

University of Iowa

External/Central IRB Reliance Process

Standard Operating Procedure (SOP)

I. OVERVIEW

The purpose of this Standard Operating Procedure is to define a process for all University of Iowa researchers engaging in an External or Central IRB collaborative relationship. This SOP provides our current thinking of the external IRB reliance review process which includes descriptions of the information flow between the IRB of Record and Relying IRB throughout the lifecycle of the initial protocol review, amendments, reporting, continuing review and study closure. This guidance includes responsibilities for the IRB of Record, Relying IRB(s), lead study team, and the relying study team(s).

ABBREVIATIONS	
CIRB	Central Institutional Review Board
CITI	Collaborative Institutional Training Initiative
COI	Conflict of Interest
FWA	Federal Wide Assurance
GPC	Greater Plains Collaborative
HIPAA	Health Insurance Portability and Accountability act
HRPP	Human Research Protections Program
HSO	Human Subjects Office
NCI	National Cancer Institute
NIH	National Institutes of Health
PCORI	Patient Centered Outcomes Research Institute
PHI	Protected Health Information
PI	Principal Investigator
POC	Point of Contact
WIRB	Western Institutional Review Board

DEFINITIONS
<i>Central IRB</i> is a single board that reviews research studies for multiple sites. A Central IRB can be any registered IRB that functions to review multiple sites but most commonly the term Central IRB references an independent IRB. Regardless of the group providing it, centralized IRB review is one review for a number of sites. Commonly, the sponsor determines which sites are to participate and suggests or requires those sites to use the Central IRB selected to perform the centralized review.
<i>External IRB</i> is outside the institutional framework. It could refer to being external to the immediate institution or to a larger system or framework of coordinating agreements. External IRBs are also called remote IRBs as they are generally geographically removed from the performance site.
<i>Internal IRB</i> exists within the institution engaged in the study.
<i>IRB of Record</i> is the lead IRB who will oversee the conduct of research related activities at all research

<p>locations. The IRB of Record could also be known as the Lead IRB or a single IRB of Record. A <i>Single IRB of Record</i> is a term adopted by the Clinical Trials Transformation Initiative (CTTI). Their website states, a Central IRB is, "...a single IRB of record for a given protocol. The Central IRB assumes all of the usual IRB responsibilities including all reviews of all relevant documents," (CTTI 2014). A Single IRB of record oversees the same research protocol across a number of locations. It might be a consortium or cooperative IRB, an IRB from another institution, a commercial or federal IRB.</p>
<p><i>Lead Study Team</i> has the obligation to submit the IRB application to the IRB of Record and comply with any requests and clarifications from the IRB or Record.</p>
<p><i>Relying IRB</i> is an internal IRB that is relying on the review by another IRB. This is rather a misnomer as it is the institution rather than the IRB that is relying on the external IRB or IRB of Record.</p>
<p><i>Relying Study Team</i> is the study team that is relying on review by an IRB outside of their institution. It is the responsibility of the <i>Relying Study Team</i> to designate a single Point of Contact who will serve as the communication portal with other Relying Site IRBs and the Lead Site IRB.</p>
<p><i>Point of Contact</i> is generally responsible for being the conduit of information, representing his or her local site, whether it is a lead or a relying institution. The Point of Contact could represent the lead study team coordinator or the IRB staff member identified as the point of contact. The Point of Contact is responsible for facilitation of communication between either the research study team(s) involved in the study or the communication between the IRB of Record and the Relying IRB.</p>
<p><i>Principal Investigator (PI)</i>, whether at a lead or a relying institution, has the primary responsibility for the conduct of the study. The PI at the lead site is accountable for the overall conduct, while the PI at a relying institution is only accountable for the research conducted at his/her institution.</p>

II. SCOPE

The policies and procedures described in this SOP apply to all parties involved in research with the University of Iowa. Any institutions or organizations engaged in research with the University of Iowa researchers must have an IRB Reliance Agreement and standard operating procedures for multisite research in place. The delegation of duties between lead and relying institution and the responsibilities of each party conducting research are outlined in the Reliance Agreement and the research application submitted to the IRB of Record.

III. APPLICABLE REGULATIONS AND GUIDELINES

The same regulatory framework applied to research reviewed by the University of Iowa IRB applies for all external IRB reliance review requests. All research involving human subjects must follow one or more of the below regulations, policies, and/or procedures.

Federal Regulations (45 CFR 46, 160, 164 & 21 CFR 50, 56 at minimum. Additional FDA regulations may apply based on the study design)
State and local regulations
Institutional Policies
ICH-GCP (E6) (as applicable)
IRB of Record Policies

Whenever possible, the IRB of Record procedures should also be consistent with the Association for the Accreditation of Human Research Protections Program's (AAHRPP) guidelines for "Reviewing IRBs."

