Reliance Agreement Guidance – GMU as Reviewing IRB

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Contents

Introduction

There are two complementary federal policies that require certain types of federally-funded research that involve multiple institutions to use one IRB to accomplish IRB review and approval for all of the institutions conducting the study/trial. See Appendix A for more information on these mandates.

The Single IRB Model allows multiple institutions that conduct the same protocol to cede to a single IRB for review. Under this model, the IRB for each institution will serve in one of two roles: the Reviewing IRB or the Relying IRB.

Whether GMU will serve as the Reviewing or Relying IRB depends on a number of factors, but every project involving human subjects research at GMU **MUST** be submitted to the IRB through RAMP prior to the start of research activities.

Eligibility for Single IRB Review

Whether a study is eligible for single IRB review depends on a number of factors, but we can provide some general guidance. You should always contact the IRB if you would like a more specific determination regarding your study.

Multi-site studies are generally eligible for single IRB review when:

- They have federal or state funding
- The sponsor requires single IRB review in order for GMU to be eligible to participate in the study
- There are other circumstances that warrant single IRB review – in this case, the study submission must include a justification for requesting single IRB review

Studies are ineligible for single IRB review when:

- They are determined to be outside the scope of IRB review (i.e., Not Human Subjects Research or Not Engaged)
- They are determined to be Exempt
- They involve international study sites

Principal Investigator Responsibilities

GMU investigators are always responsible for conducting research in accordance with federal and state regulations, GMU policies, and IRB determinations. When conducting research under a reliance agreement, each investigator has additional responsibilities depending on whether GMU is the Reviewing or Relying IRB.

Principal Investigator Responsibilities when GMU is the Reviewing IRB

As the Lead PI/study team for a study where MUSC is serving as the sIRB, the Lead PI has the ultimate responsibility for the administration and organizational support for the study. This role includes additional responsibilities. The additional responsibilities include, but are not limited to the following:

- Notifying the relying site PI of the policies of the GMU IRB and should provide these policies to the relying sites.
- Coordinating and disseminating Reliance Agreements to the sites interested in relying on GMU IRB.
- Submitting appropriate documents for GMU IRB approval including but not limited to: protocol, consent form for local site, study documents as well as consent template for the Relying Sites.
- Obtaining the information for each relying site about local requirements, local research context issues, and local ancillary reviews that are relevant to the GMU IRB's determination to oversee the external site for research that involves interactions with subjects at an external site.
- Adding each Relying site in RAMP once initial approval has been received for GMU. This will include but not limited to: adding Relying site contact staff, local context information which includes information on ancillary review approvals, and site-specific documents (as appropriate).
- Ensuring appropriate communication regarding GMU IRB approvals/requirements with the Relying Sites. The GMU PI is responsible for notifying the relying site PI's of all GMU IRB determinations and communications.
- Providing the Relying site PI with the IRB approved versions of all study documents.

After Relying Site approval, the Lead PI is responsible for:

- Coordinating the submission of any amendments for Relying Sites
- Coordinating the submission of information for continuing review from each relying site for review and approval by the GMU IRB
- Reviewing all Relying Site regulatory documents/reports and submitting them for IRB review.
- Coordinating the submission of reportable events

Principal Investigator Responsibilities When GMU is the Relying Site

As the Relying Site Investigator when MUSC is ceding IRB review to a Reviewing IRB, the Relying Site Investigator has direct responsibilities that include, but are not limited to, the following:

- Meet GMU education requirements (e.g., CITI training)
- Comply with the determinations and requirements of the Reviewing IRB, which includes conducting the research in accordance with the reviewing IRB's policies and procedures, the IRB-approved documents and conditions of approval, and any applicable laws and regulations.

- Ensure that the Reviewing Site PI has provided an approval letter for the GMU site before initiation of the research activities at GMU.
- Maintain appropriate copies of all approvals, and other correspondence from the Reviewing IRB, including approvals of all continuing reviews and modifications.
- Comply with all reporting requirements of the IRB of record. In addition, the Principal Investigator must continue to submit a **Site Modification** to the GMU IRB via RAMP for the following:
    - Local study personnel changes
    - Changes which require revision to the HIPAA authorization (if applicable)
    - Changes to conflict-of-interest status
    - Changes are made which affect local context / institutional policy / state law requirements
- **Site Updates** must continue to be submitted to the GMU IRB via RAMP for the following:
    - Status update with the Reviewing IRB's Continuing Review approval (if required)
    - Closure Report after the Reviewing IRB closes the study.
- Report promptly to the Reviewing IRB any proposed changes in the research. No changes should be initiated in the research (including changes in the consent document) without prior Reviewing IRB review and approval, except where necessary to eliminate apparent immediate hazards to the participants.
- Report to the Reviewing IRB any unanticipated problems involving risks to participants or others (Ups); non-compliance or any complaints from a subject or other person regarding the research according to the Reviewing IRB's reporting policy. **These events must also be reported to the GMU IRB in parallel with your submission to the Reviewing IRB.**

Submission Process: GMU IRB serving as the IRB of Record ("Reviewing IRB")

Introduction

Obtaining full IRB approval for projects where George Mason is serving as the **Reviewing IRB** (i.e., approval of the overall protocol and approval of each participating site(s)) occurs in approximately three phases. This document outlines our standard process for executing reliance and onboarding participating sites. However, some flexibility exists in this process (e.g., what documents are included in which modifications, number of modifications necessary, etc.), so please reach out to your assigned IRB Specialist if you have any questions.

