AT THE FOREFRONT UChicago Medicine | Office of Clinical Research

Relying on an External IRB

The University of Chicago BSD Human Research Protections Program (HRPP) has the responsibility to consider multi-center research projects that request the University of Chicago to rely upon an external reviewing IRB prior to completing a reliance agreement. In these cases, the BSD HRPP staff (in consultation with a representative from the IRB) may review the following documentation and/or appropriate information including but not limited to: the external IRB's policies and procedures, institutional information, regulatory requirements, protocol document, and consent form document.

The BSD HRPP has the responsibility to ensure investigators and staff are appropriately qualified to serve on the research team, to ensure that ancillary reviews are complete, that subject complaints and injuries are addressed, that QA/QI apply to studies that cede review to an external IRB, that the institution is compliant with the terms of the reliance agreement and that local context issues are communicated to the reviewing IRB. The AURA CIRB application allows the reliance team within the BSD HRPP to assist other departments and the IRB with completion of these activities.

Please note Institutional sign-off will be needed prior to the start of the research activities at the University of Chicago.

* It has been noted the terms external IRB, reviewing IRB, and central IRB are used interchangeably. This guidance document can be used for reliance agreements using any one of these terms when requesting reliance from UChicago.

Before submitting a request to cede review to an external IRB, consider the following:

1) Is Reliance optional or mandatory for participation in the project?
    a. If required – proceed to step 2
    b. If optional- email IRBReliance@bsd.uchicago.edu and provide an explanation as to why reliance is being sought. For example, a study network that anticipates more than one protocol focused on a specific disease/condition conducted at predetermined study locations.

2) Ensure that our institution is 'engaged' in research. For example, these activities would *not* constitute as engagement in research:
    a. Inform prospective subjects about the availability of the research
    b. Provide prospective subjects with information about the research (which may include a copy of the relevant informed consent document and other IRB approved materials) but do not obtain subjects' consent for the research or act as representatives of the investigators.
    c. Provide prospective subjects with information about contacting investigators for information or enrollment

For further guidance, please refer to the OHRP website: https://www.hhs.gov/ohrp/regulations and-policy/guidance/guidance-on-engagement-of-institutions/index.html
The Office of Human Research Protections (OHRP) Decision guide may also be used for further clarification: https://www.hhs.gov/ohrp/regulations-and-policy/decision-charts/index.html

Any additional questions may be routed to IRBReliance@bsd.uchicago.edu.

3) Review external reviewing IRBs Standard Operating Procedures (SOP) to ensure that the site (UChicago study team) has set appropriate procedures in place to adhere to these policies.

Roles and Responsibilities When Relying on an External IRB

As Principal Investigator (PI) at the University of Chicago **(Relying Institution)** for a study that may be overseen by an external IRB, you should be aware of your responsibilities.

During Consideration of Protocol

- ✓ You will be asked to submit a CIRB protocol in the AURA-IRB electronic system and upload documents received, including lead site IRB approval, protocol narrative, site-specific consent form if applicable, and any other relevant materials.
- ✓ Any reliance materials that the external IRB needs completed to document reliance should be included in the AURA IRB CIRB application.
    - This includes any reliance agreements, local context forms, communication plans, etc.
    - The BSD IRB and HRPP staff no longer review or complete these materials outside of the AURA IRB system.
- ✓ During this time, you will also be asked to provide in AURA-IRB the following:
    - The names and roles of all key study personnel on the local study team
    - Any management plans for potential conflicts of interest (COI) relevant to the study that will be ceded to the external IRB, including any new or altered management plans put in place throughout the lifespan of the study. If a copy of a finalized management plan is needed, you may reach out to the IRB Director.
    - Work with the Lead Study Team and the UChicago BSD IRB Reliance team to incorporate locally required language into the consent template to be used by the local study team, such as institutionally required compensation for injury language, local study team contact information, and additional costs that subjects may incur that differ from those identified in the template consent form.

