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1. INTRODUCTION

The following notes are intended to assist the researcher with the completion and submission of an Amendment Request.

The Tri-Council Policy Statement, the ICH-GCP's and the US Federal Regulations all require researchers to submit proposed changes to previously approved research projects to the Health Sciences North Research Ethics Board (HSN REB) for approval. All changes must be submitted prior to the changes being implemented, "except when necessary to eliminate immediate hazards to subjects or when the change(s) involve minor administrative changes such as changes in granting status, staff personnel, contact person or phone number, etc."

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.

2. DEFINITIONS

Amendment - A written description of a change 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, or change in risk regardless if risk is increased or decreased

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

Sub-Studies

The HSN 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.

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Exception

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.

3. PROCEDURES

1) Submitting an Amendment

The HSN REB Amendment 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 submission. Further details regarding version dates can be found below.

The following questions should be considered when proposing an amendment:

- Does the amendment affect the risk/benefit ratio?
- Does the amendment affect recruitment? If so, is a revised recruitment ad or letter attached?
- Does the amendment affect what the participant is asked to do or confidentiality of the data? If so, is a revised consent form attached?
  - Does the consent form adequately reflect the change in activities, risk, or confidentiality?

Amendments must be submitted in such a way that:

- The old wording is clearly identified (for example, ~~bolded strikethrough text~~).
- The new wording is clearly identified (for example, *italicized grey-shaded text*).
- It is clear why each amendment has been made.
- The amendment can be evaluated in context. Supply a copy of the protocol showing tracked changes or provide a Summary of Changes.
- It is clear whether each amendment increases risk or discomfort for the participant in any way.

The REB will not accept amendment 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.

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2) Version Dates

Version dates identify the latest edition of 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.

3) Clinical Trial Amendments:

Health Canada requires full board review for the types of amendments specified below:

i. Addition of genetic testing, new genetic tests or tissue banking where genetic testing may or will be performed;
ii. Addition of an open-label extension phase following a randomized trial;
iii. Emergency Amendments that arise because of subject safety concerns and that are submitted after implementation as a result, and;
iv. Significant changes to the protocol that may affect subject safety and may include a (but are not limited to):
   - Change in drug dosing/duration of exposure,
   - Decrease in monitoring,
   - Change in recruitment technique that may affect confidentiality or the perception of coercion,
   - Change in experimental procedures or study population.

4) 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(s) to the research protocol.

Full Board review by an REB should be the default requirement for all research involving human participants unless the REB decides to authorize delegated review based primarily on the harms that are expected to arise from the changes to the research.

Full Board Review
Amendments that qualify for full board review are reviewed at the next monthly meeting. 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.

For full board review, submit:

- One original signed copy of the typed completed Amendment Request Form + relevant study documents with changes tracked, (*or* in bold or highlighted) that accurately reflects the changes to study outlined in the request form + 4 copies, collated;
- One scanned copy of the entire package, emailed to: reb@hsnsudbury.ca.

Delegated Review
Many amendments and all administrative changes qualify for review under the delegated review process. Examples of amendments that may qualify for delegated review include amendments involving:

- minor or minimal risk changes;

- changes to consent documents that do not affect the rights and welfare of research participants, involve increased risk, affect data integrity, or require significant changes in research procedures;
- reportable events, including adverse events and safety updates such as reports from Data and Safety Monitoring Boards (DSMB) that don't result in a change to the safety profile of the product;
- minor changes to participant materials such as: recruitment posters or scripts, diaries, validated questionnaires, clinical trial identification/wallet cards;

Please contact the Research Services Office for guidance and clarification.

For delegated review, submit:

- one original signed copy of the typed completed Amendment Request Form + 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 scanned copy of the entire package, emailed to: reb@hsnsudbury.ca.

In the event that the REB finds one or more of the parts of an amendment 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.

Upon reviewing an application that was sent for delegated review, if the reviewer determines that the risks are greater than minimal, the reviewer will refer the application for review by the Full Board.

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. REFERENCES

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

Health Canada Consolidated Statutes and Regulations, Food and Drug Act, Division 5 Drugs ForClinical Trials Involving Human Subjects. August 2004.

N2/CAREB-ACCER REB SOP 401.002 Delegated Review. 2016.

N2/CAREB-ACCER REB SOP 405.002 Continuing Review. 2016.

Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans. August 1998.