

Implementation Approval

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

OFFICE OF HUMAN SUBJECTS RESEARCH PROTECTIONS

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SOP Title: IRB MEMBERSHIP AND STRUCTURE

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

Approval:



Deputy Director for Intramural
Research

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SOP 2. IRB MEMBERSHIP AND STRUCTURE

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SOP 2. IRB MEMBERSHIP AND STRUCTURE

2.1. PURPOSE

This SOP describes NIH Institutional Review Boards (IRBs) structure and membership requirements.

2.2. POLICY

The NIH Human Research Protection Program (HRPP) ensures that its IRBs are constituted consistent with federal regulatory requirements. It has procedures in place for (1) appointing and reappointing members; (2) maintaining current IRB rosters; (3) communicating members' responsibilities to them; (4) removing members for cause, and (5) clarifying their legal liability.

2.3. REQUIREMENTS FOR IRB MEMBERSHIP

2.3.1 Regulatory Requirements

Consistent with the requirements of 45 CFR 46.107 and 21 CFR 56.107, the IRB must:

- A. Be composed of at least five members with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution.
- B. Be sufficiently qualified through the experience and expertise of its members and the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.
- C. Have a membership not consisting entirely of men or entirely of women, so long as no member is chosen on the basis of gender.
- D. Have at least one member whose primary concerns are in scientific areas.
- E. Have at least one member whose primary concerns are in non-scientific areas.
- F. Have at least one member who is not otherwise affiliated with the NIH and who is not part of the immediate family of a person who is affiliated with the NIH, and

- G. If the IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, consideration shall be given to the inclusion of one or more members who have knowledge about and experience with these subjects.

One person may fulfill both the requirements of section E and those of section F.

2.3.2. IRB Member Area of Expertise and Affiliation

- A. In determining member expertise, affiliation and status as primary or alternate member, the following criteria apply:

1. **Affiliated member:** An NIH employee (or a member of that person's immediate family) is considered affiliated. Affiliated members also include, but are not limited to, individuals who are at or involved with NIH as: part-time employees; current students; trainees; members of any panel or board; paid or unpaid consultants; healthcare providers holding credentials to practice at the NIH; guest researchers; and volunteers.
2. **Unaffiliated member:** If an individual has no affiliation with the NIH, other than as an IRB member, then s/he is considered unaffiliated. Unaffiliated members may include people whose only association with the NIH is that of a research participant, or former student, trainee, contractor or employee. Paying unaffiliated members for their services would not make the member "otherwise affiliated", or cause the member to have a conflicting interest.

- a. **Note:** An IRB member will only be considered "unaffiliated" when he/she has properly completed and submitted to The NIH Office of Human Subjects Research Protections (OHSRP) a "Statement of Status as Unaffiliated Member of an NIH IRB" (see Attachment 1). OHSRP will confirm a member's unaffiliated status.

- B. **Members whose primary interests are in scientific areas:** A member whose highest level of education/training and/or occupation is from a scientific discipline or profession, e.g. the physical sciences, biomedical sciences, social/behavioral sciences, or mathematical sciences and who would be inclined to view scientific activities from these standpoints. The IRB must have members with sufficient knowledge of the specific scientific discipline(s) relevant to the research that it reviews.

1. **Member whose primary concerns are in non-scientific areas:** A member whose education, training, background, and occupation would incline him/her to view research activities from a standpoint other than any biomedical or behavioral scientific discipline should be considered a nonscientist.

2. Alternate members (see 2.3.4, below) are members who may substitute for a primary IRB member or a category of member (e.g., physician or nurse). Each alternate IRB member has experience, expertise, background, professional competence and knowledge comparable to that of the primary IRB member(s) whom the alternate would replace.
- C. OHSRP will make the final determination of whether nominated IRB members' primary concerns fall into scientific or non-scientific areas consistent with criteria provided in 2.3.1, above. This determination will be made at the time when members are nominated for appointment to the IRB through OHSRP review of the nominee's *curriculum vitae* (see 2.5, below).
 - D. Consistent with OHRP guidance, IRB members can only be appointed as either regular (primary) or alternate members. There is no category of non-voting member of the IRB.
 - E. It is the responsibility of the Director, OHSRP, in conjunction with the IRB Chair, to ensure that the IRB's overall composition meets regulatory and NIH requirements.
 - F. The IRB Chair shall at least annually notify OHSRP in writing whether the IRB regularly reviews research including any of the categories of vulnerable individuals mentioned in 2.3.1.G, above.

