Purpose of Form: This document provides helpful hints for investigators and study teams whose institutions are considering relying, or have agreed to rely, on an external IRB for a study. Investigators and study teams must work with their institutions to implement external IRB review for their studies.

Relying on an External Single IRB: FAQs for Relying Site Study Teams

What is SMART IRB?

SMART IRB is an IRB reliance platform designed to harmonize and streamline the IRB review process for multisite studies while ensuring high protection for research participants. SMART IRB is not an IRB; it is a platform encompassing a common IRB reliance agreement (the SMART IRB Agreement) and a suite of web-based resources to facilitate single IRB arrangements. Through smartirb.org, institutions can join the SMART IRB Agreement and manage their profiles. Investigators, study team members, IRB/HRPP staff, and administrators can request, track, and document single IRB (sIRB) arrangements for their studies. SMART IRB also provides essential education and flexible tools and resources to support the implementation of single IRB oversight, with a team of ambassadors available to assist in onboarding and implementation. More information about SMART IRB is at https://smartirb.org.

What is the SMART IRB Agreement?

The SMART IRB Agreement is a national reliance agreement that allows institutions to avoid negotiating individual agreements per study or group of studies. An IRB reliance agreement is a formal document that outlines the terms and conditions under which one institution agrees to rely on the IRB of another institution for the review and oversight of research involving human subjects. A list of institutions that have joined SMART IRB by signing onto the agreement is at https://smartirb.org/participating- institutions/.

What does "reliance" mean in a single IRB study?

Reliance refers to an agreement by a participating site (a relying institution) to cede IRB oversight to an external IRB (the reviewing IRB) for the life of the study. The external IRB is responsible for the ethical and regulatory review of the study. This includes initial reviews, reviews of reportable events, modifications, and continuing reviews.

What is an external IRB?

An external IRB is an IRB that operates independently of your institution. An external IRB may be located at another institution or be an independent IRB (commercial IRB). When a single external IRB oversees a multi-site study, it may be referred to as a single IRB (sIRB), a central IRB (CIRB), reviewing IRB, or the IRB of record.

What does "approval" mean in a single IRB study?

Approval means that the external IRB has conducted a regulatory review of the study and determined that it meets all applicable ethical and regulatory requirements (e.g., 45 CFR 46, 21 CFR 56). The external IRB must also approve each participating site before it can begin study activities.

What is my IRB's role?

The external IRB is responsible for the regulatory review and approval of the study. Your local IRB or other institutional offices (e.g., HRPP) may still have to review areas outside of regulatory approval, such as conflict of interest, HIPAA compliance, and specific reportable events. As noted below, your institution continues to oversee these responsibilities, even when relying on an external IRB.

What is my institution's role?

Even if an institution relies on an external IRB, the institution is still responsible for ensuring the ethical conduct of research within its organization or involving its employees. Institution staff must still provide necessary support and information to the external IRB and ensure that the research meets all relevant ethical and regulatory standards. They are also responsible for any ancillary or institutional reviews that must be completed before the activation of a study at their site.

For institutions that opt to use it, the SMART IRB Agreement clearly defines a Relying Institution's roles and responsibilities. Many responsibilities of the Relying Institution may be delegated to the institution's IRB office as a component of its human research protection program (HRPP), although these remain the institution's responsibility. (From *INSTITUTION V. IRB RESPONSIBILITIES: A Guide for Reviewing IRBs and Relying Institutions Using the SMART IRB Agreement or Other IRB Reliance Agreements*)

Why do institutions rely on an external IRB?

Institutions may rely on an external IRB to meet mandates to use a single IRB (sIRB) for multi-site research studies. Traditionally, each institution involved in a multi-site study would have its own IRB review the study protocol separately, leading to duplication of efforts, potential inconsistencies in review decisions, and delays in study initiation. Single IRB review aims to streamline this process by designating one IRB to oversee the research at all participating sites (See Introduction to Single IRB Review and SMART IRB https://smartirb.org/study-teams/). An institution may also rely on external IRBs if they do not have their own IRB or determine they do not have sufficient resources to oversee the study or that another IRB has better expertise.

