Cede Review: Navigating the World of Single IRB

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Ceding Review and SMART IRB

Learning Objectives

- Understand ceding IRB review to a Single IRB and when it is used
- Identify the procedures involved in the cede review process
- Compare the responsibilities for each institution participating in ceded research

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What is “cede review?”

- Ceding, or “relying” is when an institution agrees to use an IRB outside their institution to oversee a research study(ies)
  - “Relying” Institution cedes to the “Reviewing” Institution

- Different types of IRBs can be the Reviewing IRB
  - Other academic institutions involved in the study
  - Consortium “central” IRBs
  - Commercial IRBs

What is “cede review?”

- Why would an institution want to cede review?
  - To increase efficiency of the IRB review process
    - Only one IRB needs to conduct ethical review of the protocol/consent
    - Relying site might only involved in certain aspects of the study
  - To obtain leverage in requesting protocol or consent changes
  - Because the Institution *has* to cede to a sIRB in order to participate

What is “cede review?”

- What responsibilities does the Relying Institution cede?

This will be discussed in more detail later, but some examples:

  - The ethical review under 45 CFR 46 (“Common Rule”) and, when applicable, 21 CFR 50 and 56 (FDA regulations)
  - In certain cases, Privacy Board review (HIPAA)

What is “cede review?”

- What responsibilities does the Relying Institution retain?:

This will be discussed in more detail later, but some examples:

  - Local context issues
  - Study personnel
  - Facilitating ancillary review processes

What studies are most commonly ceded?

- Federally-supported (HHS), multi-site, non-exempt studies

Why?

Single IRB Regulations

- NIH Single IRB Policy for Multi-Site or Cooperative Research
  - Draft Single IRB (sIRB) policy published for public comments in December 2014
  - 167 comments received
    - Researchers, scientific and professional societies, patient advocacy groups generally supportive
      - Reduce unnecessary delays and additional costs caused by duplicative IRB reviews
      - Reduce inconsistencies in protocols/consents across sites
      - Could speed up recruitment
    - Academic institutions and IRBs cited concerns related to local context, recruitment and retention strategies, etc, and would prefer incentivizing sIRB
  - Final NIH Single IRB Review Policy published in June 2016

Single IRB Regulations

- NIH Single IRB Policy for Multi-Site or Cooperative Research

Applies to NIH-supported research involving:

- multiple domestic sites, and
- each site conducts the same protocol, and
- Involves non-exempt human subjects research

Single IRB Regulations

- Common Rule “Cooperative Research” 45 CFR 46.114
  - Revised Common Rule took effect January 2019
    - Federal Policy for the Protection of Human Subjects (“the Common Rule”)
    - Applies to all HHS-supported research
  - Compliance with the single IRB mandate for cooperative research, as outlined in the revised, is required as of January 20, 2020

Single IRB Regulations

- Common Rule “Cooperative Research” 45 CFR 46.114

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.

(2) The following research is not subject to this provision:

(i) Cooperative research for which more than single IRB review is required by law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe); or

(ii) Research for which any Federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate for the particular context.

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What is needed to Cede Review?

- Most institutions have an internal “cede review” process
  - For example, at BMC/BUMC, we have a short cede application
    - Later we will discuss what this process can involve at different sites
    - This helps institutions determine whether we agree to cede (or in some cases conduct the study at all)

What is needed to Cede Review?

- In order to enter into a sIRB arrangement, a reliance agreement is needed.
  - A formal, written document that provides a mechanism for an institution engaged in research to delegate institutional review board (IRB) review to an external institution.
  - Institutions that are engaged in human subjects research, where one institution will rely on the other institution's IRB, must agree to the terms of the Reliance Agreement before research can begin.

Reliance agreements are now most commonly done through SMART IRB.

What is SMART IRB?

SMART IRB is a *platform* (**not an IRB**) that enables IRB reliance among institutions who agree to collaborate under a pre-signed master SMART IRB global reliance agreement.

- Online system
- Paper forms
- Resources for researchers and IRBs/HRPPs

What is SMART IRB?

The SMART IRB agreement is a national **master agreement** that allows institutions to avoid having to negotiate individual agreements per study or group of studies.

- The agreement lays out the responsibilities of the Relying and Reviewing Institutions

BMC/BUMC, UVM, MUSC, and UF have all signed onto the SMART IRB agreement.

More information about SMART IRB is at https://smartirb.org and a list of institutions that have signed onto the agreement is at https://smartirb.org/participating-institutions/.

What is needed to Cede Review?

- Involve the local IRB early in the process
  - May or may not agree to cede:
    - Risk level
    - Local context issues
    - PI qualifications
    - Available resources

What is needed to Cede Review?

- As noted earlier, many IRBs have an initial cede review process
  - Ancillary department routing
  - Local IRB review processes
- You also have a ‘site approval’ process with the Reviewing IRB
- Post-approval, you still have some reporting responsibilities to both IRBs

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When ceding review – what local policies must the study adhere to?

DIFFERENCES BETWEEN INSTITUTIONS

Local Institutional Committee Reviews

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Facilitated Review –

a UVM committee member will review the proposed protocol to be ceded when the interventions are deemed to be ***more than minimal risk***, increased complexity of protocol, local context issues, or compliance history of the local PI

UVM will cede the function of the privacy board review to the single IRB unless the reviewing IRB does not want to be the privacy board

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Chair/Vice chair Review –

will review state and institutional regulatory requirements. Every ceded submission regardless of risk level will be reviewed to assess these issues.

They recommend to the IO if ceding is recommended/appropriate.

UF will cede the function of the privacy board review to the single IRB unless the reviewing IRB does not want to be the privacy board

BOSTON UNIVERSITY

Chair Review –

will evaluate the submission to assess whether it is appropriate given the local context for the conduct of research at Boston Medical Center and BU Medical Campus.

IRB Reliance Specialist and IRB Analyst review **review state and institutional regulatory requirements regardless of risk level**

BUMC continues to make all determinations that the study meets the requirements for waivers of HIPAA authorization for recruitment

MUSC

Chair or Designee –

The Chair and/or Designee will review the proposed protocol to be ceded and evaluate the submission including local context issues.

IRB Reliance Manager and IRB Reliance Administrator review state and institutional regulatory requirements.

MUSC will cede the function of the privacy board review to the single IRB unless the reviewing IRB does not want to be the privacy board

Congrats! Your local IRB has agreed to rely on another IRB

Local protections can occur in the form of:

- Conflict of interest reviews
- Local consent language changes
- Overseeing study team training
- Adherence to local state laws and policies
- Applying safety and facility reviews
- Monitoring the conduct of local research activities

Local Ancillary Reviews

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- Radiation Safety Committee
- Institutional Biosafety Committee
- Scientific Advisory Committee
- Investigational Pharmacy
- Billing Compliance
- Cancer Center
- Contracts
- Invoices
- Data management Office – Privacy

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- Conflict of Interest
- Billing and Compliance,
- ClinicalTrials.gov
- Cancer Center scientific review
- COVID Committee
- IBC
- Radiation safety
- Environmental Health and Safety
- International Research
- Privacy
- CTSI

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- Institutional Biosafety Committee
- Department Chair
- Investigational Pharmacy
- Chief Medical Officer
- Perinatal Research Committee
- GCRU
- Clinical Trials Office
- Radiology
- Investigational Pharmacy
- Radiation Safety Committee
- Pathology/Lab Medicine
- Others

MUSC

- Institutional Biosafety Committee
- Department Chair
- Investigational Pharmacy
- OCR-PRA
- Radiation Safety Committee
- Investigational Pharmacy
- Radiation Safety Committee
- ORSP
- Protocol Review Committee
- Conflict of Interest
- Others

Amendments

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Changes in PI or Key Personnel Protocol changes which affect required consent language Change affecting a local ancillary review	Changes in PI or Study staff Change affecting a local ancillary review Changes affecting local context review/state laws and university policies (e.g. recruitment, pregnancy testing in minors for research only, etc)	Changes in PI or Key Personnel Protocol changes which affect required consent language Change affecting a local ancillary review Change affecting local HRPP policy (LARs, Non-English speakers, LIPs in consent, etc)	Changes in PI or Key Personnel Protocol changes which affect required consent language Change affecting a local ancillary review Change affecting local HRPP policy and/or local context/state laws

Continuing Reviews

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No continuing review forms required when ceding review to another institution.	PI will only submit to UF the approval letter for CR from sIRB, updated protocol, and Informed Consent Form(s). Frequency of this "check in" is determined by the review type/regulatory status of the study as determined by sIRB. If the study is reviewed as expedited at the IRB of record, the UF PI will submit a "CR activity" every 3 years indicating that the study is still ongoing or closing the study. (status report)	Brief status check-in required every 3 years to indicate whether the study is still ongoing or should be closed. This also gives the IRB the opportunity to check that study personnel training is still valid.	Brief status update required every year to indicate whether the study is still ongoing or should be closed. Personnel training and COI is checked during this status update

Reportable Events

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- local serious or continuing noncompliance,
- local unanticipated problems, that are unexpected, related or possibly related to participation in the research and suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized

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- local serious or continuing noncompliance,
- local unanticipated problems, or
- local adverse events that are serious, unexpected, and related or more likely than not related to the study interventions.

BOSTON UNIVERSITY

- local unanticipated problems, that are unexpected, related or possibly related to participation in the research and suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized and involve harm to a local subject

MUSC

- Report to the IRB of Record
  - any unanticipated problems involving risks to participants or others according to the IRB's reporting policy
  - any non-compliance or protocol deviations according to the IRB's reporting policy.
- Report to the IRB of Record as well as the MUSC IRB any complaints from a subject or other person regarding the research.

