Overview: NIH Multi-Site Protocol Processes

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NIH Office of Intramural Research
Office of Human Subjects Research Protections

Fundamentals of single IRB review (sIRB)

Previous OHSRP Education Sessions

- What You Need to Know About Single IRB Review: Principles and Practice (Part 1) – July 7, 2020
- What You Need to Know About Single IRB Review: Principles and Practice (Part 2) – August 4, 2020

Fundamentals of single IRB review (sIRB)

In OHSRP Education presentations, the following topics were covered:

- Defined multi-site research
- Explained sIRB mandates
- Provided an overview of the sIRB review model
- Role and responsibilities of key players
- Development of protocol and consent documents
- Local Context – institutional vs study specific

eIRB Systems

With the upcoming eIRB transition from iRIS to the Huron eIRB system, PROTECT, this presentation will not focus on specific iRIS or Huron eIRB processes.

Focus of this presentation will be on multi-site workflows when:

- NIH is the reviewing IRB i.e., single IRB (sIRB) for a multi-site study
- NIH is a participating site in a multi-site study reviewed by an external IRB serving as the sIRB.

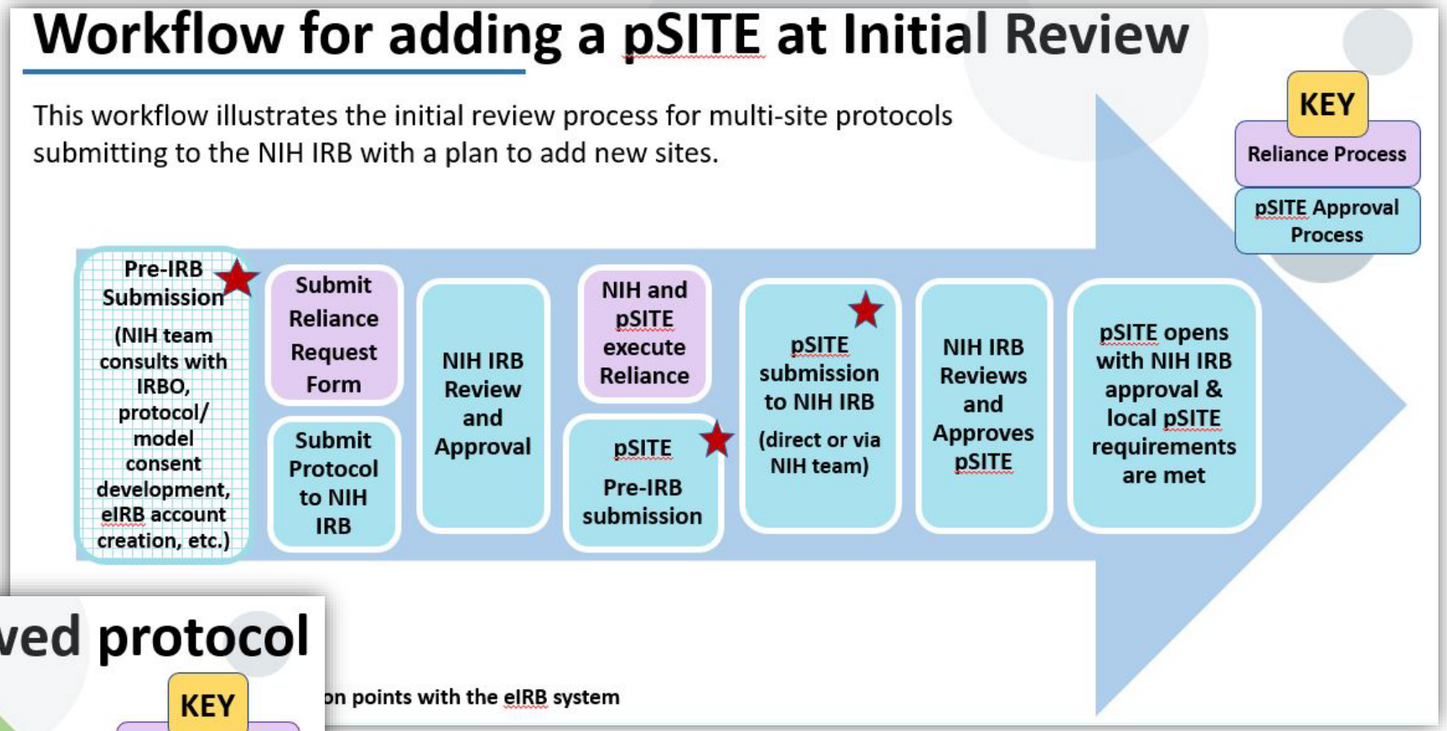
Key Terms

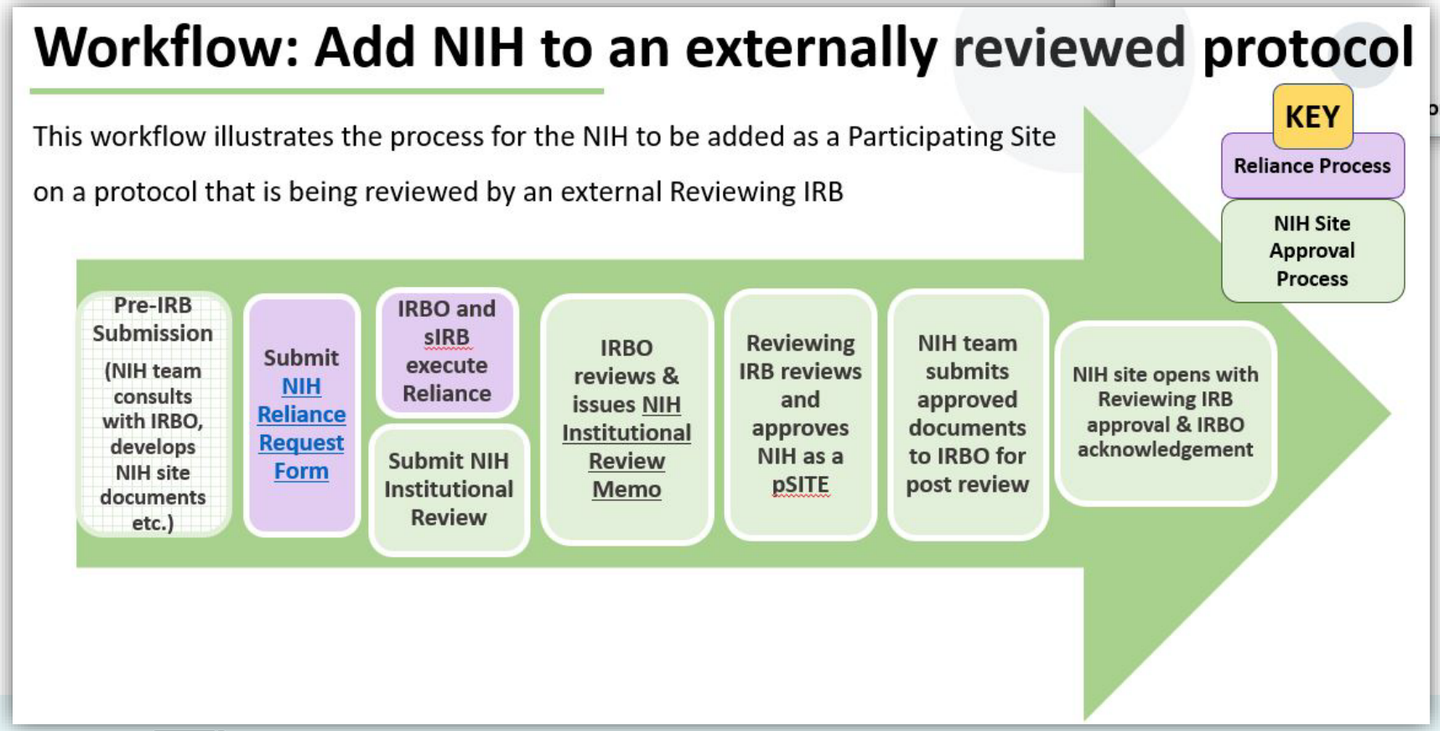
TERM	DEFINITION
Core Site	Term used to describe the lead study team**.** The core site has ultimate responsibility for the conduct and integrity of the research. It usually serves as the main study point of contact for the Reviewing IRB and serves as the conduit for communication to and from the Participating Sites. The core site can also be referred to as the 'Lead Site' or 'Main Site.
Participating Site	A research site involved in multi-site research that relies on the Reviewing IRB to provide oversight for the site. The Participating Site can also be referred to as the 'pSITE', 'local site', or 'relying site'.
Relying Institution	An institution participating in multi-site research that cedes IRB review to the Reviewing IRB for human subjects research consistent with the terms of a reliance agreement. The Relying Institution may involve more then one participating study site, e.g., one healthcare system may have multiple hospitals and/or clinics.
Reviewing IRB	The Reviewing IRB will be responsible for reviewing human subjects research and determining that the research meets the required criteria for approval under the regulatory requirements at 45 CFR 46 and, as applicable, 21 CFR 50; 312; 812. When reviewing for a multi-site study, the Reviewing IRB can also be referred to as the 'single IRB (sIRB),' 'IRB of record' or 'Central IRB.'

NIH can function as one or a combination of these designations.