How do I know whether an external IRB can review my study?

Check with the office at your institution that administers human subjects research. Most federally funded multi-site studies require sIRB review, which an external IRB often provides. Some sponsors may also require sIRB review of their studies.

Do I need authorization from my institution to use an external IRB?

Because institutions need to identify the research that falls under their purview, even if an external IRB oversees a study, they usually require researchers to at least alert their institution about a study they wish to have reviewed by an external IRB. Institutions often require institutional authorization before an external IRB can review the study. The mechanism for this authorization varies by institution. Some, for example, require researchers to provide a brief application in the local electronic submission system. Study teams should check their institution's requirements for using an external IRB.

Many institutions expect study teams to provide a protocol, template consent form, and list of sites and personnel engaged in the study, so that the institution can determine whether the study qualifies for sIRB review and/or decide which institution should serve as the Reviewing IRB. Contact the office at your institution responsible for administering human research (i.e., human research protection program or "IRB office") to learn more about the processes and procedures your institution requires for using an external IRB.

Does my institution need to execute an agreement to rely on an external IRB?

Generally, institutions must execute a written reliance agreement that allows an institution to rely on an external IRB. The agreement spells out the responsibilities of the institution providing IRB review and of the institution relying on the external IRB. The SMART IRB Agreement is a common reliance agreement that allows institutions to avoid having to negotiate individual agreements per study or group of studies (see below).

How do I request that my institution rely on an external IRB for a study?

The mechanism to request reliance varies by institution and by the reliance agreement under which IRB review will be ceded. Check with the office at your institution responsible for administering human research.

How do I submit my documents to the external IRB for review?

You will need to find out the arrangements in place for submitting to and communicating with the designated Reviewing IRB. In some cases, a lead study team, coordinating center, or sponsor will submit documents to the external IRB and provide you with documentation of the external IRB's approval for your site. Some institutions do not allow sponsors to submit applications to the external IRB on behalf of the study team. In other cases, the study team is directly responsible for

submitting documents to the external IRB.

If an external IRB reviews the study, how do I know when to start the research at my site?

Obtaining IRB approval is one of often many approvals or signoffs that study teams must have in place to activate a study. When using an external IRB, you must still meet the same institutional requirements for study activation, including reviews and approvals by other institutional committees (e.g., biosafety, radiation safety, pharmacy, conflict of interest, billing compliance), executing any clinical trial agreements, etc.

You will need to ensure you have documentation that your site has ceded review to the external sIRB, as well as documentation that the external sIRB's approval for the study covers your site. If the external IRB has approved the study before your site is ready to join, your site will need to be specifically reviewed and approved as a new site. This is usually accomplished via an amendment to the existing study. Activities at your site involving human subjects cannot occur until the external IRB approves your site's participation in the research and you have obtained all required institutional signoffs and/or approvals.

What if my institution does not have an IRB?

If your institution does not have an IRB, you may still rely on an external IRB. You will need to work with the office that administers human research studies at your institution to ensure a reliance agreement is in place and that the institutional responsibilities are met. If your institution does not have such an office, please refer to the following FAQ.

Must an institution establish its own IRB?

No. Although institutions engaged in research involving human subjects will usually have their own IRBs to oversee research conducted within the institution or by the staff of the institution, FDA regulations permit an institution without an IRB to arrange for an "outside" IRB to be responsible for initial and continuing review of studies conducted at the non-IRB institution. Such arrangements should be documented in writing. Individuals conducting research in a non-institutional setting often use established IRBs (independent or institutional) rather than form their own IRBs. See FDA Information Sheet IRB FAQs Question #6.

What if my institution does not have an office that administers human research studies?

If your institution does not have a human research protection program (HRPP) or a designated office for research oversight, identify the individual authorized to make decisions about human subjects research—this may be an institutional official, department head, or other organizational leader—and consult with them to determine if such a process exists or is needed.