# What You Need to Know About Single IRB Review: Principles and Practice (Part 1)

## NIH OHSRP EDUCATION SERIES - JULY 7, 2020

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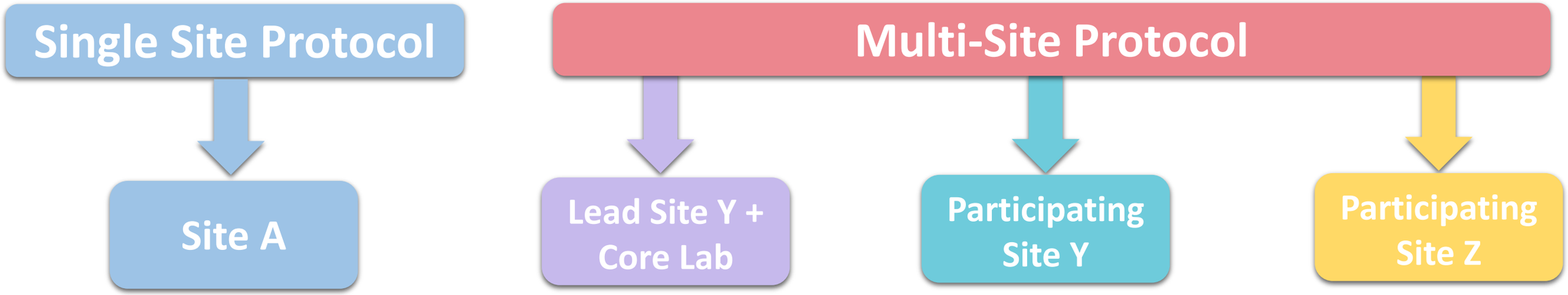
# Learning Objectives

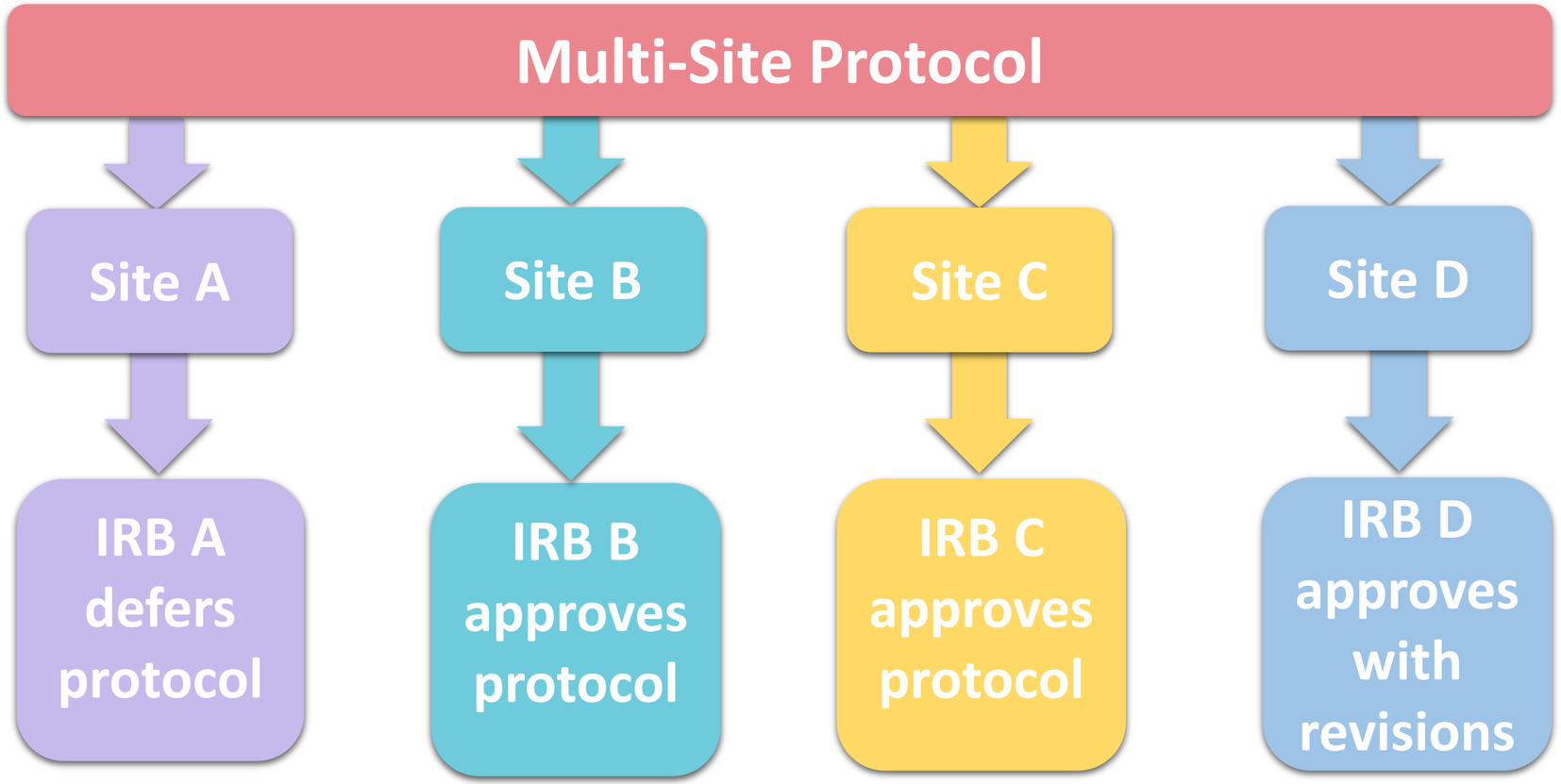
- Provide an overview of the principles behind Single Institutional Review Board (sIRB) review
- Explain what is Single IRB review; when it is required; and what is involved in reviewing research using the Single IRB review model
- Explain and provide context for terms such as “multi-site research”, “Single IRB”, and “Reviewing IRB”

# Multi-Site Research – What is it?

- Research projects (protocols) that involve more than one institution conducting the same human subjects research
- Sites may be conducting identical activities or implementing different aspects of the same protocol
- Research may be taking place within the US or internationally
- Also known as “Cooperative Research”