Throughout the Course of Study

- ✓ Be aware of the study communication plan (typically outlined in grant or protocol narrative). Promptly respond to questions or requests for information from the Lead

Study Team (or their designee) as well as from the Reviewing IRB.

- ✓ Participate, as required, in conference calls regarding a study as requested by the Lead Study Team, Reviewing IRB, or the UChicago BSD IRB Reliance Team.
- ✓ Become familiar with the reportable event policy of the Reviewing IRB to ensure that you appropriately report protocol deviations, noncompliance, significant subject complaints, subject injuries, unanticipated problems, or other events required by the Reviewing IRB to be reported and within the timeframes required.
- ✓ Ensure that all local reviews and sign offs that are required in addition to IRB approval are in place before a study is activated, such as coverage analysis, department approvals, data use agreements, material transfer agreements, ancillary committee reviews (e.g., PRMC, IBC, RADRAC, NERC, etc).
- ✓ Notify UChicago BSD IRB of any staff changes via personnel change amendment so they can confirm their training is current and help ensure any relevant COI management plans are communicated to the Reviewing IRB.
- ✓ Notify the lead PI of:
    - Any reportable events that occur locally, according to regulations and the Reviewing IRB's policy.
    - Any changes (including those related to funding and personnel) in accordance with the Reviewing IRB's policies and procedures for timing and content of such submissions.
    - Any management plans, including any updates to these plans, as relevant to the study.
    - Any applicable information for continuing review progress reports in accordance with the Reviewing IRB's policies and procedures for timing and content of such submissions.
- ✓ Follow all determinations of the Reviewing IRB.
- ✓ Only implement changes of protocol, including local variations, after the Reviewing IRB has approved them, except in cases where a change is required to avoid an apparent immediate hazard to participants. Utilize the 'Updating CIRB Study' function in AURA-IRB and ensure that all members of the UChicago study team have access to relevant study documents.
- ✓ Provide access to study records for audit by UChicago Office of Clinical Research and BSD IRB, the Reviewing IRB's institution, and other regulatory or monitoring entities upon request.

After Study Initiation the PI and study team should:

- ✓ Oversee and conduct the study in compliance with BOTH the Reviewing IRB

requirements and the applicable institutional policies and procedures.

- ✓ The PI must maintain records of all research and related activities as required by applicable federal, state and local regulations and institutional policies.

Amendments:

- ✓ The PI is responsible for submitting amendments to the Reviewing IRB either directly or through the sponsor, or their Coordination Center/Lead Study PI. The PI must verify that the Reviewing IRB approves any amendments to the protocol or approved documents prior to their implementation or use unless necessary to eliminate apparent immediate hazards to subjects.
- ✓ The PI or relying study team are responsible for updating the AURA-IRB form with newly approved documents, continuing reviews and other study related changes.
    - When new documents or study materials are provided to the University of Chicago study team related to the conduct of the study, the study team should perform the 'update CIRB study' function in AURA IRB to include these documents.
- ✓ Part of the institution's responsibility when ceding review to an external IRB is to communicate potential conflicts of interest. Personnel amendments are reviewed for conflicts and study teams will be notified when a conflict needs to be disclosed to the reviewing IRB.
    - Changes in personnel should be submitted in AURA through a personnel amendment.
    - Changes to management plans or new conflicts of interests that need to be disclosed may result in the need to update the consent form.
    - If changes to the consent form are necessary, the study team will need to provide the revised consent form to the Reviewing IRB or reviewing IRB contact for review and approval.
    - Changes to conflicts of interest may require notification to participants.

Continuing Reviews:

- ✓ The PI remains responsible for submitting any required information needed for continuing review of the research to the Reviewing IRB or to the Lead PI or sponsor for submission to the Reviewing IRB for approval.
- ✓ Continuing Review approval from the Reviewing IRB should be uploaded into AURA-IRB by completing the Update CIRB activity.
- ✓ If at any time study approval lapses, the PI must cease all human subject research work related to the study. If the PI determines that subjects who are already enrolled on the trial may be harmed if research ceases, the PI should follow the Reviewing IRB's procedure for notifying the Reviewing IRB about the individual subject(s) and the

justification for remaining on the trial.

