University Health Network
Research Ethics Board
Guidelines for Submitting Proposed Amendments, Administrative Changes and Changes in Principal Investigator

Guidelines

These guidelines are in conformity with the requirements for continuing ethical review as set out in the Tri-Council Policy Statement[i] and in compliance with the regulations governing clinical trials (Health Canada regulations for the investigational use of drugs, radiopharmaceuticals, biologics, natural health products, and medical devices)[ii], ICH GCP E6[iii], and where relevant, the U.S. Code of Federal Regulations.

All changes to the planning or conduct of approved studies – with the exception of "Administrative Changes", defined below – are considered amendments and must be submitted to the UHN Research Ethics Board (REB) for **prior review and approval** to ensure that the research remains ethically sound. The Principal Investigator (PI) must ensure that amendments are submitted to the REB for review and that written approval is received prior to implementation.

Definitions

1. Amendment – A proposed change to the planning or conduct of an REB-approved research study. Amendments include any change to any REB-Reviewed Study Documents that affects the design or conduct of a study, and may represent a change in known risks to study participants.

Some examples of Amendments include:

⇒ 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 participant(s)
⇒ Change to protocol that affects the evaluation of the clinical efficacy and safety of the investigational product
⇒ Change to protocol that alters the risk to the study participant(s)
⇒ Changes to case report forms (CRFs) **only** when the CRF is the original source document/data collection tool (e.g. – the CRF contains an embedded pain or quality-of-life scale that is filled in directly when seeing the participant).
⇒ Rephrasing a line or section of recruitment materials or informed consent form(s), or typographical or numeric corrections to these documents that may

affect the safety of participants (e.g. – change in eligibility criteria, change of dose, change in risk irrespective of whether risk to participants is increased or decreased, change in who has access to study records, etc.)

⇒ New recruitment materials or informed consent form(s)

⇒ Change of Principal Investigator

2. Administrative Change – A minor change(s) to any study document(s) that does *not* affect the design or conduct of a study, and does *not* change the known risks to study participants. There are two types of Administrative Change which require REB review and approval:

a) Changes to REB-Reviewed Study Documents to correct inaccuracies or for administrative purposes (reformatting the document, updating inconsistent headers/footers, etc.)
b) Changes to study personnel, other than the Principal Investigator that affect REB-Reviewed Study Documents. Changes in the Principal Investigator should be submitted using the Change in Principal Investigator Form**.** Please note that the Principal Investigator is responsible for documenting all changes in the study personnel in a study delegation log or equivalent. All other changes in study personnel do not require reporting to, or approval from, the REB, except when they affect REB-Reviewed Study Documents.

Examples of Administrative Changes include but are not limited to:

- Rephrasing a sentence or section of a study-related document to add clarity or correct inconsistencies
- Reformatting a study-related document
- Change of Co-Investigator, study coordinator, data abstractor, or monitor
- Change of address, telephone, or e-mail address of study personnel

Administrative Changes should only be reported to the REB if the changes affect REB-Reviewed Study Documents. Not all Administrative Changes – including some of those in the examples above – require REB review or approval. Administrative Changes that require reporting to, and approval from, the REB should be submitted through CAPCR.

3. REB-Reviewed Study Documents – The documents the REB has reviewed and referenced when initial ethical approval was granted for a study, or when the REB has provided ethical approval for an Amendment or an Administrative Change. These documents include the research protocol, informed consent form(s), and other participant-directed materials such as direct data collection tools (questionnaires, diaries) or recruitment-related documents such as advertisements or telephone scripts. For guidance on when to submit changes to investigational product documentation (Investigator Brochures, Product

Monographs, Device Manuals, etc.) please see Section 5.2.1 of the REB's Unanticipated Problem Reporting Guidance.

Sub-Studies

The UHN REB generally does not consider sub-studies, ancillary studies, rollover studies, continuation studies, or extension studies to be Amendments. These are usually considered new studies and the decision as to whether they qualify for review as amendments rests with the REB Co-Chair responsible for a given study. As such, you are encouraged to consult the REB Coordinator responsible for your study prior to preparing a submission for this type of change, to ensure that you prepare the correct type of submission. The REB Coordinator will facilitate obtaining a decision from the REB Co-Chair.