Session Objectives

PART 1: Workflow to add a Participating Site (pSITE) when NIH is the CORE Study Team and Reviewing IRB

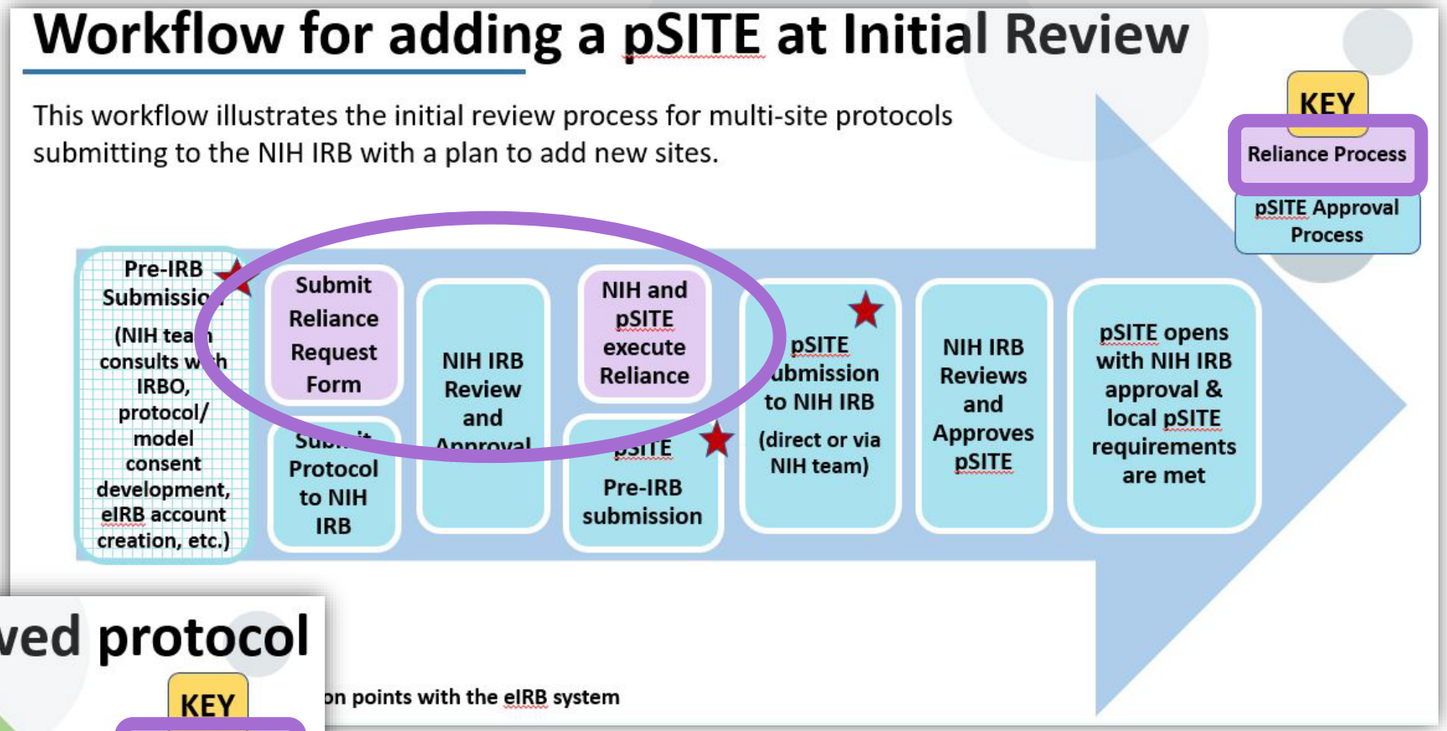


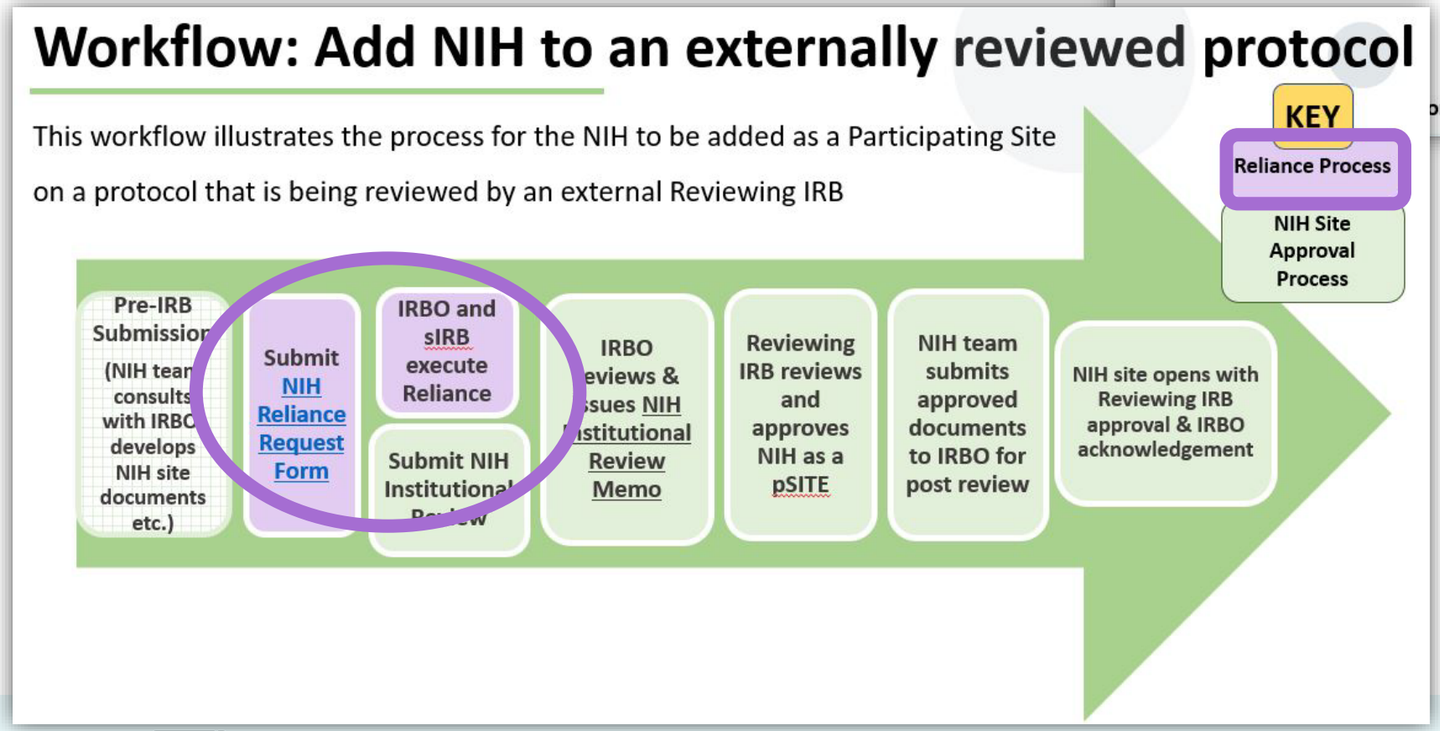


PART 2: Workflow for adding NIH as a site on a protocol that is being reviewed by an external Reviewing IRB

Session Objectives

PART 1: Workflow to add a Participating Site (pSITE) when NIH is the CORE Study Team and Reviewing IRB





PART 2: Workflow for adding NIH as a site on a protocol that is being reviewed by an external Reviewing IRB

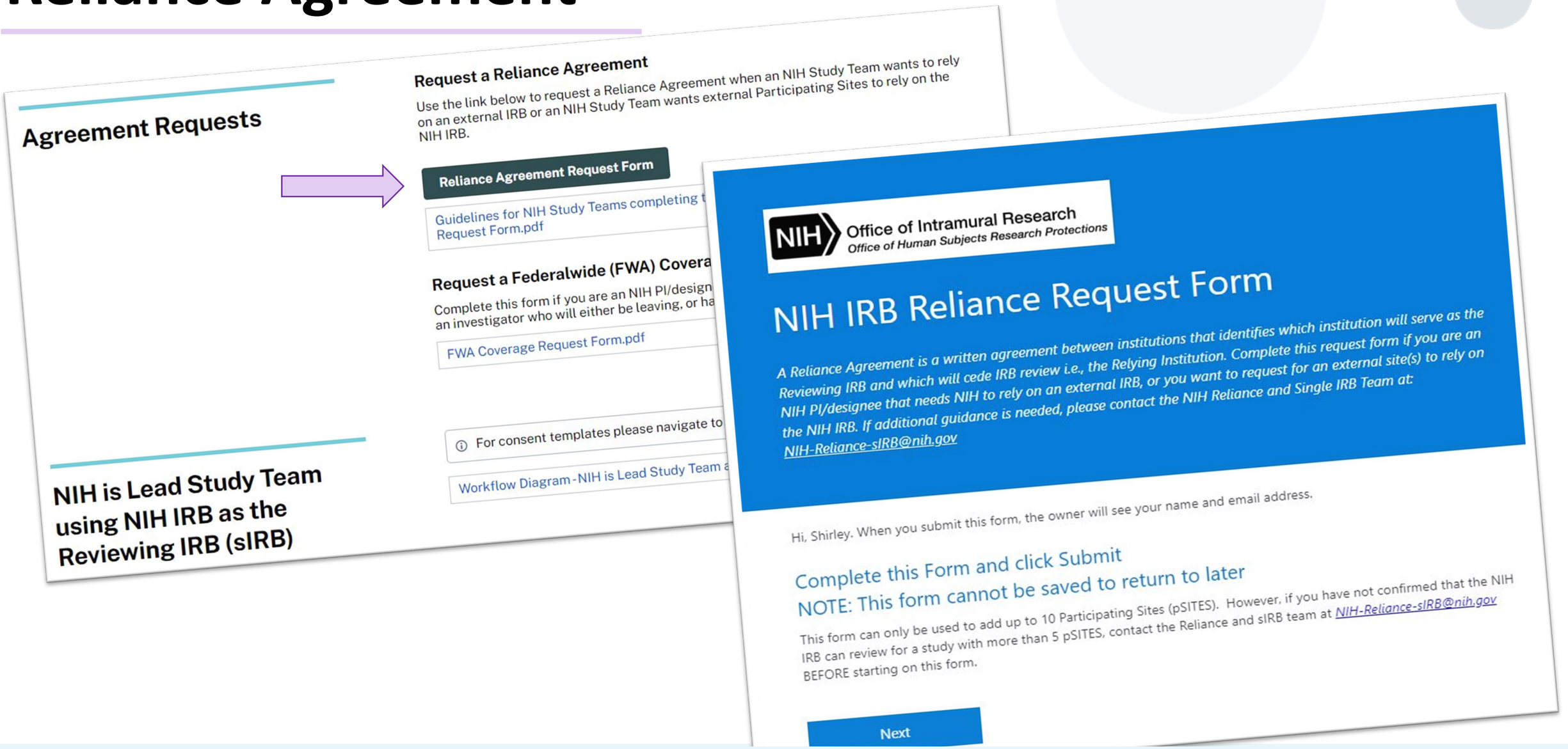
Reliance Agreement

- Agreement between two FWA-holding institutions that documents the use of the Reviewing IRB by the Relying Institution
- Delineates the institutions responsibilities for sIRB research review
- Content is generally consistent, but scope can vary
    - Programwide agreements with WCG IRB, Advarra, NCI CIRB
    - Master Agreement with SMART IRB
    - Regular NIH template for a single protocol