Phase One – Initial Protocol Review

1. Submit your project in RAMP
    a. Review GMU's IRB webpage on initial submissions for guidance on submitting your project for initial review.
    b. This submission will look very similar to a normal single-site study.
    c. Include a thorough description of activities happening at each site within the protocol
    d. Do not yet include participating sites on the "Sites" page or external study team members on the "Study Team" page. You will add these later via a modification and reliance agreements will be submitted during that review.
2. After your project is submitted in RAMP for initial review your assigned IRB Specialist will review the protocol and other study materials.
3. If the IRB Office determines it is appropriate to do so, you will be issued an initial approval letter.
    a. This letter indicates that the protocol and other study materials have been approved for use at George Mason. This letter **DOES NOT** indicate that research activities may commence at external sites as Reliance Agreements and review of external sites are not typically executed in initial submissions.
    b. To request IRB review of participating sites and execute Reliance Agreements, you will next create a modification for the project in RAMP as detailed in Phase Two.

Phase Two – Execute Reliance Agreement(s)

4. Open a modification in RAMP
    a. If the reliance pathway has not yet been determined (e.g., an IAA or SMART IRB LOA), please contact your IRB Specialist for guidance
    b. In the modification, include a draft version of the Reliance Agreement (e.g., IAA or SMART IRB LOA) using George Mason's template. Fill out the portions relevant to the George Mason study team (e.g., study title, PI name, etc.). The Reliance Agreement should not have any signatures at this stage. One Reliance Agreement should be uploaded per participating site.
    c. Add all participating sites to the "Sites" page, and add Site PIs to the External Study Team Members list and submit after you've ensured the rest of the submission is up to date.

5. After submitting your modification:
    a. Once your assigned IRB Specialist has completed their pre-review, the Reliance Team will review the reliance components of the submission and ensure the RAMP application and Reliance Agreement have been completed accurately. We will communicate any necessary changes or clarifications via RAMP.
    b. Once the Reliance Agreement is complete and accurate, the Reliance Team will facilitate the execution of the reliance agreement via RAMP. At this stage, IAAs and LOAs will be signed by George Mason's Signatory Official. Once signed, they will be returned via a comment in RAMP.
6. At this stage, you will have all currently GMU IRB approved documents. These may include, but may not be limited to...
    a. GMU signed Reliance Agreement
    b. Master consent form (if applicable)
    c. Recruitment materials (if applicable)
    d. Note: You will not have site-specific consent or HIPAA documents (if applicable) at this time as they will likely not have been submitted to RAMP yet.
7. Send all IRB approved study materials, the Institutional Profile Form, and Basic Site Information Form to your external collaborators
    a. Regarding the Consent form and HIPPA authorization, instruct participating sites to locate and delete George Mason's language related to subject injury, Conflict of Interest/Financial disclosure/compensation, and HIPAA language, and replace it with their local required language (as required)
    b. Your external collaborators will need share the partially executed reliance agreement and Institutional Profile Form with their IRB. The local IRB should be able to (a) complete the Institutional Profile Form and (b) obtain the signature of their institution's Signatory Official on the reliance agreement
    c. Remind your collaborators that they should be in communication with their local IRB to ensure their local procedures regarding ceding review are followed.
8. Once signed by the external collaborator's Signatory Official, upload the fully executed Reliance Agreement and the completed Institutional Profile Form to the RAMP modification submission.
    a. Note that at this point, while Reliance has been fully executed, the George Mason IRB Office has not reviewed or approved participating sites. Research activities at participating sites cannot occur until reliance agreements are fully executed and approval for the participating site(s) has been issued by the George Mason IRB. Review of participating site documents can either occur in the same modification where Reliance was executed, or, that modification can be approved, and a new one can be opened.

Phase Three – Review of Participating Site(s)

1. If the participating site(s) will be consenting, your collaborators should return the site-specific consent form(s), (with HIPAA authorization, if applicable) and recruitment materials. They should include their institution's required local language and site PI contact information.
2. Submit all site-specific documents in RAMP via the Sites page. Include any documents received from the participating site(s). These will be reviewed by the appropriate IRB Specialist.

3. As reliance is fully executed, the IRB Office will now review participating sites, their activities, and if applicable, their site-specific documents. The IRB Office will then issue an approval letter which lists each external site.
4. Remind your collaborators that they should be in communication with their local IRB to ensure their local procedures relating to ceding review are followed before research activities begin at each site.
5. Throughout the life of the project, while George Mason is the IRB of Record, the George Mason PI maintains the responsibility of retaining all reliance documentation, submitting continuing reviews, modifications, and submitting any Reportable New Information that comes from the George Mason site or any other participating site(s).

Appendix A: Background on Single IRB Mandates

NIH Single IRB Mandate

Effective January 25, 2018 the NIH Single IRB Policy states all competing NIH grant applications (new, renewal, revision or re-submission) for multi-site studies with NIH receipt dates on or after January 25, 2018 must include a plan describing the use of a sIRB for the study.

- Applies to: Domestic sites of NIH funded studies where each site will conduct the same protocol involving non-exempt human subjects research, whether supported by grants, cooperative agreements contracts or the NIH Intramural Research Program. It does not apply to Foreign Sites, career development (K), research training (T) or fellowship awards (F) and current awards.
- Exceptions: VA sites; international sites; sites involving tribal nations.

Cooperative Research Requirement

Effective January 20, 2020 the Common Rule Cooperative Research Requirement states projects sponsored by signatories of the revised Common Rule, involving multiple research locations conducting human subjects research, with IRB approval dates on or after January 20, 2020, must use a sIRB. This is mandated by the Cooperative Research provision which expands upon and supersedes the NIH's Single IRB policy.

- Applies to: All sites in the United States participating in a federally funded cooperative research study (involves more than one site).
- Exceptions: 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 Research for which any Federal department of agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate.