Title: Policy on Designating an Institutional Review Board of Record

Original Effective Date: February 25, 2016

Last Revised: April 26, 2022

Responsible Office/Department: Office of Research Subject Protection (ORSP)

POLICY OVERVIEW

U.S. federal regulations require Institutional Review Board (IRB) review, approval, and monitoring of all research involving human subjects in order to ensure that appropriate steps are taken to protect their rights and welfare as study subjects. The Broad Institute (“Broad”) does not maintain its own IRB, and therefore enters into IRB Authorization Agreements with other institutions to confer this authority and oversight responsibility.

The Broad makes every effort to rely upon accredited IRBs for review of its human subjects research, however, in cases where review by an unaccredited IRB is unavoidable (e.g. when a researcher’s primary employment affiliation is at an institution with an unaccredited IRB) the Broad ensures that the institution has undergone the federal Office of Human Research Subject Protection’s Division of Education and Development Quality Assessment Program or other equivalent review.

PURPOSE AND SCOPE

This policy describes required procedures and documentation associated with designating an IRB-of-record for non-exempt human subjects research conducted by Broad investigators.

This policy applies to research involving human subjects when the Broad Institute is considered engaged according to the 2008 Office of Human Research Protection’s “Guidance on Engagement of Institutions in Human Subjects Research.” (See SOP on “Determining When Activities are Overseen by the HRPP” for guidance regarding engagement determinations).

Investigators are considered subject to this policy when the human subjects research is:

1. performed as part of their Broad employment responsibilities, or
2. conducted using Broad resources/funding/space, or
3. using the name of Broad Institute as part of an individual’s credentials for
any type of publication, presentation or abstract.

DEFINITIONS AND ACRONYMS

Institutional Review Board (IRB): An institutional body charged with protecting the rights and welfare of human subjects, which reviews and has authority to approve, require modifications, or disapprove all research activities.

IRB-of-record: Used to refer to the IRB that assumes IRB responsibilities for another institution for a specific study, group of studies, or for all research conducted by the other institution. This relationship must be documented in advance by an IRB Authorization Agreement.

IRB Authorization Agreement: This is a formal agreement between two institutions that each have a Federalwide Assurance (FWA). Though often negotiated by IRB offices, it is in fact an agreement between two institutions rather than the IRBs. The agreement:

- specifies that one institution agrees to rely upon the IRB used by the other institution for some or all components of a study and
- defines the responsibilities of the IRB and for each institution

Human Subjects Research: Any activity that is either:

- Research as defined by the Department of Health and Human Services (DHHS) and involves Human Subjects as defined by that agency, or
- Research as defined by the Food and Drug Administration (FDA) and involves Human Subjects as defined by that agency.

Research (as defined by DHHS): A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. For the purpose of this definition, please note:

- “Systematic investigation” is not defined in the federal regulations, however, may be interpreted as a planned scientific or scholarly activity involving qualitative or quantitative data collection and/or data analysis that sets forth an objective(s) and a set of procedures intended to reach the objective(s), i.e., to acquire knowledge, develop a theory, or answer a question.
- “Generalizable knowledge” is not defined in the federal regulations, however, may be interpreted as information from which one may infer a general conclusion; knowledge brought into general use or that can be applied to a wider or different range of circumstances.

Human Subject (as defined by DHHS): A living individual about whom an investigator (whether professional or student) conducting research: (i) obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (ii) obtains,
uses, studies, analyzes or generates identifiable private information or identifiable biospecimens.

- **Intervention:** Includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
- **Interaction:** Communication or interpersonal contact between investigator and subject.
- **Private Information:** 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)
- **Identifiable Information:** Information that is individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information).
- **Identifiable biospecimen:** A biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

**Research, as defined by FDA:** Any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA or the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulation.

**Human Subject, as defined by FDA:** An individual who is or becomes a subject in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. A human subject includes an individual on whose specimen a medical device is used. When medical device research involves in vitro diagnostics and unidentified tissue specimens, the FDA defines the unidentified specimens as human subjects.

**Investigational New Drug Application (IND):** An IND is a request for Food and Drug Administration (FDA) authorization to administer an investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug that is not the subject of an approved new drug application. IND regulations are contained in Title 21, Code of Federal Regulations, Part 312. Copies of the regulations, further guidance regarding IND procedures, and additional forms are available at www.fda.gov.

**Investigational device exemption (IDE):** And IDE allows an investigational device to be used in a clinical study in order to collect safety and effectiveness data.
Investigational use also includes clinical evaluation of certain modifications or new intended uses of legally marketed devices. All clinical evaluations of investigational devices, unless exempt, must have an approved IDE before the study is initiated. Nonsignificant risk (NSR) devices are devices that do not pose a significant risk to the human subjects. A nonsignificant risk device study requires only IRB approval prior to initiation of a clinical study. Sponsors of studies involving nonsignificant risk devices are not required to submit an IDE application to the FDA for approval. Submissions for nonsignificant device investigations are made directly to the IRB of each participating institution. Sponsors should present to the reviewing IRB an explanation why the device does not pose a significant risk. NSR device studies do not have to have an IDE application approved by the FDA.

