

**COLUMBIA UNIVERSITY INSTITUTIONAL REVIEW BOARD
POLICY**

RESEARCH INVOLVING CHILDREN

SCOPE:

This Policy applies to all human subjects research involving children conducted under the auspices of Columbia University (the "University").

EFFECTIVE DATE: September 23, 2005

BACKGROUND:

Children are a vulnerable research population and, as such, require additional protections when they are potential research subjects. At the same time, children should not be denied the benefits of participating in research. Federal regulations and/or NIH policy require both that children be included in certain research activities unless there is a justification for excluding them and that additional precautions be taken depending on the degree of risk involved in the research. In addition, the regulations also set forth requirements for obtaining parental permission and, where appropriate, assent by the children themselves.

PROTECTION OF CHILDREN AS SUBJECTS IN RESEARCH STUDIES:

A. General

Subpart D of both 45 CFR 46, promulgated by the U.S. Department of Health and Human Services ("DHHS"), and 21 CFR 50, promulgated by the U.S. Food and Drug Administration ("FDA") (collectively, "Subpart D"), require certain additional protections for children involved as subjects in research. The requirements of Subpart D apply to all non-exempt research involving children conducted under the auspices of the University. A complete copy of the DHHS Subpart D can be found at <http://www.gpoaccess.gov/cfr/index.html> and a complete copy of the FDA Subpart D can be found at <http://www.accessdata.fda.gov>.

There are three main areas to consider under Subpart D when proposing research involving children:

- (a) risk/benefit analysis;
- (b) permission of the parents or guardian of the child; and
- (c) assent of the child.

No research involving children should be conducted without prior IRB approval. Because the IRB must make certain findings and determinations when reviewing research involving children, each investigator must submit information relevant to Subpart D determinations with the protocol describing such research. All information must be provided with sufficient specificity to permit the IRB to make the determinations it is required to make under Subpart D.

B. Important Definitions

The following terms are important to understanding the requirements of this Policy:

- 1) **Assent:** a child's affirmative agreement to participate in research.
- 2) **Child:** a person who has not attained the legal age for consent to treatments or procedures involved in the proposed research under the applicable laws of the jurisdiction in which it will be conducted.

In New York State, any person under the age of 18 who is not married or a parent should be considered a child for purposes of this Policy.

With IRB approval, a child may be able to consent to research without the permission of parents in certain other situations (e.g., emancipated minors, research involving sexually transmitted diseases, etc.).

If a research study is to be conducted in a state other than New York, the investigator should check appropriate state and local laws and regulations before conducting research to determine the definition of a child.

If an investigator is uncertain as to the determination of a child's status, whether under New York law or otherwise, he/she should call the IRB for assistance.

- 3) **Guardian:** an individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care.

In New York State, a guardian is any person who:

- (a) is over the age of 18;
- (b) is a legal resident or citizen of the United States; and
- (c) has been appointed as a guardian of the person of the child by
 - (i) a parent pursuant to a designation, deed of guardianship or will approved by a Family Court or Surrogate's Court judge; or

- (ii) a Family Court or Surrogate's Court judge pursuant to a letter or order of guardianship.

If a research study is to be conducted in a state other than New York, the investigator should check appropriate state and local laws and regulations before conducting research to determine the definition of a guardian. The IRB can provide assistance in this determination.

4) **Parent:** a child's biological or adoptive parent.

5) **Permission:** the agreement of a parent or guardian to the participation of a child in research.

6) **Ward:** any child who is under the protection of the state or any other agency, institution or entity.

In New York State, any foster child should be considered a ward for purposes of Subpart D. A foster child is any child in the care, custody or guardianship of an authorized agency, who is placed for temporary or long term care.

If a research study is to be conducted in a state other than New York, the investigator should check appropriate state and local laws and regulations before conducting research to determine the definition of a ward. The IRB can provide assistance in this determination.

7) **Minimal Risk:** the probability and magnitude of harm or discomfort anticipated in the research are no greater in themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

C. Risk/Benefit Analysis

Subpart D identifies four categories of research that the IRB may approve based on a risk/benefit analysis. The IRB must determine the appropriate category for each non-exempt research study involving children, as described below, and ensure that all conditions of that category are satisfied.