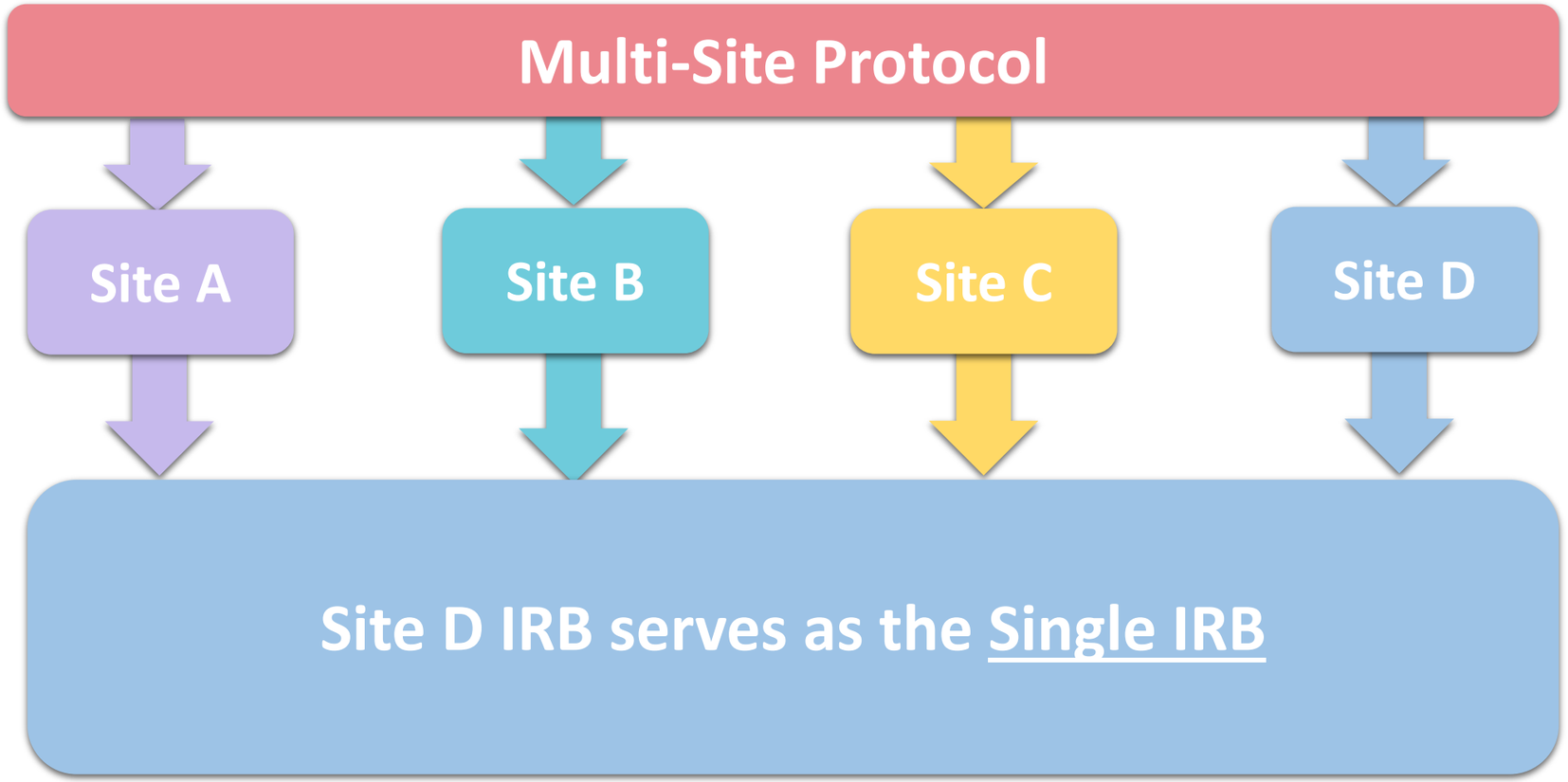
# IRB Review for Multi-Site Research – Traditional Model



# IRB Review for Multi-Site Research – Single IRB Model

- Single IRB (sIRB), also known as the Reviewing IRB, IRB of Record, or Central IRB (CIRB)
- An individual IRB reviews and approves research for all participating sites involved in a multi-site protocol instead of each site obtaining individual approvals
- Streamlines the IRB review process for study teams, institutions, sponsors and IRB professionals
- Allows research to proceed expeditiously without compromising on IRB review quality
- Different, not necessarily less, work for all involved

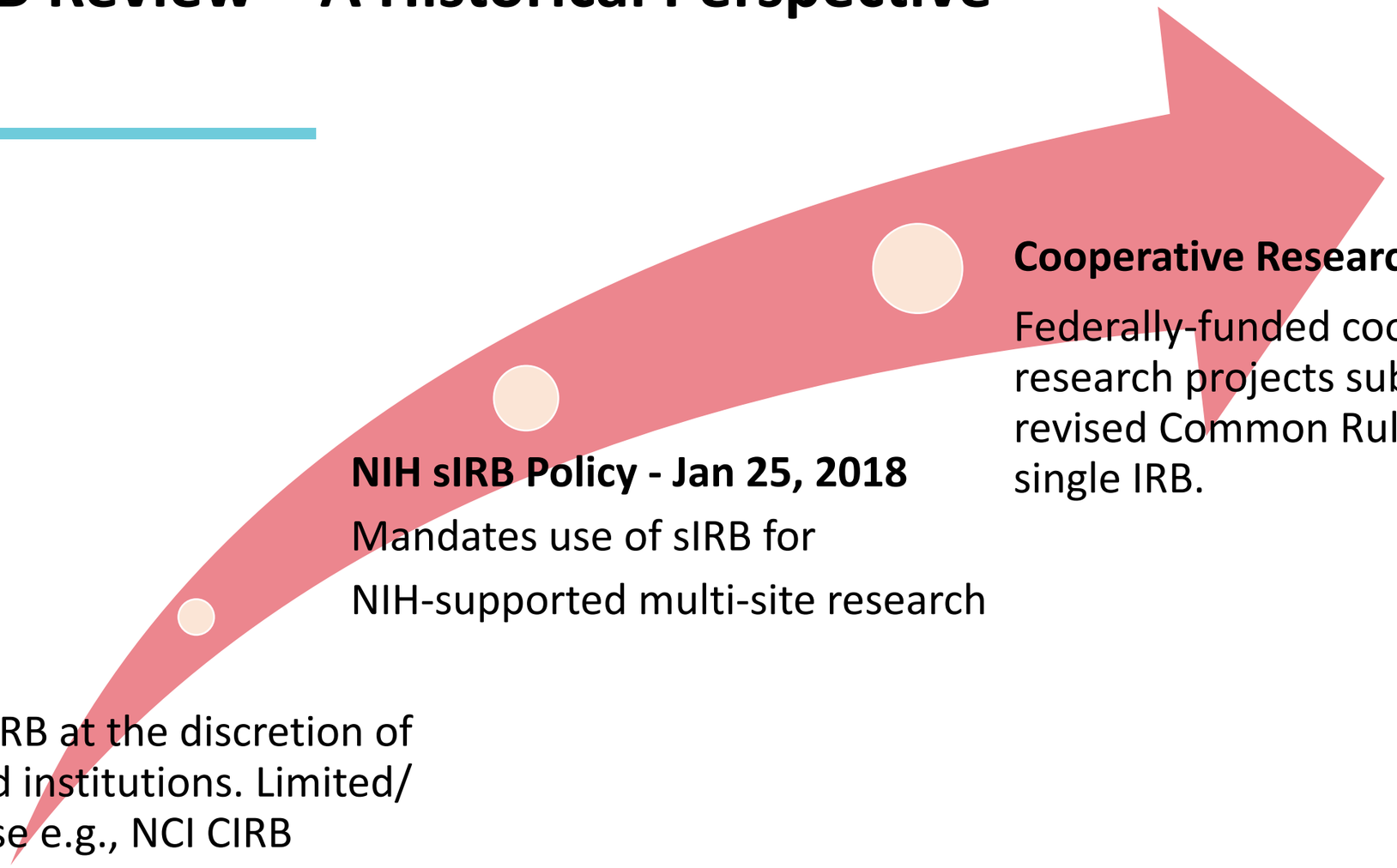
# IRB Review for Multi-Site Research – Single IRB Model



# Single IRB Review – When is it Required?

- Prior to mandates, Single IRB review model encouraged by NIH, OHRP & FDA
- Early manifestations: NCI CIRB (2001), VA CIRB (2008), and NeuroNEXT IRB (2012)
- sIRB use more commonplace given mandates - NIH sIRB Policy and revised Common Rule
- Allowing one IRB to review for all sites participating in research reduces the burden for all
- Only ceding IRB review - each participating institution retains responsibility for adhering to regulations, local requirements, and protecting participants

# Single IRB Review – A Historical Perspective



**Pre-2018**

Use of an sIRB at the discretion of the involved institutions. Limited/ specialist use e.g., NCI CIRB

**NIH sIRB Policy - Jan 25, 2018**

Mandates use of sIRB for

NIH-supported multi-site research

**Cooperative Research - Jan 20, 2020**

Federally-funded cooperative research projects subject to the revised Common Rule must use a single IRB.

