

**HRPP POLICY APPROVAL & IMPLEMENTATION**  
**OFFICE OF HUMAN SUBJECTS RESEARCH PROTECTIONS**

**Policy Number:** 402

**SOP Title:** Research Involving Children

**Distribution:** Scientific Directors; Clinical Directors; Clinical Investigators,  
IRB Chairs, IRB Administrators, Protocol Navigators

**Revision Approval:**

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**Deputy Director for Intramural  
Research**

**Implementation date:** 9/14/2020

<b>NIH Intramural Research Program</b>		
<b>Office of Human Subjects Research Protections</b>	<b>Effective Date: 09/14/2020</b>	
<b>Research Involving Children</b>	<b>Policy 402</b>	<b>Version: 1.0</b>

## POLICY

### A. PURPOSE

1. Describe regulatory and policy requirements that apply when an NIH Institutional Review Board (IRB) is reviewing, or when an NIH investigator seeks to perform, research involving children.

### B. SCOPE

1. This policy applies to all research involving children reviewed by the NIH IRB
2. This policy applies to NIH investigators when conducting research at an NIH site, whether the reviewing IRB is the NIH IRB or an external IRB.
3. This policy applies to non-NIH investigators, including Lead Site Investigators, when the NIH IRB is the reviewing IRB.
4. This policy applies to the Office of Human Subjects Research Protections (OHSRP) and its offices.

### C. POLICY

1. The protection of the rights, welfare and safety of children that are research subjects is of paramount importance to the NIH Human Research Protection Program (HRPP). Therefore, the NIH Principal Investigator (PI)/Lead Site Investigator will not initiate or conduct research (e.g., screen, enroll or perform research procedures) that involves children without IRB approval for the inclusion of children.
2. The NIH IRB will only approve research that permits the participation of children if it has determined and documented that the research meets the requirements of 45 CFR 46, including [Subpart D -Additional Protections for Children Involved as Subjects in Research](#) and, as applicable, [21 CFR 50 Subpart D](#), in addition to all other applicable regulatory and policy requirements.
3. Human subjects research that is subject to 45 CFR 46 Subpart D generally may be exempt research under 45 CFR 46.101(b) of the pre-2018 Common Rule but is subject to the following restriction:
  - a. The exemption at 45 CFR 46.101(b)(2), for research involving survey or interview procedures or observation of public behavior, does not apply to research with children (45 CFR Subpart D), except for research involving observations of public behavior

<b>NIH Intramural Research Program</b>		
<b>Office of Human Subjects Research Protections</b>	<b>Effective Date: 09/14/2020</b>	
<b>Research Involving Children</b>	<b>Policy 402</b>	<b>Version: 1.0</b>

when the investigator(s) do not participate in the activities being observed. ([45 CFR 46.101\(i\)](#)<sup>1</sup> of the pre-2018 Common Rule)

4. Human subjects research that is subject to 45 CFR 46 subpart D may be exempt research under [45 CFR 46.104](#) of the 2018 Common Rule, as follows:
  - a. Exemptions may be applied to the categories found at 45 CFR 46.104(d)(1), (4), (5), (6), (7), and (8), if the conditions of the exemption are met. ([45 CFR 46.104\(b\)\(3\)](#) of the 2018 Common Rule)
  - b. Exemptions may be applied to the category found at 45 CFR 46.104(d)(2)(i) and (ii), only when the research involves educational tests or the observation of public behavior when the investigator(s) does not participate in the activities being observed.
  - c. As written in the 2018 Common Rule, the exemption category found at 45 CFR 46.104(d)(3)) applies only to adults. Further, the exemption category found at 45 CFR 46.104(d)(2)(iii) cannot be applied or utilized.
5. When the research involves children, no child may be enrolled, screened, or have research procedures initiated, unless parental permission and child assent is obtained consistent with [45 CFR 46.408](#) and, if applicable, [21 CFR 50.55](#), unless waived by the IRB. ([45 CFR 46.116\(f\) of the 2018 Common Rule](#) and [45 CFR 46.116\(d\) of the pre-2018 Common Rule](#))
  - a. For research taking place at an NIH site, and in cases where parents share joint legal custody for medical decision-making of a child (e.g., by a custody agreement or court order), both parents must give their permission regardless of the risk level of the research. Exceptions may include if one parent has since died, become incompetent, or is not reasonably available.
  - b. The Secretarial waiver of informed consent in certain emergency research may be applicable to research involving children. ([45 CFR 46.101\(a\)](#) and [46.401\(a\)\(2\)](#))
6. For the purpose of consent when research is conducted at an NIH site, an adult is anyone 18 years or older.
  - a. For the purposes of the research, children who are legally emancipated are considered adults and the requirements of this policy do not apply.
  - b. Children that reach the age of majority during the period of the research, must provide consent in order to continue participation in the research, unless consent is not required (e.g., for certain exempt research) or if waived by the IRB.

