SMART TALK

A Community Forum to Explore Issues Surrounding Single IRB Review

Funded by the NIH National Center for Advancing Translational Sciences through its Clinical and Translational Science Awards Program, grant number 3UL1TR002541-01S1.

What Is SMART Talk?

An approximately monthly forum with:

- Presentations on topics relevant for single IRB review
- Q&A on topic presented as well as questions submitted when

Open and free to anyone with interest

Upcoming sessions

November – SMART IRB Harmonization Efforts: QA/QI

December - no SMART Talk due to PRIM&R

Future:

- Single IRB and planned emergency research
- Lessons Learned
- NIH's Approach to the Implementation of the NIH Single IRB policy

FYIs

A recording of this talk will be posted on the SMART IRB website

A link to the talk will be sent to those who registered for the talk when it is posted

If you have any questions for the panelists, please use the chat function to submit them

Today's Speakers:
Nichelle Cobb, University of Wisconsin-Madison & Director of SMART IRB Operations
Mike Linke, University of Cincinnati & StrokeNet
Carissa Minder, Washington University in St. Louis

Moderator: Polly Goodman, **SMART IRB Associate Director of Regulatory Affairs Operations**

Join us for the next
SMART Talk
November 18, 2020
2:00-3:30 pm EDT

SMART IRB Harmonization Recommendations for Study Auditing

Questions?
Contact
help@smartirb.org

Register at smartirb.org

Sign up for our mailing list to be notified of future offerings

Recommendations for Harmonization of Single IRB Continuing Review Processes

Nichelle Cobb, SMART IRB & University of Wisconsin-Madison
Carissa Minder, Washington University in St Louis
Mike Linke, University of Cincinnati & StrokeNet

Continuing Review
Working Group Membership

- John Baumann, Ambassador + Indiana University
- Nichelle Cobb, Ambassador + University of Wisconsin-Madison (Co-Lead)
- Stacey Goretzka, Ambassador + Medical University of South Carolina
- Mike Linke, StrokeNet, University of Cincinnati
- Carissa Minder, Washington University of St. Louis (Co-Lead)
- Ada Sue Selwitz, Ambassador + University of Kentucky
- Kim Summers, University of Texas Health Sciences Center at San Antonio

Continuing Review Charge

Identify, propose and harmonize best practices for continuing review requirements, taking into consideration the revisions to the Common Rule.

Basis of Working Group Recommendations

Acknowledged that the Common Rule and FDA regulations do not describe what a continuing review involves

Recommendations based on and in reaction to the OHRP and FDA guidance

The guidance make it clear that continuing review serves two purposes, which are to ensure:

- 1) the rights and welfare of research subjects continue to be protected by ensuring the research continues to meet the criteria for IRB approval; and
- 2) investigators and their study teams are in compliance with the determinations and requirements of the reviewing IRB

Cornerstones of Continuing Review

Effect of single IRB review

Identified components of continuing review affected by a single IRB arrangement, such as what information will be provided to the reviewing IRB and who provides it

- Does the reviewing IRB only need the brief project summary to describe the study progress as a whole or is it critical for the summary to capture what has occurred at each participating site?
- Who provides this information to the IRB – is it the study sponsor (if one exists), the lead investigator, each participating site, or a combination of these parties?

Overall Study vs. Site Issues

The considerations of the single reviewing IRB differ from those in multi-IRB situations because the reviewing IRB must evaluate events and other information both as they affect the overall study as well as their impact on each participation site

