Title: Establishing a Single IRB (sIRB) Reliance and sIRB Submission Process	Version Number: #1	Effective Date: 1 AUG 2024	Page **1** of **28**

Revision History		
Version No.	**Effective Date**	**Description**

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1. Purpose

This SOP is intended for cooperative research, multisite or multicenter trials involving human subjects for which University of California, San Diego (UCSD) investigators intend to serve as a participating or lead site, and for which research activities will occur at the UCSD campus. Reliance on a single IRB typically occurs with: 1) multicenter, federally-funded research which require use of a single IRB, 2) Industry-sponsored clinical trials, and 3) multicenter studies partner institutions.

2. Scope

This SOP applies to all research submitted to the UCSD IRB or relied upon IRB. The scope of the Regulatory SOP is to orient Investigators, regulatory staff, coordinators and study management on the guidelines, and expectations of submissions to an IRB. The SOP includes information related to the full lifecycle of a study from initial submission to the IRB, through management of ongoing research activities, and ending with study closure with the IRB. This regulatory SOP includes steps to follow for submissions to Kuali and Central IRBs (e.g. Advarra and WCGIRB). Smart IRB reliance agreements can be used in order to rely on other IRBs or universities.

The UCSD IRB operates under a distinct Federal Wide Assurance (FWA). With these FWA, UCSD assures that they will meet all requirements of Title 45, Part 46 of the Code of Federal Regulations (45 CFR 46) for all human subjects research supported by the federal government."

Federally funded research activities conducted at or by personnel at other UCSD campuses or external institutions, except for Rady Children's Hospital San Diego, are considered outside of the UCSD IRB purview. As such, these activities must be reviewed by their own IRB or governed by an IRB reliance agreement.

Rady Children's Hospital San Diego is under the purview of UCSD IRB.

3. Abbreviations and Definitions

COI	Conflict of Interest
CTA	Clinical Trial Agreement
DUA	Data Use Agreement
HIPAA	Health Insurance Portability and Accountability Act
IBC	Institutional Biosafety Committee
IRB	Institutional Review Board
FDA	Food and Drug Administration
HERC	Human Exposure Review Committee (AKA Radiation Safety Committee)

NIH	National Institute of Health
OHRP	Office for Human Research Protections
PI	Principal Investigator
PRMC	Protocol Review & Monitoring Committee
sIRB	Single Institutional Review Board
SOG	Standard Operating Guidelines
UCSD	University of California, San Diego
WCGIRB	Western Copernicus Group IRB

a. **Multi-site (NIH funded research)**: refers to research where the same procedures (i.e., protocol) are conducted at one or more domestic sites, each overseen by a local participating investigator. Typically, there is a lead site that receives the grant or contract directly from NIH and then establishes subawards or subcontracts with each participating site. This research can include clinical trials, observational studies, or basic clinical research studies.

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

c. **Collaborative Study:** This refers to human research involving more than one institution and/or site participating in the same research protocol. In a collaborative study, each site completes a specific portion or portions of the research procedures. This coordination ensures that different aspects of the research are conducted across various locations, all contributing to the same overarching study goals.

d. **Cooperative Research:** This refers to human research covered by 45 CFR 46 that involves more than one institution and/or site. In cooperative research, each institution and/or site is responsible for safeguarding the rights and welfare of human participants and for complying with regulatory provisions. Any institution and/or site located in the United States that is engaged in cooperative research must rely on approval by a single IRB for the portion of the research conducted within the United States.

e. **IRB of Record:** The IRB of record is the primary IRB responsible for ensuring that research is conducted ethically and in compliance with applicable regulations on behalf of an institution, site, or individual investigator. This term is often used interchangeably with "reviewing IRB" and refers to the IRB that has the main responsibility for the review and oversight of a study.

f. **Lead Site:** In federally funded research, the lead site is the primary awardee of the grant and is responsible for identifying the selected single IRB (sIRB) for cooperative research. In non-federally funded research, the lead site refers to the primary institution, organization, or site responsible for developing the research protocol.

g. **Participating Site:** An institution or site involved in multi-site research, where a local investigator is responsible for conducting the human research at their specific institution or site. Each participating site collaborates under the same research protocol and contributes to the overall study objectives.

h. **Reviewing IRB**: The reviewing IRB, also known as the "IRB of record", is the Institutional Review Board responsible for the ethical review and oversight of a specific study. This IRB conducts the initial and ongoing reviews to ensure the research complies with ethical standards and regulations. The reviewing IRB has the primary authority for approving, modifying, or disapproving the study, ensuring the protection of human participants throughout the research process.

i. **Relying IRB:** The relying IRB is an Institutional Review Board that agrees to rely (to cede) on the review and oversight of another IRB, known as the reviewing IRB. Instead of conducting its own full review, the relying IRB accepts the determinations and oversight of the reviewing IRB for the research study

Practical Examples:

Reviewing IRB (IRB of record):

- **Example**: A multi-site clinical trial is being conducted, and one institution's IRB (e.g., UCSD IRB) serves as the reviewing IRB. This IRB reviews and approves the study protocol, consent forms, and other related documents for all participating sites.

Relying IRB:

- **Example**: Other institutions participating in the same multi-site trial agree to rely on the reviewing IRB's oversight. These institutions do not conduct their own full reviews but instead accept the regulatory determinations made by the reviewing IRB and provide the reviewing IRB with local context to conduct the review for their site.

j. **Reliance Agreement (RA):** A reliance agreement is 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. Authorization agreements may be for a specific study, or for specific classes or categories of research. They

describe the responsibilities of the relying institution and researcher as well as the responsibilities of the reviewing IRB and its institution.

