SMART IRB

Reliance Agreement
Version 3.0

Standard Operating Procedures

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Introduction

The SMART IRB Standard Operating Procedures (SOPs) are the default SOPs for SMART IRB reliance arrangements, unless other SOPs are specifically documented. The SMART IRB SOPs are not intended to overlap with or replace existing institutional-level SOPs that have already been implemented internally at institutions participating in the SMART IRB Agreement. These SOPs serve as a mechanism for highlighting the unique features associated with participating in the SMART IRB Agreement, and serve as guidelines for establishing reliant review of multi-site human research conducted using the SMART IRB Agreement.

The implementation of these SOPs helps assure that institutions using the SMART IRB Agreement follow the responsibilities documented within the SMART IRB Agreement, and provides a reference and guideline for internal stakeholders and external sponsors as to how multi-site research is undertaken using the SMART IRB Agreement. Furthermore, these SOPs provide an additional training source for investigators and administrators participating in the SMART IRB Agreement.

Glossary of Terms

Agreement: SMART IRB Reliance Agreement.

Assurance: An assurance of compliance with the Federal Policy that is maintained with a federal department or agency.

Ceded Review: The transfer of authority to, and reliance on, a Reviewing IRB for IRB review and oversight of research.

Confidential Information: Any non-public, confidential and/or proprietary information, including but not limited to the scientific content of Research proposals and information provided by the Overall PI, Site Investigator(s), or other Personnel not generally known or available to the public. Information is not Confidential Information hereunder if such information (a) is or becomes known to the receiving party independently of disclosure by the disclosing party, directly or indirectly from a source other than one having an obligation of confidentiality to the disclosing party; (b) becomes publicly known or otherwise ceases to be confidential, except through a breach of this Agreement by the receiving party; or (c) is independently developed by or on behalf of the receiving party. For clarity, as used in this Agreement, the term Confidential Information has no relation to the classification level of information/documents within a federal department or agency.

Covered Activity/Covered Activities: Ceded Review of Research and Exemption Determinations, individually or collectively.

DHHS: U.S. Department of Health and Human Services.

Effective Date of the Agreement: With respect to any Participating Institution, the Effective Date of its Joinder Agreement.

Effective Date of the Indemnification Addendum: With respect to any Indemnification Participating Institution, the date on which the Indemnification Participating Institution's Institutional Official/Signatory executes the Indemnification Addendum Joinder Agreement.

Effective Date of a Joinder Agreement: The date on which the Participating Institution's Institutional Official/Signatory executes the Joinder Agreement.

Executive Committee: Composed of SMART IRB Team leadership and representatives from NCATS.

Exemption Determinations: A determination by a Reviewing IRB or Reviewing IRB Institution whether Research is exempt from some or all of the requirements of the Federal Policy.

FDA: U.S. Food and Drug Administration.

FDA Clinical Investigation Regulations: 21 CFR Parts 50, 56, 312, and 812.

Federal Institution: An Institution/Participating Institution that is a department or agency of federal government.

Federal Policy: The Federal Policy for the Protection of Human Subjects set forth in the DHHS regulations at 45 CFR Part 46, Subpart A and corresponding regulations of other federal departments and agencies adopting such Policy.

Force Majeure Event: An unforeseeable natural, political, or similar event beyond the control of a Participating Institution, including, without limitation, fire, flood, pandemics, epidemics, riots, war, acts of terrorism, or governmental actions or decrees in response to same, except as provided in Section 8.13 hereof.

FWA: The OHRP-approved Federalwide Assurance in which a research institution commits to DHHS that it will comply with the Federal Policy.

HIPAA: Collectively, the Health Insurance Portability and Accountability Act of 1996, the Health Information Technology for Economic and Clinical Health Act of 2009, and their implementing privacy and security regulations, including but not limited to the implementing privacy regulations at 45 CFR Part 160 and 45 CFR Part 164, Subparts A and E.

HIPAA Covered Entity: A health care provider, health plan, or health care clearinghouse subject to HIPAA as further defined and provided in 45 CFR 160.103.

Human Research Protection Program or HRPP: An Institution's policies, procedures, and oversight mechanisms for addressing human research protections.

Indemnification Addendum: The SMART IRB Indemnification Addendum attached to the Agreement at Exhibit C.

Indemnification Addendum Joinder Agreement: The SMART IRB Indemnification Addendum Joinder Agreement available at www.smartirb.org, which will be in substantially the same form as in Exhibit C.

Indemnification Participating Institution: A Participating Institution that joins the Indemnification Addendum.

Indemnification Terminating Institution: An Indemnification Participating Institution that terminates its participation in the Indemnification Addendum or whose participation in the Indemnification Addendum is terminated pursuant to Sections 7.2.2.2 or 7.2.2.3 hereof, respectively, or whose participation in the Indemnification Addendum ends as a result of the termination of the Indemnification Addendum in its entirety pursuant to Section 7.2.2.1.

Indemnified Party(ies): An Indemnification Participating Institution and its trustees, directors, officers, Personnel, and IRB members eligible to be held harmless, indemnified, and defended by an Indemnifying Party under the Indemnification Addendum.

Indemnifying Party: An Indemnification Participating Institution that is a Private Institution and is agreeing in the Indemnification Addendum to hold harmless, indemnify, and defend the Indemnified Parties.

Independent IRB Organization: An independent IRB organization that provides IRB review services.

Institutional Official/Signatory: The person who has the authority on behalf of an Institution to bind such Institution to the terms and conditions of the Agreement and, if applicable, the Indemnification Addendum.

IRB: Institutional Review Board(s).

Joinder Agreement: The SMART IRB Joinder Agreement available at www.smartirb.org, which will be in substantially the same form as attached to the Agreement at Exhibit B.

Limited IRB Review: The IRB review required pursuant to 45 CFR 46.104(d)(2)(iii), (d)(3)(i)(C), (d)(7), or (d)(8) or the corresponding provisions in the regulations of any federal department or agency adopting the Federal Policy in order for Research to be considered exempt under one of those provisions.

Local Considerations: Requirements of any applicable state or local laws, regulations, institutional policies, standards, or other local factors, including local ancillary reviews.

Losses: Any and all damages, judgments, liabilities, costs, expenses (including, without limitation, reasonable attorney's fees and expenses of litigation), or other losses incurred by or imposed upon any Indemnified Party(ies) or Other Party(ies) as a result of third-party claims, suits, demands, actions, or causes of action.

Mandated Policy/Policies: Federal department- or agency-mandated policies and procedures governing the conduct of a reliance relationship once it is established.

Mandated Processes: Federal department or agency processes for initiating reliance and for determination of the Reviewing IRB/Reviewing IRB Institution.

NCATS: National Center for Advancing Translational Sciences at NIH.

NIH: National Institutes of Health.

OHRP: The Office for Human Research Protections of DHHS.

Other Considerations: The requirements of any applicable federal laws or regulations or of relevant federal departments or agencies that are not readily apparent from the IRB submission for the Research or that are specific to the Relying Institution. For purposes of this Agreement, HIPAA and its requirements are not considered Other Considerations.

Other Party(ies): An Indemnification Participating Institution and its trustees, directors, officers, Personnel, and IRB members to whom a Responsible Party is responsible and who are eligible to be reimbursed by a Responsible Party Under the Indemnification Addendum.

Other Policies: Policies and procedures for the conduct of a reliance relationship that are not Mandated Policies but that Participating Institutions agree among themselves to apply to a reliance relationship under the Agreement.

Overall PI: The lead multi-site principal investigator with ultimate responsibility for the conduct and integrity of Research (generally, the initiating principal investigator or funding principal investigator, as applicable).

Party/Parties: A Participating Institution or, collectively, the Participating Institutions.

Participating Institution: An Institution (including an Independent IRB Organization) that meets the eligibility requirements set forth in the Agreement and accepts the terms and conditions of the Agreement through the execution of a SMART IRB Joinder Agreement.

Personnel: Members of a Participating Institution's team (including the Overall PI (if any) and Site Investigator(s)) involved in conducting an instance of Research. These individuals may include, as applicable, physicians, nurses, coordinators, data managers, lab technicians, postdoctoral fellows, students, volunteers and/or other personnel.

POC: Contact person or point of contact responsible for communicating on behalf of the Institution/Participating Institution with respect to matters concerning the initial and ongoing implementation of the Agreement.

Private Institution: An Institution/Participating Institution that is not a department, agency or instrumentality of federal, state, local, or other government.

Protected Health Information or PHI: Protected Health Information as defined in 45 CFR 160.103.

Public Institution: An Institution/Participating Institution that is a department, agency, or instrumentality of U.S. federal, state, local, or other domestic government.

Reliance Request: A request for Ceded Review or for an Exemption Determination, as applicable, with respect to an instance or multiple instances of Research.

Relying Institution: A Participating Institution that will obtain IRB review from a Reviewing IRB and/or determinations of exemption from IRB review from a Reviewing IRB or Reviewing IRB Institution under the Agreement.

