MedStar Health

General Guidance for External or Single IRB (sIRB) Review at MedStar Health

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Background and Key Terms

In order to help facilitate human research by allowing investigators to avoid duplicative Institutional Review Board (IRB) review while at the same time protecting the rights and welfare of human research participants, MedStar Health is willing to establish IRB reliance agreements for research involving collaborations between two or more institutions. IRB reliance agreements allow for only one IRB review for research procedures completed by all collaborating personnel.

What is a Reliance Agreement?

A reliance agreement (also called an IRB Authorization Agreement or IAA) is a document signed by two or more institutions engaged in human subject research that permit one or more institutions to cede review to another IRB. The signed agreement permits a single IRB to review human subject research activities for more than one site.

What is the purpose of a Reliance Agreement?

A reliance agreement avoids duplicate IRB initial review and continued oversight when multiple IRBs have jurisdiction for the same multi-site research protocol. Once the agreement is executed, it can lessen the administrative burden and regulatory oversight of multiple institutions' IRBs.

Important to note that such agreements are limited to IRB review, and do not include ancillary committee reviews such as radiation safety, biosafety, etc.

Reliance Agreements can be the following:

- MHRI IRB serves as the IRB of Record for a study. The IRB of record means that a reviewing IRB that assumes IRB responsibilities for another institution. .
- MedStar Health relying on another IRB (commercial, federal or another institution) for a study
- Master Reciprocal IRB agreements: MHRI relying on partner IRBs for multiple studies. For a list of master agreements, contact the Office of Research Integrity (ORI) at MHRI.

Requesting External or Single IRB (sIRB) Review at MedStar Health

Before an IRB reliance agreement may be executed a formal request for reliance, whether for MedStar to rely on others or for use of the MHRI IRB as a sIRB to be relied upon needs to be submitted to the MedStar Health Research Institute (MHRI) Office of Research Integrity (ORI).

When relying on an external IRB MHRI must first authorize reliance on the external IRB before a study specific IRB reliance request can be submitted through the electronic IRB (eIRB) system. . A request to rely on an external IRB where MHRI does not already have an established relationship should be submitted in the form of an email to the MHRI ORI helpdesk at MHRI-ORIHelpDesk@medstar.net and should include:

Name of MedStar Requestor
Department and Facility of MedStar Requestor
Contact information for requestor

Name of External IRB
Point of Contact for External IRB
Contact information for the External IRB including mailing address, email and phone number
Status of accreditation

The MHRI ORI, in collaboration with appropriate Institutional Officials (IO), will review and determine whether to proceed with IRB Reliance with an external IRB. Once authorization is obtained, MHRI ORI will proceed with establishing an institutional profile in the eIRB system so that investigative teams may proceed with a request for study specific reliance.

Who approves MedStar's IRB Reliance Agreements?

The Institutional Official (IO) is vested with the authority to make the decision whether or not to review for or rely on another IRB. At MedStar, the IO is the President of MHRI. The IO is authorized to execute IRB Reliance Agreements on MedStar's behalf and may delegate this authority.

Factors that the Institutional Official will consider when deciding whether a proposed reliance agreement is appropriate:

- **Whether other IRB's policies and procedures meet MHRI standards.** If the other IRB is part of an AAHRPP-accredited HRPP, then it will be presumed that MHRI standards are being met. There are other ways to satisfy this requirement include: a third-party or a self-assessment, accreditation by an external organization, OHRP's QA Self-Assessment Tool or FDA's Self-Evaluation Checklist for IRBs or the Association for the Accreditation of Human Research Protection Programs (AAHRPP) Evaluation Instrument for Accreditation, or another approach that includes comprehensive review of the HRPP and assessment of the IRB. Depending on its scope, an audit by a federal agency, with no major issues identified and any minor issues corrected/resolved, may also be sufficient.
- **Risk level of study:** Can the study be reviewed using an expedited review procedure (minimal risk) or does the study require review at a convened meeting of the full committee?
- **Source of funding.** Which institution is the prime grantee?
- **Location of human research activities.** If research activities are not the same at both or all institutions, where will most of the contact with the research participants occur?
- **Personnel involved:** Is PI able to provide appropriate coordination and oversight of the study activities? What is the expertise of the personnel? Where is the primary appointment of the PI?
- **IRB expertise:** Which IRB has the most appropriate expertise to conduct the review?

How is an IRB reliance agreement documented?

The MHRI ORI Director will ensure that any required IRB reliance agreement is appropriately signed by the IOs/Delegates for both or all institutions involved and is kept on file in the Office of Research Integrity (ORI) for reference and review.

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Guidance for MedStar to rely on an External IRB or a Single IRB (sIRB)

MedStar Health will generally agree to rely on an external Institutional Review Board with appropriate approvals in place when MedStar or its employees or agents are engaged in human subject research. All requests for reliance on a commercial or single IRB need to be processed through the eIRB system. You can find instructions for that process here: Submitting a Study to be Reviewed by an External IRB

Please contact the ORI at MHRI-ORIHelpDesk@medstar.net if you wish to rely on a commercial or single IRB for which an institutional profile has not yet been established.

Why does MedStar need to review the study if the research team is relying on an external IRB?

The federal regulations governing human subject research include more than IRB Committee review. MedStar Health has other institutional responsibilities, which must be met such as ensuring research teams have the appropriate resources and expertise, have received training in the protection of human subjects and that any potential conflicts of interest have been mitigated or managed amongst other items. This institutional responsibility is not delegated to the reviewing IRB but must be reviewed in the context of individual projects.

The institution conducts an administrative review of the request to confirm at a minimum that:

- the institution/site has the expertise and resources to conduct the study
- the protocol does not otherwise violate any institutional policies, norms or practices
- any potential conflicts of interest have been managed
- the informed consent form contains (or there are plans to incorporate) required institutional language addressing for example compensation for research related injury, study costs/insurance and any required HIPAA clauses.

Once the above is confirmed, the reliance is approved.

What agreements are needed for a MedStar research team to rely on an external IRB?

MedStar Health Research Institute must enter into an agreement with the reviewing IRB to give them the authority to conduct IRB review for MedStar. This agreement may be referred to as an IRB Authorization Agreement or IRB Reliance Agreement.

MHRI IRB has signed the SMART IRB Agreement, which is a national reliance agreement developed under an award from the National Center for Advancing Translational Sciences. If the reviewing IRB the study team is working with has also signed the SMART IRB Agreement, this agreement can be used to cede IRB review.

If the reviewing IRB has not signed the SMART IRB Agreement and is not interested in signing that agreement, please contact the ORI which can provide a study-specific agreement to sign.

MedStar Health has also executed master reliance agreements with many of the commercial or independent IRBs including WCG (WIRB and Copernicus) and Advarra. If using another commercial IRB for reliance check with the ORI to determine if a master IRB Reliance agreement is in place.

If the reviewing IRB has signed the SMART IRB Agreement or MedStar has a master reliance agreement in place, do any other documents need to be obtained?

Yes, we will have to document MHRI's agreement to rely on reviewing IRB for the individual study. This can be done by obtaining a "Letter of Acknowledgment" or "Letter to Approve Reliance" and will be handled by the ORI during the review process.

What documents need to be submitted when requesting MedStar to rely on an external IRB?

MedStar requires that a draft protocol and draft/template informed consent form (ICF) along with site specific information about the study team and role of the local site be submitted with the request for reliance.

To request review by an external IRB, the MedStar investigator must submit the request in the Electronic IRB (eIRB) System. The process should be done prior to submitting to the external IRB. Once the ORI receives the submission, institutional review will occur.

Once review is complete the ORI will send the investigator **"Letter of Acknowledgment"** or **"Letter to Approve Reliance"** via the eIRB system representing MedStar's authorization to use the external IRB. The letter is very important because:

a. The external IRB will usually ask the research site for the authorization letter before it will review a study.
b. The authorization letter will contain a reminder about any MedStar required language to be included in the consent form.

If the external IRB has asked for a local site questionnaire requiring the completion of institutional information by the ORI, the completed questionnaire will also be provided in the eIRB system. If applicable, the eIRB system will also include the IRB Authorization Agreement and letters of agreement or authorization, signed by MHRI.

Please do not submit to any External IRB without the reliance approval.

When you receive approval, the research site can then submit to the External IRB.

Note regarding the informed consent form to be used in the study:

- Many of the commercial IRBs provide a service whereby they will automatically include MHRI required language at the time of review. However that is not the situation when relying on all external IRBs.
- It is the study team's responsibility to request that MedStar required language regarding COI disclosure where applicable, subject compensation and appropriate HIPAA authorization is included in the consent form for use at MedStar.
- If the external IRB has agreed to release a draft ICF for site review,
    - Once a draft ICF is received back from the external IRB after initial review, the MHRI study team will confirm that MHRI language is present and send the ICF to the Sponsor or Central Coordinating Site for their review, if applicable.
    - Once the Sponsor or Central Coordinating Site has agreed to the ICF, the MHRI study team will submit that tracked ICF back through the eIRB system for final ORI sign-off, where ORI review HIPAA and injury language in particular.