4. Responsibilities

The Principal Investigator (PI) is responsible for ensuring that all human subjects research undergoes IRB review and obtains approval before initiation, including initial review, amendments, continuing review, and reporting of unanticipated problems, non-compliance, new risk information, or adverse events, while also ensuring compliance with ethical standards, regulations, and institutional policies. The research team, including regulatory staff and coordinators, is responsible for preparing and submitting, with the PI's assistance, all required regulatory documents to the IRB, facilitating communication between the IRB and the research team, maintaining accurate records of all IRB submissions and approvals, and ensuring that all team members are trained in human subjects protection. However, the PI is ultimately responsible for overseeing and ensuring compliance of all these activities. The IRB is responsible for the ethical review and oversight of all human subjects research, providing guidance and support to investigators and research teams to ensure compliance with ethical standards and regulatory requirements.

5. Establishing A Single IRB Reliance (sIRB)

5.1 Single IRB Reliance Agreement Establishment

A reliance agreement, , is an electronic or written document allowing the "Relying IRB" to cede review to the "IRB of Record" for a particular study involving human participants. An agreement must be in place to delineate the roles and responsibilities of the involved parties.

The reliance agreement may pertain to activities of a single research study or it may pertain to multiple studies (e.g., a Master Reliance Agreement). In this way, only one IRB reviews and approves human subject research activities for all campuses and sites, avoiding duplicative review and regulatory oversight.

Agreement Types

- Master Reliance Agreement (Bilateral or Multi-lateral)
  E.g. Smart IRB, WCG IRB, Advarra IRB, NCI CIRB
- IRB Authorization Agreement (IAA)

NOTE: Reliance agreements are executed by an authorized Signatory Official/Institutional Official (IO) or designated IRB representative from the Office of

IRB Administration (OIA). Investigators cannot sign themselves.

Both OHRP and the FDA permit an IRB the option to rely on the review of another IRB. While such agreements are required for federally funded cooperative research, the UCSD IRB allows reliance for Industry Sponsored or Consortium trials that are multicenter or multisite upon request.

Each institution or campus involved in the research is responsible for ensuring compliance with their site's submission requirements for any ancillary reviews, including but not limited to review by the respective campus's Institutional Biosafety Committee (IBC) and Radiation Safety Committee (HERC). Research staff from each site must consult their own institutional policies to determine if additional requirements apply.

5.2 Existing Reliance Agreements

5.2.1 UCSD IRB utilizes SMART IRB for reliance designed to facilitate single IRB (sIRB) review process for multisite studies. SMART IRB: is not an IRB, but a master reliance agreement. Over 1200 institutions and organizations across the United States have signed on to the SMART IRB Agreement, making it widely applicable for a variety of institutions. It provides a collaborative framework for institutions to rely on a single IRB, thus reducing administrative burden and improving efficiency in the IRB review process for multisite studies.

The SMART IRB master reliance agreement replaces the need to have an individual Institutional Authorization Agreement (IAA).

Acknowledging the use of the Smart IRB Agreement can be accomplished one of two ways:

- Executing a written SMART IRB Letter of Acknowledgment (LOA) or
- Using the SMART IRB Online Reliance System (ORS)

The SMART IRB ORS allows research teams to submit an electronic request to execute reliance under the terms of the SMART IRB master reliance agreement. The request is typically initiated by the lead study team whose IRB will be serving as the IRB of Record for all sites. Each person requiring access to the online reliance system will need to submit a separate request for access to the system. If you've

requested access and haven't received confirmation within a week please contact irbrely@ucsd.edu

- Request Access: https://reliance.smartirb.org/users/sign_up
- Sign In: https://reliance.smartirb.org/users/sign_in

How SMART IRB Works:

For SMART IRB to function properly, an agreement must be established between the local IRB and an external IRB from another organization or institution. Both parties must agree to use the SMART IRB system to facilitate reliance on a single IRB for ethical review and oversight.

Practical Examples:

Multi-site Clinical Trial:

- A multi-site clinical trial involves several research institutions. Each site typically has its own IRB. To streamline the process, all participating sites agree to rely on one institution's IRB as the reviewing IRB.
- For instance, if UCSD is the reviewing IRB, other institutions like UCLA and Stanford agree to rely on UCSD's IRB review and oversight for this particular study.

Collaborative Research Projects:

- Two universities, each with its own IRB, decide to collaborate on a research project. They agree to use the SMART IRB agreement to designate one of the universities' IRBs as the reviewing IRB.
- For example, Harvard University and UCSD collaborate on a study. They decide that UCSD IRB will be the reviewing IRB. Harvard's IRB relies on UCSD's IRB for the study, using the SMART IRB agreement to facilitate this arrangement.

Steps for Implementation:

- Institutional Agreement: Both the external IRB and the local IRB must sign the SMART IRB reliance agreement or accept the reliance request using the ORS. You can see what institutions have signed on to SMART IRB here: Participating Institutions | SMART IRB

- Designation of Reviewing IRB: Decide which institution's IRB will act as the reviewing IRB for the study.
- Communication and Documentation: Ensure all participating sites are informed of the SMART IRB process;
    1. The Lead PI and study team registers the study in the ORS and uploads the study documents such as protocol, approval letter, consent template, local context questionnaires, etc. when registering the study. The documents uploaded are for reference for the participating sites and their SMART IRB point of contact (POC). After the study is registered, updates cannot be made as the portal only serves to electronically document the reliance after the SMART IRB POCs agree to rely on the reviewing IRB.
    2. When using the LOA, which is not done within the ORS, then the communication is typically done via email.
- Ongoing Oversight: The reviewing IRB oversees the study and communicates with the relying IRBs as needed to ensure compliance and address any issues.

5.2.2 UCSD IRB has executed reliance agreements with the following non-commercial IRBs to serve as the IRB of Record when necessary:

- National Cancer Institute Central IRB (NCI CIRB)
- All of Us IRB

5.2.3 UCSD IRB has executed reliance agreements with the following commercial IRBs to serve as the IRB of Record when necessary, usually for pharmaceutical trials:

- Western Copernicus Group (WCG IRB)
- Advarra IRB

For trials not covered under these existing agreements, a request to establish reliance must be sought from UCSD IRB as early as feasible. Contact IRBrely@ucsd.edu for more information.

5.3 Request for Single IRB Review

When it is established that a trial will utilize single IRB review, a determination must be made regarding which institution's IRB will oversee the trial conduct. To facilitate this process, both the UCSD IRB and the external IRBs will collect and review basic information about the planned collaboration.