Reliance Agreement

- When **NIH is the Reviewing IRB**
  - The reliance request form should be submitted in parallel to the initial review or, for existing protocols, before the pSITE is added to the protocol
  - The reliance needs to be fully executed before any pSITE is added to the NIH protocol
- If NIH is **relying on external Reviewing IRB**
  - The reliance request form submission depends on the processes of the external IRB
    - If it's **WCG** or **Advarra IRB**, submit when the protocol has been approved
    - For others, submit when the protocol is submitted for initial review or has been approved by the external IRB
  - Exceptions: NIH is the lead site or the external IRB approves pSITES at initial review
  - In general, the Reliance Agreement needs to be executed BEFORE the NIH site can be added to an externally reviewed protocol

Reliance Agreement



SMART IRB Reliance Agreement

- SMART IRB is a “Master” reliance agreement not an IRB
- Signed by 993 institutions and counting
- No additional agreements are required to put the reliance in place
- Reliance arrangements still need to be documented on a study-by-study basis
    1. SMART IRB online reliance platform
    2. SMART Letter of Authorization
- Two versions exist, NIH has signed version 2
- NIH is only permitted to rely on, or be relied upon by another **v2 signatory**
- SMART SOPs are followed and, where applicable, NIH IRB SOPs
- NIH study teams are advised by IRBO if/ when the online platform is needed

SMART IRB Reliance Agreement

SMART resources: https://smartirb.org/

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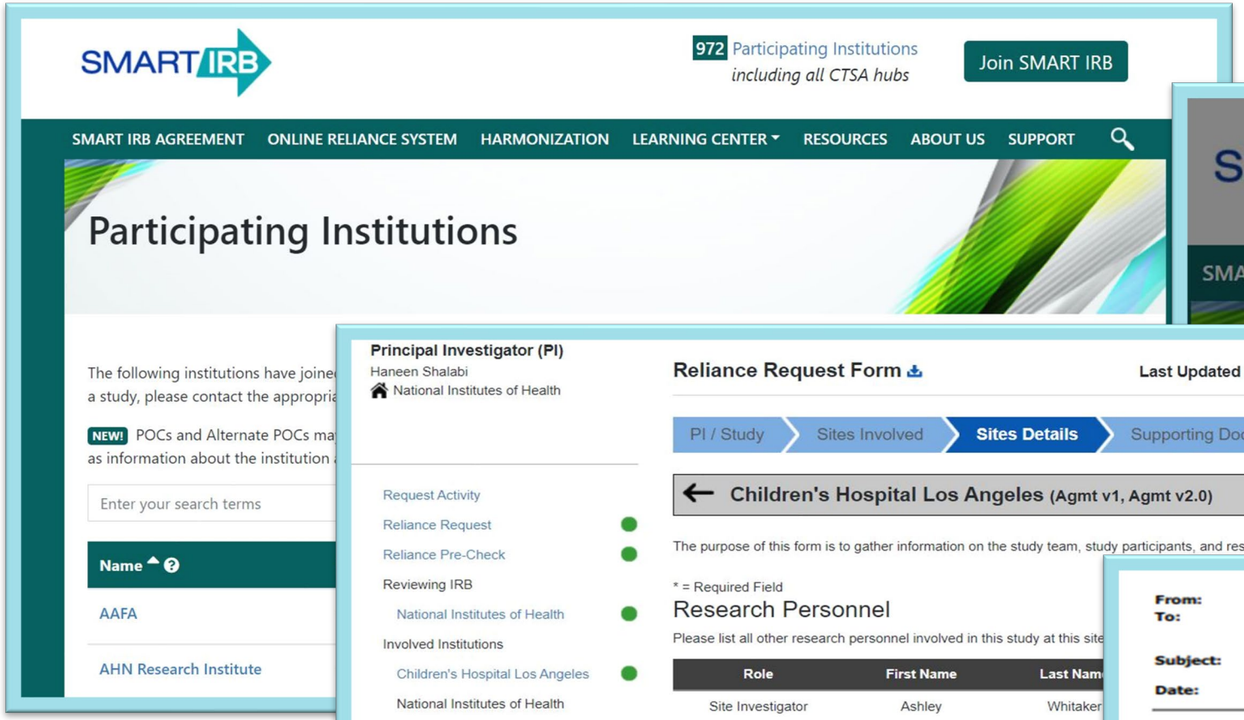

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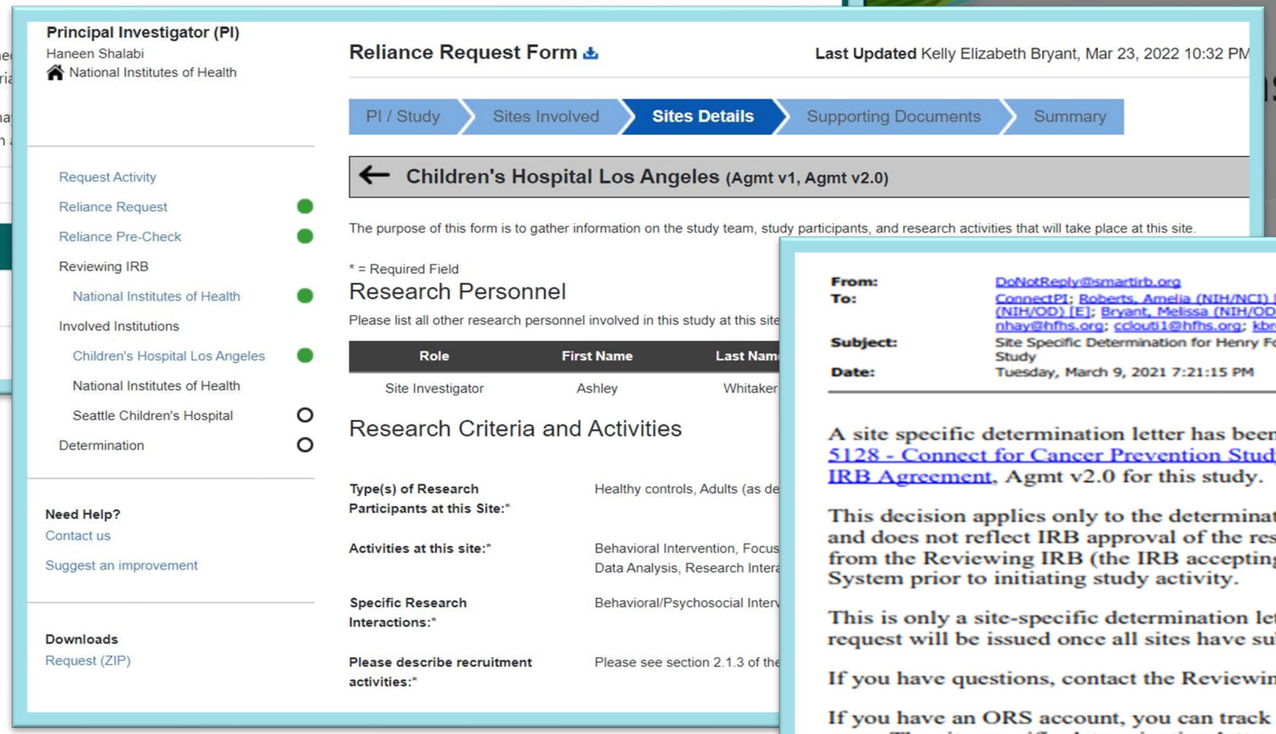

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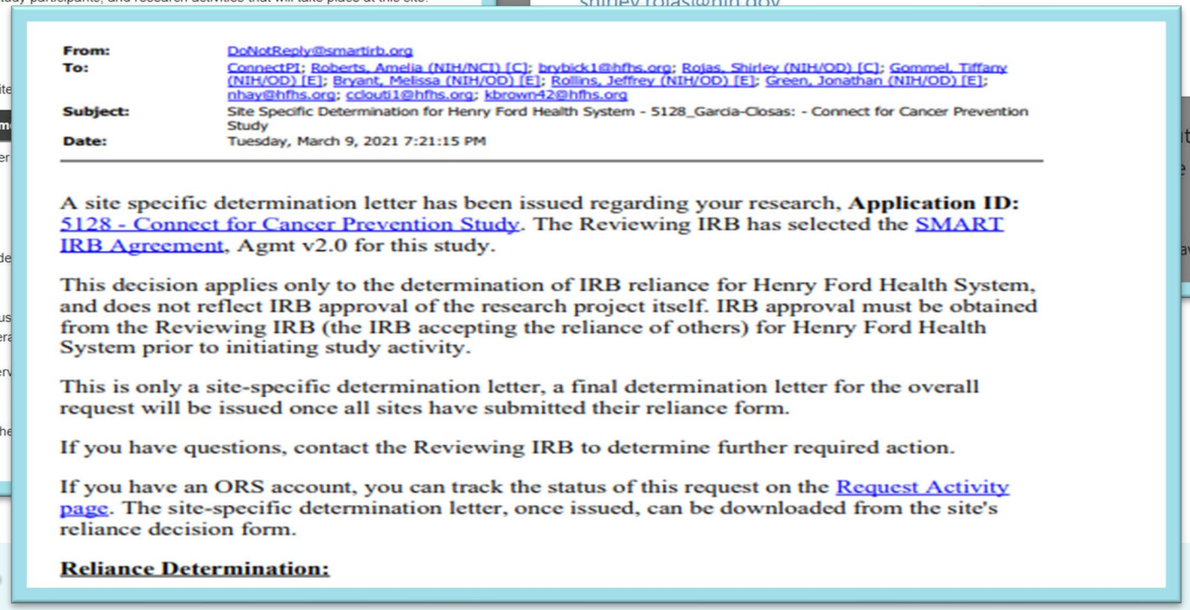


Reliance: Reviewing IRB responsibilities

The **IRB** responsibilities include but are not limited to:

- Initial Reviews, Amendments, & Continuing Reviews
- Reviews Local Context & Considerations
  - Reviews Conflicts of Interest Management Plan Summary, if applicable
  - Reviews and approves pSITE PI
  - Reviews and approves pSITE materials
- Reviews Reportable Events
- IRB-initiated audits/ investigations
- Reports to federal agencies and sponsors

This slide is <u>not</u> an exhaustive list of all the clauses in a reliance agreement that relate to the Reviewing IRB. They are focused on what relates most directly to onboarding a pSITE.

