“重塑创新涅槃”- 药品和医疗器械研发临床研究质量高峰论坛

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Single IRB Review

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Agenda

- Background on Single IRBs
- Challenges to using Single IRBs
- Model reliance structures
- Considerations when ceding or conducting a review
- Experience at Duke

Duke University – Durham North Carolina

Facts and Figures

- Duke University Health System and Medical Center have 28,000 full-time employees
- Duke University School of Medicine and School of Nursing have over 1500 faculty members.
- The Duke Clinical Research Institute is the world's largest academic research organization
- Duke Health has an annual research budget in excess of $650 million FY16

Duke Health IRB

- 9 Convened Boards
- 8,000+ Active Protocols
- 15 IRB Chairs, 16 Staff Members

	FY2011	FY2012	FY2013	FY2014	FY2015	FY2016	FY2017
New Protocol Applications	1598	1642	1634	1685	1749	1888	2005
Continuing Reviews	3485	3727	3918	3992	4032	4233	4519
Amendments & Personnel Changes	9737	12544	14296	15864	16604	18646	21006

Definitions

- Single IRB: a single IRB of record overseeing multiple clinical trial sites participating in a multisite study
  - Used interchangeably with an older term, Central IRB
  - Central IRB more often refers to a commercial IRB

Background – Single IRB

- Historically, most clinical research studies were carried out at single institutions
- Increasingly, studies are being conducted at multiple sites to help increase the number and diversity of the participants, improve operational efficiencies, and accelerate the generation of research results.
- Accelerating clinical research benefits researchers, research participants, and the general public

Background – Single IRB

- IRBs play a critical role in reviewing and approving studies involving human research participants by evaluating the potential benefits of research and risks to subjects
- However, for the majority of multi-site studies, the IRB at each participating site continues to conduct an independent review.
- This review adds time, but generally does not meaningfully enhance protections for the participants.

Background – Single IRB

- US model is very de-centralized
- Local IRBs feel that they know their population best
- Nobody likes to relinquish control
- Single IRB model is still in infancy
  - Division of responsibilities is still unclear to many institutions

Current Regulations

- 45 CFR 46.111 (DHHS): Cooperative Research
  - “With the approval of the department or agency head, an institution participating in a cooperative project may enter into a joint review arrangement, rely upon the review of another qualified IRB, or make similar arrangements for duplication of effort.”

- 21 CFR 56.114 (FDA): Cooperative Research
  - “In complying with these regulations, institutions involved in multi-institutional studies may use joint review, reliance upon the review of another qualified IRB, or similar arrangements aimed at avoidance of duplication of effort.”

New U.S. Single IRB Requirements

- National Institutes of Health
  - NIH Policy on the Use of a Single IRB for Multi-Site Research sets expectation of a single IRB.
  - Goes into effect January 2018

- Common Rule
  - Any U.S. institution engaged in cooperative research must rely upon approval of a single IRB.
  - January 2020

Proposed Benefits - NIH

- Streamline the IRB review process
- Remove redundant hurdles to the initiation of multi- site studies
- Permit research to proceed effectively and expeditiously
- Reduce administrative burdens
- Enable IRBs to focus on single site protocols thereby enhancing research oversight

Overview of Responsibilities - NIH

Single IRB

- Conducts the initial and continuing reviews
- Ensure compliance with regulatory requirements
- May also act as the Privacy Board for HIPAA purposes

Participating Sites

- Rely on the Single IRB to carry out functions for institutional compliance
- Meet other regulatory obligations:
  - obtaining informed consent,
  - reporting unanticipated problems,
  - communicate relevant local context and state regulations.

Existing Models of IRB Review

- **Facilitated Review:** A shared responsibility between central and local IRB. The central IRB makes initial decisions, and then a local IRB conducts its own review.

- **Reliance Model:** SmartIRB has established a network of shared information that allows IRBs to pool resources, compare best practices, and sometimes accept each other's decisions.

Existing Models of IRB Review

- **Lead IRBs:** A model common to NIH-funded studies. In a multi-site study, the sponsor of the study authorizes one institution's IRB to oversee research in some or all of the study's other sites.

- **Consortium/Regional:** A group of research sites share IRB oversight from some unifying element such as affiliation or location. Some university networks have IRBs, as do some research centers that are in the same area.

Independent IRBs

- Independent IRBs can have review authority over one, some, or all of the sites in one protocol.
- Independent IRBs can be privately owned and these are often called commercial IRBs.
- Some independent IRBs are funded publicly. The National Cancer Institute's central IRB is now an independent IRB.