- The study team may email UCSD OIA at IRBrely@ucsd.edu and provide

information and request confirmation that the UCSD IRB would be willing and able to serve as the reviewing IRB for a multisite study. If agreed, a traditional Kuali application will be submitted which will indicate that the UCSD IRB is serving as the IRB of Record for other sites. The UCSD site will be reviewed and approved first and the other sites will be added on later through the amendment process.

- If the UCSD IRB will rely on an external IRB, the UCSD Principal Investigator (PI) should submit a "Request for Reliance", by initiating an Administrative Registration via the Kuali IRB System. The reliance registration is an abbreviated application that is administratively reviewed by UCSD Office of IRB Administration (OIA) to collect documentation of local requirements, and also serves the purpose of facilitating transmission of information to other UCSD offices such as OCAA, OCGA, HERC, and PRMC.

- The PI or Coordinator will upload a number of documents depending on which type of agreement is being agreed upon. More details on the various processes ahead.

5.4 Determination of IRB of Record (Reviewing IRB)

Circumstances arise in which an individual who is not a university/affiliate investigator may wish to use the UCSD IRB for review and oversight of their non-exempt human subjects research or to rely on the UCSD IRB for oversight of non-exempt human subjects research.

- The UCSD IRB will generally only review studies for an external or independent investigator when that investigator is involved in non-exempt human subjects research being conducted by a collaborating UCSD investigator.
- Exceptions may be made upon consultation with the OIA director/medical director, and/or institutional official.
- Human subjects research may not commence at the independent investigator's/external investigator's site until the conditions and responsibilities specified herein are met.
- In accordance with OIA-085 SOP: Reliance Agreement, the UCSD OIA reviews reliance requests and determines whether it is appropriate to execute a reliance agreement for the UCSD IRB to serve as the single IRB

(sIRB) or IRB of record for an external or independent investigator.

- Industry Sponsored multisite research typically will utilize a commercial IRB (e.g. Advarra, WCGIRB), unless the sponsor specified their desire to use UCSD as the IRB of record.

5.5 Reliance Documentation

It is the responsibility of the UCSD Principal Investigator or designee to complete the appropriate reliance process, obtain UCSD review and approval of the reliance request, and obtain all local and external institutional signatures prior to study submission to the UCSD IRB.

- For a study to use an existing reliance agreement, email the IRB office at IRBRely@ucsd.edu for further instructions on how to proceed.
- For federally funded cooperative research (multisite or multicenter) UCSD IRB has determined that participating sites must agree to utilize the SMART IRB Master Agreement for establishing reliance, unless a master agreement is already in place. It is preferred that the study team(s) involved initiate the reliance within the SMART IRB platform.

6. Single (sIRB) Submission Process

6.1 UCSD IRB Review as the IRB of Record for external sites (in other words UCSD is reviewing for external site)

Following a determination that UCSD will act as the IRB of record (Reviewing IRB) for a particular collaboration, the UCSD PI must complete the UCSD IRB application using UCSD's protocol management system, Kuali System, according to the guidance and directions of the UCSD IRB.

A. Pre-Submission

Early Planning: Contact the IRB during the early stages of sIRB planning.

- Determine if the UCSD IRB is suitable to serve as the IRB of record.
- Confirm the number of collaborating sites and their willingness to cede IRB review.
- Identify which reliance agreement(s) to use.
- Determine any IRB fees associated with the UCSD IRB's review for external sites.

B. IRB Submission

UCSD PI Identifies IRB of Record:

- In the Kuali application, select "Yes, UCSD IRB will be IRB of record for other sites".
- In the general information section add the participating sites in the Participating Sites tab which appears at the top of the application. This can be done during an initial submission or via an amendment submission.

C. IRB Review Process

UCSD IRB Initial Review:

- After step B above, the IRB and team address any issues that could affect study documents such as protocol and consents.

UCSD IRB Review Process:

- The UCSD IRB OIA completes the review of all documents submitted and issues an IRB approval letter for UCSD to be the IRB of record.
- The UCSD PI forwards copies of the IRB approval letter and all approved study-related documents (e.g., consents, recruitment materials) to the participating sites for local consideration.
- Forward the UCSD Local Context Questionnaire (LCQ) to the sites to complete with their local IRB's help, along with a copy of the reliance agreement to be executed if one does not already exist (e.g. SMART IRB).

Amendment Submission to Kuali of Documents from Participating Sites:

- After the lead site (reviewing team) is approved by UCSD IRB OIA, the UCSD PI uploads copies of the completed LCQ (Local Context Review) and signed agreement (if applicable) in the Participating Sites tab for the respective sites.
- Any site-specific study documents requiring IRB review and stamping must be uploaded in the Supporting Information section of the application via an amendment.

Kuali IRB Approval of Relying/Participating Sites:

- A UCSD IRB Analyst reviews the amendment submission and uploaded documents.
- The Analyst issues approval for the addition of the participating sites, if no additional changes or information is needed, stamping and releasing site-specific study documents with the approval.

UCSD Forwarding Approval Documentation to Relying Sites:

- The UCSD PI forwards the amendment approval letter and approved site-specific study documents to the participating sites.