2.3.3 Additional NIH Membership Requirements

- A. Consistent with NIH Manual Chapter 3014, NIH has the following additional IRB membership requirements:
 1. A scientific or professional staff member not affiliated with the IRB's Institute.
 2. A member with expertise in statistics or an epidemiologist.
 3. A member who is either a pharmacist or pharmacologist, and
 4. An ethicist or individual who has expertise in the ethics of human subjects protection.
 - a. **Note:** For several of the intramural IRBs, a member of the senior staff of the Clinical Center Department of Clinical Bioethics participates as an ethics member. For other NIH IRBs, the Clinical Center Department of Clinical Bioethics has recommended, as possible members, individuals who have knowledge and experience with research ethics. An IRB may also independently nominate an ethicist for its committee.

5. Non–scientist members. DHHS regulations require that each IRB shall include at least one member whose primary concerns are in non-scientific areas. However, NIH strives to maintain a 20% ratio of non-scientist members on each IRB.
 6. At least one member of the IRB must represent the perspective of research participants.
 7. NIH IRB administrative staff may not be members of the IRB.
- B. Based on a written request and justification by the appropriate Institute Clinical Director(s), OHSRP can determine that an NIH IRB need not comply with some or all of the requirements set forth in 2.3.3.A.

2.3.4 Additional Requirements for Alternate Members

- A. Appointment process: The appointment process is the same as for primary members of the IRB (see 2.5, below). Alternates' names are included in the IRB's official membership roster with the designation that they are alternates together with the name(s) of the IRB member or members for whom they are an alternate.
- B. Assignment of alternates: An alternate member may be assigned as a substitute for one or more named primary members or for a category of members. Alternates must have qualifications similar to those of the member(s) for whom they are allowed to be a substitute. Alternate members receive agenda packages for all IRB meetings and are encouraged to attend as many meetings as possible, even when not required to be present to act as an IRB member.
- C. Alternate members and the quorum: When an alternate member substitutes for a regular member, the alternate member's vote counts towards the quorum in the same way as the regular member's vote.
- D. Voting by alternate members:
 1. Alternate members vote on protocols or other matters at convened meetings only when one of the primary members for whom they are an alternate is not participating in the vote (e.g., because that member is absent or has a conflict of interest). They should only participate when they have, prior to the meeting, adequately reviewed the materials distributed with regard to the protocol or other matters on which they would be voting. The IRB minutes should document the alternate member's votes.

2. A designated alternate IRB member may substitute for the primary IRB member for an entire meeting or at any time during a meeting. Substitution during a meeting commonly occurs when the primary member is (a) absent from the room for part of the meeting, or (b) recused from review of certain research protocols because the primary IRB member has a conflicting interest with respect to a specific research protocol. Whenever this occurs, the minutes of the IRB meeting should indicate clearly that the alternate IRB member has replaced the designated primary IRB member.

2.4 ROSTERS OF IRB MEMBERS

2.4.1 Maintenance of Roster

Each NIH IRB must maintain a current roster of its membership including the following information, preferably in the Excel template used by OHSRP:

- A. First and Last Name
- B. Earned Degrees
- C. Phone Number
- D. E-mail Address
- E. Term Start Date
- F. Term End Date
- G. Scientific Status (scientist or non-scientist; see 2.3, above)
- H. Affiliation Status
- I. Area of Specialty
- J. Narrative Description of Area of Expertise (e.g. brief description of all relevant experiences that describe each member's expected contributions to the IRB)
- K. IRB Office (e.g. Chair, Vice-chair)
- L. Membership Status (e.g., primary member or alternate member)
- M. Alternate Member(s) and for whom the alternate(s) can substitute (e.g. alternate for pharmacist member, etc.)

- N. Representative Capacity (indicate which, if any, vulnerable populations are being represented by this member, e.g. children, pregnant women, or prisoners, etc.; or if the member represents the perspectives of research participants)

2.4.2 Reporting Membership Changes to OHSRP

IRB administrative staff will report changes in the IRB roster as they occur and will provide OHSRP an up-to-date roster and contact information in electronic form annually, preferably in the Excel template used by OHSRP, including confirmation of the status of unaffiliated members. See Attachment 2, IRB Roster Template.

