# Geisinger IRB Investigator's Guide for Geisinger Serving as the Single IRB

**Geisinger Institutional Review Board Official Document**

Version 2/27/2023

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## Definitions

**Cooperative Research:** Non-exempt human subjects research to which the Common Rule regulations apply, that involves more than one institution engaged in the research.

**GIRB:** Geisinger Institutional Review Board

**HRPP:** Human Research Protection Program

**HRPP/Local Context Review**: Review process conducted by the relying institution's HRPP to verify compliance with state and local laws, and institutional policies. This also includes HIPAA review when the reviewing IRB does not serve as the privacy board to make HIPAA determinations.

**IRB Authorization Agreement (IAA)/Reliance Agreement**: An agreement between two or more institutions that are engaged in human subjects research, which economizes the IRB review and approval process by limiting the IRB review to one institution's IRB. The IAA documents the respective authorities, roles, responsibilities, and communication between the institution/organization providing the IRB review and the relying participating sites.

**Lead Principal Investigator (PI)/Lead PI:** In most cases, the lead PI is the Geisinger Principal Investigator. Some exceptions may include when GIRB is the sIRB, but Geisinger is not the lead site or is not a participating site in the research.

**Lead Study Team:** All individuals who are participating in coordinating and conducting the research at the lead site such as, investigators, study coordinators, project managers, regulatory managers, research assistants, biostatisticians, etc.

**Master Reliance Agreement:** An overarching IAA that is designed to cover all multi-center studies involving two or more sites.

**Point of Contact (POC):** The point of contact is an individual at a site who has been delegated to manage and coordinate communications related to the research. This individual should be knowledgeable about the research and the polices and requirements at his/her institution and serves as a liaison between their site and the other sites as well as the sIRB when necessary.

**Relying Site/Participating Site/Ceding Institution/Relying Institution/Local Site**: An institution that relies on an external reviewing IRB's regulatory review and approval and ongoing oversight for human subject research.

**Relying Site Principal Investigator (PI)/Site PI:** An investigator at a participating site who is overall responsible for the conduct of the research at the participating site.

**Relying Study Team:** All individuals who are participating in coordinating and conducting the research at a participating site such as investigators, study coordinators, project managers, regulatory managers, research assistants, biostatisticians, etc.

**Reviewing IRB/IRB of Record/External IRB/Reviewing Institution:** The IRB that is responsible for the regulatory review, approval, and continuing oversight of a particular study.

**Single IRB (sIRB):** The single IRB is the IRB that has been selected to carry out the IRB review requirements for participating sites involved in multi-site research. For multi-site research, the sIRB is the reviewing IRB.

**SMART IRB:** SMART IRB is designed to harmonize and streamline the IRB review process for multi-site studies, while ensuring a high level of protection for research participants. SMART IRB is not an IRB; rather, it's a platform that offers a master IRB reliance agreement (the SMART IRB Agreement) and a web-based system (SMART IRB's Online Reliance System) that provides a central process for participating institutions and their investigators to request, track, and document study-specific reliance arrangements. Investigators and their study teams, together with institutional and HRPP/IRB offices, use the SMART IRB platform to initiate single IRB review of a study. SMART IRB also provides a gateway to essential education as well as flexible tools and resources designed to support the adoption and implementation of single IRB review for a range of studies.

## Introduction

The use and implementation of the Single IRB (sIRB) is largely driven by regulatory requirements, including the NIH Single IRB Policy and the Department of Health and Human Services' Single IRB Requirement for Cooperative Research under the 2018 Common Rule (45 CFR 46). These sIRB requirements are intended to improve and streamline IRB review and approval for multi-site research so it can proceed as quickly as possible without compromising ethical principles and protections for human subjects that volunteer to participate in research.

The NIH Single IRB Policy took effect on January 25, 2018 and requires all domestic sites participating in multi-center research to use a sIRB when each site will conduct the same protocol. The NIH policy applies to all non-exempt human subjects research, whether supported through grants, cooperative agreements, contracts, or the NIH Intramural Research Program. The policy applies to all competing grant applications, including new grants, renewals, revisions, and resubmissions submitted on or after January 25, 2018. Please refer to the actual policy to determine if the policy applies to your research.

The requirement for sIRB review of cooperative research under the 2018 Common Rule became effective January 20, 2020. Cooperative research is defined as non-exempt human subjects research to which the regulations apply, that involves more than one institution engaged in the research. This rule requires all multi-site, domestic research supported by U.S. government funded agencies that have adopted the use of the Common Rule, to adhere to the regulations for cooperative research. Some research that is not subject to the NIH sIRB Policy may still be subject to the cooperative research requirements of the 2018 Common Rule.

GIRB is generally willing to serve as the sIRB for one or more relying sites whether or not the research is subject to the NIH Single IRB Policy and/or the 2018 Common Rule requirement for cooperative research. In all cases, when GIRB serves as the sIRB, relying sites are charged fees to offset the use of GIRB's resources including the time and effort of the IRB office staff and committee members.

While the main goal of the sIRB model is to streamline and enhance the IRB review and approval of multi-site research, sIRB processes developed at most institutions are not harmonized and vary greatly

between institutions. This document is designed to be a resource for investigators and research teams to effectively navigate Geisinger's sIRB process. Investigators are strongly encouraged to provide this document to sponsors, prime sites, lead investigators, and relying institutions when Geisinger will be the sIRB. Informing these stakeholders about our institutional sIRB process and requirements improves communication and sets clear expectations for all parties involved.

It is important to note that this guide only covers GIRB's sIRB process. Other applicable Geisinger research requirements such as those governed by Research Contracts and The Office of Sponsored Projects are not covered in this document.

## Mandatory sIRB Review

The NIH sIRB Policy and the Common Rule Cooperative Research requirement mandate the use of a sIRB for multi-site, non-exempt human subjects research unless an exception is granted. Understanding what is meant by "same protocol" is vital to knowing when the NIH Single IRB Policy applies. The NIH Single IRB FAQs state, *Protocols that address the same research questions, involve the same methodologies, and evaluate the same outcomes are considered to be the "same research protocol."* Additionally, sites that are accruing research participants for studies that are identical except for variations due to local context considerations are considered to be conducting the "same research protocol.""

The NIH further explained the concept of "same protocol" in a SMART IRB SMART Talk titled "A Conversation with NIH and OHRP about Single IRB". Sites that are engaged in research activities to address the same research questions and evaluate the same outcomes are subject to the NIH policy, regardless of whether they are conducting all or only part of the same protocol. In addition, if the NIH funds a site in a multi-site study, the NIH expects all other sites following the same protocol as the NIH-funded site to also follow the NIH Single IRB Policy (Adam Berger, NIH, Director, Division of Clinical & Healthcare Research Policy).

It is important to remember that the Common Rule may require sIRB review even when the NIH Policy does not. For instance, to determine whether the Common Rule Cooperative Research Rule applies, the cooperative research needs to be evaluated to determine if any research activities are non-exempt (i.e., one or more of the research activities or interventions are not allowable within any of the exemption categories at 45 CFR 46.104). If the cooperative research involves any non-exempt activities, the work of the employees and agents of each institution participating in the research must be evaluated under the 2008 OHRP Engagement of Institutions in Human Subjects Research Guidance. An institution engaging in any of the activities described under Section A, *Institutions Engaged in Human Subjects Research,* of the guidance, are also considered engaged in non-exempt human subjects research and the Cooperative Research Rule applies. Note that each institution that is engaged in cooperative research does not have to be conducting the same activities to be subject to the Common Rule Cooperative Research Rule.