Additional responsibilities of the UCSD Investigator as part of the submission to the IRB include:

- Ensure all persons on the list of external investigators complete a COI form disclosing their financial interests. These forms should be submitted to the UCSD IRB with the application.
- Ensure all persons on the list of external investigators have completed required training if required. UCSD requires personnel on all human subject protocols to complete training in Good Clinical Practices, in addition to human subjects research and HIPAA training. If external investigators will be conducting research procedures in UCSD spaces additional requirements must be met, including but not limited, medical clearance, etc.
- External investigators will need to provide UCSD's IRB with proof that they have completed these required trainings. Completion certificates must be attached in the personnel section of the IRB application

6.2 <u>UCSD IRB Relying on a non-UCSD IRB</u>

The use of an external IRB may be warranted when one or more of the following are applicable:

- UCSD is a sub-contracted site and IRB approval for the overall study has been provided by the external institution/organization.
- The request is mandated by the funding agency per single IRB (sIRB) review or cooperative research requirements.
- The request is mandated by the study sponsor or funding agency in order for the UCSD site to participate in the research.
- The UCSD site is collaborating with the lead site for the study and is engaged in human subjects research.
- The study is a clinical trial that is industry-authored and financially sponsored,

unless the principal investigator or sponsor requests the UCSD IRB conduct review

Following determination that an External IRB will act as the IRB of record for a collaboration as describe above, the IRB of Record must provide the documents listed under bullet points 6.2.1 and 6.2.2 below to UCSD OIA for administrative review in order for UCSD to accept the approval of an external IRB, and before UCSD faculty, and staff can engage in human research subject under external IRB oversight.

After approval to proceed is received from the IRB of Record, the UCSD PI must submit a "Request to Rely" application in Kuali IRB System for local context review as described below. If an existing study submitted as "Full/Expedited" is seeking to rely on an external IRB, an amendment must be initiated in Kuali IRB to change the review type of the study.

6.2.1 UCSD Relying on an External Non-Commercial IRB

This guide provides a detailed and step-by-step process for submitting studies to an external non-commercial Institutional Review Board (IRB). It integrates the necessary steps from the initial pre-submission phase to the final acceptance by the UCSD Office of IRB Administration (OIA), ensuring compliance with all local and external IRB requirements.

A. General Process

Pre-submission:

- Contact the IRB Early:
    - Engage with the IRB during the initial stages of sIRB planning.
    - Confirm the study meets the criteria for external IRB review.
    - Identify and provide the name of the IRB of Record.
- Reliance Agreement:
    - Determine and document the reliance agreement to be used (e.g. SMART IRB).

- Request approved study documentation from the reviewing IRB. (e.g. IRB approval of the study)

Reliance Registration for Clearance:

- Register in the Kuali IRB system for clearance, not for a second IRB review. See steps below in item 5.
- This step allows the UCSD OIA to confirm all local requirements are met.
- Detailed instructions are available in the KBA on Administrative Determinations.

Submitting to the External IRB for Approval:

- If relying on another institution's IRB, the local research team at the reviewing site submits the UCSD information and documents through their local system for review and approval.

External Review Acceptance/Approval Documentation:

- Once the reviewing IRB approves the addition of UCSD as a relying site, the study team (UCSD) must upload copies of the approval documents in the Kuali IRB system for final acceptance.
- Detailed instructions are available in the KBA on Reliance Acceptance.

B. Detailed Steps for Relying on a Non-Commercial IRB

1. UCSD PI Submits External IRB Review Registration via Kuali:
   - The UCSD Principal Investigator (PI) creates and submits a "Request to Rely on non-UCSD IRB" Administrative Registration in Kuali. This abbreviated application is administratively reviewed by UCSD OIA to collect documentation of local requirements and facilitate information transmission to other UCSD offices (e.g. OCAA, OCGA, HERC, and PRMC).
2. Required Documents for Submission:
   - Master Protocol
   - Sponsor's Consent Template(s) with UCSD site-specific consent language tracked in Word, if UCSD will be consenting participants
   - Investigator's Brochure or Package insert (if applicable)
   - When submitting initially, UCSD is not listed as a site.
   - Reviewing IRB's Overall Study Approval Letter.

- Any other study-related documents(e.g. materials specific to UCSD)
- Reliance documents provided by the reviewing IRB.

3. Administrative Screening of Kuali External IRB Registration (Clearance):
   - UCSD OIA screens the reliance registration submission in Kuali for completeness and confirms the project meets the criteria for external IRB review.
   - UCSD OIA provides the UCSD PI with a "Clearance Notification" confirming that UCSD has agreed to cede IRB review responsibility to the external IRB.
4. Providing Site-Specific Documents to the Reviewing Site:
   - The UCSD PI provides the UCSD-specific study documents to the Lead Investigator at the reviewing site, including the "Clearance" screenshot.
   - The Lead Investigator at the reviewing site submits the UCSD-specific study documents to their IRB for review and approval.
   - Note: The UCSD PI should communicate with UCSD ancillary committees as applicable. The OIA does not hold a submission for ancillary reviews to be completed.
5. External IRB Review and Approval:
   - The external IRB reviews the site submission for the addition of the UCSD PI to a particular protocol.
   - The external IRB issues an approval notice for the addition of UCSD as a relying site and approves any UCSD-specific study documents (e.g. stamped consent with UCSD language).
6. Submitting External IRB Approval Notice and Approved Documents via Kuali:
   - The Lead Investigator at the reviewing site forwards the approval documentation to the UCSD PI (consents, etc.).
   - The UCSD PI uploads the approval notice and stamped versions of the UCSD site-specific consent(s) into Kuali as a response to the initial clearance, not a new submission.
7. Final Administrative Review:
   - UCSD OIA completes an administrative review of the approval notice and approved documents from the external IRB.
   - UCSD OIA issues an "External Oversite Acceptance" letter via Kuali, signifying the completion of the UCSD OIA Administrative Review process.
   - Submit letter to reviewing IRB.

6.2.2 <u>UCSD Relying on a Commercial IRB (e.g. WCGIRB, Advarra IRB)</u>

This guide provides a detailed and step-by-step process for submitting studies to an external non-commercial Institutional Review Board (IRB). It integrates the

necessary steps from the initial pre-submission phase to the final acceptance by the UCSD Office of IRB Administration.

A. General Process

Pre-submission:

- Contact the IRB Early:
  - Engage with the IRB during the initial stages of sIRB planning.
  - Confirm the study meets the criteria for external IRB review.
  - Identify and provide the name of the IRB of Record.
- Reliance Agreement:
  - Determine and document the reliance agreement to be used (e.g. SMART IRB).
  - Request approved study documentation from the reviewing IRB. (e.g. IRB approval of the study)

Reliance Registration

- Register in the Kuali IRB system for clearance, not for a second IRB review. See steps below in item 5.
- This step allows the UCSD OIA to confirm all local requirements are met.
- Detailed instructions are available in the KBA on Administrative Determinations.