IV. IRB FEES

The charge for the coordination of your non-federally funded IRB submission is a one-time administrative fee of \$1,000. The submission fee will be deducted from the established research account by the HSO upon receiving a finalization of contract or funding notice from the Division of Sponsored Programs. This fee should be included in the study budget. There will be no F&A charges assessed on this fee.

V. EXTERNAL IRB RELIANCE REQUEST PROCEDURES

- A. All external IRB reliance requests are considered on a case by case basis by the University of Iowa *HRPP Review Committee*. The HRPP review process could involve one or more members of the UI HRPP. For studies considered greater than minimal risk, review by an IRB Chair, HSO Director, Institutional Official, Research Counsel, &/or other HRPP components may be required. Criteria reviewed by this committee include, but is not limited to, the size of the study, level of risk involved, the lead and relying study team members, institutional human research protection program committees involved, contract language (when applicable), local or state regulations, accreditation status of the institution(s) and/or expertise of the IRB.
- B. All requests to rely on an external IRB for research occurring at the University of Iowa should include, a copy of the protocol, consent document including identification of the lead PI and study coordinator submitted via the HawkIRB system for consideration by the HRPP Review Committee.
 - a. **Please Note:** Studies conducted at the VAHCS cannot utilize a central or external IRB model. This includes projects which propose the use of Veteran's Administration facilities, equipment, research staff, or patients. Full-time VA employees may not be involved as PI, Co-I, or Sub-I on any projects requesting an external IRB model.
- C. The UI HRPP Review Committee concurrence of the external IRB reliance request means, the lifecycle of the research is under the purview of the external IRB. The external IRB's policies and procedures will prevail for the conduct of the research. This includes review of the:
 - a. New Project submission.
 - b. Modification(s). Any change in the conduct of a study. Changes must be reviewed and approved by the IRB of Record prior to implementation. The exception to this is when the change is necessary to eliminate apparent immediate hazards to subjects.
 - c. Continuing Review. The IRB of Record is required to review and approve all research projects at intervals appropriate to the degree of risk, but not less than once a year.
 - d. Reportable Event(s). A Reportable Event can be any unanticipated problem, serious adverse event, receipt of new information, or a form of noncompliance. Investigators are

required to report these to his or her respective IRB, the IRB of Record, regulatory agencies and sponsors as applicable.

- e. Project Closure. When a study ends, the PI must complete a Project Closure Form.
- D. All requests for the University of Iowa Institutional Review Board(s) to serve as the lead IRB of record for a multi-site study is considered by selecting the appropriate IRB of record as designated by the affiliation of the University of Iowa Principal Investigator in the HawkIRB application. Information on this affiliation can be found in the University of Iowa Investigator's Guide in Part 1, Section 4.b.i-ii. The UI HRPP Review Committee will review the request for the University of Iowa IRB to serve as the IRB of Record for all designated research study locations outside of the University of Iowa associated campuses.
- E. *Other HRPP Committee Review* All research, regardless of the IRB of record, will be required to section V of the HawkIRB application form to ensure appropriate HRPP review and other Institutional reviews occur as per University of Iowa policies. . The responses provided in the HawkIRB application determine(s) which committee reviews will apply to the study, verification of research team member's human subjects protections training, and Institutional Conflict of Interest disclosure requirements. All committee approvals must be in place prior to final signoff to any External IRB reliance process.

VI. ROLES AND RESPONSIBILITIES

Relying on an external IRB, whether it is for a single protocol or a portion of the organization's research portfolio creates a different set of responsibilities for both the UI HRPP and the University of Iowa research team. It is important to develop a formal written agreement which clearly delineates the roles and responsibilities of each party. In addition, there should be a working and communicative relationship between the two parties. Below are roles for the IRB of Record and relying IRB(s) that should be included in written agreements.

Lead Site IRB (IRB of Record) Responsibilities

It is the responsibility of the Lead Site IRB to serve as the IRB of Record. This includes approval of new studies and consents, determining procedures for modifications and continuing reviews, instructing relying institutions how to report unanticipated problems and serious adverse events and instances of noncompliance. It is also the IRB of Record's responsibility to ensure processes for data protection, conflict of interest management, and confirmation of human subjects protection training.

The University of Iowa considers the following to always be responsibilities of the IRB of Record:

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. Suspend or terminate IRB approval.
3. Reviews unanticipated problems involving risks to participants or others.
4. Review incidents of serious or continuing non-compliance.

