Children's Hospital LOS ANGELES®

THE SABAN RESEARCH INSTITUTE

Human Subject Protection Program
Investigator Guidance
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INSTRUCTIONS FOR RELIANCE ON ANOTHER IRB FOR REVIEW AND OVERSIGHT

Purpose

This document provides detailed information about the CHLA requirements to rely on another IRB for review and oversight.

An IRB reliance agreement is necessary to allow for only one IRB review of multisite research. CHLA has established various IRB reliance agreements to allow an external IRB to serve as the Reviewing IRB for research that is conducted at more than one site. These agreements outline the responsibilities of each organization for IRB review, reporting and research oversight.

Definitions

- **Reliance Agreement:** A formal, written document that provides a mechanism for an institution engaged in research to delegate institutional review board (IRB) review to an independent IRB or an IRB of another institution. Institutions that are engaged in human

subjects 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.

- **Multisite:** Under the NIH Single IRB Review policy, "multisite" is defined as two or more sites.

- **Single IRB (sIRB):** An Institutional Review Board that oversees all sites participating in a multisite study. "Single IRB" and "sIRB" are terms used in DHHS regulations and NIH grant policy.

- **Central IRB:** A central IRB is an IRB (usually an independent IRB) chosen by the Sponsor, CRO, Foundation, Consortium to review the study and all the sites that will perform the study.

- **Reviewing IRB:** The IRB serving as the IRB of record for all participating sites in a multisite research study. A Reviewing IRB can be a Single IRB or a Central IRB.

- **SMART IRB:** The "SMART IRB" is not an IRB, but a master reliance agreement that was created in 2016 to harmonize and streamline the IRB review process for multisite studies. It enables reliance on a study-by-study basis, 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). CHLA along with 800+ institutions have already signed onto this agreement and are actively using it as the basis of reliance for multisite projects. See https://smartirb.org/participating-institutions/ for a listing of participating institutions.

- **Smart IRB Master Reliance Agreement:** This is the Master Joinder agreement for becoming a member of SMART IRB.

- **Master Joiner Agreement:** This is the SMART IRB agreement all institutions sign to become a member of the SMART IRB.

- **Flexibility Agreement:** This is an additional agreement some institutions require to cover missing elements in the SMART master joinder agreement (e.g., indemnification, insurance).

- **CHLA Clearance Letter:** This is a CHLA HSPP letter that is issued after a Ceded Review submission is made in iStar. The submission is reviewed by a HSPP team member to ensure all CHLA requirements for the conduct of research are completed, and the documents to be submitted to the central IRB are complete and accurate.

CHLA Reliance Agreements

The following agreements are in place at CHLA:

SMART IRB Agreement: CHLA is a signatory to the SMART IRB master reliance agreement. This is the most commonly used reliance agreement for academic and clinical institutions when

single IRB review is required for multicenter research. CHLA is willing to rely on another institution for IRB review using the SMART IRB agreement.

Master Agreements: CHLA has reliance agreements with several independent IRBs and consortia groups.

- **Advarra IRB**
  - ❑ Allows for central IRB review of clinical trials by the Advarra IRB
  - ❑ Applies to industry initiated and sponsored, multi-center clinical trials
  - ❑ Allows for IRB review of clinical trials by the Advarra IRB that are authorized by the Therapeutics Development Network of the Cystic Fibrosis Foundation

- **WIRB-Copernicus Group (WCG)**
  - ❑ Allows for central IRB review of clinical trials by the WCG IRB
  - ❑ Applies to industry initiated and sponsored, multi-center clinical trials

- **Sterling IRB**
  - ❑ Allows for central IRB review of clinical trials by the Sterling IRB
  - ❑ Applies to industry initiated and sponsored, multi-center clinical trials

- **National Marrow Donor Program (NMDP) IRB** - BMT-CTN, Be the Match, CIBMTR, Be the Match BioTherapies studies
  - ❑ Allows for IRB review of research studies by NMDP IRB
  - ❑ Applies to studies funded and/or supported by NMDP consortia