Submitting Process to the External IRB for Approval

- If relying on another institution's IRB, the local research team at the reviewing site submits the UCSD information and documents through their local system for review and approval.

External Review Acceptance/Approval Documentation

- Once the reviewing IRB approves the addition of UCSD as a relying site, the study team must upload copies of the approval documents in the Kuali IRB system for final acceptance.

- Detailed instructions are available in the KBA on Reliance Acceptance.

B. Detailed Steps for Relying on a Commercial IRB (Advarra and WCG IRB)

1. UCSD PI Submits External IRB Review Registration via Kuali

   - The UCSD Principal Investigator (PI) creates and submits a "Request to Rely on non-UCSD IRB" Administrative Registration in Kuali. This abbreviated application is administratively reviewed by UCSD OIA to collect documentation of local requirements and facilitate information transmission to other UCSD offices (OCAA, OCGA, HERC, PRMC).

2. Required Documents for Submission:
   - Master Protocol (sponsor protocol)
   - Sponsor's Consent Template(s) (if applicable)
   - Overall study approval letter from the commercial IRB with UCSD as a site.
   - Investigator's Brochure or Package insert (if applicable)
   - Any other study-related documents(e.g. materials specific to UCSD)

3. Administrative Screening of Kuali External IRB Registration (Clearance)

   - UCSD OIA screens the reliance registration submission in Kuali for completeness and confirms the project meets the criteria for Commercial IRB review.
   - UCSD OIA provides the UCSD PI with a "Clearance Notification" attesting that UCSD has agreed to cede IRB review responsibility to the central IRB.

4. Providing Site Specific Package to the Commercial IRB

   - The UCSD PI submits the appropriate application, including the "Clearance," to the commercial IRB using their online system. Ensure the submission is noted as affiliated to UCSD. Print and save the submission as it will be required at a later time.
   - The commercial IRB reviews the submission and communicates directly with the UCSD PI for any required revisions or additional information.

- The UCSD PI concurrently communicates with UCSD ancillary committees as applicable. Note: Ancillary reviews do not need to be completed before submitting to the Commercial IRB; they can be conducted concurrently.

5. Commercial IRB Processing and Institutional Sign-Off

   - The commercial IRB reviews the site package for the addition of the UCSD PI to a particular protocol.
   - Commercial IRB review analysts revise the consent document(s) to add UCSD required language, following the UCSD-consent requirements. The analyst will provide the site contact the prepared consent forms during the site pre-review. Site should review the prepared consent form(s) to ensure they meet UCSD Reliance Consent Minimums and aligns with the information provided to the IRB in their site application. After site and sometimes sponsor review is complete, it is routed for IRB review. If deviations to our language are submitted during this step, WCG will contact OIA Managers. Advarra does not.
   - The commercial IRB issues an Initial Site Review email notification to the UCSD OIA designated staff and requests Institutional Sign-Off. The commercial IRB places an indefinite hold on the approval documents until Institutional Sign-off.

6. UCSD OIA Reviews Approval and Provides Institutional Sign-Off

   - UCSD OIA designated staff reviews the consent document(s) to confirm UCSD Institutional requirements have been met.
   - UCSD OIA provides institutional sign-off to the commercial IRB.

7. UCSD PI Submits Commercial IRB Approval Notice and Approved Documents via Kuali

   - The commercial IRB approves the UCSD PI and provides approval documents.
   - The UCSD PI uploads the approval notice and stamped versions of the UCSD site-specific consent(s) into Kuali.

8. UCSD OIA Issues Acceptance of Commercial IRB's Review and Approval

   - UCSD OIA completes an administrative review of the approval notice and approved documents from the commercial IRB.

- UCSD OIA issues an "External Oversite Acceptance" letter via Kuali, signifying the completion of the UCSD OIA Administrative Review process and provides sign off/notification to OCTA or OCGA that study is now approved.

6.2.3 Initiating Study at UCSD

UCSD IRB must perform the local review and acknowledge the IRB approval before any research activities at the UCSD site may begin. All UCSD training and conflicts of interest requirements must be met, as well as ancillary committee reviews (e.g. PRMC, radiation safety, investigational pharmacy, etc.). It is the responsibility of the UCSD PI to determine if additional agreements, such as Data Use Agreement (DUA) or Clinical Trial Agreement (CTA), are needed for the given collaboration.

6.2.4 Informed Consent Documentation (see informed consent documentation subsections for details)

UCSD requires use of approved consent form template language when enrolling subjects at our site (see Forms & Instructions (ucsd.edu) unless the IRB of Record explicitly requires use of their template. In such case, HIPAA and Subject Injury language must be used per the UCSD template. Once the UCSD consent form has been generated, review and approval must be obtained from the IRB of Record. Confirmation of I,RB of Record approval and stamped ICF should be submitted to UCSD IRB for local context review.

6.2.5 Documentation of Local Context Review

For studies using a reliance, the UCSD IRB will provide an acknowledgment letter to capture local context review. Documents submitted will not receive a UCSD IRB Stamp, but document name and version details will be indicated on the acknowledgement letter. If a local context survey is requested by the IRB of Record, the UCSD PI or designee should complete all applicable sections, and send to the UCSD IRB for final review and signature at IRBRely@ucsd.edu. To obtain a Conflicts of Interest (COI) determination for UCSD investigators a submission in UCSD Kuali COI is required.

7. Post-Approval Responsibilities

7.1 Annual Renewals

UCSD as the IRB of Record

- annual reviews ensure ongoing compliance with ethical and regulatory standards.
- The UCSD Principal Investigator (PI) must submit a comprehensive continuing review annually, when required, including all approved documents and updates.
- If UCSD oversees multiple sites as the IRB of Record, the PI must compile comprehensive data (e.g., enrollment numbers, adverse events) from all relying sites for inclusion in the annual continuing review submission.