# Single IRB Review Mandates

## NIH sIRB Policy

All domestic sites must use a single IRB of record to review human subjects research when participating in *NIH supported* multi-site studies whether that support comes from a grant, cooperative agreement, contract, or the NIH IRP.

## Revised Common Rule

Any institution located in the United States that is engaged in cooperative research must rely upon approval by a single IRB for that portion of the research that is conducted in the United States. (***s.45 CFR 46.114, Cooperative Research***)

# Single IRB Review Mandates

| | NIH sIRB Policy applied to the NIH IRP | Revised Common Rule (2018 requirements) |
|---|---|---|
| **Effective date** | • All initial reviews submitted by IRP after January 25, 2018<br>• When IRP becomes involved in (a) New multi-site study; or (b) Existing multi-site study approved on/after January 25th, 2018. | January 20, 2020 |
| **Terminology** | Refers to “multi-site studies” | Refers to “cooperative research” |
| **Scope** | • Applies to domestic sites of NIH-funded (wholly or partially funded), non-exempt, multi-site studies<br>• Involvement of the NIH IRP as a site in any multi-site study is interpreted as NIH-funding of a project | • Applies to any institution located in the US engaged in non-exempt, federally supported cooperative research for portion of research conducted in the US<br>• Studies subject to the revised Common Rule<br>• At least 2 institutions must be receiving federal funds to trigger the mandate |
| **Exceptions** | Single IRB is not required<br>• For certain types of grants and to foreign sites<br>• If review by an sIRB would be prohibited by a federal, tribal, or state law, regulation, or policy<br>• If there is a compelling justification | Single IRB is not required when<br>• More than single IRB review required by law<br>• A Federal department/agency supporting/conducting research determines use of single IRB not appropriate |

Adapted from SMART IRB. “The NIH sIRB Policy” [Powerpoint Slides].

# Single IRB Review – The NIH Context

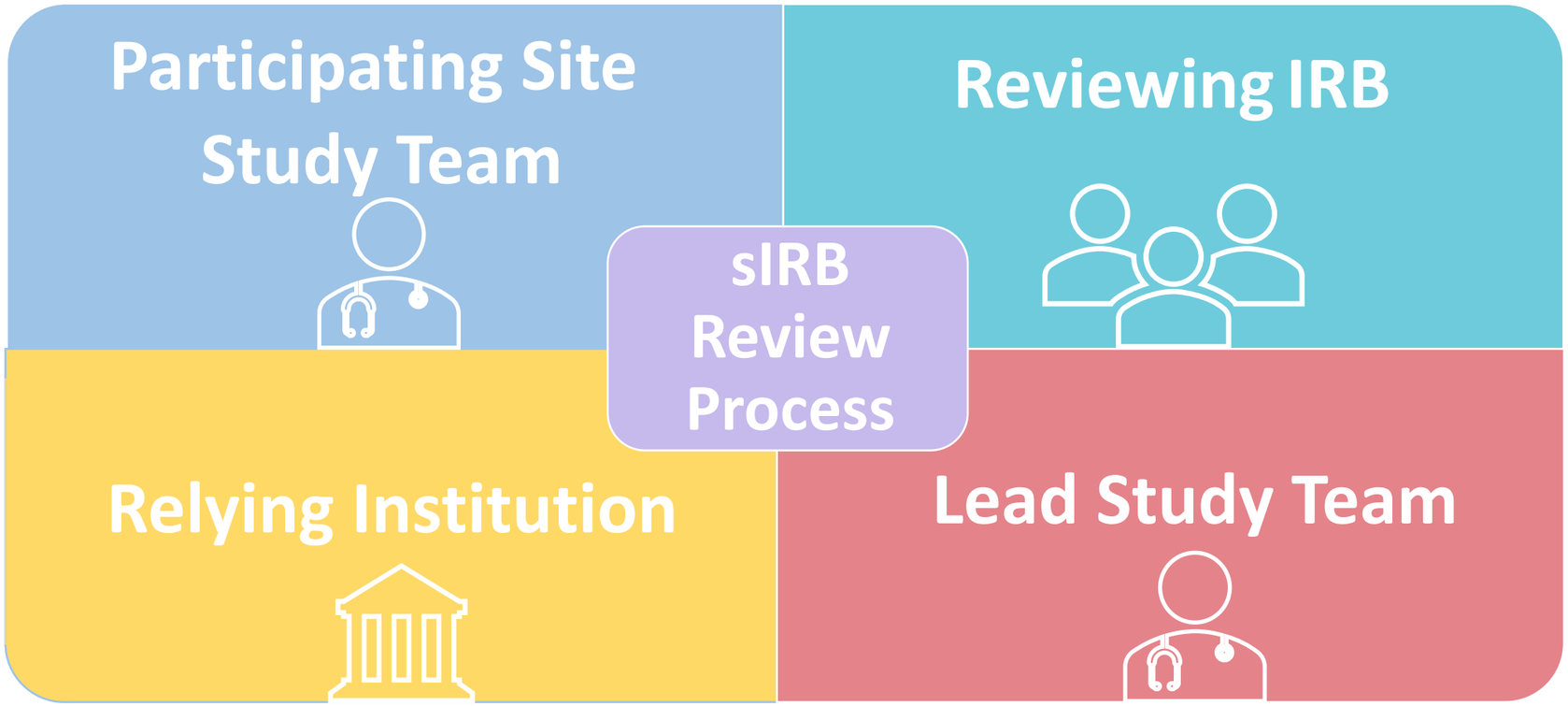
## Past sIRB Review Process at NIH

- Multiple NIH IRBs serving as sIRBs
- Separate department for Reliance Agreements

