Title:	Amendments and Administrative Changes
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Revised:	
Approved By:	REB Chair

1.0 PURPOSE

The purpose of this guideline is to describe how amendments and administrative changes are submitted to and reviewed by the REB.

2.0 POLICY STATEMENT

This guideline is in compliance with the requirements for continuing ethical review as set out in the Tri-Council Policy Statement 2 and in the regulations and guidelines governing clinical trials (Health Canada Clinical Trial Regulations for new investigational drugs, radiopharmaceuticals, biological drugs, natural health products, and medical devices), ICH GCP, and where relevant, US Codes of Federal Regulations.

All revisions, additions or deletions to approved studies are considered amendments and must be submitted to the HRH Research Ethics Board (REB) for review to ensure that the research remains scientifically and ethically sound. The Principal Investigator (PI) is responsible for ensuring that amendments are submitted to the REB for review and written approval is received prior to implementation.

3.0 PROCEDURES

3.1 Definitions

3.1.1 Amendment: A written description of a change(s) to, or formal clarification of an ongoing currently approved protocol. Amendments include any change to the study documents that affects the scientific intent, study design, patient safety, or human subject protection.

Some examples of amendments include:

- change of Principal Investigator or change of Co-Investigator(s)
- change in recruitment methods
- change in sample size or study duration
- change to inclusion/exclusion criteria
- change in study procedures

- change to protocol that affects the selection, monitoring or dismissal of a study subject(s)
- change to protocol that affects the evaluation of the clinical efficacy and safety of the drug
- change to protocol that alters the risk to the study subject(s)
  rephrasing a line or section, or typographical or numeric corrections that may affect safety of subjects (i.e. change in eligibility criteria, change of dose, change in risk regardless if risk is increased or decreased

3.1.2 Administrative Change: A minor change(s) to any study document(s) that does not affect the scientific intent of the study, study design, study subject risk, or human subject protection.

Some examples of administrative changes include:

- rephrasing a sentence or section to add clarity or correct inconsistencies
- reformatting the document
- change of study coordinator or monitor
- change of address, telephone, or e-mail address of study staff

3.2 Sub-Studies

The HRH REB generally does not consider sub-studies, ancillary studies, rollover studies, continuation studies, and extension studies to be amendments. These are usually considered new studies and the decision of whether they qualify for review as amendments rests with the REB Chair.

3.3 Exceptions

Although most amendments must be reviewed and approved prior to implementation, amendments can be implemented prior to REB review and approval under the following circumstances:

- Amendments *should* be implemented prior to REB review and approval when the amendment is essential to eliminate any immediate hazards to research subjects. These amendments must be submitted to the REB within 7 days of implementation.

- Amendments *may* be implemented prior to REB review and approval when the amendment involves only logistical or administrative aspects of the study. These administrative changes must be submitted to the REB within 30 days of implementation.

3.4 Submitting an Amendment and Administrative Change

The HRH REB Amendment and Administrative Change Form must accompany all amendments and administrative change submissions. The form directs the PI to identify change(s) to be made to study documents and to provide justification/rationale for the change(s). All study documents affected by the change must be included with the submission (e.g.):

- amendment document
- revised protocol
- informed consent form(s)
- supporting documentation (e.g. new information supporting the amendment)

All revised study documents must have version dates that reflect the most recent amendment/administrative change submission. Further details regarding version dates can be found below.

The REB will not accept amendment/administrative change submissions without the original signature of the PI. This signature attests that the PI accepts the amendment/administrative change. For amendments, the PI's signature further attests that the PI has assessed the safety implications of the amendment, its impact on study procedures and is prepared to take all necessary steps to implement the change.

Incomplete amendment/administrative change submissions will be returned to the Principal Investigator with a return notification form that indicates the documentation that is outstanding. The REB will process and review the amendment/administrative change submission once all required documentation is received.

Amendments which include a change in study personnel should also include a completed HRH REB Change of Study Personnel Form.

3.5 Version Dates

Version dates identify the latest edition of study documents. Version dates, including the day, written month, and year (e.g. 04-Jan-05) must be presented in this format in the footer of all study documents. If a study document requires further modification based on comments received during the REB review process, the version date must be modified to reflect the most recent edition of the study document. Informed Consent Forms will not be approved without revised version dates in the format outlined above.