- **University of Southern California (USC) IRB**
  - ❑ Allows for IRB review of research studies by CHLA IRB or USC IRB
  - ❑ Applies to research conducted at both CHLA and USC

- **National Cancer Institute (NCI) Central IRB (CIRB)**
  - ❑ Allows for IRB review of oncology group clinical trials (e.g., COG) by NCI CIRB
  - ❑ Applies only to clinical trials that are reviewed by the NCI CIRB

Individual IRB Authorization Agreements: In cases where an institution does not meet the eligibility criteria to sign onto the SMART IRB agreement, CHLA may use an IRB Authorization Agreement to establish a reliance relationship with an external institution.

- ❑ IRB Authorization Agreements must be reviewed by the HSPP Director and are sent to the Contracts and Clinical Research Office for signature. Fully executed reliance agreements are kept as IRB records for the CHLA HSPP.

New Master Reliance Agreements and Other Reliance Materials

- ❑ All requests for new master reliance agreements or other reliance materials from a Reviewing IRB must be initiated by the HSPP Director.

- ❑ Master reliance agreements are negotiated and signed by CHLA Contracts and Clinical Research staff. Fully executed master reliance agreements are kept as IRB records for the CHLA HSPP.

Submitting to the CHLA HSPP Office for Initial Clearance

All studies must first be cleared by the CHLA HSPP office. The clearance process is an administrative review to ensure all CHLA requirements for the conduct of research are completed, and the documents to be submitted to the central IRB are complete and accurate. The central IRB will not review a submission to add CHLA as a site without a CHLA clearance letter.

1. Submit a ceded review application in iStar to obtain CHLA HSPP clearance to rely on an external IRB.

2. All department/division and ancillary reviews must be completed **before** a submission may be cleared by the HSPP Office. To avoid delays in the CHLA clearance process, be sure to answer all of the questions in Section 50 of the iStar application – do not leave sections blank.

3. The CHLA HSPP will issue a clearance notice to the Principal Investigator (PI).

4. After receiving the clearance notice, the CHLA study team can submit for review by the external IRB.

Instructions for Submitting to the CHLA HSPP Office for Initial Clearance

IMPORTANT NOTE:

- ✓ **Do not use these instructions for submitting to the Advarra IRB, WCG IRB, Sterling IRB, or another central IRB.** Refer to, "Instructions for Making a Submission to a Central IRB for Industry Sponsored Multi-Center Clinical Trials" for details about the submission process to a central IRB.

These instructions are for studies that will not be reviewed by a central IRB:

1. Contact the lead site or study coordinating center of the study to obtain the approved protocol and approved/template consent and assent forms.

2. Working from the approved/template consent and assent forms, add **all required CHLA consent form language** using tracked (redline) changes. Use one of the following consent form checklists located on the HSPP website to make these additions:
   - ❑ Use the "**NMDP IRB Consent Form Checklist"** document for studies that will be reviewed by the NMDP IRB.
   - ❑ Use the "**NCI CIRB Boilerplate for Consent Forms"** document for studies that will be reviewed by the NCI CIRB.
   - ❑ Use the "**External IRB Consent Form Checklist"** document for all other studies that will be reviewed by an external IRB.

3. Include the following **information** in the CHLA Ceded Review Application:

   - ❑ Funding source for the study.

- ❑ For extramural funding, identify whether CHLA is the prime awardee or a subawardee.
- ❑ If NIH funded, indicate whether the award requires use of a single IRB.
- ❑ Name of Reviewing IRB.
- ❑ What IRB reliance agreement will be used (e.g., SMART IRB) – see above list.
- ❑ Any additional documentation required by the Reviewing IRB (e.g., letter to agree to rely, flexibility agreement, indemnification letter; forms to obtain CHLA local context information, CHLA institutional profile information). **Note:** CHLA study teams should not sign these documents. They must be reviewed and signed by the HSPP Director or CHLA Contracts and Clinical Research staff.