Report: A report required under applicable federal human subjects protection regulations or under the terms of a Relying Institution's Assurance to a federal human subjects research regulatory agency (e.g., OHRP, FDA) regarding any unanticipated problems involving risks to human subjects or others; serious and/or continuing noncompliance with the Federal Policy, other applicable federal human subjects protection regulations or policies, or the FDA Clinical Investigation Regulations, as applicable, or with the requirements or determinations of the Reviewing IRB; and/or any suspensions or terminations of IRB approval.

Research: Any human subjects research within the meaning of the Federal Policy or within the meaning of any other federal human subjects protection regulations or policies; any investigation/ clinical investigation within the meaning of the FDA Clinical Investigation Regulations; and any other research for which any Participating Institution seeks or is required to rely on a Reviewing IRB. Research may reference a specific study or protocol (an instance of Research) or collectively any or all of the studies or protocols eligible under the Agreement.

Responsible Party: An Indemnification Participating Institution that is a Public Institution and is agreeing in the Indemnification Addendum to be responsible to and to reimburse the Other Parties.

Reviewing IRB: The IRB of a Participating Institution that will provide IRB review and/or determinations of exemption from IRB review for a Relying Institution under the Agreement.

Reviewing IRB Institution: The Participating Institution whose IRB will become the Reviewing IRB for a Relying Institution under the Agreement and/or that will provide determinations of exemption from IRB review for a Relying Institution under this Agreement.

Site Investigator(s): An investigator(s) responsible for the conduct of the Research at their Participating Institution.

SMART IRB SOPs: The SMART IRB Standard Operating Procedures developed in support of the Agreement.

SMART IRB Team, including SMART IRB Administrators, Administration, and/or Administrative personnel: collectively, these terms include leadership, staff, and SMART IRB Ambassadors supporting the development, implementation, and operations of SMART IRB and its systems and programming.

Terminating Institution: A Participating Institution that terminates its participation in the Agreement or whose participation in the Agreement is terminated pursuant to Sections 7.2.1.2 or 7.2.1.3 hereof, respectively, or whose participation in the Agreement ends as a result of the termination of the Agreement in its entirety pursuant to Section 7.2.1

Responsibilities: PIs and Study Teams

Overall PI and Lead Study Team

The Overall PI is responsible for identifying a Lead Study Team and providing the Lead Study Team/ Coordinating Center contact information to the Site Investigators. The Overall PI and Lead Study Team (or their designees) are responsible for providing the information or performing the activities described below related to the reliance review process and once IRB review has been ceded:

- Work in collaboration with the Reviewing IRB and POC to determine and document specific roles and responsibilities for communicating and coordinating key information to Relying Institutions and the Reviewing IRB as described throughout these SOPs and summarized in the Appendix: Communication Plan.
- Promptly responding to questions or requests for information from Site Investigators, study teams, and/or IRB/HRPPs at Relying Institutions.
- Providing the Site Investigators with the IRB policies of the Reviewing Institution. This will include but is not limited to providing the Site Investigators with the IRB policies applicable to the study for reporting unanticipated problems, noncompliance, and subject complaints.
- Obtaining and collating information from Relying Site Study Teams and/or Relying Site Points of Contacts (depending on who is designated to provide that information at the Relying Institution) regarding local variations in study conduct, such as recruitment materials and process, consent process and language, and subject identification processes.
- Participating in meetings regarding a study as requested by the Reviewing IRB, Relying Site Study Team, or home institution.
- Providing participating Relying Site Study Teams with the IRB-approved versions of all study documents (e.g., consent and authorization forms, protocol, recruitment materials).
- Assisting Relying Site Study Teams and/or POCs at the Relying Institution(s) (depending on who is designated to provide that information) in ensuring consent documents follow the Reviewing IRB's template form and include applicable site-specific required language from each Relying Institution.
- When agreed upon in coordination with the Reviewing IRB, promptly reporting to the Site Investigator (or designee on the Relying Site Study Team) any unanticipated problems involving risks to subjects or others research-related subject injuries, or significant subject complaints that are related to or may affect subjects participating in the Research (i.e., the specific study or studies ceded to the Reviewing IRB) at the Relying Institution.
- Ensuring Site Investigators are notified of all Reviewing IRB determinations and communications, including those for initial review, continuing review, amendments, and reportable events, as applicable.

- If a Relying Site Study Team does not provide the Lead Study Team (or designee) with the required information before the continuing review application is submitted to the Reviewing IRB, reporting the absence of this information as part of the continuing review and notifying affected Relying Site Study Team of lapse in approval for their site and any applicable corrective action plans.
- Providing access, upon request, to study records for audit by the Relying Institution, the Reviewing IRB, and other regulatory or monitoring entities.
- Following all ceded review requirements of the Relying Institution, such as ensuring administrative requirements for documenting ceded review have been met before study activation occurs at a Relying Institution.

Relying Site Study Teams

The Relying Site Study Teams, which include Site Investigators, are responsible for providing the information or performing the activities described below related to the reliance review process and once IRB review has been ceded:

- Following all requirements of their home institution regarding ceded review, such as ensuring other reviews or sign-offs required by the institution have been completed before a study is activated.
- Promptly responding to questions or requests for information from the Lead Study Team (or designee) as well as from the Reviewing IRB through the communication mechanism(s).
- Participating in meetings regarding a study as requested by the Lead Study Team, Reviewing IRB, or home institution.
- Working with the Lead Study Team and the POC from their home institution or the Reviewing IRB, as applicable, to incorporate site-specific required language into the consent template to be used at their institution.
- Providing the applicable office (e.g. grants/contracts) at their institution with documentation that IRB oversight for a study has been ceded to and approved by an IRB external to their home institution.
- Providing the POC from their home institution with information regarding local Site Investigator or other Relying Site Study Team personnel changes.
- Reporting to their home institution POC any changes in conflict of interest (COI) disclosures and resulting changes in COI management plans related to the Research (i.e., the specific study or studies ceded to the Reviewing IRB).
- Promptly reporting to the Lead Study Team (or designee) 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.

- Reporting to the Lead Study Team (or designee) any changes (including funding changes and personnel changes), reportable events, and continuing review progress reports, for submission to the Reviewing IRB in accordance with the Reviewing IRB's policies and procedures for timing and content of such submissions.
- Promptly reporting to the Overall PI via the Lead Study Team (or designee) any unanticipated problems involving risks to subjects or others, subject injuries related to the research, or significant complaints that could impact the conduct of the Research (i.e., the specific study or studies ceded to the Reviewing IRB) in accordance with the Reviewing IRB's policies and procedures for timing and content of such submissions. Significant complaints are defined as those that cannot be resolved by the study team and a) suggest an increased or unexpected new risk or harm or b) change the risk/benefit ratio of the Research. Other complaints should be reported in accordance with the Reviewing IRB's policies and procedures.
- Promptly reporting to the Overall PI via the Lead Study Team (or designee) any potential noncompliance that occurs in relation to the Research (i.e., the specific study or studies ceded to the Reviewing IRB) in accordance with the Reviewing IRB's policies and procedures for timing of submission and content of such submissions.
- Providing, upon request, access to study records for audit by the local institution, the Reviewing IRB's institution, and other regulatory or monitoring entities.

Responsibilities: Reviewing IRBs and Relying Institutions

This section of the SOPs provides an overview of the key responsibilities of Reviewing IRBs and Relying Institutions. The responsibilities of the POC, who plays a critical role in ensuring that many of these Reviewing IRB and Relying Institution responsibilities are met, are addressed in detail in the next section.

Reviewing IRBs

The Reviewing IRB is responsible for reviewing and overseeing any studies ceded to it for the life of the study, unless the research is withdrawn from Ceded Review, Institution ends its participation in the SMART IRB Agreement or a specific study section below. In addition, the Reviewing IRB (or designee) is responsible for the following activities related to the initial reliance review process and subsequent management of the study:

- Working in collaboration with the POC and Lead Study Team (or designee) to determine and document specific roles and responsibilities for communicating key information to Relying Institutions and the Reviewing IRB as described throughout these SOPs, and as summarized in the Appendix: Communication Plan.
- Providing POCs and Relying Site Study Teams with template informed consent form(s), which indicate areas where the Relying Institutions must add information (e.g., local contacts)[1].
- Sending written notification to the Overall PI and Lead Study Team of: (i) its decision to approve or disapprove any Research (i.e., the specific study or studies ceded to the Reviewing IRB), (ii) any modifications required to secure approval of the Research, and (iii) the date by which renewal of an approval is required.
- Upon reasonable request, providing to the Relying Institution with access to relevant records related to the IRB review.
- Promptly notifying the Overall PI and relevant POCs from a Relying Institution of its findings and actions with respect to any unanticipated problems involving risks to subjects or others or any research-related subject injuries or significant subject complaints that occurred at the Relying Institution—or that occurred at another Relying Institution if such events or actions relate to or may affect the conduct of the Research or the safety, rights, or welfare of subjects participating in the Research at the Relying Institution.
- In the event a continuing review is submitted after IRB approval for the study expires or the study expires before the Reviewing IRB can reapprove the study, notifying the POCs and Relying Site Study Teams from affected sites, in addition to the Overall PI and Lead Study Team, of the lapse in IRB approval and any applicable corrective action plans.

1 Alternatively, a member of the Lead Study Team may assume responsibility for notifying Relying Site POCs and Study Team members as described in this section, if agreed upon by the POC for the Reviewing IRB.

