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pSite Investigator Manual[1]

(For Single IRB Review of Multi-Site or Collaborative Research)

BROWN

[1]This document satisfies AAHRPP element I-9

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Scope

Throughout this document “local institution” refers to the Participating Site (pSite).

What is the purpose of this manual?

This document, HRP-103 – pSite INVESTIGATOR MANUAL, is designed to guide you through policies and procedures related to the conduct of Human Research that is being reviewed externally by a sIRB.

General information regarding Human Research protections and relevant federal regulations and guidance is incorporated into the required human protections training. For additional information see below: “What training do my staff and I need in order to conduct Human Research?”

What training do my staff and I need to conduct Human Research?

This section describes the training requirements imposed by the IRB. You may have additional training imposed by other federal, state, or institutional policies.

Personnel affiliated with an institution or entity with an IRB must complete human participant protections training as required by their local institution.

Personnel affiliated with an organization without an IRB or not affiliated with any entity (e.g., independent consultant) must complete human participant protection training as described below.

Investigators and staff conducting research must complete the Collaborative Institutional Training Initiative (CITI) human subjects online training program.

The CITI site can be accessed at http://www.citiprogram.org/.

Initial education courses are valid for a three-year period, after which time the training must be repeated.

If you will collect or receive protected health information (PHI) as part your research, additional training may be required.

If the study meets the definition of a clinical trial, Good Clinical Practice training may also be required.

All members of the research team involved in the design, conduct, or reporting of the research must complete training. Research personnel who have direct contact with participants, contribute to the research in a substantive way, have contact with a participant's identifiable data or biological samples (e.g., tissue, blood, urine, plasma, saliva) or use a participant's personal information for research purposes must also complete applicable education requirements. Members of the research team who have not completed human research protections training may not take part in aspects of the research that involve human subjects.

What financial interests do my staff and I need to disclose to the sIRB to conduct Human Research?

You should follow your local institution's processes and policies regarding financial interest disclosures. You must provide the sIRB with the local institution's evaluation when any personnel (or an immediate family member of personnel) involved in the design, conduct, or reporting of the research are determined to have a financial interest Related to the Research.

What are my responsibilities as the Participating Site (pSite) Investigator?

pSite investigators are responsible for ensuring safe and appropriate performance of the research at their site and following their own local institution's processes and requirements for relying on an external IRB, including completion of local institutional ancillary reviews. The pSite study team is responsible for completing reliance documents for the lead institution to the best of their ability and providing the local institution with any documents requiring administrative or institutional attention. The items below are examples of documents that may be required:

- HRP-811 – FORM – Basic Site Information or completed submission in the electronic system (Study team)
- Site-specific study documents, including consent, authorization form if requested, and recruitment material (Study team)
- Local Context Questionnaire (Study team and Reliance administrators)
- Reliance agreement (Reliance administrators)

pSite investigators are responsible for following the policies of the external IRBs and knowing the terms and conditions of your IAA. Although an external IRB is providing overall oversight of the research, Brown University is responsible for ensuring compliance and determining that reliance remains appropriate. Site PIs are responsible for submitting updates approved by the IRB of Record and providing relevant outcome letters or determination documentation including:

<u>Continuing Reviews</u>

- HRP-812 – FORM – Site Continuing Review or completed submission in the electronic system
    - Local expiration is based on the expiration date issued at the IRB of Record.

<u>Modifications</u>

- HRP-813 – FORM – Site Modification or completed submission in the electronic system
    - Approved changes to the local research activities must be submitted for review to ensure an accurate study record and approval of our revised scope of work. It is recommended that the Site PI ensure the proposed modifications to local research activities are allowable before submitting to the IRB of Record.

<u>Reportable Events</u>

- HRP-814 – FORM – Site Reportable New Information or completed submission in the electronic system
    - Serious Adverse Events occurring at the local site should be submitted in alignment with the report to the IRB of Record to ensure a timely enactment of corrective actions.

Closures

- HRP-812 – FORM – Site Continuing Review or completed submission in the electronic system
    - The Site PI is responsible for notifying the local IRB of study closures and requests to terminate the reliance agreement.

How do I create a consent document?

Use the sIRB approved consent template document and revise it to include applicable site-specific required language.

We recommend that you date the revisions of your consent documents to ensure that you use the most recent version approved by the IRB.

What are my obligations after sIRB approval of my site?

