Geisinger IRB Investigator's Guide for Relying on an External IRB

Geisinger Institutional Review Board Official Document

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Definitions

Ceding Acknowledgement: The ceding acknowledgement signifies the completion of the relying/ceding request process, including the HRPP/local context review, ceding determination, approval from the external IRB to conduct the study at the local site, and the submission of all final documentation to Geisinger IRB. The ceding acknowledgement signifies that the conduct of the research at the local site may begin.

Ceding Determination: Following completion of the HRPP/local context review, Geisinger IRB provides a ceding determination to either accept or deny requests to rely on an external IRB.

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.

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

Documentation of IRB Approval at External/Reviewing IRB: Documentation from the reviewing IRB that indicates that the main protocol, template consent form and relevant study-wide documents have been IRB approved; or that the lead site has been approved to conduct the research.

Documentation of IRB Approval to Conduct Research at the Local Site/Documentation of IRB Approval of the Local Investigator: Documentation from the reviewing IRB that indicates that the local site is an approved site to conduct the research. Some reviewing IRBs (such as ADVARRA) approve the local investigator to conduct the research, instead of the local site. This documentation should not be obtained until after the local context review has been completed and the investigator is given permission to submit to the reviewing IRB.

GIRB: Geisinger Institutional Review Board

HRPP: Human Research Protection Program

HRPP/Local Context Review: Review process conducted by the relying institution's IRB to verify initial 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.

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 only 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.

Local Context Form/Site Information Sheet: Most reliance agreements require institutions to communicate "local context" issues to the Reviewing IRB. Local context issues can include institutional requirements for informed consent language (e.g., compensation for injury language), attesting to the adequacy of research team training, qualifications of the research team and resources available to conduct the study, and providing any relevant conflict of interest management plans (or, in the case of federal agencies, assurances that that the participation of their research

personnel is permissible and consistent with federal law). Local context issues might also include any state or local laws, regulations, institutional policies, standards, or other local factors, including site-specific ancillary reviews, relevant to the research, that could affect the approval of the reviewing IRB or the conduct of the study at the local site. The reviewing IRB usually provides the Local Context Form to the relying institution, and the form is completed by the relying IRB in collaboration with the study team.

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

Reviewing IRB/IRB of Record/External IRB: 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 multisite 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

Institutions may agree to use an IRB outside their institution to meet the regulatory review and approval requirements for research studies. This is called ceding IRB review. Ceding IRB oversight, or relying on an external reviewing IRB's regulatory review, approval and continued oversight for human subject research has become a common and widely accepted practice. Ultimately, however, the relying institution remains responsible for the oversight and conduct of the research occurring at its site. This is largely driven by regulatory requirements such as the NIH Single IRB Policy and the Department of Health and Human Services' single IRB requirement for cooperative research. The premise of these regulations is to streamline the IRB process and reduce redundant regulatory reviews of research by each institution's local IRB. The latter can lead to variances in the conduct of research between sites.

While one goal of the ceding/single IRB model is to harmonize study procedures and most documents being used at all sites involved in a multi-site research study, the processes and requirements for relying on an external reviewing IRB are not harmonized across institutions and vary greatly from one institution to the next. Due to this, investigators and research teams not familiar with Geisinger processes and requirements may find that relying on an external IRB does not result in a streamlined IRB experience. In addition, local context such as state laws and institutional polices may prevent complete harmonization of study documents, such as consent forms, across all sites.

This document is designed to be a resource for investigators and research teams to effectively navigate the Geisinger ceding process. Investigators are strongly encouraged to provide this document to sponsors, prime sites and lead investigators when relying on an external IRB. Having these stakeholders informed of our local process and requirements improves communication and sets clear expectations for all parties involved.

It is important to note that this guide only covers local Geisinger IRB (GIRB) processes for relying on an external IRB. Other applicable Geisinger research requirements such as those governed by Research Contracts and Research Grants are not covered in this document. It is also important to understand that when Geisinger relies on an external reviewing IRB, GIRB still retains responsibility to ensure investigator compliance with the protocol, the reviewing IRB's determinations, applicable federal and state regulations, and Geisinger institutional policy. GIRB ultimately bears responsibility for the local conduct of the study.

Reliance Determinations

Geisinger HRPP is responsible for determining the acceptability and appropriateness of relying on an external IRB. Geisinger HRPP must first determine that it is acceptable to rely on an external IRB before investigators can obtain IRB approval for Geisinger, from a reviewing IRB. Generally, when the use of an external IRB is required or mandated, Geisinger HRPP finds it acceptable to cede IRB oversight. Some examples include:

- Cooperative Group Cancer Research funded by the National Cancer Institute, subject to IRB review and approval by the NCI CIRB
- Federally supported research mandating sIRB review under the NIH Single IRB Policy and/or The Common Rule Cooperative Research requirement
- The principal investigator or research consortium is mandating single IRB review

Geisinger HRPP also considers requests to rely on an external IRB when single IRB review has not been mandated or required. For all reliance requests, regardless of requirements or mandates, Geisinger HRPP may consider any of the following when making a reliance determination:

- Risk level of the research
- AHRPP accreditation status of the reviewing IRB/HRPP
- Findings and sanctions related to any audits or inspections conducted by the FDA and OHRP impacting the reviewing IRB/HRPP
- Expertise of the proposed reviewing IRB verses GIRB expertise
- Resources of the reviewing IRB verses GIRB resources
- Organizational conflicts
- Institutional risk to Geisinger

In most cases, GIRB usually determines that it is acceptable to rely on an external IRB for research conducted at a Geisinger site. When making ceding determinations, Geisinger HRPP may consult with other departments and individuals such as the Office of Research Compliance, GIRB Chairs, The

Vice President of Research, the Chief Scientific Officer and/or the Institutional Official.

