

(a) The research is NOT subject to FDA regulations (Complete checklist for Determining Whether a Proposed Activity is Human Research) AND
REQUIRED ADDITIONAL PROTECTIONS FOR CHILDREN INVOLVED IN RESEARCH

(b) If permission is to be obtained from a guardian, the guardian will be an individual who is authorized under applicable State or local law to consent on behalf of the child to general medical care when general medical care is required.

C. The requirement for parental permission is waived under 45 CFR 46.116(c) (Complete checklist for Waiver or Alteration of Requirement to Obtain Informed Consent).

D. The requirement for parental permission is waived under 45 CFR 46.116(d) (Complete checklist for Waiver or Alteration of Requirement to Obtain Informed Consent).

E. The requirement for parental permission is waived because all of the following are true (1, 2, 3, and 4):

(1) The research protocol is designed for either of the following:
   (a) Conditions for which parental or guardian permission is NOT a reasonable requirement to protect the participants OR
   (b) A participant population for which parental or guardian permission is NOT a reasonable requirement to protect the participants

(2) An appropriate mechanism for protecting the children who will participate as participants in the research is substituted.

(3) The waiver is consistent with Federal, State, or local law.

(4) The research is NOT subject to FDA regulations (Complete checklist for Determining Whether a Proposed Activity is Human Research According to DHHS or FDA Regulatory Definitions).

WARDS OF THE STATE

Children who are wards of the State or other agency, institution, or entity can be included in research approved under 45 CFR 46.406 or 45 CFR.407 only if such research is either 1) related to their status as wards or 2) be conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.
REQUIRED ADDITIONAL PROTECTIONS FOR CHILDREN INVOLVED IN RESEARCH

In research approved under 45 CFR 46.406 or 45 CFR 407, the IRB must require appointment of an advocate for each child who is a ward. This advocate serves in addition to any other individual acting on behalf of the child as a 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 the guardian organization.