I Have Ceded Review – Now What to Do?

MATTHEW OGRODNIK, MS, CIP
DIRECTOR, OFFICE OF HUMAN RESEARCH AFFAIRS, BOSTON MEDICAL CENTER/BOSTON UNIVERSITY MEDICAL CAMPUS

I Have Ceded Review – Now What to Do?

Learning Objectives

- Discuss the different roles and responsibilities of reviewing IRBs and relying institutions
- Learn about our BMC/BUMC HRPP Policies and Procedures for maintaining compliance when ceding
- Review case studies related to ceded responsibilities for deviations, amendments, recruitment materials, and more!

I Have Ceded Review – Now What to Do?

Learning Objectives

- Discuss the different roles and responsibilities of reviewing IRBs and relying institutions
- Learn about our BMC/BUMC HRPP Policies and Procedures for maintaining compliance when ceding
- Review case studies related to ceded responsibilities for deviations, amendments, recruitment materials, and more!

3

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

4

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

5

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

6

What studies are most commonly ceded?

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

Why?

7

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

8

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.

11

Retained and Ceded Responsibilities

- What responsibilities does the Relying Institution cede?

These will be discussed in detail, but broadly:

- 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)

12

Retained Responsibilities

- Evaluation of requests to cede review; and
- Determinations that the study meets the requirements for waivers of HIPAA authorization for research uses and disclosures of subjects' protected health information; and
- Conflict of interest reporting and evaluation: Investigators are required to report their financial interests, and BMC and BU are responsible for evaluating whether the interests constitute Financial Conflicts of Interest that require management, and if so, for communicating management plans to the reviewing IRB; and
- Reviews performed by special routing; and

Retained Responsibilities

- Monitoring research: The compliance provisions of Section 11 apply to all human subjects research conducted by BMC/BUMC investigators, including ceded research.
  - For QA Reviews, the QA Review Report will inform the study team which findings are reportable to the IRB of record
    - In addition, a summary of reportable findings will be provided to the IRB of record.
  - For targeted audits, the BMC and BUMC HRPP will notify the IRB of record of any potential noncompliance with applicable human subjects protection regulations or with the requirements or determinations of the IRB of record; and

Retained Responsibilities

- Investigator qualifications:
  - The process for ceding review includes providing training for investigators and research staff and assuring that all study staff meet the qualifications and training requirements, including personnel added to the study after initial approval; and
- Organizational conflicts of interest: BMC and BU are responsible for notifying the external IRB of any organizational conflicts of interest

15

Ceded Responsibilities

- Performing the scientific review of the protocol; and
- Ensuring concordance between any applicable grant and the protocol; and
- Reviewing potential noncompliance, including complaints, protocol deviations, and results of audits and making determinations of noncompliance according to the policies and procedures of the IRB of record; and
- Evaluating the protections provided by management plans for conflicts of interests and imposing additional requirements if necessary to protect the rights and welfare of subjects; and

16

Ceded Responsibilities

- Obtaining any additional approvals from DHHS when the research involves pregnant women, fetuses, and neonates; or children; or prisoners; and
- Reporting to regulatory agencies and sponsors concerning serious or continuing noncompliance, unanticipated problems, and suspensions or terminations of IRB approval.
  - The IRB of record is expected to provide the BMC and BUMC HRPP the opportunity to review and comment on the report before it is sent to regulatory agencies or sponsors.

17

I Have Ceded Review – Now What to Do?

Learning Objectives

- Discuss the different roles and responsibilities of reviewing IRBs and relying institutions
- Learn about our BMC/BUMC HRPP Policies and Procedures for maintaining compliance when ceding
- Review case studies related to ceded responsibilities for deviations, amendments, recruitment materials, and more!

18

I Have Ceded Review – Now What to Do?

Learning Objectives

- Discuss the different roles and responsibilities of reviewing IRBs and relying institutions
- Learn about our BMC/BUMC HRPP Policies and Procedures for maintaining compliance when ceding
- Review case studies related to ceded responsibilities for deviations, amendments, recruitment materials, and more!