Reliance: pSITE responsibilities

pSITE responsibilities include but are not limited to:

- Providing pSITE-specific protocol and consent documents, recruitment materials etc.
  - Communicates findings from ancillary reviews that impact risk/ benefit
  - Provides the Reviewing IRB with information about local study conduct that differs from approved protocol
- Notifying Reviewing IRB of reportable events according to NIH IRB policies
- **Providing Local Context**
  State/ local laws and regulations, institutional requirements, local factors
  - Reviews and approves study personnel
  - Provides Conflicts of Interest management plan summary, if applicable
- **Providing Documentation/ Assurances**
  pSITE study team appropriate qualifications & training, local HRPP confirms local context accurate

This slide is <u>not</u> an exhaustive list of all the clauses in a reliance agreement that relate to the pSITE. They focus on what relates most directly to onboarding a pSITE.

PART 1:

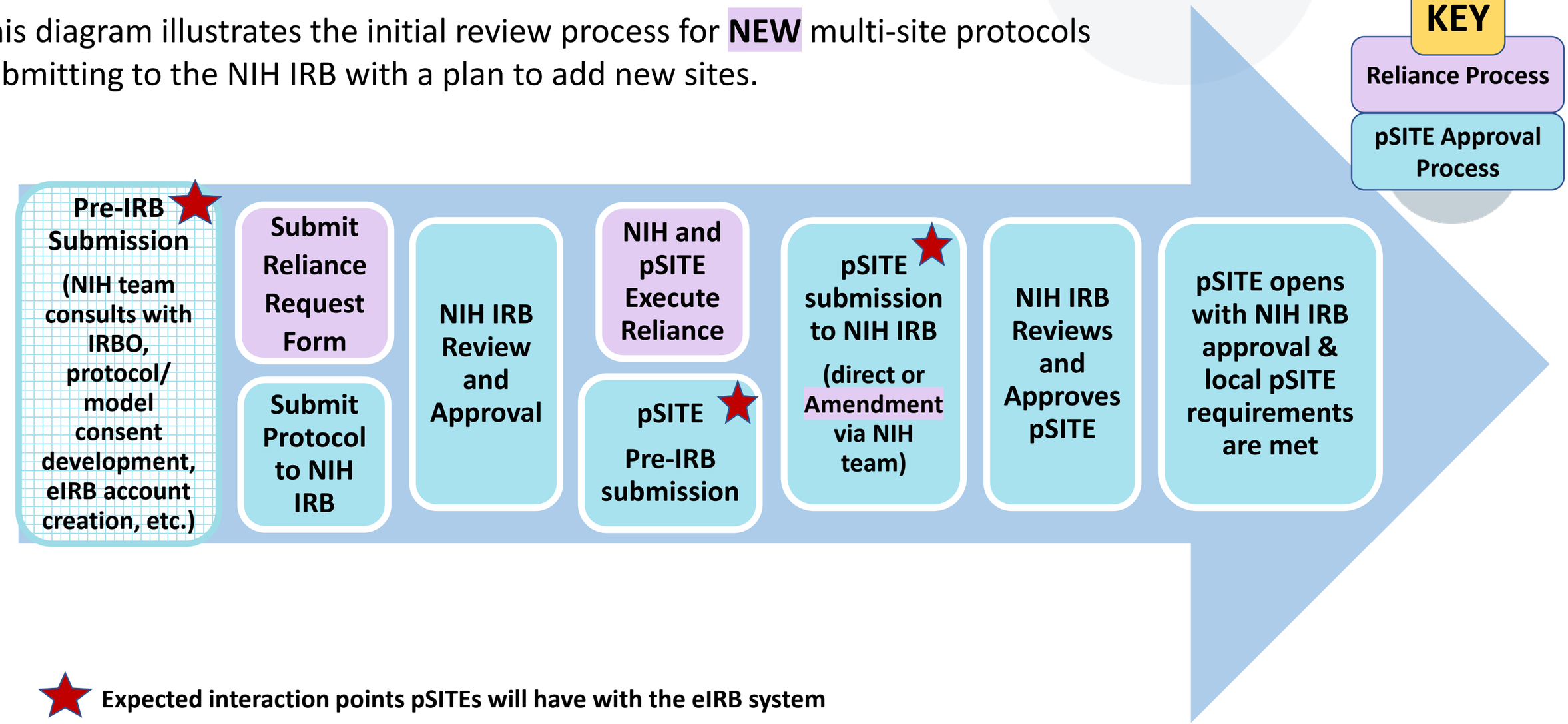
Workflow to add a Participating Site when NIH is the CORE Study Team and Reviewing IRB

Part 1: Session Objectives

- Reliance Agreement process
- Adding a Participating Site (pSITE) to an NIH protocol
- Review NIH study team (CORE) role and responsibilities
- Review pSITE study team role and responsibilities

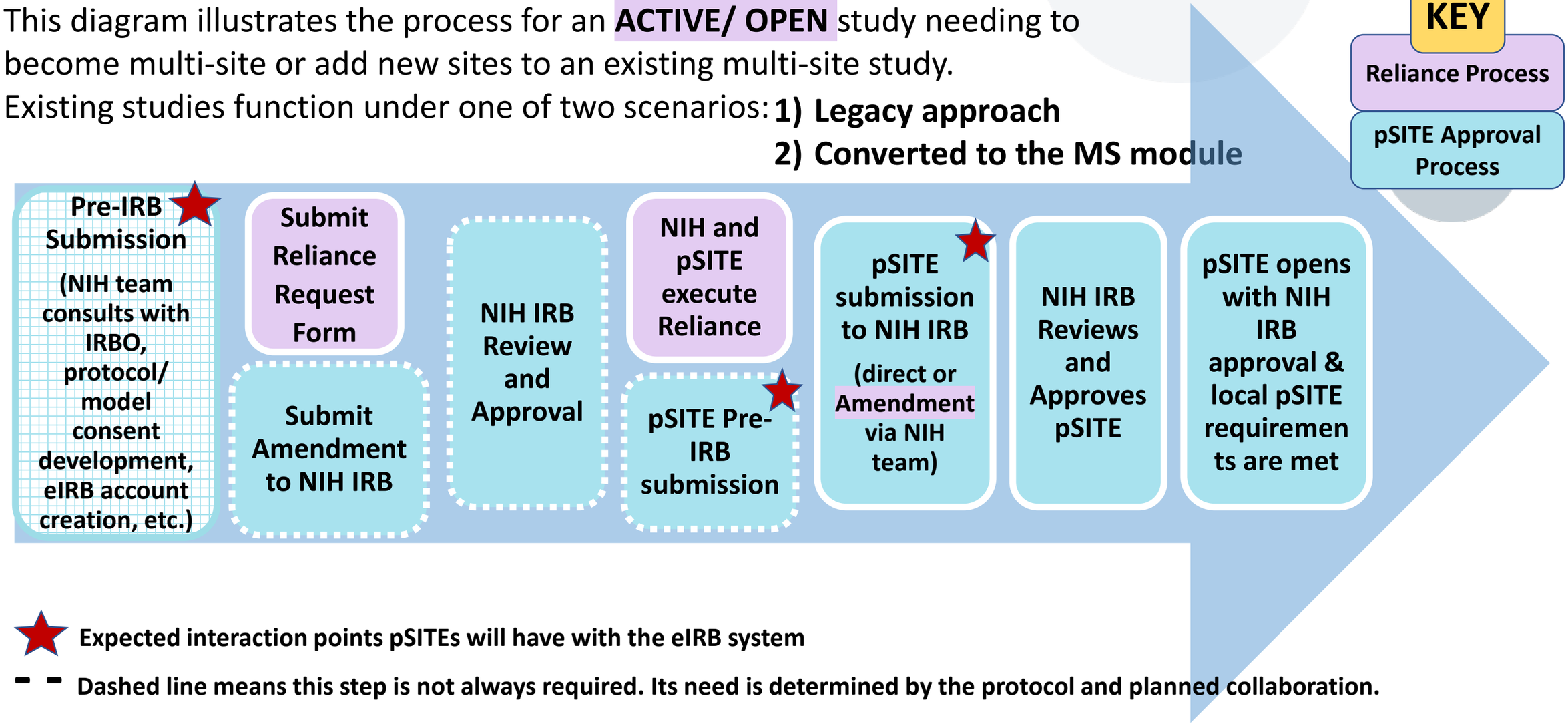
Workflow for adding a pSITE at Initial Review

This diagram illustrates the initial review process for **NEW** multi-site protocols submitting to the NIH IRB with a plan to add new sites.



