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GUIDANCE NOTES FOR REQUEST FOR AMENDMENT OF A PREVIOUSLY APPROVED RESEARCH STUDY

INTRODUCTION

The following Guidance Notes [GN], which comprise some of the FH Research Ethics Board's [FHREB] standard operating policies and procedures, are intended to ensure that the applicant has the necessary information to be able to complete the 'Request for Amendment of a Previously Approved Project' correctly. These Guidance Notes have been adapted with the permission of the University of British Columbia.

The FHREB policies/procedures correspond to, and therefore comply with, the current version of the Tri-Council Policy Statement (TCPS) on 'Ethical Conduct for Research Involving Humans'[1], specifically TCPS 2, Article 6.16 which states that "Researchers shall submit to their REBs in a timely manner requests for substantive changes to their originally approved research. REBs shall decide on the ethical acceptability of those changes to the research in accordance with a proportionate approach to research ethics review."

With respect to clinical trials, the ICH Good Clinical Practice (ICH GCP) Guidelines[2] Article 3.3.7 states:
"…no deviations from, or changes of, the protocol should be initiated without prior written IRB/IEC approval/favourable opinion of an appropriate amendment, except when necessary to eliminate immediate hazards to the subjects or when the change(s) involves only logistical or administrative aspects of the trial (e.g. change of monitor(s), telephone numbers(s))".

Both the Tri-Council Policy Statement and the ICH GCP Guidelines have their origin in the ethical principles that were developed in the Declaration of Helsinki.[3] The FHEB operates under the authority of the most current version of the following Fraser Health Authority policies: 1) "FH Research" and 2) "The Ethical Conduct of Research and Other Studies Involving Human Subjects".

These Guidance Notes (GNs) are not meant to be a substitute for the current version of the Tri-council Policy. Please refer to the original documents for complete information.

GUIDANCE NOTE #1: WHAT RESEARCHERS NEED TO KNOW PRIOR TO SUBMITTING A REQUEST FOR AMENDMENT

Obligations of the Principal Investigator

The Principal Investigator for a study is responsible for ensuring that amendments are submitted to the FHREB prior to implementation and for understanding and adhering to the TCPS and other relevant guidelines, including ICH GCP when applicable. In particular, ICH GCP 4.5.2 specifies that:
"The investigator should not implement any deviation from, or changes of the protocol without agreement by the sponsor and prior review and documented approval/favourable opinion from the IRB/IEC of an amendment…".

Studies Requiring Amendment Before Initial Approval Is Obtained

[1] Canada: Tri-Council Policy Statement2: Ethical Conduct for Research Involving Humans. December 2010. Available at www.pre.ethics.gc.ca
[2] Canada: Good Clinical Practice: Consolidated Guideline. ICH Harmonised Tripartite Guideline. 1997. Available at http://www.ncehr-cnerh.org/english/gcp/
[3] World Medical Association: Declaration of Helsinki. http://www.wma.net/e/policy/b3.htm

Amendments should only be submitted for review AFTER the study has received initial approval from the FHREB.

Amendments Submitted With A Request For Annual Renewal

If necessary, amendments may be submitted at the same time as the request for annual renewal, using the Integrated Post-Approval Application Form. However, the amendment may be processed separately from the annual renewal if deemed necessary by the FHREB.

Approval Period for Amendments

The term of the approval for the amendment expires at the same time as the initial approval/annual renewal for the study.

Change of Investigator or Contact Person's Contact Information

Submit changes to any of the investigator's/contact person's contact information (i.e. address, telephone/fax number, email). Ensure that all studies affected by the change(s) are specified in the letter. See Guidance Note #3 regarding additional requirements for a change of principal investigator.

The FH Research Office will send an acknowledgement to the designated contact.

GUIDANCE NOTE #2: SUBMISSION CRITERIA

Any amendment must be submitted using the Integrated Post-Approval Application form. The FHREB will decide on the ethical acceptability of substantive changes to the originally proposed research in accordance with a proportionate approach to research ethics review.

Updated 2016 November 17: All submissions and accompanying documents/correspondence may be emailed to: REB @fraserhealth.ca or the current REB Coordinator.

2.1 Delegated Review

The TCPS 2 Article 6.12 stipulates that the FHREB can delegate the authority for the approval of amendments to the co-Chair (or designate) of the FHREB under the category of 'Delegated Review'.

Most amendments can be reviewed under the Delegated Review process. Refer to Guidance Note 2.2.1 for criteria that designate which type of amendments must receive Full Board review.

The co-Chair (or designate) may at any time put forward a request for approval of an amendment to the Full Board.

2.1.1 Timelines for Delegated Review

2.1.1.1 Review

Updated 2016 November 17: Amendments are reviewed on a rolling basis. The time from submission of an amendment to review will vary according to the volume of submitted amendments as well as renewal applications.