1. **Research not involving greater than minimal risk** (45 CFR 46.404; 21 CFR 50.51) ("Section 404 Research").

2. **Research involving greater than minimal risk, but presenting the prospect of direct benefit to the individual subjects** (45 CFR 46.405; 21 CFR 50.52) ("Section 405 Research"). Section 405 Research may be conducted only if:

- (a) the risk is justified by the anticipated benefit to the subject;

- (b) the relation of the anticipated benefit to the risk is at least as favorable to the 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 parents or guardians, as set forth in 45 CFR 46.408.

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; 21 CFR 50.53) ("Section 406 Research").

Section 406 Research may be conducted only if:

- (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 subjects' disorder or condition that is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and
- (d) adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in 45 CFR 46.408.

Although Subpart D does not define what a "minor increase" over minimal risk is, according to the Report on Research Involving Children of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (1977), "while [minor increase] goes beyond the boundaries of minimal risk, it poses no significant threat to the child's health or well being."

4. Research which does not meet the criteria of Section 404, 405 or 406 of Subpart D, but which presents an opportunity to understand, prevent, or alleviate a serious problem that affects the health or welfare of children (45 CFR 46.407; 21 CFR 50.54) ("Section 407 Research"). Section 407 Research may be conducted only if:

- (a) the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem that affects the health or welfare of children; and
- (b) the Secretary of DHHS or the Commissioner of the FDA, after consultation with a panel of experts in pertinent disciplines (e.g., science, medicine, education, ethics, law) and following the opportunity for public review and comment, has determined that either:
 - (i) the research satisfies the criteria of Section 404, 405 or 406 of Subpart D; or

(ii) the following conditions are met:

- (1) the research presents a reasonable opportunity to further the understanding, prevention or alleviation of a serious problem that affects the health and welfare of children;
- (2) the research will be conducted in accordance with ethical principles; and
- (3) adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in 45 CFR 46.408.

In considering the risks of a study involving children, the investigator should note the following:

- (a) Minimal risk should be considered in relation to the normal experiences of average, healthy, normal children.
- (b) The potential harm or discomfort anticipated in research should be considered in relation to the harm or discomfort that average, healthy, normal children may encounter in their daily lives or experience in routine physical or psychological examinations or tests.
- (c) The risk of harm or discomfort should be considered in relation to the ages of the children to be studied.
- (d) The duration, as well as the probability and magnitude, of potential harm or discomfort should be considered.

D. Parental Permission

1. Sections 408(b) and 55 (b) of Subpart D require that adequate provisions be made for soliciting the permission of the parents or guardian of each child involved in a research study. All of the requirements concerning informed consent apply to obtaining parental permission and the appropriate elements of consent must be included in a written informed consent document (i.e., a consent form that could apply to both adult participants in the study and parents of children in the study or a separate Parental Permission Form), unless otherwise waived by the IRB.

2. The IRB may waive the requirement for obtaining parental permission if it determines that:

- (a) the relevant 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 (for example, neglected or abused children);

(b) an appropriate mechanism for protecting children who will be subjects is substituted; and

(c) the waiver is not inconsistent with federal, state or local law.

3. The IRB may also waive the requirement for obtaining parental permission if it determines that:

(a) the research involves no more than minimal risk to the subjects;

(b) the waiver will not adversely affect the rights and welfare of the subjects;

(c) the research could not practicably be carried out without the waiver; and

(d) whenever appropriate, the subjects will be provided with additional information after participation.

4. If the IRB has not waived the requirement of parental permission, obtaining the permission of only **one** parent is acceptable for Section 404 Research or Section 405 Research unless the IRB determines that permission from both parents is warranted.

5. If the IRB has not waived the requirement of parental permission, obtaining the permission of **both** parents must be obtained for Section 406 Research or Section 407 Research unless

(a) one parent is deceased, unknown or lacks capacity to provide permission;

(b) one parent is not reasonably available; or

(c) only one parent has legal responsibility for the care and custody of the child.

The investigator should document in the research record the efforts made to obtain permission from both parents unless not required to do so by the IRB.