Workflow for adding a pSITE for an on-going study

- This diagram illustrates the process for an **ACTIVE/ OPEN** study needing to become multi-site or add new sites to an existing multi-site study.
- Existing studies function under one of two scenarios: **1) Legacy approach**
  2) Converted to the MS module

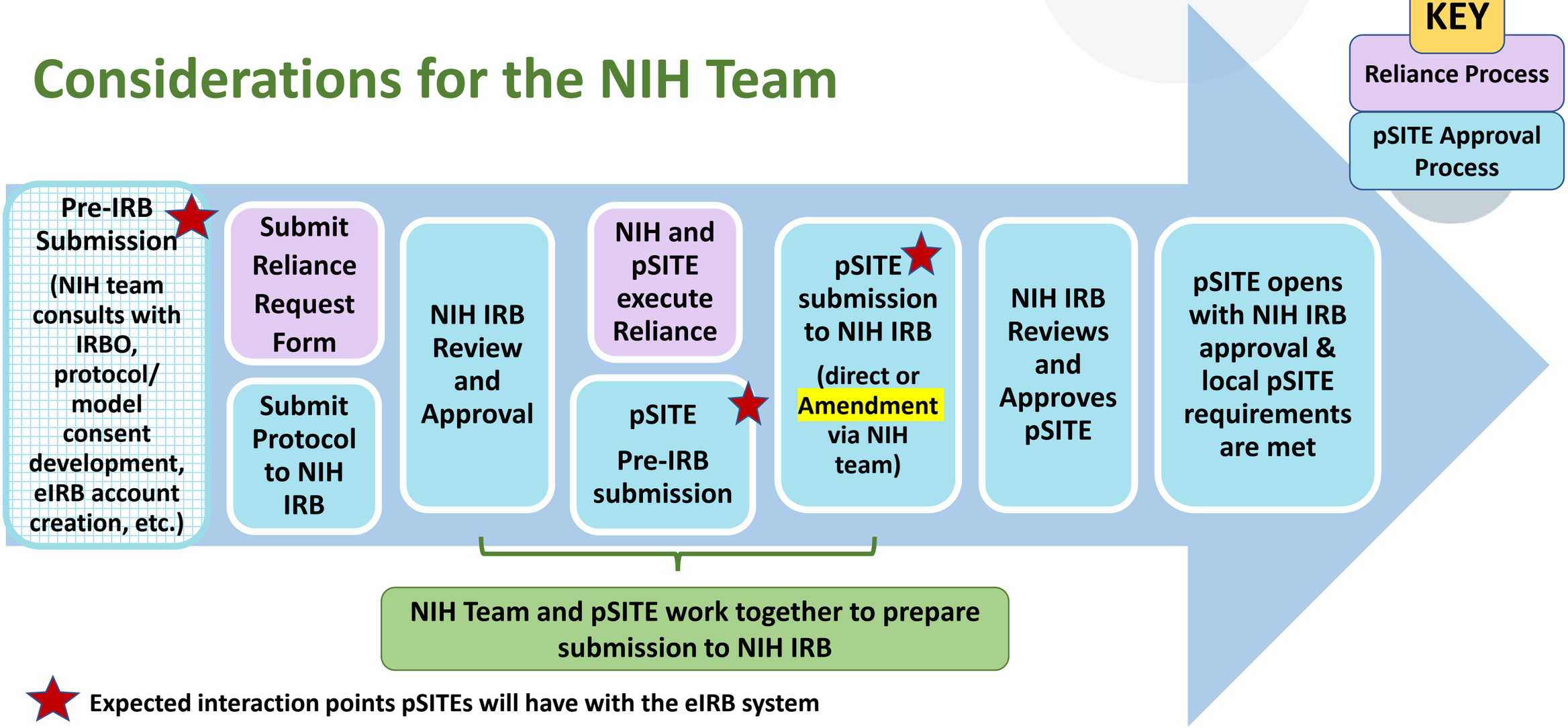


★ **Expected interaction points pSITEs will have with the eIRB system**

- - Dashed line means this step is not always required. Its need is determined by the protocol and planned collaboration.

Workflow for adding a pSITE at Initial Review

Considerations for the NIH Team



Role of NIH PI and NIH Study Team

- NIH PI assumes leadership and has ultimate responsibility for conduct of the research study
- Leads the development of the protocol, model consent documents, model recruitment materials, study instruments
- Ensures study coordination, communication, and routing of IRB submissions (in collaboration with Reviewing IRB)
- Verifies that pSITES have approved protocol and model study materials (consent/ recruitment template) and ensure they understand what sections can be revised during the development of their documents
- Ensures study teams are aware of NIH IRB policies and procedures
- Facilitates submissions to the NIH IRB for all pSITES
- Provides information to the NIH IRB at the time of continuing review about the study's progress and conduct
- Ensures IRB-approved materials/determinations are provided to all pSITE study teams

NIH Study Team, pSITEs, and NIH IRB Communication

Legacy approach

- All study information flows to the NIH IRB through the NIH study team; pSITE PIs send information to NIH PI/ designee for processing
- No direct communication between pSITE team and NIH IRB

eIRB model utilizing multi-site functionality

- Study-wide information can more easily flow between the NIH IRB, the NIH study team, and pSITE team(s)
- pSITE study information submitted directly to the NIH IRB via the pSITE study team; NIH PI/ designee serves as a gatekeeper (current eIRB model) –
  - Opportunity for the NIH study team to vet submission before it reaches NIH IRB
- Still need to maintain good communication between NIH study team and pSITEs

Communication Plan

- Keep in mind that the way NIH PI/ Lead Site and pSITEs communicate differs when using an eIRB multi-site system vs the Legacy Module
  - Presents different challenges
  - Consider differences when developing/ executing a communication plan
  - Do not rely solely on the eIRB system to facilitate communication across sites
  - Suggest NIH Study team have regular communication with the pSITEs
    - Site initiation meetings; regular conference calls; newsletter; email blasts; training materials
- Can work in collaboration with the NIH IRB to determine best plan for communicating and coordinating information to pSITEs

Protocol - NIH PI/Study Team Responsibilities

- Study-wide protocol should be written in a way that incorporates all human subjects research activities; not only NIH specific
  - List the number of sites involved in the protocol
    - Do not list the name of each site or the pSITE PI
      - this is currently listed in the iRIS study application
  - Include all potential subject types e.g., if only one site is enrolling children, the protocol still needs to list this population
  - Number of subjects to be recruited from each pSITE, if not competitive enrollment
  - Recruitment and Screening Procedures
  - Compensation plan
  - Multi-site safety monitoring coordination plan
  - Refer to NIH Protocol Template for other guidelines regarding multi-site protocols

Model Recruitment Forms - Lead PI/Study Team Responsibilities

- Model recruitment materials are created if they will be used at more than one site.
  - **IRB approval is not required at the pSITE level** if pSITE changes consist only of inserting institutional logos and/or contact information e.g., phone number; email address; contact name
  - These changes can be made administratively by the pSITE without IRB review/approval
    - Any other changes at the pSITE level would require IRB review/approval
  - NIH IRB suggests NO other changes to model recruitment material at the pSITE level unless warranted by policy at that institution
- Some pSITEs may have specific site recruitment materials that will be used only at that site. Submit to the NIH IRB for approval with the pSITE application

Model Consent Forms - Lead PI/Study Team Responsibilities

- Responsible for the creation of the Model Consent/ Assent forms (in addition to the NIH site specific versions)
  - Use the Model Consent Template on the IRBO website
    - Some sections will apply to all sites, other sections will need modifications
    - Not one size fits all – there can be exceptions
      - Costs, compensation, and/or reimbursement sections could be different
      - COI (if a conflict exists), research related injury language, who to contact in case of complaint would mostly likely be different
      - Anything specific at the site should be added e.g., if a scan or survey will only take place at the site or is different in some way
- Assent process may be different at each institution, anticipate differences e.g., signature requirements may be different

Coordinating Center

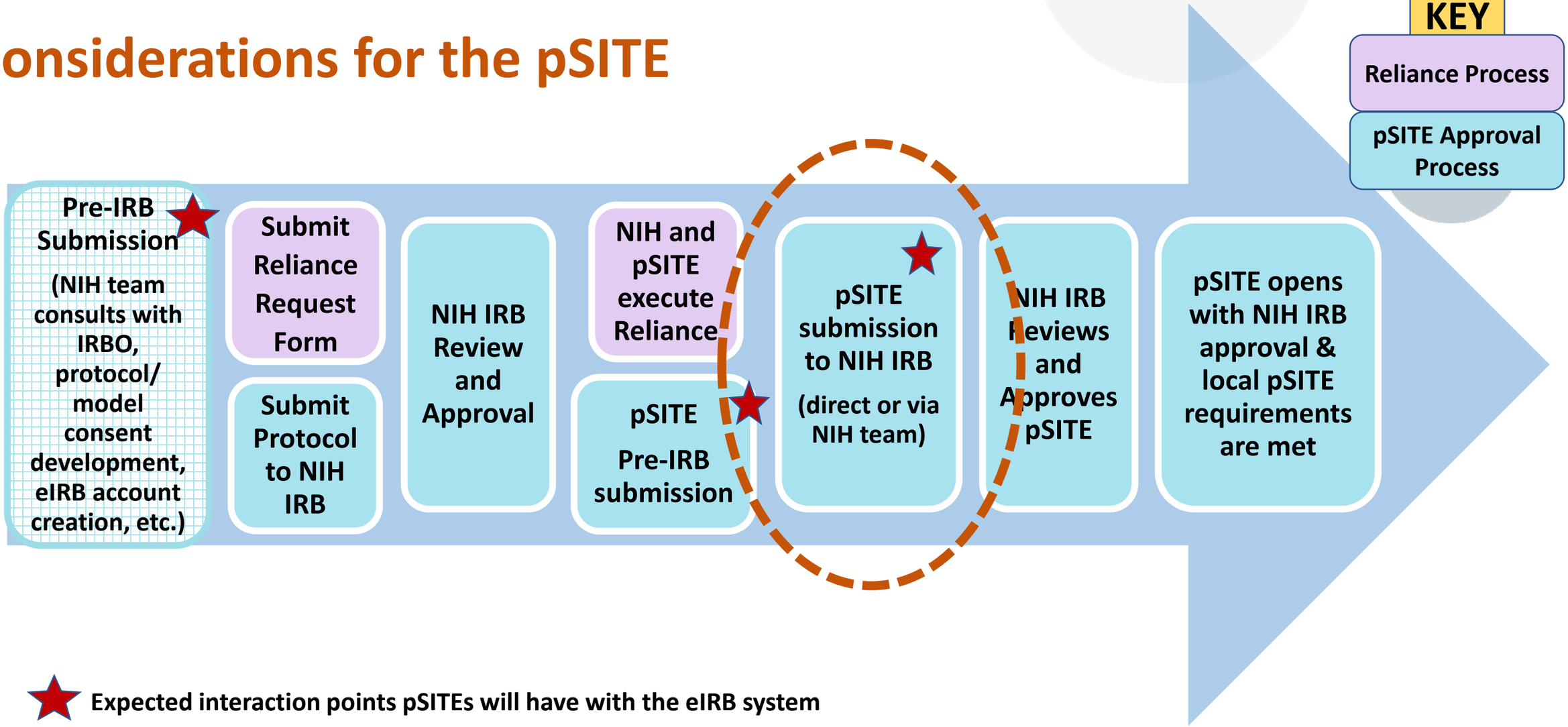
- **Not one definitive definition of a Coordinating Center**
- **The term ‘Coordinating Center’ can cover several very different research-related activities**
  - Can be the NIH PI/Lead Site or delegated to another entity
  - Some only handle data center functions
  - Some have study-wide responsibilities of most or all aspects of the multi-site protocol e.g., consent form development, coordinate data collection, create and manage the overall operations of a study
  - Contract and/or grant should outline scope of work to outline Coordinating Center activities and those of the pSITE(s)
  - Coordinating Center functions need to be clearly described in the protocol

