

TITLE	404: Ongoing HREB Review Activities
SCOPE	All research submitted to the Human Research Ethics Board operating under the direct authority of Trinity Western University
RESPONSIBILITIES	The Vice-Provost, Research & Graduate Studies, all Human Research Ethics Board (HREB) members, including the Chair(s) and Coordinator, and TWU researchers
APPROVAL AUTHORITY	The Vice-Provost, Research & Graduate Studies
EFFECTIVE DATE	November 14, 2019
Supersedes documents dated	N/A

1.0 PURPOSE

This standard operating procedure (SOP) describes the procedures for the ongoing review activities that occur after the initial Human Research Ethics Board (HREB) approval of a research project and prior to the formally scheduled continuing review of the research project.

2.0 SCOPE

This SOP pertains to HREBs that review human participant research in compliance with applicable regulations and guidelines.

3.0 RESPONSIBILITIES

The Researcher is responsible for reporting to the HREB any new information generated throughout the course of the research that might affect the rights, safety and well-being of research participants, including reportable events that meet the reporting criteria as per this SOP.

The Researcher is responsible for reporting to the HREB any information about the conduct of the research that could affect the rights, safety and well-being of research participants, including information about any serious or continuing non-compliance.

When action is taken to ensure the protection of the rights, safety, and well-being of participants (e.g., for an unanticipated problem involving risks to participants or others) the HREB is responsible for reporting to the Researcher and the Organizational Official(s) and has the authority to notify the sponsor and/or the appropriate regulatory authorities of any events that meet the reporting criteria. The HREB may delegate regulatory authority reporting (as applicable) to the organization.

The HREB Chair or designee is responsible for reviewing all reportable events submitted to the HREB as well as any proposed amendments to the research, and for determining the type of review (i.e., delegated or Full Board) or action required.

The HREB members are responsible for reviewing any new information, reportable events 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 PROCEDURE

It may be that the real risk/benefit ratio can be evaluated only after the research has begun; therefore, in addition to the formally scheduled continuing review, the HREB 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. Such information may include:

- Modifications or changes to the previously approved research,
- Reports of unanticipated problems involving risks to participants or others,
- Reports of any serious or continuing non-compliance,
- Reports of any changes significantly affecting the conduct of the research or increasing the risk to research participants,
- Results of any interim analysis or Data and Safety Monitoring Board (DSMB) assessments,
- Deviations to the previously approved research,
- Adverse events that meet the reporting criteria,
- Reports of any privacy breaches,
- Summary reports of any audits and inspections,
- Any other new information that may affect adversely the safety of the research participants or the conduct of the research,

Modifications to the approved research may not be initiated without prior HREB review and approval except where necessary to eliminate apparent immediate hazards to human participants. If changes are made to eliminate immediate hazards, the Researcher must notify the HREB immediately.

5.1 Amendments to the Approved Research

- 5.1.1 The Researcher is responsible for submitting to the HREB any changes to the approved research in the form of an amendment. Changes to the approved research include modifications including (for example) modifications to the research, to the consent form, to the Investigator Brochure (IB) or product monograph (PM), changes in participant

materials (e.g., wallet cards, diary cards, recruitment materials), a change in the Researcher etc.;

- 5.1.2 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;
- 5.1.3 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;
- 5.1.4 The HREB Chair or designee reviews the amendment to determine the appropriate level of HREB review required (i.e., Full Board or delegated review);
- 5.1.5 The HREB Chair or designee also may use delegated review procedures for review of amendments when the conditions are met:
- 5.1.6 If the proposed change represents more than minimal risk, it must be reviewed by the HREB 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:
 1. A change in drug dosing/duration of exposure,
 2. A change in recruitment that may affect confidentiality or the perception of coercion,
 3. A change in experimental procedure or research population;
- 5.1.7 For amendments requiring Full Board review, the responsible HREB Office Personnel assigns the amendment to the next available Full Board meeting. For amendments that meet the criteria for delegated review, the responsible HREB Office Personnel will forward the amendment to the designated reviewer;
- 5.1.8 When an amendment involves a revised consent, the HREB 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;
- 5.1.9 The HREB must find that the criteria for approval are still met in order to approve the amendment;

5.1.10 The amended research may not be implemented prior to the HREB review and approval, except when necessary to eliminate immediate hazards to participants.