2.5 APPOINTMENT AND REAPPOINTMENT PROCEDURES AND TERMS OF SERVICE

2.5.1 Procedures for Initial Appointment to the IRB

- A. Identifying members: The Institute Clinical Director or Clinical Directors (in the case of multi-Institute IRBs), the IRB Chair, and, at the discretion of each IC, the Scientific Director, recommend the appointment of the IRB Chair, the IRB Vice Chair and IRB members (including alternate members). In making such recommendations, consideration will be given to the requirements above for IRB membership and representation.
1. Nominees and their supervisors should agree to the nomination.
 2. The Director, Scientific Director and Clinical Director of the Institute and other Institutes may not serve as a member, IRB Chair or Vice Chair of any NIH IRB.
- B. Nomination memorandum: Recommendations are made by a memorandum from the Clinical Director(s) to the Deputy Director for Intramural Research (DDIR) through the Office of Human Subjects Research Protections (OHSRP), and, at the discretion of the IC, through the Scientific Director. The memorandum describes how the qualifications of the nominee will serve the IRB. It specifies an appointment term and includes as an attachment curriculum *vitae* for the person being nominated. Appointment terms are specified in 2.5.E. below. In addition, if the member is being appointed as a person who is not affiliated with the NIH (see 2.3.2.A., above), the memorandum should be accompanied by a copy of the “Statement of Status as Unaffiliated Member of an NIH IRB” (see Attachment 1), signed by the nominee.
- C. Specific considerations for nomination of Chair and Vice Chairs: Nominees for IRB Chair and Vice Chair should have experience in human subjects research, which could include previous experience

serving on an IRB; be knowledgeable about the scientific mission and clinical program of the particular Institute or Institutes for which the IRB serves as the primary IRB, and be familiar with the federal regulations for the protection of human subjects (45 CFR 46 and 21 CFR 50 and 56) and the ethical basis for the regulations (The Belmont Report).

- D. Completion of required training: Before beginning service as a member of the IRB, all nominees, including those for Chair and Vice Chair, must complete the training requirements that are specified in SOP 25, "Training Requirements for the NIH HRPP."
- E. Appointment letters: After completion of required training, the DDIR, acting through OHSRP, sends a letter to the approved nominees appointing them to the Institute's IRB for an initial one-, two-, or three-year term (see Attachment 3). Appointment letters are copied to the Clinical Director, IRB Chair, and the IRB administrative office. This letter should be in the personnel file of NIH and other Federal employees whose IRB service is part of their official duty (see 2.10.2., below)
 - 1. **Note:** Nominees do not become a member of the IRB until they have received an appointment letter from the DDIR, although, at the discretion of the Chair, they may participate in IRB meetings prior to that time as consultants, consistent with the rules relating to such participation as a consultant (see 2.11).

2.5.2 Reappointment Procedures

- A. IRB administrative staff is responsible for allowing enough time in advance of members' term end dates for the submission and processing of reappointment requests or the appointment of new members.
- B. Reappointment letters: Reappointment requests are made by memorandum from the Institute Clinical Director to the Director, OHSRP, who has delegated authority from the DDIR for approving such requests (see Attachment 4.) Term lengths for reappointments (including of Chairs and Vice Chairs) can be for one, two or three years.
 - a. Reappointment letters are copied to the Clinical Director, IRB Chair and the IRB administrative office.
- C. Expiration of Terms: After the expiration of the term of an appointment, an individual is no longer a member of the IRB and may not participate in IRB meetings (except as a consultant, according to the requirements at 2.11, below) until the reappointment memorandum from the OHSRP Director has been signed.

2.5.3 Terms of Service

- A. Unless reappointed, Chairs, Vice Chairs and members rotate off the Board when their terms expire and have not been renewed; when members tender their resignations, or when members are removed for cause.
- B. IRB Chairs, Vice Chairs and members may be reappointed in conformity with the rules stated in 2.5.2, above. There is no limit on the total number of years members may serve as a result of being reappointed multiple times, unless Institute management wishes to impose a limit.
- C. Chairs and Vice Chairs may serve as regular IRB members on the same IRB or another NIH IRB after their terms as Chair and Vice Chair are completed.

2.5.4 Removal for Cause of a Member

- A. Justification for Removal: To remove a member of an IRB, including the Chair or Vice Chair, before the end of that person's appointed term, just cause must be shown of that person's inability to meet his/her responsibilities, such as failure to attend meetings regularly; failure to follow applicable laws, regulations and policies; mismanagement; misconduct, or an unresolved conflict of interest for which recusal is insufficient.
- B. Procedures for Removal: The Institute Clinical Director, after consultation with the Institute Scientific Director and the Chair (if the Chair is not the member in question) should prepare a written memorandum to the DDIR through the Director, OHSRP, with the reasons for recommending premature termination of membership. The DDIR makes the final decision on termination and sends a termination letter to the member if he concurs with the recommendation for the member's removal from the IRB.
- C. Termination letters are copied to the Clinical Director, IRB Chair and the IRB administrative office.
- D. Reconsideration for Terminated Members. Terminated members or those who are about to be terminated may ask the Deputy Director for Intramural Research for reconsideration.