Coordinating Center cont'd

- **Possible Coordinating Center Responsibilities (not inclusive)**
  - Develop the protocol, model consent documents, model recruitment materials, study instruments
  - Conduct data and/or statistical analysis
  - Lead communication efforts across all pSITEs to include current enrollment numbers, study progression, upcoming revisions
  - Ensure pSITEs are receiving IRB correspondence and notification of Amendments, Progress Reports, etc. (Legacy vs eIRB multi-site module approach needs to be considered, especially during the eIRB transition)
    - Coordinating Center or NIH PI/ Lead Site is responsible for ensuring distribution of study-wide documents to the pSITEs
  - Overseeing data transmissions amongst sites

Workflow for adding a pSITE at Initial Review

Considerations for the pSITE



Expected interaction points pSITEs will have with the eIRB system

Role of pSITE Study Team

- Responsible for conduct of the research at the pSITE
- Follow NIH IRB policies and procedures (e.g., for reportable events, personnel changes) **and** applicable pSITE requirements
- Use NIH IRB approved materials including the consent form template (except for locally required language that can be added/ changed)
- Work with pSITE HRPP/IRB to ensure that appropriate local context information is provided to the NIH IRB
- Provide NIH Study Team with ***pSITE information*** when initially being added, on study progress for continuing review, and local problem events so that they can be reported to the NIH IRB
    - Via eIRB system and/ or with supporting documents (protocol addendum and site consents)

Current pSITE submission

- pSITE Application -
If using the multi-site module in iRIS

- **pSITE Protocol Addendum –**
A legacy and multi-site module version exists

- pSITE Consent(s)/ Assent(s) -
Approved model templates plus pSITE edits

- Recruitment materials -
Only when changes go beyond fillable fields in model recruitment materials

- pSITE HRPP/ IRB "Cede Letter" -
Per NIH Policy 105: Notification indicating institutional requirements have been met and local context information approved by the pSITE institution e.g., letter, email, memo etc.

- **Other Supporting Materials –**

Content of a pSITE submission

- Initial Review approves the research protocol and NIH Site
- Baseline assumption for the pSITES will therefore be based on how the research is described in the protocol and how it will be implemented at the NIH
- Focus for the pSITE submission is to:
  - Provide the NIH IRB *pertinent* pSITE information to provide oversight
  - Have the pSITE's implementation of the protocol approved
- The pSITE submission therefore needs to describe
  - Pertinent local context information about the pSITE
  - When the pSITE will:
    - Not implement the research in the way described, or
    - Implement it in a different way, or
    - Do something in addition to what is approved in the protocol

Content of a pSITE submission

Study Procedures	Medical records review, obtaining informed consent, research interactions, recruitment etc.
Recruitment	Description needed if recruitment activities will differ from the protocol
Costs, Compensation & Reimbursement	Billing of insurance, local rates of compensation, and availability of reimbursement
Consent Process and Forms	Use of NIH / local short forms, assent, waivers of consent, e-consent, management of consent process when subjects lack decision-making capacity etc.
Data/ Specimens Use & Storage	**Data**: Analysis, banking, creation of repository **Specimen**: anonymous, coded/ deidentified etc. Centrally vs locally stored, local security measures, duration of storage, etc.

Content of a pSITE submission

Types of research subject	Adults, Children, Employees, Students, Adults lacking decision-making capacity etc.
Local Context	Regulatory, local, and institutional requirements age of majority, who can obtain consent, required state reporting etc.
Ancillary Reviews	Conflicts of Interest, Pharmacy, Radiation Safety, Biostatistics, Nursing etc. Verify completion but should also be used to provide rationale for protocol/ consent edits
Conflict of Interest	Whether investigator has a financial interest and, if so, provide summary
Study team qualifications & HRPP training	pSITE confirm that study team are qualified and have completed HRPP training

pSITE Consent Documents

- Typically developed from the **NIH Model Consent**
- The **NIH Model Consent**(s) has sections that are the **same** for each site and sections that **allow customization** by the pSITE to address local context
- pSITE study team should work with the pSITE HRPP/ IRB to identify institutional language that needs to be included in the pSITE consent
- Suggested changes should be substantiated:
  - The way the protocol will be implemented at the pSITE
  - State and local laws, or institutional policies and procedures
- Exceptions: Some pSITEs may have a site specific ICF e.g., only a survey is taking place at that site (no need for a model ICF in this case)
- pSITE HRPP/IRB may issue confirmation that consent is appropriate

Mandatory sections in pSITE Consent Documents

- Aside from regulatory-required language, structure (e.g., key information etc.) and study procedures, the following should be in the pSITE consent:

  - Certificate of Confidentiality
    - Cannot be removed from a domestic pSITE
  - Privacy Act text
    - When identifiable information will be sent to the NIH
  - Standard language about clinicaltrials.gov
  - The NIH IRB identified as the Reviewing IRB and with contact details

Flexibilities in the pSITE Consent Documents

NIH IRB permitted changes include ***but are not limited*** to:

- Header/Footer – provided there is space for the NIH IRB stamp
- pSITE PI and study team contact information
- The inclusion of references to the pSITE
- Compensation, Costs, and Reimbursement
- Conflicts of Interest
- Radiation Safety language
  - A local ancillary review that may generate a need to amend the protocol and/ or consent form as it alters the risk/benefit analysis
  - NIH model text can be added to by the pSITE.
  - Rationale needed if it is to be deleted e.g., no radiation use at pSITE
- GINA language: Some states mandate use of specific language

Flexibilities in the pSITE Consent Documents

- Confidentiality language
  - May be replaced or augmented provided consistent with how data/ samples will be managed study-wide
- Subject complaints
  - pSITE HRPP/IRB office contact information can be added
- Study procedures can be deleted, changed, or added to when the pSITE is implementing the protocol differently
- Use and storage of data/ samples may be altered
- Research-related injury language & statement about available medical treatment
- Assent process
  - pSITES will have different processes (e.g., documenting assent via signature not research record); need to anticipate the impact of those differences

HIPAA in pSITE Consent Documents

- The NIH's position is that:
    - NIH is not a covered entity and
    - NIH IRB will not serve as a privacy board
- pSITEs therefore need to address their own HIPAA obligations locally
- NIH IRB *prefers* HIPAA is dealt with in a stand-alone form which does not need to be provided to the NIH IRB
- However, a pSITE consent form that is combined with a HIPAA authorization is permitted. The NIH IRB will only review the consent portion.

pSITE Approval

When can a pSITE begin Human Subjects Research (HSR) activities?