2.1.1.2 Issuing FHREB Decisions

All decisions arising from the review are emailed to the contact person identified in the Application Form and copied to the Principal Investigator.

Certificates of Approval for approved amendments are usually issued within 1-2 business day from the REB decision. A pdf certificate with the digital signature of the FHREB Co-Chair (or designate) is emailed to the contact person and the Principal Investigator and is the FHREB official notification of the decision

Modification Memos are emailed usually within 1-2 business day from the decision of the co-Chair.

2.2 Full Board Review

2.2.1 FHREB Criteria

Updated 2016 November 17: The following types of amendments for previously approved studies that are clinical trials [drug, device, natural health product] must be referred to the Full Board for review as required by Health Canada.

1. Addition of genetic testing, new genetic tests or tissue banking where genetic testing may or will be performed;
2. Addition of an open label extension phase following a randomized trial;
3. Emergency amendments that arise because of subject safety concerns and that are submitted after implementation as a result, and;
4. amendments to the protocol that affect the selection, monitoring or dismissal of a clinical trial subject;
5. amendments to the protocol that affect the evaluation of the clinical efficacy of the drug;
6. amendments to the protocol that alter the risk to the health of a clinical trial subject;
7. amendments to the protocol that affect the safety evaluation of the drug;
8. amendments to the protocol that extend the duration of the clinical trial; and
9. amendments to the chemistry and manufacturing information that may affect the safety or quality of the drug.
10. (Amendments 4 to 9 are a requirement of Health Canada Regulations Amending the Food and Drug Regulations (1024 - clinical trials) Division 5, C.05.008 Drugs For Clinical Trials Involving Human Subjects Amendment 2 (a) to (f). (downloaded on November 24, 2011 from http://www.hc-sc.gc.ca/dhp-mps/compli-conform/clini-pract-prat/reg/1024-eng.php

2.2.2 Sponsors that Require Full Board Review

Some sponsors require Full Board Review for amendments. These requirements are described below. For studies that require Full Board Review, refer to GN 8 for details on the required documentation.

2.2.2.1 Studies sponsored by the United States Department of Health and Human Services

Studies sponsored by the United States Department of Health and Human Services (DHHS) (e.g. NIH and its related institutes including NCI, U.S. Centre for Disease Control) may require Full Board Review under 45 CFR 46.109 (e) and 46 CFR 110 (Code of Federal Regulations).

Refer to the following link for guidance on the interpretation of 45 CFR 46.109 (e) as it applies to studies sponsored by the DHHS.
http://www.hhs.gov/ohrp/assurances/assurances_index.html;

This link can also be used to access the relevant articles under 46 CFR.

2.2.2.2 Studies sponsored by other United States federal agencies (Updated 15 November 2003)

Studies that are funded by other American federal agencies (e.g. United States Department of Defence) may require Full Board Review under 21 CFR 56.110.

Refer to the following link for guidance on the interpretation of 21 CFR 56.110 as it applies to studies with this funding source.

http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm.

2.2.3 Timelines for Full Board Review

2.2.3.1 Review

The full board meets on the 2nd Wednesday of each month.

2.2.3.2 FHREB Decisions

All decisions arising from the review are sent to the contact person identified in the Amendment Application Form.

Certificates of Approval for approved amendments are usually issued within five business days of the approval of the full board. A pdf certificate with the digital signature of the FHREB co-Chair is emailed to the contact person and the Principal Investigator and is the FHREB's official notification of the decision.

Modification or deferral memos are emailed usually within five business days from the date of the board meeting.

GUIDANCE NOTE #3: CHANGE OF PRINCIPAL INVESTIGATOR

This is considered an administrative amendment and does not affect the ongoing enrolment of subjects.

In order to change the Principal Investigator, the original Principal Investigator must sign the Application Form for Amendment which indicates the change required. The amendment form should identify the new Principal Investigator and also include any documents that require revision due to the change in Principal Investigator, i.e. consent form, recruitment posters, etc.

NB: All consent forms will have the FHREB Approval date stamp as of January 2009.

For studies submitting consent forms, ensure that the consent form is the most recently approved version (check to ensure that the correct version number/date is on every page of the consent form). All approved consent form(s) will be electronically stamped with the FHREB approval date and returned via email with the amendment certificate of approval.

The new Principal Investigator signs the Change of Principal Investigator Form. This form is required so that the appropriate contact information is included for the new Principal Investigator and so that there is documentation of the new Principal Investigator's attestation to abide by the Tri-Council Policy.

In addition, the new Principal Investigator must declare any potential conflict of interest that could arise from assuming this role.

GUIDANCE NOTE #4: CHANGES TO CO-INVESTIGATORS

Changes to co-investigators are considered administrative amendments and do not affect the ongoing enrolment of subjects.

GUIDANCE NOTE #5: SITE CHANGES

Indicate if any FH or other sites have been added to OR removed from the study.