Relying on Non-AAHRPP Accredited Organizations

Geisinger maintains accreditation through the Association for the Accreditation of Human Subject Protection Programs (AAHRPP). AAHRPP standards require additional steps when relying on an IRB at a non-accredited organization to ensure participants in the research are properly protected. The necessary steps are largely dependent upon the level of risk presented by the study, with the possibility of greater than minimal risk research requiring additional oversight measures. Geisinger will employ any combination of the following steps when relying on non-accredited organizations:

1. Minimal risk research
    - Obtain an assurance from the non-accredited IRB that it will conduct its review in accordance with applicable ethical standards and regulations and report regulatory violations or investigations of the reviewing IRB by any regulatory agencies*
    - Request the reviewing IRB to attest that it has its own internal quality review process such as:
        i. AAHRPP's Evaluation Instrument for Accreditation
        ii. US FDA's self-evaluation checklist for IRBs
        iii. Other processes deemed to be satisfactory
2. Greater than minimal risk research
    - Review relevant parts of the IRB minutes where the particular study was reviewed
    - Review IRB records of a particular study being reviewed
    - Evaluate relevant polices and procedures of the reviewing IRB
    - Observe portion of IRB meeting where the particular study is reviewed
    - Having an individual form Geisinger serve as a consultant to the non-accredited IRB for the particular study
    - Conducting non-for-cause monitoring of the IRB

    * A reliance agreement can be used in lieu of an assurance when it adequately covers that the reviewing IRB will conduct its review in accordance with applicable ethical standards and regulations and report regulatory violations or investigations of the reviewing IRB by any regulatory agencies

Geisinger HRPP Communication with Reviewing IRB

Geisinger HRPP collects contact information for the reviewing IRB in the *Application for Request for Ceding to an External IRB* submitted in the iRIS electronic submission system. The GIRB Reliance Team uses this information to communicate with the reviewing IRB should the need arise. This information is also used to execute reliance agreements after making ceding determinations.

The GIRB Reliance Team provides its contact information to the reviewing IRB when completing local context forms. Additionally, Geisinger investigators can provide GIRB Reliance Team contact information to the reviewing IRB when requested.

Procedures and Requirements

An investigator who wants to request to rely on an external IRB must complete and submit an *Application for Request for Ceding to an External IRB* in the iRIS electronic submission system along with all required documents (see steps below). **NOTE: This request must be submitted and accepted PRIOR to obtaining approval from the reviewing IRB to conduct the study at the local site (e.g. Geisinger).** In addition, before submitting this application request to GIRB, the reviewing IRB needs to have approved the study at the lead site, or approved the main protocol, template consent form and relevant study-wide documents. GIRB will not conduct HRPP/local context reviews unless the investigator includes documentation that the reviewing IRB has approved the lead site and/or the study-wide documents with the *Application for Request for Ceding to an External IRB.* The only exceptions include studies relying on the National Cancer Institute Central Institutional Review Board (NCI CIRB), which are not required to submit this documentation and any study requesting to rely on an external IRB where the study will only be conducted at the local site (i.e. the study is not a multi-site study).

Even after the external IRB has approved the research, human subjects research activity may not begin at Geisinger until after a number of steps are completed. For Geisinger to agree to cede review to an external IRB, the GIRB must confirm that the consent form aligns with Geisinger requirements, Geisinger Ancillary Committees may need to review and approve the study, compliance with local context needs to be ensured, and an IRB Authorization Agreement between Geisinger and the reviewing IRB might need to be executed. Further, industry sponsored studies and grant funded studies and/or studies with billable patient charges will still need to flow through the Research Contracts, Research Grants and billing determination processes, respectively.

Sections 1-3 below cover the procedures for completing a request to rely on an external IRB. Use the following guidelines to ensure that the correct process is followed. Please refer to the diagrams and Flow Charts included as Appendixes for overviews of the below processes. Appendix 3 can be used to help determine the appropriate process to follow.

The procedures and requirements in Section 1 should be utilized when the following is true:

- The reviewing IRB is not NCI CIRB;
- The reviewing IRB is not ADVARRA; or
- The Reviewing IRB is ADVARRA and ADVARRA consent services will not be utilized (See Section 3 below)

See Appendix 1 and Appendix 4 for an overview of this process.

The procedures and requirements in Section 2 should be followed when the study will rely on NCI CIRB.

See Appendix 2 and Appendix 6 for an overview of this process.

The procedures and requirements in Section 3 should be followed when the study will rely on ADVARRA and utilize ADVARRA consent services to develop the final consent form to be used at the local site.

See Appendix 5 for an overview of this process.

The procedures and requirements in Sections 4, 5, 6, and 7 apply to <u>all</u> ceded studies regardless of the reviewing IRB.

1. Procedures for requests to rely on an external IRB EXCEPT NCI CIRB and ADVARRA when ADVARRA consent services will be utilized

1.1 Investigators must first prepare and submit a new study in iRIS using the *Application for Request for Ceding to an External IRB.* Investigators must submit the following documents as attachments when they are applicable to the study:

- Protocol
- Consent/Parental Permission/Assent/LAR Forms – Geisinger versions AND Templates
- HIPAA Authorization Forms
- Billing Determinations
- Recruitment Materials
- Documentation of Security, Compliance and Privacy (SCP) Research Pre-Screen Questionnaire/CORL Review completion
- MyCode Data and Sample Request Form and MyCode Governing Board Approval
- Radiation Safety Review
- IBC Approval
- GHP proposals and approvals
- Local Context Form (see section 1.2 below; to be completed by GIRB for the reviewing IRB)
- Documentation of IRB approval at external/reviewing IRB
- Any other materials at the request of the IRB

Generally, it is not acceptable to submit an incomplete application for local context review. For instance, if the study requires a billing determination and SCP review, the billing determination and documentation that the SCP process has been completed must be included with the initial submission or the local context review will not proceed.

1.2 If the reviewing IRB requires Geisinger to complete a Local Context form, it must be submitted with the *Application for Request for Ceding to an External IRB*. Upon making a ceding determination, IRB staff will complete this form and upload it into iRIS where the investigator can access the completed form to provide it to the reviewing IRB. Under most circumstances, GIRB will not complete these forms prior to the submission of the *Application for Request for Ceding to an External IRB* because review of the template consent form and protocol is typically required for IRB staff to answer the Local Context review questions. This results in duplicative efforts since the protocol and consent forms will also need to be reviewed when the *Application for Request for Ceding to an External IRB* is submitted for local context review.

1.3 Upon submission of an *Application for Request for Ceding to an External IRB* and all required documents, GIRB conducts an HRPP/local context review to verify that the protocol, consent form and other study wide documents are compliant with all state and local laws, as well as Geisinger Institutional polices.