- Promptly notifying relevant POCs and Relying Site Study Teams, in addition to the Overall PI and Lead Study Team, of any finding of serious and or/continuing noncompliance that may affect the conduct of the Research or the safety, rights, or welfare of human subjects participating in the Research at the Relying Institution(s). If the finding of serious and/or continuing noncompliance has a study-wide impact, all Relying Institutions must be notified.
- Promptly notifying the Overall PI, Lead Study Team, relevant POCs, and relevant Relying Site Study Teams of any suspension or termination of IRB approval for that portion of the Research taking place at those Relying Institutions. If the suspension or termination is study-wide, all Relying Institutions must be notified.
- Unless an alternate reporting arrangement has been previously agreed upon between the Relying Institutions and Reviewing IRB, reporting to regulatory agencies and/or sponsors any findings of unanticipated problems involving risks to subjects or others, determinations of serious and/or continuing noncompliance, and/or any suspensions or terminations of IRB approval on behalf of all applicable institutions covered by this Agreement. The Reviewing IRB will also provide the involved Relying Institutions the opportunity to review and comment on the report before it is sent to federal authorities, such as OHRP, the FDA, or others.
- If the Reviewing IRB ends its participation in the SMART IRB Agreement or a specific study, informing all Relying Institutions of this change, as described in the “Ending Site Participation in the SMART IRB Agreement or Specific Studies” section below.

Relying Institutions

Relying Institutions are responsible for the following activities related to the initial reliance review process and subsequent management of the study; these will generally occur through the Overall PI and Lead Study Team:

- Communicating local considerations to the Reviewing IRB, including requirements of applicable state or local laws, regulations, institutional policies and standards, and other local factors including ancillary review processes as are relevant to the Research (i.e., the specific study or studies ceded to the Reviewing IRB). Generally, this will occur through the POC (see sections below).
- Communicating other considerations including the requirements of any applicable federal laws or regulations of relevant federal departments or agencies that may not be apparent from the research submission or that are specific to the relying institution that would affect the conduct by or approval of the research.
- Providing information about local restrictions, stipulations, or requested substitutions to informed consent documents for approval by the Reviewing IRB, Generally, this will occur through the POC (see sections below).
- Ensuring there is a mechanism for which significant complaints about the research may be received locally.

- Notifying the Reviewing IRB of the following:
  - Any unanticipated problems or potential noncompliance that occurred
  - Findings of serious and/or continuing noncompliance that occurred on research that has not been ceded under this Agreement but that may have relevance to ceded Research
  - Any significant research participant complaints
  - Any suspension or restriction of a Relying Site's Study Team member(s) ability to conduct human subjects research.
- Maintaining policies regarding the disclosure and management of personnel conflicts of interest related to the research submitted for ceded review and sharing those policies with Reviewing IRB, as requested.
- Disclosing any COI related to Research conducted under this Agreement and providing applicable management plans to the Reviewing IRB; this may occur through the Lead Study Team or the Relying Institution POC.
- If the Reviewing IRB requests an audit, the Relying Institution will cooperate, and report audit findings to the Reviewing IRB within a reasonable timeframe.
- Report to federal funding agencies, sponsors, and/or other federal authorities and that are required related to the ceded research but not made by the Reviewing IRB (e.g., report of a determination of serious noncompliance to a study sponsor).
- Notifying the Reviewing IRB(s) of communications regarding Research covered by this Agreement to/from the Relying Institution and FDA, OHRP, and/or other regulatory agencies (e.g., re. unanticipated problems or serious and/or continuing noncompliance), as applicable.
- Informing the Reviewing IRB if the Relying Institution ends its participation in the SMART IRB Agreement or a specific study.

Responsibilities: SMART IRB Points of Contact (POCs)

This section of the SOPs provides an overview of the key responsibilities of SMART IRB POCs during the reliance review process and after IRB review is ceded.

Each Participating Institution must designate a primary POC and an (optional) alternate POC. Generally, the POC is associated with the Participating Institution's IRB. However, some Participating Institutions will not have IRBs or will appoint an individual outside of the local IRB office to serve as a POC.

All Participating Institutions are responsible for designating an individual (a SMART IRB POC) to carry out the following activities; Participating Institutions may designate some of these activities to personnel other than the designated SMART IRB POC (e.g., Research Integrity Officers, legal counsels, Institutional Officials, or post-approval monitoring programs):

- Communicating to other SMART IRB POCs, the Lead Study Team, and to their Site Investigator the institution's decisions to serve as the Reviewing IRB, cede review to the proposed Reviewing IRB, or retain local IRB review of Research.
- Promptly reviewing reliance requests and any supporting materials to determine whether ceding IRB review or serving as the Reviewing IRB is appropriate, in accordance with that institution's policies and procedures.
- On a study-by-study basis, communicating with SMART IRB POCs at other institutions identified as potential study sites to identify a single Reviewing IRB and determine which institutions choose to rely on the identified Reviewing IRB.
- Consulting, as needed, with individuals and resources (e.g., other IRB staff, legal counsel) at the institution regarding ceding IRB review or accepting IRB oversight for Research under the SMART IRB Agreement.
- Addressing any questions from the Site PI and/or potential Relying Site Study Team regarding the SMART IRB Agreement reliance review process and status of the reliance request.
- Notifying Relying Institutions of any legal action related to Research that had been ceded to the institution's IRB under the SMART IRB Agreement.
- Notifying the Reviewing IRB regarding the outcome of any internal audit findings related to Research ceded under the SMART IRB Agreement that represent reportable information per the Reviewing IRB's policies and procedures (e.g. unanticipated problems, serious or continuing noncompliance, or other reportable information).
- As appropriate, notifying other SMART IRB POCs regarding the outcome of any other audit findings not addressed above and related to Research that had been ceded under the SMART IRB Agreement.
- Promptly communicating to the SMART IRB Team, and to SMART IRB POCs at Participating Institutions with which the institution is engaged, any changes in the institution's designated SMART IRB POC(s).

- In regard to the institution's FWA or other Federal Assurance, notifying POCs at other Participating Institutions of:
  - A suspension or restriction to the institution's FWA or other assurance
  - A modification to the scope of research to which the FWA or other assurance applies
  - Invalidation of the institution's FWA or other assurance for any reason (e.g., termination or expiration)
  - Filing of a new or updated Federal Assurance (e.g. FWA or other assurance)
- Notifying the SMART IRB Team of changes in the components of the institution that are covered under the FWA or other assurance.
- When the POC's institution serves as the Reviewing IRB:
  - Working in collaboration with the Reviewing IRB and Lead Study Team to determine and document specific roles and responsibilities for communicating key information to Relying Institutions and the Reviewing IRB as described throughout these SOPs and as summarized in the Appendix: Communication Plan.
  - Verifying that any changes in Site PIs or Relying Site Study Team personnel have been signed-off on by the Relying Institution POC for submission to the Reviewing IRB.
  - Communicating lapses in IRB approval to affected Relying Institutions as addressed in the "Continuing Review Submission and Review Process" section below.
  - Communicating information related to reportable events to affected Relying Institutions as addressed in "Reportable Event Submission and Review Process" below.
- When a POC's institution is a Relying Institution:
  - Communicating to the Reviewing IRB POC any questions or concerns about the Research and local considerations (e.g., State law and any outstanding institutional requirements that must be met), in coordination with the Relying Site Study Team.
  - Verifying, in coordination with the Reviewing IRB POC, that Site Investigator or Relying Site Study Team personnel meet the institutional requirements for the Relying Institution, including education, training, and qualifications to perform the Research and safeguard the rights and welfare of research participants. This verification includes, but is not limited to, having any local institutionally required professional staff appointments, credentialing, insurance or other liability coverage (if required), and training in human subjects protections, and background checks for their assigned role in the Research.
  - For any proposed changes in Site PI or Relying Site Study Team personnel, verifying, in coordination with the Reviewing IRB POC, that any institutional requirements for investigators and study team members are met, including education, training, qualifications, and resources to perform the Research and safeguard the rights and welfare of research subjects. This verification includes, but is not limited to, having any local institutionally required professional staff appointments, credentialing, insurance or other liability coverage (if required), training in human subjects protections, and background checks for their assigned role in the Research.

- Notifying the Reviewing IRB's POC regarding events that occur at the Relying Institution that may alter the Reviewing IRB's decision to accept IRB oversight for the Relying Institution or the Relying Institution's decision to cede review, such as suspension of research privileges of a Site Investigator at a Relying Institution. NOTE: This notification would be limited to events that might not otherwise be reported to the Reviewing IRB by the Lead Study Team (e.g., noncompliance concerns identified by the Relying Institution on a study not ceded to the Reviewing IRB).
- Responding promptly to any requests for assistance or information from the Reviewing IRB's POC (e.g., gathering information on behalf of the Reviewing IRB regarding reportable events occurring at the Relying Institution)

Establishing the Reviewing IRB

This section describes the process for establishing a Reviewing IRB for any studies conducted under the SMART IRB Agreement. The process begins when a proposed human research study has been identified and an “Overall PI” has been established.