- *Reminder that Participating Sites are reviewed and approved **after** the NIH Site is approved*

- From the IRB's perspective, once a site has full IRB approval, HSR activities can begin

- However, the pSITE must ensure that all local reviews/ approvals required by its institution are in place
  - Examples of other reviews that may be required are coverage analysis, specific department approvals, data use agreements, material transfer agreements, ancillary committee reviews (e.g., radiology, nursing, and pharmacy)
    - *Communicate with the pSITEs so expectations on when they can begin research activities are established*

Top Tips: Adding a pSITE to an NIH protocol

- Establish effective communication pathways
- Is the pSITE a SMART signatory?
- Ask the pSITE to find out what is required from them by their HRPP/ IRB in order to rely on an external IRB
- Does a model consent need to be developed?
- Provide the pSITE with guidance to develop the pSITE consent
- Try to limit customization of documents at the pSITE level e.g., recruitment materials

Part 1: Session Objectives

- Reliance Agreement process
- Adding a Participating Site (pSITE) to an NIH protocol
- Review NIH study team (CORE) role and responsibilities
- Review pSITE study team role and responsibilities

PART 2:

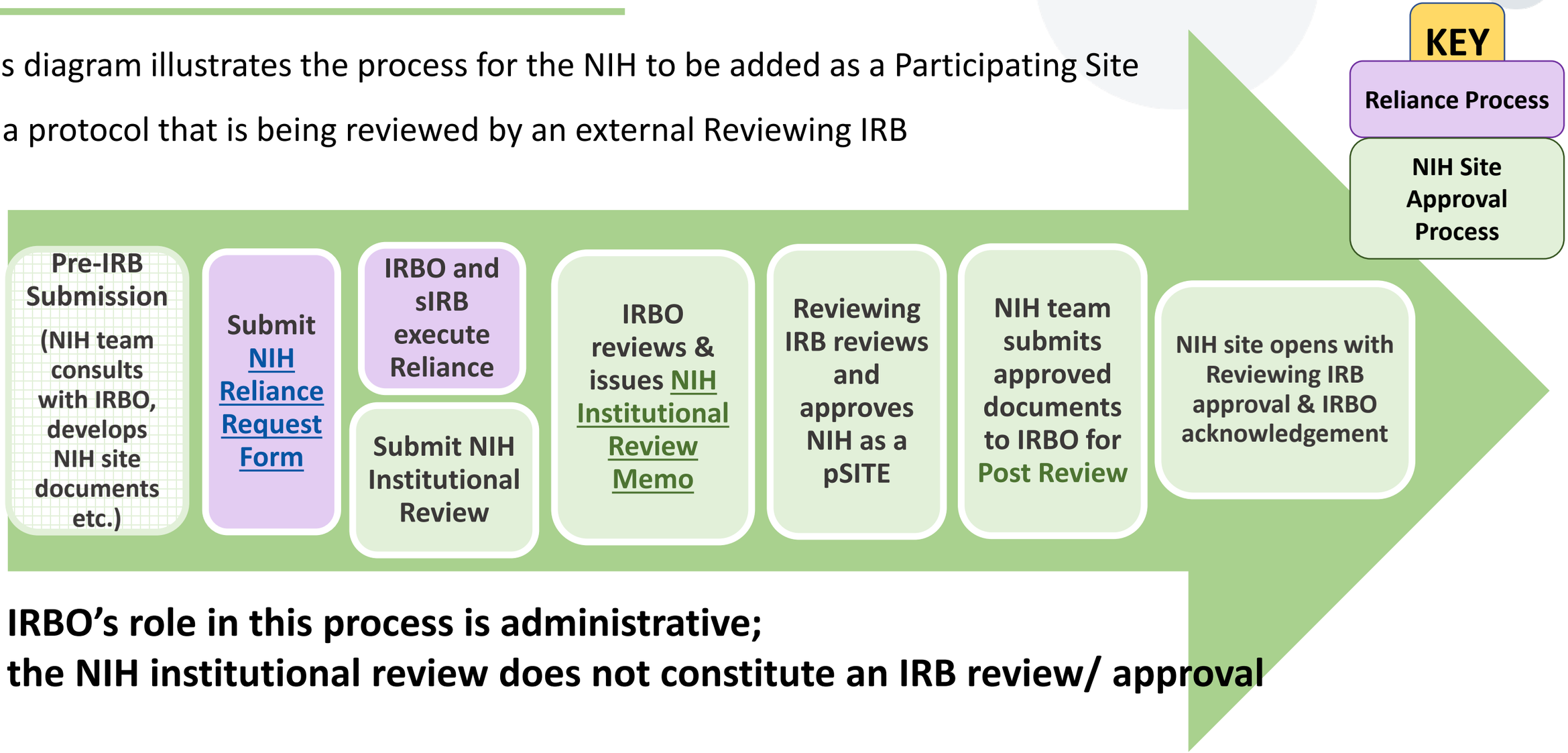
Workflow: Adding NIH as a site on a protocol that is being reviewed by an external Reviewing IRB

Part 2: Session Objectives

- Reliance Agreement process
- Review principles of relying on an external IRB
- Review NIH study team role and responsibilities
- Preparing a submission for an NIH Institutional Review

Workflow: Add NIH to an externally reviewed protocol

This diagram illustrates the process for the NIH to be added as a Participating Site on a protocol that is being reviewed by an external Reviewing IRB

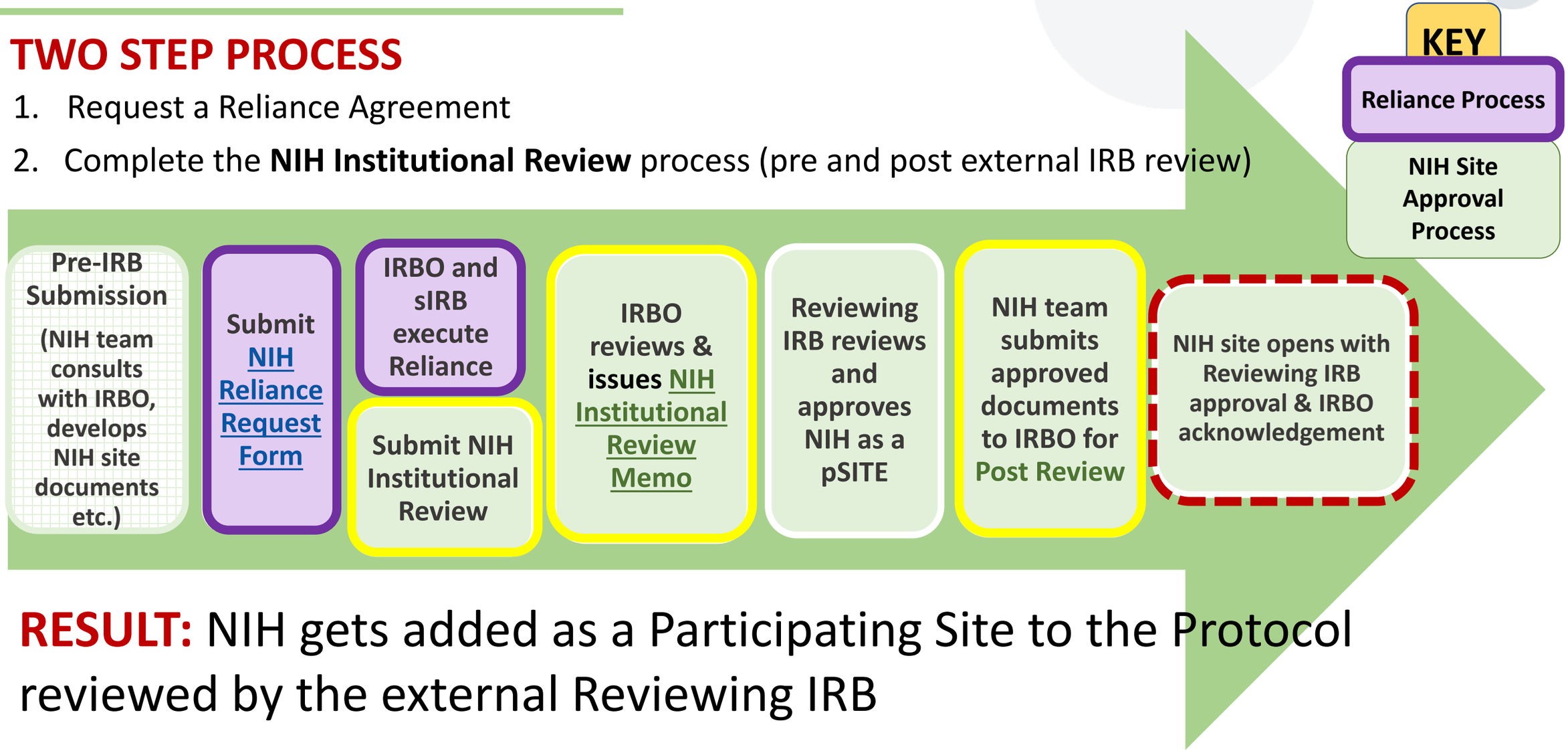


IRBO's role in this process is administrative;
the NIH institutional review does not constitute an IRB review/ approval