1.4 If the external IRB is not serving as the privacy board, the GIRB will maintain its role as the privacy board and will review all submissions to verify compliance with HIPAA, as well as ensure that all requests for partial and full waivers of HIPAA Authorization and alterations of HIPAA Authorization are sufficiently justified. This is usually addressed in the IAA; however, the reviewing IRB can always confirm whether or not they will be serving as the privacy board.

1.4.1 If the reviewing IRB is serving as the privacy board, there is no need to select a partial or full waiver, or an alteration of HIPAA Authorization in the *Application for Request for Ceding to an External IRB*. This request would be made to the reviewing IRB.

1.4.2 If the reviewing IRB is not serving as the privacy board, the investigator needs to make and justify all requests for full and partial waivers, as well as alterations of HIPAA Authorization in the *Application for Request for Ceding to an External IRB*.

1.5 If all HRPP and local context requirements are met, a ceding determination is made.

1.5.1 If the request to rely on an external IRB is accepted, the IRB staff notifies the investigator with an outcome letter, that the investigator can now submit to the external IRB for IRB approval to conduct the study at the local site. **Note: Investigators cannot submit to the reviewing IRB prior to receiving permission from GIRB.**

1.5.2 If not already in existence, an IAA with the reviewing IRB will need to be initiated once the HRPP/local context review has been completed and the request to rely on an external IRB has been accepted. Generally, GIRB will not execute an IAA until the local context review has been completed and the investigator is given approval to submit to the reviewing IRB (see section 5 below).

1.5.3 If GIRB does not accept the request to cede oversight, the investigator will be notified via an iRIS outcome letter. The outcome letter will include the reason(s) why the GIRB is not willing to rely on an external IRB.

1.6 If any modifications are necessary prior to making a ceding determination, the investigator is notified with an outcome letter. The investigator must address the deficiencies and submit a submission response to GIRB. If this is the case, the local investigator cannot yet submit to the reviewing IRB. When received, GIRB reviews the response to determine if the deficiencies have been adequately addressed.

1.6.1 If all deficiencies are adequately addressed, then the procedures in section 1.5 above are followed.

1.6.2 If there are outstanding deficiencies, or new deficiencies arise based on the revisions, another outcome letter requesting clarifications and/or revisions is sent to the investigator for response and the investigator must wait to submit to the reviewing IRB. This cycle will continue until the investigator has satisfied all deficiencies.

1.7 After approval is granted from the external IRB to conduct the research at the local site, the following documentation must be submitted through iRIS, to GIRB before any research activities occur:

- Documentation that clearly identifies the local site as an approved research site, or the local investigator as an approved investigator. **Note: Please see definition for**

"Documentation of IRB Approval to Conduct Research at the Local Site/Documentation of IRB Approval of the Local Investigator".

- Fully executed IAA (if not using SMART IRB or other Master Reliance Agreement; see section 6.0 below)
- Contract reconciliation from Research Contracts for all studies that are sponsored externally through industry or clinical trials managed by Research Contracts; or
- Grant reconciliation from Research Grants for all studies that are sponsored externally through nonprofit organizations or the federal government.

1.8 If there is missing documentation or deficiencies requiring modifications or clarifications, the IRB will notify the investigator with an outcome letter that outlines the deficiencies. The investigator must submit a response which includes any missing documentation and/or addresses any deficiencies. If this occurs, the research cannot begin at the local site.

1.9 Once all of the required documentation has been verified, GIRB will send an acknowledgement outcome letter notifying the investigator that the research may now begin at the local site.

2. Procedures for requests to rely on the National Cancer Institute (NCI) CIRB

2.1 Investigators must first prepare and submit a new study in iRIS using the *Application for Request for Ceding to an External IRB.* Investigators must submit the following documents as attachments when they are applicable to the study:

- Coverage Analysis Worksheet
- Documentation of Security, Compliance and Privacy (SCP) Research Pre-Screen Questionnaire/CORL Review completion
- Radiation Safety Review
- IBC Approval
- Research Contracts approved Patient Information Sheets
- GHP proposals and approvals
- Any other materials at the request of the IRB

2.2 For all requests to rely on the NCI CIRB, the IRB conducts an HRPP/local context review of all new *Application for Request for Ceding to an External IRB*, to verify that the protocol consent form and other study wide documents are compliant with all state and local laws, as well as Geisinger Institutional polices.

2.3 The NCI CIRB does not serve as the privacy board, so GIRB maintains this role and reviews all submissions to verify compliance with HIPAA and ensures that all requests for partial and full waivers of HIPAA Authorization and alterations of HIPAA Authorization are sufficiently justified. Therefore, investigators need to make and justify all requests for full and partial waivers as well as alterations of HIPAA Authorization in the *Application for Request for Ceding to an External IRB.*

2.3.1 All protocols, consent/parental permission/assent forms are available to GIRB through

the *Cancer Trials Support Network* (CTSU) website. Investigators are not required to submit these documents as attachments with the *Application for Request for Ceding to an External IRB* in iRIS. IRB staff will access these documents as needed via the CTSU website.

2.3.2 GIRB has an overarching IAA with NCI CIRB, so submission of the IAA in iRIS is not required.

2.3.3 The NCI CIRB approves boilerplate/templated language with the submission of the NCI CIRB *Annual Institutional Worksheet About Local Context* which is added to the NCI CIRB approved consent forms. It is the responsibility of the investigator to verify that the language has been appropriately incorporated into the consent document prior to enrolling participants. There is no requirement to submit consent forms to the GIRB for studies relying on NCI CIRB.

2.3.4 GIRB has approved a template HIPAA Authorization Form for use in all studies relying on NCI CIRB. Investigators are not required to submit the HIPAA Authorization Form to the GIRB.

2.4 If all HRPP and local context requirements are met, a ceding determination is made.

2.4.1 If the request to rely on NCI CIRB is accepted, IRB staff notifies the investigator with an outcome letter, that the investigator may now submit the *Study Specific Worksheet* to NCI CIRB for approval to conduct the study at the local site.

2.4.2 If GIRB does not accept the request to cede oversight, the investigator will be notified with an iRIS outcome letter. The outcome letter will include the reason(s) why the GIRB is not willing to rely on NCI CIRB.