Reportable Events and Unanticipated Problems:

- ✓ Each Reviewing IRB may have different report requirements with regard to what should be reported and the timeframe for reporting.
- ✓ The relying PI is responsible for notifying their Reviewing IRB of any event meeting the Reviewing IRB's requirement for reporting via the mechanism the Reviewing IRB determines to be appropriate.
- ✓ The relying PI is responsible for reporting to the UChicago BSD IRB as consistent with local policies: https://biologicalsciences.uchicago.edu/irb/irb-policies

Study Closure:

- ✓ Once the study is complete and has been closed out with the Reviewing IRB, the PI is responsible for terminating the study within AURA-IRB.

Submitting a request to rely on an external IRB in AURA IRB

Once it has been determined that the use of a single IRB is appropriate. A CIRB study application should be submitted in AURA-IRB, by clicking on the Create CIRB study button. The CIRB form is designed to collect information that the Institution will utilize to make appropriate reliance determinations. The CIRB form also collects information to be utilized by multiple clinical research operational systems, many of which extract data directly from the AURA-IRB system. For example, data feeds into EPIC, Pharmacy, Oncore, etc.

Much of the CIRB form will reflect a subset of the same questions on the standard AURA-IRB submission form. However, there are some questions that may not appear on the standard AURA-IRB form. Suggestions for how to answer these questions can be found below:

- ✓ View 1.1, question 1, requests the name of the organization/IRB that is requesting to serve as the IRB of record. Please note: If the organization/IRB is not listed in the drop down list, please contact the AURA Help Desk at AURA-Help@uchicago.edu to request that this institution be added.

- ✓ View 1.1 question 2, the type of IRB agreement that will be used by the Reviewing IRB should be selected. If the Reviewing IRB is an institution in which the University of Chicago has a master agreement with or they wish to utilize the SMART IRB cede letter or SMART IRB reliance platform, you should check the option for yes and select the appropriate agreement type.
    - If the reviewing IRB is utilizing the SMART IRB cede letter, please upload the agreement after selecting the SMART IRB Cede letter or addendum to the SMART IRB agreement.
    - As of 5/14/2024, the BSD IRB has reliance agreements with:

- **NCI CIRB** (The National Cancer Institute (NCI) funds an extensive national program of cancer research, including pilot, phase 1, phase 2, and phase 3 clinical trials in adults and children focused on cancer prevention, cancer care and delivery, and treatment. The NCI CIRB is an independent organization that provides reviews of NCI-funded clinical studies.)
- **CHAIRb** (Chicago Area IRB for studies funded and/or sponsored by Chicago PCORI CAPRICORN group). The Chicago Area Institutional Review Board (CHAIRb) is the IRB of record for all CAPriCORN research. CHAIRb is made up of experienced IRB members from all of the CAPriCORN institutions.
- **All of Us** The *All of Us* Research Program is a historic effort to collect and study data from one million or more people living in the United States. The goal of the program is better health for all of us. The protocol was reviewed by the Institutional Review Board (IRB) of the *All of Us* Research Program. The *All of Us* IRB follows the regulations and guidance of the NIH Office for Human Research Protections for all studies, ensuring that the rights and welfare of research participants are overseen and protected uniformly.
- **NEALS** NEALS has developed a strong infrastructure that facilitates rapid institution and support of trials sponsored by industry, foundations, and federal granting agencies. The NEALS **Coordinating Centers** include the Clinical Coordination Center (CCC) and the Data Coordination Center (DCC) located at the Neurological Clinical Research Institute at Massachusetts General Hospital (MGH-NCRI), as well as the Outcomes and Monitoring Center at Barrow Neurological Institute. A sponsor may contract with a NEALS Coordination Center to manage an entire trial or just a portion of the work.
- **PCORI** The Patient-Centered Outcomes Research Institute (PCORI) is an independent, nonprofit research organization that seeks to empower patients and others with actionable information about their health and healthcare choices. Although PCORI's primary purpose is to fund extramural investigators in conducting health research, PCORI's Science Team needs intermittent, periodic Institutional Review Board (IRB) services for the protection of human subjects participating in research conducted by PCORI staff.
- **StrokeNet** In September 2013, the National Institutes of Health funded the stroke trials network, NIH StrokeNet. The National Institute of Neurological Disorders and Stroke (NINDS) established the National Institutes of Health (NIH) StrokeNet to facilitate the rapid initiation and efficient implementation of small and large multisite exploratory and confirmatory clinical trials

