IRB Review When NIH is the Reviewing IRB for Multi-site Research

The NIH IRB will serve as the Reviewing IRB in domestic multi-site studies when the use of a single IRB is mandated by either the NIH sIRB policy and/or the Cooperative Research single IRB mandate in the revised Common Rule. A key determinant for the mandates is study funding, specifically whether it is from the NIH or a different federal source. When serving as the Reviewing IRB for multi-site research, NIH enters into a Reliance Agreement with Participating Sites (pSites) who will rely on the NIH for IRB oversight. A Reliance (Authorization) Agreement provides a mechanism to delegate IRB review and documents the authorities, roles, and responsibilities of the Reviewing IRB and participating institutions. The agreement may apply to a single study or to certain categories of studies. The NIH typically uses the Streamlined, Multisite, Accelerated Resources for Trials (SMART) Agreement v2.0 to document reliance arrangements. Otherwise, for non-SMART signatories, the NIH's Reliance Agreement Template is used. The SMART Agreement was developed under an award from the NIH National Center for Advancing Translational Sciences (NCATS) to streamline the IRB review process and assist investigators and IRBs in initiating multisite research. When using the SMART Agreement, the reliance is confirmed either using the SMART online platform or a SMART Letter of Authorization (LoA) signed by the Reviewing IRB and pSITE.

Role of the IRBO (via Reliance Specialist and/or IRBO Analyst) **Prior to New Site Being Added**

- Review the NIH protocol and ensure it is clearly written as a multi-site (MS) protocol.
- Establish a Reliance Agreement with each pSite before they are added to the protocol.
- Review Local Context information and pSite documents (protocol addendum, site specific consents etc.).
- For pSites, confirm that institutional requirements of the Relying Institution have been met.

Review of the NIH Protocol

- An MS protocol reviewed by the NIH IRB is study-wide and includes the NIH's role in the study; this is called the main or core site. pSites only get reviewed and approved after the core/main site is approved.
- Study will be identified as MS in PROTECT, so branching appears and sites can be created. Note, this can be done at the time of initial review or later via submission of a modification.
- The protocol will be more generic than when NIH is a single site; it will not be as NIH-focused since it applies to all sites, as applicable. (e.g., Sites will enroll potential Non-English-speaking subjects per institutional policies.)
- Determinations for vulnerable populations and/or waivers of consent are determined at the core/main site level. For example, if only one non-NIH site is enrolling children, a subpart D, Additional Protections for Children Involved as Subjects in Research, determination will be made. These determinations are not made at pSITE level.
- The protocol should include how the study will be managed across multiple sites and, if applicable, include information about any international sites involved even though these typically do not rely on the NIH IRB for oversight.
- MS studies normally include model documents (e.g., model consent forms, model recruitment materials) which are reviewed and approved by the NIH IRB before being used by the pSITEs to create site-specific documents.
- Planned enrollment may be described differently (e.g., cumulative enrollment across all sites or a designated enrollment ceiling per site).