**Overall Principal Investigator (PI):** Overall Principal Investigator has the ultimate responsibility for the conduct of research to ensure subject safety and data integrity for research that will be carried out collaboratively among two or more institutions.

**Site Investigator (Site PI):** The Site Investigator is responsible for the conduct of research at the institution where they are employed.

**Research Personnel:** Persons who have direct contact with research participants, contribute to the research in a substantive way, have contact with participants’ identifiable data or biological samples (e.g., tissue, blood, urine, plasma, saliva), or use participant's personal information.

**Relying and Reviewing Institution:** When an institution cedes its IRB review to another institution's IRB, the former is called the "Relying Institution" and the latter is called the "Reviewing Institution."

**Primary Employment:** Although investigators may have appointments at multiple institutions, investigators are usually considered "an employee" or a "workforce member" of one institution. The institution from which the investigator receives their paycheck is generally considered the institution of primary employment.

**Unanticipated Problems Involving Risks to Participants or Others:** Problems encountered during the research that are a.) unanticipated or unexpected, b.) related to the research, or c.) involves new or increased risks to participants or others. A new or increased risk is defined as one that requires some action (e.g., modification of the consent process or informing participants).

**Federalwide Assurance (FWA):** An assurance of compliance accepted and approved by OHRP for institutions engaged in non-exempt human subjects research conducted or supported by the department of Health and Human Services.

**DESCRIPTION**

Procedures carried out by the Broad's Office of Research Protections (ORSP)
1. In accordance with the Broad’s Policy, “Determining When Activities are Overseen by the Human Research Protection Plan,” ORSP reviews project activities and determines if IRB review is required.

2. Because Broad does not maintain its own IRB, all studies that require IRB review are eligible for review by another organization's IRB. In such cases, ORSP and project leaders determine the appropriate IRB to review the project. Considerations include, but are not limited to: PI’s primary employment affiliation, subject population, study risk factors, and scientific and regulatory expertise.

3. Requests to rely on an AAHRPP (Association for the Accreditation of Human Research Protection Programs) accredited IRB are generally acceptable. Requests to rely on a

4. Non-AAHRPP accredited IRB will be evaluated by ORSP administration on a case-by-case basis by reviewing policies and procedures and the IRB application of the unaccredited IRB to ensure the IRB meets equivalent standards of human subject protection. This may involve a member of ORSP staff serving on the IRB or completion of the AAHRPP Evaluation Checklist (https://aahrpp.org/).

5. If an IRB authorization agreement is not already in place, ORSP initiates this process in accordance with the selected IRB’s standard operating procedures.

6. As needed, ORSP updates the Broad’s FWA to include identifying all IRBs with which the Broad maintains reliance agreements. ORSP may not approve research subject to the reliance agreement until it has been approved by the reviewing IRB.

7. ORSP may conduct monitoring in addition to, or in cooperation with, the reviewing IRB, when appropriate

**Procedures carried out by Broad Institute (the relying institution) and Broad investigators carrying out research involving human subjects:**

1. Broad affiliated researchers must comply with the determinations and requirements of the IRB and the Broad relying organization is responsible for ensuring compliance with the IRB’s requirements at the research site.

2. Prior to IRB review, the Broad must provide the IRB with any local context issues relevant to the research protocol.

3. Research may be further reviewed and approved or disapproved by Broad officials of the relying organization, but they may not approve the research if it has not been approved by the reviewing IRB.
4. The Broad and its affiliated organization and the researchers acknowledge and agree to cooperate with the IRB responsible for initial and continuing review, record keeping, and reporting. All information requested by the IRB will be provided in a timely manner.

5. Broad researchers and research staff agree to disclose financial conflicts of interest according to the agreed-upon process and comply with any conflict management plans that may result.

6. The Broad organization or its affiliated researchers will report promptly to the IRB any proposed changes in the research. The investigator will not initiate changes in the research (including changes in the consent document) without prior IRB review and approval, except where necessary to eliminate apparent immediate hazards to the participants.

7. Broad researchers will not enroll individuals in research prior to review and approval by the IRB, and meeting all other applicable requirements and approvals for the study.

8. Broad researchers, when responsible for enrolling participants, will obtain, document, and maintain records of consent for each participant or each participant's legally authorized representative.

9. Broad researchers will report to the IRB any unanticipated problems involving risks to participants or others according to the requirements specified in the IRB reliance agreement.

10. Broad researchers will provide to the IRB any data safety monitoring reports they receive, according to the IRB's reporting policy.

11. Broad researchers will report non-compliance, participant complaints, protocol deviations or other events according to the requirements specified in the IRB reliance agreement. (See Policy: "Addressing Allegations and Findings of IRB Protocol Noncompliance."). Researchers are responsible for communicating decisions of the IRB-of-record to ORSP.

12. Emergency medical care may be delivered without IRB review and approval to the extent permitted under applicable federal regulations and state law.

