

Implementation Approval

HRPP STANDARD OPERATING PROCEDURE/POLICY APPROVAL &
IMPLEMENTATION

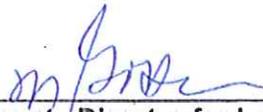
OFFICE OF HUMAN SUBJECTS RESEARCH PROTECTIONS

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

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SOP 19 INVESTIGATOR RESPONSIBILITIES

TABLE OF CONTENTS

19.1 PURPOSE	1
19.2 POLICY	1
19.3 DEFINITIONS, QUALIFICATIONS AND RESPONSIBILITIES OF INVESTIGATORS.....	1
19.3.1 INVESTIGATOR	1
19.3.2 PRINCIPAL INVESTIGATOR (PI)	2
19.3.3. ADJUNCT PRINCIPAL INVESTIGATOR	3
19.3.4. MEDICALLY ADVISORY INVESTIGATOR (MAI)	3
19.3.5 LEAD ASSOCIATE INVESTIGATOR (LAI).....	3
19.3.6. ASSOCIATE INVESTIGATORS (AI).....	3
19.3.7 ACCOUNTABLE INVESTIGATOR	4
19.3.8 RESEARCH CONTACT (RC)	4
19.4 GENERAL RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR (PI).....	4
19.5 SPECIFIC RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR (PI)	5
19.5.1 SUPERVISING THE CONDUCT OF THE RESEARCH PROTOCOL/STUDY	7
19.5.2 ADEQUATE RESOURCES TO CONDUCT THE RESEARCH.....	8
19.5.3 RESEARCH RECORDS MANAGEMENT	8
19.5.4 PROTOCOL COMPLIANCE	9
19.5.5 ADMINISTRATIVE HOLD, SUSPENSIONS AND TERMINATIONS	9
REFERENCES	1

SOP 19 INVESTIGATOR RESPONSIBILITIES

19.1 PURPOSE

This policy describes the roles and responsibilities of investigators, particularly Principal Investigators (PIs), in the conduct and supervision of research protocols involving human subjects. Additional requirements for PIs conducting research regulated by the Food and Drug Administration (FDA) are provided in SOP 15 “Research Regulated by the FDA: General Procedures for Both IND and IDE Applications”.

19.2 POLICY

It is the policy of the NIH Human Research Protection Program (HRPP) that each protocol approved by an NIH Institutional Review Board (IRB) has a single Principal Investigator (PI) who is responsible for its design and conduct. Upon IRB approval, the PI may delegate specific aspects of the conduct of the research to other members of the research team but he/she retains overall responsibility.

19.3 DEFINITIONS, QUALIFICATIONS AND RESPONSIBILITIES OF INVESTIGATORS

19.3.1 Investigator

The Department of Health and Human Service’s Office of Human Research Protections (OHRP) considers an “investigator” to be any individual who is involved in conducting human subjects research studies. Such involvement includes: (1) obtaining information about living individuals by intervening or interacting with them for research purposes; (2) obtaining identifiable private information about living individuals for research purposes; (3) obtaining voluntary informed consent of individuals to be subjects in research, and (4) studying, interpreting, or analyzing identifiable private information or data for research purposes. See Policy & Guidance for Investigators*, see SOP15, “Research Regulated by the Food and Drug Administration (FDA): General Procedures for Both IND and IDE Applications”, for the FDA’s definition of an investigator.

19.3.2 Principal Investigator (PI)

All investigators engaged in human subjects research are responsible for the ethical treatment of the participants.

The Principal Investigator is responsible for assuring that all investigators are qualified by education, training, and experience needed to perform their delegated roles in conduct of the study (see **19.5.1**).

The PI is responsible overall for the design and conduct of the IRB-approved research protocol. There can be only one PI for each protocol (see Responsibilities of the PI, **19.4** and **19.5**).

At the NIH, consultants or students may not be PIs. The following requirements determine who may be a PI:

- A. NIH employees including PHS commissioned officers assigned to the NIH:** To be a PI, an NIH employee will have appropriate credentialing. At the NIH Clinical Research Center (CC) a PI will be a member of the senior or junior medical, research or adjunct staff. When the PI is not a member of the senior or junior medical staff, or when an IRB, IC Clinical Director, or the Director, CC consider it warranted, a Medically Advisory Investigator must be identified in the protocol and approved by the IRB (see **19.3.4**).