4. Include the following **documents** with the CHLA Ceded Review Application:

- ❑ The approved or final study protocol that all participating sites will follow.
- ❑ Reviewing IRB study approval letter (if the *study* is approved). Note: This is *not* the CHLA site IRB approval letter.
- ❑ Reviewing IRB's template consent/assent documents.
- ❑ CHLA specific consent/assent forms containing CHLA required language (using redline tracked changes).
- ❑ CHLA Conflict of Interest Research Committee (COIRC) management plan (if required).
- ❑ Any other CHLA specific materials to be used by CHLA study team (e.g., ads, flyers, etc.)

Submitting to the Reviewing IRB

After you receive a CHLA clearance letter you can submit to the Reviewing IRB. **Include these documents with your submission to the Reviewing IRB:**

- ➢ CHLA HSPP Clearance Notice of Ceded Review Clearance Letter.
- ➢ CHLA specific consent/assent forms (versions cleared by CHLA HSPP).
- ➢ CHLA specific materials (as applicable – versions cleared by CHLA HSPP).
- ➢ CHLA Institutional Profile Information Sheet (CHLA Local Context). This document is located on the CHLA HSPP Website.
- ➢ Other Reviewing IRB documents (e.g., application or submission form) required for review.

Submitting an Amendment to the CHLA Ceded Review Application

1. Once the Reviewing IRB approval is received, there is **one last step** before subjects may be enrolled into the study. The CHLA study team will need to **file an amendment in iStar** to upload the following approved documents to the CHLA ceded review application:

- ❑ Reviewing IRB approval letter
- ❑ Reviewing IRB approved CHLA consent and assent forms
- ❑ Any approved CHLA specific recruitment or subject materials

2. CHLA study teams also are responsible for submitting **additional amendments** to the CHLA ceded review application in iStar when **new approval letters and study documents** are issued by the central IRB.

3. Amendments are processed by the CHLA HSPP staff. The purpose of filing amendments to the CHLA ceded review application is to ensure currently approved documents appear in iStar and OnCore for use by the CHLA study team.

Managing Your Approved Study with the Reviewing IRB

IMPORTANT NOTE: These requirements apply to all studies that are reviewed by an external IRB, including studies reviewed by a central IRB.

1. CHLA study teams are responsible for keeping **all the IRB approved protocol documents and information** in the research regulatory binder/e-Reg for the study.

2. If your **study contacts change**, be sure to revise them with the Reviewing IRB, so that the correct people receive email correspondence about the study.

3. CHLA study teams are responsible for assuring all **CHLA site amendments, continuing reviews, and reportable events** are reviewed by the Reviewing IRB.

4. CHLA study teams are responsible for **understanding the Reviewing IRB's requirements for review and oversight of the research**. These requirements may be different than CHLA IRB requirements. For example, requirements for translation and submission of new information that requires prompt reporting. **NOTE:** Always access the Reviewing IRB's website and resources **from the source** to ensure you are referring to the most current versions of the documents.

FAQs for Managing Studies Approved by an External IRB

➢ When is CHLA Clearance Required for Amendments?

Amendments do not require any CHLA clearance with the exception of the following:

- ✓ Change of the CHLA Principal Investigator (PI)
- ✓ Change or addition of CHLA Co-Investigators (Co-I)

❑ PI and Co-I changes must be submitted and cleared by the CHLA HSPP office to verify human research training requirements are completed and to identify any financial conflicts of interest that require review by the COIRC. Submit an amendment in iStar for clearance.

- ✓ **NOTE:** Personnel changes may or may not require approval from the Reviewing IRB. CHLA study teams are responsible for understanding and complying with the submission requirements of the Reviewing IRB for study personnel amendments.