<b>NIH Intramural Research Program</b>		
<b>Office of Human Subjects Research Protections</b>	<b>Effective Date: 09/14/2020</b>	
<b>Research Involving Children</b>	<b>Policy 402</b>	<b>Version: 1.0</b>

- c. If the child who has reached the age of majority lacks the capacity to consent to the research, the NIH investigator will follow the requirements in *Policy 403 Research Involving Adults Who Lack Decision-making Capacity to Consent to Research Participation*, unless the IRB has waived consent consistent with [45 CFR 46.116\(f\)\(3\) of the 2018 Common Rule and 45 CFR 46.116\(d\) of the pre-2018 Common Rule](#).

#### **D. DEFINITIONS**

1. *Advocate* – 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 Institutional Review Board (IRB)) with the research, the investigators(s), or the guardian organization. (See [45 CFR 46.409\(b\)](#).)
2. *Assent* – The affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent. (See [45 CFR 46.402\(b\)](#) of the 2018 Common Rule.)
3. *Children* – Are 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. ([45 CFR 46.402\(a\)](#)) Also described as a “child” in policy 402.
4. *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\(e\)](#))
5. *Minimal Risk* – 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. [45 CFR 46.102\(i\)](#) (pre-2018 Common Rule), [45 CFR 46.102\(j\)](#) (2018 Common Rule) and [21 CFR 50.3\(k\)](#) (FDA regulations).
6. *Parent* – A child’s biological or adoptive parent. ([45 CFR 46.402\(d\)](#))
7. *Permission* – The agreement of parent(s) or a guardian to the participation of their child or ward in research. ([45 CFR 46.402\(c\)](#)).
8. *Ward* – A child who is placed under the protection of, and in the legal custody of, the State or other agency, institution, or entity (including guardians), consistent with applicable State or local law.

<b>NIH Intramural Research Program</b>		
<b>Office of Human Subjects Research Protections</b>	<b>Effective Date: 09/14/2020</b>	
<b>Research Involving Children</b>	<b>Policy 402</b>	<b>Version: 1.0</b>

## E. RESPONSIBILITIES AND REQUIREMENTS

### 1. Responsibilities of Investigators:

- a. The NIH Principal Investigator (PI)/Lead site investigator may not initiate or conduct research that involves children unless IRB approval has been obtained in accordance with this policy.
- b. The NIH Principal Investigator (PI)/Lead Site Investigator is responsible for determining if it is scientifically and ethically appropriate to enroll children in the research protocol and must document this rationale in the protocol.
- c. In addition to the requirements for informed consent described in 45 CFR 46 Subpart A, when the research involves children, the consent requirements at 45 CFR 46 Subpart D must also be met.
  - I. When the research involves children, the NIH PI/Lead Site Investigator must provide a plan in the protocol for obtaining parental permission as well as assent from the child, as applicable, or they must provide a justification for requesting a waiver of parental permission and/or assent (consistent with [C.5](#) above).
  - II. All investigators are responsible for complying with the Reviewing IRB requirements for obtaining and documenting parental permission and assent, and consistent with [C.4](#) and [C.5](#) above, as applicable. ([45 CFR 46.408\(d\) and \(e\)](#))
  - III. When child subjects reach the age of majority, investigators must seek legally effective informed consent from the now-adult subject, consistent with [C.6.\(c\)](#) above, or withdraw the subject from the research. (See *Policy 301 Informed Consent*.)
    - i. Alternatively, the investigator may request a waiver of consent from the IRB for the subjects continued participation if the ongoing research meets the criteria for a waiver specified in [45 CFR 46.116\(f\)\(3\) of the 2018 Common Rule and 45 CFR 46.116\(d\) of the pre-2018 Common Rule](#). For example, a request may be to continue to use tissue specimens collected when the participant was a minor.
    - ii. If the now-adult subject is unable to provide legally effective informed consent, the requirements of *Policy 403 Research Involving Adults*

<b>NIH Intramural Research Program</b>		
<b>Office of Human Subjects Research Protections</b>	<b>Effective Date: 09/14/2020</b>	
<b>Research Involving Children</b>	<b>Policy 402</b>	<b>Version: 1.0</b>

*Who Lack Decision-making Capacity to Consent to Research Participation* must be followed.