- B. Non-NIH Federal employees:** Non-NIH Federal employees may serve as PIs on an NIH protocol on a case-by-case basis with the following conditions:
 1. The Deputy Director for Intramural Research (DDIR) must approve in writing a request for a non-NIH Federal employee to serve as a PI. The DDIR's approval is submitted with the protocol to the appropriate NIH IRB for review and approval.

 2. There must be an official letter in the IRB office's protocol file (and a copy kept by the PI) from the individual's employing agency stating that the activities at the NIH are a part of his/her official duties.

 3. The protocol must list an NIH Accountable Investigator (see **19.3.7**).

4. Applicable medical staff credentialing requirements for the research site will be met.
5. The DDIR may make exceptions in writing to the above conditions.

C. Non-NIH, non-Federal employees: Extramural researchers (e.g., in academia, practicing at a community hospital) may serve as Adjunct Principal Investigators on a protocol where the PI is an NIH employee.

19.3.3. Adjunct Principal Investigator

An Adjunct Principal Investigator is an individual serving as the Principal investigator who is not an NIH employee. If the protocol has an Adjunct Principal Investigator, there must be a named NIH Principal Investigator who is an employee and who will be responsible for the conduct and conflicts analysis of the protocol. The relationship between the Adjunct PI and the NIH PI will allow for the conduct of collaborative protocols.

19.3.4. Medically Advisory Investigator (MAI)

An MAI must be identified when the PI is not a member of the junior or senior medical staff, or when the Clinical Director, IRB, or Director, CC consider it warranted. The MAI must be an appropriately qualified member of the medical staff at the research site and is responsible for assisting the Principal Investigator in the development of clinical aspects of the protocol and for providing direct medical care to protocol participants. There is only one MAI per protocol.

19.3.5 Lead Associate Investigator (LAI)

An individual who plays a leading role in the formulation, writing, and implementation of a clinical research protocol under the mentorship of the protocol's PI. A LAI may be a physician, a dentist, a PhD, an RN, a member of the allied health professions or a trainee. There is only one LAI per protocol.

19.3.6. Associate Investigators (AI)

Individuals, other than the PI, who make substantial contributions to the conception, design of the study, and execution of the study including, but not limited to, obtaining informed consent from protocol participants, the acquisition of data, or to the analysis and interpretation of data. There may be several AIs on a protocol. Contractors, NIH trainees, students and non-NIH collaborators may serve as AIs.

19.3.7 Accountable Investigator

Accountable Investigators are tenured, tenure-track investigators, or senior clinicians who are responsible and accountable for the expenditure of resources for clinical research protocols.

19.3.8 Research Contact (RC)

The person(s) to whom potential research subjects may be referred for participation in a particular research protocol

19.4 GENERAL RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR (PI)

The PI is responsible for designing and personally conducting, or properly supervising the conduct of the IRB-approved protocol. The PI is also responsible for protecting the rights, safety, and welfare of the research participants. The PI ensures that the research is conducted in an ethical manner consistent with:

- A. The Belmont Report
- B. Relevant federal regulations (45 CFR 46 and 21 CFR 50 and 56)
- C. Guideline for Good Clinical Practice (GCP) as applicable
- D. The Standard Operating Procedures (SOPs) of the NIH Human Research Protection Program (HRPP)
- E. The Standards for Clinical Research Within the NIH Intramural Research Program; and

- F. Other NIH IRB requirements, as appropriate such as those of the: Radiation Safety Committee, the Recombinant DNA Advisory Committee (RAC), and the NIH Biosafety Committee.

19.5 SPECIFIC RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR (PI)

The PI ensures that:

- A. Research involving human subjects begins only after NIH IRB review and approval or, when appropriate, after the NIH Office of Human Subjects Research Protections (OHSRP) grants a written exemption. See SOP 6, “Exemptions and Not Human Subjects Research (NHSR) Determinations Made by the Office of Human Subjects Research Protections (OHSRP) under 45 CFR 46.”
- B. Guidance has been sought from the IRB and/or OHSRP if it is unclear whether or not the research involves human subjects. See SOP 5, “NIH Research Activities with Human Specimens and Data.”
- C. The research is conducted in accordance with the NIH IRB-approved protocol, including the approved recruitment and consent procedures.
- D. The contents of protocols and supporting documents submitted for initial review, continuing review, and amendments meet NIH criteria as provided in SOPs 7A, “Requirements for Expedited Review of Research by NIH IRBs”; SOP 8, “Procedures & Required Documentation for Initial Review of Protocols by a Convened NIH IRB”; SOP 9, “Continuing Review by the Convened IRB” and SOP 10, “Amendments to IRB-Approved Research.”
- E. The NIH IRB Review Standards will be used in his/her oral presentation of the protocol to the IRB as required by the NIH HRPP SOPs. See References for the link to the NIH IRB Review Standards.
- F. When informed consent is required, it is obtained and documented before research participation begins as delineated by the IRB-approved protocol (see SOP 12, “Requirements for Informed Consent from Research Subjects”).
- G. When drugs, biological products, and devices are being investigated or used, they are managed as required by NIH/CC policy, including MAS 80-3(rev), and, when applicable, FDA regulations 21 CFR 312 and 21 CFR

- 812 (see SOP 15 “Research Regulated by the FDA: General Procedures for Both IND and IDE Applications”) or other regulations.
- H. Changes to NIH IRB-approved protocols and/or consent documents are not initiated without prospective IRB approval unless necessary to eliminate apparent immediate hazards to the subject (see SOP 16, “Reporting Requirements for Unanticipated Problems, Adverse Events, Protocol Violations and Protocol Deviations”).
 - I. Unanticipated problems involving risks to subjects or others (including adverse events and protocol violations) are reported to the IRB in accordance with requirements set forth in SOP 16 “Reporting Requirements for Unanticipated Problems, Adverse Events, Protocol Violations and Protocol Deviations” and SOP 16A “Allegations and Incidents of Non-compliance.”
 - J. When applicable, Data and Safety Monitoring Board/Data Monitoring Committee or other monitoring individual or group reports are submitted promptly to the IRB for review (see SOP 17, “Data and Safety Monitoring”).
 - K. The continuing review submission to the IRB should be submitted with sufficient time to allow for IRB review and approval and provide an opportunity for response by the Principal Investigator to any stipulations of the IRB (see SOP 9 “Continuing Review by the Convened IRB”).
 - L. When the research protocol ends, a final report is submitted to the appropriate NIH IRB (see SOP 11, “Suspensions and Terminations of IRB Approved Research and Administrative Holds”).
 - M. Adequate and accurate research records are kept and retained as required by this SOP (see **19.5.3**) and other applicable policies.
 - N. Upon request for monitoring and oversight of the research, research records are made available to OHSRP, the IC Quality Improvement Program, and when applicable, the DSMB, the sponsor, the DHHS Office for Human Research Protections (OHRP), and the Food and Drug Administration (FDA) (see SOP 23, Quality Management System for the HRPP”).
 - O. Documents are completed properly, submitted, and approved consistent

with NIH Conflict of Interest policy (see SOP 21, “Conflict of Interest Requirements for Researchers and Research Staff, Appendix A: A Guide to Avoiding Financial and Non-financial Conflicts or Perceived Conflicts of Interest in Clinical Research as NIH”.)

19.5.1 Supervising the Conduct of the Research Protocol/Study

- A. The PI is responsible for the design and conduct of the IRB-approved research protocol. S/he may delegate study-related tasks but must properly supervise investigators and other study personnel to whom tasks are assigned.

- B. The intensity of the PI’s supervision will take into account the research study personnel, the nature of the research, and the subject population. When supervising the conduct of the research, the PI ensures that study personnel:
 - 1. Are qualified by training and experience, and credentialed if necessary, to perform study-related tasks that have been assigned to them.
 - 2. Are aware of regulatory and policy requirements and standards for the conduct of human subjects research.
 - 3. Have a complete understanding of the details of the protocol relevant to the tasks they will be performing.
 - 4. Follow the IRB-approved protocol.
 - 5. Are informed of any pertinent changes to the protocol during the conduct of the study and are educated or given additional training, as appropriate.

- C. IRB approval may be required for protocol-related activity delegations. For example, the IRB approved protocol must identify who, in addition to or instead of the PI, will obtain informed consent from subjects. These delegated persons or categories of persons must fulfill requirements in 19.5.1.B or as provided in the IRB-approved protocol.

- D. The PI ensures that research personnel certify completion of all NIH training requirements consistent with SOP 25 “Training Requirements for the NIH HRPP.”

