Guidelines for CHLA as Single Reviewing IRB (sIRB)

Purpose: The purpose of this document is to establish parameters for when CHLA may serve as the **Reviewing IRB** (IRB of record) for a multi-site study. To facilitate the conduct of human research, and to comply with the NIH's grants policy and federal regulations requiring the use of a single IRB for review of multisite research, CHLA is willing to serve as the single Reviewing IRB for federally funded multisite research.

Federal Policy: Effective January 25, 2018, the National Institutes of Health (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.

Definitions for NIH-funded research
"Multi-site" means that the same research procedures (i.e., protocol) are being conducted at one or more domestic sites and each site is under the control of a local participating investigator. This typically involves a lead site that receives a grant or contract directly from NIH and then establishes a subaward or subcontract to each participating site.

"Same Research Protocol" means protocols that address the same research questions, involve the same methodologies, and evaluate the same outcomes. Additionally, sites that are accruing research participants for studies that are identical except for variations due to local context consideration are considered to be conducting the "same research protocol." If a study involves a separate site for study coordination or coordination of data and statistical analyses and the site is conducting the same protocol as the other participating sites, then all sites would be expected to rely on the designated sIRB.

This also includes multi-site studies where most sites are conducting the same protocol but one or a few sites are responsible solely for overall study coordination, laboratory services, statistical services, or other study support functions.

CHLA As Single Relying IRB
Decisions related to whether the CHLA IRB will agree to serve as the sIRB of a research study are made by the CHLA Human Subjects Protection Program (HSPP) on a protocol-specific, case-by-case basis. Several factors may affect the decision, including, but not limited to:

- The funding source
- Whether appropriate resources (i.e., personnel and financial support) are available to support the plans for sIRB review
- The number of sites participating in a study that will be enrolling (maximum 6 sites)
- The specific subject populations under study
- The number of cohorts in the study design
- The number of subjects anticipated to be enrolled
- The complexity and risk level of the study protocol

The CHLA IRB will not serve as the sIRB under the following circumstances:

- Exempt and Not Human Subjects research
- When unable to meet the needs of specific populations (e.g., prisoners, veterans)
- Local IRB is required by federal, tribal, or state laws
- Foreign sites
- Research conducted is under career development, research training or fellowship awards

- When study involves more than six Relying Sites
- Collaborative projects in which multiple sites are involved but different sites may complete different parts of the study

Identifying the Reviewing IRB

Establishing Reliance Agreements
The Reviewing IRB and the Relying Sites are responsible for working together to identify the sIRB for any given study. This decision must be documented in writing via an IRB Authorization Agreement, also called a Reliance Agreement. The Reliance Agreement outlines the obligations and responsibilities of both parties. When the CHLA IRB will be the reviewing IRB, the SMART IRB agreement will be utilized, unless extenuating circumstances prevent its use. This will avoid negotiating the terms of the agreement for each study with every participating site and managing the study according to different terms for each site.

Costs of sIRB Review
The costs for IRB review at a single institution by that institution's IRB have typically been considered an indirect cost covered under an institution's Facilities and Administration (F&A) rate (except for industry-initiated-and-sponsored studies). However, NIH expects that many sIRBs will charge fees to review for other sites and these can be part of the **direct costs**. The fees are the responsibility of the prime site and should be included in the grant budget.

Fees for CHLA IRB as sIRB
The table below outlines the IRB fee schedule that must be built into your budget.

Service Provided	**CHLA IRB Fee**
Initial review (full or expedited)	$0 for protocol and CHLA site $1,500 per site for external sites
Continuing review (full or expedited) – required at least annually, but may be required more frequently	$0 for CHLA site $1,000 per site for external sites
Amendment review (excluding administrative/editorial changes)	$0 for CHLA site $500 per site for external sites

Protocol and Consent Form Development
As with any study, the protocol must be developed and finalized. This is primarily the responsibility of the lead study team, although the participating PIs and study teams may also provide input as part of a collaborative effort.