2.5 If any modifications are necessary prior to making a ceding determination, the investigator is notified via an outcome letter. The investigator must address the deficiencies and submit a submission response to GIRB. If this is the case, the local investigator cannot yet submit the *Study Specific Worksheet* to the NCI CIRB. Once a response is received, GIRB will review the response to determine if the deficiencies are adequately addressed.

2.5.1 If all deficiencies are adequately addressed, the procedures in section 2.4 above are followed.

2.5.2 If there are outstanding deficiencies, or new deficiencies arise based on revisions, another outcome letter requesting clarifications and/or revisions is sent to the investigator for response and the investigator must wait to submit the *Study Specific Worksheet* to the NCI CIRB. This cycle will continue until the Investigator has satisfied all deficiencies.

2.6 After approval from the NCI CIRB is granted, the following documentation must be submitted through iRIS to GIRB before any research activities occur:

- Documentation that clearly identifies Geisinger as an approved research site
- Note: Grant reconciliation documentation is not required for NCI CIRB studies that fall under Geisinger's umbrella grant

2.7 If there is missing documentation or deficiencies requiring modifications or clarifications, the

IRB will notify the investigator with an outcome letter. The investigator must submit a response which includes any missing documentation and/or addresses any deficiencies. If this occurs, the research cannot begin at the local site.

2.8 Once all the required documentation has been verified, GIRB will send an acknowledgement outcome letter notifying the investigator that the research may now begin at the local site.

3. Procedures for requests to rely on ADVARRA when ADVARRA will create the local consent form

3.1 Upon request, ADVARRA provides consent form services for investigators when ADVARRA is the IRB of record. This includes developing consent forms that comply with Geisinger readability standards outlined in section 5 below.

3.1.1 Generally, this service is only used for industry supported research; however, this process can be modified and followed for research supported via other means when relying on ADVARRA.

3.1.2 ADVARRA charges a fee for this service and GIRB will not cover this fee. Prior to using this service, local investigators need to consult with sponsors, prime sites and/or the lead investigator to determine if there are sufficient resources to cover the service.

3.2 The GIRB HRPP/local context review occurs prior to the ADVARRA consent team generating the consent form for the local site. The HRPP/local context review relies on the sponsor's template consent form and the provided Research Contract Consent Form Memo (provided by Research Contracts and contains mandatory language for subject injury, cost and payment; ADVARRA must incorporate this language into the site-specific consent document).

3.3 Investigators must first prepare and submit a new study in iRIS using the *Application for Request for Ceding to an External IRB.* Investigators must submit the following documents when they are applicable to the study:

- Protocol
- Consent/Parental Permission/Assent/LAR Forms – Sponsor Templates
- Research Contract Consent Form Memo
- HIPAA Authorization Forms
- Billing Determinations
- Recruitment Materials
- Documentation of Security, Compliance and Privacy (SCP) Research Pre-Screen Questionnaire/CORL Review completion
- MyCode Data and Sample Request Form and MyCode Governing Board Approval
- Radiation Safety Review
- IBC Approval
- GHP proposals and approvals
- Local Context Form
- Documentation of IRB approval at external/reviewing IRB
- Any other materials at the request of the IRB

3.4 GIRB conducts a HRPP/local context review of all new *Applications for Request for Ceding to an External IRB*, to verify that the protocol is compliant with all state and local laws, as well as Geisinger Institutional polices.

3.5 ADVARRA generally serves as the privacy board and will review all requests for waivers and alterations of HIPAA Authorization.

3.5.1 If ADVARRA is serving as the privacy board, there is no need to select a partial or full waiver, or an alteration of HIPAA Authorization in the *Application for Request for Ceding to an External IRB*.

3.5.2 If ADVARRA is not serving as the privacy board, the investigator needs to make and justify all requests for full and partial waivers as well as alterations of HIPAA Authorization in the *Application for Request for Ceding to an External IRB*.

3.6 If all HRPP and Local Context requirements are met, a ceding determination is made.

3.6.1 If the request to rely on ADVARRA is accepted, the IRB notifies the investigator with an outcome letter, that the investigator can now submit to ADVARRA for IRB approval to conduct the study at the local site. Note: This is when ADVARRA will generate the local site consent form.

3.6.2 If the request to rely on ADVARRA is not accepted, the investigator will be notified with an outcome letter. The outcome letter will include the reason(s) why the GIRB is not willing to rely on ADVARRA.

3.7 If any modifications are necessary prior to making a ceding determination, the investigator is notified with an outcome letter. The investigator must address the deficiencies and submit a submission response to GIRB. If this is the case, the local investigator cannot yet submit to the reviewing IRB. When received, GIRB will review the response to determine if the deficiencies are adequately addressed. Once all deficiencies are addressed, the IRB follows the procedures in section 3.6 above.

3.8 Prior to submitting a submission response in iRIS to GIRB:

3.8.1 The ADVARRA created consent form using the required language from the Research Contracts Consent Form Memo must be approved by the sponsor.

3.8.2 Any changes or deviations from the language in the provided Research Contracts Consent Form Memo need to be reviewed and approved by Research Contracts.

3.8.3 The investigator must email the ADVARRA generated and sponsor approved consent form to be used at the local site to GIRB staff for acceptance prior to submitting a response in iRIS.

3.8.4 Once the GIRB accepts the ADVARRA generated and approved consent form, IRB staff will notify Research Contracts that the consent form is acceptable. Research Contracts will then provide the reconciliation required to finalize the ceding process, once the reconciliation can occur.

3.9 The investigator must then submit the following documentation in iRIS, to the GIRB before any research activities occur:

- Documentation that clearly identifies the local site as an approved research site
- GIRB has a Master Reliance Agreement with ADVARRA, so submission f the IAA is not required.
- Contract reconciliation from Research Contracts for all studies that are sponsored externally through industry or clinical trials managed by Research Contracts; or
- Grant reconciliation from Research Grants for all studies that are sponsored externally through nonprofit organizations or the federal government.

3.10 If there is missing documentation or deficiencies requiring modifications or clarifications, the IRB will notify the investigator with an outcome letter that outlines the deficiencies. The investigator must submit a response which includes any missing documentation and/or addresses any deficiencies. If this occurs, the research cannot begin at the local site.

3.11 Once all of the required documentation has been verified, GIRB will send an acknowledgement outcome letter notifying the investigator that the research may now begin at the local site.