19

Initial Cede Process

- Most institutions have an internal "cede review" process
  - For example, at BMC/BUMC, we have a short cede application
    - This helps institutions determine whether we agree to cede (or in some cases conduct the study at all)
    - Please see the September 2020 seminar for more information on submitting your initial cede application:

    Cede Review and You — How to Navigate this Evolving "New World" of IRB Review

20

Requirements After Initial Cede Approval

- Once the initial request to cede review has been granted, you may begin research activities.
- When the BMC and BUMC IRB has entered into a reliance agreement with another IRB that acts as the IRB of record, the Principal Investigator (PI) must comply with all reporting requirements of the IRB of record.
  - For example: deviations, AEs/SAEs, Unanticipated Problems (UPs), enrollment numbers
  - However, you are still responsible for certain reporting requirements to the relying BMC/BUMC IRB.

21

Reporting to relying BMC/BUMC IRB

- Submit Internal Study Personnel Changes to the BMC/BUMC IRB for administrative approval
  - The reviewing IRB may or may not wish to be informed about non-PI personnel changes; check with them!
- Submit Reportable Events and New Information (RENI) forms to report any UPs or changes made to eliminate an apparent immediate hazard to subjects that occur at the BMC or BUMC site ("internal Unanticipated Problems" and "internal immediate apparent hazards to subjects").
  - This requirement is in addition to required reporting to the IRB of record according to its reporting requirements for (UPs) and changes made to eliminate an apparent immediate hazard to subjects

22

Reporting to relying BMC/BUMC IRB

- Submit RENI forms to report any **serious and/or continuing noncompliance determinations made by the reviewing IRB** in relation to event(s) that occur at the BMC or BUMC site.
  - This form must be submitted to the IRB **within 7 days** of the investigator or research staff becoming aware of the reviewing IRB determination; and
- Submit a Status Check-In Report form prior to the status check-in due date
- Submit a Final Report after the IRB of record closes the study

23

Reporting to relying BMC/BUMC IRB

- Submit Change Request and Amendment forms if the proposed changes:

Affect compliance with local policies or seek to modify previously-granted policy exception requests for enrollment of:

- Decisionally-impaired subjects who require the use of Legally Authorized Representatives (see Section 9.5)
  - Policy: Who is an allowable Legally-Authorized Representative?
- Non-English speaking subjects (see Section 8.4.5)
  - Policy: minors may not be interpreters; adult family members may only be interpreters if the study does not require an interpreter with a medical background; use of the short form consent process is not allowed with prior approval by BMC/BUMC IRB
- Wards of the State (see Section 9.2.3); and
  - Policy: When may wards be enrolled? Limited- and non-readers (see Section 8.4.6); and

24

Reporting to relying BMC/BUMC IRB

- Submit Change Request and Amendment forms if the proposed changes:

Affect compliance with local policies or seek to modify previously-granted policy exception requests for enrollment of:

  - Students, trainees, and employees (see Section 9.6) and
    - Policy: adding new targeted recruitment of these groups or enrolling those who report directly to any of the investigators
  - Patients of Substance Use Disorder Clinic(s) (see Section 7.2.2.10); or
    - Policy: Use of data under 42 CFR Part 2

Reporting to relying BMC/BUMC IRB

- Submit Change Request and Amendment forms if the proposed changes:
  - Affect compliance with local policies or seek to modify previously-granted policy exception requests for individuals involved the consent discussion for studies involving drugs, devices, or surgical procedures
    - For these studies, a Licensed Independent Professional (LIP, for example, physician, dentist, physician assistant, nurse practitioner) must discuss the purpose, risks, benefits, and alternatives with potential subjects.

Reporting to relying BMC/BUMC IRB

- Submit Change Request and Amendment forms if the proposed changes:

Affect information provided regarding:

- the plan to prevent disclosure of HIV testing status to any non-Boston Medical Center research staff prior to written consent being obtained; or
- the plan to share data with a third-party vendor or software application or program; or
- recruitment procedures; or
- add new or modify existing recruitment materials; or
- affect information provided for a waiver of authorization for use and disclosure of Protected Health Information (see Section 8.5.2.2); or

Reporting to relying BMC/BUMC IRB

- Submit Change Request and Amendment forms if the proposed changes:

Affect information provided regarding:

- the plan to prevent disclosure of HIV testing status to any non-Boston Medical Center research staff prior to written consent being obtained; or
- the plan to share data with a third-party vendor or software application or program; or
- recruitment procedures;

Or if the changes involve:

- adding new or modify existing recruitment materials; or
- adding a new or modifying an existing waiver of authorization for use and disclosure of Protected Health Information (see Section 8.5.2.2); or

Reporting to relying BMC/BUMC IRB

- Submit Change Request and Amendment forms if the proposed changes:
  - Require review by a special routing individual or entity that was not involved during initial the review process (see Section 7.2.2.2); or
  - Add new or modify existing investigator or research staff Financial Conflicts of Interest as determined by Boston Medical Center/Boston University Faculty Review Committee on Research Financial Conflicts of Interest; or
  - Affect information provided regarding organizational conflicts of interest review
  - Add new study cohorts and/or new consent forms

As noted earlier, Status Check-In Reports for ceded studies will be evaluated to determine whether any information was not reported as required and whether any follow-up actions are required. A revised cede letter with the new status check-in due date will be provided via the electronic system.

29

I Have Ceded Review – Now What to Do?

Learning Objectives

- Discuss the different roles and responsibilities of reviewing IRBs and relying institutions
- Learn about our BMC/BUMC HRPP Policies and Procedures for maintaining compliance when ceding
- Review case studies related to ceded responsibilities for deviations, amendments, recruitment materials, and more!

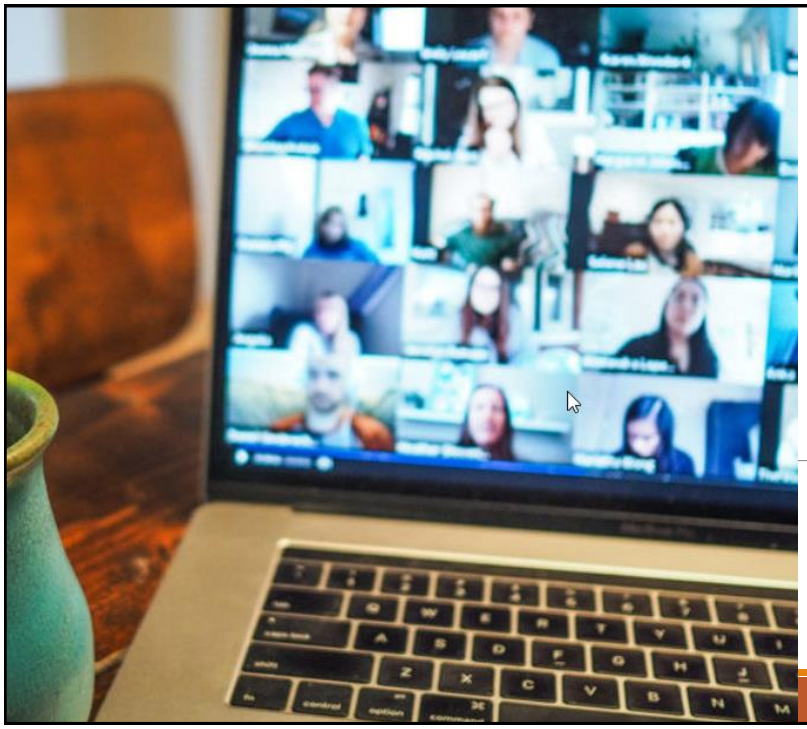
30

I Have Ceded Review – Now What to Do?

Learning Objectives

- Discuss the different roles and responsibilities of reviewing IRBs and relying institutions
- Learn about our BMC/BUMC HRPP Policies and Procedures for maintaining compliance when ceding
- Review case studies related to ceded responsibilities for deviations, amendments, recruitment materials, and more!

31



GROUP DISCUSSION

32

You are ready to submit your summary of expected adverse events at the time of Continuing Review.

Which IRB do you submit to?

A. The external REVIEWING IRB

B. The local RELYING IRB

C. Both IRB's

33

You are ready to submit your summary of expected adverse events at the time of Continuing Review.

Which IRB do you submit to?

A. The external REVIEWING IRB

B. The local RELYING IRB

C. Both IRB's

34

Your local PI has recently retired, and a new local PI has been identified.

Which IRB needs notification of the Change?

A. The external REVIEWING IRB

B. The local RELYING IRB

C. Both IRB's

35

Your local PI has recently retired, and a new local PI has been identified.

Which IRB needs notification of the Change?

