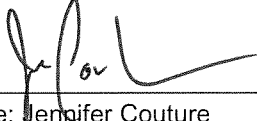
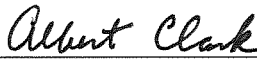



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|------------------------|----------------------------------|
| Section 400: | Review of Research |
| Title: | HSREB Amendment Reporting |
| SOP Code: | 404.003 |
| Effective Date: | 2016SEP12 |

Site Approvals

| | | |
|--------------------------------------|--|---------------------|
| Signature of Responsible Individual: | | |
| Ethics Compliance Advisor |  | Date: 2016 Sep 14 |
| | Name: Jennifer Couture | |
| Approval Authority: | | |
| Chair, HSREB |  | Date: Sept 14, 2016 |
| | Name: Dr. Albert Clark | |
| Approval Authority: | | |
| Director, Research Ethics Compliance |  | Date: 2016 Sep 15 |
| | Name: Dr. Andrew Winterborn | |

1.0 PURPOSE

This standard operating procedure (SOP) describes the procedures for the ongoing submission and review of amendments, following the initial HSREB ethical clearance of a research project.

2.0 SCOPE

This SOP pertains to the HSREB that reviews human participant research in compliance with applicable regulations, guidelines and current and emerging best practices.

3.0 RESPONSIBILITIES

All HSREB members, HSREB Office Personnel and Researchers are responsible for ensuring that the requirements of this SOP are met.

The Researcher is responsible for reporting to the HSREB and applicable authorities any new information generated throughout the course of the research that might affect the rights, safety and well-being of research participants, including any changes to the ethically cleared research in the form of an amendment, as outlined in this SOP and/or in the research protocol.

The HSREB Chair or designee is responsible for reviewing any proposed amendments to the research, and for determining the type of review (i.e., delegated or Full Board) or action required.

HSREB Members are responsible for reviewing any new information or proposed amendments that are assigned to them or that are assigned to a Full Board meeting, and for recommending the appropriate course of action.

4.0 DEFINITIONS

See Glossary of Terms.

5.0 PROCEDURES

The HSREB must receive and review any new information generated throughout the course of the research that might affect the rights, safety and well-being of research participants.

Modifications to the ethically cleared research may not be initiated without prior HSREB review and ethical clearance except where necessary to eliminate apparent immediate hazards to participants. If changes are made to eliminate immediate hazards, the Researcher must notify the HSREB as soon as they become aware of the modification.

5.1 Amendments to the Research

In order for the research to receive HSREB ethical clearance, the HSREB will take the following into consideration:

- 5.1.1 The Researcher is responsible for submitting any changes to the ethically cleared research to the HSREB in the form of an amendment using the HSREB Multi-Use Amendment/Full Board Renewal Form in TRAQ;
- 5.1.2 Changes to the ethically cleared research may include modifications to the research, to the consent form, participant material (e.g., patient diary, handouts), to the Investigator Brochure (IB) or product monograph (PM), changes in participant materials (e.g., wallet cards, diary cards, recruitment materials) or recruitment process, a change in the Researcher, etc.;
- 5.1.3 When the amendment includes a change to the consent form, the Researcher must indicate his/her recommendation for the provision of the new information to current and/or past research participants;
- 5.1.4 The Researcher must indicate the type of review being requested (i.e., Full Board, delegated review or acknowledgement for a minor

- correction). Supporting correspondence documentation and/or background information may be appended to the amendment submission;
- 5.1.5 The Health Canada No Objection Letter (NOL), must be included with the amendment to be granted ethics clearance (where applicable);
- 5.1.6 The HSREB Chair or designee reviews the amendment to determine the appropriate level of HSREB review required (i.e., Full Board or delegated review);
- 5.1.7 The HSREB Chair or designee also may use delegated review procedures for review of amendments when the conditions for delegated review are met;
- 5.1.8 If the proposed change represents an increase in risk (e.g., increase in drug dose, frequency of dosing, etc.), it may be reviewed by the HSREB at a Full Board meeting. Amendments that may be classified as more than minimal risk may include:
- Addition of genetic testing, new genetic tests, or tissue banking where genetic testing may or will be performed,
 - Addition of an open label extension phase following a randomized trial,
 - Emergency amendments that arise because of participant safety and may include, but are not limited to:
 - A change in drug dosing/duration of exposure,
 - A change in recruitment that may affect confidentiality or the perception of coercion,
 - A change in experimental procedure or research population;
- 5.1.9 For amendments requiring Full Board review, the HSREB Ethics Coordinator or designee assigns the amendment to the next available Full Board meeting. For amendments that meet the criteria for delegated review, the HSREB Ethics Coordinator or designee will forward the amendment to the designated reviewer;
- 5.1.10 When an amendment involves a revised consent, the HSREB will consider the recommendations of the Researcher in determining if, how and when the new information should be provided to the research participants and whether re-consent is required;
- 5.1.11 The HSREB must find that the criteria for ethics clearance are still met in order to approve the amendment;
- 5.1.12 The amended research may not be implemented prior to the HSREB review and ethical clearance, except when necessary to eliminate immediate hazards to participants;
- 5.1.13 **Other Reportable Amendments:** The Researcher is responsible for reporting to the HSREB other findings, such as:

- Any new information (e.g., sponsor's safety notice or action letter) that would cause the sponsor to modify the Investigator's Brochure, the research or the consent form, or would prompt other action by the HSREB to ensure protection of research participants,
- Any changes to the risks or potential benefits of the research, such as:
 - An interim analysis indicates that participants have a lower rate of response to treatment than initially expected,
 - Safety monitoring indicates that a particular side effect is more severe, or more frequent than initially expected,
 - Information is published from another research project that shows that an arm of the research is of no therapeutic value;
- A change in Health Canada or FDA safety labeling or withdrawal from marketing of a drug, device, health product, genetic therapy or biologic used in research;
- The Researcher is also responsible for submitting to the HSREB other types of findings, such as:
 - DSMB reports,
 - Interim analysis results,
 - Any other events that could significantly impact the overall conduct of the research or alter the HSREB's ethics clearance or favourable opinion to continue the research;
- Other reportable events must be submitted in a timely manner to the HSREB;

5.1.14 **Audit or Inspection Findings:** The Researcher must report to the HSREB a summary of any relevant audit or inspection findings following a Health Canada inspection, an FDA or other regulatory audit, audit sponsor, an internal QA audit, or other audits at the site.

5.2 Review of Amendments by the HSREB

- 5.2.1 The HSREB Ethics Coordinator or designee will screen the amendment submission for completeness;
- 5.2.2 The HSREB Ethics Coordinator or designee may route the submission back to the Researcher to request clarifications, missing documents or additional information;
- 5.2.3 If the event raises concerns or involves risk to research participants such that HSREB action may be required, the item is added to the agenda of the next Full Board meeting;

- 5.2.4 For reportable events reviewed at a Full Board meeting, the HSREB determines whether further action is required. Possible actions that could be taken by the HSREB include, but are not limited to:
- Placing a hold on the research pending receipt of further information from the Researcher,
 - Requesting modifications to the research,
 - Requesting modifications to the consent form,
 - Providing additional information to past participants,
 - Notifying current participants when such information might affect the participants willingness to continue to take part in the research, and requiring that current participants re-consent for ongoing participation,
 - Altering the frequency for renewal of ethics clearance,
 - Observing the research or the consent process,
 - Requiring additional training of the PI and research staff,
 - Termination or suspension of the research,
 - If the HSREB determines that the event does not raise concerns about risks to research participants, the HSREB may decide that no further action needs to be taken;
- 5.2.5 When action is taken to ensure the protection of the rights, safety, and well-being of participants the Researcher is responsible for reporting to the appropriate authorities. If it becomes known that no action has been taken by the Researcher, then the HSREB Chair or designee is responsible for reporting to Queen's University and Affiliated Teaching Hospital Official(s) as applicable, and has the authority to notify the sponsor and the appropriate regulatory authorities, as applicable. The HSREB may delegate regulatory authority reporting as applicable.

6.0 REFERENCES

See References.

7.0 APPENDICES

None.

8.0 REVISION HISTORY

| SOP Title | Version | Updates |
|---------------------------------|------------------------|--|
| Ongoing HSREB Review Activities | v.404.001 2015MAY25 | Original: Adoption of standardized SOPs developed by CAREB/N2 with an effective date of 2014SEP15. Minor modifications were made to the CAREB/N2 SOPs to reflect institutional policies |
| HSREB Amendment Reporting | v.404.002 2016JAN28 | Replaces SOP v.404.001 Ongoing HSREB Review Activities 2015MAY25, which now is divided into 3 SOPs: 404.002 (Amendment Reporting); 408.001 (Protocol Deviation Reporting); and 410.001 (SAE Reporting). |
| HSREB Amendment Reporting | v.404.003 2016SEP12 | <ol style="list-style-type: none"> 1. Revisions purpose, scope, responsibilities, and minor formatting changes in document. 2. References to 'reportable events' changed to amendments. 3. 5.1.1 Reference to Multi-Use Amendment/Full Board Renewal Form added. 4. 5.1.8: Section on Emergency amendments added (formerly section 5.1.6). 5. 5.1.11: Section of Health Canada NOLs moved to section 5.1.5. |