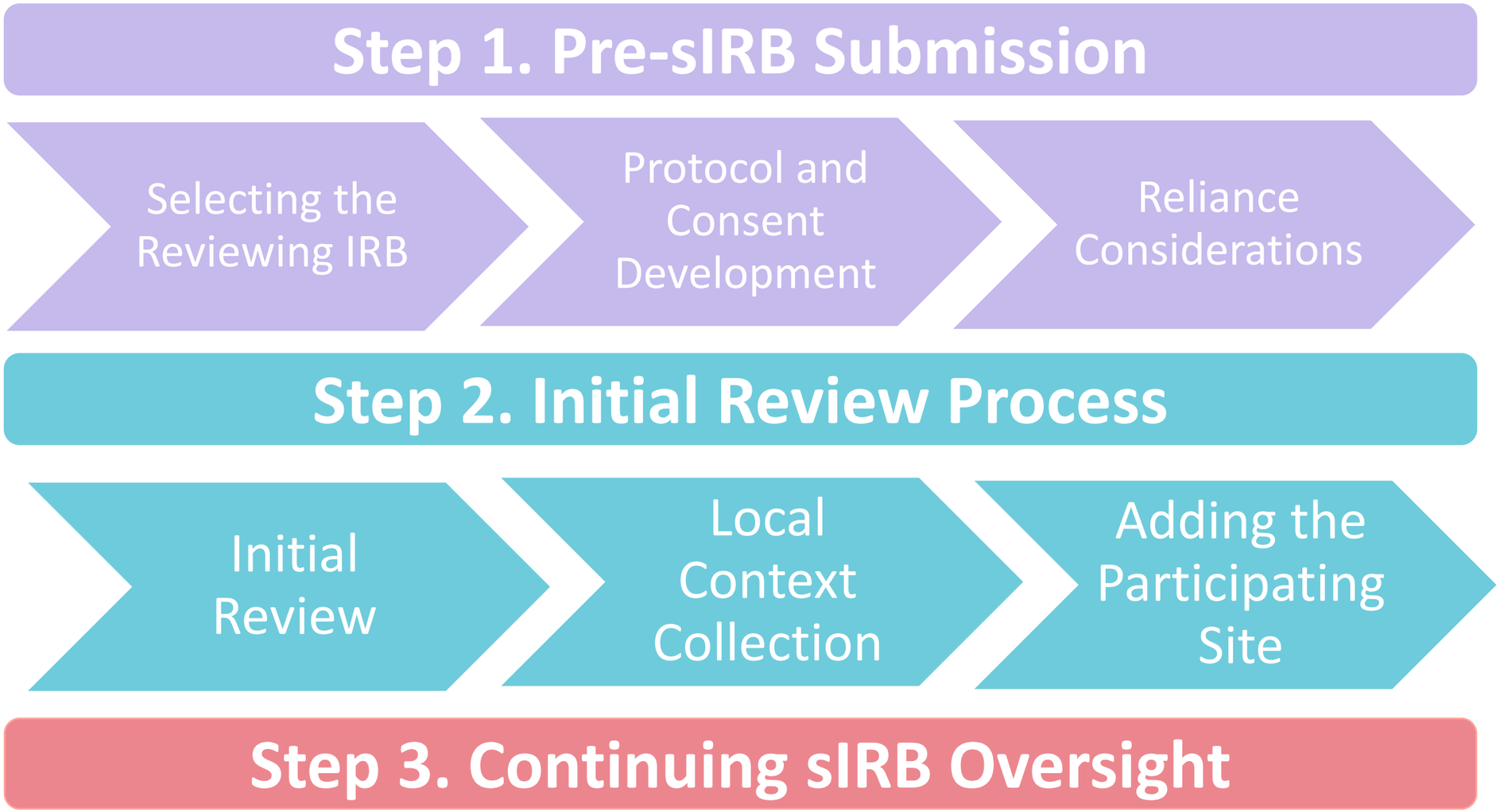
## Current sIRB Review Process at NIH

- NIH as the Reviewing IRB
  - The NIH IRB serves as sIRB
  - Reliance and sIRB Team in IRBO allows for coordinated and consistent reviews
- NIH as the Relying Institution
  - Reliance agreements now possible with commercial IRBs
  - NIH Institutional Review
  - Requirements for shadow protocol in electronic IRB system

# Single IRB Review – The Key Players



# Single IRB Review – The Essential Steps



# Selecting the Reviewing IRB

- The sIRB may be embedded within an academic, medical, or academic medical institution that is also a Participating Site, or could be a commercial IRB e.g., Advarra, Western IRB
- Selection is dependent on a variety of factors including:
  - Sponsor
  - Funding
  - Subject-matter expertise
  - Experience and infrastructure for reviewing large multi-site studies
  - Protocol is embedded in a network or consortium
- The IRB at the Lead Study Team's home institution commonly serves as the Reviewing IRB
- Not the default and generally operates on principle of "right of first refusal"
- Reviewing IRB must agree to act in that capacity

# Protocol & Consent Development

## Lead Study Team Considerations

- Protocol Content
  - Consult with HRPP office to discuss multi-site protocol and sIRB arrangements
  - Ensure that protocol provides Relying Institution with adequate information to determine if they can implement the study and comply with local requirements
  - Develop Model documents that can be customized later by Participating Site
- Protocol Implementation
  - Establish an effective communication strategy for liaising with IRB and Participating Sites
  - Devise a data/safety monitoring plan that can be operationalized across all Participating Sites
  - Consider compliance obligations required by the Reviewing IRB and Participating Site HRPPs

# Reliance Agreement

- Written agreement between institutions performing multi-site research that identifies which institution will serve as the Reviewing IRB and which will cede IRB review i.e., Relying Institution
- Outlines the roles and responsibilities of the Reviewing IRB and Relying Institution
- Negotiated by the respective Human Research Protections Program (HRPP)
- Executed by the respective Institutional Official or designee
- May apply to a single study or apply to a broader arrangement
  - Certain categories of studies e.g., NCI CIRB
  - Studies involving established/ frequent research partners e.g., NIH-Walter Reed National Military Medical Center (WRNMMC)
  - Programmatic agreements allow review by an sIRB of all submitted studies and the relying institution decides which to submit e.g., Advarra, Western IRB (WIRB)

# Reliance Considerations

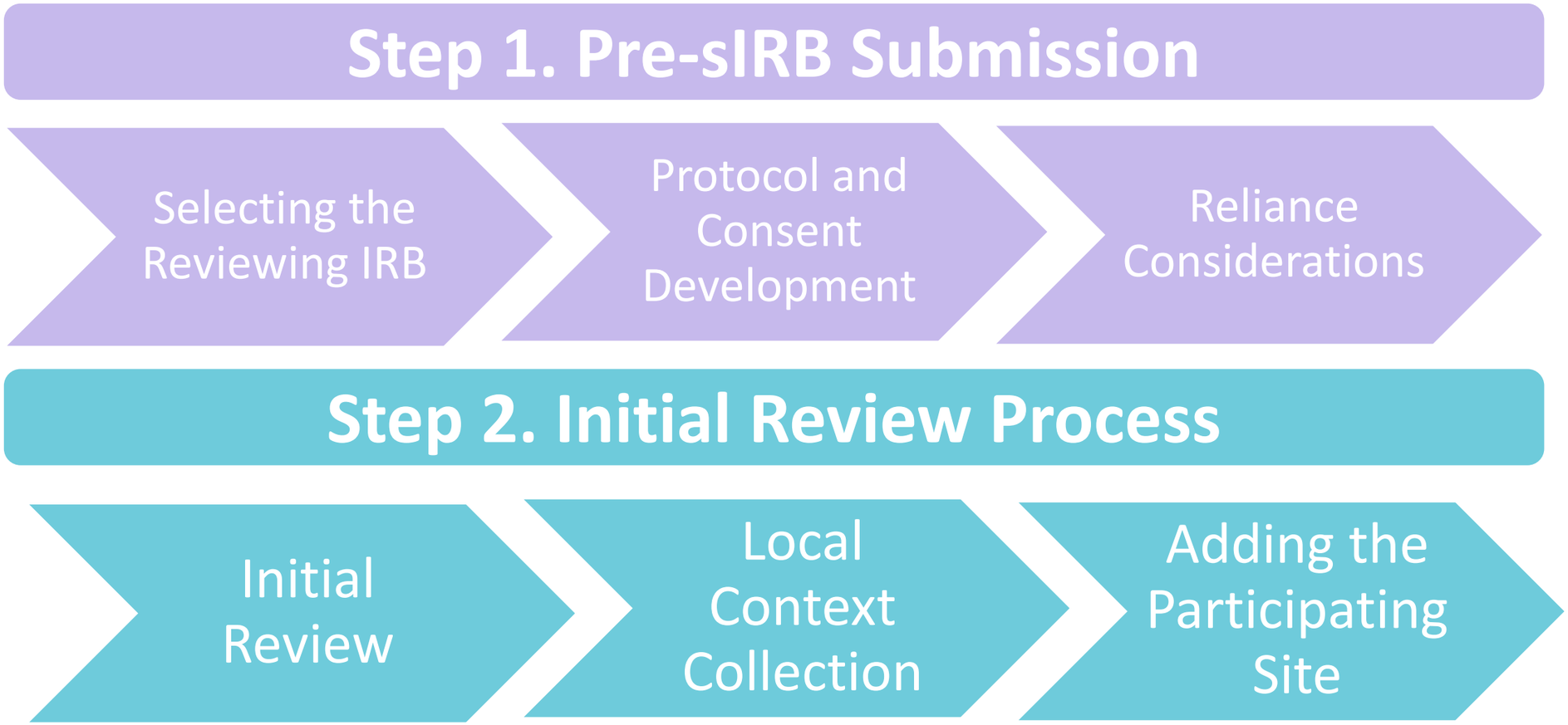
**Q. Does the Participating Site Institution need the oversight of an IRB?**