Which policies to follow?

- Examples of differing definitions related to deviations

IRB	Policy
IRB 1	A protocol deviation is any variance from the protocol involving a subject or subjects that is not approved by the IRB….The PI must submit all protocol deviations that occur during the course of a study to the IRB immediately upon discovering them and no later than 10 working days following the discovery….
IRB 2	Major deviations are deviations that may 1) harm the participant's rights, safety or well-being, 2) significantly damage the overall reliability of the study data or 3) …. Major deviations must be reported to the IRB within 7 days of the investigator or research staff becoming aware of the event.
IRB 3	Things that need to be promptly reported: New or increased risk; Protocol deviation that harmed a participant or placed participant at risk of harm; Protocol deviation made without prior IRB approval to eliminate an immediate hazard to a participant; Audit, inspection, or inquiry by a federal agency; Written reports of federal agencies (e.g., FDA Form 483); Allegation of Noncompliance or Finding of Noncompliance; Breach of confidentiality; Unresolved participant complaint; Suspension or premature termination by the sponsor, investigator, or institution; Incarceration of a participant in a research study not approved to involve prisoners; Adverse events or IND safety reports that require a change to the protocol or consent; State Medical Board actions; Unanticipated adverse device effects; Information where the sponsor requires prompt reporting to the IRB. Information not listed above does not require prompt reporting to xxxxxx IRB.

Which policies to follow?

- Examples of differing policies on enrolling limited/non-readers

Reviewing IRB (External, or IRB of Record)	Relying IRB (local IRB)
When a person cannot read the consent form, the entire consent form may be provided as an audio recording that the person can listen to, in an electronic format that the computer can read to the person or, for persons who are visually impaired and able to read Braille, in Braille… When the consent form is provided in these formats, the investigator or person obtaining informed consent should confirm that the subject listened to the audio version or electronic consent form, or read the Braille consent form when they begin the consent discussion and provide an opportunity to review the information and ask questions. When following ICH-GCP (E6) guidance, if a participant or their legally authorized representative is unable to read, an impartial witness should be present during the entire informed consent discussion.	Unless the exclusion of limited- and non-readers is determined to be justified by the IRB, studies that are greater than minimal risk must either include a plan to have an impartial witness who is present throughout the consent process or propose some other method, such as a quiz or a “teach-back” process, to ensure comprehension. This latter approach can be used when consent is obtained just from limited- or non-readers, or can be used for all subjects. If the research is being performed according to the standards of the International Conference on Harmonisation – Good Clinical Practices, an impartial witness is required for obtaining consent from limited- and non-readers.

GROUP DISCUSSION

Your institution has ceded review and is participating in an NIH funded multi-site protocol. Your local PI has recently retired, and a new local PI has been identified.

Which IRB needs notification of the Change?

A. The REVIEWING IRB needs notification

B. The RELYING IRB needs notification

C. Both IRBs need notification

Your institution has ceded review to an external IRB participating in an NIH funded multi-site protocol. Your local PI has recently retired, and a new local PI has been identified.

Which IRB needs notification of the Change?

C. Both IRBs need notification

Your institution is participating in a multi-site study and is relying on another IRB. The lead site has issued a protocol amendment revising the protocol and consent to add additional questionnaires.

Which IRB needs notification of the Change?

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The independent DSMB releases their quarterly report which recommends continuation without changes. Which IRB needs to review?

Which IRB needs notification of the recommendation?

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The RELYING IRB needs notification

Both IRBs require notification

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Which IRB needs notification of the recommendation?

The REVIEWING IRB needs notification

You are ready to submit your summary of expected adverse events at the time of annual continuing review for a greater than minimal risk study that has an expiration date. Which IRB do you notify and submit your AEs to?

- Which IRB needs notification of the recommendation?
- The REVIEWING IRB needs notification
- The RELYING IRB needs notification
- Both IRBs require notification

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Which IRB needs notification of the recommendation?

The REVIEWING IRB needs notification

What are some of the biggest challenges your study team has faced when ceding review?

What are some best practices your study team has put into place when ceding review?

Cede Review: Institution-specific links

BU/BMC	UVM	UF	MUSC
Submission Requirements for Cede review Retained and ceded responsibilities 2.5.3.2 Requirements for Relying on another IRB 7.2.2.18 Evaluation of requests to Cede Review 10.2.3.1.1	Procedures for Relying on External IRB for Federally Funded Research	Single IRB (sIRB) POLICY: UF Single IRB (sIRB) UF sIRB Request	IRB reliance requests HRPP 9.5 Relying on an External IRB

Cede Review

Thank you!

What questions do you have?