

Implementation Approval

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

OFFICE OF HUMAN SUBJECTS RESEARCH PROTECTIONS

SOP Number: 1

SOP Title: HUMAN SUBJECTS RESEARCH AND THE NIH IRB SYSTEM

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

Approval:



Deputy Director for Intramural
Research

1/15/13
Date

Date of Implementation: 1-19-2013

SUMMARY OF SOP # 1 – HUMAN SUBJECTS RESEARCH AND THE NIH IRB SYSTEM

A. Summary

1. Applicability of DHHS and FDA regulations to NIH research and HRPP SOPs
2. Regulatory definitions of “Research”, “Human Subject”, “Intervention”, “Interaction” and “Private Information”
3. Explanation of when NIH employees are engaged in human subjects research (HSR)
4. List of NIH Institutional Review Boards (IRBs) and registration numbers
5. IRBs’ jurisdiction and authorities
6. Scientific Directors’ (SDs) and Clinical Directors’ (CDs) administrative responsibility for the IRBs, including nominating IRB members and provision of resources for pre-IRB scientific review (see SOP 7) and data and safety monitoring (see SOP 17)
7. Requirements for IRB review of protocols where Principal Investigator is an Institute or Center (IC) Director, SD or CD (see SOP 21)
8. NIH IRBs’ interactions with other committees involved in safety and monitoring: NIH Radiation Safety Committee (RSC); the Radioactive Drug Research Committee (RDRC), the Office of Biological Activities (OBA) and the Recombinant DNA Advisory Committee; the Institutional Biosafety Committee (IBC).

B. Change from previous material

There was no previous SOP or information sheet that provided an overview of Human Subjects Research (HSR) and a description of the NIH IRB system. Old SOP 1, Section A provided a one-paragraph statement of the purpose of an IRB. Old SOP 4, Section A referenced Federal regulations (one paragraph) and old SOP 4, Section B described the applicability of Maryland State law (one paragraph).

C. Material Superseded

1. Old SOP Chapter 1 – Preamble
2. Old SOP Chapter 4 – The Authorities of the IRB

SOP 1. HUMAN SUBJECTS RESEARCH AND THE NIH IRB SYSTEM

TABLE OF CONTENTS

1.1 PURPOSE..... 2

1.2 POLICY..... 2

1.3 INTRODUCTION..... 2

1.4 DEFINITIONS..... 2

1.5 DETERMINATIONS REGARDING ENGAGEMENT IN HUMAN SUBJECTS

RESEARCH BY NIH..... 3

1.6 REQUIREMENT FOR REVIEW BY NIH’s IRBS..... 3

1.7. DESCRIPTION OF THE NIH IRBs 4

1.8. JURISDICTION OF EACH IRB..... 5

1.9. AUTHORITY OF THE IRBs 6

1.10 FREQUENCY OF MEETINGS 6

1.11 ADMINISTRATIVE RESPONSIBILITY FOR NIH IRBs 6

1.12 REVIEW OF IRBs’ PERFORMANCE 7

1.13 INDEPENDENCE OF THE IRBs..... 7

1.14. NIH IRBs’ INTERACTIONS WITH OTHER NIH COMMITTEES INVOLVED IN

SAFETY AND MONITORING 8

APPENDIX 1: LIST OF NIH COMPONENTS NOT ASSIGNED TO A SPECIFIC IRB 10

APPENDIX 2: REFERENCES 11

SOP 1. HUMAN SUBJECTS RESEARCH AND THE NIH IRB SYSTEM

1.1 PURPOSE

This Standard Operating Procedure (SOP) provides an overview of human subjects research and a description of the NIH IRB system.

1.2 POLICY

NIH Institutional Review Boards (IRBs) will review research involving human subjects in accordance with Department of Human Health Services (DHHS) regulations at 45 CFR 46 and the relevant NIH Standard Operating Procedures (SOPs). This policy applies only to human subjects research that is reviewed by IRBs, and does not apply to research exempt from IRB review (see SOP 6 – “Exemptions and Not Human Subjects Research (NHSR) Made by the Office of Human Subjects Research Protections (OHSRP) under 45 CFR 46”).

1.3 INTRODUCTION

DHHS regulations apply to all research at NIH and to all NIH SOPs. In certain situations, where applicable, the Food and Drug Administration (FDA) regulations at 21 CFR 50, 56, 312 and 812 also apply. See SOP 15 “Research Regulated by the Food and Drug Administration.”