UCSD Relying on an External IRB

- The UCSD PI is responsible for providing a detailed report to the external IRB, including enrollment numbers and reportable events.
- Once the external IRB provides renewal approval, the UCSD PI must promptly submit this approval to the UCSD Kuali System. This ensures compliance with both UCSD's local policies and those specified by the external IRB.
- Research activities may continue without interruption unless otherwise directed by the External IRB, UCSD's IRB, or the Institutional Official at the Office of IRB Administration.

7.2 Amendments

UCSD Relying on an External IRB

Significant amendments to the protocol or ICF documents should first be approved by the IRB of Record. The UCSD PI has the obligation for submitting the following amendments to the Kuali IRB system:

- Change in Principal Investigator* or study personnel
    i. Affiliated with the institution, eligible to participate depending on their role, have completed appropriate training.
- New or changes in COI for investigators
- New or changes in HIPAA determination (made by UCSD)
- New or changes in funding/budgeting

- New or additional ancillary review required (e.g., Radiation Safety Committee HERC)
- Changes to the table of assessments (e.g. new procedure, additional visit, etc.)
- Any other changes that affect the UCSD required information in the consent document*.

NOTE: Items marked above with an * should be submitted to OIA for clearance before being submitted to the reviewing IRB for approval.

As soon as receiving the approval notice from the external IRB of significant amendment, UCSD investigators should submit the amendment to the UCSD IRB through Kuali IRB for local context review. A local context review will be performed, and an Acknowledgement letter will be provided. The amendment to the research activity may be implemented upon receipt of approval by the IRB of Record. Please note that the IRB local context review may determine that the amended research is not acceptable for UCSD, which may result in halting of the research project while a resolution is sought.

Any amendments to a research PI at UCSD should first be reviewed and approved by the UCSD IRB, unless stipulated otherwise by the IRB of Record in the reliance agreement or associated workflow documents governing the reliance.

7.3 Reportable Events: Unanticipated Problems/Continuing or Serious Non-compliance, Suspensions or Terminations.

If the event meets the reporting requirement of the reviewing IRB, these events need to be reported to the reviewing IRB per their event reporting process.

After the reviewing IRB completes its assessment of the event and determines it falls under categories such as Unanticipated Problems, Continuing or Serious Non-compliance, Suspension, or Termination, the Principal Investigator or their delegate must report the event and its determination to Kuali IRB system using the Reportable Event tab for acknowledgment by UCSD OIA.

NOTE: Terms of the agreement may specify reporting requirements.

- 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.

7.4 Coverage Analysis (CA) for Studies with Significant Amendments

Office of Coverage Analysis Administration (OCAA) utilizes the Kuali IRB system to keep coverage analyses up to date for study teams. A request for coverage analysis for amendments involving significant changes to, protocol, investigator's brochure (IB), or informed consent form (ICF) and PI are triggered by:

- Amendment submission in Kuali
- Emailing OCAA to informed them of the need of a CA review due to a significant amendment.
- To ease researcher and OIA staff burden in submitting and processing these amendments, OIA has a specific question in Section A of the Kuali IRB amendment application (see appendix B) that asks if this submission is only for OCAA review. If your study has a coverage analysis, is reviewed by an External IRB, and does not involve amendments listed in Section 7.2, answer this question as "yes." This will allow you to bypass all other amendment questions to save time in submitting for OCAA review purposes. Note that most significant amendments will also require a Coverage Analysis review, this ensures that billing and funding for the study is updated according to the updated information.

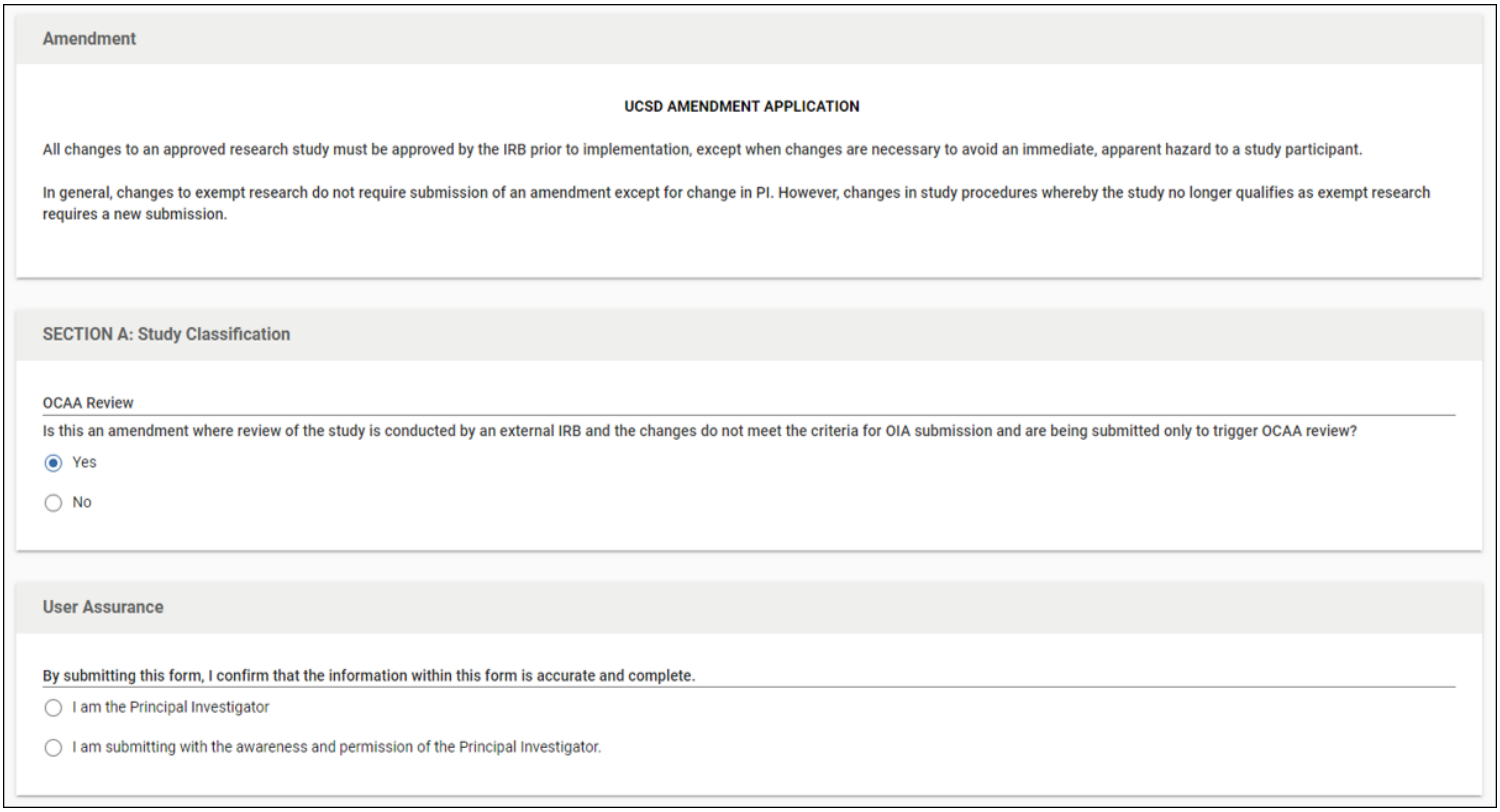
If you have questions about whether OCAA review is required, please email OCAA directly at ocaa@ucsd.edu.