2.6 RESPONSIBILITIES OF THE IRB CHAIR

2.6.1 Leadership Requirements for IRB Chairs

- A. The Chair shall embody the following leadership requirements:
- B. The ability to conduct meetings of the IRB in an efficient, expeditious and fair manner; attentiveness to the details and requirements of the Federal regulations and NIH policies in the context of NIH IRP protocol review;

application of the requirements to foster ethically and scientifically sound biomedical research.

- C. The promotion of methodical and systematic IRB review by applying the NIH IRB Protocol Review Standards (Attachment 5).
- D. The ability to set a tone of openness that encourages dialogue in IRB meetings.
- E. Respect for the diverse backgrounds, perspectives and sources of expertise of all IRB members, especially for the contributions of the non-scientists, and the ability to foster such respect among the IRB members.
- F. The confidence and ability to uphold IRB judgments that may not always be popular with Principal Investigators, and
- G. Investment of adequate time, interest and commitment to provide guidance and expertise to IRB members and investigators.

2.6.2 Duties of the Chair

The Chair either votes or abstains from voting on all actions for which votes are taken, unless recused. Chairs will recuse themselves, as appropriate, when conflicts of interest exist.

- A. Provides guidance and expertise about human subjects research to IRB members, investigators and others. Ensures that investigators and IRB members receive information on new or revised policies and regulations pertinent to human subjects research.
- B. Upholds the independent decisions of the IRB with investigators and Institute officials.
- C. Works closely with the IRB administrative staff to carry out the functions of the IRB and IRB office. For example, the Chair sets agendas and scheduling of convened meetings as often as required to accomplish the business of the IRB.
- D. Stays informed of established and emerging policies and guidance pertaining to the protection of human subjects involved in research.
- E. Promotes continuing education of IRB members and IRB staff, including providing IRB members and staff with information about relevant educational opportunities.

- F. Serves as a member of the Human Subjects Research Advisory Committee (HSRAC) regularly attends HSRAC meetings, and shares issues discussed at them with the IRB members and investigators as appropriate.
- G. When a Chair and/or Vice Chair needs to recuse himself/herself from the meeting, he/she designates an IRB member to serve temporarily as Acting Chair or Acting Vice Chair of the meeting.
- H. Conducts expedited reviews or delegates them to the Vice Chair or other qualified IRB members and assures that determinations are documented as required by SOP 7A, “Requirements for Expedited Review of Research by NIH IRBs.”
- I. As directed by the IRB, reviews and approves stipulations in cases where no more than simple concurrence is required, i.e., the stipulations do not have to be reviewed and approved by the convened IRB.
- J. Prepares for and handles any audits by OHRP or the FDA.
- K. Coordinates education of investigators with the appropriate Clinical Director
- L. Ensures that reports to OHSRP are completed in a timely fashion.

2.6.3 Conduct of Convened Meetings

- A. Ensures the presence of a quorum.
- B. Conducts IRB meetings based on Roberts Rules of Order. That is, at a minimum, the Chair is in charge of the meeting, there is a predetermined agenda, the minutes of the prior meeting are voted upon, and all actions and resolutions require the voice or show-of-hands vote of the members present following the making and seconding of a motion and discussion.
- C. Leads IRB discussions by identifying regulatory requirements of 45 CFR 46, 21 CFR 50 and 56, the ethical principles of The Belmont Report, and NIH policy as the criteria for the review of all research studies.
- D. Determines if any IRB members have a conflict of interest with regard to any given protocol or action under consideration by the IRB. The Chair will exclude members with a conflict of interest from participating in the deliberations and voting on that action. That member must leave the meeting room during the deliberations and vote (see SOP 21, “Managing Conflict of Interest in Research”).
- E. Ensures that all IRB members who are not recused have the opportunity to contribute to the IRB's deliberations;

- F. In IRBs where a primary and/or primary and secondary reviewer system is used, chooses the reviewers and ensures that they are qualified to conduct the review. In cases where additional expertise is required, selects consultants to assist in review.
- G. Ensures that the NIH IRB Protocol Review Standards are addressed by the PI for all initial protocol reviews.*
- H. Ensures that the IRB addresses and documents in the minutes all the regulatory standards embodied in the NIH IRB Protocol Review Standards for every initial review or uses an appropriate review tool for this purpose.
- I. Ensures thorough evaluation of initial and continuing reviews, amendments and unanticipated problems including adverse events.

2.7 RESPONSIBILITIES OF THE VICE CHAIR

Each IRB is required to have a Vice Chair. The Vice Chair, in the Chair's absence, exerts all authorities ordinarily vested in the Chair (see 2.6, above).