13. The Broad organization and its affiliated researchers acknowledge that they are primarily responsible for safeguarding the rights and welfare of each research participant and that the participant's rights and welfare must take precedence over the goals and requirements of the research.

14. The Broad relying organization may conduct post-approval monitoring in addition to, or in cooperation with, the reviewing IRB.

15. The IRB Authorization Agreement does not preclude the Broad or its affiliated researchers from taking part in research not covered by the agreement.
16. The IRB Authorization Agreement must specify the institutional contact person and provide contact information to the reviewing organization.

17. Broad investigators and research staff must implement any additional safeguard required by the reviewing IRB to protect vulnerable populations.

18. Broad must ensure appropriate education and continuing education of researchers and research staff. (See Policy: Oversight of Education regarding Protection of Research Subject Rights and Welfare.)

19. The Broad is responsible for disclosure and management of financial conflict of interest, and disclosing these to the IRB-of-Record in a timely manner prior to approval decisions by the IRB. (See Policy: Conflict of Interest and Conflict of Commitment.)

20. The Broad is responsible for managing organizational conflict of interest related to the research. (See Policy: Conflict of Interest and Conflict of Commitment.)

21. Broad investigators must continually monitor the resources allocated for their research and notify the IRB-of-record if any change in the availability of resources may adversely impact the rights and welfare of participants.

22. A Broad investigator who holds an Investigational New Drug Application (IND) and who is the Sponsor of the research (i.e., in the case of an investigator-initiated trial) has additional responsibilities that must be adhered to in order to properly conduct the research. In such cases, the investigator must provide documentation to the IRB-of-record that research will be conducted under an IND. Once the IND is submitted to the FDA, the Sponsor must wait thirty (30) calendar days before initiating any clinical trials. If the sponsor does not receive notification from the FDA within the thirty (30) day period, the IND is considered acknowledged and in effect by the FDA.

23. An investigator conducting an investigational device study is responsible for providing the reviewing IRB an explanation of its risk determination (significant or non-significant risk) and should provide any other information that may help the IRB in evaluating the risk of the study.

24. Investigators are responsible for ensuring that research staff are qualified (e.g., including but not limited to appropriate training, education, expertise, credentials and, when relevant privileges) to perform procedures assigned to them during the study.
Procedures carried out by the IRB-of-record (the reviewing institution):

1. Conduct review of research according to all applicable regulations and laws, including initial review, continuing review, and review of modification to previously approved research.

2. Grant, suspend, or terminate IRB approval.

3. Review unanticipated problems involving risks to participants or others.

4. Review incidents of serious or continuing noncompliance.

5. Notify the researchers and organizations in writing of its decisions.

6. Make available relevant IRB minutes to the relying organization upon request.

7. When appropriate, conduct on-site or remote post-approval monitoring or audits, unless delegated to the relying organization.

8. Ensure that research is scientifically valid.

9. Specify the IRB contact person and provide contact information to the relying institution.

10. Specify the IRB contact person, and provide contact information to be included in consent documents, who will serve as an individual who is unaffiliated with a specific research study to discuss research participants’ problems, concerns and questions.

11. Ensure that:
   
   - Risks to participants are minimized by using procedures that are consistent with sound research design and that do not unnecessarily expose participants to risk.
   - Risks to participants are minimized, when appropriate, by using procedures already being performed on the participants for diagnostic or treatment purposes.
   - Risks to participants are reasonable in relationship to the potential benefits, if any, to participants and the importance of the knowledge that may be expected to result.

12. Ensure that participants are recruited in a fair and equitable manner.

13. Has the authority to observe the consent process as a method to protect participants.

14. Ensure that researchers have access to adequate resources to carry out the proposed research.

15. Report to organizational officials, regulatory agencies, and sponsors of any serious or continuing non-compliance, unanticipated problems involving risks to participants or others, suspensions or terminations of IRB approval.

16. Ensure that research using any investigational or unlicensed test article complies with all applicable legal and regulatory requirements. For research being conducted under an IND, the Broad’s IRBs of record require the IND number be included in the application. As confirmation that the IND number is valid, the IRBs require
documentation from the sponsor or the FDA of the IND number. Research is not approved by the IRB until the IND is in effect. For studies of investigational devices, unless FDA has already made a risk determination for the study, the IRB must review the sponsor's SR or NSR determination for every investigational medical device study reviewed and modify the determination if the IRB disagrees with the investigator/sponsor.

REFERENCES

- **Code of Federal Regulations: Title 45, Public Welfare, Department of Health and Human Services: Part 46, Protection of Human Subjects.**
  http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html
- **Code of Federal Regulations: Title 21, Food and Drugs, Food and Drug Administration: Part 56, Institutional Review Boards.**
- Broad Institute policy: “Determining When Activities are Overseen by the HRPP”
- Broad Institute policy: “Oversight of Education regarding Protection of Research Subject Rights and Welfare”
- Broad Institute policy: “Conflict of Interest and Conflict of Commitment”

CONTACTS AND SUBJECT MATTER EXPERTS

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KEYWORDS

IRB

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