1.4 DEFINITIONS

- A. Research** means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge (45 CFR 46.102(d)).
- B. Human subject** means a living individual about whom an investigator (whether professional or student) conducting research obtains
 1. Data through **intervention** or **interaction** with the individual.
 2. Identifiable **private information**.
- C. Intervention** includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject’s environment that are performed for research purposes.
- D. Interaction** includes communication or interpersonal contact between investigator and subject.

- E. Private information** includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects. (45 CFR.102 (f) (1) (2))

1.5 DETERMINATIONS REGARDING ENGAGEMENT IN HUMAN SUBJECTS RESEARCH BY NIH

The NIH is engaged in human subjects research projects when its employees or agents for the purposes of the research project obtain: (1) data about the subjects of the research through intervention or interaction with them; (2) identifiable private information about the subjects of the research; or (3) the informed consent of human subjects for the research.”

Engagement of NIH employees or agents in human subjects research may also occur during cooperative or collaborative research. See SOP 20, “NIH HRPP Requirements for Collaborative Research” and OHRP “Guidance on Engagement of Institutions in Human Subjects Research”*

“Agents” of the NIH, for purposes of this SOP, means members of the NIH workforce who act on behalf of the institution or perform institutionally-designated activities. Employees and agents include professional staff, students/fellows, contractors, and volunteers, among others, regardless of whether the individual is being paid by NIH.

1.6 REQUIREMENT FOR REVIEW BY NIH’S IRBS

Except as otherwise provided in these SOPs, when NIH investigators become engaged in human subjects research, such research must be reviewed, prospectively approved, and subject to continuing review by an NIH IRB. Officials at the NIH may not approve the conduct of research unless it receives IRB approval or is viewed as exempt by OHSRP. The most common exceptions to the requirement for such NIH IRB review will be:

- A.** Studies that meet the requirements for an exemption under 45 CFR 46.101(b) (see SOP 6, “Exemptions and Not Human Subjects Research (NHSR) Determinations Made by the OHSR under 45 CFR 46”); and,

* See Appendix 2: References, page 9

- B.** Studies that would otherwise require review by an NIH IRB, but for which NIH enters into a reliance agreement to rely on IRB review by a non-NIH IRB (see SOP 20, “NIH HRP Requirements for Collaborative Research”).

1.7. DESCRIPTION OF THE NIH IRBs

The NIH IRB system is composed of 12 active IRBs with discrete missions and research portfolios. Except as otherwise stated in these SOPs, each of the NIH IRBs will follow the requirements of the NIH Federalwide Assurance (FWA) and of these SOPs. The NIH IRBs are:

Name	Primary Institute(s) Assigned	IRB Registration
National Cancer Institute	NCI	IRB 00000001
National Cancer Institute Special Studies	NCI	IRB 00000002
National Heart, Lung and Blood Institute	NHLBI	IRB 00000004
National Institute of Allergy and Infectious Diseases	NIAID	IRB 00000005
National Institute of Digestive and Kidney Diseases & National Institute of Arthritis and Musculoskeletal Diseases	NIDDK/NIAMS	IRB 00000006
Combined Neurosciences Purple Panel	NIDCR	IRB 00000007
National Institute of Child Health and Human Development	NICHHD	IRB 00000008
Addictions IRB	NIDA, NIAAA	IRB 00000012
National Institute of Environmental Health Sciences	NIEHS	IRB 00000013
National Human Genome Research Institute	NHGRI	IRB 00000014
Combined Neurosciences Blue Panel	NEI, NINDS, NIDCD, NINR	IRB 00000016
Combined Neurosciences White Panel	NIMH	IRB 00000017

Unless otherwise stated in these SOPs, the use of the term IRB refers to any of these twelve IRBs.

1.8. JURISDICTION OF EACH IRB

Institutes with designated IRBs (single-Institute IRBs- see **1.12**, below) generally review protocols from their own investigators. There are, however, exceptions to this rule, as follows:

A. PIs from other Institutes

When the Principal Investigator of a research protocol is an employee of an NIH IC that is not assigned to an IRB in **1.7**, above, (see Appendix 1: List of NIH Components Not Assigned to an IRB), that protocol will be reviewed by the IRB whose expertise is most closely related to the protocol's research topic. The Principal Investigator initially contacts the administrative staff of the IRB that appears most appropriate. The appropriateness of that protocol for review is determined by the IRB's Chair. A research study submitted to one NIH IRB for review may not be submitted to a different NIH IRB either at the same time or subsequently, unless to avoid a conflict of interest of the institute leadership (see **1.9.C** below).