- ❑ CHLA clearance is not required for amendments initiated by the lead site, sponsor or Reviewing IRB.

➢ When is an amendment to the Ceded Review Application in iStar required?

- ❑ When amendments approved by the Reviewing IRB require changes to the study protocol, CHLA site consent and assents forms, or recruitment materials, submit an amendment in iStar to describe the changes in the research and provide the newly approved documents.

➢ Is CHLA Clearance Required for Continuing Reviews and Closure Reports?

No. Continuing reviews and closure reports do not require CHLA clearance.

➢ When is an amendment to the Ceded Review Application in iStar required?

- ❑ When continuing review approval is granted by the Reviewing IRB, submit an amendment in iStar to indicate continuing review of the study has been performed and upload the new approval letter, approved protocol (if changed), updated consent/assent form(s), and any other documentation provided by the Reviewing IRB.

- ❑ When the study has been closed with the Reviewing IRB, submit a closure report in iStar (by selecting the "Close IRB" function) for the Ceded Review Application to close the ceded review submission at CHLA.

➢ Is CHLA Clearance or CHLA IRB Review Required for Reportable New Information and Events?

No. CHLA clearance or CHLA IRB review is not required for reportable new information and events.

- ❑ **Do not submit any reportable events in iStar.** The CHLA IRB is not the Reviewing IRB.

➢ Does the CHLA HSPP Office Require Any Notification of Reportable New Information and Events that Occur at CHLA?

Yes. Once a submission for a **CHLA reportable event** has been made to the Reviewing IRB, send the following information to the CHLA HSPP Office. Use the IRB Reliance email address for this purpose (**irbreliance@chla.usc.edu)**:

- ❑ Details of the submission made to the Reviewing IRB.
- ❑ The Reviewing IRB's review of the event and its determination(s).

This email submission provides the CHLA HSPP office with information that will be used to communicate with the Reviewing IRB for events that happen at CHLA. The HSPP Office will ensure any local CHLA requirements are considered by the Reviewing IRB, and will partner

with the Reviewing IRB in the event that any information needs to be reported to federal agencies.

Reviewing IRB Authorities

The Reviewing IRB is responsible for review and oversight of the study for all sites conducting the research. The Reviewing IRB has authority to:

- Approve, require modifications to secure approval, and disapprove all human subject research activities overseen and conducted under its purview.
- Suspend or terminate approval of human subject research not being conducted in accordance with its requirements or that had been associated with unexpected serious harm to participants.
- Observe, or have a third party observe, the consent process and the conduct of the human subject research activities.
- Decide whether financial interests related to the research and the management, if any, allow approval of the human subjects research.

CHLA Investigator Responsibilities When Relying On An External IRB

- Do not commence research until you have the Reviewing IRB approval letter and obtain all other required department/division and ancillary approvals.
- Comply with all requirements and determinations of the Reviewing IRB.
- Ensure that there are adequate resources to carry out the research safely. This includes, but is not limited to, sufficient investigator time, appropriately qualified research team members, equipment, and space.
- Ensure that research staff are qualified (e.g., including but not limited to appropriate training, education, expertise, credentials, protocol requirements and, when relevant, privileges) to perform procedures and duties assigned to them during the study.
- Personally conduct or supervise the research.
- Conduct the research in accordance with the relevant current protocol approved by the Reviewing IRB.
- Protect the rights, safety, and welfare of subjects involved in the research.
- Submit proposed amendments to the Reviewing IRB prior to their implementation.
- Do not make modifications to the research without prior Reviewing IRB approval unless necessary to eliminate apparent immediate hazards to subjects.

- Submit continuing reviews when requested by the Reviewing IRB.

- Submit a closure form to the Reviewing IRB to close research when requested by the Reviewing IRB.

- If research approval expires, stop all research activities and immediately contact the Reviewing IRB.

- Promptly report to the Reviewing IRB any new information that requires prompt reporting (refer to Reviewing IRB requirements).