The default prioritization scheme used for identifying potential Reviewing IRBs will be as follows:

1. Reviewing IRB that has been pre-determined by study sponsor or grant or established by prior arrangement (e.g., network central IRB).
2. Overall PI’s Home Institution (HI) IRB. (NOTE: the HI is where the Overall PI is primarily employed or is affiliated.)
3. Another Participating Institution IRB, when Overall PI HI does not have an IRB or Reviewing IRB(s) is selected based on type of procedures to be performed, subject population, or other criteria; more than one Reviewing IRB may be appropriate if these will significantly vary among participating sites.

Note: For research that is subject to federal regulations or funding policies mandating reliance on a single IRB, specific federal department or agency processes for initiating reliance and for determination of the Reviewing IRB/Reviewing IRB Institution will apply and should be used to establish the Reviewing IRB/Reviewing IRB Institution.

Each Participating Institution will determine whether the responsibility for submitting reliance request is assigned to the Overall PI, Lead Study Team, or the IRB POC. The Overall PI or designee submits a request and supporting documents via the mechanism established by the HI IRB and identifies a proposed Reviewing IRB, which may be the IRB at the HI or an external IRB. If the Overall PI HI does not have an IRB, the Overall PI will follow the institution’s policies for requesting the use of an external IRB.

The SMART IRB POC at the Overall PI’s HI reviews the request and supporting documents and determines, in consultation with other Participating Institutions as necessary, if the institution’s IRB will serve as the Reviewing IRB for the Overall PI and other sites. If the SMART IRB POC determines that the HI IRB agrees serve as the Reviewing IRB, the POC will notify the Overall PI of the decision, and proceed to the section below on “Establishing the Relying Institutions.”

If the HI has an IRB and declines to serve as the Reviewing IRB for all Participating Institutions, the HI SMART IRB POC will then determine whether the HI is willing to cede review to another IRB to serve as the Reviewing IRB for the Overall PI. If the HI is willing to cede review to another institution, the HI SMART IRB POC contacts the POC(s) for potential alternate Reviewing IRB(s) identified by the Overall PI. The Overall PI may participate in this process where necessary. Once the Reviewing IRB has been established, the SMART IRB POC (on behalf of the Reviewing IRB) will notify the Overall PI of the decision, and proceed to the section below on “Establishing the Relying Institutions.” If the HI is unwilling to cede review to another institution, the HI IRB proceeds to conduct a review of the study for its own study team. The other Site Investigators are referred to new potential Reviewing IRBs identified by the Overall PI or by the HI POC.

The Overall PI, SMART IRB POC, and representative(s) from the Reviewing IRB will establish and document the party who will assume responsibility for the reliance-related communication and administrative functions described within these SOPs for which flexibility exists (e.g., whether the Reviewing IRB will review waivers and alterations of authorization on behalf of Relying Institutions. A sample “Communication Plan” matrix is attached to these SOPs.

NOTE: There may be situations where the Overall PI does not seek Ceded Review but a sub-group of POCs determine Ceded Review is appropriate for the Research. If the Overall PI and/or the POC for the Overall PI’s HI do not object, Participating Institutions may still participate in Ceded Review for the Research. In this case, a Site Investigator may make a request for Ceded Review to their HI IRB.

2 For example, it may be appropriate to identify more than one Reviewing IRB for a single study if a study involves both pediatric and adult populations and separate reviewing IRBs are established to oversee each population.

Establishing the Relying Institutions – Prior to IRB Approval

Once the proposed Reviewing IRB has been established, the SMART IRB POC from the Reviewing IRB Institution contacts the SMART IRB POCs at the other known Participating Institutions engaged in the proposed research, providing these sites access to the available materials provided by the Overall PI. These potential Relying Institutions should complete the following steps within 14 calendar days:

1. Review the materials provided by the Overall PI.
2. Render a determination about ceding IRB review to the proposed Reviewing IRB.

If a potential Relying Institution agrees to cede review to the proposed Reviewing IRB, the Relying Institution SMART IRB POC provides the following information to the Reviewing IRB POC, Overall PI, and local Site Investigator:

1. The decision to cede review.
2. Any outstanding concerns or requirements that must be addressed before the Reviewing IRB approves the Research for that Relying Institution.
3. Any local considerations or other considerations related to the Research that the Reviewing IRB must consider.

NOTE: Once informed consent document (ICD) templates are available for site-specific customization, Relying Institutions will provide institution-specific language for a limited number of areas as described in the "Customization, Submission, and Review of Informed Consent Documents" section below.

If a potential Relying Institution declines to cede review to the proposed Reviewing IRB, the SMART IRB POC for the institution communicates this determination to the proposed Reviewing IRB POC, Overall PI, and local Site Investigator. If the institution still plans to conduct the research, the institution will do so by maintaining local IRB oversight, ceding to a different Participating Institution IRB or ceding to an IRB that is not part of the SMART IRB Agreement. On the rare occasion that more than one Reviewing IRB becomes involved in overseeing a multi-site study[2], it is the Overall PI's responsibility to ensure coordination among the reviewing IRBs.

2 For example, it may be appropriate to identify more than one Reviewing IRB for a single study if a study involves both pediatric and adult populations and separate reviewing IRBs are established to oversee each population.

Adding New Relying Institutions – Post-IRB Approval

This section describes the process for adding a new Relying Institution for Research already reviewed and approved by a Reviewing IRB under the SMART IRB Agreement.

This process begins when the Overall PI/Lead Study Team provides the new proposed Relying Institution Site Investigator and SMART IRB POC with available study materials. The POC completes the following:

1. Reviews the materials provided by the Overall PI (or designee).
2. Renders a determination about ceding IRB review to the proposed Reviewing IRB.

If the potential new Relying Institution agrees to cede review to the Reviewing IRB, the Relying Institution SMART IRB POC provides the following information to the Reviewing IRB POC, Overall PI, and local Site Investigator:

1. The decision to cede review.
2. Any outstanding concerns or requirements that must be addressed before the Reviewing IRB approves the Research for that Relying Institution.
3. Any local considerations or other considerations related to the Research that the Reviewing IRB must consider.

The Overall PI (or designee) then completes and submits a protocol amendment to add the proposed new Relying Institution to the study in accordance with the SOP section on “Protocol Amendment Submission and Review Process.”

Coordination of IRB Review when a Single Central IRB is Not Identified

Under some circumstances, more than one Reviewing IRB may be established for a particular study. In these cases, it is the responsibility of the Overall PI to coordinate and communicate to each Reviewing IRB the necessary information related to the conduct of the study across all institutions throughout the life of the Research, not just information related to the sites overseen by each Reviewing IRB. Such information must be communicated in accordance with each Reviewing IRB's applicable policies and procedures.

Initial Review: Submission and Review Process

This section describes the IRB review process and responsibilities of the Reviewing IRB, Relying Institutions, Overall PI and Lead Study Team, Site Investigators and Relying Site Study Teams, and SMART IRB POCs.

Once the determination has been made regarding which institution will provide IRB oversight (i.e., act as the Reviewing IRB), as described in the "Identifying the Reviewing IRB" section above, the Lead Study Team submits an application for initial review to the designated Reviewing IRB following the processes and policies and using the forms established by the Reviewing IRB. The initial review application must contain sufficient information to allow the Reviewing IRB to identify a) all known institutions engaged in human subjects research that intend to cede review to the Reviewing IRB (Relying Institutions), b) the activities performed at each institution, and c) the Overall PI and Lead Study Team for the study.

The Reviewing IRB will review initial applications for new Research in accordance with the human subject protection requirements of each Relying Institution's FWA or other federal assurance, the federal regulations and ethical principles referenced therein, any other applicable federal human subjects research regulations or policies, and any local considerations communicated to the Reviewing IRB (e.g., state law). The processes and procedures for review will be in accord with the Reviewing IRB's own policies and procedures. As part of its responsibilities for conducting the initial review, the Reviewing IRB must:

- Take into consideration the local considerations and other considerations provided to it by the SMART IRB POCs from the Relying Institutions as part of their decision to cede review, including institution-specific information for any informed consent documents. This information will be provided to the Reviewing IRB as described in the section above on "Establishing the Relying Institutions."
- If agreed upon by both institutions, review and make any applicable determinations regarding requests for waivers or alterations of authorization under the HIPAA Privacy Rule, per the SOP section below titled 'HIPAA Privacy Rule'.

Unless an issue is discovered during the course of review that requires input from the Relying Institution, the Reviewing IRB generally will not provide any direct communication to the Relying Institution regarding the initial review of the application other than notifications about the Research review.

The Reviewing IRB will notify the Lead Study Team when it has approved the Research through its established processes. The Reviewing IRB may rely on the Lead Study Team to notify the Overall PI and Relying Site Study Teams of the IRB approval or notify the Relying Site Study Team directly.

If the Reviewing IRB disapproves the Research or disapproves a Relying Institution's participation in the Research, the Reviewing IRB POC will inform the Overall PI and Lead Study Team. The Lead Study Team is responsible for notifying relevant institutions of the IRB's determination to disapprove the study or the proposed Relying Institution's participation in the Research. If the Research is disapproved by a Reviewing IRB, and the Overall PI chooses to seek approval from a different IRB rather than substantively revise the protocol materials to address the concerns of the IRB that disapproved the study, the study cannot be subsequently submitted to another Participating Institution for review without disclosing the nature of the previous Reviewing IRB's disapproval.