- Determined by the Participating Site's involvement in the study
- Establish whether the Participating Site Study Team will be obtaining informed consent or interacting, intervening or collecting identifiable private information from living individuals for research purposes
- If so, considered to be "engaged" in non-exempt human subjects research and need oversight
- OHRP Guidance Engagement of Institutions in Human Subjects Research (2008)

**Q. Is the Participating Site willing to rely on the Reviewing IRB?**

- Limited discretion to opt out due to sIRB mandates
- By policy can require certain safeguards
  - Reviewing IRB must be AAHRPP accredited
  - Shadow Protocol

# Single IRB Review – The Essential Steps



# Approaches to sIRB Submission

| | |
|---|---|
| **COMBINED SUBMISSION** | • **Lead** and **Participating Sites** submit IRB application at Initial Review<br>• sIRB approves all sites included in initial submission<br>• All sites commence research at the same time<br>• Further addition of sites managed later by amendment |
| **TWO PART SUBMISSION** | • **Lead Site** submit IRB application at Initial Review<br>  • sIRB reviews protocol and model documents e.g., consent, recruitment materials<br>• sIRB approves Lead Site only<br>• **Participating Sites** approved later by separate IRB action<br>  • Submit local context information and site-specific documents |

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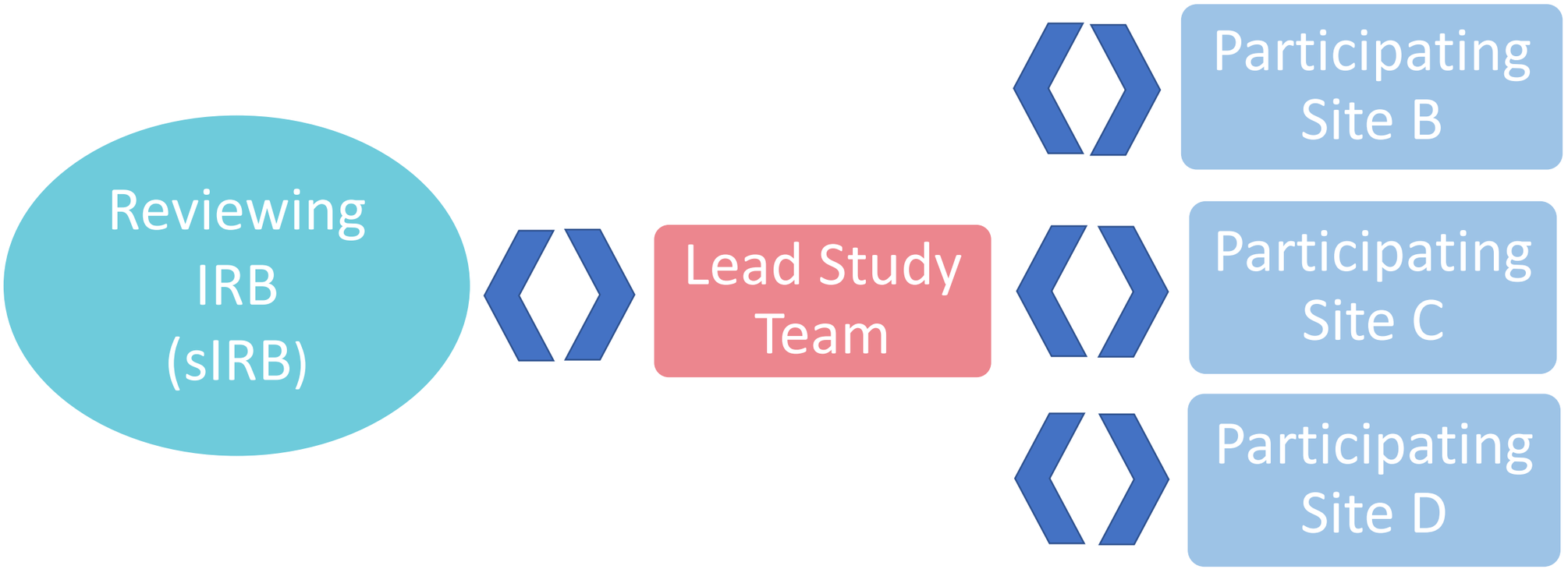
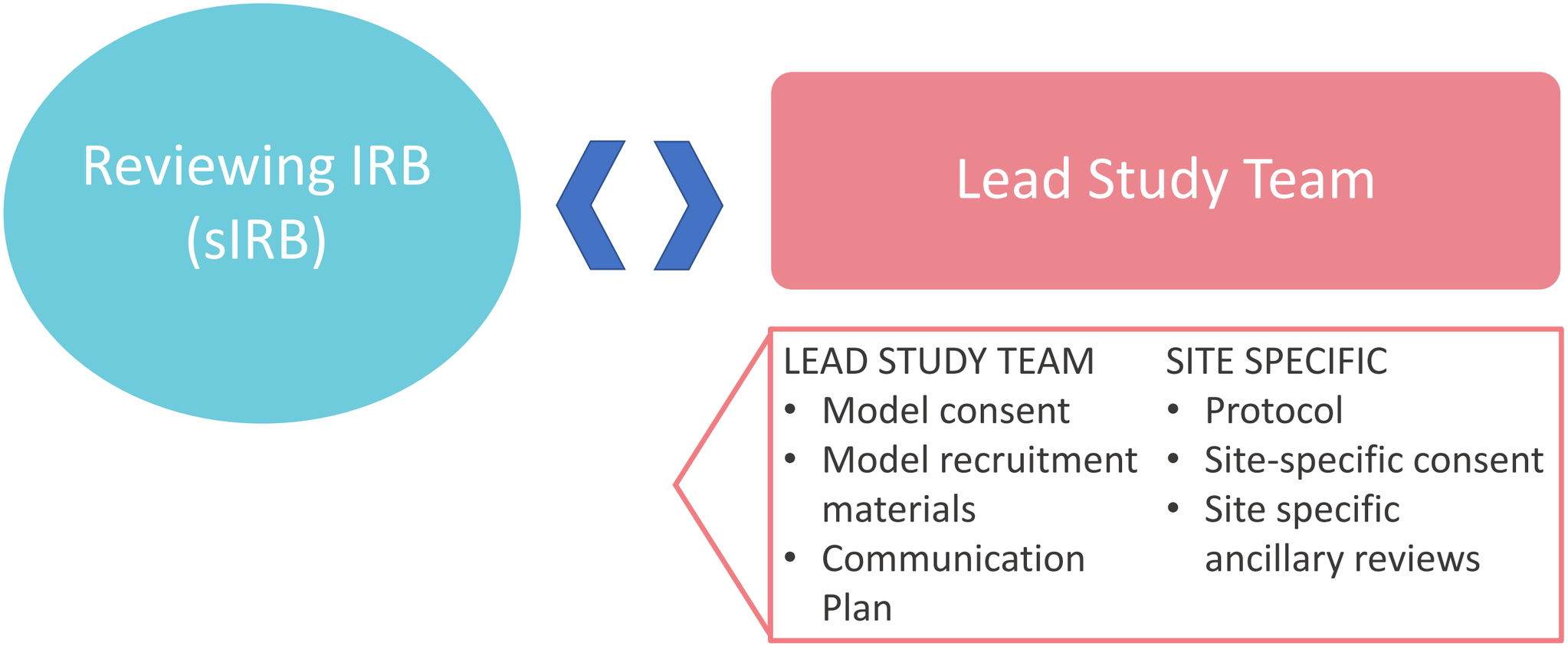
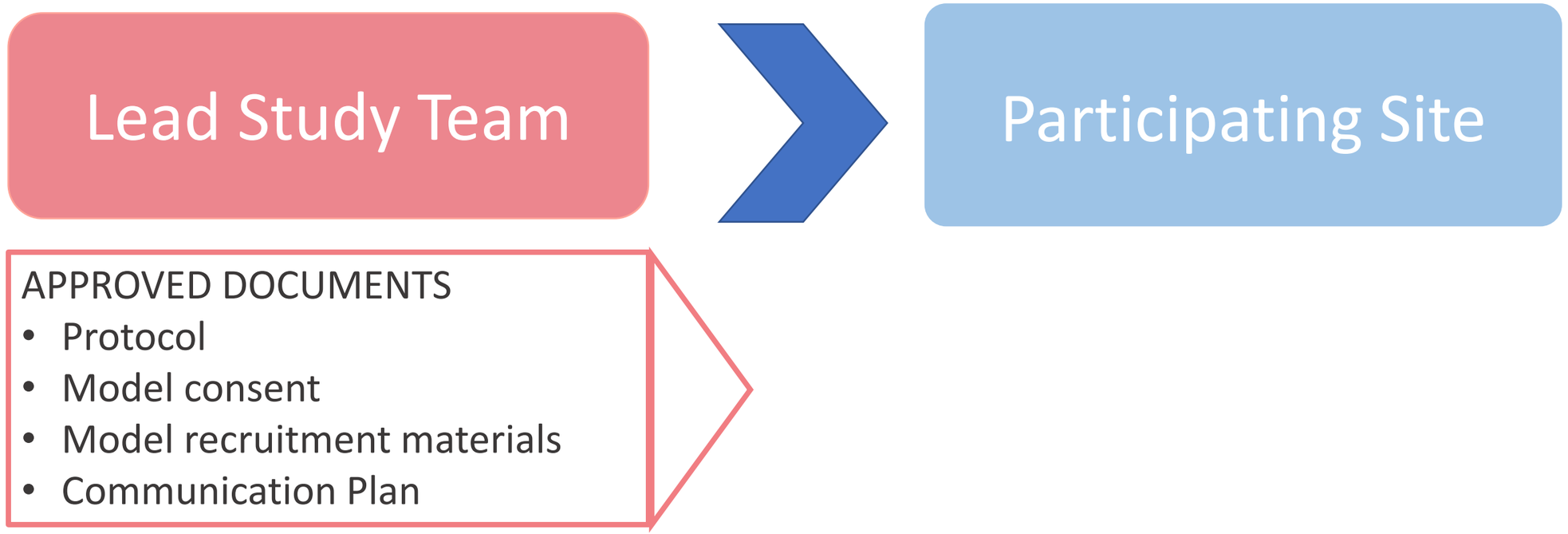
# sIRB Initial Review Submission – Overview of Two-Part Process