Addition of Participating Sites to the NIH Protocol

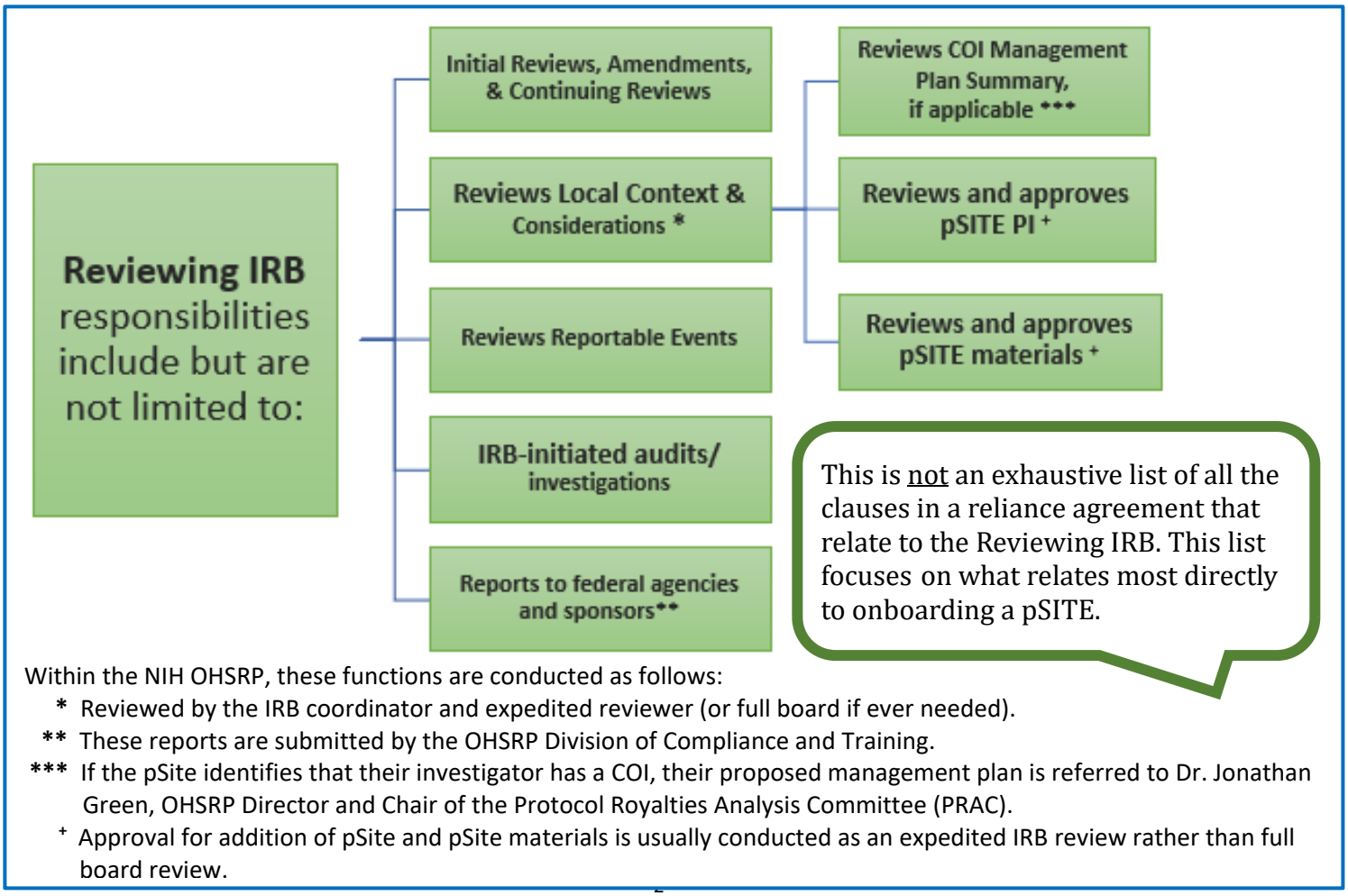
- When pSites are added, the review and approval of all study related materials (e.g., site specific addendum, site - specific consents etc.) is usually conducted under expedited review by Designated Reviewers in the NIH IRBO and not by the convened IRB.
- Information about specific pSites is found under the documents tab in PROTECT in the section titled Site Related Documents. The reliance agreement NIH has with the pSite for specific protocols is found in the Institutional Profiles tab by clicking on the pencil and paper icon () to the left of the name of the pSite.
- The IRB reviews only one Continuing Review (CR) submission that includes CR data from both the NIH site and all pSITEs. pSITEs do not submit separate CR applications.

IRB Member Responsibilities When NIH is the Reviewing IRB for Multi-Site Research (~ 150 active studies with pSITEs)

- Perform review of IRs, CRs, modifications and submitted study-wide and pSite documents (model consent form, protocol, recruitment materials, site consents, etc.)

- Review Reportable New Information (RNI) forms submitted by the pSite that have been reviewed by OHSRP leadership in their weekly RNI review and subsequently referred (e.g., possible unanticipated problems, possible serious or continuing noncompliance, or possible new information that may impact subject's decision to enroll or remain on study.)
    - For an event that is a potential unanticipated problem, or possible new information that may impact a subject's decision to enroll or remain on the study, review is conducted by the NIH IRB.
    - For an event that is potential serious and/or continuing noncompliance, review is conducted by the Research Compliance Review Committee (RCRC).
    - In its review of RNIs, the NIH IRB and the RCRC have the authority to:
        - Request additional information;
        - Require modification of the protocol or consent(s);
        - Require subject notification;
        - Increase the type and/or frequency of safety monitoring;
        - Change the review period of the protocol;
        - Implement measures to protect the rights, safety, and welfare of subjects;
        - Suspend or terminate IRB approval (e.g., research associated with unexpected serious subject harm) or suspend new enrollment.
- When the NIH is the Reviewing IRB, and the NIH IRB is informed of a financial conflict of interest for an investigator from the pSite, the IRBO analyst refers the information and the summary management plan (if one has been provided) to Dr. Jonathan Green, Chair of the Protocol Royalties Analysis Committee (via Chris Witwer who coordinates this process with Dr. Green), for initial review to determine if additional measures are needed to protect the rights and welfare of subjects participating on the research consistent with the terms of the reliance agreement.

Reliance: Reviewing IRB Responsibilities



Within the NIH OHSRP, these functions are conducted as follows:

* Reviewed by the IRB coordinator and expedited reviewer (or full board if ever needed).

** These reports are submitted by the OHSRP Division of Compliance and Training.

*** If the pSite identifies that their investigator has a COI, their proposed management plan is referred to Dr. Jonathan Green, OHSRP Director and Chair of the Protocol Royalties Analysis Committee (PRAC).

\+ Approval for addition of pSite and pSite materials is usually conducted as an expedited IRB review rather than full board review.

For additional guidance, please contact the NIH Reliance and Single IRB Team at NIH-Reliance-sIRB@nih.gov.