

Institutional Review Board (IRB) Policies & Procedures Manual



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Single IRB Review

Purpose

This policy describes the procedures for ensuring the rights and welfare of research participants are protected when Boston Children's Hospital Institutional Review Board (IRB) is sharing oversight of research with another organization.

Policy

Boston Children's Hospital (BCH) may enter into formal agreements with other institutions that are not legal entities of BCH to serve as the reviewing IRB or to rely on another institution's IRB for research conducted by BCH Investigators. BCH enters into these types of arrangements through a Reliance agreement. In both situations review and approval is required for each request in accordance with the single IRB review policy.

BCH protects the rights and welfare of participants when collaborating with other organizations for the oversight of research.

BCH has established procedures to define the responsibilities of each institution/investigator, coordinate communication among responsible IRBs, promote compliance of all involved institutions and investigators, and manage information shared in external or multi-site research to ensure the protection of human subjects.

Definitions

Reliance Agreement/Authorization Agreement: Identifies and describes the respective authorities, roles, responsibilities, and methods of communication between an institution/organization providing the ethical review of research and a participating site relying on the institution/organization. Institutions that are engaged in human subject research, where one institution will rely on the other institution's IRB, must agree to the terms of the Reliance Agreement before research can begin.

Multi-site: Two or more sites conducting non-exempt human subject research.

Relying Site or Organization: Relying on the review of or has ceded IRB review to another IRB to provide oversight for a specific research study or set of studies. This process is also referred to as deferring IRB review.

Reviewing IRB: The selected IRB of record that conducts the ethical review of research for all participating sites of a multi-site study (also referred to as the IRB of record, central IRB or single IRB (sIRB)).

External IRB: An Institutional review board outside of BCH

Master Protocol: The protocol submitted at BCH and approved to which relying sites can be added.

SMART IRB: The “*SMART IRB*” master reliance agreement is an agreement created in 2016 to harmonize and streamline the IRB review process for multisite studies. It enables reliance on a study-by-study basis, clearly defines roles and responsibilities of relying institutions and reviewing IRBs and eliminates the need to sign reliance agreements for each study [e.g., a non-SMART IRB agreement].

When is Single IRB Required?

NIH Policy

Effective January 25, 2018, the NIH requires use of a Single IRB [sIRB] for the review of NIH-funded multisite studies where each site will conduct the same protocol involving non-exempt human subjects research, whether supported through grants, cooperative agreements, contracts, or the NIH Intramural Research Program.

This Policy applies to domestic sites only. Implementation of the NIH sIRB policy is expected to reduce unnecessary administrative burdens and systemic inefficiencies while maintaining appropriate human subjects protections. Under the policy, “multi-site” is defined as two or more sites. For more information, see: [**Final NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research**](#)

Revised Common Rule

The Common Rule is a federal policy regarding Human Subjects Protection that applies to 17 Federal agencies and offices. Under the new Final Rule governing human subjects protections approved by the DHHS in January 2017, most U.S. government funded cooperative studies that meet the criteria for non-exempt “human subjects research”, and involve more than one site, will also require sIRB review. This requirement went into effect January 20, 2020.

For more information, see: [**The Revised Common Rule's Cooperative Research Provision \(45 CFR 46.114\)**](#)

Boston Children’s Hospital will consider utilizing reliance agreements in other situations on a case-by-case basis. Some additional examples when single IRB review may be considered are:

- Study is part of an existing network, consortium, or agency which encourages or mandates single IRB review
- Proposed external IRB has already reviewed the study or a similar study
- IRB expertise concerns (e.g., special subject population, untypical research design, sensitive topics)
- Efficiency considerations, especially for collaborating research

Reliance Agreements

Boston Children’s Hospital will enter into a written reliance agreement with other institutions to take on oversight of some or all participating sites in a multi-site study or (ii) rely on the review of another qualified IRB when engaged in multi-site human subject research.