2.8 RESPONSIBILITIES OF IRB MEMBERS

Members of the IRB (including the Chair, Vice Chair, and alternate members) must:

- A. In convened meetings, apply the NIH IRB Protocol Review Standards or an appropriate reviewer tool when reviewing initial protocols.
- B. Attend IRB meetings regularly (at least 75% of meetings per year) and in those instances in which they are unable to attend a meeting, provide the longest possible notice of their inability to attend.
- C. Be well prepared to discuss each meeting agenda item as a result of having spent sufficient time prior to the meeting reviewing the materials distributed for that meeting, and reviewing the minutes of previous meetings for accuracy.
- D. Maintain the confidentiality of IRB discussions, the votes of individual members, and the protocols and related materials, including any proprietary information (see SOP 7B.9 “Confidentiality of Proceedings”).
- E. Participate in required training and continuing education opportunities, or IRB retreats (see SOP 25, “Training Requirements for the NIH HRPP”), and

* See Appendix 1: References page 15

- F. Inform the IRB immediately if their status changes in a way that might impact their membership (such as a new affiliation with the NIH for a member who was previously considered unaffiliated).

2.9 COMPENSATION OF IRB MEMBERS

Annually, each IRB will provide information to OHSRP in writing about if, and how, IRB members, including the Chair and Vice-Chair, are compensated for their IRB service.

2.10 LIABILITY COVERAGE FOR IRB MEMBERS AFFILIATED WITH NIH THROUGH ANY OF THE FOLLOWING FOUR CATEGORIES: SPECIAL GOVERNMENT EMPLOYEES (SGEs), SPECIAL VOLUNTEER, CONTRACTOR, OR EMPLOYEE

2.10.1. Background

Liability coverage for IRB members differs depending on whether they are federal employees (either full-time or as a special government employee), or non-Federal employees who serve on the IRB without compensation (i.e., a volunteer member) or who are compensated.

2.10.2. NIH and Other Federal Employees

The Federal Tort Claims Act (FTCA) (28 U.S.C. 2671 et seq.) generally covers Federal employees in litigation when there are allegations of negligence that occurred within the scope of their employment.

- A. NIH and other federal employees, whose IRB service is considered part of their official duties, are covered by the FTCA. Employees should have documentation in their personnel files that their IRB service is an official duty.
- B. An individual who is not presently an employee may be appointed as a special government employee (SGE) specifically for service as an IRB member. The individual must complete various personnel forms, including a financial disclosure form and agree to abide by applicable Federal ethics requirements.

2.10.3. Volunteer Members of the IRB

It is considered that volunteers may be eligible under the FTCA for coverage from personal liability for damages or injuries that arise from actions occurring within the scope of their federal assignment as NIH IRB members and while under the direct supervision of a federal employee. However, the ultimate decision on issues of liability and coverage depends on the circumstances of each situation as it does for federal employees and is made by the U.S.

Department of Justice. These individuals must obtain a Special Volunteer appointment at the NIH.

2.10.4. Compensated IRB Members Who are Not Federal Employees

Compensated non-Federal employees may receive compensation for services as contractors. They are not covered by FTCA but may purchase private liability coverage for IRB services. The cost of such coverage may be reimbursed under their contract with NIH.

2.11 SELECTION AND USE OF CONSULTANTS FOR REVIEW

2.11.1. Use of Consultants

Consistent with requirements set forth at 45 CFR 45.117(f), an NIH IRB may choose to invite individuals with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that available on the IRB. This may include experts in scientific aspects of the research or related to human subjects protections.

2.11.2. Choosing Consultants

The IRB Chair, in cooperation with the Clinical Director(s), will identify appropriate experts (based on their *curriculum vitae*, current work in the relevant scientific discipline, etc.). Consultants may be drawn from the scientific or other NIH staff as well as from outside the NIH.

2.11.3. Consultants' Conflict of Interest

Consultants are subject to the same NIH conflict of interest rules as IRB members and are required to certify they have no conflict of interest (see SOP 21, "Managing Conflict of Interest in Research").

2.11.4. Provision of Consultant Advice

- A. The IRB administrative office ensures that the consultant understands his/her confidentiality obligations and receives a copy of the proposed protocol and any other supporting documentation in a timely manner.
- B. Consultants may attend IRB meetings in person or submit a written report to the Board. Consultants may attend the convened IRB meeting; question the protocol's Principal Investigator (PI) during the PI's presentation; provide an oral critique of the protocol after the PI has left the room, and participate in discussions of the protocol with other IRB members.

- C. Consultants do not vote and are excused from the meeting prior to the vote. Their presence is noted in the IRB meeting minutes.

