USING THE ADVARRA IRB AT THE NIH

NIH OHSRP/ IRBO PRESENTATION: SEPT 22, 2020

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Presentation Overview

Part 1: NIH OHSRP/ IRBO will outline:

- Circumstances when an NIH Study Team may need to use the Advarra IRB
- NIH requirements before submitting to the Advarra IRB
  - Investigator Responsibilities
  - Institutional and study-specific Local Context
- On-going responsibilities following approval by the Advarra IRB

Part 2: Advarra will:

- Introduce the team working with the NIH
- Explain their submission and review process
- Answer questions from prospective and current NIH users

Using the Advarra IRB: Background and Context

- When Advarra reviews for the NIH, it is typically serving as the *Reviewing IRB* in a multi-site study
  - This is an example of single IRB (sIRB) Review i.e., where an IRB reviews and approves research for all Participating Sites in a multi-site study instead of each site obtaining individual approvals
  - Approach has become more commonplace given sIRB mandates i.e., NIH sIRB Policy and the Cooperative Research requirement in the revised Common Rule
  - Participating Sites cede IRB review via a "Reliance Agreement"*
- NIH Study Teams can use the Advarra IRB as there is a program-wide Reliance Agreement in place
  - Only the IRB review is being ceded
  - NIH retains responsibility for adhering to regulations, local requirements, and protecting participants

*For additional guidance please review the OHSRP Education Sessions from July and August 2020

Using the Advarra IRB: When can a NIH Investigator use it?

- Advarra IRB review is appropriate when an **NIH Study Team** is undertaking non-exempt human subjects research (HSR) in two situations:
  - ***NIH Study Team plans to serve as a Participating Site***
    An external Sponsor has identified the Advarra IRB and the NIH investigator wishes to join a new/existing multi-site study; **or**
  - ***NIH Study Team plans to serve as a Sponsor and Participating Site***
    An NIH investigator initiates a multi-site study, and the NIH IRB cannot serve as the single IRB
- In addition, the NIH Study Team needs to:
  - Complete a *NIH Institutional Review*; and
  - Address how IRB fees will be covered

Before submitting to the Advarra IRB: IRBO Pre-Review Requirements

Before Submitting to the Advarra IRB: NIH IRBO Requirements

IRBO Consult *(Optional)*	• Establish if NIH is engaged in HSR and needs IRB oversight • Establish which sIRB mandates apply, if any • Discuss Study Planning i.e. study resources, communication plan etc. • Advise teams to review Advarra IRB policies and procedures in their "IRB Handbook" • Advise study teams to address fee issues
Reliance Agreement	• Apply for the Reliance Agreement for tracking purposes and to confirm coverage
NIH Institutional Review	• IRBO will conduct a pre-review of the protocol and NIH site-specific documents to ensure all NIH Institutional requirements have been met • Undertaken in the iRIS system • This is NOT equivalent an official IRB review • Issues "**NIH Institutional Review Memo**" confirming all NIH requirements are met

NIH Institutional Review

NIH Study Team

(Participating Site Study Team)

Submits into iRIS as Initial Review:

- Sponsor/Core Protocol
- Model Consent(s)/Assent(s)
- NIH Protocol Addendum
- NIH Consent(s)/Assent(s)
- Study Personnel Page
- Ancillary Reviews e.g., DEC, RSC, Scientific Review, IBC, PRIA etc.
- Initial Review IRB Approval Letter*

NIH IRBO (Relying Institution)

Conducts Institutional Review

- Ensures NIH Protocol Addendum meets NIH requirements
- Confirms NIH required language in consent documents
- Verifies Ancillary Reviews
- Checks HRPP Training Records

Once completed, IRBO issues via iRIS:

NIH Institutional Review Memo

PLUS a Stipulation

- Confirms that submission meets NIH institutional requirements
- Serves as "green light" to NIH Study Team and should be submitted to the Advarra IRB
- Advarra IRB will not review the study without the NIH Institutional Review Memo