Customization, Submission, and Review of Informed Consent Documents (ICD)

This section describes how consent documents will be handled and certain language from Relying Institutions incorporated into them.

When informed consent documents (ICDs) are required for a study reviewed under the SMART IRB Agreement, the ICD template(s) of the Reviewing IRB will be used by all Relying Institutions for that Research, except for key areas where regulatory or institutional areas have been identified as requiring site-specific changes to the ICD. If the Reviewing IRB uses a stamp to indicate approval of ICDs, the stamp of the Reviewing IRB will be used. However, Reviewing IRBs are not obligated to stamp approved ICDs, unless required by their own institutional policy or other regulatory requirement.

The Reviewing IRB will determine the content of ICDs except for sections for which Relying Institutions may provide their institution-specific language, as applicable. The institution-specific language in the ICD to be provided by Relying Institutions is generally limited to:

- Compensation for injury
- Availability of treatment for injury
- Payment or reimbursement of research costs incurred by subjects
- Local study team contact(s) for questions about the study
- Changes to address legal or regulatory issues, federal department or agency-specific requirements, or institutional requirements

HIPAA waiver and authorization language is addressed separately in the “Waivers and Alterations of Authorization” section of these SOPs.

Relying Institutions will customize these sections of the ICD by one of two mechanisms, as determined through coordination between the SMART IRB POC and Relying Site Study Team:

1. The Relying Institution POC requests the local Relying Site Study Team incorporate the information into the appropriate section(s) of the ICD(s). Once this has been finalized, the Relying Institution POC provides the local language to the Reviewing IRB POC for reference. The Relying Site Study Team is responsible for forwarding the ICD(s) to the Lead Study Team for submission to the Reviewing IRB through the Reviewing IRB’s established processes.

OR

2. The Relying Institution POC takes responsibility for incorporating the information into the local ICD(s). Once finalized, the Relying Institution POC forwards the ICD(s) to the Lead Study Team for communication to the Reviewing IRB in accordance with the Reviewing IRB’s established processes.

The Reviewing IRB will ensure a copy of the approved ICD(s) is sent to the Relying Institution POC, Overall PI, Lead Study Team, and Site Investigators. The Reviewing IRB may rely on the Lead Study Team to distribute the IRB-approved ICD(s). If a Relying Site Study Team or Relying Institution requires changes to its local language after the Reviewing IRB has approved the ICD(s) for that site, an amendment must be submitted to and approved by the Reviewing IRB before revised ICDs can be used at that institution.

Continuing Review: Submission and Review Process

This section describes the key components for continuing review and responsibilities of the Reviewing IRB, Relying Institutions, Lead Study Team, Relying Site Study Team, and SMART IRB POCs during this process.

The Lead Study Team will submit a continuing review progress report to the Reviewing IRB in accordance with the Reviewing IRB's policies and procedures (e.g., when the report is due and the mechanism through which it is submitted to the IRB). The Lead Study Team (or designee) is responsible for obtaining information from each Relying Site Study Team, regardless of whether the institution is under the purview of the Reviewing IRB, so that the Reviewing IRB can assess a comprehensive report regarding study progress, new information, and problems that have occurred. If a Relying Site Study Team does not provide the Lead Study Team with required information before the continuing review application is submitted to the Reviewing IRB, the Lead Study Team must report the absence of this information as part of the continuing review submission.

The Reviewing IRB is responsible for reviewing all relevant information for the Lead Study Team's and Relying Study Team's sites until the Research is closed. The Reviewing IRB will conduct continuing reviews in accordance with the human subject protection requirements of each Relying Institution's FWA or other federal assurance, the federal regulations and ethical principles referenced therein, any other applicable federal human subjects research regulations or policies, and any local requirements communicated to the Reviewing IRB (e.g., state law). The processes and procedures for review will be in accord with the Reviewing IRB's own policies and procedures.

Unless a Reportable Event is discovered in the course of the continuing review, the Reviewing IRB generally will not provide any direct communication to the Relying Institution regarding the review. The Reviewing IRB will notify the Lead Study Team when it has reapproved the Research through its established processes. The Reviewing IRB may rely on the Lead Study Team to notify Relying Site Study Teams of the IRB reapproval (or disapproval) of the Research or notify the Relying Site Study Team directly. If Research is disapproved by a Reviewing IRB at continuing review, and the Overall PI chooses to seek approval from a different IRB rather than substantively revise the study materials to address the concerns of the IRB that disapproved the Research, the Research cannot be subsequently submitted to another Participating Institution for review without disclosing the nature of the previous IRB's disapproval.

In the event a continuing review is submitted after IRB approval for the study expires or the study expires before the Reviewing IRB can reapprove the study, the Reviewing IRB will notify all participating site SMART IRB POCs, Overall PI, Lead Study Team, and Relying Site Investigators of the expiration of IRB approval. The Reviewing IRB will notify the Lead Study Team and applicable Relying Institution POCs of any applicable corrective action plans required.

Relying Site Study Teams may be required by their home institutions to provide study updates to local officials (e.g., local IRB offices) and are responsible for meeting these requirements.

Protocol Amendment: Submission and Review Process

This section describes the process for reviewing study amendments (i.e., changes to the study or supporting documents) and associated responsibilities of the Reviewing IRB, Relying Institution, Lead Study Team, Relying Site Study Team, and SMART IRB POCs during this process.

The Lead Study Team is responsible for submitting amendments (studywide or local amendments for Relying Sites) to the Reviewing IRB for review in accordance with the Reviewing IRB's policies and procedures (e.g., timing and mechanism of submission).

The Reviewing IRB will conduct reviews of changes in research in accordance with the human subject protection requirements of each Relying Institution's FWA(s) or other federal assurance(s), the federal regulations and ethical principles referenced therein, any other applicable federal human subjects research regulations or policies, and any local considerations communicated to the Reviewing IRB (e.g., state law). The processes and procedures for review will be in accord with the Reviewing IRB's own policies and procedures. A Relying Institution POC must authorize their Relying Site Study Team's submissions of the following types of changes to the Lead Study Team for consideration by the Reviewing IRB POC:

- Changes to a Site Investigator or other Relying Site Study Team personnel, in order to ensure these personnel meet the institutional requirements for the Relying Institution;
- Changes that appear to affect any state law or local considerations or other considerations a Relying Institution noted as part of its agreement to cede review; or
- Changes that indicate a newly identified COI.

Relying Site Study Teams will report changes in COI to their local Relying Institution in accordance with the local procedures and policies for COI reporting and management already established at each site. Relying Institution POCs will coordinate with local COI administrators and the local Relying Site Study Team in order to communicate this information to the Reviewing IRB. Reporting new or updated COI information, as well as personnel changes, to local SMART IRB POCs will occur in accord with the Relying Institution's processes.

The Reviewing IRB will notify the Lead Study Team when it has approved an amendment/change in research through its established processes. The Reviewing IRB may rely on the Lead Study Team to notify applicable Relying Institutions of the IRB approval. In advance, determine and document specific roles and responsibilities for communicating and coordinating key information to Relying Institutions and the Reviewing IRB. In the case of local amendments (e.g. local recruitment materials, site-specific changes to consent documents) that do not affect all Relying Institutions, only the sites affected by the approved amendment must be notified of the IRB approval.

Record Keeping and Document Retention

This section describes the process for maintaining and storing SMART IRB administrative records and the responsibilities of SMART IRB Administration, Reviewing IRBs, and Relying Institutions for the maintenance of these records, covering SMART IRB administrative records and study-specific IRB records related to reliance, but not the investigators' Research files.

SMART IRB Administrators, Reviewing IRBs, and Relying Institutions will maintain the following records in the locations specified in the table below:

SMART IRB Records

RECORD TYPE	RESPONSIBLE PARTY	STORAGE LOCATION
Current SMART IRB policies and procedures including: SOPs, forms, templates, etc.	SMART IRB Administrators	SMARTIRB.org
Current executed SMART IRB Reliance Agreements and Joinder Agreements, as well as any amendments	SMART IRB Administrators and Participating Institutions	SMARTIRB.org and at Participating Institutions
Study-specific reliance requests including: identification of Reviewing IRB(s) and Relying Institutions, and Study Team information	Participating Institutions	Local storage at Participating Institutions
Minutes from IRB meetings at which Research ceded under the SMART IRB Agreement was reviewed; portions of the minutes that are relevant to a Relying Institution available upon request to designated officials of the Relying Institution.	Reviewing IRB	Local storage; available to Relying Institution(s) upon request
Records of any applicable COI management plans provided by the Relying Institution and received by the Reviewing Institution	Reviewing IRB and Relying Institution	Local storage
Records of events reported by Relying Institution and received by the Reviewing Institutions	Reviewing IRB and Relying Institution	Local storage; available to Relying Institutions upon request
Study-specific review and approval notifications	Reviewing IRB and Relying Institutions	Reviewing IRB and Lead Study Team
Other general correspondence between the Relying Institution and the Reviewing IRB	Reviewing IRB and Relying Institution	Reviewing IRB and Lead Study Team; available to Relying Institutions upon request
Study-specific determinations related to ceding review to a Reviewing IRB (e.g., forms documenting decision to cede review; any outstanding concerns or requirements that must be addressed by the Reviewing IRB, and any institutional requirements related to the ceded study that the Reviewing IRB must take into consideration.)	Relying Institution and Reviewing Institution	Local storage

Document Retention

The records described in the table above will be retained by the respective responsible parties for a minimum of seven years after the closure or termination of the study by the Reviewing IRB. Participating Institutions, including Lead Study Teams and Relying Site Study Teams, are advised to refer to their local institutional policies, as they may require a longer period of retention.