3.6 Review Process

Full board review of amendments is the default requirement for all research involving human subjects. The decision of whether an amendment qualifies for delegated review is based primarily on the risks that are expected to arise from the change to the research protocol. The decision of whether an amendment qualifies for delegated review rests with the REB Chair.

3.6.1 Full Board Review

The following types of amendments will be considered for full board review and approval:

- changes that increase the risks to the study subject(s) and/or changes that significantly affect the study procedures, study design, or conduct of the study

- changes that have been implemented to eliminate any immediate hazards to study subjects without prior REB approval. (The REB office will review these amendments and provide a preliminary decision; however, the final decision rests with the full board.)

Amendments that qualify for full board review are reviewed at the next monthly meeting of the board that conducted the initial review of the study. REB questions or concerns regarding amendment submissions are communicated to the PI in a written format that is sent to the PI following the review.

Health Canada No Objection letters (NOLs) must be included with amendment submissions for clinical trials when applicable. REB approval will not be granted until the NOL is received.

For full board review, attach:

- five copies of relevant study documents with changes tracked, (*or* in bold or highlighted) that accurately reflects the changes to study outlined in the request form
- one clean copy of relevant study documents (without tracked changes, handwritten notes or highlights)

3.6.2 Delegated Review

Many amendments and all administrative changes qualify for review under the delegated review process. REB questions, concerns and/or recommendations regarding amendment/administrative change submissions are generally communicated to the PI via email.

For delegated review attach:

- one copy of relevant study documents with changes tracked (*or* in bold or highlighted) that accurately reflects the changes (additions and deletions to study outlined in the amendment form.
- one clean copy of relevant study documents (without tracked changes, handwritten notes or highlights)

In the event that the REB finds one or more of the parts of an amendment/administrative change submission unacceptable, the PI will be informed via written letter or email communication of what was not acceptable and why. The PI will have the opportunity to submit a revised amendment that corrects the issues outlined by the REB or provides additional justification to support the original request.

3.7 Acknowledgement of Receipt

The HRH REB does not routinely "acknowledge receipt" of documents received. Acknowledgement of Receipt is reserved primarily for those documents related to safety review and Health Canada communications.

Requests for Acknowledgement of Receipt for documents other than those listed below will not be provided. The sender is instructed to document "proof of submission" to indicate on their records that the document has been sent to the REB. The REB website posts this policy should the sender require a copy for their files.

Documents Acknowledged by the REB include:

- Investigator Brochures submitted after the initial approval date
- Product Monographs
- Safety Reports
- DSMB Reports
- Health Canada "No Objection Letter" (NOL) or other Health Canada communications.

These documents are stamped with the "REB Date Received" stamp and the cover page is emailed/faxed/mailed back to the PI or acknowledged in an accompanying approval letter. The REB copies of faxed documents contain a date faxed stamp as confirmation of acknowledgment.

Documents not acknowledged are filed in the REB Office.

3.8 Amendments Submitted During the Initial Review Process

Whether an amendment submitted for a study that has not yet been approved by the REB is reviewed by the full board or qualifies for expedited review depends upon the risk(s) associated with it.

Amendments that have greater than minimal risk(s) associated with them will be reviewed at the next meeting of the same full board that conducted the initial review of the study. Once all of the concerns are addressed, the initial approval and the amendment to study will be approved in separate approval letters that reflect the dates of the full board meetings where the review of each was conducted.

Amendments that have minimal risk(s) associated with them will be expedited and once all of the concerns are addressed, the initial approval and the amendment to study will be approved in separate approval letters that reflect the dates and types of review.

3.9 Amendments Not Approved by the REB

In the event that the concerns of the REB cannot be resolved and an acceptable alternative cannot be found, the amendment will not be approved and the reasons will be communicated to the Principal Investigator. In accordance with Division 5 C.05.008 (C)(ii), it is the responsibility of the Sponsor (for clinical trials only) to inform Health Canada that the amendment was not approved by the REB and the reasons for this.

4.0 REFERENCES

1. Tri-Council Policy Statement 2: Ethical Conduct for Research Involving Humans. 2010.

2. Good Clinical Practice: Consolidated Guideline. ICH Harmonised Tripartite Guideline. 1997.

3. Health Canada, Consolidated Statutes and Regulations, Food and Drug Act, Division 5 Drugs For Clinical Trials Involving Human Subjects.

4. Personal Health Information Protection Act, 2004.