**2. Responsibilities of the NIH IRB:**

- a. When reviewing research involving children, the IRB shall only approve research that satisfies all applicable sections of 45 CFR 46 Subpart D and the other applicable regulatory and policy requirements as described in [Section C](#) above. ([45 CFR 46.403](#) and, as applicable, [21 CFR 50.50](#))
- b. The NIH IRB is responsible for making and documenting in the minutes, the appropriate risk benefit ratio, consistent with [45 CFR 46.404](#), [45 CFR 46.405](#) or [45 CFR 46.406](#) and, as applicable, [21 CFR 50.51](#), [50.52](#), or [50.53](#). The NIH IRB is responsible for making and documenting in the minutes, the other required determinations consistent with 45 CFR Subparts A and D, and, as applicable, 21 CFR parts 50 and 56.
- c. If the IRB does not believe the research meets the requirements of 45 CFR 46.404, 46.405, or 46.406, but presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children, then the requirements of [45 CFR 46.407](#) and, as applicable, [21 CFR 50.54](#) must be satisfied prior to review by the Secretary of HHS. In this case, the IRB must determine and document in the meeting minutes 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.
- d. The NIH IRB is responsible for determining the parental permission and signature requirements, consistent with 45 CFR 46.116, 45 CFR 46.117, and [45 CFR 46.408](#) and, as applicable, [21 CFR 50.55](#). The IRB will ensure that adequate provisions are made for soliciting the permission of each child's parents or guardian, unless waived by the IRB consistent with the regulations.
  - I. In cases where parents share joint legal custody for medical decision-making of a child (e.g., by a custody agreement or court order), NIH policy requires that at NIH sites both parents give their permission regardless of the risk level of the research. Exceptions may include if one parent has since died, become incompetent, or is not reasonably available.

<b>NIH Intramural Research Program</b>		
<b>Office of Human Subjects Research Protections</b>	<b>Effective Date: 09/14/2020</b>	
<b>Research Involving Children</b>	<b>Policy 402</b>	<b>Version: 1.0</b>

- e. The IRB will determine that adequate provisions are made for soliciting the assent of children capable of assenting as described in [45 CFR 46.408\(a\)](#) and consistent with applicable provisions of 45 CFR 46.116.
  - I. When the IRB determines that assent is required, it shall determine whether and how assent must be documented. The assent process may be either verbal or written. ([45 CFR 46.408\(e\)](#)).
  - II. The IRB may only waive assent of the child if it determines that the conditions of [45 CFR 46.116](#), and [45 CFR 46.408](#) and, as applicable, [21 CFR 50.55](#) are met.
- f. If the proposed research will involve wards, the IRB may only approve the research when consistent with the requirements at [45 CFR 46.409](#), and, as applicable [21 CFR 50.56](#).
  - I. When the IRB reviews research involving wards, 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*, and consistent with the requirements at [45 CFR 46.409\(b\)](#), and, as applicable [21 CFR 50.56\(b\)](#).

**3. Responsibilities of OHSRP:**

- a. When proposed research has been determined by the IRB to satisfy the requirements at [45 CFR 46.407](#), and, as applicable, [21 CFR 50.54](#), OHSRP is responsible for providing the research protocol and other relevant documents, e.g., the IRB minutes, to the HHS Office for Human Research Protections (OHRP) for review by the Secretary in accordance with [45 CFR 46.407](#); and, as applicable, to the Food and Drug Administration, for review by the Commissioner of Food and Drugs in accordance with [21 CFR 50.54](#).

**F. REFERENCES**

**1. Federal Regulations**

HHS: [45 CFR 46](#) and [45 CFR 46 Subpart D](#)  
 FDA: 21 CFR parts [50](#), [56](#) and [21 CFR 50 Subpart D](#)

**2. NIH Policies**

Policy 301 Informed Consent

<b>NIH Intramural Research Program</b>		
<b>Office of Human Subjects Research Protections</b>	<b>Effective Date: 09/14/2020</b>	
<b>Research Involving Children</b>	<b>Policy 402</b>	<b>Version: 1.0</b>

Policy 403 Research Involving Adults Who Lack Decision-making Capacity to Consent to Research Participation

**3. Guidance**

OHRP Research with Children FAQs: <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/children-research/index.html>

OHRP Special Protections for Children as Research Subjects:  
<https://www.hhs.gov/ohrp/regulations-and-policy/guidance/special-protections-for-children/index.html>

OHRP Children as Research Subjects and the HHS "407" Process:  
<https://www.hhs.gov/ohrp/regulations-and-policy/guidance/guidance-on-407-review-process/index.html>

**G. APPENDICES:** N/A

**H. REVISION HISTORY:** NA

**I. SUPERSEDES DATE:** 09/14/2020

SOP 14A Research Involving Vulnerable Subjects (General Considerations)

SOP 14D Research Involving Children