1) Do not start Human Research activities until you have the final IRB approval letter.
2) Do not start Human Research activities until you have obtained all other required local institutional approvals.
3) Ensure that there are adequate resources to carry out the research safely. This includes, but is not limited to, sufficient investigator time, appropriately qualified research team members, equipment, and space.
4) Ensure that Research Staff are qualified (e.g., including but not limited to appropriate training, education, expertise, credentials, protocol requirements and, when relevant, privileges) to perform procedures and duties assigned to them during the study.
5) Personally conduct or supervise the Human Research. Recognize that the investigator is accountable for the failures of any study team member.
    a) Conduct the Human Research in accordance with the relevant current protocol as approved by the IRB, and in accordance with applicable federal regulations and local laws.
    b) When required by the IRB ensure that consent or permission is obtained in accordance with the relevant current protocol as approved by the IRB.
    c) Do not modify the Human Research without prior IRB review and approval unless necessary to eliminate apparent immediate hazards to subjects.
    d) Protect the rights, safety, and welfare of subjects involved in the research.
6) Submit to the lead study team and sIRB:
    a) Proposed modifications as described in this manual. (See "What are my responsibilities as the Participating Site (pSite) Investigator?")
        i) Single subject protocol exceptions should be submitted via the modification process.

b) A continuing review application as requested in the approval letter. (See “What are my responsibilities as the Participating Site (pSite) Investigator?”
c) A continuing review application when the Human Research is closed. (See “What are my responsibilities as the Participating Site (pSite) Investigator?”)

7) Submit to the local IRB:
   a) Modifications approved by the sIRB that directly impact the research activities at the local site
   b) Modifications for review and approval of local study personnel
   c) Continuing review forms for ongoing research with documented approval by the sIRB
   d) Continuing review forms when the Human Research is closed with documented approval by the sIRB
8) Complete HRP-814 – FORM – Site Reportable New Information or complete a submission in the electronic system so that it can be submitted to the sIRB within five business days of becoming aware of the event for any of the following information items that occur at the local site:
   a) Information that indicates a new or increased risk, or a new safety issue. For example:
      i) New information (e.g., an interim analysis, safety monitoring report, publication in the literature, sponsor report, or investigator finding) indicates an increase in the frequency or magnitude of a previously known risk, or uncovers a new risk.
      ii) An investigator brochure, package insert, or device labeling is revised to indicate an increase in the frequency or magnitude of a previously known risk, or describe a new risk
      iii) Withdrawal, restriction, or modification of a marketed approval of a drug, device, or biologic used in a research protocol
      iv) Protocol violation that harmed subjects or others or that indicates subjects or others might be at increased risk of harm
      v) Complaint of a subject that indicates subjects or others might be at increased risk of harm or at risk of a new harm
      vi) Any changes significantly affecting the conduct of the research
   b) Harm experienced by a subject or other individual, which in the opinion of the investigator are **unexpected** and **probably related** to the research procedures.
      i) A harm is “unexpected” when its specificity or severity are inconsistent with risk information previously reviewed and approved by the IRB in terms of nature, severity, frequency, and characteristics of the study population.
      ii) A harm is “probably related” to the research procedures if in the opinion of the investigator, the research procedures more likely than not caused the harm.
   c) Non-compliance with the federal regulations governing human research or with the requirements or determinations of the IRB, or an allegation of such non-compliance.
   d) Audit, inspection, or inquiry by a federal agency and any resulting reports (e.g. FDA Form 483.)
   e) Written reports of study monitors.
   f) Failure to follow the protocol due to the action or inaction of the investigator or research staff.
   g) Breach of confidentiality.

h) Change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a subject.
i) Incarceration of a subject in a study not approved by the IRB to involve prisoners.
j) Complaint of a subject that cannot be resolved by the research team.
k) Premature suspension or termination of the protocol by the sponsor, investigator, or institution.
l) Unanticipated adverse device effect (any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects).

9) Complete HRP-813 – FORM – Site Modification and provide to lead study team to report an updated disclosure of financial interests within thirty days of discovering or acquiring (e.g., through purchase, marriage, or inheritance) a new financial interest. Attach the pSite institution's evaluation of the financial interest.
10) Do not accept or provide payments to professionals in exchange for referrals of potential subjects ("finder's fees.")
11) Do not accept payments designed to accelerate recruitment that were tied to the rate or timing of enrollment ("bonus payments.")
12) See sIRB requirements of federal agencies in Appendix A.
13) If the study is a clinical trial and supported by a Common Rule agency, one IRB-approved version of a consent form that has been used to enroll participants must be posted on a public federal website designated for posting such consent forms. The form must be posted after recruitment closes, and no later than 60 days after the last study visit. Please contact the study sponsor with any questions.
    a) If certain information should not be made publicly available on a Federal website (e.g. confidential commercial information), the supporting Federal department or agency may permit or require redactions to the information posted. Contact the Federal department or agency supporting the clinical trial for a formal determination.
    b) Contact the supporting Federal department or agency sponsor with any other questions regarding consent form posting obligations.

How do I document consent?

Use the signature block approved by the sIRB on the consent form(s). Complete all items in the signature block, including dates.

The following are the requirements for long form consent documents:

- The subject or representative signs and dates the consent document.
    - If the subject/representative is physically unable to sign the consent form, note this on the consent form and document the method used for communication with the prospective subject/representative and the specific means by which their agreement was communicated.
- The individual obtaining consent signs and dates the consent document.

- Whenever the sIRB or the sponsor require a witness to the oral presentation, the witness signs and dates the consent document.
- For subjects who cannot read and whenever required by the IRB or the sponsor, a witness to the oral presentation signs and dates the consent document.
- A copy of the signed and dated consent document is to be provided to the subject.

The following are the requirements for short form consent documents:

- The subject or representative signs and dates the short form consent document.
- The person obtaining consent signs and dates the summary.
- The impartial witness (fluent in both English and the language spoken by the subject/representative) to the oral presentation signs and dates the short form consent document and the summary. The witness and the interpreter may be the same person.
- Copies of the signed and dated consent document and summary are provided to the subject/representative
- If the study is FDA regulated, obtain a translated copy of the IRB-approved English version of the long form consent promptly and submit to the IRB for review.
    - After the IRB approval of the translated version, provide it to the subject or LAR as soon as possible.

How do I get additional information and answers to questions?

This document and the policies and procedures for the Human Research Protection Program are available on the Brown University website: https://division-research.brown.edu/research-cycle/conduct-research/human-subjects-research.

If you have any questions or concerns, about the Human Research Protection Program (HRPP), contact the HRPP at:

Alexandra Boutros, BS, CIP
Brown University Human Research Protection Program (HRPP)
350 Eddy St. Box 1986
Providence, RI 02912
Email: IRB@brown.edu
(401) 863-3050

You may also contact your local institution IRB Office or Human Research Protection Program.

Appendix A-1 ***Single IRB Studies***

1. That National Institutes of Health expects that all sites participating in multi-site studies involving non-exempt human subjects research funded by the NIH will use a single Institutional Review Board (sIRB) to conduct the ethical review required by the Department of Health and Human Services regulations for the Protection of Human Subjects at 45 CFR Part 46.
    a. This policy applies to the domestic sites of NIH-funded multi-site studies where each site will conduct the same protocol involving non-exempt human subjects research, whether supported through grants, cooperative agreements, contracts, or the NIH Intramural Research Program. It does not apply to career development, research training or fellowship awards.
    b. This policy applies to domestic awardees and participating domestic sites. Foreign sites participating in NIH-funded, multi-site studies will not be expected to follow this policy.
    c. Exceptions to the NIH policy will be made where review by the proposed sIRB would be prohibited by a federal, tribal, or state law, regulation, or policy. Requests for exceptions that are not based on a legal, regulatory, or policy requirement will be considered if there is a compelling justification for the exception. The NIH will determine whether to grant an exception following an assessment of the need.
2. The Office for Human Research Protections expects that all sites located in the United States participating in cooperative research must rely upon approval by a single IRB for that portion of the research that is conducted in the United States. The reviewing IRB will be identified by the Federal department or agency supporting or conducting the research or proposed by the lead institution subject to the acceptance of the Federal department or agency supporting the research.

    The following research is not subject to this provision:

    a. Cooperative research for which more than single IRB review is required by law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe); or
    b. Research for which any Federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate for the particular context.
    c. For research not subject to paragraph (b) of this section, an institution participating in a cooperative project may enter into a joint review arrangement, rely on the review of another IRB, or make similar arrangements for avoiding duplication of effort.