* Optional

Investigator Responsibilities when Submitting to Advarra IRB

Investigator Responsibilities When NIH is a Participating Site

- When the NIH is a ***Participating Site*** in an industry-sponsored, industry-initiated (external sponsor) multi-site study, the NIH site will be added to the study after the protocol has received initial approval via an Amendment/Modification

- The Amendment/ Modification takes place *after* the **NIH Institutional Review** has been completed

- NIH Study Teams need to submit an *"Investigator Application"* to Advarra via their electronic system (CIRBI) identifying the NIH as a Participating Site (Investigational/Research Location). The submission should include appropriate NIH site-specific documents i.e.,
  - NIH site-specific Protocol Addendum
  - NIH site Consent and/or Assent document(s) i.e., Model Advarra/ Sponsor Consent/Assent with NIH required language inserted
  - NIH Institutional Review Memo

Investigator Responsibilities When Initiating New Research as a Sponsor and Participating Site

- When the NIH is serving as the **Sponsor/ Lead Site/ CRO** for a multi-site study, the NIH site needs to first obtain initial approval for the protocol before Participating Sites can be added via subsequent Amendments/Modifications
- After IRBO has conducted its **NIH Institutional Review**, the NIH Study Team will need to submit a *"Protocol Application"* to Advarra via CIRBI and submit appropriate study documents which will include:
  - Master/ Core protocol
  - Model consent document(s)
  - Model recruitment material(s)
  - NIH Conflict of Interest certification
  - NIH Institutional Review Memo

  Model documents allow for customization by the Participating Sites
- After Initial Review, NIH and other institutions can be added as Participating Sites to the study.
- NIH Study Team should complete Advarra *"Investigator Application"* i.e., as a (Investigational/Research Location)

Investigator Responsibilities Regarding Consent

- The NIH Study Team will be responsible for drafting the consent and/or assent document(s) to be used at the NIH site and the consent template language will depend on the role of NIH:
  - If the NIH PI is **initiating** the research and acting as the Sponsor/CRO, then a "model" consent document will need to be developed and approved by Advarra IRB first
  - If the NIH is a **Participating Site** and enrolling subjects, an NIH site-specific consent must be developed based on the Sponsor's model consent template and the NIH investigator is responsible for inserting the NIH required language into that template as well as making any appropriate deletions
- In both instances, the consent documents undergo NIH institutional review to verify that appropriate NIH language is inserted into the model and/or NIH site-specific consents
- For additional guidance on how to develop model documents refer to the Advarra model consent template as well as the NIH model consent template on the IRBO website
- For guidance on customizing the model consents to the NIH context, refer to the OHSRP Education Session presentation from August 4th and a *soon-to-be-available* consent template on the IRBO website

Institutional and Study-Specific Local Context

NIH Institutional and Study-Specific Local Context

- The Advarra IRB needs to understand the NIH's specific policies, as well as local norms, special requirements, culture, etc. in order to conduct its review. This is called "Local Context".
- Comprised of information specific to NIH as the ***Relying Institution*** AND ***study-specific*** information relating to how the protocol will be implemented at the NIH site
- Identifying pertinent local context information is a collaborative effort involving the NIH Study Team and NIH IRBO
- *NIH Institutional local context* has been provided to Advarra as part of reliance negotiations and any additional information will be provided via the Institutional Review Memo
- *Study-specific local context* is provided by the NIH PI to Advarra IRB via protocol documents e.g., site-specific consents and NIH protocol addendums
- NIH IRBO ultimately signs off on information provided
- Local context is an initial and on-going consideration for all parties

Examples of Institutional and Study-Specific Local Context

Institutional local context includes:

- NIH is a Federal Preserve – State laws do not apply
- NIH is subject to the Privacy Act of 1974, not HIPAA
- NIH has no ER and the closest is at Suburban Hospital

Study-specific local context includes:

- Specific populations being enrolled (e.g. adults lacking capacity to give informed consent; employees and students)
- Local expertise, special equipment, policies etc.

