

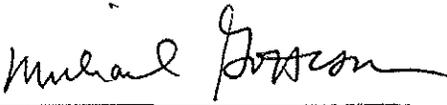
**HRPP STANDARD OPERATING PROCEDURE/POLICY APPROVAL &
IMPLEMENTATION**

OFFICE OF HUMAN SUBJECTS RESEARCH PROTECTIONS

SOP Number: SOP 14A

**SOP Title: RESEARCH INVOLVING VULNERABLE SUBJECTS (GENERAL
CONSIDERATIONS)**

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

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SOP 14A – RESEARCH INVOLVING VULNERABLE SUBJECTS (GENERAL CONSIDERATIONS)

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SOP 14A RESEARCH INVOLVING VULNERABLE SUBJECTS (GENERAL CONSIDERATIONS)

14A.1 PURPOSE

This Standard Operating Procedure (SOP) describes the responsibilities of the NIH Institutional Review Boards (IRBs), Principal Investigators (PIs) and members of the research team pertaining to research conducted on vulnerable subjects.

14A.2 POLICY

The NIH Human Research Protection Program (HRPP) abides by Federal regulatory requirements to provide appropriate additional protections for vulnerable subjects (Department of Health and Human Services (DHHS) regulations at 45 CFR 46.111(b) and, if applicable, FDA regulations at 21 CFR 56.111(b)).

14A.3 REQUIREMENTS FOR RESEARCH INVOLVING VULNERABLE SUBJECTS

14A.3.1. GENERAL DHHS REGULATORY REQUIREMENTS

- A. 45 CFR 46.111(b) states “when some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.”
- B. Composition of the IRB: NIH IRBs that regularly review research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, shall give consideration to the inclusion of one or more members who have knowledge about and experience with these subjects (45 CFR 46.107(a)). In some cases, additional membership is expressly required. For additional regulatory requirements regarding IRB membership, see SOP 2 - IRB Membership and Structure.
 - 1. An NIH IRB may seek expertise or information from non-voting consultants as described in SOP 2 - IRB Membership and Structure.

14A.3.2 SPECIFIC DHHS REGULATORY REQUIREMENTS

DHHS Federal regulations (45 CFR Part 46) put into place the following specific additional protections that are followed by the NIH HRPP:

Subpart B - Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research (see SOP 14B - Research Involving Pregnant Women, Human Fetuses and Neonates).

Subpart C - Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects (see SOP 14C - Research Involving Prisoners).

Subpart D - Additional Protections for Children Involved as Subjects in Research (see SOP 14D - Research Involving Children).

14A.3.3 ADDITIONAL NIH REQUIREMENTS

- A. In addition to the requirements of **14A.3.1** and **14A.3.2** above, the NIH HRPP has additional protections for adult subjects who are or may be unable to consent (see SOP 14E - Research Involving Adults Who Are or May be Unable to Consent) and for subjects who are also NIH staff (see SOP 14F - Research Involving NIH Staff as Subjects).
- B. In addition to the specific protections required under 45 CFR 46 Subparts B, C and D, the NIH HRPP expects IRBs to use their judgment when determining if subjects enrolling into particular protocols are considered vulnerable and if additional protections are warranted. For example, students and very ill persons may be considered vulnerable subjects.

14A.4 PROCEDURES FOR THE INITIAL REVIEW OF A RESEARCH STUDY INVOLVING VULNERABLE SUBJECTS

- A. The policy of other relevant SOPs on initial review of research applies when vulnerable populations are the anticipated subjects. Relevant SOPs include: SOP 7 - Requirements for the Ethical and Regulatory Review of Research by NIH Institutional Review Boards (IRBs), SOP 7A - Requirements for Expedited Review of Research by NIH Institutional Review Boards, and SOP 8 - Procedures and Required Documentation for Submission and Initial Review of Protocols. At NIH, expedited review for minimal risk studies including vulnerable subjects is permitted generally, but expedited review is not permitted for any research involving prisoners.
- B. The PI will complete the NIH Intramural Clinical Initial Protocol Application and ensure that the protocol contains the information described in the Supplements relevant to the subjects to be enrolled, i.e., Supplement D (Children), Supplement E (Prisoners), Supplement F (Pregnant Women, etc.) and Supplement G (Adults Who Are or May be Unable to Consent to Research). The IRB will review the NIH Intramural Clinical Initial Protocol Application in its entirety.

- C. In addition to its obligations outlined in other SOPs, including SOPs 14B, 14C, 14D, 14E and 14F, the IRB:
1. Ensures that the PI identifies the potential to enroll vulnerable subjects in the proposed research at initial review and provides the justification for their inclusion in the study.
 2. Ensures that the PI provides appropriate safeguards to protect the subject's rights and welfare.
 3. Shall give consideration to, and require as needed, the inclusion, either as members or *ad hoc* consultants, of individuals who have experience with the vulnerable populations involved in the proposed research. (Prisoner representatives must be IRB members, not consultants.)
 4. Reviews the PI's justifications for including vulnerable populations in the proposed research.
 5. Ensures that additional safeguards have been included in the proposed research to protect the rights and welfare of vulnerable subjects, as needed, and assesses the adequacy of additional protections for vulnerable populations provided by the PI.
 6. Evaluates the proposed plan for consent and, as needed, assent of the specific vulnerable populations involved.
 7. Evaluates the proposed research to determine the need for additional safety monitoring.
 8. Documents a separate risk and benefit assessment for each cohort involved in the protocol. Documentation for vulnerable populations (children, prisoners, pregnant women, fetuses, employees and individuals unable to provide consent) should also include protocol-specific findings that support and justify the risk and benefit assessment.

14A.5 PROCEDURES FOR THE CONTINUING REVIEW OF A RESEARCH STUDY INVOLVING VULNERABLE SUBJECTS

NIH IRBs will conduct continuing reviews consistent with SOP 9 - Continuing Review by the Convened IRB. When vulnerable subjects are involved they will also:

- A. Review information provided by the PI on the number and types of vulnerable subjects enrolled.
- B. Determine whether the protections for vulnerable subjects continue to be adequate.

14A.6 PROCEDURES FOR AMENDMENTS TO AN IRB-APPROVED RESEARCH STUDY INVOLVING VULNERABLE SUBJECTS

NIH IRBs will review amendments consistent with SOP 10 - Amendments to IRB-approved Research. When the amendment concerns the inclusion of vulnerable subjects, or the proposed change/s will impact vulnerable subjects enrolled on the study, the IRB will:

- A. Review existing safeguards to protect the rights and welfare of vulnerable subjects in the protocol to ensure that they continue to be adequate.
- B. Ensure that additional safeguards, if required, are included in the study to protect the rights and welfare of these subjects.
- C. Determine whether current or past subjects must be informed of the amendment and, if so, how they will be informed (verbally and/or in writing). Current and past subjects must be notified if the study amendment affects their safety and welfare, and current subjects re-consented if the amendment changes future clinical study procedures.

These procedures will be undertaken in addition to those outlined in **section 14.A.4.C** above.