OHRP has issued draft guidance for using a sIRB for cooperative research, which can be accessed here.

## Exempt Research

GIRB does not routinely make exempt determinations for other sites participating in multi-site research and will only consider requests to do so for 1) Student-Based sIRB Exceptions that meets the criteria described under the *Procedures* section, below and 2) on a case-by-case basis. Institutions with an established IRB generally need to rely on their designated IRB for exempt determinations. If a study meets exempt criteria at 45 CFR 46.104, GIRB will not serve as a sIRB unless there is a justifiable reason to make an exception.

## Requesting GIRB as the sIRB

Before agreeing that GIRB will act as the sIRB, the lead principal investigator (PI) needs to complete and submit the GIRB Single IRB Intake Form. After submission of this form, GIRB will review the submitted information and may schedule a meeting with the research team to talk in more detail about the study and the sIRB situation, if necessary. Based on the intake form and the meeting (if necessary), GIRB will determine whether it is willing to serve as the sIRB based on the expertise and resources required for the review and fulfillment of sIRB responsibilities. A Letter of Support will be provided if GIRB is willing to serve as the sIRB. Investigators are not able to indicate that GIRB is willing to serve as a sIRB without receiving a Letter of Support.

If this information is required to submit a grant application, the intake form needs to be submitted at least 4 weeks prior to the grant submission deadline.

## sIRB Fees

Fees apply when GIRB is the sIRB for a multi-site study. Fees will vary depending upon how the study is funded or supported, the type of IRB review required (expedite or full board) and the number of sites relying on GIRB. The current GIRB sIRB Fee Schedule can be found here. GIRB sIRB fees are a one-time upfront fee charged upon IRB review.

sIRB fees are estimated during review of the sIRB intake form. If GIRB determines it is willing to serve as the sIRB, the Letter of Support will include an estimate of the associated fees. The sIRB fees provided in the Letter of Support are an estimate and are subject to change based on the actual number of sites that rely on GIRB.

There are some research funding mechanisms for which GIRB may provide an exception and not charge sIRB fees. These include the Lehigh-Geisinger Joint Research Initiative and the Bucknell-Geisinger Research Initiative. During review of the sIRB Intake Form, GIRB will evaluate the sIRB resources required for the study and determine if the fees can be waived.

## sIRB Study Management

Lead PIs should contact relying site PIs and discuss the GIRB submission requirements and IRB review

process. Overall PIs should provide relying site PIs with this Investigator's Guide to help investigators get started. The relying site PIs should discuss the GIRB sIRB process with their local IRB office and ensure that they comply with their own institution's requirements for relying on a sIRB. Many relying institutions conduct an abbreviated review called an HRPP/local context review before agreeing to cede IRB oversight to an external IRB.
The lead PI and lead research team should plan to have resources and time available to assist and follow up with sites during the course of the study to manage the sIRB. Relying sites may need reminders and assistance from the lead PI and lead research team to properly navigate and comply with GIRB sIRB processes and requirements. The GIRB Reliance Team is happy to answer questions and talk with research teams at relying sites; however, it is the lead PI/research team's responsibility to regularly follow-up with relying sites to ensure that they are progressing. Relying sites that wish to meet with GIRB to discuss requirements and processes can contact the GIRB Reliance Team at irbreliance@geisinger.edu to schedule a meeting.

## IRB Reliance Agreements

A Reliance Agreement or IRB Authorization Agreement (IAA) is a written agreement between institutions participating in multi-site research that establishes the reviewing IRB for the research. The agreement is generally composed of terms that delineate the roles and responsibilities for each institution in the review, oversight, and conduct of the research. This includes the responsibilities related to local requirements, state law, and federal regulations. Reliance agreements can be established for a single study or for multiple studies (often referred to as a Master Reliance Agreement).

GIRB is willing to enter into Reliance Agreements to serve as the sIRB for multi-site research. The IAA can be a Master Reliance Agreement that applies to all human subjects research involving two or more sites, or it can apply to a single study.

Geisinger prefers to use the SMART IRB Master Reliance Agreement. SMART IRB was created to streamline the IRB reliance agreement process between institutions. The SMART IRB Master Reliance Agreement is a national master agreement that facilitates the authorization agreement process for participating institutions. A list of the signatories to the SMART IRB agreement is available on the SMART IRB participating institution webpage. Geisinger is a signatory to the SMART IRB Agreement.

If relying sites have not signed the SMART IRB agreement, an alternative agreement can be provided by GIRB. In these situations, the Geisinger standard Reliance Agreement may be used as is, or in modified form.

When GIRB is the sIRB, the GIRB Reliance Team will ensure that a reliance agreement is in place with each relying site and that the appropriate documentation is retained. The reliance agreement will be approved and executed by the appropriate officials of the organizations involved. If the reliance agreement has not been previously executed, GIRB will contact the appropriate individuals at relying sites to execute an agreement when it receives submissions to add relying sites to a study.

## Forms Required for sIRB Review

### 1. Single IRB Intake Form

The Single IRB Intake Form is used to initiate the sIRB process with GIRB. Prior to committing GIRB as the sIRB for a multi-site study or submitting anything for review to GIRB, investigators intending to use GIRB as a sIRB must first submit the sIRB Intake Form. This form is used to collect information required to determine whether GIRB is willing to serve as the sIRB and to provide a Letter of Support if it is determined that GIRB has the expertise and resources to fulfill this role. Investigators are not permitted to indicate that GIRB is willing to serve as the sIRB without receiving a Letter of Support. The sIRB Intake Form is also used to establish and provide IRB fees associated with sIRB review.

The sIRB Intake form is required for all research studies requesting to use GIRB as the sIRB, regardless of the funding (federal, NIH, industry, foundation, non-profit, internal Geisinger funding, etc.). Investigators submitting grant applications generally need to include sIRB fees in the overall grant budget at the time of grant submission. The sIRB Intake Form must be submitted to GIRB at least 4 weeks prior to the grant submission deadline to ensure sufficient time for GIRB review. GIRB reserves the right to decline serving as the sIRB when investigators do not budget for sIRB fees.

### 2. Local Context Form/Site Information Form

GIRB does not generally use a stand-alone local context form or site information sheet to obtain local context information from relying sites. Instead, the Relying Site Application referenced below includes local context information. In rare instances, GIRB may determine that the use of the entire Relying Site Application is not necessary and only require local context information. In these cases, the Relying Site Application will still be used, but not all sections will need to be completed.

### 3. Relying Site Application

The Relying Site Application is used to capture site and protocol specific details for each relying site. The Relying Site Application captures site specific details around many things including, but not limited to, local context, the plan and process for identifying and recruiting participants, the consent process, site specific differences in the study plan, vulnerable populations, HIPAA authorization and waivers, as well as the measures in place to maintain the privacy of the participants and the confidentiality of the data. The Relying Site application is not required for Student-Based sIRB Exceptions (see subsection for *Exception to Traditional Approach*, below, under the main *Procedures* section).