For questions about collaboration on human subjects research that are not addressed in this document, or need further guidance you may contact IRBRely@ucsd.edu.

8. Appendixes

Appendix A: External Reliance Flow Chart

Appendix B: Amendment – OCAA Review Required



Amendment

UCSD AMENDMENT APPLICATION

All changes to an approved research study must be approved by the IRB prior to implementation, except when changes are necessary to avoid an immediate, apparent hazard to a study participant.

In general, changes to exempt research do not require submission of an amendment except for change in PI. However, changes in study procedures whereby the study no longer qualifies as exempt research requires a new submission.

SECTION A: Study Classification

OCAA Review

Is this an amendment where review of the study is conducted by an external IRB and the changes do not meet the criteria for OIA submission and are being submitted only to trigger OCAA review?

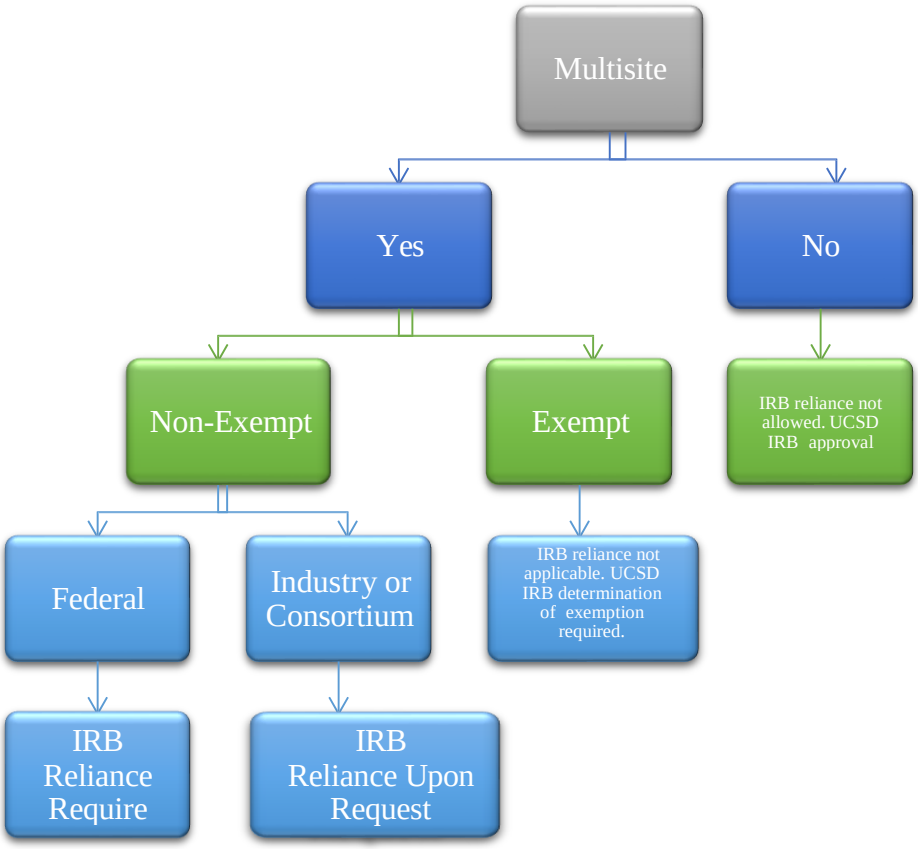
- (●) Yes
- ( ) No

User Assurance

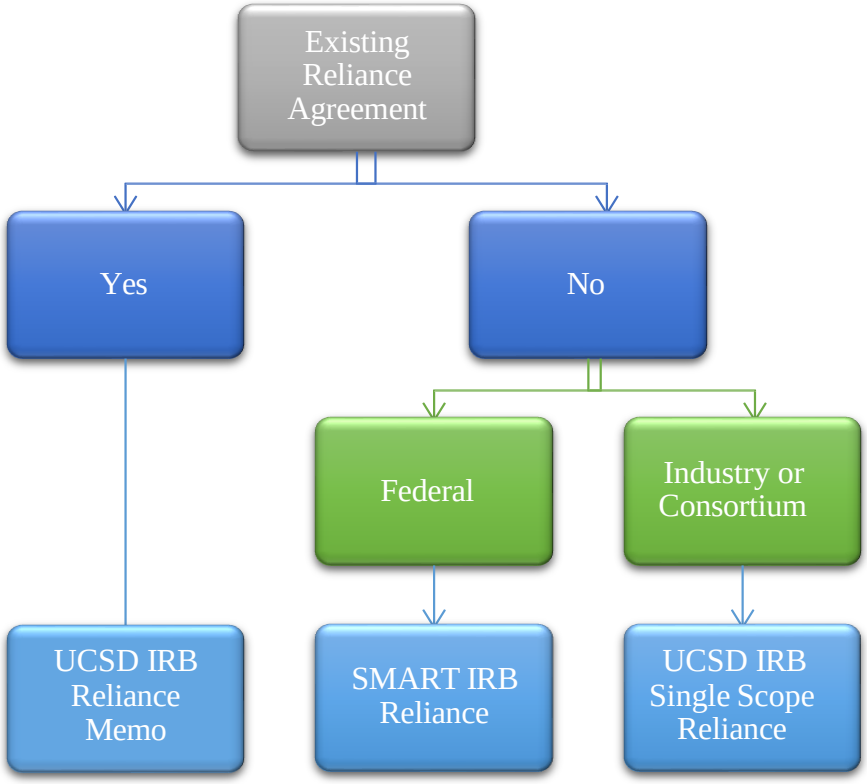
By submitting this form, I confirm that the information within this form is accurate and complete.

