Title: Policy on Determining When Activities are Overseen by the Human Research Protection Plan

Original Effective Date: October 30, 2015

Last Revised: April 6, 2022

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

POLICY OVERVIEW

It is the Broad’s policy to ensure faithful adherence to all applicable federal regulations and guidelines governing the protection of human research participants by ensuring accurate assessment of all Broad projects that involve the use of human data or biospecimens. The Broad’s Office of Research Subject Protection (ORSP) is responsible for this assessment and for identifying the subsequent regulatory activities needed to ensure appropriate compliance.

PURPOSE AND SCOPE

The purpose of this policy is to establish the process to determine whether Broad scientific activities constitute research involving human subjects, whether the Broad is "engaged" in research involving human subjects, and thereby identify whether the activities fall within the scope of the Broad’s Human Research Protection Program (HRPP).

This policy applies to scientific activities conducted at the Broad by a Broad staff member, researcher, or affiliate, which involve use of biological specimens or data derived from humans. The Chief Compliance Officer and ORSP are responsible for determining when activities are overseen by HRPP. Please note: Projects that involve data requested from a controlled-access repository (e.g. dbGaP, UK Biobank) are excluded from this policy.

DEFINITIONS AND ACRONYMS

Clinical trial: A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health outcomes.

Exempt research: Research involving human subjects that meet one of seven criteria outlined in the Code of Federal Regulations, and which are therefore exempt from some federal regulations that apply to non-exempt research. Research exemptions for Broad-based projects must be made by the Broad’s Office of Research Subject Protection or the project’s IRB-of-record.
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.

The following activities are not considered research:

- Scholarly and journalistic activities (e.g. oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.
- Public health surveillance activities conducted by a public health authority, limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance.
  - Including the collection and testing of information or biospecimens, conducted, supported, ordered, required, or authorized by a public health authority.
  - Including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products.
  - Including those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).
- Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.
- Authorized operational activities (as determined by the relevant federal agency) in support of intelligence, homeland security, defense, or other national security missions.
- Secondary research involving non-identifiable newborn screening blood spots.

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. For the purpose of this definition:

- **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** includes communication or interpersonal contact between investigator and subject.

- **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 that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record).

- **Identifiable private information** is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

- **An identifiable biospecimen** is 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.

**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.

**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 in, or disapprove all research activities. Currently, Broad does not have their own IRB but rather has reliance agreements with our partner institutions.

**ORSP Portal:** The Office of Research Subject Protection’s (ORSP) online project submission and documentation storage system. Accessible at https://orsp.broadinstitute.org to individuals who have been assigned a Broad username and password.

**IRB Protocol:** A research project subject to review by an Institutional Review Board (IRB).
“Not Human Subjects Research” Determination: A determination made by the ORSP that a project’s activities do not meet the Department of Health and Human Services’ (DHHS) definition, as described in the Code of Federal Regulations (45CFR46), of both research and involvement of a human subject.

“Not Engaged in Human Subjects Research” Determination: A determination made by the ORSP that the Broad’s research activities do not meet the regulatory criteria associated with “engagement” in human subjects research, as defined in the 2008 OHRP Guidance on Engagement of Institutions in Humans Subjects Research.

Employees or agents: As defined by OHRP, individuals who (1) act on behalf of the institution; (2) exercise institutional authority or responsibility; or (3) perform institutionally designated activities. “Employees and agents” can include staff, students, contractors, and volunteers, among others, regardless of whether the individual is receiving compensation from the Broad. All individuals who have been assigned a Broad email address are considered to be employees or agents.

DESCRIPTION

1. A researcher and/or members of their study staff contact ORSP via email, the ORSP Portal (at https://orsp.broadinstitute.org), or in-person meeting regarding a new project, or new activities associated with an existing project.

2. The researcher or designated member of the project’s study staff enters the project details into the ORSP Portal.

3. Using the “ORSP Review Decision Tree” (appendix A) as a reference, an ORSP staff member, with guidance from the Chief Compliance Officer as needed, performs an initial evaluation of the project, to determine:

   a. Whether a project’s activities appear to meet either the FDA or HHS regulatory criteria that define research involving human subjects. According to HHS regulations, to constitute research involving human subjects, the project must:

      o Constitute a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge, and,

      o Involve a living individual about whom an investigator conducting research obtains (1) Data through intervention or interaction with the individual, or (2) Identifiable private information.