focused on promising interventions for stroke prevention, treatment, and recovery, as well as validation studies of biomarkers or outcome measures. The StrokeNet infrastructure consists of 27 regional coordinating centers across the US, a national coordinating center at the University of Cincinnati, and a national data management and statistical center (Medical University of South Carolina). The network also has a Central IRB that is located at the University of Cincinnati and is responsible for the human subjects protection.

- **TrialNet** The TrialNet family is made up of physicians, scientists and healthcare teams at the forefront of type 1 diabetes research.
- **SMARTIRB** (An authorization agreement established by the NIH National Center for Advancing Translational Sciences (NCATS) that allows institutions to rely upon each other under one agreement). Please go to https://smartirb.org/ to determine if the reviewing IRB is a part of SMART IRB: https://smartirb.org/participating-institutions/.

- If the Reviewing IRB we are being asked to rely upon is not listed above *and* the institution is NOT part of SMART IRB, an authorization agreement will need to be established with that institution and you should check the option for no and upload a copy of the IRB Authorization that will be utilized to document reliance between the institution and the reviewing IRB.

2. **Will a master agreement or the SMART IRB agreement be used to document reliance between the University of Chicago and the organization/IRB listed above?**

● **Yes** ○ **No** Clear

* **Please check an option:**

- ☐ **IREX (Only check this option if the Reviewing IRB is asking for reliance to be document only in IREX and the University of Chicago will not be asked to sign a reliance agreement).**
- ☐ **STROKENET**
- ☐ **NCI IRB**
- ☐ **PCORI**
- ☑ **TRIALNET**
- ☐ **NMDP**
- ☐ **All of Us**
- ☐ **SMART IRB Reliance System (Only check this option if the Reviewing IRB is not requesting the University of Chicago to sign a reliance agreement and will ask the SMART IRB POC to login to SMART to cede review)**
- ☐ **SMART IRB Cede Letter or addendum to the SMART IRB Agreement o If this option is chosen, attach a copy of the agreement that will be signed.**
- ☐ **NEALS**
- ☐ **CHAIRb**

✓ In View 1.1 question 3, provide the original IRB approval date of the study.

- ✓ In View 1.1 question 4, the approval for the study along with the approval for our site should be uploaded.
    - The approval letter can be the original approval of the study but should be current. If the approval letter is greater than a year old, please also attach a copy of the most recent Continuing Review.
    - In addition, the memo or approval letter showing approval of The University of Chicago as a study site should be provided in this question.

- ✓ In View 1.1 question 5, if the reviewing IRB is requesting completion of a local context questionnaire or reliance materials that are not the reliance agreement, please check the option for yes and attach a copy of the documents that need to be completed by the IRB.
    - The local context form should be started by the study team with relevant study details, but the institutional policies should be addressed by the IRB office.

- ✓ In View 3.2 Purpose Question 2, if the University of Chicago is not participating in all aspects of the protocol, please check the option for no. If the University of Chicago is participating in all aspects of the research, please check the option for yes.
    - Checking the option for no in this question, will open an additional question. Please select the activities that will be conducted at the University of Chicago.
    - If you check the option for Data Analysis only, an additional text box will open. Please describe the type(s) of data the University of Chicago team will have access to. A full description of data types can be found in the help (?) button within the question.
    - If you check the option for limited activities, an additional text box will open. Please describe the specific activities that will be completed by UChicago researchers.