  - ORI will provide confirmation via the eIRB system that the ICF is acceptable, and the MHRI study team will then send the ICF back to the IRB for final review and approval.
- If the external IRB does not have a process to release a draft ICF for site review,
  - The study team will need to add MedStar template language to the ICF prior to reliance submission
  - Once the Sponsor or Central Coordinating Site has agreed to the ICF, the MHRI study team will submit that tracked ICF back through the eIRB system for final ORI sign-off, where ORI review HIPAA and injury language in particular.
  - ORI will provide confirmation via the eIRB system that the ICF is acceptable, and the MHRI study team will then send the ICF back to the IRB for final review and approval.

If I have approval to rely on an external IRB, do I need to submit anything to MedStar or MHRI in the future?

It is important to understand, that investigators still have reporting obligations, despite relying on an external IRB.

AFTER INITIAL IRB APPROVAL AND MEDSTAR INSTITUTIONAL APPROVAL:

- ***Reportable Events:*** All studies using an external IRB, regardless of when they started or received approval, must submit Reportable Events (i.e. ***unanticipated problems involving risks to subjects or others***) promptly to the IRB of Record, AND to the ORI. This is accomplished in the eIRB system through the Reportable New Information (RNI) process.
- ***Modifications***:
  a. ***Changes in Study Personnel***: All studies using an external IRB, regardless of when they started or received approval, must submit any *personnel modifications* to the ORI. The ORI will issue an institutional approval letter to add or remove the personnel. This is accomplished in the eIRB system through the Modification process. The PI needs institutional approval, and approval from the IRB of Record, if required by the IRB, to add the personnel.
  b. ***Changes or additions to MedStar locations/facilities*** All internal study location sites (additions or deletions of sites within MedStar) must be submitted as modifications to the ORI. The ORI will issue an institutional approval letter to add the site. These may also require review and approval by the sIRB
  c. ***Protocol and Consent Modifications***: All studies using an external IRB must submit any protocol or consent form modifications to the IRB of Record. Submissions to the ORI are **NOT** required.
  d. ***Submissions for Continuing Review, Recruitment materials*** (flyers, advertisements, etc.), ***Patient facing materials, and study progress reports*** do **NOT** need submission to ORI.

Final Reports:

A Final Report should be submitted via the eIRB system to the ORI when a study has been formally closed with the IRB of Record.

Guidance on Using MHRI IRB as a Single IRB (sIRB)

MHRI IRB may serve as a Single IRB for Multi-site studies on a limited case-by-case basis. If your site would like to use MHRI IRB as a single IRB, you should call the Office of Research Integrity (ORI) for guidance on whether MHRI would agree to serve this role and how to accurately budget and forecast costs in your proposal. There are costs associated with the use of MHRI as an sIRB

You may also opt and are encouraged to pursue the use of a commercial or independent IRB as the sIRB of record for your multicenter study. The ORI has contracts and contacts with most of the major commercial independent IRBs in the United States and will obtain a proposal for you if you wish to pursue this option.

What agreements are needed for an external site to rely on MHRI IRB to review and approve research from their site?

A relying institution (external site) must enter into an agreement with MHRI IRB to give us the authority to conduct IRB review for them. This agreement may be referred to as an IRB Authorization Agreement or IRB Reliance Agreement.

MHRI IRB has signed the SMART IRB Agreement, which is a national reliance agreement developed under an award from the National Center for Advancing Translational Sciences. If the other institutions you are working with have also signed the SMART IRB Agreement, this agreement can be used to cede IRB review.

If the external site has not signed the SMART IRB Agreement and is not interested in signing that agreement, please contact the ORI at MHRI-ORIHelpDesk@medstar.net, and we can provide a study-specific agreement to sign.

If the relying institution has signed the SMART IRB Agreement, do any other documents need to be signed?

Yes, we will have to document the relying institution's agreement to rely on MHRI IRB. This can be done by obtaining signatures on the "Letter of Acknowledgment".

How do I add an external site during the initial IRB review of this study?

External Sites can be added in the eIRB system when completing the initial submission application. On the application page titled "Study Locations," you should answer "yes" to the question "Does the study involve external sites?"

Additional questions will then follow, where you can indicate that external sites will be relying on MHRI IRB.

An "External Site Questionnaire" or "External Team Member List" should be completed for each relying institution. For example, if you have 5 relying institutions, this form should be complete 5 times. This form will then need to be uploaded into the eIRB system.