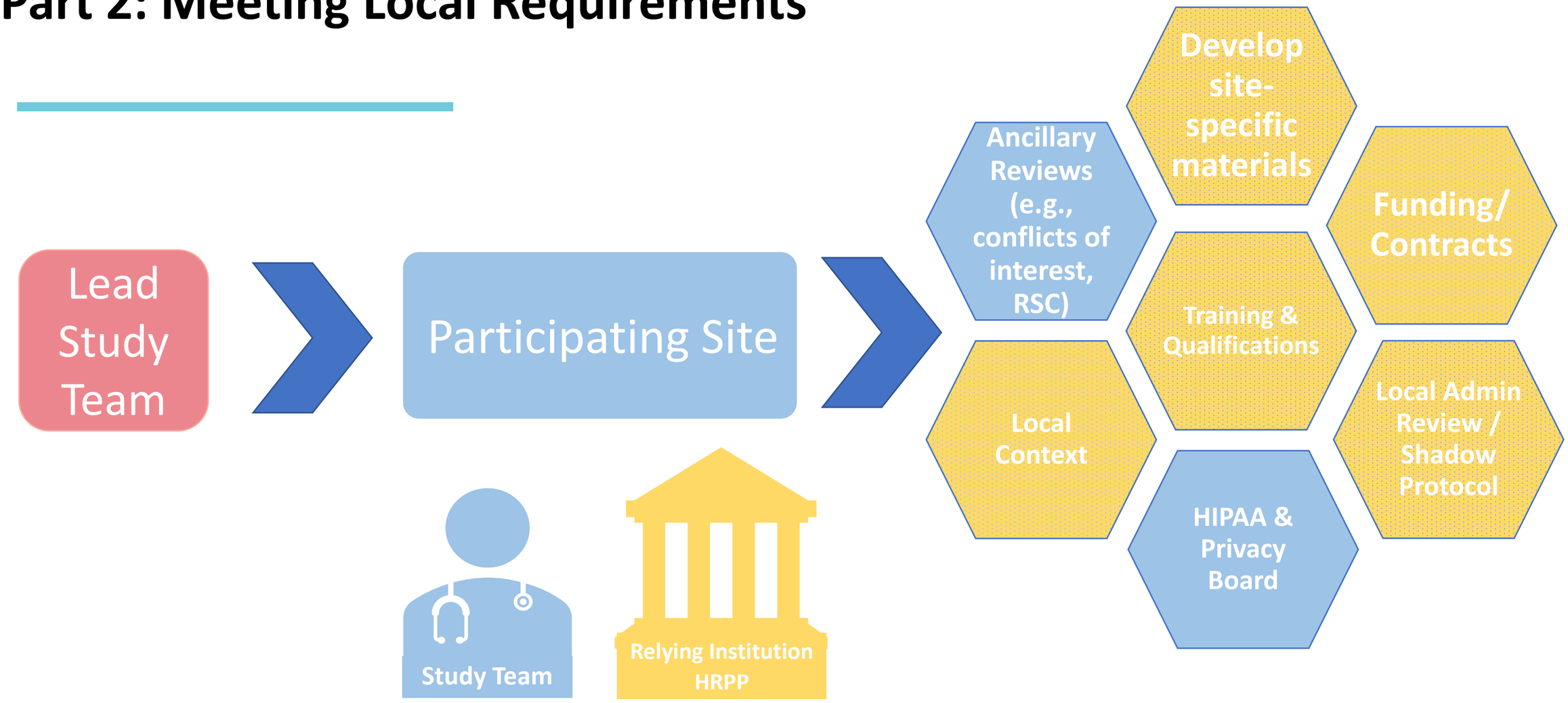
# Part 1: Lead Site Submission to the Reviewing IRB