   Note: The Broad also adheres to OHRP’s 2008 “Guidance on Research Involving Coded Private Information or Biological
Specimens," which states that if the individuals who provide coded information or specimens collaborate on other activities related to the conduct of this research with the investigators who receive such information or specimens, then the additional activities constitute involvement in the conduct of research. Examples of such additional activities include, but are not limited to: (1) the study, interpretation, or analysis of the data resulting from the coded information or specimens; and (2) authorship of presentations or manuscripts related to the research.

b. If the project's activities do not meet the criteria defining human subjects research, an ORSP staff member approves the application, and the study team is notified of its “not human subjects research” determination in an email automatically generated by the ORSP Portal. This status is also recorded in the ORSP Portal record.

c. If the project does involve human subjects research ORSP is responsible for determining whether the Broad is “engaged” in that human subjects research. The Broad is not “engaged” in human subjects research if is not a recipient of an award through a grant, contract, or cooperative agreement directly from HHS for the human subjects research and either:

- Is performing commercial services (i.e., fee-for-service) for investigators provided that,
  - the services do not merit professional recognition or publication privileges, b) the services are typically also performed for non-research purposes, AND c) the Broad's employees or agents do not administer any study interventions.
  - Or, is in receipt of coded information or biological specimens, for which employees and agents do not have access to a key that might allow them to readily ascertain the identity of the research subjects.

Note: For both of the above categories, Broad employees or agents do not obtain data about research participants through an intervention or interaction, and do not solicit informed consent from research participants.

d. If the Broad is not engaged in human subjects research, an ORSP staff member approves the application, and the study team is notified of its “not engaged in human subjects research” determination in an email automatically generated by the ORSP Portal. This status is also recorded in the ORSP Portal record.
2. If, based on the information provided in the ORSP Portal, the project constitutes non-exempt human subjects research, in which the Broad is engaged, the applicant is directed to the submissions materials for the appropriate IRB of record. ORSP members provide assistance as needed with the IRB submission, and ensure that all IRB documentation is stored in the ORSP Portal. Because Broad does not maintain its own IRB, all non-exempt studies in which the Broad is engaged, are eligible for review by another organization’s IRB.

3. If, based on the information provided in the ORSP Portal, the project constitutes exempt human subjects research, the study team will either be directed to the appropriate submission materials at the IRB of record, or will complete a paper-based exemption request provided by ORSP. The particular route will depend on whether the relevant IRB is willing to make an exemption determination on behalf of the Broad; this varies among institutions. Both scenarios are recorded in the ORSP Portal.

NON-COMPLIANCE

Noncompliance will be considered a violation of this policy and may be grounds for denial of entry into Broad facilities and serious disciplinary action, up to and including termination of employment.

ADDITIONAL REVIEW

Appendix A: ORSP Decision Tree

REFERENCES

CONTACTS AND SUBJECT MATTER EXPERTS

Chief Compliance Officer

Office of Research Subject Protection (orsp@broadinstitute.org)

KEYWORDS

ORSP, IRB
ORSP REVIEW DECISION TREE

Is this a "fee-for-service" project? (e.g., Broad is providing sequencing or analysis as commercial service only)

- No

Is a Broad affiliate conducting research (i.e., generating, contributing to generalizable knowledge)? (excluding case studies and internal technology development projects)

- Yes
  - Are all subjects who provided samples and/or data now deceased?
    - Yes
    - No
  - No

Is the Broad affiliated researcher obtaining information or biospecimens through an interaction with living human subjects or, b) obtaining/analyzing/generating identifiable private information or identifiable biospecimens (Coded data are considered identifiable if researcher has access to key)

- Yes
  - Is the project a secondary use of biospecimens? (i.e., were specimens originally collected for a different purpose?)
    - Yes
    - No
    - No
  - No

Will information be recorded by the investigator in such a manner that the identity of the subjects cannot be readily ascertained, directly or through identifiers linked to subjects AND the investigator will not try to re-identify subjects?

- Yes
  - Submit IRB application
- No

Submit exempt application to ORSP or IRB

Is Broad receiving direct federal funding? (i.e., Broad is the ‘prime awardee’ on federally funded grant)

- Yes
  - Broad investigators affiliated with other institutions should check with their IRBs to determine whether they require additional reviews or approvals
- No

"Not Engaged" eligible. Must submit to ORSP portal.

Are samples/data being provided by an investigator who has identifiers or obtains samples through an interaction (i.e., is conducting human subjects research)?

- Yes
  - Does the Broad affiliated researcher have access to identifiers (either directly or via a code)?
    - Yes
    - No
    - No
  - No

Is the Broad affiliate co-publishing or doing joint analysis with investigator who has access to identifiers?

- Yes
  - NHSR eligible. Must submit to ORSP Portal
- No