

Summary Table for 45 CFR 46, Subpart D Reviewing Research Involving Children

For all research studies involving children, the investigator should make an initial determination of the appropriate risk category. As required by the Office for Human Research Protections (OHRP), the IRB will make the final determination of category and reflect it in the letters and minutes of the IRB meeting.

45 CFR 46	Category	Explanation	Permission/Assent
§46.404	Research not involving greater than minimal risk ¹	The IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians.	Permission/Consent from one parent is sufficient. Assent of child is required.
§46.405	Research involving greater than minimal risk ¹ but presenting the prospect of direct benefit to the individual subjects	<ul style="list-style-type: none"> a. The risk is justified by the anticipated benefit to the subjects; b. The relation of the anticipated benefit to the risk is as least as favorable to the subjects as that presented by available alternative approaches; and c. <i>Adequate provisions are made for soliciting the assent of the children</i> and permission of their parents or guardians, as set forth in §46.408. 	Permission/Consent from one parent is sufficient. Assent of child is required.
§46.406	Research involving greater than minimal risk ¹ and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition	<ul style="list-style-type: none"> 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 which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and d. <i>Adequate provisions are made for soliciting assent of the children</i> and permission of their parents or guardians, as set forth in §46.408. 	Permission/Consent must be obtained from both parents if they have custody and are reasonably available. Assent of child is required.
§46.407	Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children <i>(very rarely used)</i>	<ul style="list-style-type: none"> 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; and b. The Secretary of DHHS, 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 either: <ul style="list-style-type: none"> 1. That the research in fact satisfies the conditions of §46.404, §46.405, or §46.406, as applicable, or 2. The following: <ul style="list-style-type: none"> i. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health and welfare of children; ii. The research will be conducted in accordance with sound ethical principles; iii. <i>Adequate provisions are made for soliciting the assent of children</i> and the 	Permission/Consent must be obtained from both parents if they have custody and are reasonably available. Assent of child is required.

		permission of their parents or guardians, as set forth in §46.408 .	
§46.408	<p>Requirements for permission by parents or guardians and for assent by children</p> <p>Waiver of assent and permission/consent conditions</p>	<p>a. “[T]he IRB shall determine that adequate provisions are made for soliciting assent...when in the judgment of the IRB the children are capable of assenting. [In determining this], the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children...under a particular protocol or for each child, as the IRB deems appropriate.”</p> <p>“If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted, or that 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, the assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accord with §46.116 of Subpart A.”</p> <p>b. “[T]he IRB shall determine, in accordance with...§46.116 of Subpart A, 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 the permission of one parent is sufficient for research to be conducted under §46.404 or §46.405. Where research is covered by §46.406 and §46.407 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 responsibility for the care and custody of the child.”</p> <p>c. “In addition to the provisions for waiver contained in §46.116 of Subpart A, 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 (for example, neglected or abused children), it may waive the consent requirements in Subpart A of this part and paragraph (b) of this section, provided that:</p> <ol style="list-style-type: none"> 1. an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and 2. the waiver is not inconsistent with Federal, State, or local law.” <p>d. “Permission by parents or guardians shall be documented in accordance with and to the extent required by §46.117 of Subpart A.”</p> <p>e. “When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.”</p>	<p><i>Requirements for Permission/Consent of the parent or assent of the child if the study falls under:</i></p> <p><i>46.404 & 46.405</i> IRB may find that permission of one parent is sufficient</p> <p><i>46.406 & 46.407</i> Permission/Consent must be obtained from both parents if they have custody and are reasonably available.</p> <p>Assent of the child is required unless appropriately waived.</p>

§46.409	Wards	<p>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:</p> <ol style="list-style-type: none"> 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.” <p>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 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.”</p>	<p><i>Requirements for Permission/Consent or assent if the study falls under:</i></p> <p><i>46.406 & 46.407</i> Permission/Consent must be obtained from both child advocate and any other individual acting on behalf of the child as guardian or in <i>loco parentis</i></p>
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¹ “*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,” 45CFR46.102