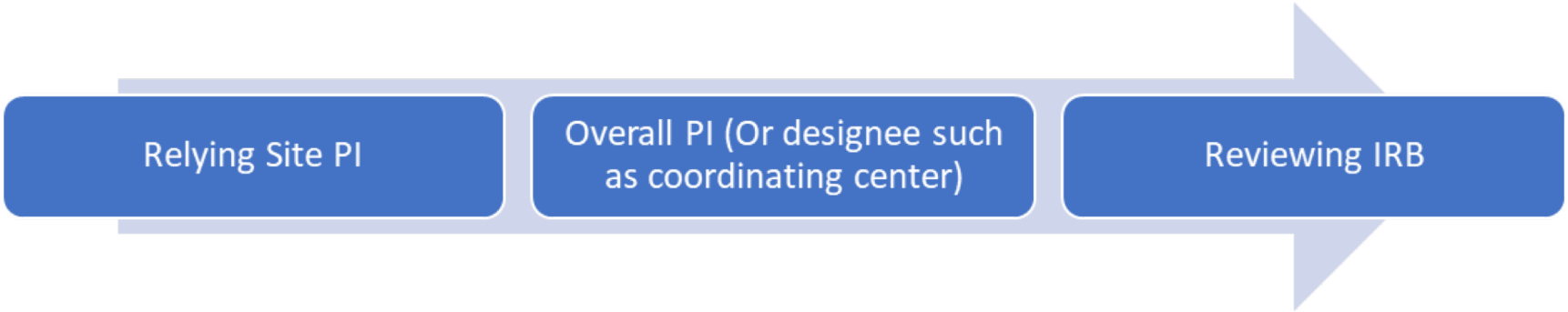
- For example, the reviewing IRB assumes responsibility for assessing how an event that occurs at one study site affects that site as well as the entire study, including what site-specific versus studywide actions may be necessary (e.g., suspending research activities at a particular site versus the entire study).

Recommendations Structure

Outlined by role

- Overall PI
- Relying site PIs
- Reviewing IRB
- Relying Institution

Recommended Flow of Information for Continuing Review



Expectation that the Overall PI assumes significant responsibility for information collection, evaluation, and dissemination at continuing review.

Overall PI Responsibilities

Collates Information

Identifies what studywide information should be collected and maintained centrally and communicates this to relying site study teams

Maintains studywide data or delegates a designee to manage and maintain studywide data (e.g., a coordinating center)

Identifies how and when participating site study teams provide their information for central data storage

Sets Expectations for Information Collection

Site PI status, qualifications, and resources to conduct the study and site study team conflicts of interest (COIs) that could affect the study

About safety monitoring

About auditing and monitoring from all sites to identify items that may need to be reported to the reviewing IRB

Assesses Information

Assess any new and relevant information, published or unpublished, that has arisen since the last IRB review, especially information about risks associated with the research.

- When a research study has a sponsor, the sponsor may provide studywide information either directly to the reviewing IRB or an Overall PI, depending on the IRB's processes.
- In the case of research without a sponsor, the Overall PI should be responsible for this activity, but may wish to obtain input from other participating investigators to ensure as complete and accurate an assessment of study risks and monitoring as possible.

Monitoring study progress & conduct

Ensures **study data provided to the designated entity in a timely manner** and are of **sufficient quality and completeness** based on the reporting requirements of the reviewing IRB
Ensures **adherence with applicable data monitoring plans** approved by the reviewing IRB
Assesses safety monitoring information to promptly address any issues identified
Assesses adverse events and other information (e.g., protocol deviations) to **identify potential changes in risks** to subjects based on the frequency or severity of the events
Identifies and communicates to the reviewing IRB any **data reporting or other issues that could affect study progress**
Assesses **whether reports contain information that may need to be reported to the reviewing IRB or require other action** (e.g., halting enrollment at a site, investigation of a site deviation, corrective action plan)
Ensures the **plan** the reviewing IRB approved **for equitable subject selection** (e.g., number of subjects as well as subject demographics) is **being followed**

Relying Site PI Responsibilities

Provides information to the Overall PI

The number of withdrawals and the reason for these withdrawals

A description of subject complaints that could not be resolved by their study team or their home institution

The status of each enrolled subject (e.g., active, in follow up, completed, withdrawn)

Provide study data in a timely manner

Can Provide Attestation That…

All events the reviewing IRB requires to be reported have been submitted to the Overall PI previously

No material changes have been made at that site without prior IRB approval unless to avoid an apparent immediate hazard to subjects

Any changes in their situation and qualifications would not adversely affect their participation in the study

There are no changes in the acceptability of the proposed research in terms of their institution's commitments and applicable regulations, State and local law, or standards of professional conduct or practice

There have been no changes in the COI status or management plans for personnel added to or removed from the study at that site

There are no updates to funding at that site

Reviewing IRB Responsibilities

Setting Expectations

Informing the Overall PI of their requirements for continuing review submissions, including when reports should be submitted, content of reports, and who should communicate the information to the reviewing IRB

Expiration Dates

Determining the appropriate expiration date for the overall study

Assigning the same expiration date for all sites regardless of when the individual sites obtain IRB approval

Study Status

To identify when a study may qualify for an expedited or excused from continuing review, at minimum whether:

- Some or all sites have ongoing participant enrollment
- Enrollment is complete, but study interventions are ongoing
- Study activities are limited to long-term follow-up of participants at some or all sites or
- Enrollment is closed, study interventions complete, and study activities are limited to data analysis

Study Progress

Information about studywide progress

Overall enrollment of the study including withdrawals and reasons for them

Risk Assessment

- Data safety monitoring reports or safety monitoring information to ensure the approved safety monitoring plan is being followed and that any designated DSMB/DMC has determined the research is appropriate to continue or that the review conducted as part of the IRB-approved data monitoring plan has not uncovered any concerns
- A summary of any new and relevant information, published or unpublished, that has arisen since the last IRB review (i.e., initial review or the prior continuing review, whichever was more recent)

Informed consent

Compliance assessment

- Confirming that all study teams are using the most recently approved version(s) of the informed consent document(s)

New information assessment

- Ensuring that any new and relevant information provided at continuing review is reflected in informed the consent document(s), requesting revisions to informed consent documents as needed and, if changes to consent document are necessary, determining which subjects must informed of the new information

Institutional & Investigator Issues

Obtaining Attestation That…	
	All events the reviewing IRB requires to be reported have been submitted previously
	No material changes have been made without prior IRB approval unless to avoid an apparent immediate hazard to subjects
	None of the participating investigators' situations or qualifications have changed such that the change would adversely affect their participation in the study
	There are no changes in the acceptability of the proposed research for each of the participating sites in terms of institutional commitments and applicable regulations, State and local law, or standards of professional conduct or practice
	No changes in COI status or management plans have occurred for personnel added to or removed from the study
	There are no updates to funding (which can affect the regulations applied to a study)

Relying Institution Responsibilities

Compliance

Ensuring their study teams comply with reviewing IRB requirements for continuing review

Issues Debated by the Working Group

No Continuing Review Situations

Declined to make recommendations about

Processes institutions may put in place in the absence of continuing review	When a continuing might be assigned even if not required under the regulations

When to obtain documents or summaries from investigators

OHRP/FDA guidance recommends IRBs obtain

- Summaries of any amendments to the research approved by the IRB since the IRB's initial review or the last continuing review
- Summaries of any unanticipated problems and available information regarding adverse events
- The latest version of the IRB-approved protocol and sample informed consent document(s)

The Working Group discussed when and why such summaries or documents would be needed, especially when IRBs should have these documents in their files/systems

Also reluctant to recommend a summary of AEs, especially when a DSMB/DMC in place or when AEs are not unanticipated problems

Implementing these recommendations

Proposed Changes to StrokeNet Process

Event Reporting

- Currently- events that occur during the reporting period that do not require prompt reporting are submitted at the time of CR
- Recommendation
  - Not require reporting of these events
  - Reviewed as part of the safety monitoring plan

Proposed Changes to StrokeNet Process

- Informed Consent Document Verification
  - Currently - each site is required to submit a copy of the last de-identified ICD at the time of CR
  - Recommendation
    - Not require submission of the last deidentified ICD
    - NDMC consent monitoring process

Proposed Changes to StrokeNet Process

- Equitable subject selection
  - Currently - gender and ethnicity category is submitted for each site at the time of CR
  - Recommendation –
    - Not collect this information
    - StrokeNet process ensures there is equitable subject selection

Discussion & Questions

Ada Sue Selwitz, University of Kentucky
John Baumann, Indiana University
Kim Summers, UTHSCSA