

**HRPP STANDARD OPERATING PROCEDURE/POLICY APPROVAL &  
IMPLEMENTATION**

**OFFICE OF HUMAN SUBJECTS RESEARCH PROTECTIONS**

**Policy Number: 400**

**SOP Title: Research Involving Pregnant Women, Human Fetuses and Neonates**

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

**Revision Approval:**

  
**Deputy Director for Intramural  
Research**

**Approval Date:**

9/25/19

**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 Pregnant Women, Human Fetuses, and Neonates</b>	<b>Policy 400</b>	<b>Version: 1.0</b>

## POLICY

### A. PURPOSE

1. Describe general considerations and certain regulatory requirements that apply when an NIH Institutional Review Board (IRB) is reviewing, or when an NIH investigator seeks to perform research involving pregnant women, human fetuses, neonates, and/or research involving, after delivery, the placenta, the dead fetus, or fetal material.

### B. SCOPE

1. This policy applies to research conducted by NIH investigators involving pregnant women, human fetuses, and neonates, and/or research involving, after delivery, the placenta, the dead fetus, or fetal material. This policy also applies when such research is being reviewed by the NIH IRB.
2. This policy is not intended to be an exhaustive listing of statutory, regulatory, and policy requirements. For more complete information, NIH Investigators and IRBs should refer to [45 CFR 46 Subpart B](#). Further, for research involving fetal tissue, Principal Investigators must consult the Office of Intramural Research (OIR) for information on additional requirements and restrictions. The [OIR Sourcebook: Special Research Concerns](#) includes additional requirements related to prohibited research and research with human embryonic stem cells (hESCs), human induced pluripotent stem cells (iPSCs), and adult stem cells.

### C. POLICY

1. NIH investigators and the NIH IRB must comply with the basic requirements for Protection of Human Subjects at 45 CFR 46 [Subpart A](#) and to the requirements for Protections for Pregnant Women, Human Fetuses, and Neonates Involved in Research at 45 CFR 46 Subpart B when applicable. In addition:
  - a. When the pregnant woman is also a child or the research involves a viable neonate, the NIH investigator and the NIH IRB must also comply with the requirements at 45 CFR 46 [Subpart D](#). (See *Policy 402 Research Involving Children*.)
2. NIH investigators and the IRB must comply with Food and Drug Administration (FDA) and Department of Health and Human Services (referred to as HHS in this policy) regulations, as applicable. In limited circumstances, FDA and HHS regulations allow for exception(s) from informed consent requirements for emergency research, but this waiver

<b>NIH Intramural Research Program</b>		
<b>Office of Human Subjects Research Protections</b>	<b>Effective Date: 09/14/2020</b>	
<b>Research Involving Pregnant Women, Human Fetuses, and Neonates</b>	<b>Policy 400</b>	<b>Version: 1.0</b>

may not be applied to research subject to 45 CFR 46, Subpart B (e.g., pregnant women, human fetuses, or neonates). ([21 CFR part 50.24](#))

3. NIH investigators must comply with applicable regulatory and federal policy requirements. (See [B.2.](#) above.)
4. For exempt human subjects research involving pregnant women, human fetuses, or neonates, and/or research involving, after delivery, the placenta, the dead fetus, or fetal material:
  - a. When the research is subject to the pre-2018 Common Rule, the exemptions at 45 CFR 46.101(b)(1) through (6) may apply as long as the conditions of the exemption are met.
  - b. When the research is subject to the requirements of the 2018 Common Rule, the exemptions at 45 CFR 46.104(d)(1) through (8) may apply to research as long as the conditions of the exemption are met.<sup>1</sup>
5. For non-exempt human subjects research subject to 45 CFR 46, Subpart B (e.g., involving pregnant women, human fetuses, or neonates), in addition to the basic requirements of Subpart A (described in [C.1.](#) above), the following regulatory requirements must be satisfied, when applicable:
  - a. Research involving pregnant women and/or human fetuses may be conducted only in accordance with all the conditions of [45 CFR 46.204](#).
  - b. Research involving neonates varies by viability. Research with neonates may be approved only if the following requirements are satisfied:
    - I. Research involving viable neonates may be conducted only in accordance with the conditions of [45 CFR 46.205\(d\)](#). (See *Policy 402 Research Involving Children*.)
    - II. Research involving neonates of uncertain viability may be conducted only in accordance with the conditions of [45 CFR 46.205 \(a\)](#) and [\(b\)](#).
    - III. Research involving nonviable neonates may be conducted only in accordance with the conditions of 45 CFR [46.205\(a\)](#) and [\(c\)](#).

---

<sup>1</sup> Exemptions related to broad consent for the maintenance, storage and secondary use of identifiable private information or identifiable biospecimens at 45 CFR 46.104(d)(7) or (8) are not being implemented in the NIH IRP at this time.

