OHRS Information Sheet
Additional Protections for Children

Summary Guide to Additional Protections for Children as Subjects in Research

Instructions: This document outlines the categories of research that are permissible in children if the requirements listed below are met.

Adequate provisions are required for soliciting permission from both parents or guardians, if reasonably available, and soliciting the assent of each child when the IRB deems the children are capable of assent. (See requirements on reverse.)

Minimal risk is also defined and explained. (See reverse.)

RESEARCH CATEGORY REQUIREMENTS

I. DHHS §46.404; FDA 50.51 Research not involving greater than minimal risk to children

DHHS will conduct or fund research in which the IRB finds that **no greater than minimal risk to children** is presented, only if the IRB finds that: adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in §46.408.

II. DHHS §46.405; FDA 50.52 Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects

DHHS will conduct or fund research in which the IRB finds that **more than minimal risk to children** is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual subject, or by a monitoring procedure that is likely to contribute to the subject's well-being, only if the IRB finds that: (a) the risk is justified by the anticipated benefit to subjects;
(b) the relation of anticipated benefit to the risk is at least as favorable to subjects as that presented by available alternative approaches; and
(c) adequate provisions are made for soliciting the assent of the children and permission of their parent/s or guardians, as set forth in §46.408.

III. DHHS §46.406; FDA 50.53 Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subjects' disorder or condition

DHHS will conduct or fund research in which the IRB finds that 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 subject, or by a monitoring procedure which is not likely to contribute to the well-being of the subject, only if the IRB finds that:
(a) the risk represents a **minor increase over minimal risk;**
(b) the intervention or procedure presents **experiences** to subjects that are **reasonably commensurate with** those inherent in their **actual or expected medical, dental, psychological, social, or educational situations**;

(c) the intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and
(d) adequate provisions are made for soliciting assent of the children and permission of their parents or guardians, as set forth in §46.408.

IV. DHHS §46.407; FDA 50.54 Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children

DHHS will conduct or fund research that the IRB does not believe meets the requirements of §46.404, §46.405, or §46.406 only if:
(a) the IRB finds that 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) the research is considered by the Secretary of DHHS in consultation with a panel of experts, with opportunity for public comment.

V. DHHS §46.409; FDA 50.55 Wards

(a) Children who are wards of the State or any other agency, institution, or entity can be included in research approved under §46.406 or §46.407, only if such research is:
(1) related to their status as wards; or
(2) conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.
(b) If the research is approved under paragraph (a) of this section , 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. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of 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.

DEFINITION OF MINIMAL RISK

Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Examples of minimal risk procedures per FDA guidance include: clean-catch urinalysis, obtaining stool samples, administering electroencephalograms, requiring minimal changes in diet or daily routine, taste test of an excipient, tests of devices involving temperature readings orally or in ear, and use of standard psychological tests; also, there may be some circumstances under which products with established safety profile in adults may present no more than minimal risk in children.

DHHS §46.408: REQUIREMENTS FOR PERMISSION BY PARENTS OR GUARDIANS AND FOR ASSENT BY CHILDREN

Permission: Adequate provisions are required for soliciting permission of parent(s) or guardian.

For minimal risk research (Cat. 1) and research involving greater than minimal risk with prospect of benefit (Cat. 2) the IRB may find that the permission of one parent/guardian is sufficient, if consistent with state law.

For research involving greater than minimal risk with no prospect of direct benefit permission of both parents/guardian is required, unless one parent is not reasonably available or one parent has custody.

Exception: The parental permission requirement may be waived if the subject population is one for which parental or guardian permission is not a reasonable requirement (e.g., neglect, abuse) provided an appropriate mechanism for protecting the children is substituted, or permission may be waived if the standard waiver criteria (listed below) are met.

Parental or Guardian Permission

The IRB shall determine, in accord with and to the extent that consent is required (per §46.116) that adequate provisions are made for soliciting the permission of each child's parents or guardian. Where parental permission is to be obtained, the IRB may find that permission of one parent is sufficient for research to be conducted under §46.404 (minimal risk research – Cat. 1) or §46.405 (research with direct benefit – Cat. 2).

When research is covered by §46.406 and §46.407 (Cat. 3 and 4) and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal custody of the child.

Waiver of Permission Requirements

In addition to the provisions for waver contained in §46.116 of Subpart A (the standard waiver criteria, listed below), if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (e.g., neglected or abused children), it may waive the permission requirements, provided an appropriate mechanism for protection of the children who will participate in the research is substituted, and that 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 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.

Standard Waiver Criteria §46.116

1.) The research involves no more than minimal risk to subjects;
2.) The waiver or alteration will not adversely affect the rights and welfare of subjects;
3.) The research could not practicably be carried out without waiver or alteration; and
4.) When appropriate, subjects will be provided with additional pertinent information after participation.

Assent: The IRB determines if the children are capable of providing assent and if documentation is required.

When the IRB determines that assent is required, it shall also determine if and how assent must be documented.

The assent requirement may be waived if the intervention offers direct benefit important to the child's well-being and is available only via the research (or if the usual requirements for consent waiver apply).

Assent of Children

The IRB shall determine that adequate provisions are made for soliciting the assent of children when in the judgment of the IRB the children are capable of providing assent. 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.

When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

The assent of children is not a necessary requirement for proceeding with the research if:

1.) The IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted;
2.) 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; or
3.) The IRB determines that, although the children are capable, the assent requirement may be waived because the standard criteria for waiver of consent (§46.116, listed above) have been met.