2.12 USE OF SUBCOMMITTEES FOR REVIEW

Subcommittees of the IRB may be created as needed at the discretion of the Chair. They may be constituted to consider a specific issue or issues, or to review and approve a protocol under an expedited review process (SOP 7A, “Requirements for Expedited Review of Research by NIH IRBs”) or to review an investigator’s response to stipulations when this authority has been specifically delegated to them by the IRB Chair or convened IRB. If a HRPP Standard Operating Procedure (SOP) requires that an issue be reviewed at a convened meeting of an IRB, then review by a subcommittee can never serve as a substitute for that convened IRB review. Subcommittee actions are reported to the full Board at the next convened meeting.

2.13 EVALUATION OF IRB MEMBERS

See SOP 26 “Evaluation of NIH IRB Chairs, Vice Chairs and Members, IRB Activities and IRB Administrative Staff.”

2.14 TRAINING, EDUCATION AND PROFESSIONAL DEVELOPMENT FOR IRB MEMBERS

See SOP 25 “Training Requirements for the NIH HRPP.”

APPENDIX 1: REFERENCES

NIH IRB Protocol Review Standards:

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

ATTACHMENTS

Attachment 1. Statement of Status as an Unaffiliated IRB Member

Attachment 2. OHSR IRB Roster Template

Attachment 3. Sample Appointment Letter

Attachment 4. Sample Reappointment Letter

Attachment 5. NIH Protocol Review Standards

Statement of Status as Unaffiliated Member of an NIH IRB

I, _____, am already serving on the _____ NIH IRB, or am now being invited to serve on that IRB, in the role of a member who will be considered **not** “affiliated” with the NIH. I have read the guidance on the bottom half of this page which provides an explanation of when someone is considered to be affiliated with the NIH. Based on that guidance, I have concluded that there are no circumstances that I am aware of which would suggest that either I, or a member of my immediate family, is affiliated with the NIH. If I ever become aware of such circumstances, I will contact the administrator of the IRB so that my status as an unaffiliated member can be changed.

Signature

Date

The following paragraph describes what it means to be “affiliated” with the NIH. If you have any questions about how it applies to your circumstances, please be sure to ask the administrator of the IRB.

An employee or agent of the NIH (or a member of that person’s immediate family) is considered affiliated. Affiliated members include, but are not limited to individuals who are: part-time employees; current students; members of any governing panel or board of the NIH; paid or unpaid consultants; healthcare providers holding credentials to practice at the NIH; and volunteers working at NIH on business unrelated to the IRB. An individual that has no affiliation with the NIH, other than as an IRB member, is considered unaffiliated with the NIH. Unaffiliated members may include people whose only association with the NIH is that of a patient, subject, or former student at the NIH.

Name	Degree	Gender	Specialty	IRB Position	NIH Affiliated	Term End	Current Address	Phone
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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

Date

[Name of recommended IRB member]
Mailing Address

Dear Dr/Mr./Ms. [Last name of recommended IRB member]:

Drs. [names of Clinical Director, Scientific Director, IRB Chair], [IC Name] have recommended your appointment to serve as [a full voting, non/affiliated, non/scientist] member of the [---] IRB for a [---] year term.

I am pleased to confirm this [---] year appointment, effective Date.

The IRBs play a vital part in ensuring that the clinical research done at NIH is of the highest scientific and ethical standards, and that the safety and welfare of the people who participate in the research are protected. I am grateful that you are willing to take part in this very important process.

Sincerely yours,

Michael M. Gottesman, M.D.
Deputy Director for Intramural Research

cc: Clinical Director
Scientific Director
IRB Chair
IRB Administrator



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

[Date]

[Name of Appointee]

[Address]

Dear Dr. [Name]:

Drs. [CD, SD, Chair, IRB], have recommended your reappointment to serve as a [primary voting, affiliated, scientist] member of the [IRB], for a [___] year term. I am pleased to confirm this [___] year appointment, effective [Date].

The IRBs play a vital part in ensuring that the clinical research done at NIH is of the highest scientific and ethical standards, and that the safety and welfare of the people who participate in the research are protected. I am grateful that you are willing to continue to take part in this very important process.

Sincerely yours,

Charlotte Holden, JD
Deputy Director, Office of Human Subjects Research

cc: Clinical Director
Scientific Director
Chair, IRB
IRB Administrator

NIH IRB PROTOCOL REVIEW STANDARDS
Principal Investigator and IRB Member Review Tool:
Minimal Regulatory Requirements for IRB Review, Discussion and
Documentation in the IRB Meeting Minutes

Section I – Regulatory Criteria for IRB Approval for Initial Reviews

(To be used by the Principal Investigator at the initial protocol presentation to the IRB)

