Title: Policy on Evaluating Scientific Validity of Proposed Research Involving Human Subjects

Original Effective Date: January 26, 2016

Last Revised: April 19, 2022

 Responsible Office/Area: Office of Research Subject Protection

**POLICY OVERVIEW**

In order to ensure adherence to the Belmont Report’s ethical principle of beneficence, or “do no harm,” all human subjects research must undergo review of its scientific validity. At the Broad, this is accomplished through two mechanisms: 1) scientific review by funding sponsors (either internal or external to the institution), and 2) scientific review by the Broad’s Institutional Review Boards of record in accordance with their standard operating policies and procedures.

**PURPOSE AND SCOPE**

This policy outlines the ways in which the scientific validity of research involving human subjects is reviewed, and by whom.

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 “Policy on Determining When Activities are Overseen by the HRPP” for guidance regarding engagement determinations).

**DEFINITIONS AND ACRONYMS**

Federalwide Assurance (FWA) is an agreement to comply with federal regulations concerning research involving human subjects, including the ethical principles outlined in the Belmont Report and the DHHS regulations 45 CFR Part 46.

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.

IRB-of-record: An IRB is considered the IRB-of-record when it assumes IRB responsibilities for another institution.

IRB Authorization Agreement: This is a formal agreement between two institutions that each have a 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
• Defines the responsibilities for 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 procedure 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 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 Information: Private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.
• Identifiable biospecimens: 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 also includes an individual on whose specimen a medical device is used.

### DESCRIPTION

1. Review of the scientific validity of proposed research is typically first carried out by the institution or entity that may provide funding for the project. At the Broad Institute, funding sources typically fall into one of three categories: NIH (or other federal funding agency), institutional, and non-federal/external.
   a. In the case of projects that may be funded by the NIH, scientific review is an integral part of the evaluation process applied to each research proposal.
      i. The first level of NIH review is carried out by a Scientific Review Group (SRG) composed primarily of non-federal scientists who have expertise in relevant scientific disciplines and current research areas.
      ii. The second level of NIH review is performed by Institute and Center (IC) National Advisory Councils or Boards. Councils are composed of both scientific and public representatives chosen for their expertise, interest, or activity in matters related to health and disease. Only applications that are recommended for approval by both the SRG and the Advisory Council may be recommended for funding. Final funding decisions are made by the IC Directors.
   b. In the case of projects that are applying for Broad-based institutional funding (e.g. Broad Next 10, Broad Ignite, SPARC: Scientific Projects to Accelerate Research and Collaboration), scientific review is performed by the internal funding committee, typically composed of Broad Principal Investigators and senior scientific leadership.
   c. For projects seeking non-federal, external funding support (e.g. the Gates Foundation), proposals are subject to review by the sponsors’ internal scientific review mechanisms.
   d. At the discretion of the Broad’s Chief Compliance Officer, additional scientific review by individuals with relevant expert knowledge may be required.

2. All non-exempt human subjects research, when the Broad has been determined to be engaged, must be reviewed by an Institutional Review Board with which the Broad has an IRB Authorization Agreement (a Broad IRB-of-record), where it is also subjected to independent scientific review in accordance with that IRB’s policies, as well as the requirements of 45CFR46, to ensure sound scientific design. IRB approval of human subjects research is required prior to study initiation. 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.

### CONTACTS AND SUBJECT MATTER EXPERTS

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KEYWORDS

ORSP, IRB, Scientific Validity