Access to Locally Stored Records and Reliance-Related Documents

The SMART IRB Team and Participating Institution personnel, including POCs, Study Team members, and Reviewing IRBs will have access, where relevant and appropriate, to records listed in the table above for all studies for which they serve either as a Reviewing IRB or as a Relying Institution.

All other reasonable requests for access to records not listed above, or records stored locally, will be granted upon request by the applicable SMART IRB Team member, Reviewing IRB POC, or Relying Site POC, within a reasonable timeframe, and in accordance with the policies of the institution storing the records and applicable state and federal laws or regulations.

Supplemental Study Protocol Content

This section describes the additional content (beyond that which is typically included in a human research protocol) that should be provided to the Reviewing IRB. This additional information addresses coordinating the conduct of the research across multiple sites and establishing roles and responsibilities that supplement the high-level information already included in these SOPs.

Recommendations for information that should be collected at key points during the reliant review process are outlined below.

When requests to cede IRB review are made the following should be identified:

- The Overall PI and Lead Study Team, which retains overall responsibility for the Research.
- Any applicable Coordinating Center, which is responsible for coordinating activities at all other sites, receiving and analyzing data, and developing and updating the study protocol as needed. The Coordinating Center may be the same as the Lead Study Team.

The following should be collected about potential Relying Institutions:

- All Institutions that will be involved in the conduct of the Research
- Types of activities that will occur at each site (e.g., subject recruitment, laboratory analyses, and/or data analyses)
- Nature of the site(s) at which various research activities will occur (e.g., hospital, academic medical center, research clinic, medical office).
- If the study involves sample banking, identification of all institutions at which samples will be stored, what samples will be stored at which site(s).
- Description of any differences among performance sites in study procedures, subject remuneration, or subject populations.

On a study-by-study basis, the following additional information may need to be provided to the Reviewing IRB using forms/format specific to the Reviewing IRB:

- Description of how potential subjects are identified and the recruitment methods used at each recruiting site.
- Description of how informed consent is obtained at each site and who conducts the consent and/or assent process, including any special processes for subjects, such as those who may be non-English speaking, illiterate, have impaired decision-making capacity, or who may be children.
- Description of data storage, including all sites at which data will be stored, what data will be stored at what site(s), data security measures employed, who will have access to identifiable data at a site, when data will be anonymized or destroyed, or if data will be transferred to a central site for storage.
- If the Research involves sample banking, additional information regarding how sample confidentiality will be protected, who will have access to identifiable samples, will whether an honest broker system will be used (and if so, who the honest broker is), when samples will be anonymized or destroyed, and what types of analyses may be conducted on the banked samples.

In addition to the information above, Lead Study Teams (or designee, such as a Coordinating Center) will need to establish processes to address the following issues:

- How they will ensure all Relying Site Study Teams have the most current version of the protocol, consent documents, and other supporting materials.
- How they will ensure that all Relying Site Study Teams use the same version of the protocol, including a description of the procedures that must be followed in order to amend the protocol.
- How they will communicate with, collect information from, and disseminate information to other sites, regarding:
  - Local ICD requirements
  - Study updates (e.g., recruitment holds for interim analyses, closure to enrollment) or other changes to the study
  - Continuing reviews
  - Local changes of protocol (e.g., personnel updates, COI updates)
  - Reportable events
  - Study closure
  - The plan for collection and management of data from all sites

Federal Grant Congruency Review

The Lead Study Team is responsible for submitting any federal grant award or proposal that supports a proposed or approved study to the Reviewing IRB at the time of initial review or as an amendment (change of protocol) if the funds are awarded after initial IRB approval. If the federal grant is not held by a member of the Lead Study Team but by a Relying Site Study Team instead, the Relying Site Study Team must provide a copy of the federal grant to the Lead Study Team for submission to the Reviewing IRB. The Reviewing IRB is expected to review a copy of the entire proposal in order to understand the scope of a project.

The Participating Institution, rather than the Reviewing IRB, that holds the grant is responsible for providing documentation of congruency (when required) for certification to its local sponsored programs office per local policies and procedures. Relying Institutions retain responsibility for making relevant certifications to a Federal Department or Agency for awards their Institution receives.

HIPAA Privacy Rule

This section describes how determinations related to the Health Insurance Portability and Accountability Act of 1996 (HIPAA) will be handled under the SMART IRB Agreement.

Under the SMART IRB Agreement Protected Health Information (PHI) will not be used or disclosed among collaborating institutions unless there is: (1) appropriate authorization to use and disclose such information for the purposes of research; (2) an appropriate waiver or alteration of such authorization has been granted by the Reviewing IRB in accordance with the HIPAA Privacy Rule, or; (3) the information constitutes a Limited Data Set and is shared pursuant to a Data Use Agreement as those terms are defined in HIPAA.

Waivers and Alterations of Authorization

Relying Institutions who are covered entities under HIPAA are responsible for making determinations regarding waivers or alterations of authorization under the HIPAA Privacy Rule for their institution, and will follow their institutional policies and procedures as well as federal regulations for the review and approval of waivers or alterations of authorization.

If agreed by both the Reviewing IRB and the Relying Institution, the Reviewing IRB may make determinations regarding waivers or alterations of authorization under the HIPAA Privacy Rule for Relying Institutions that are Covered Entities. When considering waivers or alterations of authorization, Reviewing IRBs will not approve waivers for the release of directly identifiable data outside the Covered Entity without consulting with Relying Institution POCs to determine whether the policies of the Relying Institutions would allow such a disclosure.

If the Reviewing IRB approves a waiver of authorization for use and disclosure of PHI, a Relying Institution may rely on the Reviewing IRB's determination to the extent that it comports with institutional requirements.

If the Relying Institution has a concern about a waiver, partial waiver, or alteration of authorization the Reviewing IRB has granted, then the Relying Institution should discuss alternative approaches with the Reviewing IRB. Until an alternative approach is agreed upon between the Reviewing IRB and the Relying Institution, the Relying Site Study Team cannot perform the activity covered by the waiver, partial waiver, or alteration of authorization.

If a research subject revokes permission to use his or her PHI, the affected investigator will determine whether the revocation occurred due to circumstances that require reporting to the Reviewing IRB in accordance with the Reviewing IRB's policies and procedures.

HIPAA Authorization Language

The language required under the HIPAA Privacy Rule to obtain authorization for the use and/or disclosure of PHI will be provided by the Relying Institution, and may be incorporated into the (ICD) or as a separate HIPAA authorization form. The Relying Institution will provide any relevant local considerations information that require a HIPAA authorization form or language to be separate from the consent document(s). If the Relying Institution does not provide a separate HIPAA authorization form or section to be incorporated into the ICD, the Reviewing IRB will provide the Relying Institution with the proposed HIPAA authorization form/section, ensure that certain elements of authorization are sufficiently broad to cover the Relying Institutions (e.g., the sources of the PHI, who may use the PHI, and to whom the covered entity may disclose the PHI), and consider any institution-specific requirements for HIPAA authorization language that a Relying Institution wishes to be incorporated into combined consent/authorization documents. A Relying Institution can delegate this responsibility for communicating Institution-specific HIPAA authorization language to the Relying Site Study Team or Relying Institution POC.

Potential Breaches of PHI

Participating Institutions are responsible for investigating and reporting to appropriate authorities, including Privacy Officers at affected institutions, breaches of PHI in accordance with institutional policies.

In the event that a potential privacy breach is discovered, Relying Site Study Teams must promptly notify their local Privacy Officer. The local Privacy Officer must then determine if a breach occurred. If it is determined that a breach occurred, the Relying Site POC (or designee) should ensure that the Lead Study Team and Reviewing IRB are notified of the breach, and should be involved in any subsequent investigation of the breach as well as any notifications individuals or offices required by local institutional policy (e.g., their local Institutional Official for the Protection of Human Subjects).

The Reviewing IRB may review the reported breach as a potential unanticipated problem in accordance with the Reviewing IRB’s policies and procedures for unanticipated problems.

Financial and Other Conflicts of Interest

This section describes key components of the process for communicating and evaluating financial conflicts of interest (henceforth COIs) for Research under the SMART IRB Agreement, and responsibilities of the Federal and non-federal Relying Institutions, Reviewing IRB, Lead Study Team, Relying Site Study Teams, and POCs.