Regional IRBs

- Not very common in the US in the true sense of “regional”
- More common to see:
  - IRBs for health systems
  - IRBs for cooperative groups
  - Consortiums of IRBs
- Regional IRBs in the US can take the place of all local IRB review OR local sites can conduct an also conduct an administrative review
  - Different models: some sites have their own IRBs and cede review, others have no IRB

Regional and Network IRBs

CAROLINAS COLLABORATIVE

MARCH
MIDWEST AREA RESEARCH CONSORTIUM FOR HEALTH

The Greater Plains Collaborative (GPC)

NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY
Funded by a Grant from the National Institutes of Health

INDIAN HEALTH SERVICE · PHS · 1955 ·

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Conflicts Between Single and Local IRBs

- It is very common for local IRBs to conduct their own administrative review of studies reviewed by a Single IRB

- Different institutions have different levels of review
  - Some require a full review of all study documents
  - Others only require seeing the reliance agreement

- Poses the dilemma of conflicts between determinations of Single and Local IRBs

Pros and Cons to Single IRB Review

- Pros
  - One point of review
  - Faster process
  - More consistent study design

- Cons
  - A big cultural shift
  - Loss of local control
  - Unclear division of responsibilities
  - Retooling of IRB offices

Dealing with Conflicts of Interest

- **AAHRPP:** Either the central IRB or the referring IRB may obtain disclosure and institute management of financial conflict of interests.

  "If the relying organization maintains responsibility for this issue, any disclosure or management plan will be provided to the IRB in timely manner prior to the decision by the IRB."

- **Unsettled issue:** Does the central IRB have responsibility to seek disclosures of, and to manage, institutional conflicts of interest?

AAHRPP Accreditation Standard 1.9

Standard I-9: The organization has written policies and procedures to ensure that, when sharing oversight of research with another organization, the rights and welfare of research participants are protected.

AAHRPP Guidance

Part A: General Considerations

Organizations should define responsibilities, roles, and workflows related to Standard I.9. Suggested information for policies and procedures may include a description of:

- Required written agreements. Policies and procedures should identify which agreement terms are required, those that are negotiable, and the process for adding participating sites or additional research to existing agreements.
- The process to ensure the organization maintains a record of all research conducted by the organization
- The process for ensuring organizational compliance with the requirements of other parts of the HRPP.
- How researchers are provided information on the process to use a reviewing IRB or EC and to rely on another IRB or EC.

AAHRPP Guidance

- Part B: Role of the Reviewing IRB or EC When providing IRB or EC review services to other organizations, written materials must describe the responsibilities of the relying organizations, such as expectations for relying organizations to follow the reporting policies of the reviewing IRB or EC. The IRB or EC must be able to access sufficient information to conduct an analysis of the criteria for approval for each relying organization for all applicable studies.

Decisions for a Relying Institution

What information is needed to make a reliance decision?

- Is the institution engaged in research?
- Who is the reviewing IRB?
- What types of accreditation does the reviewing IRB maintain?
- Does the study fit the institution’s policy for reliance?

Decisions for Reviewing Institution

What considerations should be made before agreeing to serve as an IRB of record?

- Does this fulfill the institutional mission?
- How is the reviewing institution engaged?
  - Lead PI? Site?
- Is there risk to the reviewing institution?
- Does the reviewing institution have the capacity to serve as the IRB of record?

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Duke’s Experience as a sIRB

- Individual reliance agreements
- The Duke Health IRB has served as the single IRB for numerous Duke Oncology Network (DON) studies and served as the IRB for regional sites.
- In the first pilot of the SMART IRB platform, Duke Health serves as the single IRB for the CARRA Registry, involving juvenile arthritis patients.

Reliance Agreement

The legal document allowing institutions to cede/rely on each other.

- Contractual mechanism among 2 or more sites.
- Allows an institution to identify another IRB that is able to review their human subjects research.
- Establishes the division of responsibilities.
- May be specific to one study, a specific consortium or may be a master agreement.
- Master agreements are becoming the standard.

Typical Terms - Master IRB Agreement

Qualifications to join defined

- Independent assessment of site's HRPP
- Internal monitoring capability at site
- Federal Wide Assurance
- Indemnification of both parties

Relying site responsibilities

- Ensure qualifications of site study team
- Ensure compliance with IRB determinations
- Maintain institutional SOPs for conduct of research
- Adequate monitoring and QI/QA programs

IRB-of-Record responsibilities

- Conduct IRB review in accordance with all regulations and guidance
- Prompt reporting of UPIRTSOs and serious/continuing noncompliance to sites and regulatory agencies

IRB Reliance on a National Scale

Funded by NCATS: July 2016-April 2018

Harvard University, University of Wisconsin-Madison & Dartmouth College

A team of SMART IRB Ambassadors from CTSAs across the nation

Streamlined, **M**ultisite, **A**ccelerated **R**esources for **T**rials - SMARTIRB

Implement NIH Policy on the Use of a Single IRB for Multi-Site Research

JOIN

ENABLE

HARMONIZE

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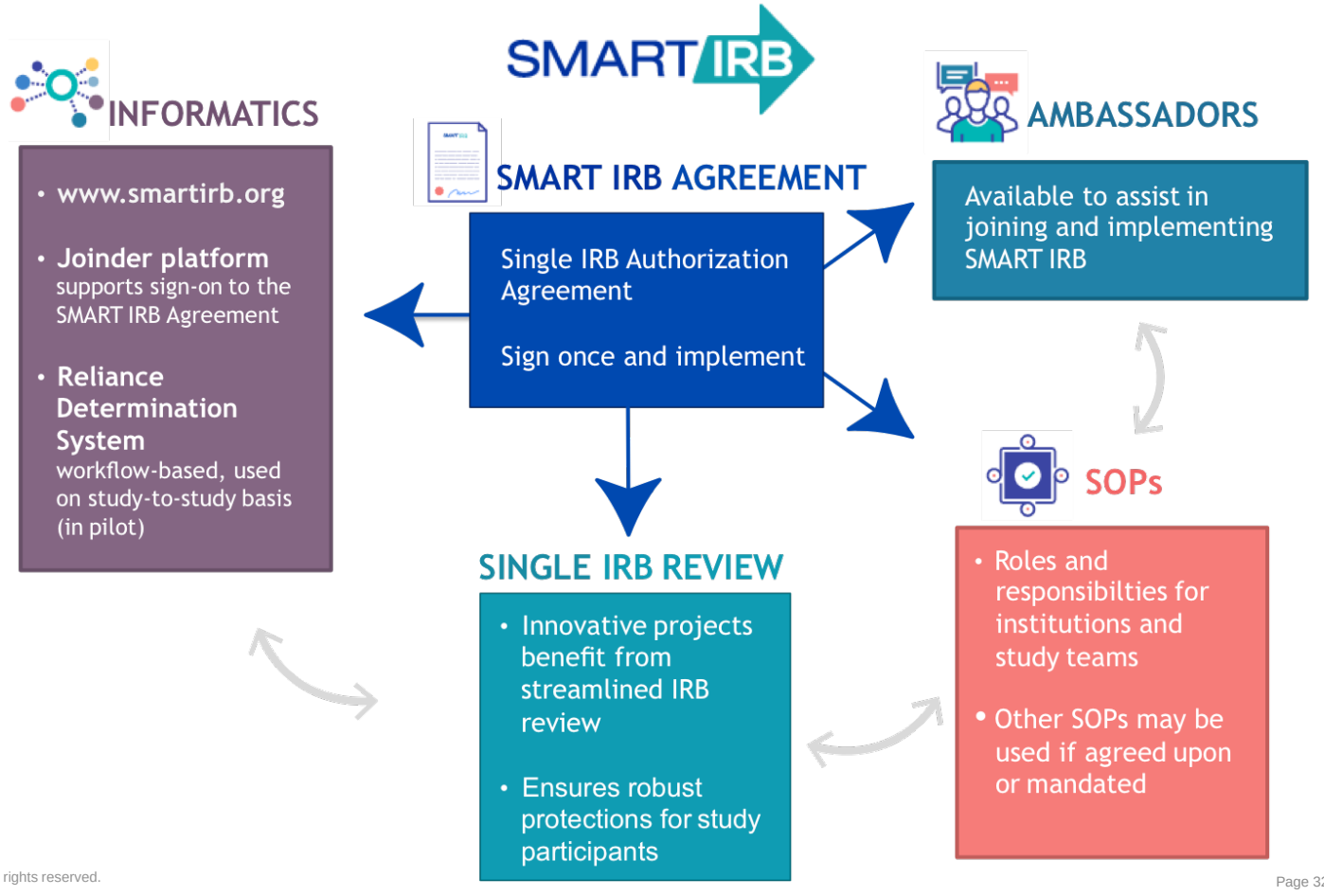
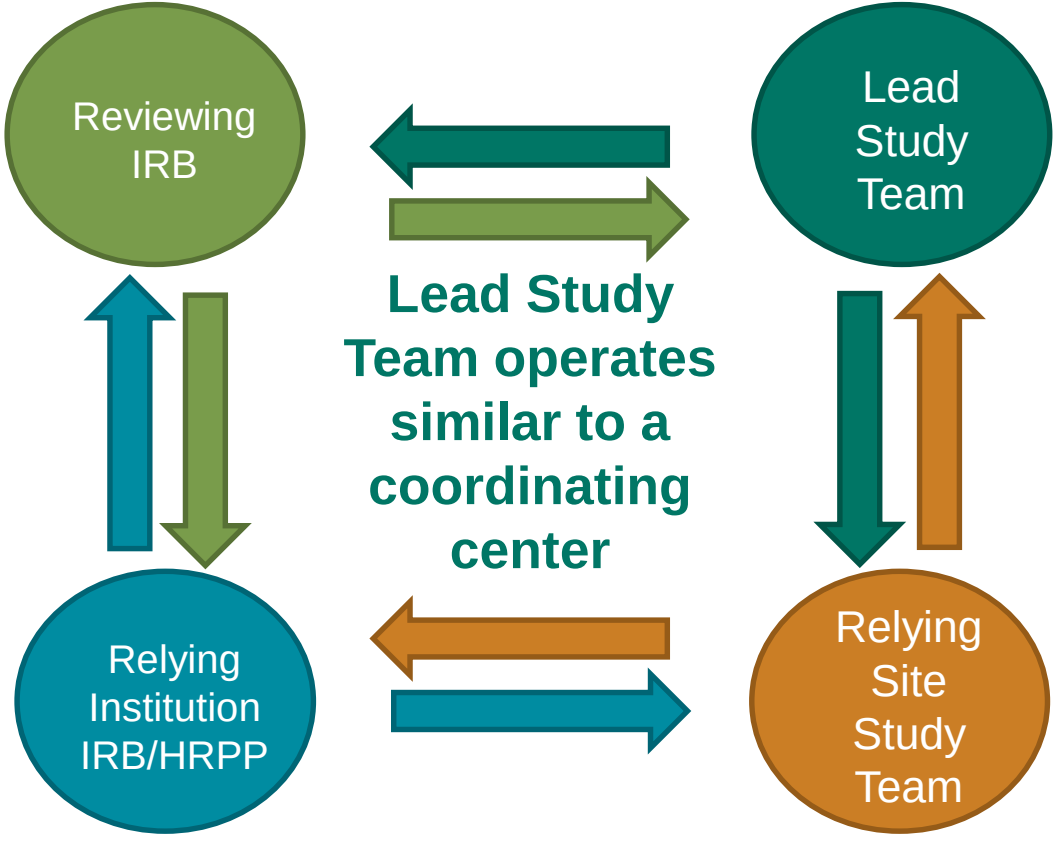
Single IRB Review on a National Scale



SMART IRB Communication Model



Key Roles in the Reliance Process

Overall PI

Home Institution Point of Contact (POC)

Reviewing IRB POC

Relying Institution POC

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Requesting Single IRB Review: Step 1

Overall PI (or designee)

Contact Overall PI's Home Institution POC to discuss a reliance arrangement, including a proposed Reviewing IRB and mechanism to request single IRB review.

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Requesting Single IRB Review: Step 2

Overall PI (or designee)

Submits a request for reliance via the SMART IRB Online Reliance System* and proposes a Reviewing IRB

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Requesting Single IRB Review: Step 3

Home Institution Point of Contact (POC)

Determines if the study is eligible for single IRB review and, if so, either confirms the proposed Reviewing IRB or proposes a new Reviewing IRB

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Requesting Single IRB Review: Step 4

Proposed Reviewing IRB POC

If PI's Home Institution will serve as Reviewing IRB, this will be the same as the Home Institution POC.

Proposed Reviewing IRB POC reviews materials and communicates to proposed Relying Institution POCs whether his/her institution will serve as the Reviewing IRB for the study.

Proposed Relying Institution POCs notified by Online Reliance System or via other mechanism

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Requesting Single IRB Review: Step 5

Proposed Relying Institution POCs

Review materials related to the request and communicate decision whether to rely on the proposed Reviewing IRB.

If agree to rely, also communicate key local context information.

Proposed Relying Institution POCs can record determination and include local context information in the Online Reliance System

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Requesting Single IRB Review: Step 6

After receiving decisions/information from other institutions, Proposed Reviewing IRB POC:

- Reviews provided local context information
- Confirms for which institutions the IRB will oversee the research
- Documents the reliance determination
- Communicates which SOPs it will follow

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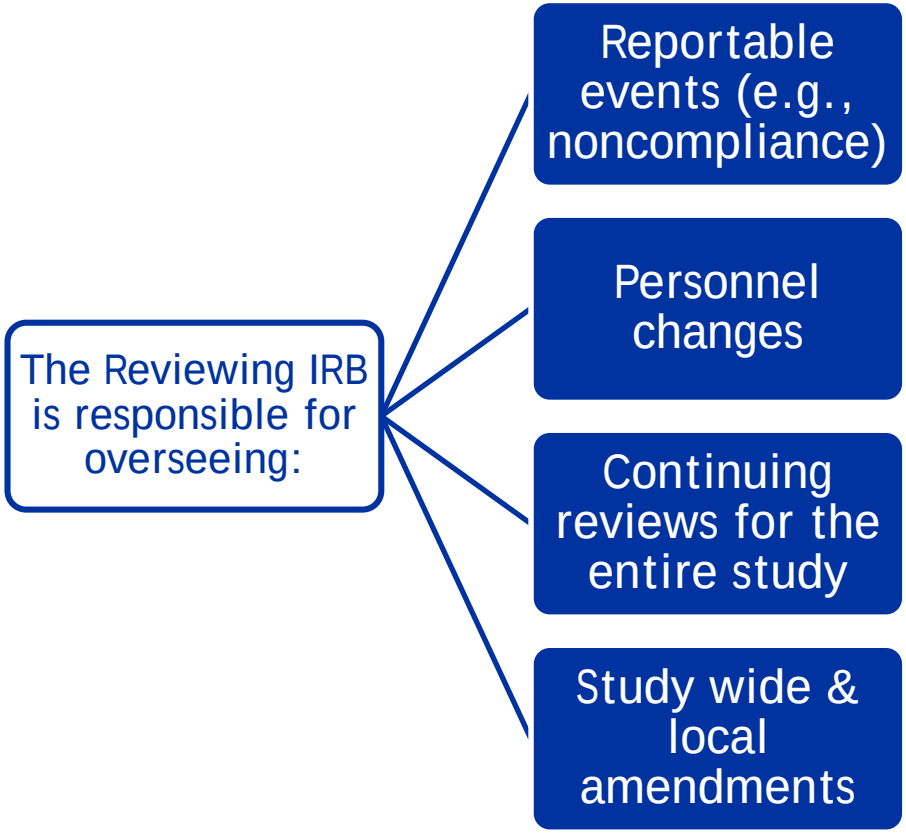
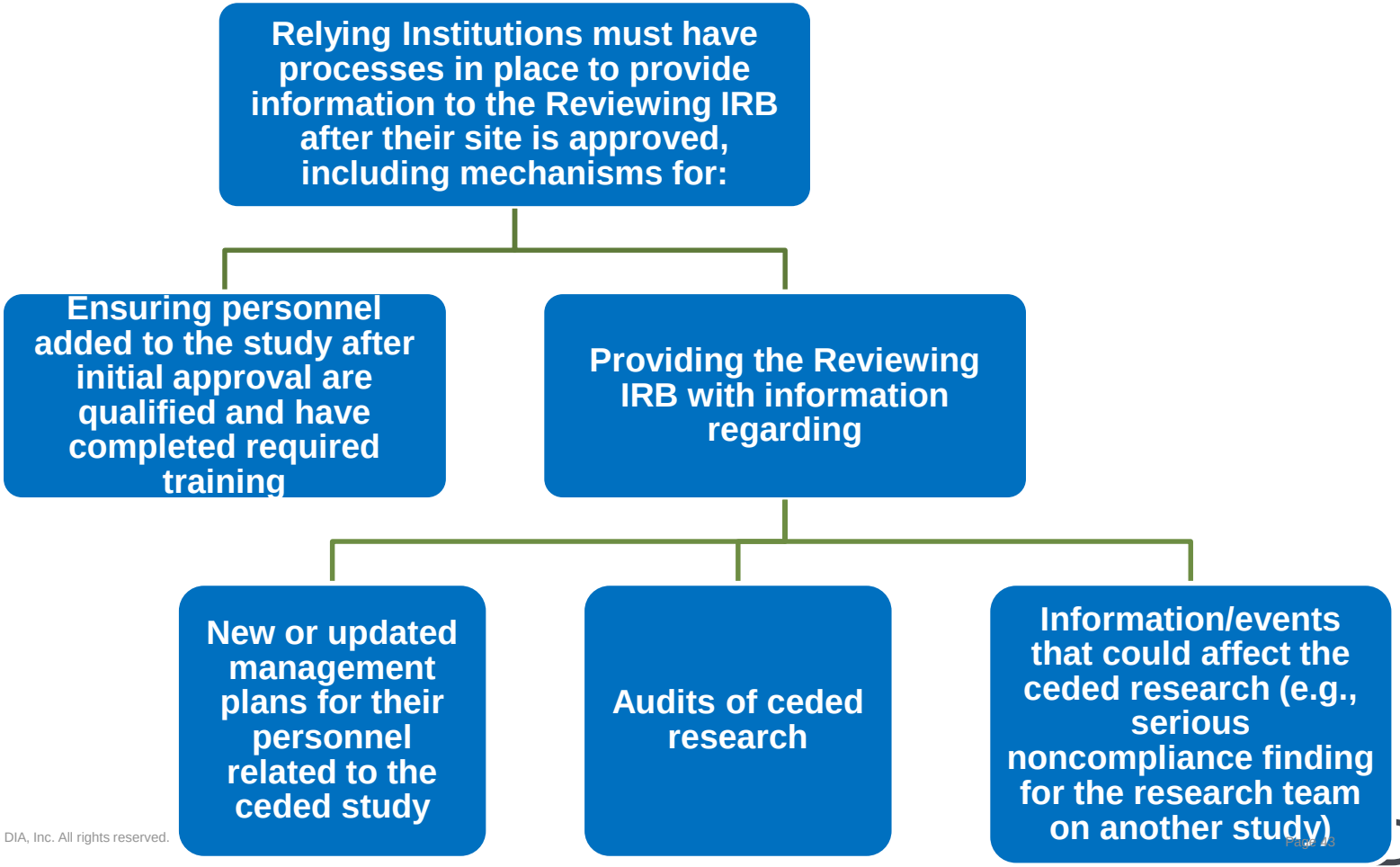
After Initial Review: Reviewing IRB