A. The external REVIEWING IRB

B. The local RELYING IRB

C. Both IRB's

36

The lead site has issued a protocol amendment revising the protocol and consent to add additional questionnaires.

Which IRB needs notification of the Change?

A. The external REVIEWING IRB

B. The local RELYING IRB

C. Both IRBs

37

The lead site has issued a protocol amendment revising the protocol and consent to add additional questionnaires.

Which IRB needs notification of the Change?

A. The external REVIEWING IRB

B. The local RELYING IRB

C. Both IRBs

38

The independent DSMB releases their quarterly report which recommends continuation without changes.

Which IRB needs to review?

A. The external REVIEWING IRB

B. The local RELYING IRB

C. Both IRBs

39

The independent DSMB releases their quarterly report which recommends continuation without changes.

Which IRB needs to review?

A. The external REVIEWING IRB

B. The local RELYING IRB

C. Both IRBs

40

Enrollment into the study has been slow, and you wish to add a new recruitment method – mailing out opt-out letters to potential participants.

Which IRB needs to review the proposed change?

A. The external REVIEWING IRB

B. The local RELYING IRB

C. Both IRBs

41

Enrollment into the study has been slow, and you wish to add a new recruitment method – mailing out opt-out letters to potential participants.

Which IRB needs to review the proposed change?

A. The external REVIEWING IRB

B. The local RELYING IRB

C. Both IRBs

42

Your study undergoes a Quality Assurance review, which identifies 2 major deviations.

Which IRB needs to review these major deviations?

A. The external REVIEWING IRB

B. The local RELYING IRB

C. Both IRBs

43

Your study undergoes a Quality Assurance review, which identifies 2 major deviations.

Which IRB needs to review these major deviations?

A. The external REVIEWING IRB

B. The local RELYING IRB

C. Both IRBs

44

After reviewing the 2 major deviations, the reviewing IRB determines that 1 of the major deviations represents serious noncompliance.

Do you need to report this to the local relying IRB?

A. Yes

B. No

45

After reviewing the 2 major deviations, the reviewing IRB determines that 1 of the major deviations represents serious noncompliance.

Do you need to report this to the local relying IRB?

A. Yes

B. No

46

As your approved study is ongoing, you realize that some eligible patients speak unanticipated languages. You wish to add use of the short form consent process for unanticipated languages.

Which IRB needs to approve this change?

A. The external REVIEWING IRB

B. The local RELYING IRB

C. Both IRBs

47

As your approved study is ongoing, you realize that some eligible patients speak unanticipated languages. You wish to add use of the short form consent process for unanticipated languages.

Which IRB needs to approve this change?

A. The external REVIEWING IRB

B. The local RELYING IRB

C. Both IRBs

48

The eligibility criteria for the study are revised to increase the upper age limit. Previously, the age range was 18-50 years old, but an amendment proposes to change this to 18-60 years old.

Which IRB needs to review this proposed change?

A. The external REVIEWING IRB

B. The local RELYING IRB

C. Both IRBs

49

The eligibility criteria for the study are revised to increase the upper age limit. Previously, the age range was 18-50 years old, but an amendment proposes to change this to 18-60 years old.

Which IRB needs to review this proposed change?

A. The external REVIEWING IRB

B. The local RELYING IRB

C. Both IRBs

50

The study protocol is being revised to add a third arm – observation-only. This is for patients who do not wish to be randomized, but are willing to participate via longitudinal review of medical records. The amendment includes a new consent form to be used for enrollment into this arm.

Which IRB needs to review this proposed change?

A. The external REVIEWING IRB

B. The local RELYING IRB

C. Both IRBs

51

The study protocol is being revised to add a third arm – observation-only. This is for patients who do not wish to be randomized, but are willing to participate via longitudinal review of medical records. The amendment includes a new consent form to be used for enrollment into this arm.

Which IRB needs to review this proposed change?

A. The external REVIEWING IRB

B. The local RELYING IRB

C. Both IRBs

52

Cede Review in INSPIR

Some Helpful Links:

- Ceding Review: https://www.bumc.bu.edu/irb/submission-requirements/when-to-submit/ceding-review/
- Cede Review Resources: https://www.bumc.bu.edu/irb/submission-requirements/when-to-submit/ceding-review/cede-review-resources/

53

Cede Review

Thank you!

What questions do you have?

54