BC Ethics Harmonization Initiative

Guidance for Harmonized Ethics Review of Multi-Jurisdictional Studies

Includes Minimal Risk and Above Minimal Risk Studies

1 PURPOSE

To provide guidance on the use of the models for harmonized ethics review of multi-jurisdictional research studies.

2 SCOPE AND APPLICABILITY

2.1 This guidance is intended for use by Research Ethics Board1 (REB) administrators and members for harmonized multi-jurisdictional research studies where three or more2 partner institutions in the BC Ethics Harmonization Initiative (BCEHI) will be reviewing a research ethics application.

2.2 Research is considered either minimal risk or above minimal risk, in accordance with the Minimal Risk Criteria Guideline. The workflow diagrams for each model describe the process for determining risk level.

2.3 This guidance is not intended to address sponsored clinical trials or retrospective chart reviews.

2.4 This is guidance only and emphasis is on flexibility in the models, which may be required in certain circumstances.

2.5 Although the Board of Record (BoR) will be responsible for providing the PI with contact information for operational approvals, this guidance does not address institution-specific approvals that may be required in addition to ethical approval.

2.6 Privacy review is considered an institutional approval. If a privacy review creates a requirement to change an ethics application, the REB involved will notify the BoR that an amendment will be required.

3 RESPONSE TIMES FOR ETHICS REVIEW

3.1 REBs will determine the BoR and confirm risk level within five business days of ethics application submission.

3.2 If an REB is unable to participate in a harmonized review, they will notify the participating REBs and the PI in writing as soon as possible, but within five business days of receiving the notification. It is recognized that in order to make this determination, the REBs may require additional information, such as the cover sheet and/or the application itself.

3.3 Other REBs should deliver their provisos to the BoR within 10 business days of receiving the application and provisos from the BoR.

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[1] Throughout this document, "Research Ethics Board" and "REB" are intended to include the Northern Health Research Ethics Committee.

[2] REBs engaged in dyad ethics reviews are welcome to follow the procedures outlined for harmonized multi-jurisdictional review.

3.4 In accordance with Section **Error! Reference source not found.** below, if an REB requests to see the PI's proviso responses, they will respond to the BoR within three business days of receiving the proviso response.

4 INITIATION OF ETHICS APPLICATION

4.1 The Principal Investigator (PI) will initiate the ethics application by contacting their primary REB office, by submitting a Cover Sheet, via their application, or by other means (e.g. phone, email, or in person).

4.2 The ethics application will be submitted by whatever medium is particular to the institution receiving the initial application (electronic through RISe or other platform, email, or hard copy).

4.3 The Cover Sheet should be completed by the PI and submitted in advance or as part of their application. Completion of a Cover Sheet is required to facilitate information exchange between REBs and the PI/research team. The recipient REB may assist the PI with the completion of the coversheet as needed.

4.4 The recipient REB will confirm which REBs are involved and will initiate communication among them to determine the BoR.

4.5 Participating REBs may opt in advance for full reciprocity with the BoR (choose to accept the BoR review and decision) and opt to receive a copy of the Certificate of Approval (CoA), once issued, and a full package of the final documents for their records. Until there is the ability to issue a joint CoA, the CoA will be issued as outlined below.

4.6 If a REB decides to reject a study, they may do so at any time during the review and approval process, by notifying the BoR in writing and by contacting the PI/research team.

5 BOARD OF RECORD

5.1 The BoR for a multi-jurisdictional study will be decided based upon a discussion between the involved REBs, and taking into consideration the following elements:

a. Location of majority of participants and/or study team;
b. Which institution is best placed to mitigate risk to participants/data;
c. The expertise of the involved REBs (for example: BCCA and cancer studies);
d. Proportion of the study that is hospital-based and community-based; and
e. Other unique factors that the participating boards agree are relevant.

5.2 These are guidelines only and participating REBs will use their best judgment to determine the BoR on a case-by-case basis and, where appropriate, in consultation with the PI.

5.3 If Northern Health is the primary location for the study, the PI's home institution will be the BoR, and the Northern Health (NH) Research Committee will be included in the process for proportionate review. In the event the PI is a NH employee, UNBC will act as the BoR.

5.4 Once the BoR has been confirmed, the BoR administrator will discuss and agree with the PI on the most efficient way to submit the complete application to the BoR.

5.5 Upon receipt of the ethics application, the BoR will:

a. Confirm via email to the participating REBs that the ethics application has been received, including the study title and PI name in the subject line (recommended for all harmonized study communications)
b. Provide the PI with a copy of the Partner Contacts for Operational Approval

6 MINIMAL RISK MODEL

6.1 Delegated review will be conducted by the BoR in accordance with their usual practice.

6.2 Reviews will be conducted in a timely manner to ensure that local REB issues can be addressed within a reasonable timeframe.

6.3 If full reciprocity (see 4.5) is not chosen by all the participating REBs, all provisos resulting from the BoR's delegated review will be shared with the participating REBs. The participating REBs will respond either by:

a. Accepting the BoR's review
Or
b. Conducting a proportionate and site specific review: avoiding duplication of provisos; submitting their provisos to the BoR; and indicating which proviso responses, if any, they need to review.

6.4 The BoR will compile the provisos and provide them to the PI as per their usual practices.

6.5 The BoR will work with the PI to address all provisos.

6.6 The BoR will notify a participating REB of a PI's responses only if specifically requested as outlined in 6.3.b.

7 CERTIFICATE OF APPROVAL

7.1 When all provisos have been satisfied, the BoR will notify the participating REBs that the BoR is ready to issue a Certificate of Approval.

7.2 The BoR will provide the PI with the Joint CoA.

7.3 If separate CoAs are being created for each REB, the BoR will notify the participating REBs that the BoR is ready to issue a CoA and confirm the certificate's expiry date. All other participating REBs will send their CoAs with the confirmed expiry date to the BoR.

7.4 If separate CoAs are being created and the BoR is using RISe they can either:

a. Attach all partner CoAs (if available) to the BoR CoA upon issuing
Or
b. Issue the BoR CoA to the PI on RISe, and then upload participating REB CoAs to the RISe application as they are received. In this option, the participating REBs are responsible for sending their own certificates to their local PIs.

7.5 If separate CoAs are being created and the BoR is **not** using RISe they can either:

a. Attach all participating REB CoAs (if available) upon issuing the BoR CoA
Or

b. Issue the BoR CoA to the PI and then append all the participating REB CoAs to the study file as they are received. In this option, the participating REBs are responsible for sending their own certificates to their local PIs.

7.6 The BoR will email the CoA and final copies of all approved documents listed on the CoA to each participating REB, except when the review was conducted through RISe.

8 ABOVE MINIMAL RISK MODEL

8.1 Following the decision on which REB will form the BoR, the BoR will normally take the lead in determining whether the study is above minimal risk. If required, the BoR will consult with the affected REBs about the level of risk designation.

8.2 If the study does not require full board review, the BoR will follow the minimal risk process outlined in Section 6.

8.3 If a full board review is required, the board will consist of the BoR plus one or more voting members from each participating REB.

8.4 The Chair will be the Chair of the BoR.

8.5 Notice of the full board meeting will be sent out as quickly as possible to the REB administrators of the participating REBs in order to ensure they have a member available for the meeting date.

8.6 In order to ensure a fair review period for guest reviewers, the BoR must make every attempt to provide a minimum 2 week notice for all reviewers. If the BoR cannot provide the other REB(s) with at least 2 week notice prior to the full board meeting, then the BoR must provide the PI with the choice to:

a. Apply an adapted harmonized approach by having separate reviews by the other participating REBs with the option for other REBs to accept the initial BoR application form to start the process and use the provisos from the BoR review as appropriate

Or

b. Wait until the BoR's next full board meeting in order to get a harmonized review by all required partner REBs.

8.7 Participation in the full board meeting may be proportionate to the risks identified and can occur by one of the following methods:

a. Attending in person
b. Attending by video conference
c. Attending by teleconference
d. Submitting review comments prior to the meeting to be considered by the Chair in the decision process
e. Confirming full reciprocity in advance of the meeting in which case the partner REB will not participate in any way

8.8 A reasonable effort will be made by the BoR to accommodate the participation method chosen by additional members.

8.9 If, due to connectivity problems or last minute scheduling difficulties, a +1 REB member is unable to participate in the meeting, the meeting will continue and provision will be made by the BoR to have the absent REB member participate by other means.

8.10 Quorum will be defined by the BoR's policy and, at a minimum, will meet the TCPS2 standards:

a. At least two members who have relevant knowledge and expertise in the content area
b. At least one member who is knowledgeable in ethics
c. At least one member who is knowledgeable in the relevant law
d. At least one member who has no affiliation with the institution, but is recruited from the community
e. Quorum is based on who is present at the meeting (physically and remotely). This includes designated members of other REBs who participate in the collaborative review. In the event of a vote, the designated members of the other REBs are entitled to vote.
f. Attendees who are voting members of their own REB will be considered voting members to meet the quorum.

8.11 The meeting minutes will record if a member of the involved REB(s) requests notification of a response by a PI to a proviso to ensure it has been met to their satisfaction. Otherwise, the BoR will be responsible for determining when all provisos have been met.

8.12 The BoR will address the provisos on behalf of the participating REB(s) unless instructed otherwise as in 8.11.

8.13 The BoR will process the CoA as described in Section 7 above.

9 CONTINUING REVIEW – MINIMAL RISK AND ABOVE MINIMAL RISK STUDIES

9.1 All continuing review activities, including approvals, annual renewals, amendments, and communications with the PI, will be coordinated through the BoR.

9.2 The BoR's forms will be used for each type of continuing review activity.

9.3 When available, the study team's forms will be accepted for various continuing review scenarios, including annual renewals, amendments, local serious adverse events, protocol deviations, periodic safety update reports and administrative letters. If the study team does not have a specific form for the purpose, they will use the forms belonging to the BoR.

9.4 Upon submission by the PI of a continuing review activity, the BoR will determine if a consultation with the participating REBs is required, depending on whether:

a. The continuing review activity is specific to the jurisdiction of a participating REB (e.g. security and privacy breach at a particular site, new funding, change in study team membership from an institution, addition of animal care ethics, addition of bio-safety factors or patient data to the protocol)

   And/Or

b. The information provided in the continuing review activity increases the overall risk to participants above the level approved in the original application.
c. If consultation is required, the BoR will contact the partner REB's to notify them that they are required to review this post approval activity and comments should be posted within 2

business days. Any automatic notifications (e.g. RISe) should be ignored until the BoR confirms review is required.

d. The participating REBs will confirm if they request notification of the PI's response to a proviso to determine if it has been met to their satisfaction.

e. If a participating REB requires review of the PI's response, they agree to provide any additional comments or confirm their agreement within three working days of receipt of the PI response.

9.5 If no consultation is required, the BoR will NOT contact the partner REBs and will process the continuing review activity in accordance with their REB policies and procedures. The BoR will issue the appropriate documentation to the PI and will provide the other REBs with a copy of the related documentation (e.g. certificate).

ABOVE MINIMAL RISK CONTINUING REVIEW ACTIVITIES

9.6 If full board review is required in accordance with regulatory and TCPS2 guidance, the BoR will follow the same process as outlined in the sections above for forming a full board and conducting the review.

9.7 If a full board review is not required, the BoR will facilitate consultation between the REBs to determine the specific disposition of the continuing review activity following steps 9.4 through 9.5

9.8 The participating REBs will be advised of the continuing review activity (event/outcome), and will be provided with a copy of the appropriate acknowledgement or CoA.

10 ADDITION OF NEW SITES AFTER INITIAL ETHICS APPROVAL:

10.1 The PI will be asked to submit the added sites as a separate amendment prior to submitting other amendments for review and approval.

10.2 The originating REB will notify the affected REBs and request their decision re: harmonization.

10.3 The BoR will provide the new REB(s) with the original application and provisos to date for review and a decision on status.

10.4 If there are additional provisos related to the new REB:

a. The new REB will communicate directly with the PI to resolve and copy the BoR on correspondence

b. The PI will submit revised documentation to the BoR for review and approval

c. The BoR approves the amendment for adding sites and advises the PI that other amendments (if any) may be submitted for review

10.5 If there are no additional provisos related to the new REB:

a. The new REB submits a Letter of Acknowledgement to the BoR

b. The BoR approves the new REB amendment and advises the PI that other amendments (if any) may be submitted for review

10.6 The certificate date of the originating REB will be considered the default date for expiry and renewal purposes.

11 HARMONIZATION OF AN ETHICS FILE WHEN INITIAL APPROVAL WAS NOT HARMONIZED:

11.1 Designation of the BoR will be decided using the original decision criteria (see Section 5).

11.2 The harmonized certificate date will be the earliest of the participating REB's expiry dates.

12 STUDY CLOSURE

12.1 Individual REBs are responsible for ensuring that administrative requirements related to study closure are completed by the research team.

12.2 The BoR will be advised by the PI when the study is closing in any jurisdiction, using the customary continuing review procedures.

12.3 The BoR will notify the affected REB(s) and facilitate documentation of study closure activities.

12.4 If a participating REB is notified by the research team of closure at their site, the other REB will inform the BoR and provide the related paperwork for inclusion in the ethics application documentation.

12.5 The BoR will remove an REB from the study once the REB has confirmed all their requirements have been met.

12.6 The BoR will ensure that study closure documentation for each site is included in the BoR file.

13 PARTICIPANT COMPLAINTS

13.1 The contact details for participants to file a complaint will be listed for each REB on the informed consent and/or assent form(s).

13.2 The submission of a participant complaint will be managed jointly by the REB that receives it and the BoR, involving other REBs as outlined in 8.4.

13.3 The BoR will consult with participating REBs depending on the type of complaint, its jurisdiction, and whether the complaint results in an amendment being required.

14 DOCUMENTATION

14.1 The BoR will be responsible for maintaining complete documentation of the ethics application and all continuing review activities, including notification of study closure.

14.2 The BoR will share updated documents with the participating REBs. This may involve emailing or uploading documents to a shared repository.

15 SUPPORTING RESOURCES (available from the Resources tab at bcethics.ca)

Research Ethics Review Workflows (Minimal Risk and Above Minimal Risk)

Harmonized Review Cover Sheet (MSWord)

Partner Contacts for Operational Approval