When using sIRB review, it is important to ensure that the protocol includes a detailed recruitment plan, consent process, and data and safety monitoring plans. The investigators should also consider standard of care procedures that may differ from one institution to another, and how this may affect the conduct of the research. These details will not only help the sIRB have complete information for their review but will also ensure that the relying sites have enough information to determine if the study meets local

requirements. The participating PIs and study teams should provide information about their local requirements, such that the protocol can address the needs at each site.

The CHLA consent and assent document(s) should be submitted with the initial application. Master consent and assent form templates will be developed once the CHLA forms have been finalized. The lead study team will be required to provide the approved master templates to the relying sites once the initial CHLA application has been approved by the CHLA IRB.

Reviewing IRB Determinations

- If the CHLA IRB reviews and disapproves the research, the research cannot be deferred to any other IRB for review.
- The IRB will document all protocol-specific determinations for relying sites on the approval letter.
- Continuing review will be required for all multi-site research for which CHLA is serving as the single Reviewing IRB.
- Any proposed changes or modifications to the study will require submission of an Amendment application.

Responsibilities of the Lead Study Team

As part of the grant preparation process that occurs prior to IRB submission, the overall PI for a multisite study that will use a sIRB should identify who will take on the role of the lead study team. This may be the PI's own study team, a coordinating center, both, or a Contract Research Organization (CRO).

The lead study team has responsibilities associated with the use of a sIRB. Consideration of these responsibilities is essential for realizing the potential efficiencies of using a sIRB. Study teams can find a list of many of these described in the Overall Principal Investigator/Lead Study Team Guidance and Checklist provided by SMART IRB. The lead PI should carefully consider the staffing of the lead study team when constructing the grant budget.

The sIRB is responsible for reporting events to federal agencies. It is expected that the draft letter be shared with collaborating institutions prior to submission to the Office of Human Research Protections (OHRP) or U.S. Food and Drug Administration (FDA).

Additional Lead Study Team Requirements for Using CHLA As Single Relying IRB

- Use of the SMART IRB Master Reliance Agreement and reciprocal IRB reliance model
- Use of IREX or SMART IRB portal to document reliance, capture local considerations, and share sIRB approval with relying sites
- Use of Advarra eRegulatory Management System (eReg) for Clinical Trials
- Development of a robust communication plan identifying and documenting how the CHLA study team will communicate with Relying Site Study Teams
- PI must have dedicated high level study staff and have the capacity to take on coordinating responsibilities

Studies with more than three sites will require significant additional staffing resources to manage the complex communications, coordination, and document management associated with the use of a sIRB across sites. This role is being called the "IRB Liaison" by CHLA and many other institutions. It is typically a staff member on the lead study team. This may be 1.0 FTE supported by direct cost extramural research funds, depending upon the size and complexity of the study. See the template Communication

Plan for Single IRB Review provided by SMART IRB for a description of the key communication roles related to sIRB review.

Primary duties of IRB Liaison:

- Understand and communicate the policies and processes of the reviewing IRB, and be familiar with the research protocol and the sites
- Work with the sites and their research compliance or IRB offices to establish reliance agreements with the reviewing IRB
- Coordinate the timing of initial review and modifications across all sites
- Assist the participating sites with completing and submitting materials to the reviewing IRB, which may include preparing and submitting all materials on their behalf
- Facilitate the continuing IRB review for the entire study by collecting information from all sites and submitting it to the reviewing IRB
- Serve as an intermediary between the reviewing IRB and the participating sites
- Obtain local context considerations (e.g., a state's age of majority) for each site and ensure that the information is provided to the reviewing IRB
- Assist the participating sites with responding to IRB requests
- Plan IRB and other regulatory approval timelines and troubleshoot challenging situations
- Coordinate the payment of IRB fees by the lead site

Resources

Final NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research
NIH FAQs on the Single IRB Policy for Multi-Site Research

CHLA HSPP Webpage: https://www.chla.org/research/human-subjects-protection-program-hspp-and-institutional-review-board-irb