When following DHHS or FDA regulations or requirements, the reliance must address:

- Whether the relying organization applies its FWA to some or all research, and ensuring that the IRB review is consistent with the requirements of the relying organization's FWA.
- Which organization is responsible for obtaining any additional approvals for DHHS when the research involves pregnant women, fetuses, neonates, or children (or any other applicable federal agency or department requirements).
- Which organization is responsible for reporting serious or continuing noncompliance; unanticipated problems involving risks to participants or others; and suspensions or terminations of IRB approval. Reporting may be done by the reviewing IRB, the relying organization, or jointly, but must be clearly defined in the reliance agreement.

The reliance agreement or accompanying flexibility terms, may also address responsibilities which can be delegated to the Reviewing IRB or the Relying Site, including:

- Providing education to researchers and research staff.
- Conducting scientific review.
- Ensuring concordance between any applicable grant and the IRB application/protocol
- Reviewing potential noncompliance, including complaints, protocol deviations, and result audits, including
 - Identifying which organization is responsible for deciding whether an allegation of noncompliance has a basis in fact;
 - Identifying which organization's process is used to decide whether an incident of noncompliance is serious or continuing.
- Obtaining management plans for researcher and research staff conflicts of interest. If the relying organization maintains responsibility for this issue, the management plan must be provided prior to the decision by the IRB.
- Managing organizational conflict of interest related to the research.
- Ensuring that, should termination of a reliance agreement occur, one of the parties is clearly responsible for continued oversight of active research until closure or a mutually agreed upon transfer of the studies.

SMART IRB

Boston Children's Hospital (BCH) is a signatory to the SMART IRB master reliance agreement.

It is the preference of Boston Children's Hospital to use the SMART IRB agreement as the basis of reliance for all studies where BCH relies on another institution's IRB or agrees to serve as the sIRB.

Boston Children's Hospital has the discretion to require the use of SMART IRB if it is determined by the BCH IRB office that it is the most efficient and effective way to enter into a reliance arrangement.

Master Agreements

Boston Children's Hospital has executed broad reliance agreements with commercial IRBs, central IRBs, and consortium groups for either individual protocols or specific groups of studies.

Other Individual IRB Reliance Agreements

The use of single IRB reliance agreements was commonly used before SMART IRB so there are multisite research activities that continue to operate under existing single reliance agreements. Going forward in cases where an institution does not meet the eligibility criteria to sign onto the SMART IRB agreement or has not signed on to SMART IRB, Boston Children's Hospital may use an IRB Reliance/Authorization Agreement (IAA) to establish a reliance relationship with an external institution for an individual research protocol.

Authority to Approve and Sign and Reliance Agreements

The Institutional Official (IO, Vice President of Research Administration) is vested with the authority to make the final decision whether or not to serve as the sIRB for multiple sites or rely on another institutions IRB.

The IO has delegated authority to the Senior Director of Clinical Research and the IRB Reliance Specialist to make ongoing determinations about IRB reliance arrangements under the SMART IRB or other master agreements.

All new reliance agreements are signed by the IO. The IO will consult with the Senior Director of Clinical Research Compliance, the IRB Chair and General Counsel as necessary to make these decisions.

Factors considered when deciding whether a proposed reliance agreement is appropriate:

- Where there are regulatory requirements or funding policies that mandate the use of reliance agreements.
- Whether the other IRB's policies and procedures meet BCH standards. If the other IRB is part of an Association for the Accreditation of Human Research Protections Program (AAHRP) accredited Human Research Protections Program (HRPP), then it will be presumed that BCH standards are being met. However, accreditation status does not in itself necessarily suffice as a basis for the decision; nor does not being accredited necessarily mean BCH will not rely on another IRB or serve as sIRB for non- accredited sites
- Whether single IRB review is mandated.
- Source of funding: Which institution is the prime grantee?
- Location of human research activities. If research activities are not the same at both or all institutions, where will most of the contact with the research participants occur?
 - Personnel involved: Is PI able to provide appropriate coordination and oversight of the study activities? What is the expertise of the personnel?
- IRB expertise: Which IRB has the most appropriate expertise to conduct the review?