In order to approve relying sites, GIRB must have a clear understanding of all research activities that will occur at each relying site, at the same level of detail GIRB requires to know this information for Geisinger sites. This information is essential to ensure that the proposed research conducted at each site meets IRB approval criteria. The Relying Site Application concisely captures the necessary study details so GIRB does not need to try and piece details together that may be scattered throughout the study application, protocol, and other study

documents.

While specific details may sometimes be included in the existing iRIS Study Application and/or protocol documents, the Relying Site Application will generally always be required when adding a relying site under GIRB approval. GIRB strongly encourages limiting details in the main study application to details about the conduct of the research at the lead site. The only exception is when the consent and HIPAA Authorization requirements for a relying site differ from the provisions that GIRB has approved for other sites. Requests for additional waivers or alterations of consent and HIPAA Authorization for relying sites need to be indicated and justified in the main study application. When different provisions apply to only certain sites relying on GIRB, the iRIS Study Application should indicate the specific sites for which HIPAA waivers and/or alterations are requested.

This form is a living document. When study specific details change that impact the information in the Relying Site Application, a revised form will need to be submitted to the IRB for review and approval.

The Relying Site Application should be provided to the study team point of contact (POC) at the relying site. The relying site study team POC should work with the site PI, other members of the relying site research team (as necessary), and a member of the relying site IRB and/or HRPP Office to complete the application. Once completed, the application should be provided back to the lead study team POC for submission to GIRB. A Relying Site Application is required for each relying site.

There are instructions built into the Relying Site Application to guide relying sites that are considered to be data only sites (see subsection for *Streamlined Approach for Data Only Sites*, below, under the main *Procedures* section). These sites will only need to complete the applicable sections outlined in the Relying Site Application.

4. Relying Site Continuing Review Form

The Relying Site Continuing Review Form is only used for studies that are subject to continuing review requirements. This form is used to collect information about the conduct of the research over the past approval period, at a relying site. A Relying Site Continuing Review Form is required for each relying site each time a continuing review is submitted. Each Relying Site's Continuing Review Form must be submitted as attachments to the lead site's Continuing Review submission to GIRB.

## Division of Responsibilities

There are several key stakeholders involved in the processes required for sIRB review, approval and continued oversight, and each maintains different responsibilities essential to the establishment of an effective sIRB relationship and adequate protection of human research participants. The table below outlines the key stakeholders responsible for several key aspects of GIRB's sIRB process. Most tasks are able to be delegated by the responsible key stakeholder; however, there are some pieces that should not be delegated, such as a relying sites' HRPP involvement in completing the Relying Site Application.

| Task | Responsible Stakeholder(s) |
|---|---|
| 1. Requesting GIRB as the sIRB via sIRB Intake Form | Lead Site Principal Investigator/Lead Site Study Team |
| 2. sIRB fee estimate | GIRB |
| 3. Communication of GIRB sIRB processes, requirements and relevant policies to participating sites[1] | Lead Site Principal Investigator/Lead Site Study Team[2] |
| 4. Initial Submission for sIRB oversight via iRIS | Lead Site Principal Investigator/Lead Site Study Team |
| 5. Completion of Relying Site Application | Relying Site Principal Investigator/Relying Site Point of Contact AND Relying Site HRPP[3] |
| 6. Development of Participating Site study documents and materials | Relying Site Principal Investigator/Relying Site Point of Contact |
| 7. IRB submissions to GIRB via iRIS for the addition of participating sites | Lead Site Principal Investigator/Lead Site Study Team |
| 8. Execution of Reliance Agreement | GIRB and Relying Site HRPP |
| 9. Completion of the Relying Site Continuing Review Form | Relying Site Principal Investigator/Relying Site Point of Contact |
| 10. Obtaining and collecting study-wide information for continuing review submission to GIRB | Lead Site Principal Investigator/Lead Site Study Team |
| 11. Continuing Review and Amendment submissions to GIRB via iRIS | Lead Site Principal Investigator/Lead Site Study Team |
| 12. Ethical review, approval and oversight of all human subjects research activities in accordance with IRB approval criteria set forth in 45 CFR Part 46.111 and 21 CFR Part 56.111 | GIRB |
| 13. Written notification to participating sites and investigators of GIRB's decisions to approve, disapprove or require modifications to proposed research activity | GIRB |
| 14. Providing copies of IRB approved materials to Relying Site Principal Investigator/Relying Site Study Team | Lead Site Principal Investigator/Lead Site Study Team |
| 15. Initial notification to GIRB of all apparent serious or continuing non-compliance and/or unanticipated problems | Lead Site Principal Investigator/Lead Site Study Team and/or Relying Site Principal Investigator/Relying Site Point of Contact and/or Relying Site Principal Investigator/Relying Site Point of Contact |
| 16. Formal submission of all apparent serious or continuing non-compliance and/or unanticipated problems to GIRB via iRIS | Lead Site Principal Investigator/Lead Site Study Team |
| 17. Determinations of serious or continuing | GIRB |

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|---|---|
| non-compliance and/or unanticipated problems | |
| 18. External reporting for serious or continuing non-compliance and/or unanticipated problems | GIRB and/or Relying Site HRPP[4] |
| 19. Study closure reports via iRIS | Lead Site Principal Investigator/Lead Site Study Team |

[1] GIRB will meet with participating site key stakeholders upon request; however, initial communication of GIRB's sIRB processes and requirements is the responsibility of the Lead Site Principal Investigator and/or Lead Site Study Team
[2] When Geisinger is a participating site, the Geisinger PI and Study Team already have access to this information and relevant documents. They are responsible for providing the information to the other sites. When Geisinger is not a participating site, the GIRB Reliance Team will meet with the non-Geisinger Lead Site PI and Study Team and provide them the necessary documentation. The Lead Site Principal Investigator/Lead Site Study Team is then responsible for providing the information to the relying sites
[3] An individual from the participating sites' HRPP is required to sign off on the Relying Site Application to confirm that all regulatory details pertaining to the IRB review and approval of the site are accurately reflected in the Relying Site Application
[4] GIRB generally assumes responsibility for all external reporting of events determined to meet the criteria for serious or continuing non-compliance and/or unanticipated problems; however, there may be circumstances where the Relying Site HRPP is better positioned to prepare the and send reports

## Communication with Relying Sites

As the reviewing IRB, GIRB is responsible for communicating its decisions related to the review of research to relying institutions and investigators. When relying site study personnel are added in accordance with the requirements under the *Key Study Personnel* section below, the individuals added to the iRIS study application as "Study Contacts" will receive official electronic correspondences outlining GIRB's decisions and/or requirements for obtaining approval.

The HRPP at a relying institution may also request to receive such correspondences. This needs to be directly communicated to GIRB so an iRIS user account can be created for the HRPP office. Investigators will need to add the iRIS user account for the HRPP office as a study contact in section 3.0 of the iRIS Study Application.

