

NIH HRPP SOP 8 v1

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

OFFICE OF HUMAN SUBJECTS RESEARCH PROTECTIONS

SOP Number: 8

**SOP Title: PROCEDURES AND REQUIRED DOCUMENTATION FOR SUBMISSION
AND INITIAL REVIEW OF PROTOCOLS**

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

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AND INITIAL REVIEW OF PROTOCOLS**

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SOP 8 PROCEDURES AND REQUIRED DOCUMENTATION FOR SUBMISSION AND INITIAL REVIEW OF PROTOCOLS

8.1 PURPOSE

This SOP describes procedures and documents required for submission and initial review of a new protocol by an NIH IRB.

8.2. POLICY

In fulfilling their mandate to protect the rights and safeguard the welfare of research subjects, a PI's submitted protocol and an NIH IRB's initial review of protocols must take into account federal regulatory requirements and those of the NIH Human Research Protection Program (HRPP).

8.3 REQUIRED ELEMENTS FOR NEW APPLICATIONS TO AN NIH IRB

- A. The PI will complete and submit to the IRB an NIH Intramural Initial Clinical Protocol Application (Attachment 1) including any supplements that are relevant to the protocol (Attachment 2).
- B. All Applications will be completed electronically, using either PTMS or iRIS.
- C. An NIH IRB administrative staff member will review the Initial Review Application to assure its completeness before its review by the convened IRB.

8.3.1. DOCUMENTS TO BE ATTACHED TO THE ELECTRONIC APPLICATION

- A. A written protocol that includes the sections listed in 8.4, below, as applicable. The format of the written protocol may be determined by the individual IRBs, as long as all sections required by this SOP are present.
- B. A written consent document(s) (NIH 2514-1, if at the Clinical Center) and, if appropriate, an assent document(s) (NIH 2514-2, if at the Clinical Center).

1. The consent document(s) and assent document(s) shall include the components listed in SOP 12, "Requirements for Informed Consent", and the requirements of SOP 14D, "Research Involving Children", and, when the research is regulated by the FDA, the requirements of SOP 15, "Research Regulated by the Food and Drug Administration (FDA): General Procedures for Both IND and IDE Applications".
 2. The consent document shall use specific headings and/or language required by the reviewing NIH IRB.
 3. If there are multiple consent documents, each should be individually identified and labeled, e.g., "cohort 1", "cohort 2", "healthy volunteer."
- C. A copy of the Institute or Center scientific review and approval, (when applicable).
- D. For FDA-regulated research (if applicable): A copy of the Clinical Investigator's Brochure along with any other required documents or correspondence, as applicable (see SOP 15, "Research Regulated by the Food and Drug Administration (FDA): General Procedures for Both IND and IDE Applications").
- E. Other required approvals, such as those of the Radiation Safety Committee, Recombinant DNA Advisory Committee (RAC), as applicable.
- F. The completed Clearance of NIH Investigator Personal Financial Holdings (PFH) form(s) (see SOP 21 "Conflict of Interest Requirements for Researchers and Research Staff").

8.4 REQUIRED PROTOCOL SECTIONS

- A. Précis: In 400 words or fewer, provide a description of the objectives, study population, design, and outcome parameters.
- B. Table of Contents
- C. Background
- D. Study Objectives: including primary endpoint(s) and secondary endpoint(s), if applicable.

- E. Study design and methods: including a description of the randomization procedure, if applicable.
- F. Inclusion and Exclusion Criteria
- G. Clinical and Laboratory Methods
- H. Collection and Storage of Human Specimens or Data: All NIH IRB-approved research studies in which IRP researchers intend to collect and store human specimens or data must include:
 - 1. A written description of the intended use of the samples.
 - 2. How they will be stored.
 - 3. How they will be tracked.
 - 4. What will happen to the samples/specimens/data at the completion of the study.
 - 5. What circumstances would prompt the PI to report to the IRB loss or destruction of samples. For additional information, see SOP 5, "NIH Research Activities with Human Data/Specimens" or contact OHSRP at 301-402-3444.
- I. Statistical Analysis (as applicable)
- J. For Phase III or IV clinical trials: The protocol should discuss the required sample size and how the trial will be analyzed statistically.
- K. Multiple-site studies: If the study involves subject enrollment at multiple sites, describe plans for ensuring appropriate IRB review and approval at each site.
- L. Human subjects protection plan should include at least:
 - 1. The responsibilities of investigators.