I’m IRB approved, what’s next?
The NIH Post-Review and on-going requirements

Approval and Activation of NIH as Participating Site

- After you receive your IRB approval from Advarra IRB you will need to prepare submission to activate the NIH as a site
- The submission includes
  - IRB approval letter
  - IRB approved Protocol and NIH Protocol Addendum
  - IRB approved consent(s)/assent(s)
    - Clean version of documents unless Advarra has made changes
- IRBO reviews the documents to ensure remain consistent with NIH institutional requirements
- IRBO activates the NIH Site in iRIS e.g., “Open – Recruiting”
- If at the NIH Clinical Center, documents forwarded to Office of Protocol Services (OPS) for administrative processing

Ongoing NIH Participating Site Study Team Responsibilities

- Comply with Advarra IRB requirements
  - Reporting requirements
  - Submitting Amendments and Continuing Reviews via their electronic system
- NIH only cedes IRB review. This means that other NIH requirements still apply to your research and the NIH Study Team retains responsibilities for managing all non-IRB requirements at the NIH for the duration of the study
  - Reporting events to OHSRP per Policy 801 via iRIS
  - Maintaining a *Shadow Protocol*
    - Currently approved protocol, protocol addendum, consent and assent documents must be in iRIS
    - Each study lifecycle action must be submitted into iRIS *after* Advarra has reviewed and approved it e.g., amendment, continuing review, progress report forms etc.
      - An exception to this approach would be where a new consent form has been developed. In those cases, reach out to IRBO as we may want to carry out a mini-institutional review before it's submitted to Advarra
    - The Advarra IRB determination/approval letter for the action must always be included
      - No batch submissions please
    - KSP changes need to be submitted to IRBO
      - Advarra IRB reviews and approves the Site PI
      - It will look at sub-investigators but including them is not an Advarra IRB requirement
      - In all cases, submit to the NIH IRB as an amendment when there are KSP changes

Top Tips for NIH PIs

- NIH PI is Responsible for:
  - Confirming budget or payment for IRB services
  - Following applicable NIH institutional policies and becoming familiar with the Advarra IRB's policies i.e., "Advarra IRB Handbook"
  - Using the appropriate consent template
  - Appointing a study staff member to be the Point of Contact for Advarra IRB
  - Providing Local Context - institutional and study-specific

Top Tips for NIH PIs: Conflict of Interest

- NIH PI must always comply with **NIH Conflict of Interest requirements**, specifically:
  - Covered protocols must be submitted for DEC clearance and the resulting outcome letter submitted for the NIH Institutional Review and later provided to Advarra
  - For Not Covered protocols, PI's need to complete the *"Documentation of NIH Completion of Conflict of Interest Requirements"* and provide it to the Advarra IRB, not the Personal Financial Holdings (PFH) form
  - When completing the Advarra IRB study application via their electronic system (CIRBI), answer "No" to conflict of interest questions

Points of Contact

NIH IRBO

- Contact Shirley Rojas if you want to use Advarra IRB
- Contact the IRBO Reliance and sIRB Team (Jeffrey Rollins and Shirley Rojas) for any questions or concerns relating to the NIH Institutional Review, local context issues etc.
- NIH IRB Office of Operations

Advarra IRB

- Contact Advarra IRB's Points of Contact for:
  - Clarification on Advarra IRB's policies and procedures
  - Help with individual submissions
  - Questions about an IRB determination

Advarra IRB Team

- Kathleen (Rankin) Dietrich (Kathleen.Dietrich@advarra.com)

  Director, Business Development

- Betsy Casillo (Betsy.Casillo@advarra.com)

  Associate Director of Client Success, Institutional Services

- Jessica Reis (Jessica.Reis@advarra.com)

  Senior Client Services Coordinator

We are happy to answer your questions but please hold off until after the Advarra IRB presentation.