Regulatory review requirement to be addressed for new protocols by the PI at the convened IRB meeting	Suggested questions for IRB discussion
1. Scientific Design: The proposed research design is scientifically sound & will not unnecessarily expose subjects to risk.	<ul style="list-style-type: none"> a. Is the hypothesis clear? Is it clearly stated? b. Is the study design appropriate to prove the hypothesis? c. Will the research contribute to generalizable knowledge and is it worth exposing subjects to risk?
2. Risks to subjects are reasonable in relation to anticipated benefits (45 CFR 46.111(a)(2)) : if any, to subjects, and the importance of knowledge that may reasonably be expected to result. Risks to subjects include physical, psychological, social, legal and socioeconomic risks.	<ul style="list-style-type: none"> a. What does the PI consider the level of risk/discomfort/inconvenience to be? (See risk assessment guide attached to this form). b. Does the IRB agree with the PI's risk assessment? c. Is there prospect of direct benefit to subjects? (See benefit assessment guide attached to this form.) d. Are risks reasonable in relation to anticipated benefits, if any to subjects?
3. Subject selection is equitable (45 CFR 46.111(a)(3)) taking into account the purpose and setting of the research	<ul style="list-style-type: none"> a. Who is to be enrolled? Men? Women? Ethnic minorities? Children (rationale for inclusion/exclusion addressed)? Seriously-ill persons? Adults who may be unable to give consent? Healthy volunteers? b. Are these subjects appropriate for the protocol?
4. Vulnerable Subjects: Additional safeguards required	<ul style="list-style-type: none"> a. Are appropriate protections in place for vulnerable subjects, e.g., pregnant women,

for subjects likely to be vulnerable to coercion or undue influence. (45 CFR 46.111(b))	fetuses, socially- or economically-disadvantaged, prisoners, adults who may be unable to give consent?
5. Risks to subjects are minimized (45 CFR 46.111(a)(1))	Are data and safety monitoring plans consistent with NIH requirements?
6. Monitoring of Data to ensure safety of subjects (45 CFR 46.111(a)(6))	The research makes adequate provisions for data monitoring.
7. Subject privacy & confidentiality are maximized (45 CFR 46.111(a)(7))	<ul style="list-style-type: none"> a. Will personally-identifiable research data be protected to the extent possible from access or use? b. Are any special privacy & confidentiality issues properly addressed, e.g., use of genetic information?
8. Informed consent process is adequate and appropriately documented (45 CFR 46.111(a)(4), 46.116, 46.117 and for FDA-regulated research, 21.CFR 50)	<ul style="list-style-type: none"> a. Does the informed consent document include the eight required elements? b. Is the consent document understandable to subjects? c. Who will obtain informed consent (PI, nurse, other?) & in what setting? d. If appropriate, is there a children's assent? e. Is the IRB requested to waive or alter any informed consent requirement?
<u>Additional considerations</u> <i>(as applicable)</i>	
1. Ionizing radiation.	If ionizing radiation is used in this protocol is it medically indicated or for research use only?
2. Collaborative research.	Is this domestic/international collaborative research? If so, are FWAs or other assurances required for the sites involved? Is there a CRADA?
3. FDA-regulated research	Is an IND or IDE involved in this protocol? Is an IND/IDE required? (For help in determining the need for an IND/IDE see SOP 15).
4. Duration of approval	Does the protocol require review more frequently than annually?

Section II –Points to Consider by the IRB at Continuing Review and for Amendments

1. Regulatory criteria.	Does the protocol meet all the regulatory criteria as approved at initial review?
2. Continuing review/amendment requirements	Have the relevant continuing review/amendment requirements as set forth on the NIH Intramural Clinical Protocol Application been met?
3. Research progress and rationale for continuing the study	Is the research progressing as proposed/expected? Should the study continue?
4. Changes in previously approved research	Does the protocol require verification from sources other than the investigator(s) that <i>no material changes</i> have occurred since the previous review? (<i>Material changes</i> mean any change that would affect the determination of whether the research meets the regulatory criteria for IRB approval.)
5. Significant new findings	Are there any significant new findings that might affect the subjects' willingness to continue participation in research?
6. Protocol recruitment	Is the protocol meeting its recruitment goals?
7. Unanticipated problems (see Section III, below)	Review the summary of AEs, PDs, and Non-compliance ; Have there been any unanticipated problems involving risks to subjects since the last review? If so, is amendment of the protocol required?
8. Scientific Design: The proposed research design is scientifically sound & will not unnecessarily expose subjects to risk. (<i>when applicable, e.g. amendment</i>)	Have the activities in the past year suggested an impact on the scientific design? Is there a change to the scientific design with this submission?
8. Informed consent process is adequate and appropriately documented (45 CFR 46.111(a)(4), 46.116, 46.117 and for FDA-regulated research, 21.CFR 50) (<i>when applicable, e.g. amendment</i>)	Have the activities in the past year suggested an impact on the informed consent process? <ol style="list-style-type: none"> Does the informed consent document include the eight required elements? Is the consent document understandable to subjects? Who will obtain informed consent (PI, nurse, other?) & in what setting? If appropriate, is there a children's assent? Is the IRB requested to waive or alter any