Procedure

Procedures for When BCH Serves as the Reviewing IRB

Please note: BCH's IRB will not serve as the Reviewing IRB for exempt activities or activities deemed to be not human subject research (exceptions may be made on a case-by-case basis).

1. For multi-site research where BCH IRB is serving as the sIRB of record the BCH IRB will ensure that all relying sites are reviewed and approved consistent with the applicable IRB Reliance Agreement.
2. When a BCH principal investigator (PI) requests that the BCH IRB serve as the reviewing sIRB for a non-BCH research site, the BCH IRB must first review and approve a protocol application before relying site submissions may be reviewed and approved.'
3. The IRB submission will, at a minimum, consist of the following:
 - Master Protocol, including a description of the multi-site oversight process
Consent(s) (if applicable)
 - Recruitment Materials (if applicable)
 - Request for BCH to serve as the Single IRB and names of sites if known
4. Initial review of the Master IRB submission/study documentation (e.g. consent) will be completed as per applicable BCH IRB SOPs.
5. Once the Master Protocol is approved by the BCH IRB, relying sites will be submitted, reviewed and approved individually as reliance requests. These will be typically reviewed and approved using an administrative review process but may be referred to the full IRB as necessary.
6. A Relying Institution must submit information about the relying site to the overall study PI or designee will then submit the following information to the BCH IRB as a reliance request for that specific site:
 - Reliance "Application" with local context information that includes information about the completion of any local ancillary reviews required.
 - IRB Reliance agreement or indication which reliance agreement will be used (i.e. SMART IRB)
 - Required Site specific consent/assent form(s) language that includes site specific HIPPA authorization language or a separate HIPPA authorization form (if applicable)
 - Site specific study documents e.g. recruitment (if applicable)
 - Any conflict of interest and associated management plan
7. The BCH Reliance Specialist will review and approve the reliance request and issue individual letters of acceptance (approval) and finalized consents/assents and study documents (as applicable) for each site relying on BCH IRB.
8. **Continuing review for BCH master protocols:** The overall study PI or designee will submit the continuing review submission in the Boston Children's Hospital electronic Research

Portal (CHERP). The overall study PI is responsible for collecting and combining all information from relying sites for the continuing review.

9. **Review of modifications/amendments for BCH protocols:** Modifications to the master protocol will be reviewed according to existing BCH IRB SOPs/policies. If there are site specific amendments needed, the overall study PI is required to submit the modification or amendment summarizing the change required for the specific site. Any revised protocol materials or consent forms for the specific site must also be included.
10. **Review of UAPs for relying sites under BCH master protocols:** UAPs for other sites submitted through the BCH master protocols will be reviewed according to existing applicable BCH SOPs/policies. Any event submitted from a relying site that is deemed reportable will be managed and evaluated in accordance with the BCH SOPs/policies. BCH will work with the relying site if local investigation and corrective actions are required. The investigation, review and reconciliation and reporting process (if required) will be managed in accordance with the terms of the applicable reliance agreement.
11. The BCH IRB will make available relevant IRB records, including (but not limited to) minutes and other records that document the IRB's determinations to the relying organization, upon request.

Reliance on an External IRB

1. When a BCH principal investigator (PI) requests the use of an external IRB for a protocol for which they will be engaged in human subject research, a request to allow this reliance arrangement must be reviewed and approved. This is accomplished through submission of a **"Rely on another IRB"** application within CHERP.

The submission requires:

- a. The completion of SmartForm questions that will trigger any necessary BCH non-IRB ancillary reviews and completion of the ancillary reviews is required to approve the "Rely on another IRB" application within CHERP
- b. The Master Protocol, including a description of the multi-site oversight process
- c. Editable Consent(s) (if applicable)
- d. Recruitment Materials (if applicable)
- e. Letter of initial and continuing (as applicable) approval from the reviewing IRB

In general an approved protocol and consent are required before making any decision about relying on another IRB; however exceptions may be made based on the nature of the research, level of engagement in research, funding agency, time sensitivity, and as necessary to collaborate with other IRB's office procedures that have different processes.