2. The names of investigators who will obtain informed consent. Those designated must be identified in the protocol as well as in the Intramural Initial Clinical Protocol Application and approved by the IRB.
3. Rationale for subject selection based on a review of gender/ethnic/race categories at risk for the disease/condition being studied.
4. Recruitment plan, including recruitment materials, advertisements, etc.
5. Rationale for involvement of vulnerable populations.
6. When discussing the research involvement of vulnerable subjects, include the appropriate requirements of:
 - a. SOP 14A, "Research Involving Vulnerable Subjects (General Considerations)"
 - b. SOP 14B, "Research Involving Pregnant Women, Human Fetuses and Neonates"
 - c. SOP 14C, "Research Involving Prisoners"
 - d. SOP 14D, "Research Involving Children"
 - e. SOP 14E, "Research Involving Adults Who Are or May be Unable to Consent"
 - f. SOP 14F, "Research Involving NIH Employees as Subjects"
7. Justification for exclusion of vulnerable populations
8. Evaluation of Risks/Discomforts and Benefits ratio: Discuss why the risks to subjects are reasonable in relation to the anticipated benefits and in relation to the importance of the knowledge that may reasonably be expected to result.
 - a. Describe the potential benefits to subjects or to others that may reasonably be expected from the research.
 - b. Describe any potential risks -- physical, psychological, social, legal, or other -- and assess their likelihood and seriousness.

- c. Where appropriate, describe alternative treatments and procedures that might be advantageous to the subjects.
 - d. Describe the procedures for protecting against or minimizing any potential risks, such as violations of confidentiality, and assess their likely effectiveness.
 - e. Where appropriate, discuss provisions for ensuring that necessary medical or professional intervention is available in the case of adverse events to the subjects.
- L. Protection of Participants' Privacy and Confidentiality: Describe how privacy and confidentiality will be protected. See SOP 18, "Privacy and Confidentiality."
- M. Study Agents/Interventions: Describe the research drugs/devices or interventions to be used.
- N. Plan for reporting unanticipated problems and adverse events: This must be consistent with the requirements of SOP 16, "Reporting Requirements for Unanticipated Problems, Adverse Events and Protocol Deviations."
- O. Data Safety and Monitoring Plan: This must be consistent with the requirements of SOP 17, "Data and Safety Monitoring."
- P. Clinical Monitoring Plan (if applicable): This must be consistent with the requirements of SOP 23, "Quality Management System for the NIH HRPP."
- Q. Data/Records Management: Describe how the research data will be managed and the safeguards in place to ensure confidentiality; see SOP 11A "Study Closure" and SOP 18 "Privacy and Confidentiality" for more information about records management.
- R. Compensation: Describe the rationale for and amount of any proposed compensation consistent with SOP 13, "Recruitment, Selection and Compensation of Research Subjects."
- S. Scientific references

T. Appendices (if applicable)

8.5 INITIAL IRB REVIEW OF PROTOCOLS

- A. The IRB will conduct its initial review consistent with the requirements in SOP 7 “Requirements for the Ethical and Regulatory Review of Research by NIH Institutional Review Boards”, SOP 7A “Requirements for Expedited Review of Research by NIH Institutional Review Boards” and SOP 7B, “Requirements for the Conduct of Research Review at a Convened NIH Institutional Review Board (IRB) Meeting.”
- B. IRB minutes and records related to its initial review will be consistent with the requirements of SOP 4, “HRPP Documentation and Records.”

8.6 OFFICE OF PROTOCOL SERVICES (OPS) ACTIONS ON INITIAL REVIEW PACKAGES

8.6.1 SUBMISSION TO AND PROCESSING BY OPS OF IRB-APPROVED PROTOCOLS

When IRB approval is complete, the protocol package is sent to OPS electronically.

- A. OPS staff will review the IRB-approved protocol and identify missing or incomplete information. Depending on the extent of the information that needs to be resolved, the action may be returned to the IRB administrative staff for resolution.
- B. Required data are extracted from the IRB-approved protocol and stored in the NIH Intramural Research Program data repository.
- C. The completed package is forwarded to the Director, Clinical Center (CC) for Patient Safety/Resource review and signature when research is conducted at the NIH Clinical Center, or the Director, Office of Human Subjects Research Protections (OHSRP) when the research is not conducted at the NIH Clinical Center.

- D. Upon receipt of the signed protocol from the Director, CC, or from the Deputy Director Intramural Clinical Research (DDICR), a protocol number is assigned, and for research conducted at the NIH CC, consent documents are posted to the intranet, and data elements are further transmitted as necessary (i.e., to the CC Clinical Research Information System (CRIS) and Clinicaltrials.gov).

- E. OPS provides the PI and IRB a copy of the protocol signed by the Director, CC, or from the Director, OHSRP and the consent/assent document(s), which includes the CC watermark for studies conducted at the CC.

8.7 WHEN RESEARCH MAY BEGIN

Research may begin after completion of all steps in 8.6.1, above.

LIST OF ATTACHMENTS

Attachment 1: National Institutes of Health Intramural Initial Clinical Protocol Application.

Attachment 2: Supplements A through Q of the NIH Intramural Initial Clinical Protocol Application.