## Procedures

### 1. Submitting a New sIRB Study

There are three main pathways that can be followed to submit a new sIRB study to GIRB, and the appropriate pathway is dependent upon the study design and involvement of each relying site engaged in the research. The pathways include:

1. **Traditional Approach** - Submit initial application to obtain IRB approval for Geisinger or the lead site, followed by amendment(s) to obtain approval for the relying site(s)
2. **Streamlined Approach for Data Only Sites** - Submit initial application to obtain IRB approval for Geisinger or the lead site and include any sites where the engagement in research is limited to providing or working with data
3. **Exception to Traditional Approach** - Alternate approach for student-based research and alternate approaches determined on a case-by-case basis

It is important to note that any sIRB scenario may allow for both the Traditional Approach and the Streamlined Approach for Data Only Sites to be employed. Sites only providing or working with data for the study can be added following the procedures outlined under the Streamlined Approach for Data Only Sites, whereas sites engaged in other research activities must be added under the procedures detailed under the Traditional Approach, unless GIRB determined that the sIRB scenario presented an Exception to the Traditional Approach.

It is also important to be aware that the Policies and Procedures at the relying institution may prevent the Streamlined Approach for Data Only Sites to be used. Many institutions require for a multi-site study to have IRB approval at the lead site before they will conduct a local context review and agree to ceded oversight. In these cases, the Traditional Approach will need to be followed, submitting for initial IRB approval at the lead site, followed by amendments to add relying sites.

Regardless of the approach to be followed, at the time of initial submission, the main Geisinger study application should be completed as follows:

| **Study Application – Section 4.5 – Multi-Site Study** |
|---|
| Is this a multi-site study?<br><br>☒ Yes ☐ No<br><br>*Check "Yes"* |
| Is Geisinger the lead site of the multi-site study? (Note: This question will appear if the previous question was answered to indicate that this is a multi-site study)<br><br>☒ Yes ☐ No<br><br>*Provide appropriate answer* |
| **Study Application – Section 4.6 – Location of Research** |
| The research will be conducted at (check all that apply):<br><br>☐ Geisinger/Geisinger affiliated facility<br>☐ Non-Geisinger facility that is engaged in human subjects research<br>☐ Non-Geisinger facility that is not engaged in human subjects research<br><br>*From the available selections, select all that apply to the current multi-site research study that is being submitted to GIRB as the sIRB.* |
| You have indicated that non-Geisinger sites are engaged in human subjects research. Will any other sites participating in the research rely on Geisinger IRB (GIRB) review and approval? **If some sites will rely on GIRB and some sites will rely on another IRB, please check both options**. (Note: this question appears if the response to the previous question) includes "Non-Geisinger facility that is engaged in human subjects research")<br><br>☐ Yes, other sites will rely on GIRB as the reviewing IRB<br>☐ No, other sites will obtain their own IRB approval |

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|---|
| Please list other sites that will rely on GIRB IRB Review (Note: this question appears if the response to the previous question includes “Yes, other sites will rely on GIRB as the reviewing IRB”) |

## 1. Traditional Approach

These procedures should be followed when the relying sites are engaged in research activities that are not limited to providing data (e.g., data within the electronic health record at an institution) and/or working with data collected as part of the study (e.g., performing data analysis). Institutions that are involved in recruitment, consenting, interacting with, and conducting interventions with subjects will typically need to follow these steps.

The initial submission, review, and approval for a sIRB study will only cover Geisinger (or the lead site if not Geisinger). The initial review will include review of the study protocol, Geisinger/lead site/template consent form, any study wide forms and documents (including templates) intended for use at all sites, as well as all necessary Geisinger ancillary reviews. For an initial submission under the Traditional Approach, the main study application must not contain any investigators or other study personnel from sites that will be relying on Geisinger, in Section 3.0 of the main study application.

All relevant documents customized for Geisinger or the lead site need to be included with the initial submission, or clearly state in the submission that they will be submitted as a future amendment prior to use. Investigators must submit the following documents as attachments to the initial submission when they are applicable to the study:

- Protocol
- Consent/Parental Permission/Assent/LAR Forms – Geisinger* or lead site versions AND Templates
- Lead site and template recruitment forms
- HIPAA Authorization Forms
- Geisinger Billing Determinations*
- Geisinger*, study wide and/or template recruitment materials
- Case Report Forms
- Investigator Brochures
- FDA Letters
- Study Wide Forms and Documents (lead site specific and templates)
- Documentation of Geisinger Security, Compliance and Privacy (SCP) Research Pre-Screen Questionnaire/CORL Review completion*
- MyCode Data and Sample Request Form and MyCode Governing Board Approval
- Geisinger Radiation Safety Review*
- Geisinger IBC Approval*
- Geisinger Health Plan (GHP) proposals and approvals*
- Any other materials at the request of the IRB

* Should only be included with the initial submission when Geisinger is the lead site

Note that in most cases, the lead site consent form and HIPAA Authorization form can serve as the template. If this is the case, there is no need to create a separate template for sites to follow, they can follow the lead site's version.

GIRB recognizes that study protocols may be created to include site specific details for other participating relying sites. Regardless of the information for relying sites included in the protocol, the initial review and approval under the Traditional Approach will generally only cover Geisinger sites and/or the lead study site, if not a Geisinger site. For simplification of the review process, GIRB strongly encourages investigators to omit from the initial submission, when able, study specific details pertinent to relying sites.

After an Investigator receives an approval letter for the lead site and all relevant study documents and materials, an amendment can be submitted to add relying sites. See subsection for *Adding a New Relying Site* below.

### 2. Streamlined Approach for Data Only Sites

Initial study submission procedures for the Streamlined Approach for Data Only Sites can be followed for the lead site and any relying sites that are only engaged in research activities limited to providing data such as data encompassed with in the electronic health record at that institution and/or working with data collected as part of the study, such as performing data analysis.

Submission of the initial application must include a Relying Site Application for each data only site relying on GIRB. The Relying Site Application includes specific instructions for Data Only Sites since some of the information collected on the application will not be applicable. In addition, investigators must submit the following documents as attachments to the initial submission when they are applicable to the study:

- Protocol
- Consent/Parental Permission/Assent/LAR Forms – Geisinger* or lead site versions AND Templates
- HIPAA Authorization Forms
- Geisinger Billing Determinations*
- Geisinger*, study wide and/or template recruitment materials
- Case Report Forms
- Investigator Brochures
- FDA Letters
- Documentation of Geisinger Security, Compliance and Privacy (SCP) Research Pre-Screen Questionnaire/CORL Review completion*
- MyCode Data and Sample Request Form and MyCode Governing Board Approval
- Geisinger Radiation Safety Review*

- Geisinger IBC Approval*
- Geisinger Health Plan (GHP) proposals and approvals*
- All additional documents specific to the conduct of the research at the relying sites being added following the streamlined approach
- Any other materials at the request of the IRB

* Should only be included with the initial submission when Geisinger is the lead site

Approval of the initial study application following the streamlined approach will include approval for Geisinger (or the lead study site) and any site where the research activities are limited to providing or working with data. Sites engaged in other research activities will need to be added following the steps outlined under the Traditional Approach above, unless GIRB makes an exception as described below.

## 3. Exception to Traditional Approach

There are two types of exceptions that GIRB considers which are described below. The two exceptions are 1) Student Based sIRB Exception and 2) Other Exceptions.

1. Student-Based sIRB Exception

   Students are often onboarded as part of the Geisinger Clinic workforce for a variety of academic reasons. Often times students need to complete research through their experience at Geisinger in order to fulfill academic requirements. In these situations, the student's involvement in the research may engage both Geisinger and their academic institution when the research is conducted to fulfill the student's academic requirements.

   Student-based research is research that is being conducted fully or partly to meet the student's academic needs, but the engagement of the academic institution in research is limited to the student's involvement in the research and no other individuals at the academic intuition (e.g. Thesis Advisor) are engaged in human subjects research activities. Note, other individuals at the academic institution may be engaged in other non-human subject research activities.

   In these situations the academic institution may prefer to enter into a reliance agreement with GIRB. When the student is the only individual engaging the academic institution in the research, GIRB will enter into a reliance agreement for both exempt and non-exempt student-based human subjects research.

   For Student-Based sRIB exceptions, The Relying Site Application does not need to be completed and submitted to GIRB. A site PI from the academic institution can be identified and added to the iRIS application as an Additional Principal Investigator and a Study Contact. This can be a mentor, thesis advisor, or other personnel willing to fulfil the responsibility. However, this individual should not be engaged in human subjects research unless GIRB makes an additional exception. The Student-Based Research

Exception is specific to research that is being conducted fully or partly to meet the student's academic needs, but the engagement of the academic institution in research is limited to the student's involvement in the research and no other individuals at the academic intuition are engaged in human subjects research activities.

If a site PI is not identified or appointed, either an individual from the academic institution who should receive IRB correspondences about the study should be added as a study contact in the main iRIS study application, or a general mailbox should be provided to which the IRB correspondences can be sent. GIRB must comply with the regulatory requirements at 45 CFR 46.109(d). As the sIRB, GIRB needs to notify investigators and institutions in writing of its requests, determinations and actions related to research under its oversight. It is recommended to consult with the academic institution's HRPP about who should receive IRB correspondences related to the study, if there is no one to serve as the PI for the academic institution.

2. Other Exceptions

   Since sIRB scenarios can be very cumbersome to navigate, GIRB may grant an Exception to the Traditional Approach on a case-by-case bases. GIRB will consider additional exceptions on a case-by-case basis for multi-site research, such as when each site is responsible for conducting separate parts of the protocol to meet the study aims and the entirety of the initial IRB approval is dependent upon understanding each site's role in the research to ensure IRB approval criteria are met. Please note, that not every study that where each site is only conducting a separate part of the protocol will qualify for an exception.

   Investigators who believe that their sIRB scenario may require an exception to the Traditional Approach or the Streamlined Approach for Data Only Studies should contact the Geisinger IRB Office and request a consultation. IRB staff will provide further guidance on the appropriate steps and documents to be submitted following a detailed discussion about the study and the sIRB scenario.

Regardless of the approach to be followed, initial submissions for sIRB studies follow the same review process as any expedite or full board study submission. Once training and conflict of interest are verified, submissions are assigned to the GIRB Reliance Team for pre-review. After a pre-review determines that the submission is complete and absent any major deficiencies, the submission is assigned to the appropriate review process. During IRB review of the initial submission, investigators can be notified by an outcome letter whenever revisions, clarifications, or additional information are required to assist the IRB in determining whether the proposed research meets IRB approval criteria. Receiving such an outcome letter requires the investigator to prepare and submit a submission response, addressing the stipulations in the outcome letter. If the submission response is adequate, it will be routed to the appropriate stage of the review process.

## 2. Adding a Relying Site

Adding a relying site generally involves submitting a completed Relying Site Application and site-specific study documents to GIRB for review and approval. The Relying Site Application is not a form built within iRIS, but rather it is a separate fillable document that is completed and then added as an attachment to a submission form in iRIS as an "Other Study Document".

The Geisinger or lead site research team must provide a copy of the Relying Site Application to relying site POC and have the relying site investigators and/or research teams, along with their IRB/HRPP Offices complete the form with the study-specific and regulatory details that pertain to their respective sites. This must be done prior to submission to GIRB to add a relying site.

Under most circumstances, the lead site PI is responsible for submitting all submissions to GIRB. On occasion, GIRB may be the sIRB for a multi-site study where Geisinger is not the lead site. When this occurs, the Geisinger lead investigator can assume all IRB submission responsibilities for the multi-site study since he/she is likely most familiar with GIRB's electronic submission requirements and processes. When Geisinger is not a participating site in the research, the lead site PI is responsible for submitting all IRB submissions to GIRB. Geisinger's iRIS system is not set-up in a manner that easily allows participating sites to submit their own site-specific IRB submissions for review and approval. Having one site responsible for all sIRB submissions centralizes the management and oversight of all study related IRB manners and allows GIRB to maintain clear records for IRB reviews and approvals.

### 1. Adding a Relying Site under the Traditional Approach

Under the Traditional Approach, after GIRB has initially approved Geisinger (and/or the lead study site), relying sites are added by submitting amendments. Geisinger (or the lead site) investigator will need to submit an IRB amendment (or series of amendments) in iRIS along with completed Relying Site Applications. The amendment needs to include all study materials specific to the sites being added (site specific consent forms, recruitment materials, scripts, etc.). The amendment form needs to identify the relying site(s) that are being added with the amendment and the individual who will serve as the PI at each site. If an additional POC is also being added, this individual and their role on the study also need to be identified in the amendment form. If multiple sites are being added with one amendment, a completed Relying Site Application needs to be attached for each site that is being added. Not all sites need to be added with one amendment.

Section 3.0 of the main study application needs to be revised to add the appropriate study personnel from the relying sites. The addition of relying site study personnel needs to follow the requirements outlined in the *Key Study Personnel* section, below.

Amendments to add relying sites are generally considered a minor modification to the study and are reviewed through expedite review procedures when the site will following the same protocol that has already been reviewed and approved, and site specific variances in the conduct of the research related to local context information do not present more than minimal risk to the participants.

### 2. Adding a Relying Site under the Streamlined Approach for Data Only Sites

Under the Streamlined Approach for Data Only Sites, data only sites can be included and approved with the initial IRB submission. The initial submission must clearly identify the data only sites that are being included for approval with the initial submission and needs to include all study materials specific to the sites being added. Section 3.0 of the main study application must be completed with the appropriate study personnel from the relying sites. The addition of relying site study personnel needs to follow the requirements outlined in the *Key Study Personnel* section, below.

### 3. Adding a Relying Site under an Exception to the Traditional Approach

1. Student-Based sIRB Exception

   Under the Student-Based sIRB Exception, the addition of academic institutions only engaged in research through student involvement in a research project at Geisinger can be included and approved with the initial IRB submission. In cases when an active study is being transitioned to accommodate student-based research, an amendment can be submitted to add the student and academic institution.

2. Other Exceptions

   The addition of relying sites for other Exceptions to the Traditional Approach are determined on a case-by-case basis. GIRB will provide customized instructions for adding relying sites based on each unique situation.

### 3. Modifying a Previously Approved GIRB Study to a sIRB

Situations may arise where an investigator opens a study that was not initially intended to be a multi-site study, or it was not intended for other sites participating in a multi-site study to rely on GIRB. In either case, an investigator can amend an already approved study and request for GIRB to be the sIRB for other sites participating in the study. In these instances, investigators should first contact GIRB Office to discuss the necessary steps to be taken. Generally, IRB fees will still apply.

## Continuing Review

Continuing review requirements are determined by the approval status of the study. Studies subject to Food and Drug Administration (FDA) regulations are required to submit for continuing review in accordance with FDA regulations at 21 CFR Part 56.109(f). Research not subject to FDA regulations will follow the requirements of the Common Rule at 45 CFR Part 46.109(e) and (f).

The lead site PI is responsible for collecting all necessary information from each relying site and submitting it to GIRB on a Continuing Review Form in iRIS. The Relying Site Continuing Review Form must be completed by each relying site lead PI and submitted as an attachment to the Continuing

Review Form in iRIS when it is submitted. While this form gives the Geisinger IRB specific details about the research activity at each relying site, it also helps the lead PI collect and organize the information necessary for submitting the continuing review. Section 1.8 of the iRIS Continuing Review Form should reflect the continuing review details for both Geisinger and/or the lead site, as well as the combined research activity at all sites. For example:

| **Continuing Review Form – Section 1.8 – Number of Subjects (from start of study):** |
|---|
| Number contacted: *Lead site – 27; Total – 89* |
| Number screened: *Lead site – 22; Total – 76* |
| Number screen failures: *Lead site – 5; Total – 16* |
| Number enrolled: *Lead site – 17; Total – 60* |
| Number withdrawn: *Lead site – 3; Total – 11* |
| Explain why withdrawn: Lead site details only; relying site details are captured in The Relying Site Continuing Review Form. |
| Number deceased: *Lead site – 0; Total – 0* |
| Number completed: *Lead site – 0; Total 3* |

Sections 1.9, 1.12, 1.16, 1.17, 1.18. 1.19, and 1.20 should be answered in context of the overall study.

Sections 1.13, 1.14 and 1.15 of the iRIS continuing review form should be completed with the details specific to the lead site AND the overall study. For example:

| **Continuing Review Form – Section 1.15 - Have there been any protocol deviations over the past review period?** |
|---|
| ☒ Yes ☐ No<br><br>If yes, please provide an overview or upload a copy of the spreadsheet outlining the protocol deviations*.<br><br>*Geisinger – 2 subjects had their end of study follow-up visits out of window*<br>*Relying Site 1– 3 subjects were not asked to complete the quality-of-life questionnaires at study visit 3*<br>*Relying Site 2 – 1 subject had the three-month CT scan out of window*<br><br>*Instead of detailing out all deviations as shown above, a spreadsheet detailing all deviations can be uploaded and attached to the iRIS Continuing Review Form. |

When the first Continuing review form is submitted, each Relying Site Continuing Review Form should be uploaded as a new study document. It is recommended to clearly title the document when uploading to iRIS (2022 Continuing Review Form for [INSERT NAME OF RELYING SITE]). For each subsequent continuing review, Relying Site Continuing Review Forms must be checked-in using the check-in/checkout function in iRIS, to make use of the document library and keep the files organized. All continuing reviews should be submitted in iRIS no later than 30 days prior to the study's expiration date. GIRB recommends submitting continuing review forms at least 60 days prior to the study's expiration

date in case any significant deficiencies are discovered that must be remedied to grant IRB approval for study continuation.

## Modifications to sIRB Studies Following Initial Approval

After initial approval of an sIRB study, changes to the research and study documents must be submitted to GIRB as an amendment via an iRIS Amendment/Modification form. All changes and revised documents need to be submitted to GIRB for review and approval prior to implementation unless an immediate change is necessary to eliminate an apparent hazard to subjects.

Amendments may impact study wide materials and/or some or all sites where the research is being conducted. Modifications to template documents should also be reflected in customized, site-specific documents when applicable. Revised documents must be checked-in and not uploaded as a new study document. GIRB will approve the revised templates (if applicable) as well as the revised site-specific documents. Revised Relying Site Applications must be submitted when the study changes impact relying site specific information within the form. Revised Relying Site Applications must be checked-in and not simply uploaded as a new study document.

Generally, review of amendments will be dependent upon the risk level of the study and the type and level modifications being proposed with the amendment. Amendments not impacting the risk/benefit ratio and/or not making alterations the present greater than minimal risk to participants will be assigned for expedited review. Changes that largely impact the risk/benefit ratio and/or present greater than minimal risk to participants will be assigned for convened review.

## Key Study Personnel

When GIRB is the sIRB, the relying institution and investigators have the primary responsibility to assess the study personnel qualifications and training at the time of initial review and throughout the life of the study. Relying institutions may use a coordinating center to perform this role, but this must be clearly documented and communicated to GIRB. The SMART IRB Harmonization Guidance, *Responsibilities Associated with the Review of Study Personnel* serves the basis to GIRBs approach to managing and overseeing the training and qualifications of research personnel at relying institutions. Under most circumstances, the relying institution is responsible for overseeing the training and conflict of interest reporting of the local investigators and study team members (Standard Approach, described below).

There are two scenarios that dictate GIRB's approaches to managing and reviewing Key Study Personnel as a sIRB, and they are dependent upon whether or not the relying Institution is following Geisinger's Financial Conflict of Interest (COI) policy and whether or not the relying institution is following Geisinger's policy for human subjects training requirements for study personnel.

The two scenarios that dictate GIRBs approaches to managing and reviewing Key Study Personnel as the sIRB are:

1. Standard Approach: The relying institution is not following Geisinger's COI policy or Geisinger's policy for human subjects training requirements

2. Reliance Approach: The relying institution is following Geisinger's COI policy and/or the relying institution is following Geisinger's policy for human subjects training requirements

If the relying institution does not have training requirements for investigators and study staff, there are two options:

1. Follow GIRBs
2. Follow an alternate strategy

If following an alternate strategy, details need to be provided in Part C of the Relying Site Application. GIRB will assess these details and determine if they are adequate and support proper oversight of human subject research training.

Please refer to the Conflict-of-Interest section below for more information around how Geisinger HRPP manages financial conflicts of interest when GIRB is the sIRB.

### 1. Standard Approach

The Standard Approach should be used when:

- The relying institution is not following Geisinger's COI policy, and
- Has their own human subjects training requirements for investigators and study staff, or
- Is following an acceptable alternate strategy to monitor and oversee human subjects training

When following the standard approach, the individual serving as the relying site principal investigator must be listed on the iRIS Study Application in Section 3.0, *Assign Key Study Personnel (KSP) Access to the Study*, as an "Additional Principal Investigator". This individual must also be listed as a "Study Contact" so that he/she receives correspondence related to IRB decisions and actions that impact the research. When institutions are not following Geisinger's COI Policy, no other members of the relying site research team should be added to Section 3.0 of the Study Application unless there is an additional person who should receive IRB correspondences for the study (e.g., relying site POC).

### 2. Reliance Approach

The Reliance Approach should be used when:

- The relying institution is following Geisinger's COI Policy, and/or
- The relying institution does not have human subjects training requirements for investigators and research staff and is following Geisinger's requirements

When following the Reliance Approach, all individuals serving as an investigator must be listed on the iRIS Study Application in Section 3.0, *Assign Key Study Personnel (KSP) Access to the Study*. An Investigator is the principal investigator or program director and any other senior/key personnel, regardless of title or position, who is responsible for the design, conduct, or reporting of research (which may include, for example, collaborators and consultants), regardless of

research funding source.

- The individual serving as the relying site principal investigator must be listed as an "Additional Principal Investigator". This individual must also be listed as a "Study Contact" so that he/she receives correspondence related to IRB decisions and actions that impact the research.
- If the relying institution is ONLY following Geisinger's COI policy - All other investigators at the relying site must be listed as "co/sub-investigators". Since Geisinger HRPP is responsible for the review and management of COI for these investigators, they must all be included on the Study Application to facilitate adequate oversite of COI. No other members of the relying site research team should be added to Section 3.0 of the Study Application unless there is an additional person who should receive IRB correspondences for the study.

If the relying site is following Geisinger's training requirements and therefore completing CITI training under affiliation with Geisinger - all investigators and members of the research team (at the relying site) should be added to section 3.0 of the Study Application in their appropriate roles, in this situation. Geisinger HRPP is responsible for the review and oversight of training for these individuals, so they must be included on the Study Application to facilitate adequate oversite.

For either approach (Standard or Reliance), if there is another member of the research team who will serve as a POC and needs to receive IRB related study correspondence, he/she should be listed as a "Study Contact" in Section 3.0 of the Study Application. Often, the POC may be a study coordinator or other member of the research team who helps oversee the management of the research at the relying site.

Any individual given a formal role in Section 3.0 of the Study Application, such as "Additional Principal Investigator," "Co/sub-investigator," "Study Coordinator," "Research Assistant," etc., is required to have a CV and/or NIH biosketch uploaded under his/her iRIS user profile and training will need to be validated and entered into the iRIS account as well. COI must also be documented in iRIS accounts for investigators (anytime they are listed on the iRIS Study Application), regardless of whether they are following Geisinger's COI Policy. Please consult with the Office of Research Compliance to verify the adequacy of training and COI reporting prior to sending requests to GIRB for iRIS user accounts.

Since most external study personnel will not need iRIS log-in access, GIRB staff will upload CVs/biosketches into individual iRIS user accounts when they are created for external individuals being added to a sIRB study. When requesting iRIS accounts for external users, lead investigators will need to indicate when the external user will need log-in access and provide justification for the access.

### Financial Conflict of Interest

When serving as a sIRB, GIRB employs a flexible approach that is consistent with SMART IRB recommendations for reviewing and managing financial conflicts of interest (COI). There are three scenarios that dictate the review and management of COI for a study under sIRB:

1. The research is Public Health Service (PHS) funded, and the relying institution has a PHS compliant policy
2. The research is PHS funded, and the relying institution does not have a PHS compliant policy
3. The research is not PHS funded and/or the relying institution does not have a COI policy

When the research is PHS funded, the COI Policy must comply with the federal regulations at 42 CFR 50, Subpart F. Polices meeting these standards are PHS compliant polices. The Federal Demonstration Partnership (FDP) website can be searched to determine if a relying institution has a PHS/FDP compliant process.

The below three subsections outline Geisinger requirements for each of the three scenarios listed above.

### 1. The research is PHS funded, and the relying institution has a PHS compliant policy

Under this scenario, the relying institution will review and manage COI under its own policy and is responsible for identifying conflicts of interest at the time of initial review, as well as throughout the life of the study. The relying institution is responsible for determining which conflicts are considered significant financial interests and which require disclosure and a management plan. The relying institution must also develop management plans, notify GIRB of any financial COIs, as well as provide any management plans to GIRB for IRB review. If specific language is required in the consent document to disclose the conflict, the relying institution is also required to provide this language to GIRB.

### 2. The research is PHS funded, and the relying institution does not have a PHS compliant policy

Under this scenario, the relying institution can follow Geisinger's Research Financial Conflict of Interest policy. The Geisinger research team must contact the Geisinger Office of Research Compliance (ORC) at orc@geisinger.edu to initiate conflict of interest reporting through Geisinger's COI-Smart platform for all relying site investigators. The Geisinger Research Team should also obtain from ORC, details about Geisinger's COI policy and provide it to the relying site investigators.

### 3. The research is not PHS funded and/or the relying institution does not have a COI policy

Geisinger HRPP has traditionally required all external investigators to follow a 42 CFR 50, subpart F compliant COI policy, but this is not the case when GIRB serves as a sIRB. When GIRB is the sIRB for a multi-site study and the research is not PHS funded, investigators at relying sites can follow polices that are not in compliance with PHS regulations. If the relying institution has its own COI policy, the relying institution will review for COI and will develop a management plan when a COI is identified. The relying institution must provide management plans and any required disclosure language to GIRB for IRB review. When the relying institution's policy is being followed, the relying institution must notify GIRB of any COIs and provide management plans and required disclosure language to GIRB for IRB review.

If the relying institution does not have its own COI policy, the relying institution can rely on Geisinger's policy.

GIRB will review all COIs and management plans in context of human subject protections. Information about COIs will initially be collected on the Relying Site Application. Information about COIs, including management plans must be submitted to GIRB through iRIS, either as part of an amendment to approve conducting the research at a relying site where a local investigator on the study has a COI, or as a follow-up amendment after a new COI is identified at a relying site. As part of the IRB review, GIRB will determine if the management plan is adequate, or if additional management strategies are needed for human subjects protections. If additional measures are requested, GIRB will notify the relying institution and work collaboratively to come to resolution.

For relying institutions following Geisinger's COI Policy, all investigators must be listed in Section 3.0 – *Assign Key Study Personnel (KSP) Access to the Study*, of the Study Application. Please refer to the *Key Study Personnel* Section for more information. The requirements for completing Section 3.0 of the Study Application are different when adding KSP (investigators) for a site relying on both GIRB as the sIRB and Geisinger's COI Policy.

## Ancillary Reviews

All Geisinger ancillary reviews must be submitted to GIRB with the initial submission of a sIRB study unless an alternate process or exception is granted.

All non-Geisinger sites are responsible for ensuring that any required ancillary reviews have been completed for their site or will be completed for their site before the research starts or before the activities impacted by the ancillary review begin. Information about required Ancillary reviews and their completion status will be collected from each relying site on the Relying Site Application. In cases where ancillary reviews may impact IRB review and approval at relying sites (such as radiation safety review), investigators must submit supporting documents to GIRB at the time the relying site is being submitted to GIRB for review. Completion of such ancillary reviews is required to be completed before GIRB can approve a participating site.

In the case where a relying institution is not capable of performing a required ancillary review, GIRB should be notified.

## Prompt Reporting

For sIRB studies, GIRB is following definitions from the SMART IRB Harmonization Guidance for Reportable Events . Prompt Reporting is defined as the initial notification of an event to the reviewing IRB.