GUIDANCE NOTE #6: CHANGES TO FUNDING AGENCY

Submit any changes regarding who is funding the study and/or name changes of funding agencies (e.g. when the funding agency's name is changed from Roche Products Ltd. to Hoffmann-LaRoche Limited).

When ANY funding agency is changed/renamed, a revised consent form is also required and must be submitted with the application. Refer to GN 13.2 for further details.

GUIDANCE NOTE #7: NEW STUDY TITLES

Changes to study titles must also be submitted using the amendment application form. This information is important to ensure that the title on a Certificate of Approval coincides with the correct funding agency as there may be somewhat different study titles for different funding agencies

The FH Research Office will only authorize the release of specific project funds to the researcher if the Certificate of Approval includes the funding agency that matches the correct study title.

GUIDANCE NOTE #8: SUBMISSION PROCESS

8.1 General Requirements

All necessary documents must be submitted with the correct number of copies required for either Full Board Review (see 8.2) or Delegated Review (see 8.3). Incomplete submissions will not be reviewed and will have to be resubmitted.

8.1.1 Amended Documents

Amended documents must be submitted in such a way that any changes are clearly identified, either in tracked changes format, or highlighted.

8.1.1.1 Protocol Amendments

Protocol amendments may include a separate document that lists both the original section(s) and the subsequent revision(s) so changes to the original text are easily seen.

8.1.1.2 Consent Forms

Submit the amended consent form with the changes tracked or in highlighted so that it is easy to see how the original consent form has been altered. The amended consent form should include a footer with an updated version number and/or date.

NB: As of January 2009 all consent forms will have the FHREB Approval date stamp.

For studies submitting consent forms, ensure that the consent form is the most recently approved version (check to ensure that the correct version number/date is on every page of the consent form). All approved consent form(s) will be electronically stamped with the FHREB approval date and returned via email with the amendment certificate of approval.

8.2 Required Documentation for Full Board Review

Submit the Application Form with signature, the revised protocol, if applicable, and all other documents to be amended via email to REB@fraserhealth.ca.

8.3 Required Documentation for Delegated Review

Submit the signature copy of the Application Form, revised protocol, if applicable and all other documents to be amended.

8.3.1 Investigator Brochures (IB) and Safety Data Reports

A Certificate of Approval is issued only if the updated IB is accompanied by documentation that summarizes the changes to the IB. Otherwise, the submission of Investigator Brochures and Safety Data Reports as amendments will be acknowledged by memo only.

Certificates of Approval are not issued for IB's submitted after the initial review and approval of the FHREB.

8.4 Documents Listed on Certificates of Approval

Documents listed in the Application Form must be recorded accurately with their complete title and version numbers because this information is included in the amendment box of the approval certificate.

GUIDANCE NOTE #9 PRINCIPAL INVESTIGATOR'S SIGNATURE

If the Principal Investigator's signature cannot be obtained by the time of submission, please indicate by memo to the FHREB office that the signed first page of the application form will follow, and by when.

The review of the amendment will not be delayed if the Principal Investigator's signature cannot be obtained by the time of submission.

GUIDANCE NOTE #10: CONTACT PERSON

All Certificates and Notices are issued to the contact person specified in the Application and copied to the Principal Investigator.

GUIDANCE NOTE #11: SUMMARY OF AMENDMENTS

For both Full Board and Delegated Review, the FHREB reviewers require a list and summary of the nature of any previous amendments so that it is easy to track how the study has been amended over time.

This summary should include only those amendments that had been submitted either after the initial approval or subsequent annual renewal (i.e. amendments submitted within the approval period for the entire study; this may be between the date of initial approval to submission for initial renewal OR between the date of subsequent annual approval for renewal to submission of the next request for annual renewal).

GUIDANCE NOTE #12: CHANGES TO STUDY DESIGN

Describe any changes to the study, involving the study's objectives, research design, sample size, inclusion/exclusion criteria, and/or changes to the treatment/intervention procedures/dosage and explain how any changes will affect the study.

Describe any changes to consent form(s) (and any other documentation, such as advertisements/information sheets, questionnaires) in this section of the Application Form as well.

GUIDANCE NOTE #13: RECONSENT

Include information on how the subjects (who are enrolled already) will be contacted and how the new information about their participation in the study will be given to them.

13.1 Additional Information About Risks

The notification of a new risk(s) must be documented in a revised consent form for new subjects. Depending on the nature of the risk the FHREB may require that subjects already enrolled in the study be reconsented.

13.2 Change in Industry Sponsor

The FHREB may request that subjects already enrolled are either notified by letter or asked to give consent again when significant changes are made in the sponsorship of the research.

Re-consenting subjects may be considered by the FHREB for studies that involve tissue/DNA banking when the sponsor has changed or a different storage facility is used to store the subjects' specimens. Alternatively, the FHREB may require that subjects be informed of the change to the study via a letter, which gives the subjects the opportunity to withdraw their tissue from storage should they have any concerns.