Unless the Reviewing IRB and a non-federal relying institution agrees to an alternative approach, the non-federal Relying Institutions are responsible for review and management of any COIs related to Research ceded to an external Reviewing IRB under the SMART IRB Agreement. Non-federal Relying Institution POCs will take into consideration COIs and applicable management plans when determining whether Research will be ceded to the proposed Reviewing IRB or continue to be ceded to the Reviewing IRB (if the potential or new COI is identified after the study has been approved). If a study will be ceded to the proposed Reviewing IRB, the non-federal Relying Institution POC will coordinate with the appropriate COI administrator at their institution to ensure any COIs and applicable management plans are communicated to the Reviewing IRB. The non-federal Relying Institution POC may communicate this COI information directly to the POC for the Reviewing IRB or delegate this responsibility to the local Relying Site Study Team for submission to Lead Study Team, who will provide this information to the Reviewing IRB. If the non-federal Relying Institution's policies require IRB review of institutional COI, the Reviewing IRB will review such conflicts upon request.

Relying Site Study Teams must disclose any COI and applicable management plans to their SMART IRB POCs and the Lead Study Team at the time a reliance request is submitted and when the initial review application is submitted to the Reviewing IRB. Any new COIs identified for any Study Team member or updates to management plans must be reported to the Reviewing IRB. In these cases, non-federal Relying Site Study Teams provide information about new COIs or updated management plans to their local SMART IRB POC through the process established at their institution. The non-federal Relying Institution POC will coordinate with the appropriate COI administrator at their institution to determine whether any additional action is required by their institution regarding the new COI and/or updated management plan.

Relying Site Study Teams are also responsible for disclosing to the Lead Study Team any new COIs or updated management plans issued by the non-federal Relying Institution after the study is ceded. The Relying Site Study Teams must inform their SMART IRB POCs of these updates and obtain confirmation from their POCs that this new information does not affect the decision to cede IRB review and ensure no additional actions must be taken (e.g., potential removal of a study team member or restriction of some personnel's activities). The Lead Study Team is responsible for submitting information about new COIs or updated management plans to the Reviewing IRB in accordance with the Reviewing IRB's policies and procedures (e.g., timing and mechanism for submission).

If a Relying Institution is a Federal Institution, the Federal Institution provides assurances to the Reviewing IRB that it has completed conflict of interest analyses under existing relevant federal policies and that the participation of federal department or agency Personnel is permissible and consistent with federal law.

The Reviewing IRB is responsible for the consideration of any Federal Institution assurances or non-federal Relying Institution COIs and applicable management plan(s) for Study Teams participating in Research that has been ceded to them under the SMART IRB Agreement. The Reviewing IRB will ensure that any management plan is incorporated into its deliberations and that any mandated disclosures to subjects are included in the approved informed consent documents, as the Reviewing IRB deems applicable. The Reviewing IRB may not modify any management plan or mandated disclosure to subjects without discussion and acceptance by the Relying Institution, and retains the authority to impose additional prohibitions or conflict management requirements that are more stringent or restrictive than those included in the Relying Institution's management plan. In the extraordinary circumstance that the Reviewing IRB is unable to rely upon Federal Assurances or implement or approve a non-federal Relying Institution's prohibitions or management plans, the Reviewing IRB will so inform the Relying Institution and withdraw the Ceded Review with respect to that Relying Institution.

If a proposed Reviewing IRB knows of any institutional COI involving its institution, that IRB should decline to serve as the Reviewing IRB, following the procedures in "Establishing the Reviewing IRB".

Reportable Event Submission and Review Process

This section describes the key components of the process for review of reportable events after reliance decisions have been finalized and a study has been approved by the Reviewing IRB, as well as the responsibilities of the Reviewing IRB, Relying Institutions, Lead Study Team, Relying Site Study Teams, and POCs during this process.

All study teams under the purview of the Reviewing IRB will follow the Reviewing IRB's policies and procedures for reportable events (e.g., what requires reporting, reporting timeframes, and mechanism for reporting). The Reviewing IRB will conduct reviews of reportable events in accordance with the SMART IRB Agreement and SOPs as well as its own policies and procedures. Relying Site Study Teams may be required by their local institutions to provide additional reports to local officials (e.g., local IRB offices) and are responsible for meeting these requirements.

Noncompliance and Unanticipated Problems

Reports of potential or actual noncompliance and potential or actual unanticipated problems will be submitted to the Reviewing IRB by the Lead Study Team, unless otherwise delegated. These submissions will be reviewed by the Reviewing IRB in accordance with its own policies and procedures. Upon becoming aware of such a report, the Reviewing IRB will notify and work with any Relying Institution(s) involved in or affected by the report as follows:

- Reviewing IRB POCs will promptly inform any Relying Institution POCs not already aware of reports of noncompliance and unanticipated problems occurring at or involving that institution, even if the Reviewing IRB Institution's information gathering regarding the report is ongoing.
- As needed, the Reviewing IRB Institution may request assistance from Relying Institution POCs in gathering information about the reported event.
- The Reviewing IRB POC will notify the Relying Institution POC(s) and Site PIs from the affected Relying Institutions, as well as, in some circumstances, those from unaffected Relying Institutions, of the Reviewing IRB's determination regarding the reportable event.
- In the event that reporting to a regulatory agency(ies), sponsor, funding agency(ies), and/or other oversight authority(ies) is required under federal regulations or under the terms of a Relying Institution's FWA or other federal assurance, the Reviewing Institution will provide the Relying Institutions with opportunity to review and provide input on such reports (no fewer than 5 business days) before they are sent to the applicable entity(ies).
- If the Reviewing Institution agreed to cede the obligation to report to federal authorities to the Relying Institution, the Relying Institution will provide the Reviewing Institution with the opportunity to review and comment on the report (no fewer than 5 business days) before it is sent to the applicable entity(ies). The Reviewing Institution will promptly provide any comments on the report to the Relying Institution.

Relying Institutions remain responsible for ensuring that any additional actions regarding the reportable event are taken as required by that Institution's policies and procedures.

Serious Adverse Events, Deviations, Subject Complaints, and Other Types of Reportable Events

Reports of serious adverse events, deviations, significant subject complaints and other events specifically requiring reporting to the Reviewing IRB in accordance with Reviewing IRB policies and procedures will be submitted to and reviewed by the Reviewing IRB. If such a report is found to constitute serious or continuing noncompliance or an unanticipated problem, the Reviewing IRB will notify and work with any Relying Institutions involved in or affected by the report as described in the section above on “Noncompliance and Unanticipated Problems.”

Suspensions and Terminations of Reviewing IRB Approval

The Reviewing IRB will suspend or terminate the approval of studies in accordance its own policies and procedures. If the Research as a whole is suspended or terminated, the Reviewing IRB POC will promptly notify in writing all Relying Institution POC(s), Overall PI, Lead Study Team, and Site Investigator(s) of the suspension or termination. If a Relying Institution(s) is suspended or terminated, the Reviewing IRB POC will promptly notify the Relying Institution POC(s), Overall PI, Lead Study Team, and Site Investigator(s) from affected Relying Institution(s) (and in some circumstances other sites) in writing of the decision to suspend or terminate the site(s). In the event of a suspension, the Reviewing IRB will determine whether it can continue to accept IRB oversight for the Relying Institution(s) or determine that it will end its oversight or participation in the specific Research.

Research Misconduct

Both the Reviewing Institution and Relying Institutions are responsible for notifying each other regarding potential research misconduct.

Any individual at a Reviewing or Relying Institution who becomes aware of a potential instance of research misconduct must notify their local Research Integrity Officer (RIO) in accordance with local policies and procedures for handling cases of potential research misconduct. When the research involves a study ceded under SMART IRB, the local RIO will notify and confer with the RIOs at other affected institutions, including the Reviewing IRB’s institution.

If a Reviewing IRB discovers or receives information regarding potential or actual research misconduct, the Reviewing IRB will handle the report as a potential unanticipated problem with further notifications to Relying Institutions as outlined under that section of these SOPs.

Other Reporting Requirements

This section describes other events that may occur that require reporting to the Reviewing IRB Institution and/or Relying Institutions.

CHANGES IN FEDERAL ASSURANCE, IRB REGISTRATION, OR ACCREDITATION STATUS

Reviewing IRB Institution and Relying Institutions are responsible for notifications regarding changes to FWA or accreditation status (also described in the Responsibilities section of this SOP):

- A Reviewing IRB Institution will promptly notify in writing all Participating Institutions and SMART IRB Administration:
  - If its Federal Assurance is suspended or restricted, lapses, or changes in scope.
  - Of any loss or change in its accreditation status.
  - Of any expiration of or change to its IRB registration status.
- Relying Sites will promptly notify:
  - All Participating Institutions and SMART IRB Administration if their FWA is suspended or restricted or if its Federal Assurance lapses or changes in scope.
  - SMART IRB Administration of any loss or change in its accreditation status.

Reviewing IRB Institutions and Relying Institutions are responsible for designating a point person for these types of communications, which may be the SMART IRB POC.

FEDERAL AUDITS AND LEGAL ACTIONS

The Reviewing IRB and Relying Institutions are responsible for notifying each other regarding audit findings related to studies ceded under the SMART IRB Agreement that represent reportable information per the Reviewing IRB's policies and procedures (e.g., unanticipated problems, serious or continuing noncompliance, or other reportable information) as well as legal actions related to any studies for which the Reviewing IRB provides IRB oversight. Participating Institutions will assist as appropriate in investigating and responding to such issues. The Reviewing Institutions and Relying Institutions are responsible for designating a point person for these types of communications, which may be the SMART IRB POC.