4. Key study personnel requirements

4.1 Key study personnel requirements are not impacted by relying on an external IRB. Study personnel must be added to all ceded study applications prior to performing any study related activities. Geisinger requirements for research training (CITI), conflict of interest (COI) and for each individual listed on a study to have a curriculum vitae, resume or NIH biosketch uploaded under his/her iRIS user account, still apply when an investigator submits an *Application for Request for Ceding to an External IRB.*

4.2 KSP amendments must be submitted for all ceded studies to:

- Add personnel
- Remove personnel

5. Geisinger consent requirements when relying on an external IRB

5.1 GIRB generally enforces the following consent document standards for all consent forms used at any Geisinger or Geisinger affiliated sites:

- Flesch-Kincaid Grade Level = 6-8; or
- Flesch Reading Ease > 60
- Font = Arial
- Spacing = multiple @1.15

5.2 GIRB enforces the above consent form requirements when relying on an external IRB; however, sometimes factors beyond the local investigator's control prevent editing the template consent form to comply with the local readability requirements. If the template consent form cannot be edited to meet these requirements, investigators are required to

follow the hierarchy of acceptable alternatives.

5.2.1 When the hierarchy is followed, documentation stating that the template consent form cannot be modified to meet the readability requirements needs to be submitted to the GIRB in iRIS.

5.2.2 The hierarchy is not just a list of acceptable alternatives for the investigator to select from. The processes in the hierarchy need to each be pursued in ranked order as viable alternatives. For instance, if the template consent form cannot be revised to meet Geisinger readability requirements, then the investigator must develop a Key Information Sheet that is written at an acceptable reading level. This would need to be eliminated as an acceptable option prior to seeking approval to developing a verbal script that is written at an acceptable reading level.

5.2.3 When submitting an *Application for Request for Ceding to an External IRB* and utilizing the hierarchy, documentation that each ordered process was deemed unacceptable needs to be included with the application. For instance, a study that is using a verbal script would need to include documentation that the template consent form could not be revised to meet the readability requirements and documentation that the development and use of a Key Information Sheet was not acceptable.

5.2.4 When using the hierarchy, the documents that are produced (i.e. key information sheet, verbal script, etc.) need to also be included as attachments with the *Application for Request for Ceding to an External IRB*.

6. Institutional authorization agreements

6.1 When a Geisinger investigator intends to rely on an external reviewing IRB, Geisinger must enter into an agreement referred to as an IRB Authorization Agreement (IAA) or IRB Reliance Agreement. This agreement is executed between the reviewing IRB and the relying institution and it delineates the roles and responsibilities of the involved parties. The agreements can be for a single research study or for multiple studies (often referred to as a Master Reliance Agreement).

6.2 Geisinger is willing to enter into a Reliance Agreement to assign another IRB as the reviewing IRB for 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. Generally, GIRB will not execute a new IAA with an external IRB until the local context review has been completed and the local investigator has been given permission to submit to the external IRB for approval to conduct the study at Geisinger. There are exceptions to this rule if sufficient justification can be provided.

6.3 Negotiating a Reliance Agreement can take weeks to months. To facilitate the process, Geisinger has entered into several Master Reliance agreements. When a Master Reliance Agreement is used, investigators are not required to submit the fully executed reliance agreement in iRIS to the GIRB. Geisinger has the following Master Reliance Agreements:

- NCI CIRB
- ADVARRA
- WIRB

- SMART IRB Agreement

6.4 When the reviewing IRB is not an institution which Geisinger has a Master Reliance Agreement with, a standalone IAA can be initiated.

6.4.1 Typically the reviewing IRB's standard reliance agreement is used. However, some IRBs do not have a standard Reliance Agreement. In these situations, the Geisinger standard Reliance Agreement may be used as is, or in modified form. The external reviewing IRB usually signs the IAA before it is sent to Geisinger for signature. The investigator should contact the GIRB office and request for the appropriate individual to contact the reviewing IRB to negotiate the agreement.

6.5 IAAs can also be executed through SMART IRB. 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/relying institutions. A list of the signatories to the SMART IRB agreement is available on the SMART IRB Participating Institutions webpage. Geisinger is a signatory to the SMART IRB Agreement.

6.5.1 SMART IRB offers several options for documenting reliance between institutions for a specific research study. IRB staff is responsible for completing this documentation. It is up to the Reviewing IRB to determine which of the following documentation methods will be used for a specific study:

- Letter of Acknowledgement; or
- The SMART IRB Online Reliance System

6.6 After the outcome letter notifying the local investigator that he/she can submit to the reviewing IRB has been sent to the investigator, GIRB staff will use the contact information provided in the *Application for Request for Ceding to an External IRB* to initiate an IAA, unless there is a Master Agreement already in place.

7. Geisinger IRB Actions

7.1 GIRB only accepts or denies requests to rely on or cede to an external IRB and acknowledges when the initial ceding process is completed and when the research can begin at the local site. Documents, such as protocols and consent forms, or iRIS submission forms do not get approved by the GIRB. GIRB only acknowledges actions of the external IRB. Documents submitted to the GIRB as part of a request to rely on an external IRB are not given an outcome in iRIS. Consent forms and protocols do not get stamped with approvals and dates in iRIS.

8. Submission requirements following ceding acknowledgement

8.1 Amendments

8.1.1 Research that is ceded to an external IRB is not subject to the same GIRB submission requirements following IRB approval from the reviewing IRB and Ceding Acknowledgement from the GIRB. Investigators are required to submit the following to the GIRB through the iRIS electronic submission system:

- Key study personnel changes
- Study title changes
- Changes to participant compensation
- Modifications to data sharing which require changes to data sharing agreements
- Changes that impact the billing determination
- Changes to HIPAA including authorization language, waivers, and alterations (only when GIRB is serving as the privacy board)
- Changes to any use and/or disclosure of highly protected health information (HPHI)
- Any significant study modifications that may affect the GIRB's decision to cede authority

8.1.2 Investigators are encouraged to consult with the GIRB Reliance Team anytime time uncertainty arises around whether or not a modification requires a submission to the Geisinger IRB. The GIRB Reliance Team can be reached by phone at 570-271-8663 or email at irbreliance@geisinger.edu.