- ( ) I am the Principal Investigator
- ( ) I am submitting with the awareness and permission of the Principal Investigator.

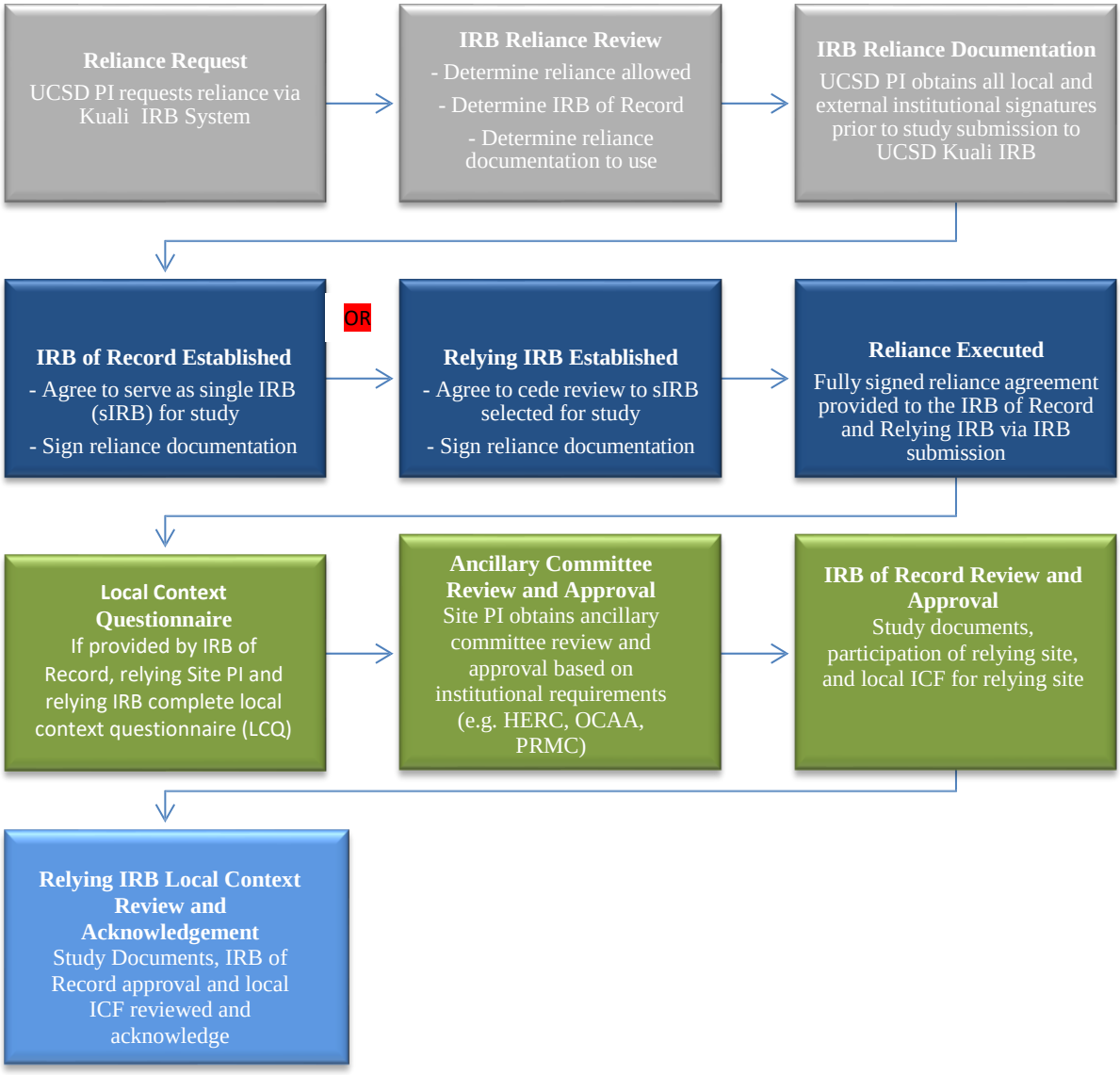
Appendix C: Flowchart for Single IRB (sIRB) Reliance Agreement Establishment:



Appendix D: Flowchart for IRB Reliance Agreement Establishment:



Appendix E: Preferred Workflow for Single IRB (sIRB) Review and Agreement:



9. References

- https://irb.ucsd.edu/researchers/guidance.html
- https://www.wcgclinical.com/solutions/study-review/
- https://www.cirbi.net/CIRBI/sd/Rooms/DisplayPages/LayoutInitial?Container=com.webridge.entity.Entity[OID[AC482809EC03C442A46F2C8EEC4D75D3
- https://reliance.smartirb.org/users/sign_up
- https://reliance.smartirb.org/users/sign_in
- https://support.ucsd.edu/research?id=kb_view&kb_id=e8c95c82dbfd0450008c9837db9619c1

10. Document Approval

- Name and Title of Approver
- Date in the format (MM/DD/YYYY)
- Insert Name and Title below Signature

Approved By: Date:

_____ _____

Insert Name and Title