<b>NIH Intramural Research Program</b>		
<b>Office of Human Subjects Research Protections</b>	<b>Effective Date: 09/14/2020</b>	
<b>Research Involving Pregnant Women, Human Fetuses, and Neonates</b>	<b>Policy 400</b>	<b>Version: 1.0</b>

- c. Research involving, after delivery, the placenta, the dead fetus, or fetal material may be conducted only in accordance with [45 CFR 46.206](#).
- d. Research that is not otherwise approvable under 45 CFR 46.204 and 45 CFR 46.205 (described in subsections [C.5.a.-C.5.c.](#) above) but which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, human fetuses, or neonates, requires additional review and approval by the Secretary, HHS. ([45 CFR 46.207](#))

**D. DEFINITIONS**

1. *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. (See [45 CFR 46.402\(a\)](#).)
2. *Dead Fetus* – A fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord. ([45 CFR 46.202\(a\)](#))
3. *Delivery* – Complete separation of the fetus from the woman by expulsion or extraction or any other means. ([45 CFR 46.202\(b\)](#))
4. *Fetus* – The product of conception from implantation until delivery. ([45 CFR 46.202\(c\)](#))
5. *Neonate* – A newborn. ([45 CFR 46.202\(d\)](#))
6. *Nonviable Neonate* – A neonate after delivery that, although living, is not viable. ([45 CFR 46.202\(e\)](#))
7. *Pregnancy* – The period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery. ([45 CFR 46.202\(f\)](#))
8. *Secretary* – The Secretary of Health and Human Services (HHS) and any other officer or employee of HHS to whom authority has been delegated. ([45 CFR 46.202\(g\)](#))
9. *Viable* – As it pertains to the neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration. The Secretary may from time to time, taking into account medical advances, publish in the Federal Register guidelines to assist in determining whether a neonate is viable for purposes of this subpart. If a neonate is viable then it may be included in research only to the extent permitted and in accordance with the requirements of 45 CFR 46 [Subpart A](#) and [Subpart D of this part](#). ([45 CFR 46.202\(h\)](#))

<b>NIH Intramural Research Program</b>		
<b>Office of Human Subjects Research Protections</b>	<b>Effective Date: 09/14/2020</b>	
<b>Research Involving Pregnant Women, Human Fetuses, and Neonates</b>	<b>Policy 400</b>	<b>Version: 1.0</b>

## **E. RESPONSIBILITIES AND REQUIREMENTS**

### **1. Investigator Responsibilities**

- a. When conducting research subject to 45 CFR 46, Subpart B (e.g., involving pregnant women, human fetuses and neonates), Principal Investigators (PIs)/Lead Site Investigators must ensure that the protocol and the performance of the research is in compliance with all applicable sections of Subpart B and the other applicable Subparts of 45 CFR 46 as described in Section C, above, as well as requirements noted in Section B.
- b. In addition to the requirements for informed consent described in 45 CFR 46 Subpart A, when the research involves pregnant women, human fetuses, or neonates, and/or research involving, after delivery, the placenta, the dead fetus, or fetal material, the consent requirements at 45 CFR 46 Subpart B must also be met, as well as the other applicable Subparts. For more information, review *Appendix A - Subpart B Informed Consent table*.

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

- a. When reviewing research involving pregnant women, human fetuses, and neonates, and/or research involving, after delivery, the placenta, the dead fetus, or fetal material, the IRB shall only approve research that satisfies all applicable sections of Subpart B and the other applicable Subparts of 45 CFR 46 as described in Section C. above. ([45 CFR 46.203](#))
- b. The IRB will document that applicable regulatory protections are satisfied during its review and approval of the proposed research.
- c. When reviewing research that might be subject to [45 CFR 46.207](#), and prior to review by the Secretary HHS, the IRB must determine and document in the 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 pregnant women, human fetuses, or neonates.
  - I. When the proposed research in this category has been determined by the IRB to satisfy the requirements at [45 CFR 46.207](#), the IRB will send the IRB Minutes documenting its determination and the research protocol to the NIH Office of Human Subjects Research Protections (OHSRP).
  - II. OHSRP is responsible for forwarding the research protocol and other relevant documents, e.g., the IRB minutes, to the HHS Office for Human Research

<b>NIH Intramural Research Program</b>		
<b>Office of Human Subjects Research Protections</b>	<b>Effective Date: 09/14/2020</b>	
<b>Research Involving Pregnant Women, Human Fetuses, and Neonates</b>	<b>Policy 400</b>	<b>Version: 1.0</b>

Protections (OHRP) for review by the Secretary in accordance with [45 CFR 46.207](#).

**F. REFERENCES**

**1. Federal regulations**

HHS: [Subpart A](#), [Subpart B](#), [Subpart D](#); [Subpart C](#)  
FDA: [21 CFR part 50](#)

**2. NIH Policies**

Policy 402 Research Involving Children

**3. Guidance**

[NIH Human Embryonic Stem Cell Registry](#) (lines eligible for use with NIH funds)  
NIH Guidelines for Human Embryonic and Induced Pluripotent Stem Cells:  
<https://stemcells.nih.gov/policy/2009-guidelines.htm>  
[NIH Guidelines for Human Stem Cell Research](#) (the policy that applies to NIH-funded research using hESCs and iPSCs)  
[NIH Stem Cell Website](#) (general info)  
[NIH Stem Cell FAQs](#)

**G. APPENDICES:** NA

**H. REVISION HISTORY:** NA

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

SOP 14B Research Involving Pregnant Women, Human Fetuses and Neonates