- ✓ In View 15.1 Informed Consent Determination, select the option for how the reviewing IRB has approved for University of Chicago team to obtain consent.
    - Checking the option for Written Consent Form, Request to Waive Written Consent or Request to Alter Consent will open view 16.0 Consent and Assent Documents. Please provide the clean and tracked changes version of the consent provided by the Reviewing IRB with the University of Chicago site specific information included.
    - Checking the option for University of Chicago Study Team Will Not Consent or Enroll Participants will also populate view 16.0 Consent and Assent Documents. If the University of Chicago is not consenting or enrolling participants but will have contribute to data analysis for the project, the template consent form approved by the Reviewing IRB should be attached.

15.1 Informed Consent Determination

1. * **Will there be any type of consent process for this study (in person, online, or over the phone)? Please indicate the type(s) of consent process that will be involved (check all that apply).**
   - ☐ **Written Consent Form**
   - ☐ **Request to Waive Signed Consent – Verbal/Oral Consent**
   - ☐ **Request to Alter Consent (Some Elements of Consent Waived)**
   - ☐ **Request to Waive Consent/Parental Permission – Consent is not being obtained**
   - ☐ **Request to Waive Parental Consent – parental consent is not being obtained**
   - ☐ **University of Chicago Study Team Will Not Consent or Enroll Participants**

16.0 Consent/Assent Documents

1. **Attach consent forms, assent forms, short forms/summary documents, oral consent scripts, HIPAA authorizations, translated consent forms or information sheets.**

   + Add Drag and drop files to upload

- ✓ Upon completion of the form and attachment of all required documents, please perform the activity "Submit to the IRB."
- ✓ As needed, budget and contract/agreement documentation should be submitted by the department in accordance with the concurrent routing guidelines.
- ✓ Upon receipt of the CIRB submission, the Office of Clinical Research (OCR) will route the submission to:
  - OCR Research Operations and Conduct (ROC)
  - IRB staff member to determine any HIPAA Privacy Board concerns and confirm consistency with institutional policies on research related injury, recruitment and other issues that need further clarification or revision.
  - If any issues from the ROC or IRB staff member review require revisions, an email will be sent to the primary contact for revisions/clarification.
- ✓ Once all Institutional issues are addressed, an Institutional acknowledgement letter will be generated and the research may begin at the institution (once contract and other issues have been addressed). When there is an external agreement (master or study specific), institutional acknowledgement is dependent upon the execution of the final agreement.

Updating CIRB Activity

When the University of Chicago BSD IRB has ceded review to an external IRB, there is still a responsibility to report changes to the study to the BSD IRB.

After a CIRB study has been acknowledged in AURA IRB, a button will become available that allows the University of Chicago study team to provide the BSD IRB with updates to the study.

The Update CIRB Activity should be completed when the reviewing IRB or lead site provides the University of Chicago study team with new study materials; including but not limited to:

- ✓ Changes to recruitment
- ✓ Changes to the study design
- ✓ Changes to the consent form
- ✓ Changes to the protocol
- ✓ The continuing review approval
- ✓ Other changes such as data storage, data sharing, data collection, etc.

Selecting the Update CIRB activity in AURA will allow the user to edit the SmartForm and make any changes necessary. Once the CIRB application has been updated, the Update Study Activity completed button should be selected.

Personnel Amendments

As part of the reliance agreement between the University of Chicago and the reviewing IRB, the University of Chicago has a responsibility to review any changes to study personnel. This review ensures that study personnel are qualified (for example have completed human subjects training according to BSD policy) and to ensure that no new or additional conflicts of interest need to be reported to the reviewing IRB.

Changes in study personnel should be submitted through a personnel amendment. Personnel amendments are reviewed by BSD IRB staff to ensure compliance with the terms of the reliance agreement and other University of Chicago institutional policies.

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Purpose of form: This document provides information for University of Chicago BSD study teams or principal investigators that have been designated as a participating site that will cede review to an external IRB. Please contact IRBReliance@bsd.uchicago.edu for any questions related to single-IRB.