8.2 Continuing reviews

8.2.1 After initial ceding determination, investigators are not required to submit continuing reviews or continuing review approvals from the reviewing IRB.

8.3 Prompt Reporting

8.3.1 The Prompt Reporting requirements outlined in this section are specific to incidents occurring at a Geisinger or a Geisinger affiliated site. Incidents not involving Geisinger sites or participants enrolled through Geisinger do not require reporting to GIRB.

8.3.2 Geisinger Investigators are required to promptly report all incidents of apparent serious or continuing non-compliance and/or unanticipated problems in accordance with the reviewing IRB's policies and procedures and/or the agreed upon policies and procedures identified in a reliance agreement. The report must be made to the reviewing IRB.

8.3.3 Geisinger Investigators are also required to promptly submit an informal report via email to GIRB HRPP at irbrelaince@geisinger.edu, for all incidents of apparent serious or continuing non-compliance and/or unanticipated problems, occurring at a Geisinger or a Geisinger affiliated site.

8.3.4 Both the reviewing IRB and GIRB HRPP may conduct their own investigations. GIRB HRPP may take action to prevent immediate hazards presented to human participants. GIRB will notify the reviewing IRB if this occurs.

8.3.5 If the reviewing IRB determines that an incident constitutes serious or continuing non-

compliance and/or an unanticipated problem, Geisinger investigators must submit an amendment with a detailed report of the incident, all correspondences related to the incident, required remediation plans or action plans based on the incident, and official documentation of the reviewing IRB's determination.

8.3.6 If the reviewing IRB determines that a reported incident does not constitute serious or continuing non-compliance and/or unanticipated problem, Geisinger investigators must submit an amendment with a detailed report of the incident and official documentation of the revieing IRB's determination.

8.4 Final reports

8.4.1 Investigators are required to submit final reports in iRIS to formally close out open studies under an external IRB's oversight. Final reports should not be submitted until all human subjects research activities have been completed at Geisinger. Investigators should consult with the Reviewing IRB if there are questions related to the acceptability of closing a study at Geisinger.

9. Investigator responsibilities following ceding acknowledgement

The responsibilities of the research team remain largely the same, and include:

- Communicating information about study progress to the Reviewing IRB via the mechanism established for such communications (e.g., either to the IRB directly or to the lead study team or to a coordinating center)
- Tracking personnel updates, ensuring personnel are qualified and appropriately trained to perform their roles, and providing information about relevant personnel changes to GIRB and the Reviewing IRB (including confirming personnel are qualified and appropriately trained) to the Reviewing IRB when required and via the mechanism established for such communications (e.g., either to the IRB directly, or to the lead study team or coordinating center)
- Reporting unanticipated problems, noncompliance, and significant new information to the Reviewing IRB via the mechanism established for such communications
- Complying with the Reviewing IRB's policies (e.g., reporting noncompliance, unanticipated problems, and subject complaints)
- Complying with the determinations of the Reviewing IRB
- Using the most current IRB-approved documents, including the protocol, consent forms, and recruitment documents
- Complying with Geisinger's applicable policies from the local institution (e.g., conflict of interest, training and education, research subject compensation processes, billing compliance)
- Working with the lead investigator to make any local updates to the protocol or other approved documents (e.g., consent form or recruitment materials) and ensuring the Reviewing IRB approves these changes before they are implemented
- Communicating applicable study updates with other relevant local institution committees and/or offices (e.g., research billing, radiation safety committees, pharmacy, oncology review committees)

- Complying with any other Geisinger Institutional requirements, as applicable

Conclusion

GIRB generally accepts requests to rely on external IRBs and sIRBs but has a clear, systematic process that must be followed. GIRB must complete a local context review prior to an external IRB approving Geisinger as a site to conduct the research. Relying on an external IRB only means that the regulatory review process under the federal research regulations, and sometimes HIPAA, is conducted by an outside IRB. All other Geisinger institutional requirements remain intact, including approvals from ancillary committees, Research Grant and Research Contract requirements. In addition, the Geisinger IRB consent form readability requirements extend to all studies in which IRB oversight is ceded. An executed Institutional Authorization Agreement between Geisinger and the reviewing IRB is required before any research can be conducted at Geisinger. Once an investigator has completed the entire ceding process and has been granted permission to start the study at the local site, the post ceding submission requirements to Geisinger IRB are not as extensive as when Geisinger is the reviewing IRB.

Appendix 1: Relying on an External IRB: Process Overview: Non-NCI CIRB Studies

Relying on an External IRB: Process Overview
Non-NCI CIRB Studies

Step 1

- Submit an *Application for Request for Ceding to an External IRB* in iRIS to Geisinger IRB for HRPP/Local Context Review
- Include all applicable documents
- Respond to any deficiencies received in a modification request outcome letter with a submission response in iRIS
- Step 1 is completed when the *Pending Reviewing IRB Approval and Grant/ Contract Reconciliation* letter is received

Step 2

- After receiving the "*Pending"* letter, submit to the reviewing IRB for IRB approval
- Geisinger IRB will initiate the IAA with the reviewing IRB
- Once approval from the reviewing IRB is received, submit in iRIS a submission response that includes:

  1. Documentation that identifies Geisinger as an approved research site
  2. Fully Executed IAA
  3. Grant and/or Contract reconciliation

Step 3

- Geisinger IRB verifies receipt of all required documentation
- Geisinger IRB finalizes HRPP/Local Context re*view*
- The ceding process is completed when the *Ceding IRB Oversight Acknowledgement Notice* letter is received

Step 4

- Begin conducting the research

Appendix 2: Relying on an External IRB: Process Overview: NCI CIRB Studies

Relying on an External IRB: Process Overview
NCI CIRB Studies

Step 1

- Submit an *Application for Request for Ceding to an External IRB* in iRIS to Geisinger IRB for HRPP/Local Context Review
- Include all applicable documents
- Respond to any deficiencies received in a modification request outcome letter with a submission response in iRIS
- Step 1 is completed when the *Pending Acknowledgement of Ceding Decision to CIRB* letter is received

Step 2

- After receiving the "*Pending"* letter, submit to the NCI CIRB for IRB approval
- Geisinger has a Master Reliance Agreement with the NCI
- Once approval from the NCI CIRB is received, submit in iRIS a submission response that includes:

  1. Documentation that identifies Geisinger as an approved research site

Step 3

- Geisinger IRB verifies receipt of all required documentation
- Geisinger IRB finalizes HRPP/Local Context r*eview*
- The ceding process is completed when the *Acknowledgement – CIRB Notice* letter is received

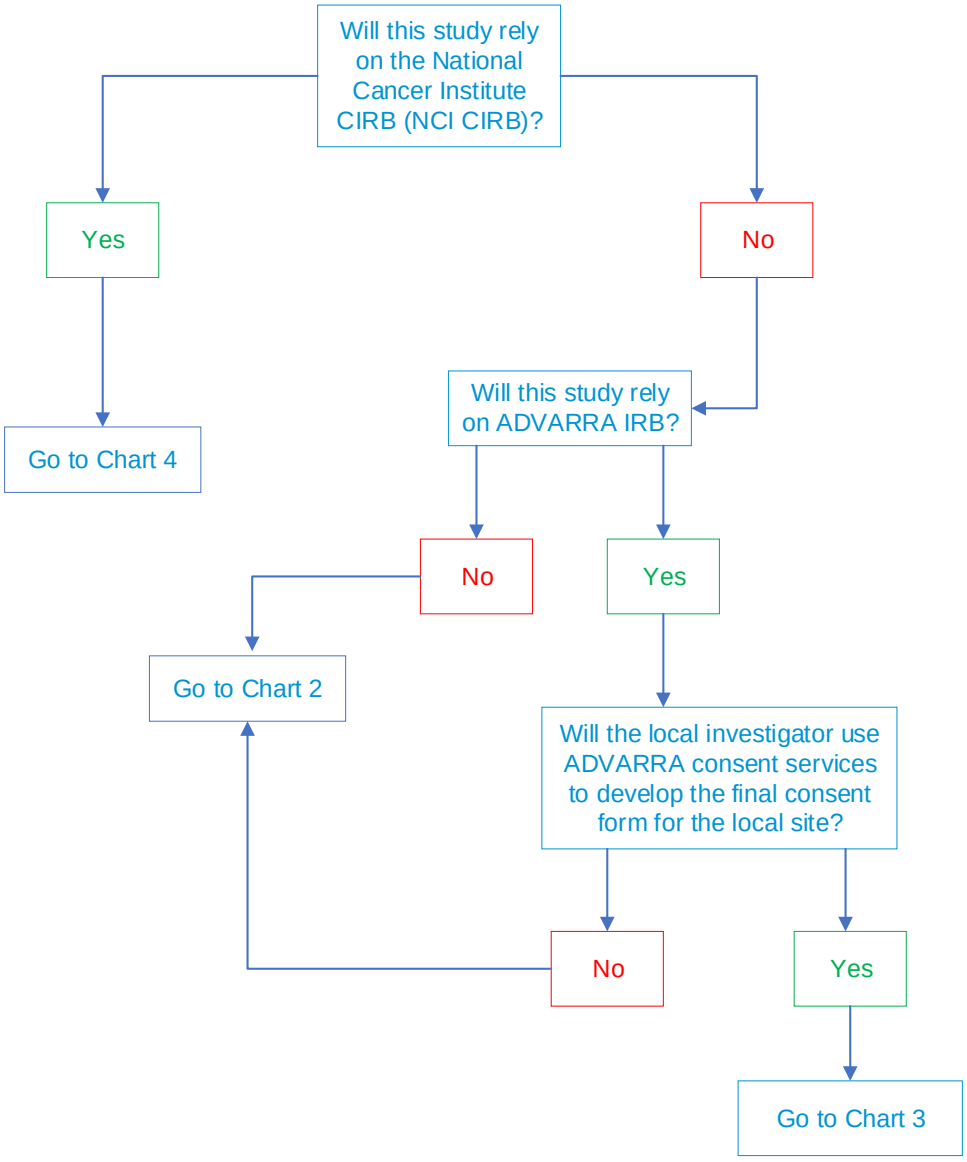
Step 4

- Begin conducting the research

Appendix 3: Relying on an External IRB: Process Overview Flow: Chart 1

Relying on an External IRB: Process Overview Flow

Chart 1

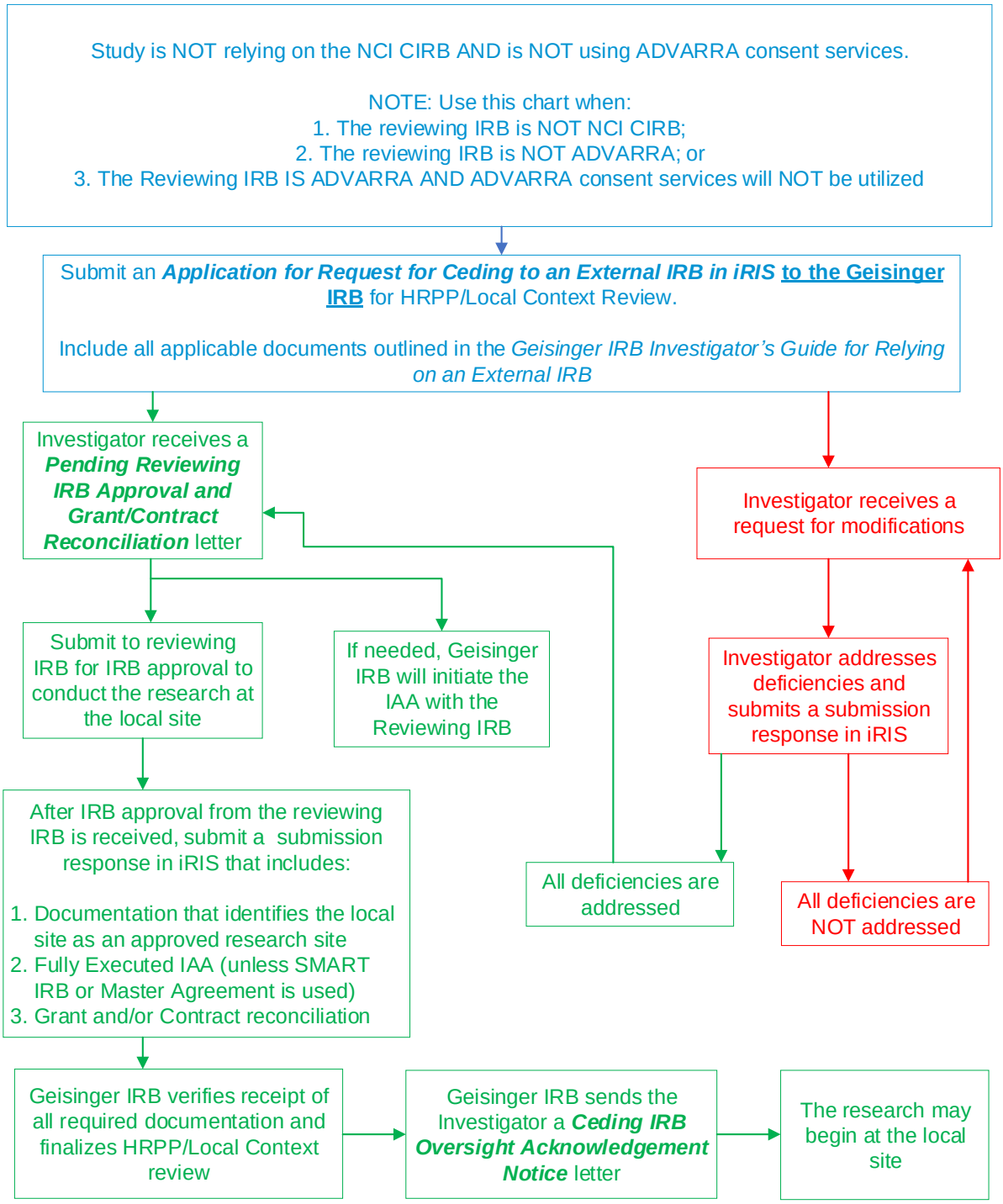


Please Note: Charts 2, 3 and 4 are high level overviews of the processes for relying on each type of reviewing IRB. At any point in those processes, if