Exceptions

Although most Amendments must be reviewed and approved by the REB 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 or reduce any apparent immediate hazards to study participants. These Amendments must be submitted to the REB within 7 calendar days of implementation.

- Amendments that require REB approval *may* be implemented prior to – or in some cases, without a requirement for – REB review and approval when the Amendment involves only logistical or administrative aspects of the study and the change constitutes an Administrative Change. When in doubt, please consult the REB Coordinator responsible for your study prior to implementing the changes.

    - Amendments that involve only logistical or administrative aspects of the study need only be approved by the REB when they affect REB-Reviewed Study Documents, or when they materially affect the conduct of the study in a way that affects study participants.

Procedures

1. Submitting an Amendment, an Administrative Change, or a Change in PI

All amendments, administrative changes, and changes in PI must be submitted through CAPCR.

The CAPCR form directs the PI to identify change(s) to be made to study documents and to provide justification/rationale for the change(s). All REB-Reviewed Study Documents affected by the change must be included with the submission.

Examples include:

- Revised protocol (one copy with tracked changes and a clean copy of the updated protocol)
- Informed consent form(s) (one copy with tracked changes and a clean copy of the updated consent form[s])
- Supporting documentation (e.g. – DSMB report, Unanticipated Problem report)

All revised study documents must have version dates that reflect the most recent Amendment or Administrative Change form submission. Further details regarding version dates can be found below.

The PI must complete the attestation form in CAPCR. Please consult the UHN REB website for current submission procedures and requirements.

Incomplete submissions will not be accepted for review. The UHN REB will accept the Amendment, Administrative Change or Change in Principal Investigator Form for review once a complete submission is received.

2. Version Dates

Version dates identify the latest edition of study documents. Version dates, including the day, written month, and year should be included 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. Revisions to informed consent forms will not be approved without revised version dates.

3. Review Process

Full board review of Amendments is the default requirement for all research involving human subjects. The decision regarding 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 Co-Chair.

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 or reduce any immediate hazards to study subjects without prior REB approval will be reviewed by the UHN REB to determine whether or not the changes affect the ethical acceptability of the study

Amendments that qualify for full board review are reviewed at the next meeting of the REB review panel that conducted the initial review of the study.

Health Canada "No Objection" letters (NOLs) or equivalent must be included with Amendment submissions for regulated clinical trials when applicable. When applicable, REB approval for an Amendment will not be granted until the NOL or equivalent Health Canada authorization (ITA, NOA, etc.) is received.

Delegated Review

Many Amendments and all Administrative Changes qualify for review under the delegated review process.

Following the review, REB questions or concerns regarding Amendment or Administrative Change submissions are communicated to the PI through CAPCR. The PI will have an opportunity to submit additional information and/or a revised submission that addresses any issues raised in the REB review.

4. Amendments/Changes Submitted During the Initial Review Process

Amended documents or changes to proposed studies submitted during the initial REB review process are considered as part of the initial REB review. Where the changes affect the potential risks to study participants or otherwise raise significant ethical issues, the study may require (re-)review at a full board (convened) meeting.

Once the initial REB review has concluded, if the study is approved, the most recent version of any REB-Reviewed Study Documents will be listed on the REB approval letter for the study.

Amendments Not Approved by the REB

In the event that any issues raised by the REB cannot be resolved and acceptable alternatives cannot be found, the Amendment will not be approved and the reasons for the decision will be communicated to the Principal

Investigator through CAPCR. It is the responsibility of the PI to inform affected parties such as the study sponsor, about negative REB review outcomes.

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[i] Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans. December 2010.

[ii] Health Canada, Consolidated Statutes and Regulations, Food and Drug Act, Division 5 Drugs For Clinical Trials Involving Human Subjects. August 2004.

[iii] Good Clinical Practice: Consolidated Guideline E6. ICH Harmonised Tripartite Guideline. 1997.