Suspension or Restriction of Relying Site Investigator or Relying Site Study Team Member

Relying Institution POCs are responsible for promptly notifying the Reviewing IRB of any suspension or restriction of Site PI or Relying Site Study Team member status to conduct research at the institution.

Withdrawal from Ceded Review

If a Relying Institution determines that it must withdraw the Research from Ceded Review, it will notify the Reviewing IRB of this determination. Participating Institutions are responsible for designating a point person for these types of communications, which may be the SMART IRB POC.

When a change in acceptance of reliance occurs, the Reviewing IRB and Relying Institution(s) will work together to facilitate the transfer of IRB oversight with the goal of limiting the potential disruption to the Research and continuing human subjects protections. Until oversight is transferred, the Reviewing IRB will continue to assume oversight responsibility.

If a Reviewing IRB determines based on significant cause as described in the SMART IRB Agreement that it must withdraw from providing review and oversight of the Research for a Relying Institution, the Reviewing IRB will provide sixty (60) business days' prior written notice to the Relying Institution explaining the significant cause for the Reviewing IRB's withdrawal.

Standard Operating Procedure (SOP) Development, Adoption, Modification, and Maintenance

This section describes the process to create and update SMART IRB SOPs and associated materials.

The Executive Committee (or designee) is responsible for determining whether new SOPs must be created or whether revisions to existing SOPs are necessary. Once a determination has been made that SMART IRB SOPs or associated materials (templates, forms, etc.) must be developed or revised, the Executive Committee (or designee) will designate an individual or group to draft or revise those document(s).

During the drafting process, the individual(s) drafting the new/revised SOPs and associated materials will seek input from the individuals or committees identified by the Executive Committee (or designee). Materials will be revised based on the review and feedback from these individuals/committees.

New or revised SOPs will be approved for finalization by the Executive Committee (or designee).

Once the necessary feedback and revisions have been incorporated into the draft SOPs and/or associated materials, SMART IRB Administrative personnel will finalize the documents by:

- Updating the “version date,” “approved by,” and “approval date” sections of the SMART IRB SOPs.
- Posting the updated SOP Manual and associated materials on the SMARTIRB.org website.
- Archiving the previous version of the materials.
- Notifying all affected Participating Institutions in writing of any material changes.

Purpose of the form: This form should be used to document key communication roles/responsibilities for specific studies. Reviewing IRB/HRPPs may use this form to document general expectations of study teams and relying site IRB/HRPPs, or less formally to guide conversations among the Reviewing IRB, Relying Institutions, and Lead Study Team. The SMART IRB recommends this form be kept up to date with all key information throughout the life of a study.

Communication Plan Template

Definitions:

+ **REVIEWING IRB – Point of Contact (POC):** Main person responsible for addressing questions related to the Reviewing IRB's policies and procedures and review status for a ceded study
+ **LEAD STUDY TEAM – Representative:** Main person responsible for communication with the Reviewing IRB and facilitating communication between relying site study teams and the Reviewing IRB regarding the ceded study
+ **RELYING SITE – POC:** Main person responsible for communication with the Reviewing IRB and local study team regarding the ceded study (e.g., personnel in the local IRB office or local human research protection program personnel)
+ **RELYING SITE STUDY TEAM – Representative:** Main person responsible for communication with the Lead Study Team regarding the ceded study

ROLE	NAME, TITLE, INSTITUTION	CONTACT INFORMATION
Reviewing IRB POC		
Lead Study Team Representative		
Relying Site POC		
Relying Site Study Team Representative		
Study Name		
Overall PI (Lead PI)		
Site Investigator (Local PI)		

Purpose of the form: This form should be used to document key communication roles/responsibilities for specific studies. Reviewing IRB/HRPPs may use this form to document general expectations of study teams and relying site IRB/HRPPs, or less formally to guide conversations among the Reviewing IRB, Relying Institutions, and Lead Study Team. The SMART IRB recommends this form be kept up to date with all key information throughout the life of a study.

AREA OF COMMUNICATION RESPONSIBILITY	RESPONSIBLE PARTY (*TYPICAL PARTY IDENTIFIED)	NOTES
Conflict of Interest: Providing applicable Relying Site Conflict of Interest management plans to the Reviewing IRB	☐ Relying Site Study Team ☐ Relying Site POC ☐ Lead Study Team* ☐ Other, specify:	
Study Team Training & Qualifications: Providing confirmation to the Reviewing IRB that relying site study teams have completed relevant training and are qualified to conduct the proposed research	☐ Relying Site Study Team ☐ Relying Site POC ☐ Lead Study Team* ☐ Other, specify:	
Local Considerations: Collecting local information related to Relying Institution's local and state laws; federalwide assurance applicability (e.g. "checking the box"); institutional requirements; unique cultural, language, geography, or socioeconomic factors; or standard of care	☐ Relying Site Study Team* ☐ Relying Site POC* ☐ Lead Study Team ☐ Other, specify:	
Local Considerations: Providing completed local context information to the Reviewing IRB throughout the study	☐ Relying Site Study Team ☐ Relying Site POC ☐ Lead Study Team* ☐ Other, specify:	
IRB Application – Studywide: Preparing and submitting the initial studywide application and studywide amendments to the Reviewing IRB	☐ Relying Site Study Team ☐ Relying Site POC ☐ Lead Study Team* ☐ Other, specify:	
IRB Application – Site-Specific: Preparing and submitting the site-specific applications to the Reviewing IRB	☐ Relying Site Study Team ☐ Relying Site POC ☐ Lead Study Team* ☐ Other, specify:	

Purpose of the form: This form should be used to document key communication roles/responsibilities for specific studies. Reviewing IRB/HRPPs may use this form to document general expectations of study teams and relying site IRB/HRPPs, or less formally to guide conversations among the Reviewing IRB, Relying Institutions, and Lead Study Team. The SMART IRB recommends this form be kept up to date with all key information throughout the life of a study.

AREA OF COMMUNICATION RESPONSIBILITY	RESPONSIBLE PARTY (*TYPICAL PARTY IDENTIFIED)	NOTES
IRB Determinations: Providing documentation of IRB determinations to relying site study teams	☐ Reviewing IRB POC ☐ Lead Study Team* ☐ Relying Site POC ☐ Other, specify:	
IRB-Approved Documents: Providing copies of IRB-approved materials to the lead study team	☐ Reviewing IRB POC* ☐ Relying Site POC ☐ Relying Site Study Team ☐ Other, specify:	
IRB-Approved Documents – Relying Sites: Providing copies of the most current versions of IRB-approved materials to relying site study teams	☐ Reviewing IRB POC ☐ Lead Study Team* ☐ Relying Site POC ☐ Other, specify:	
Consent Form Template: Providing the consent form template to relying site study teams	☐ Reviewing IRB POC ☐ Relying Site POC ☐ Lead Study Team* ☐ Other, specify:	
Consent Form Language: Incorporating site-specific language into consent form(s) and providing these consent form(s) to the Reviewing IRB	☐ Relying Site Study Team ☐ Relying Site POC ☐ Lead Study Team* ☐ Other, specify:	
Reviewing IRB Policies (Lead Study Team): Providing relevant Reviewing IRB policies to the Lead Study Team	☐ Reviewing IRB POC* ☐ Relying Site POC ☐ Relying Site Study Team ☐ Other, specify:	

Purpose of the form: This form should be used to document key communication roles/responsibilities for specific studies. Reviewing IRB/HRPPs may use this form to document general expectations of study teams and relying site IRB/HRPPs, or less formally to guide conversations among the Reviewing IRB, Relying Institutions, and Lead Study Team. The SMART IRB recommends this form be kept up to date with all key information throughout the life of a study.

AREA OF COMMUNICATION RESPONSIBILITY	RESPONSIBLE PARTY (*TYPICAL PARTY IDENTIFIED)	NOTES
Reviewing IRB Policies (Relying Sites): Providing relevant Reviewing IRB policies to Relying Site study teams	☐ Reviewing IRB POC ☐ Lead Study Team* ☐ Relying Site POC ☐ Other, specify:	
Continuing Review Information: Obtaining and collating studywide information for continuing review to the Reviewing IRB	☐ Relying Site Study Team* ☐ Relying Site POC ☐ Lead Study Team* ☐ Other, specify:	
Continuing Review Submission: Submitting continuing review progress report to the Reviewing IRB	☐ Relying Site Study Team ☐ Relying Site POC ☐ Lead Study Team* ☐ Other, specify:	
Reportable Events: Providing reportable events to the Reviewing IRB (e.g., unanticipated problems, noncompliance, significant subject complaints)	☐ Relying Site Study Team ☐ Relying Site POC ☐ Lead Study Team* ☐ Other, specify:	
Closure Reports: Providing the Reviewing IRB with required information when all research activities are completed at a Relying Site	☐ Relying Site Study Team ☐ Relying Site POC ☐ Lead Study Team* ☐ Other, specify:	