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. Specify the contact person and provide contact information for the reviewing IRB.
9. Reportable events reviewed according to policies and procedures outlined by the IRB of Record. Additional reporting may occur by relying IRBs if federal funding or other local institutional policies apply
10. If items 2, 3, or 4 should occur, the IRB of Record is responsible for reporting these occurrences to the Relying IRB(s).

Relying IRB Responsibilities

Each Relying IRB is responsible for ensuring compliance with respective local context issues and requirements. Relying IRBs are responsible for adhering to all content outlined in the IRB Reliance agreement (i.e. financial interest disclosure, record documentation, etc.).

The University of Iowa considers the following to always be Relying Site responsibilities:

1. Researchers must comply with the determinations and requirements of the IRB of Record. The lead study team is responsible for ensuring compliance with the IRB of Record requirements at the research site.
2. Prior to the IRB of Record review, provide the IRB of Record with any local context issues relevant to the research protocol.
3. Research may be disapproved by officials of the relying organization, but they may not approve the research if it has not been approved by the designated IRB of Record.
4. The Relying IRB and the researchers acknowledge and agree to cooperate in the IRB of Record's responsibility for initial and continuing review, record keeping and reporting requirements. All information requested by the Relying IRB will be provided in a timely manner.
5. 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. If their institution has a PHS-compliant conflict of interest policy, they must comply with all aspects of that policy. All managed financial conflicts of interest will be reported to the IRB of Record. If a Relying IRB does not have a PHS-compliant conflict of interest policy, it will follow the conflict of interest policy of the IRB of Record.
6. The Relying IRB or researchers will report promptly to the IRB of Record any proposed changes in the research. The investigator will not initiate changes in the research (including changes in the consent document) without prior IRB of Record review and approval, except where necessary to eliminate apparent immediate hazards to the participants.

7. Researchers will not enroll individuals in research prior to review and approval by the IRB of Record.
8. The researchers, when responsible for enrolling participants, will obtain, document, and maintain records of consent for each participant or each participants legally authorized representative as stipulated by the IRB of Record.
9. Researchers will report to the IRB of Record any unanticipated problems involving risks to participants or others according to the IRB of Record's reporting policy.
10. Researchers will provide any data safety monitoring reports they receive, either at continuing review, upon request by the IRB of Record, or on an emergent basis if appropriate.
11. Researchers will report, to the IRB of Record, any non-compliance, research misconduct, or protocol deviations according to the IRB of Record's reporting policy. If a University of Iowa researcher reports such an instance to the IRB of Record, the IRB of Record will report it to the UI IRB.
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 organization and 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 relying IRB may conduct post-approval monitoring in addition to, or in cooperation with, the IRB of Record.
15. The written agreement does not preclude the organization or researchers from taking part in research not covered by the agreement.
16. Specify points of contact for both the research team and the relying IRB to the IRB of Record for ongoing communication.

Lead Site Study Team Responsibilities

The lead study team will typically be the study team affiliated with the institution serving as the IRB of Record. The Lead Site Study Team's responsibilities include, but are not limited to:

1. Serve as the coordinating center for the study. This includes coordinating communication across sites throughout the course of the study and ensuring that all participating sites are provided with the IRB-approved versions of all study documents (e.g. consent and authorization forms, protocol, recruitment materials).
2. Designate a single point of contact whose responsibilities will include responding to questions or requests for information from the study teams at relying sites.
3. Assist study teams from relying sites in ensuring consent documents use the IRB of Record's template form and include the applicable institutional required language (e.g. compensation for injury, who to contact with questions) from each relying site.

4. Notify other study teams' points of contact of all IRB of Record determinations and communications, including those for initial review, continuing review, amendments, and reportable events.
5. Upon request, provide access to study records for audit by the relying sites' institutions, the IRB of Record's institution, and other regulatory or monitoring entities.
6. Obtain information from relying sites regarding local variations in study conduct, such as in regard to recruitment materials and process, consent process, and subject identification process.

Relying Site Study Team Responsibilities

Study teams from sites which are approved to rely on UI IRB as a single IRB of Record for a study have responsibilities that include, but are not limited to the following:

1. Designate a single point of contact. The primary role of the point of contact is to serve as the single point of contact for the study team throughout the review process and after the study has been approved by the UI IRB of Record.
2. Promptly respond to questions or requests for information from the lead study team.
3. Each relying site study team will be responsible for drafting consent documents using the UI IRB of Record template, including applicable institutionally required language (e.g. compensation for injury, who to contact with questions) from the relying site.
4. Upon request, provide access to study records for audit by the relying site's institution, the IRB of Record's institution, and other regulatory or monitoring entities.
5. Report to the lead study team any changes (including funding changes and personnel changes), reportable events, and information applicable for continuing review progress reports in accordance with the UI IRB of Record's policies and procedures.