Workflow: Add NIH to an externally reviewed protocol

TWO STEP PROCESS

1. Request a Reliance Agreement
2. Complete the **NIH Institutional Review** process (pre and post external IRB review)

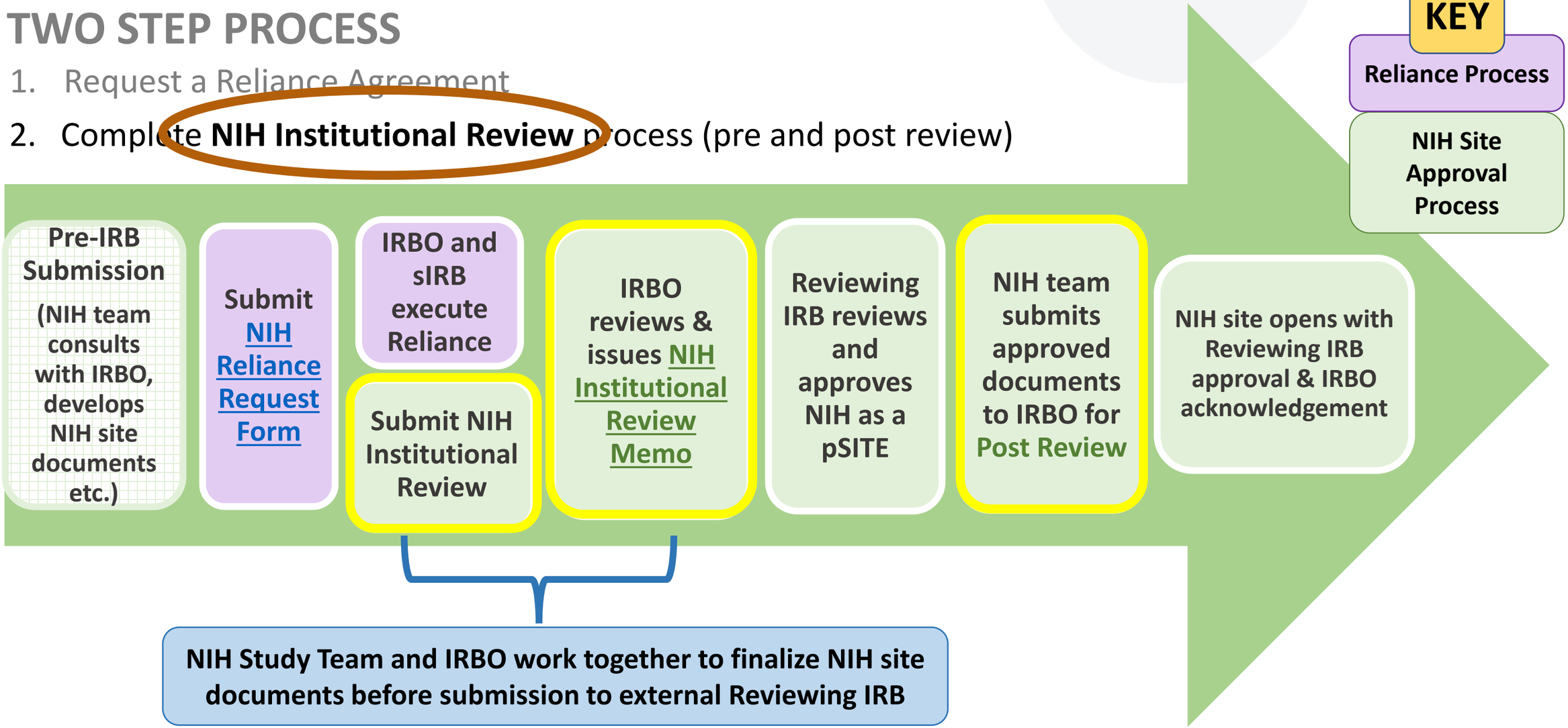


RESULT: NIH gets added as a Participating Site to the Protocol reviewed by the external Reviewing IRB

Workflow: Add NIH to an externally reviewed protocol

TWO STEP PROCESS

1. Request a Reliance Agreement
2. Complete **NIH Institutional Review** process (pre and post review)



Principles of Relying on an external Reviewing IRB

- NIH is not the Reviewing IRB and has ***ceded*** IRB review to an external IRB
  - *The institutional review by IRBO is not a review by the NIH IRB*
- NIH retains responsibilities as an FWA-holding institution e.g., training & qualifications, resources, ancillary reviews etc.
- IRBO's administrative reviews and the maintenance of a shadow protocol is the main mechanism used by the NIH to address these responsibilities
  - Ensures NIH study teams are also compliant with NIH requirements
- Reviewing IRB ***approves*** the NIH site, NIH IRBO ***acknowledges*** the approval
- NIH Site can commence research activities once it has
  - Approval from the Reviewing IRB and
  - Completed the NIH Institutional Review process

Role of NIH Study Team

- Responsible for conduct of the research at the NIH
- Follow the reviewing IRB's policies and procedures (e.g., for reportable events, personnel changes) **and** applicable NIH HRPP requirements
  - Note that there are dual reporting requirements
- Use Reviewing IRB approved materials including the consent form template (adding/ changing appropriate locally required language)
- Complete all applicable NIH ancillary reviews
- Submit documents for NIH Institutional Review
- Work with NIH IRBO to ensure that appropriate local context information is provided to the Reviewing IRB when initially being added as a site

NIH Institutional Review Submission

NIH Study Team
(Participating Site Study Team)

Submits in eIRB system:

- 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.
- Recruitment Materials, if unique
- Investigator Brochure

NIH IRBO (Relying Institution)

Conducts Institutional Review

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

Once completed, IRBO issues:

NIH Institutional Review Memo
PLUS a Stipulation

- Confirms that submission meets NIH institutional requirements
- Serves as “green light” to NIH Study Team that can move forward and submit to Reviewing IRB
- If required, provides additional guidance on submission
- Provide to Reviewing IRB

* If NIH is the lead site

NIH Protocol Addendum

- Describe NIH's proposed role in the research and applicable institutional requirements
- Ensures that Reviewing IRB understands protocol implementation at the NIH
- Supplements the Main Protocol Document and must be read in conjunction with it
  - Expands on protocol content by:
    - Correcting statements that something will be done at the NIH site when it won't *and/or*
    - Describes when NIH will do something *differently/ in addition* to the protocol
- Avoid defaulting to language that is submitted when NIH is the reviewing IRB
- Should not duplicate the protocol

➢ **Distinct** from NIH Protocol Supplements developed when the NIH is going to be implementing a Sponsor Protocol and the NIH is the Reviewing IRB.
  - These supplements tend to be more comprehensive documents as they need to satisfy all NIH HRPP and IRB requirements

NIH Protocol Addendum – Examples of Typical Content

Institutional and Operational Requirements:

- Adding NIH IRB# and identifying involved NIH sites, especially when go beyond the NIH CC
- NIH not subject to state law, will not bill insurance, and primarily a research facility
- NIH study team will report events to OHSRP in addition to reporting to the Reviewing IRB

Protocol Implementation:

- Describing ways in which screening, recruitment, compensation, reimbursement, or procedures will be conducted differently, or not at all, at the NIH, such as:
  - NIH will enroll a specific cohort
  - Data in CRIS will go to BTRIS
  - NIH will perform an extra scan and questionnaire
  - Not permit sponsor GDPR language

Consent Implementation:

- Assent process for children e.g., format, variation by age group, documentation method etc.
- Determining subject capacity and adherence to NIH HRPP Policy 403
- Enrolment of non-English speakers and use of NIH short form consent
- Re-consenting of subjects who reach 18 and requesting waiver of consent
- Varying consent process to fit the NIH context e.g., documenting assent on research record not consent form, e-consent method etc.

NIH Consent/ Assent

- Developed from the Reviewing IRB-approved “Model Consent/Assent”
- NIH study team needs to customize to include NIH institutional requirements and communicate how the protocol is going to be implemented at the NIH
- Usually involves inserting NIH language into the Model Consent with NIH edits tracked. Do not initiate using NIH template.
- Acceptable to retain language from the Model Consent when equivalent to NIH template language
    - Exceptions e.g., research-related injury, Certificate of Confidentiality etc.
- Needs to be consistent with the NIH Protocol Addendum
- Evolving craft where still learning what are true non-negotiables and need to be flexible as external IRBs take different approaches e.g., using 2-part consents
- Where possible, prudent to establish what are the acceptable parameters for the Sponsor, the Reviewing IRB, NIH, and/or the Lead Study Team

NIH Site Consent – Examples of Typical Customization

Additions:

- NIH IRB number
- NIH CC header and footer, including consent #
- Compensation & reimbursement text
- NIH research-related injury language
- Certificate of Confidentiality and Privacy Act language
- Appropriate sections of the NIH signature block
- Key Information section and revised Common Rule elements

Deletions:

- HIPAA-related text
- Assertions that insurance will be billed
- Assertions that subjects can continue clinical care at the NIH if withdraw from study
- References that combine Sponsor and Study Site conduct or responsibilities

Additional Requirements by the Reviewing IRB

- Reviewing IRB can impose additional requirements on the NIH:
  - ***Method*** by which they want to receive the protocol and/ or local context submission by the NIH study team i.e., via a conduit (lead study team, coordinating center etc.), directly using their eIRB system, via a third-party website (iREX) etc.
  - ***Sequence*** for submission may not align with NIH's workflow
    - Reliance is executed when NIH is added as a site or request local context information when reliance is executed. Discuss with IRBO to try to sync up processes.

- Request **Local Context information** in a stand-alone local context form or institutional profile
  - Reviewing IRB is trying to understand applicable NIH policies, local norms, special requirements, culture, etc. in order to conduct its review
  - Usually comprises 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 is a collaborative effort between NIH Study Team and IRBO
  - NIH IRBO needs to ultimately sign off on information provided
  - Additional forms should be submitted by email to IRBO at the time of NIH Institutional Review

Approval and Activation of NIH as Participating Site

Submission to Reviewing IRB

- NIH Study Team submits to the Reviewing IRB requesting to be added as a site to the protocol
- NIH Protocol Addendum and Consent/ Assent documents should be the last version seen by IRBO
- Once NIH is approved as a site by the Reviewing IRB, the NIH Study Team must submit the approved protocol and consent documents, and corresponding IRB approval back to NIH IRBO

IRBO Activation Review "Post-Review"

- NIH Study Team submits a "Response Review Submission Form" in response to the single stipulation issued at the time of the NIH Institutional Review Memo
- Clean version of documents should be submitted unless the Reviewing IRB has made changes
- IRBO reviews the documents to ensure remain consistent with NIH institutional requirements
  - Captures pertinent information e.g., risk determination for a specific population, CR date etc.
  - Activates NIH Site according to Initial Review Form study status e.g., "*Open – Recruiting*"
  - *Acknowledges* the NIH is approved as a site and all approved documents
- If at the NIH Clinical Center, documents forwarded to Office of Protocol Services for processing

Shadow Protocol: NIH Relying on External Reviewing IRB

- Maintain Shadow Protocol in eIRB system
    - Currently approved protocol, consent and assent documents
    - Consent/ assent must be Reviewing IRB-approved version
- Each study lifecycle action must be submitted e.g., amendment, continuing review
    - No batch submissions
- External IRB determination/approval letter must be included with submissions
- If External IRB does not approve research personnel, NIH study personnel changes are submitted to IRBO for review
- Close study via Progress Report Form

Top Tips: Add NIH to an externally reviewed protocol

- Has the study been reviewed under the revised Common Rule?
- What is the sequence of the reliance being documented vs the submission to add NIH as a site?
- How does the Reviewing IRB want the consent forms managed – NIH site consent only or in 2 parts?
- Will additional local context information be requested?
- How does the Reviewing IRB want to receive the NIH's submission?

Part 2: Session Objectives

- Reliance Agreement process
- Review principles of relying on an external IRB
- Review NIH study team role and responsibilities
- Preparing a submission for an NIH Institutional Review

Contact Us

NIH IRB Reliance & sIRB Team

For further guidance or questions:

Web: Reliance and sIRB IRBO webpage
Multi-Site Research (nih.gov)

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Questions?