2. The designated IRB reliance specialist will:

- a. Confirm that Conflict of Interest (COI) and CITI Training have been completed for BCH personnel per applicable BCH IRB Office SOP.
 - b. Confirm the “Rely on Another IRB” application has been submitted with all critical documentation may include the following as appropriate to the research study:
 - i. Indication of which reliance agreement will be utilized, if known
 - ii. Evidence of external IRB approval (required: Initial or continuing review)
 - iii. Protocol (required)
 - iv. Assent, Consent and Parental Permission forms (if applicable)
 - v. Recruitment/Consent Plan (if applicable)
3. The designated Reliance Specialist will also confirm that:
- a. The external IRB has a Federalwide Assurance of compliance.
 - b. The external IRB is accredited by the Association for the Accreditation of Human Research Protection Programs (AAHRPP) or other external quality review process.
 - c. If the institution is not accredited, additional steps may be taken to assure equivalent human subject protections are in place, considering AAHRPP accreditation standards. Depending on the level of risk of the research, the evaluation may include requesting the external IRB attest to conducting their own quality assessment or a review of written materials such as policies, procedures, application forms, and other relevant documents and meetings or interactions with external IRB.
 - d. If the institution is found to have equivalent protections, an appropriate reliance agreement is executed between the BCH IRB and the external IRB. In general, and when possible, SMART IRB will be the preferred reliance agreement.
 - e. The administrative review of the “Rely on Another IRB” submission is complete and including any local ancillary reviews.
 - f. That the investigator and research team have completed appropriate human subject training.
 - g. Provide local context information to the reviewing IRB including local consent form language, ancillary review information and any COI management plans.
4. Upon receipt of necessary documentation as detailed above, the designated IRB specialist has the authority to determine whether reliance on an external IRB is acceptable. Once confirmed, they are authorized to accept the reliance request on behalf of BCH. If there are any questions or concerns, they will be referred to the Senior Director of Clinical Research Compliance before any final decision is made
5. The IRB reliance specialist will generate appropriate correspondence back to the investigator describing the BCH IRB’s acceptance of the external IRB’s review, including the date the determination was made. This will be accomplished through CHERP. Any questions may be referred to the Senior Director of Research Compliance before accepting the reliance arrangement.
6. When a determination that BCH will rely on the review of an external IRB is made, members of the BCH IRB will be notified for informational purposes. These reliance agreements will be reported and listed in the minutes of the next meeting.

7. Ongoing Maintenance of Research Reviewed by an External IRB

- a. On an annual basis, the BCH investigator who relies on an external IRB will be asked to provide an administrative update through CHERP.
 - b. The BCH investigator is required to report only local Unanticipated Problems that have the potential to cause risk as well as serious or continuing noncompliance to the BCH IRB.
 - c. The BCH IRB may at any time during the course of the research (pursuant to the specific terms in the reliance agreement) determine that reliance on the review of the external IRB is no longer appropriate and transfer oversight of the research back to the BCH IRB.
8. If potential concerns regarding the external IRB’s oversight of the research are noted by an individual, the concerns will be forwarded as appropriate to the Senior Director of Clinical Research Compliance and/or the IRB Chair for consideration. The BCH Office of Education and Quality Improvement (EQuIP) may audit any investigator that is serving as the lead or relying PI to determine that all reliance policies are being followed.
9. When additional reviews relevant to the HRPP are conducted by an external organization, the HRPP will:
- Inform the external IRB that additional regulatory requirements, for example, those of DoD or DoJ, may apply.
 - Provide education to researchers regarding additional relevant reviews.

Related Content

Federal Guidance

[***Final NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research***](#)

[***The Revised Common Rule's Cooperative Research Provision \(45 CFR 46.114\)***](#)

Document Attributes

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