Guidance for Establishing Reliance with External IRB of Record

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Guidance for Establishing Reliance with External IRB of Record

Overview: Reliance Agreements and Deferrals to an External IRB of Record

Institutions may defer IRB review to an external entity, streamlining oversight for multicenter research. Researchers at Children's Wisconsin (CW) needing a reliance agreement should coordinate with the CW HRPP reliance team. This document outlines key considerations, institutional responsibilities, and steps for establishing reliance agreements.

What is a Reliance Agreement?

A reliance agreement (also known as an IRB Authorization Agreement or IAA) is a formal contract that enables an institution to rely on an external IRB for review and approval of human subjects research. This agreement clarifies responsibilities for both the reviewing IRB and the relying institution. While this eliminates the need for each site to conduct separate regulatory IRB reviews, each relying institution will still need to evaluate the research for local context considerations.

Why Use a Reliance Agreement?

- Federal regulations or funding agencies mandate reliance agreements.
- Duplicative reviews are reduced, ensuring consistency across institutions.
- Approval process for multisite studies is streamlined.
- Administrative burden for researchers and IRBs is reduced.

Can a Study Be Ceded to an External IRB?

To determine if a study qualifies for ceded review, researchers must consult the CW HRPP Reliance Team at CWReliance@childrenswi.org . The reliance team will:

- Assess eligibility for reliance.
- Outline the request process.
- Verify any pre-existing or master reliance agreements.

Institutional Sign-Off Requirements

Researchers must obtain CW HRPP approval before using an external IRB. Sign-off ensures compliance with local policies and institutional oversight requirements. Details on this process are provided in the Reliance Process section.

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Types of Agreements

IRB Authorization Agreement (IAA)

An IAA is a type of reliance agreement that specifically outlines how one institution's IRB will act as the IRB of record for another institution. This agreement specifies the scope of research, review responsibilities, and how communication and compliance will be managed between the institutions.

SMART IRB

SMART IRB manages a platform designed to ease common challenges associated with initiating multisite research and to provide a roadmap for institutions to implement the NIH Single IRB Review policy (effective date: January 25, 2018) as well as other mandated or desired reliance relationships. Freely available for institutions and investigators, SMART IRB is an integrated, comprehensive platform that allows flexibility in the size and scope of collaboration to enable IRB reliance for multisite studies across the nation, regardless of funding status.

The SMART IRB agreement is a national master IAA that allows institutions to avoid having to negotiate individual agreements per study or group of studies. Children's Wisconsin has signed onto the SMART IRB agreement. Click here for more information about SMART IRB. Click here for a list of institutions that have signed onto the agreement.

CW HRPP **strongly prefers** use of the SMART IRB reliance agreement. The reliance agreement language has been vetted by CW legal and use of this agreement will streamline the process. If for some reason your SIRB cannot use the SMART IRB Reliance Agreement, the CW HRPP can also negotiate a study-specific agreement; however, this will require review by CW legal and could extend the processing timeline.

General Differences Between the IRB and HRPP

The IRB and HRPP serve complementary but distinct roles in the ethical oversight of research involving human subjects. These differences become especially important when entering into reliance agreements:

General IRB Responsibilities

- Conduct ethical and regulatory review of research.
- Approve study protocols, consent forms, and recruitment materials.
- Ensure compliance with federal regulations (e.g., 45 CFR 46, 21 CFR 50 and 56).
- Monitor research for deviations, non-compliance, and adverse events.
- Communicates directly with the research team about study approvals, required modifications, compliance issues, study status and relevant IRB determinations.
- Submit required reports to federal agencies, funding bodies, and collaborating institutions in cases of unanticipated problems, non-compliance, or protocol changes.

General Institutional Responsibilities (HRPP)

- Ensure compliance with policies and regulations at the local level.

- At initial submission and periodically during the study, will conduct internal quality reviews.
- Provide local context information to the reviewing IRB.
- Verify research team training, qualifications, and conflict-of-interest disclosures.
- Support investigators in meeting institutional and IRB requirements.
- Manage communication between the institution, the reviewing IRB, and external collaborators.
- Coordinate local resources to ensure that the study meets all institutional requirements and policies, and ensures that any local reporting requirements are met.

Most reliance agreements, such as the SMART IRB Agreement, require institutions to communicate "local context" considerations to the Reviewing IRB. Local context considerations include addressing institutional requirements for informed consent language (e.g., compensation for injury language); attesting to the adequacy of training and qualifications of the research team; ensuring resources are available to conduct the study locally; and identifying and managing 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). The CW HRPP office will assist teams to provide local context information to the reviewing IRB. This is typically done via a site survey process during local context review. This local context review process is described later in this document.

Obligations when an external IRB is responsible for reviewing a research study

Researchers relying on an external IRB must:

- Obtain initial approval to be included as a participating study site,
- Obtain CW HRPP approval to proceed with the reliance process,
- Use IRB-approved study documents,
- Use the communication mechanisms established in the reliance agreement (e.g., either to the IRB directly or to the lead study team or to a coordinating center and shadow submission to the CW HRPP),
- Report:
  - Unanticipated problems, noncompliance, and significant new information,
  - Study progress,
  - Local updates (e.g., consent form or recruitment materials, local research staff changes),
  - Communicating applicable study updates with other relevant local institution committees and/ or offices (e.g., research billing, radiation safety committees, pharmacy, oncology review committees).
- Ensure research staff are qualified and appropriately trained,
- Maintain compliance with both Reviewing IRB and local institutional policies as found in HRPP SOP Manual and
- Comply with the determinations of the Reviewing IRB and any special requirements of the CW HRPP.