The forms are available on the MHRI website at https://www.medstarhealth.org/mhri/research-support/office-of-research-integrity-and-hrpp/human-research-protection/georgetown-medstar-eirb/#Policies

What is the "External Site Questionnaire"?

The External Site Questionnaire is the form we use to collect local information from the site when the study involves an intervention with human subjects. The form can be completed by the local MHRI study team in

conjunction with the external site and the form must be signed by the external site PI. The form is part electronic (data inputted directly to the eIRB system) and part Microsoft word document.

The PI of the local site does not need to be an account holder in the eIRB system. They are considered external team members and you would upload the external site questionnaire in the section for external team members.

Note: A separate form must be completed for each site.

What is the "External Team Member List"?

This is the form we use to collect the local information from the site when the study involves SOLELY the collection or analysis of biospecimens, data or information about human subjects from an external site. It should be completed by the local MHRI study team. However, the information in the form will need to be obtained in conjunction with the external site. The form is part electronic (data inputted directly to the eIRB system) and part Microsoft word document.

This form differs from the External Site Questionnaire as we recognize the activities and potential risks of an interventional study differ from those of a study which solely involves the collection or analysis of data or information about human subjects. Therefore the External Team Member List is an abbreviated document that does not go into as much detail as the External Site Questionnaire.

The PI and study team members of the external site do not need to be account holders in the eIRB system. They are considered external team members and you may upload the form in the section for external team members.

Note: A separate form must be completed for each site.

How do I add an external site after the study has already been approved?

After initial approval, the addition of an external site can be done through an Application for Modification and completion of the “External Site Questionnaire” or for studies only involving sharing of data the “External Team Member List”.

What training is required from investigators at external sites?

Study teams/investigators at external sites should follow the training requirements of their institution. If they do not have training requirements at their own institution, then they should follow the training requirements of MHRI Investigators

Do investigators at external sites need to submit an external interest questionnaire through MHRI’s COI Smart system?

No, Investigators at external sites should be using their own institution’s COI disclosure process and should not submit through the MHRI system. If an external site does not have its own COI Committee, please contact the ORI at MHRI to find the best strategy forward.

Is there a fee when MHRI IRB reviews for an external site?

Yes, MHRI IRB charges a fee to review for external sites. This fee is calculated based on the complexity of the project and the number of sites involved.

Could MHRI Research Compliance audit the non-MHRI sites?

Generally, auditing of external sites will be performed by that institution's compliance oversight mechanism, rather than MHRI Research Compliance. However, the authority for MHRI Research Compliance to audit will be outlined in the IRB Authorization Agreement.

Do external sites have any obligations to their own institution?

Study teams of all external sites are responsible for following the policies and procedures of their own institution when relying on an external IRB. They may or may not have an application process they must follow through at their own institution.

In addition, to following their Institutions policy and procedures, they will need to follow the ORI Policy and Procedures related to the MHRI IRB.

MedStar Health

Single IRB Plan for Multisite Study NIH Grant Applications – Where MHRI is the PRIME

Guidance and Instructions

Effective for applications received on or after January 25, 2018, the NIH requires multi-site grant applications to include a Single IRB Plan.

If your study falls under this mandate: Please email a formal request for reliance, whether for MedStar to rely on others or for use of the MHRI IRB as a SIRB to be relied upon to the Office of Research Integrity (ORI) as soon in the grant application process as possible and wait for the ORI's response before moving forward with the Single IRB Plan. You must consider the cost of a single IRB when planning your budget, whether utilizing an institutional or commercial/independent IRB. The ORI will provide you with a budget based on the number of protocols and sites contained within the grant proposal.

The request in the form of an email to should include:

- Name of MedStar Requestor
- Department and Facility of MedStar Requestor
- Contact information for requestor

- Name of National/Lead PI
- Institution of National/Lead PI

- Number of Sites that will rely on the MHRI IRB
- Name of Local PI(s) at each site
- Name of the Institution for each local PI

- Title of the Project
- Funding Source
- Copy of the Protocol/Grant/Summary of the project (which ever is available)
- MedStar's role in the project
- Expected number of human subject research projects which will be supported by the grant

Note: A formal, fully executed reliance agreement is NOT required to be in place prior to receiving NIH funding; nor is a final decision about which IRB will be used. It is sufficient to include in the Single IRB Plan that the participating sites are dedicated to using a single IRB to be determined in the future. Additionally, letters of support from participating sites can express that they are dedicated to relying on a single IRB, even if that single IRB has not yet been chosen, or if the decision to rely is contingent upon the institution's vetting of the single IRB's policies and procedures.