B. PI transfers to another Institute

If a PI transfers to another Institute, the appropriateness of transferring the study to another IRB will be evaluated. In the event that there is any uncertainty or dispute regarding which IRB should review a protocol, the Deputy Director for Intramural Research (DDIR) will make the final determination, or delegate that authority to OHSRP.

C. IC Directors, Scientific Directors, and Clinical Directors

1. The NIH *Guide to Avoiding Financial and Non-Financial Conflicts or Perceived Conflicts of Interest in Human Subjects Research* (see SOP 21, "Managing Conflict of Interest in Research", Appendix A) states that Institute Directors and Institute Scientific Directors must have their protocols reviewed by an IRB not affiliated with their Institute.
2. IRBs have the prerogative to review the protocols of their Institute's Clinical Director (CD) or refer them to another Institute's IRB. IRBs reviewing protocols in which their CD is the PI must have a majority of members who are not employed by the CD's Institute, otherwise any alternative plan must have prior approval by the Director, CC and the Deputy Director for Intramural Research (DDIR).

D. Other Circumstances

Circumstances may justify having a protocol reviewed by an NIH IRB other than the one to which it would be assigned under the rules above. The DDIR has the authority to determine which IRB will have jurisdiction over such a protocol or may delegate the authority to OHSRP.

1.9. AUTHORITY OF THE IRBs

1.9.1. General Authorities

Each NIH IRB has the regulatory authority to:

- A. Approve, modify or disapprove research (45 CFR 46.109(a)).
- B. Suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. (45 CFR 46.113).
- C. Observe, or have a third party observe, the consent process (45 CFR 46.109(e)).
- D. The IRBs also have authorities associated with:
- E. The consent process (45 CFR 46.109(b)-(c), 45 CFR 46.116).
- F. Continuing review (45 CFR 46.109(e)).
- G. Applicable authorities per the FDA.

1.9.2. Exemptions

Neither NIH investigators nor NIH IRBs have the authority to determine whether a research protocol is exempt from the Federal regulations (45 CFR 46.101(b)) – i.e., is exempt from IRB review. This authority is delegated to OHSRP, as described in SOP 6, “Exemptions and Not Human Subjects Research (NHSR) Made by the OHSRP under 45 CFR 46.”

1.10 FREQUENCY OF MEETINGS

Each of the NIH IRBs has regularly scheduled meetings. If necessary, IRBs may convene special meetings.

1.11 ADMINISTRATIVE RESPONSIBILITY FOR NIH IRBs

- A. **Single Institute IRBs** The Scientific Director of the Institute has administrative responsibility for each of the IRBs assigned to a single Institute. Some of the responsibilities listed below may be delegated to the CD. Administrative responsibility includes:

1. Allocation of resources for the IRB, including budget, space, and staff.
2. In conjunction with the CD (or by delegation to the CD), nominating IRB Chairs, Vice-Chairs and members for the DDIR's approval and appointment.
3. Providing resources for Data and Safety Monitoring Boards (see SOP 17, "Data and Safety Monitoring").
4. Providing resources for pre-IRB Scientific Review Committees (see SOP 7, "Requirements for the Ethical and Regulatory Review of Research by NIH IRBs").
5. Ensuring the independence of the IRB, and upholding its decisions.

B. Multiple-Institute IRBs

1. As noted in **1.7**, above, several IRBs (currently the NIDDK/NIAMS IRB, the CNS White IRB, and the CNS Blue IRB) are designated as the primary IRB for more than one NIH Institute.
2. Each of these multiple-institute IRBs must provide OHSRP with a written policy, signed by all the Scientific Directors for the Institutes assigned to that IRB, describing which SD and/or CD will assume, for that IRB, the administrative responsibilities assigned to SDs described in **1.11.A** above.

1.12 REVIEW OF IRBs' PERFORMANCE

IRBs' performance is reviewed and evaluated as described in SOP 26 "Evaluation of NIH IRB Chairs, Vice Chairs and Members, IRB Activities and IRB Administrative Staff."

1.13 INDEPENDENCE OF THE IRBs

- A.** In exercising the authority provided to them under **1.9**, above, the NIH IRBs will at all times maintain their independence. The DDIR, who serves as the Institutional Official, will oversee the NIH Human Research Protection Program in a manner that assures that the IRBs can exercise their authority independently.
- B.** An IRB member who experiences undue influence should first report the occurrence to the Chair of that IRB, who will attempt to mediate or resolve the concern, in consultation with the applicable Clinical Director, the staff of the IRB or of OHSRP, or other NIH officials, as necessary or appropriate.

- C. An IRB Chair who experiences undue influence should first report the occurrence to OHSRP, which will attempt to mediate or resolve the concern, in consultation with the applicable Clinical Director, the DDIR or other NIH officials, as necessary or appropriate.
- D. Any individual who believes that undue influence is being exerted by an official in one of the above reporting chains, or who believes that the undue influence has not been appropriately resolved in a timely manner, should report to the next higher level in the reporting chain, and ultimately to the DDIR.

1.14. NIH IRBs' INTERACTIONS WITH OTHER NIH COMMITTEES INVOLVED IN SAFETY AND MONITORING

In addition to the NIH IRBs, there are several specialized NIH committees involved in ensuring the safety of IRP research subjects and NIH staff during the conduct of research protocols. If applicable, the following specialized NIH committee(s) will review protocols, regardless of location (i.e., NIH Clinical Center and NIH off-site locations):

- A. **The NIH Radiation Safety Committee (RSC)** is responsible to the Director, NIH for oversight of the NIH Radiation Safety Program to ensure the safe use of radioactive materials and all sources of ionizing radiation throughout NIH and those NIH-occupied buildings included in the NIH Radiation Safety Program. The RSC is responsible for formulating policy with regard to radiation protection matters in the intramural program that involve NIH employees and members of the general public, routine clinical and research programs, and protection of the environment to ensure compliance with Federal regulations, including those of the U.S. Nuclear Regulatory Commission.

PIs must obtain clearance from the RSC for protocols whose subjects may be exposed to radiation before the protocol can be approved (See SOP 7, "Requirements for the Ethical and Regulatory Review of Research by NIH IRBs").

- B. **The Radioactive Drug Research Committee (RDRC)** functions as a subcommittee of the RSC and is mandated by the FDA Regulations, 21 CFR Part 361.1, "Radioactive Drugs for Certain Research Uses," to review and approve the use of radioactive drugs for research purposes in humans for which an approved New Drug Application (NDA) or an approved Investigational New Drug Application (INDA) does not exist.
- C. **The Office of Biological Activities (OBA), and the Recombinant DNA Advisory Committee** OBA is responsible for oversight and policy development regarding scientific, safety, and ethical issues associated with basic and clinical recombinant NIH research. This role includes implementation of the *NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines)*, which articulate principles of containment and biosafety review for

this type of research. A key element of this system of oversight is the NIH Recombinant DNA Advisory Committee (RAC), which reviews human gene transfer protocols and makes recommendations to PIs and others on improving the science, safety and ethics of their trials. The RAC also advises the NIH on scientific, safety, and policy matters related to the use of recombinant DNA in research generally, including needed modifications of the *NIH Guidelines*. Most intramural trials involving human gene transfer need to be registered with OBA and reviewed by the RAC. Further, basic and clinical research involving recombinant DNA should be registered, and in many cases reviewed, by the NIH Institutional Biosafety Committee (IBC). More information on the RAC and IBC can be found at their website.*

D. The Institutional Biosafety Committee (IBC), Office of Research Services

This committee, created pursuant to the *NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines)**, reviews basic and clinical research involving recombinant DNA, including human gene transfer, to ensure that proper containment and biosafety practices are employed. When reviewing human gene transfer protocols, the IBC also oversees compliance with Appendix M of the *NIH Guidelines*, which details points to consider in the design of human gene transfer protocols and their submission to the NIH Office of Biotechnology Activities.

APPENDIX 1: LIST OF NIH COMPONENTS NOT ASSIGNED TO A SPECIFIC IRB

The National Institute on Aging

The National Institute of Biomedical Imaging and Bioengineering

The National Institute of General Medical Sciences

The National Library of Medicine

The NIH Clinical Center

The Center for Information Technology

The Center for Scientific Review

The John E. Fogarty International Center for Advanced Study in the Health Sciences

The National Center for Complementary and Alternative Medicine

The National Institute on Minority Health and Health Disparities

National Center for Advancing Translational Science

The NIH Office of the Director

APPENDIX 2: REFERENCES

OHRP “Guidance on Engagement of Institutions in Human Subjects Research”
<http://www.hhs.gov/ohrp/policy/engage08.html>.

RAC and IBC guidance: <http://oba.od.nih.gov/oba/>

NIH Guidelines for Research Involving Recombinant DNA Molecules
<http://oba.od.nih.gov/oba/>