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Process for Setting Up a Reliance Agreement at Children's Wisconsin

An invitation to rely on a SIRB is sent to participating sites. We call this a Reliance Invitation. Sometimes the SIRB sends the invitation directly to site Human Research Protection Programs (HRPP), and sometimes the study teams receive instructions to connect with their HRPP. At Children's, we require the invitation from the study team before initiating reliance activities.

Step 1: Initial Review and Institutional Signoff

1. **Consult with Director, Clinical Trial Operations to assess study feasibility**

2. **Consult with Children's HRPP Office Reliance Team**
   - Evaluate whether the study involves multiple institutions and if a reliance agreement is necessary or beneficial for IRB review.
   - Engage the HRPP early in the process to discuss reliance options; again Children's strongly prefers to utilize the SMART IRB Reliance Agreement, but the HRPP Office can help determine the best pathway for reliance.

3. **Submit Reliance Request in eBridge:**

   Reliance requests must be initiated in eBridge.

   1. Once logged into eBridge, select "New Human Research Project" on the left-hand side of the dashboard.
   2. When you get to question 3.1, select the option that reads, "Research Project requesting reliance on another IRB."
   3. Then, select the type of reliance (e.g., NCI CIRB).
   4. Follow the directions to upload required documents and complete the application.
   5. In Section 7, you will select "No," and fill out the boxes as a multisite study to indicate what, specifically, will be happening at MCW/FH/Versiti/Children's Wisconsin.
   6. Follow the additional prompts throughout the SmartForm to complete the submission and upload any required reliance documents in Section 52. At a minimum, include:

      - SMART Acknowledgement Letter or IAA
      - Site survey (if applicable)
      - Protocol
      - Consent forms (tracked changes is preferred)
      - HIPAA forms (if separate)
      - Surveys (if applicable)
      - Applicable local letters of support

   Please note that you will have to create consent forms and other subject facing materials which meet local requirements based on the model documents provided by the coordinating center. This may be done by copying/pasting locally required language from MCW/Children's consent templates to the IRB of record's consent templates. MCW/Children's consent templates are located here. If you need assistance, please contact

the Children's Wisconsin IRB reliance team at CWReliance@childrenswi.org. These customized documents are reviewed for local context at this stage as well.

4. **The CW HRPP analyst reviews compliance with institutional requirements.**

   Study teams will work with an HRPP Analyst to confirm all local requirements, including consent language and reliance agreement materials, have been addressed. This is the step at which the Local Context (LC) review will occur. The same institutional LC requirements must be met for study activation as those when using the local IRB (MCW). Examples include, reviews and approvals by other institutional committees (e.g., biosafety, radiation safety, pharmacy, conflict of interest, billing compliance, departmental sign offs) and executing any clinical trials agreements.

   During this time, the Agreement is finalized. Teams will work with the Children's HRPP Office and collaborating institutions to negotiate and finalize the reliance agreement, ensuring all parties are aligned on responsibilities, timelines, and communication channels. If the SMART IRB reliance agreement is being used (HIGHLY RECOMMENDED), there may be different requirements depending on the IRB of record. For example, the IRB of record may require the relying institution to complete a site survey or Letter of Acknowledgement (LOA).

5. **Once approved, the Step 1 letter is issued allowing submission to the IRB of record.**

   - Once the review of the local submission is complete, the HRPP Analyst will publish our "Step 1" letter. This letter describes that Children's is willing to rely on the proposed IRB of record and gives the study team instructions to submit back to the IRB of record for local site approval.
   - When the letter is published in eBridge, the project will move from a status of "Pre IRB Review" to "Action Required."

Step 2: Final IRB approval and study activation

1. **Obtain approval from the IRB of record for CW as a participating site**
   - Once the Part 1 letter is issued, submit the necessary documents to the reviewing IRB. This may include protocol, informed consent documents customized for CW, and any documents to be used locally and if required by the reviewing IRB, site survey or LOA.

2. **Submit approved documents to CW HRPP for consistency review**
   - Once the IRB of record has approved Children's Wisconsin as a site, the local study team should submit IRB of record approval letter and documents approved for local use in the eBridge PRO.
   - Once received, the IRB approved documents will be reviewed by the HRPP Analyst for congruence. The purpose of this final review is to confirm what was originally reviewed is what has been approved. If it is not, additional review may be required.

3. **Part 2 letter is issued confirming all local requirements have been met**
   - **Enrollment may begin at our site ONLY when this Part 2 letter is issued in eBridge.**
   - This communication should be provided to the IRB of record as evidence that all site requirements have been satisfactorily addressed.

Other Topics

Collaborators

For multicenter research, clear communication of responsibilities is essential. Collaborators must adhere to both IRB determinations and local institutional policies.

Consortia Group Research

Some research networks have pre-established reliance agreements with CW to streamline oversight:

- COG
- NMDP