What content is needed in the sIRB plan?

- Describe how you plan to comply with the NIH sIRB policy. If requesting an exception for some or all participating sites, see NIH Guidance for Requesting an Exception.
- Provide the name of the IRB which will serve as the single IRB of record (sIRB)
- State that all currently identified participating sites have agreed to rely on said sIRB (or on a single IRB in general, if one has not been chosen).
- State that any sites which will be added in the future must agree to rely on the chosen sIRB.
- Describe the communication policy between the sIRB and participating sites

- State that all participating sites will sign an individual authorization agreement (IAA), also known as a reliance agreement, prior to initiating the study. State that the IAA/reliance agreement will specify the division of responsibilities between the sites.
- State which institution(s) will be responsible for maintaining records related to the IAA/reliance agreements and for maintaining a copy of the communication plan.
- *If your study meets the criteria for "delayed onset" human subjects research, do not create a separate sIRB plan, and instead see below.*

Delayed-onset multi-site research?

Delayed-onset human subjects studies are those for which there is no well-defined, detailed plan for human subjects involvement at the time of submission. If the delayed-onset research is likely to involve multiple sites, the delayed onset justification attachment (*not* a separate single IRB attachment) must:

- Include information about how the study will comply with the sIRB policy, and
- State that an sIRB plan will be provided prior to initiating the study.

Letters of Support/Commitments to Rely on Single IRB (Optional)

While the NIH does not specifically require Letters of Support, providing Letters of Support is one way to confirm that all participating sites are willing to rely on the selected sIRB (or on some sIRB, if none has yet been selected).

MedStar Health

Use of a sIRB administered by the Trial Innovation Network (TIN)

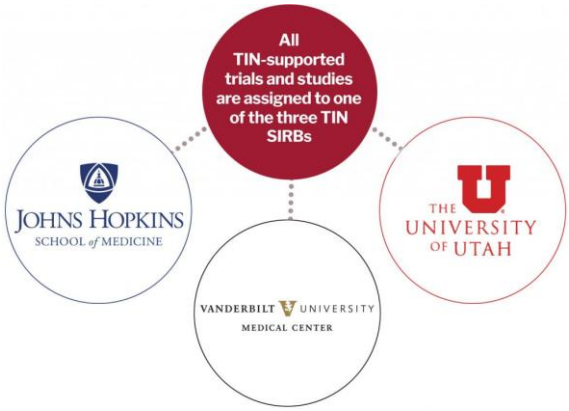
What is the Trial Innovation Network (TIN)?

The Trial Innovation Network is a collaborative initiative within the federally funded CTSA Program and is composed of three key partners – the CTSA Program Hubs, the Trial Innovation Centers (TICs), and the Recruitment Innovation Center (RIC). The Trial Innovation Network features a single IRB system, master contracting agreements, quality by design approaches, and a focus on evidence-based strategies to recruitment and patient engagement.

- ***MedStar Health Research Institute (MHRI) is a partner in the Georgetown and Howard Universities Center for Clinical and Translational Science known as GHUCCTS funded by the CTSA program.*** For more information: http://www.georgetownhowardctsa.org/home
- ***Investigators conducting federally sponsored research may apply for services provided by the GHUCCTS and the TINs including use of the TINs SIRBs.***

What is the Trial Innovation Network (TIN) single IRB (sIRB)?

The Trial Innovation Network (TIN) single IRB (SIRB) is a central IRB process and operating system that supports federally sponsored multi-center studies on a national level. It leverages the SMART IRB agreement. For more information: https://trialinnovationnetwork.org/elements/central-irb/



The TIN SIRB Goals:

- Serve as the single IRB for multi-center clinical trials and studies (learn who can and how to request resources here)
- Organize and harmonize SIRB activities and SOPs with other TIC SIRBs across the TIN
- Develop and disseminate operational innovations that support the single IRB review process
- Develop and disseminate educational materials for all single IRB stakeholders – IRBs, Coordinating Centers and Study Teams
- Create a framework for local workflows for when using a SIRB

Costs for single IRB review and coordination

The high demand for TIN single IRB (SIRB) review plus the time required from TIN staff to coordinate review of multi-center studies and trials has made it necessary to recover costs for both the review and the coordination. Coordination involves providing SIRB documentation and submission preparation, including navigation assistance from TIC personnel. Costs of SIRB review for federally-funded research may be included in a study budget as direct costs. The costs related to the single IRB process will be discussed with you by the Trial Innovation Center single IRB to which you are assigned.