6. If a person other than a parent signs a Parental Permission Form, the principal investigator should, if possible, obtain documentary evidence that such person has been legally appointed as a guardian or, in the case of wards or foster children, that a state agency has legal custody or guardianship of the child. If such documentation is not available, the investigator should call the IRB for assistance. A foster parent is not ordinarily authorized to provide parental or guardian permission.

E. Assent

Section 408(a) and 55(a) of Subpart D requires that adequate provisions be made for soliciting the assent of all children involved in research, when the children are capable of providing assent. In determining whether children are capable of assenting, the ages, maturity and psychological state of the children should be taken into account.

Please note that mere failure of the child to object should not, absent affirmative agreement, be construed as assent.

The following guidelines apply to obtaining the assent of children:

1. Assent is required for all non-exempt research involving children aged 7 years or more unless the IRB determines that:

- (a) the capability of the child is so limited that he/she cannot reasonably be consulted;
- (b) the research holds out the prospect of a direct benefit that is only available through participation in the research (i.e., research that offers a therapeutic benefit); or
- (c) all of the following factors are present and the IRB has specifically waived the requirement to obtain assent:
 - (i) the research involves no more than minimal risk;
 - (ii) the waiver will not adversely affect the rights and welfare of the subjects;
 - (iii) the research could not practically be carried out without the waiver; and
 - (iv) if appropriate, the subjects will be provided with additional pertinent information.

2. In general, children should be given developmentally appropriate information about a research study in language that is understandable to them, given their age, maturity and previous experiences. This information may be provided verbally. However, the provision of information is a matter of judgment for the investigator and the child's parents or guardian and there may be circumstances where information should not be given to a child. The IRB can provide assistance in this determination.

3. If assent is required, the process for obtaining assent, the content of the information provided and the format of the assent document, if any, depends on the age of the child.

- (a) **Children aged 7-11 years:** If assent is not waived by the IRB, except as otherwise provided in paragraph (2) above, children in this age group should be fully informed about the research, using language appropriate to their age and maturity, and assent should be obtained from those deemed capable of making a meaningful decision. Assent should be solicited in the presence of a parent or guardian and the Parental Permission Form should include an acknowledgement by the investigator and the parent or guardian that verbal assent was obtained. If assent is not solicited, the reason for not soliciting assent should be noted in the research record for the subject.

- (b) **Children ages 11-17:** If assent is not waived by the IRB, except as otherwise provided in paragraph (2) above children in this age group should be fully informed about the research and documented assent should be obtained. The child may either sign his/her own Assent Form or may co-sign the Parental Permission Form, so long as in either case, the Form is written in age appropriate language. If documented assent is not obtained, the reason for not obtaining assent should be noted in the research record for the subject.

In any research study that involves continuing diagnostic or therapeutic procedures, or any other form of research intervention (e.g., surveys) over time, attention should be paid to revising the information and assent documentation as the age of a child changes. In any case, any child who turns 18 during the course of a study must provide informed consent before his/her participation in the study continues.

F. Wards

1. Children who are wards may be included in Section 404 Research or Section 405 Research.

2. Children who are wards may be included in Section 406 Research or Section 407 Research only if such research is:
 - (a) related to their status as wards; or

 - (b) conducted in schools, camps, hospitals, institutions or similar settings in which the majority of children involved as subjects are not wards.


3. If wards are to be included in any research study, the investigator must provide the IRB with detailed information about the proposed informed consent process as well as identity and authority of the individuals who will provide the consent.

4. If wards are to be included in Section 406 Research or Section 407 Research, an advocate for each ward must be appointed 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 should be an individual who has the background and experience to act in the best interest of the child for the duration of the child's participation in the study and who is not associated in any other way with the research, the investigator or the guardian organization.

5. In New York City, if wards are to be included in Section 406 Research or Section 407 Research, the Administration for Children's Services ("ACS") must be notified and agree to the inclusion of wards in the study. In addition, permission for the enrollment of each ward in the study must be obtained from the person designated by the ACS to give such permission.

6. If a research study is to be conducted outside of New York City, the investigator should check appropriate state or local laws and regulations before conducting research to determine whether there are similar regulatory requirements and, if so, contact the appropriate governmental agency. The IRB can provide assistance in this determination.

George Gasparis	Executive Director, CU IRB		September 23, 2005
Guidance Approved by	Title	Signature	Date