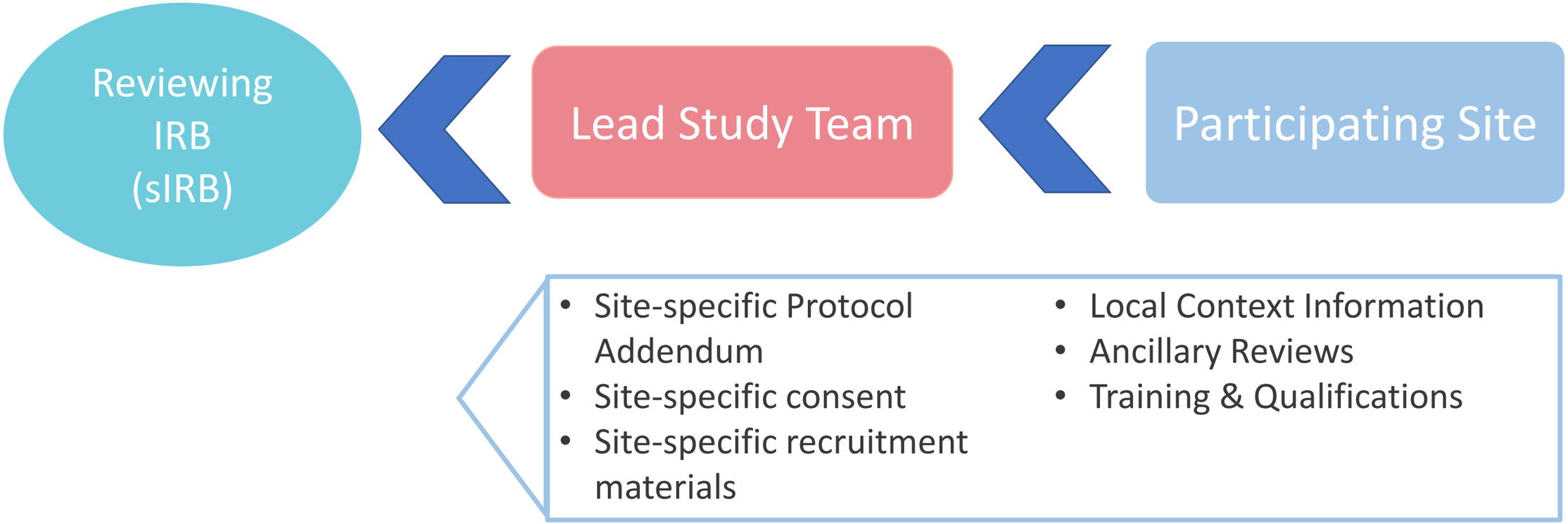
# Part 2: Process for Adding the Participating Site



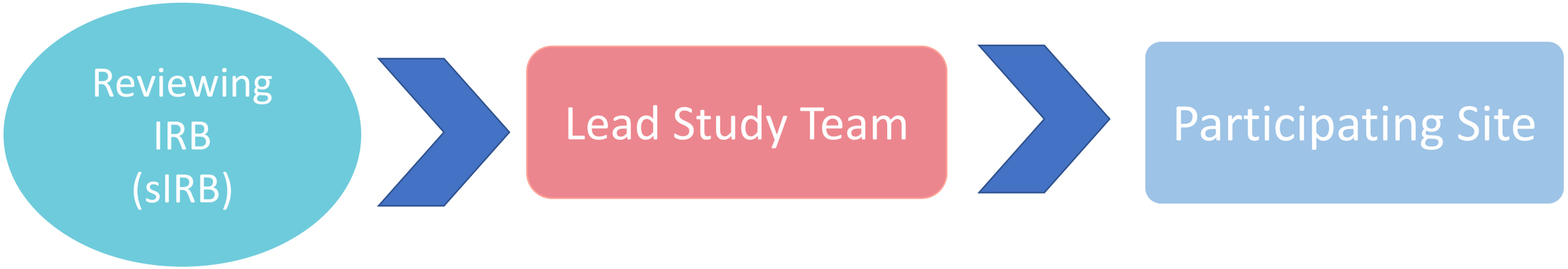
# Part 2: Meeting Local Requirements



# Part 2: Participating Site Submission to the Reviewing IRB



# Part 2: Participating Site IRB Approval




- Reviewing IRB approves all submitted documents.
- IRB issues approval determination
- Lead Study Team communicates to Participating Site.
- Participating Site approved as a site

- Approved documents may need post review at Relying Institution
- Submitted into local shadow protocol.

# sIRB Initial Review Submission Process

## Lead Study Team

- Obtain IRB review and approval of protocol and model documents
- Provide Participating Sites appropriate study documents to consider and customize
- Obtain local context information and site-specific documents from Participating Sites to submit to the Reviewing IRB
- Provide Participating Site information to the Reviewing IRB for review and approval

# sIRB Initial Review Submission Process

## Participating Site Study Team

- Customize model documents according to Participating Site policies
- Meet all local requirements, may include
  - A local administrative review
  - Creating and maintaining a Shadow Protocol
- Complete all applicable Ancillary Reviews e.g., Conflicts of Interest, RSC, Scientific Review, HIPAA etc.
- Communicate accurate local context to the Reviewing IRB via Lead Study Team/ Coordinating Center/ IRB electronic system

# sIRB Initial Review Submission Process

## Relying Institution



- Evaluate Training & Qualifications
- Assess Conflicts of Interest
- Confirm all local institutional requirements are met
- Provide institutional local context to Reviewing IRB (directly/ indirectly)
- Educate and support Participate Study Team
- Undertake institutional review – varies by institution

# sIRB Initial Review Submission Process

## Reviewing IRB

- Review and approve Lead Site and all Participating Sites according to applicable regulations and IRB policies
- Consider all local context information provided by the Participating Sites
- Communicate IRB determinations to the Lead Study Team and all Participating Sites
- Provide IRB policies and ensure adherence to them
- Protect human subjects

# Local Context

- Reviewing IRB needs to understand applicable Participating Sites policies, as well as local norms, special requirements, culture, etc. in order to conduct its review. This is called “Local Context”
- Local Context is comprised of information specific to the **Relying Institution** AND **study-specific** information about how the protocol will be implemented at that Participating Site
- Collaborative effort involving the Participating Site Study Team and HRPP/ IRB office
- Captured in forms, study documents (e.g., site-specific consents), protocol addendums, institutional profiles or policies
- Initial and on-going consideration for all parties