1. Definitions

2. **Noncompliance is any failure to follow:**

- Applicable federal regulations, state and local laws, or institutional polices governing human subjects protections, or
- The requirements or determinations of the IRB, including the requirements of the approved investigational plan (i.e., protocol deviations)

3. **Serious noncompliance** is any noncompliance that increases risk of harm to subjects; adversely affects the rights, safety, or welfare of subjects; or adversely affects the integrity of the data and research
   - **Apparent serious noncompliance** describes an event that *appears* to constitute serious noncompliance, and so requires reporting to the IRB for consideration. The term "apparent" is used because the IRB has not yet made a formal assessment of the event

4. **Continuing noncompliance** is a pattern or repeated noncompliance which continues after initial discovery, including inadequate efforts to take corrective actions within a reasonable timeframe
   - **Apparent continuing noncompliance** describes an event that *appears* to constitute noncompliance, and so requires reporting to the IRB for consideration. The term "apparent" is used because the IRB has not yet made a formal assessment of the event

5. **Unanticipated Problem*** is any incident, experience, or outcome that meets all the following criteria:
   - Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
   - Related, or possibly related to participation in the research (i.e., reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
   - Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economical, or social harm) than was previously known or recognized.

   GIRB follows the Office of Human Research Protections (OHRP) guidance regarding the types of events that constitute unanticipated problems. For research that falls under FDA purview, GIRB follows FDA guidance to help assess whether adverse events also constitute unanticipated problems.

## 2. Procedures for Prompt Reporting

Investigators are responsible for promptly reporting only events that constitute apparent serious or continuing noncompliance or unanticipated problems when the events occur at a site where GIRB is the reviewing IRB. It is the responsibility of the site investigators to promptly report such events that have occurred at their site.

### 1. Initial Notification

Prompt Reporting is the initial notification of apparent serious or continuing noncompliance or events that appear to meet the definition of unanticipated problems, to GIRB. Initial notification can be completed by sending a high priority email to the GIRB Reliance Team at irbreliance@geisinger.edu, when an investigator needs to collect more information and sufficient details required for a formal report are not completely understood. Such reports must describe the event and all currently known information. It is likely that GIRB will have follow-up questions based on initial reports.

**Initial notification must occur within 10 working days of recognizing apparent serious or continuing noncompliance or unanticipated problems, except for adverse events that are unexpected, fatal, or life threatening, and related or possibly related to the research, GIRB must be notified within 24 hours of discovering an event meeting this criteria**.

Initial notification can be submitted to GIRB by relying site investigators and/or their designees with the lead site PI being copied on the email. When the event is being reported by a whistleblower and the lead site PI can't be copied for confidentiality reasons, the whistleblower need not copy any parties when confidentiality concerns may exist.

If all or sufficient detail about the event are known, a formal report can be submitted as described immediately below.

### 2. Formal Notification

Once all pertinent details have been obtained and there is enough information to submit a formal report in iRIS, the lead site PI should submit a Prompt Report Form in iRIS on behalf of the sites impacted by the event. Note, when an event impacts multiple sites relying on GIRB, only one Prompt Report Form needs to be submitted, but the form should clearly identify the sites that have been impacted by the details in the report. Please do not submit separate reports for each site involved in the event. However, independent events should generally be submitted on separate reports.

In cases where the reportable event involves a whistleblower, GIRB staff will work directly with the whistleblower to compile the needed information when it is not possible to have the lead site PI submit the formal report because it presents confidentiality issues.

## 3. IRB Review of Prompt Reports

### 1. Triage

Prompt Reports submitted are triaged to a member of the GIRB Reliance Team to make an initial assessment. The Reliance Team may reach out with questions for additional information to help make an initial assessment. They may also consult with an IRB Chair to help make an initial assessment.

Reports that do not meet the definition of an apparent serious or continuing noncompliance or unanticipated problems are returned with an outcome letter notifying the investigators that the submitted report was determined not be an alleged serious or continuing noncompliance or unanticipated problem. Reports that meet the definition of apparent serous or continuing noncompliance or unanticipated problems are assigned to an IRB reviewer and scheduled for review at a convened IRB meeting. The convened IRB committee will discuss the event and related details and make a determination as to whether allegations of noncompliance meet the definition of serious or continuing noncompliance and/or whether events meet the definition of unanticipated problems. At any point in the review process, a prompt report may be returned to the investigator with questions or requests for additional information or clarifications.

## 2. IRB Review of Prompt Reports

All reports of apparent serious or continuing noncompliance and unanticipated problems involving risks to subjects are reviewed at a convened IRB meeting unless an initial assessment determines that the event does not meet reporting criteria. GIRB bases determinations on the definitions included above, at the beginning of this section. GIRB also relies on relevant guidance's from OHRP, SACHRP and the FDA as applicable.

### 1. Unfounded Prompt Reports

Prompt Reports determined to be neither serious or continuing noncompliance or unanticipated problems involving risks to subjects are completed by notifying the lead site, the lead site PI, and other applicable parties (such as relying sites that were impacted by the reported event and their respective PIs) that the submitted report was determined not to meet criteria for prompt reporting and whether any actions are required by the investigators.

### 2. Founded Prompt Reports

When GIRB determines that an event is serious or continuing noncompliance and/or an unanticipated problem, GIRB promptly notifies the relying institutions that may be impacted by the event.

In some situations, the relying institution may be better positioned to prepare the report for required external reporting. In these cases, the external institution will draft the report and share it with GIRB for review and comment prior to sending it to the relevant parties. Relying institutions should provide the draft report to GIRB within 10 working days after officially being notified about a serious or continuing noncompliance and/or unanticipated problem determination. GIRB will provide comments and recommendations back to the relying institution within 5 business days of receiving the draft report. The relying institution will send the final report to relevant parties within 30 working days from the convened IRB making a

determination.

In other cases, GIRB may be better positioned to prepare the external report. Following a determination of a serious or continuing noncompliance or unanticipated problem, GIRB will promptly notify the relying institutions impacted by the event, to obtain their input, as appropriate, regarding the event and any proposed corrective actions. GIRB will provide this information to relying institutions within 10 working days following a determination by the convened IRB. Relying institutions will be provided with a draft of the IRB outcome letter and a draft of the report detailing the corrective action measures. The relying institution has 5 business days to review and comment on the draft report before GIRB sends the report to external recipients. GIRB is under no obligation to adopt comments of any relying institution.

Following receipt of feedback from impacted relying institutions, GIRB will modify all reports and corrective action measures as determined necessary and send the IRB outcome letter to the lead site and lead principal investigator as well as the impacted relying sites and relying site principal investigators.

The institution responsible for preparing and sending the external report will be determined on a case-by-case basis.

### 4. External Reporting by GIRB

Unless an alternate reporting structure is established, GIRB will promptly report (within 30 working days of the convened IRB making a determination) the finding to:

- All applicable Institutional Officials
- All applicable regulatory or oversight agencies (such as OHRP and FDA)
- Study sponsor and/or funding agency
- Contract research organizations
- Other performance sites involved in the research affected by the event

## When the Lead Site is Not Geisinger

GIRB is generally willing to serve as the sIRB for multi-site research when Geisinger is not the lead study site, both when Geisinger is a participating site in the research as well as when Geisinger is not a participating site in the research. In situations where Geisinger is a participating site in the research, the Lead PI can delegate IRB submission requirements to the Geisinger Site PI and research team or choose to handle IRB submission responsibilities on his/her own. In situations where Geisinger is not a participating site, the Lead PI and research team are responsible for handling IRB submission responsibilities.