Role of Relying Site

- Relying site is often an afterthought in efforts to establish sIRB review models.
- Important to understand what is involved in getting a trial started in a larger university or academic medical center.
- Role of the relying site's HRPP in this process (may or may not need to involve the local IRB)
- Many functions that still need to be completed by the relying site…other than actual IRB review.

After Initial Review: Relying Institution



Policies – Relying Organization

- Relying organization should have policies that describe:
  - Which studies are eligible for review by another IRB
  - Ensuring that researchers have information on how to use an external IRB
  - Complying with the determinations and requirements of the reviewing IRB Notifying reviewing IRB of changes in local policies
  - Ensuring that relying organization officials cannot approve research not approved by reviewing IRB

Policies – Relying Organization

- Relying organizations researchers must follow reviewing IRB's policies
- Relying researchers must disclose conflicts of interest
- Providing local context
- Prompt reporting of any changes in research
- Ensuring that researchers will not enroll subjects prior to IRB approval
- Ensuring that researchers will obtain, document, and maintain consent
- Reporting unanticipated problems

Challenges

Relying Site

- What type of review will you do locally?
  - Will you maintain a full shadow file?
  - How will institutional reviews be conducted?
- Who assesses whether a project moves forward?
  - How will feasibility be determined?
- How will you address differences in institutional requirements?

Reviewing site

- Adequately determining all of the activities occurring at individual sites
- How will you consider local context?

Duke as a Relying Site

- Special application type in our electronic IRB system
- Used for any request to rely, regardless of type of reviewing IRB
- Investigators required to submit a full study application for administrative review
  - Protocol, consent, study-specific documents
- Collects institutional requirements
  - Training, COI

Tips for Working with Research Teams

- Set expectations
  - Single IRB review does not always mean faster
  - Study teams may struggle with different policies
  - Not all institutions have the same level of experience with single IRB review
- Agree on a template agreement

Tips for IRB Offices

- Identify specific staff members to serve as Single IRB experts
- Be sure that agreements clearly identify responsibilities
- Be clear on the communication plan
- Leverage Single IRB resources like SMART IRB

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