19.5.2 Adequate Resources to Conduct the Research

The PI will conduct the research only when adequate resources to protect research subjects exist. These resources may include:

- A. Access to population(s) that allow recruitment and enrollment of subjects consistent with the IRB-approved protocol.
- B. Sufficient time to be devoted by the PI and other research staff to conduct and complete the research.
- C. Adequate numbers of qualified and trained staff.
- D. Adequate budget, facilities, and space.
- E. Access to medical or psychological care for problems that may arise during subjects’ participation in research.

19.5.3 Research Records Management

- A. General considerations: “*The NIH Standards for Clinical Research in the NIH Intramural Research Program*”^{*} specify that each Institute sponsoring clinical research should develop a central clinical investigations database that maintains all data specified to be collected in the clinical study (either intervention or natural history). The Institutes require data-management infrastructures to maintain their central data registries; to enhance existing databases; to provide eligibility checklists; to record patient randomization and entry into protocols; to provide report generation, data warehousing, and data entry forms; and, to monitor data collection.
- B. PI responsibilities include but are not limited to:
 - 1. Ensuring the accuracy, completeness, legibility, and timeliness of the data.
 - 2. Following internal procedures for the appropriate documentation of research related tests and procedures.

3. Maintaining the confidentiality of data at all times

- C. FDA-regulated research: Data collection, record-keeping and record retention will be consistent with the Guideline for Good Clinical Practice (GCP) and requirements set forth in SOP 15 “Research Regulated by the Food and Drug Administration (FDA): General Procedures for Both IND and IDE Applications.”
- D. Retention of research records: Records retention will be consistent with NIH Manual Chapter 1743, Keeping and Destroying Records, and other applicable policies*

19.5.4 Protocol Compliance

- A. General considerations: Routine monitoring of the conduct of research protocols is a requirement of the NIH HRPP. This includes monitoring by the PI and the research team and through the Institute or Center’s (IC) quality assurance/quality improvement (QA/QI) plan. Also, there may be “not-for-cause” and “for cause” audits (by the NIH, FDA, OHRP, sponsor, etc...).
- B. PI cooperation with the IC QA/QI plan and NIH or other monitoring and compliance activities: The PI is responsible for ensuring the cooperation of all research personnel with monitoring and audit activities. This includes, but is not limited to, preparing for routine monitoring or other required audits and being available as needed, (see SOP 23, “Quality Management System for the HRPP”).
- C. FDA regulated research: IC, PI and research staff compliance activities for these protocols will be consistent with the requirements set forth in SOP 15 “Research Regulated by the Food and Drug Administration: General Procedures for Both IND and IDE Applications.”

19.5.5 Administrative Hold, Suspensions and Terminations

- A. Administrative hold: A Principal Investigator may request an administrative hold on a study when he/she wishes temporarily to stop or as a preliminary step before permanently stopping some or all approved research activities. An administrative hold may be in response to a directive from a sponsor or the FDA or other review body. Administrative

holds are not suspensions or terminations. Studies on administrative hold require continuing review by the IRB prior to the expiration date. The procedures for initiating administrative holds, suspensions, and terminations are found in SOP 11, "Suspensions and Terminations of IRB Approved Research and Administrative Holds."

- B. Suspensions or terminations by study sponsors: The PI promptly reports any study that is suspended or terminated prematurely (by the sponsor, etc.) for any reason to the IRB and appropriate institutional officials (see SOP 11).

REFERENCES

Policy & Guidance for Investigators: <http://www.hhs.gov/ohrp/>

The Belmont Report:

<http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html>

Guideline for Good Clinical Practice (GCP) as applicable

(<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073122.pdf>).

The Standards for Clinical Research Within NIH Intramural Research:

(http://clinicalcenter.nih.gov/ccc/patientcare/pdf/cc_research_standards.pdf)

NIH IRB Review Standards:

<http://citfm.cit.nih.gov/ohrdocs/Protocol%20Review%20Standards%20v%209-2011.pdf>

The NIH Standards for Clinical Research in the NIH Intramural Research Program:

http://clinicalcenter.nih.gov/ccc/patientcare/pdf/cc_research_standards.pdf

NIH Manual Chapter 1743, Keeping and Destroying Records, and other

applicable policies: <http://oma.od.nih.gov/manualchapters/management/1743/>