# Local Context

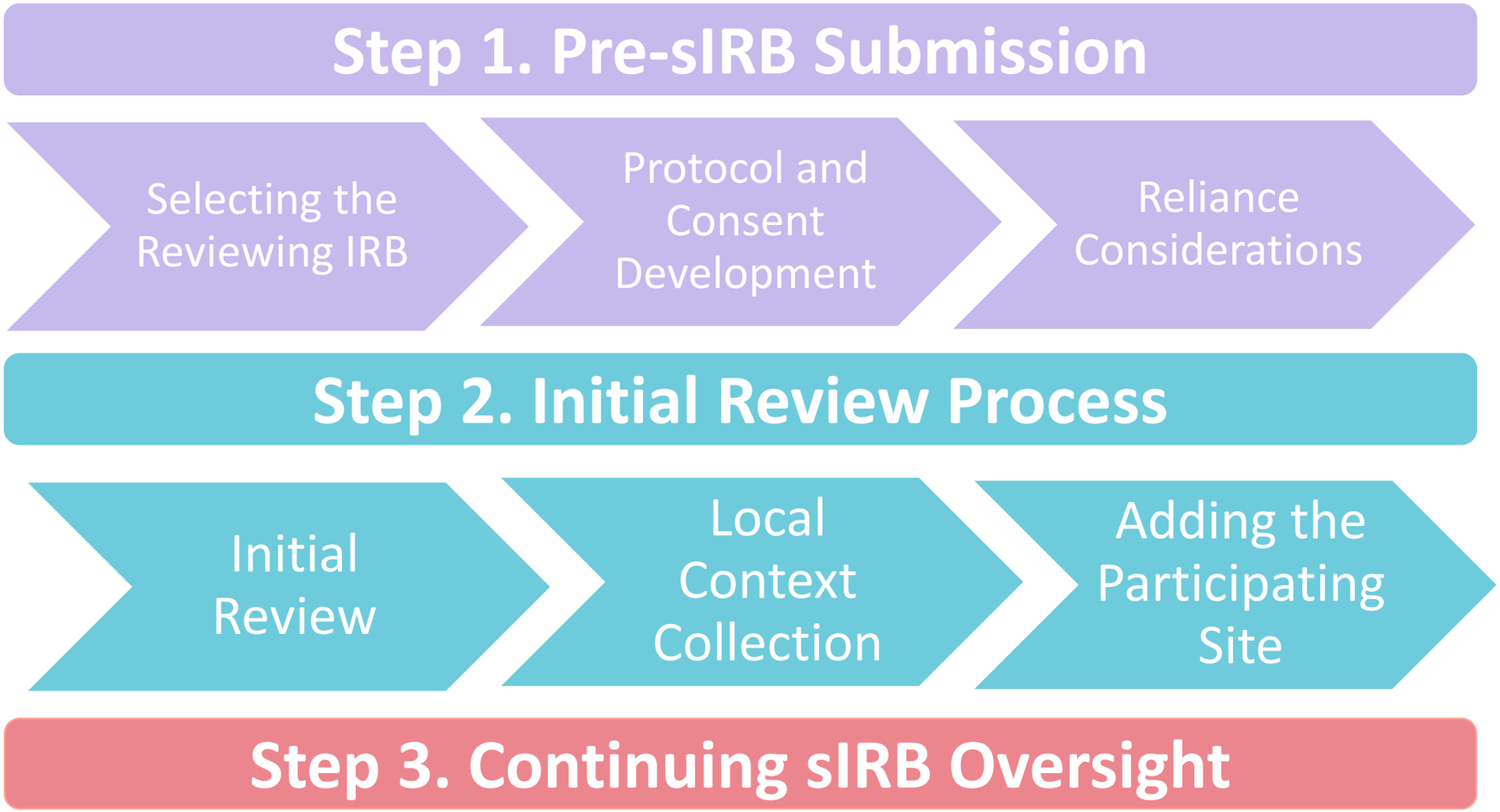
## Institutional local context may include:

- NIH is a Federal Preserve – State laws do not apply
- NIH is subject to the Privacy Act of 1974, not HIPAA
- Site X has no ER and the closest ER is 10 miles away

## Study-specific local context may include:

- Specific populations being enrolled (e.g. adults lacking capacity to give informed consent; employees and students)
- Consent Process
  - Risk level determines that consent must be obtained by physician
  - Use of short-form triggers the need to translate the long form consent
- Local expertise, special equipment, policies etc.

# Single IRB Review – The Essential Steps



# Continuing sIRB Oversight

## Lead Study Team

- Lead responsibility for submission of Amendments, Continuing Review, Event Reporting, and Closures - study-wide and at the level of individual sites
- Facilitate site-specific IRB submission
- Ensure protocol compliance and safety monitoring
- Facilitate audits
- Key communicator between the Reviewing IRB and Participating Sites
  - IRB electronic system may allow Participating Sites more direct access
  - Delegate to coordinating center
  - Additional actors may become involved e.g., Sponsor, FDA

# Continuing sIRB Oversight

## Participating Site Study Team

- Comply with the requirements of the Reviewing IRB
- Responsible for managing all non-IRB requirements at home institution for the course of the study
- Maintain communication with the Lead Study Team to ensure that have all current approvals from the IRB and are communicating all changes to the protocol, consent, conflicts of interest, and local problem reports.
- Maintain shadow protocol

# Continuing sIRB Oversight

## Relying Institution

- Work with local study team to ensure all non-IRB requirements are met and, if necessary, may require changes to site documents
- Safeguard protocol compliance by ensuring monitoring according to local policies
- Assist with addressing problem events and instances of non-compliance
- Maintain communication with the Reviewing IRB
- Maintain a shadow review – degree varies by institution

# Continuing sIRB Oversight

## Reviewing IRB

- Perform standard IRB functions to ensure continued approval of the research and the protection of participants
- Review according to applicable regulations and policies for amendments, continuing reviews and problem reports
- Ensure necessary compliance monitoring of all sites conducting the research
- Communicate with the relying HRPPs to address problem events or to consult before reporting to the regulatory bodies

# Single IRB Review – The Takeaways

- Understand your role in the multi-site research project and the applicable sIRB review process
- Once established, this will determine your responsibilities at the pre-submission phase, initial review and for the duration of the protocol lifecycle
- Study teams and their respective HRPPs need to work together to facilitate the sIRB review process
- The sIRB review process can vary significantly depending on the specific Reviewing IRB and Relying Institution – important to become aware of what is required from you in each specific instance

Join us for **What You Need to Know About Single IRB Review: Principles and Practice (Part 2)** on **August 4, 2020** when we will present how IRBO is putting these sIRB principles into practice within the NIH IRP.

# Key Terms

| TERM | DEFINITION |
| --- | --- |
| **Ceded Review** | When IRB review and oversight is transferred via a reliance agreement to another institution's IRB. "Relying Out" has the same meaning. |
| **Engagement** | An institution is engaged in human subjects research when its employees or agents either intervene or interact with living individuals for research purposes or obtain individually identifiable private information for research purposes. |
| **Reliance Agreement** | An agreement between institutions performing multi-site research that provides a mechanism to delegate IRB review, and that sets forth the authorities, roles, and responsibilities of the IRB and participating institutions. The agreement may apply to a single study or to certain categories of studies. |
| **Participating Site** | A research site involved in multi-site research. |

# Key Terms

| TERM | DEFINITION |
| --- | --- |
| **Lead Study Team** | Designated by the Lead Principal Investigator (PI) and is generally located at the Reviewing IRB's institution. Main point of contact with the Reviewing IRB and facilitates communication pathways to and from Participating Sites to include IRB submissions to the Reviewing IRB. |
| **Lead Principal Investigator** | The Overall PI or multi-site PI has ultimate responsibility for the conduct and integrity of research. This PI is usually part of the Lead Study Team. |
| **Relying Institution** | An institution participating in multi-site research that cedes IRB review to an external reviewing IRB for human subjects research consistent with the terms of a reliance agreement. |
| **Reviewing IRB** | The IRB 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, the pertinent Subparts of 21 CFR parts 50. The IRB can also be referred to as the single IRB, IRB of record or central IRB. |

# References and Helpful Links


SMART IRB. “The NIH sIRB Policy” [Powerpoint Slides]. Retrieved from https://smartirb.org/irb-admin/#adminResources where renamed Overview of the NIH Single IRB Policy for Researchers.

Johnson, A. Mumford, S. 2017. “Considerations for a Single IRB Model” [Powerpoint Slides Video]. Retrieved from https://irb.utah.edu/training/video-sirb-model.php

Final NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research

Revised Common Rule, 2018 Requirements, 45 CFR 46

OHRP Guidance Engagement of Institutions in Human Subjects Research (2008)

NIH IRBO Website

IRBO Reliance Resources

# Questions?

Submit via NIH Videocast website

# Contact Us

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