an incomplete submission or response is received, or there are modifications or clarifications required, an outcome letter may be sent to the investigator. The response will pick back up within the last step of the process which the study had reached.

Appendix 4: Relying on an External IRB: Process Overview Flow: Chart 2

Relying on an External IRB: Process Overview Flow

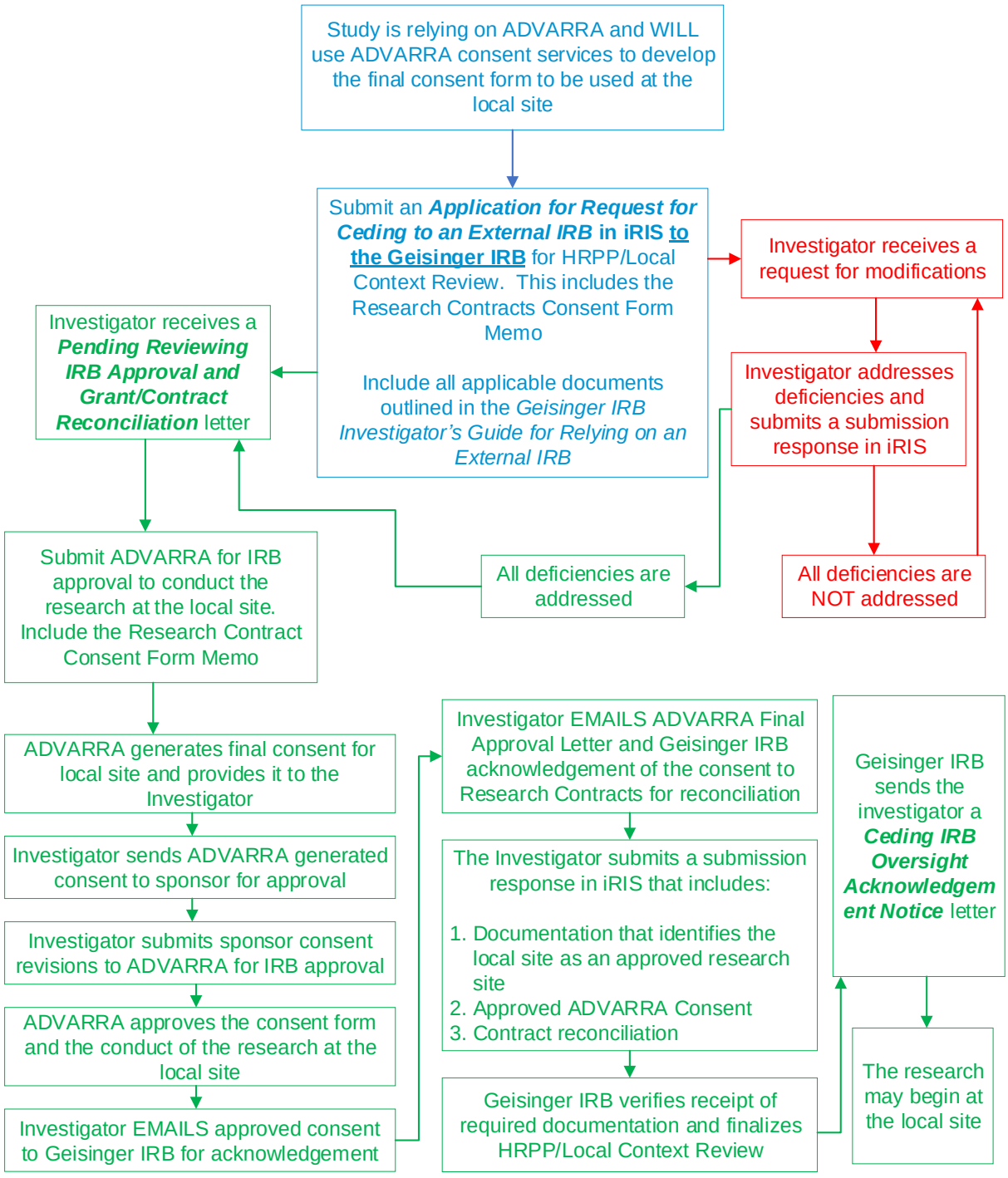
Chart 2



Appendix 5: Relying on an External IRB: Process Overview Flow: Chart 3

Relying on an External IRB: Process Overview Flow

Chart 3



Appendix 6: Relying on an External IRB: Process Overview Flow: Chart 4

Relying on an External IRB: Process Overview Flow

Chart 4