	informed consent requirement?
9. Vulnerable Subjects: Additional safeguards required for subjects likely to be vulnerable to coercion or undue influence. (45 CFR 46.111(b)) <i>(when applicable, e.g. amendment)</i>	a. Are appropriate protections in place for vulnerable subjects, e.g., pregnant women, fetuses, socially- or economically-disadvantaged, prisoners, adults who may be unable to give consent?
10. Monitoring of Data to ensure safety of subjects (45 CFR 46.111(a)(6)) <i>(when applicable, i.e. amendment)</i>	The Research makes adequate provisions for data monitoring.
11. Subject privacy & confidentiality are maximized (45 CFR 46.111(a)(7)) <i>(when applicable, e.g. amendment)</i>	a. Will personally-identifiable research data be protected to the extent possible from access or use? (b) Are any special privacy & confidentiality issues properly addressed, e.g., use of genetic information?
12. Research risks	Has any information appeared in the literature or evolved from this or similar research that might affect the IRB's evaluation of the risk/benefit analysis of human subjects involved in this protocol?
<u>Additional considerations</u> <i>(as applicable)</i>	
1. Ionizing radiation.	If ionizing radiation is used in this protocol is it medically indicated or for research use only?
2. Collaborative research.	Is this domestic/international collaborative research? If so, are FWAs or other assurances required for the sites involved? Is there a CRADA?
3. FDA-regulated research	Is an IND or IDE involved in this protocol? Is an IND/IDE required? (For help in determining the need for an IND/IDE see SOP 15).
4. Duration of approval	Does the protocol require review more frequently than annually?

Section III. Points to consider when reviewing unanticipated problems/protocol deviations in previously approved research

<p>Definition of an Unanticipated Problem (UP) An unanticipated problem is any incident, experience or outcome that: (a) Is unexpected in terms of nature, severity or frequency in relation to (i) the research risks that are described in the IRB-approved research protocol and informed consent document; Investigator’s Brochure or other study documents, and (ii) the characteristics of the subject population being studied, AND (b) is related or possibly related to participation the research, AND (c) places subjects or others at a <i>greater risk of harm</i> (including physical, psychological, economic or social harm) than was previously know or recognized.</p>	<p>a. Is the incident, experience or outcome unexpected given the research procedures that are described in the IRB-approved research protocol and consent and the characteristics of the subject population being studied? b. Does the incident, experience or outcome suggest that the research places subjects or others at greater risk of harm? c. Is there a pattern of UPs/protocol deviations (PDs)? b. (d) Is any action required on the part of the IRB or the PI as a result of UPs/PDs (e.g., change in protocol procedures/change in consent document)?(e) Should the UP be reported to OHSRP?</p>
<p>Definition of a Protocol Deviation (PD) Any change, divergence, or departure from the IRB-approved study procedures in a research protocol. PDs may be serious or non-serious. For examples of PDs see SOP 16, Appendix D.</p>	<p>a. Is this PD also a UP? (b) Does this PD represent serious or continuing non-compliance (see SOP 16A)? (c) Will the PD result in change to the risk/benefit analysis or to the protocol or informed consent? (d) Should the PD be reported to OHSRP?</p>

Risk/Benefit Assessment

Regulatory definition of minimal risk: Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (45 CFR 46.102(h)(i)).

RISK LEVEL FOR ADULTS

Check appropriate risk category:

1. _____ Research involving greater than minimal risk to subjects
2. _____ Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects.
3. _____ Research involving greater than minimal risk and no prospect of direct benefit to individual subjects.

RISK LEVEL FOR CHILDREN (see SOP 14D "Research Involving Children")

Check appropriate risk category

1. _____ Research not involving greater than minimal risk to subjects (45 CFR 46.404)
2. _____ Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects (45 CFR 46.405)
3. _____ Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition (45 CFR 46.406)
4. _____ Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (CFR 46.407)

BENEFIT

Definition: A research benefit is considered to be something of health-related, psychosocial, or other value to an individual research subject, or something that will contribute to the acquisition of generalizable knowledge. Money or other compensation for participation in research is not considered to be a benefit, but rather compensation for research-related inconveniences.

Check appropriate benefit category:

1. ____no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition;
2. ____no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge to further society's understanding of the disorder or condition under study;
3. ____the research involves the prospect of direct benefit to individual subjects.