5.2 Reportable Events

5.2.1 The Researcher is responsible for submitting reportable events that meet the HREB's reporting criteria according to the local procedures;

5.2.2 Local Adverse Events (AE): The Researcher must report the following to the HREB within a time frame specified by the HREB:

- Any local AE that in the opinion of the Researcher meets the definition of an unanticipated problem,
- The completed sponsor's serious adverse event (SAE) form (if applicable) must be appended to the reportable event form,
- All reports submitted to the HREB must have all research participant identifiers removed (i.e., participant research number only),
- The sponsor's SAE report (if applicable) must be signed by the Researcher or medical designee,
- Once a local SAE is acknowledged by the HREB, subsequent important follow-up reports related to the SAE should be submitted when available, as SAE update(s). The sponsor's follow-up reporting form(s) signed by the Researcher or medical designee must be appended to the updated reportable event. All initial and subsequent follow-up reports will be retained with the reportable event;

5.2.3 Non-Local (External) Adverse Events: Upon receipt of an external adverse event (EAE) or a periodic safety update or safety summary report, the Researcher must determine if it meets the HREB reporting criteria:

- Non-local adverse event reports are reportable to the HREB, if in the opinion of the Researcher, it meets the definition of an unanticipated problem AND requires a change to the research and/or informed consent form and/or requires immediate notification to participants for safety reasons,
- The report submitted to the HREB must include **all** of the following information:
 - The description of the serious and unexpected event(s),
 - All previous safety reports concerning similar adverse events,
 - An analysis of the significance of the current adverse event(s) in light of the previous reports, **and**
 - The proposed research changes, informed consent form changes or other corrective actions to be taken by the sponsor in response to the event(s),

- The individual AE reports or periodic safety updates or safety summary reports that meet the reporting criteria must be submitted to the HREB within a time frame specified by the HREB;
- 5.2.4 Other Reportable Events: The Researcher is responsible for reporting to the HREB other events or 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 HREB 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 HREB other types of reportable events, such as:
 - DSMB reports,
 - Interim analysis results,
 - Any unanticipated problems or other events that could significantly impact the overall conduct of the research or alter the HREB’s approval or favorable opinion to continue the research,
 - A change to the research that was initiated without prior HREB review to eliminate an apparent immediate hazard to a research participant,
 - Any unanticipated problems or other events that could significantly impact the conduct of the research at the site (e.g., concerns of non-compliance),
 - Other reportable events must be submitted to the HREB within a time frame specified by the HREB;
- 5.2.5 Deviations to Previously Approved Research: The Researcher must report to the HREB any deviations that meet the following reporting criteria:
- Deviations that in the opinion of the Researcher jeopardize the safety of research participants, or that jeopardize the research efficacy or data integrity,

- Any sponsor-approved waivers to the participant eligibility criteria,
 - Any change in the approved process for obtaining consent (e.g., improper translation, current ICF not implemented),
 - Any deviations that lead to an SAE,
 - Deviations must be reported within a time frame specified by the HREB; deviations that lead to an SAE should be reported within a time frame specified by the HREB;
- 5.2.6 Privacy Breaches: The Researcher must report to the HREB any unauthorized collection, use, or disclosure of personal information (PI) including, but not limited to:
- The collection, use and disclosure of PI that is not in compliance with the jurisdictional legislation or its regulation,
 - Circumstances where PI is stolen, lost or subject to unauthorized use or disclosure or where records of PI are subjected to unauthorized copying, modifications or disposal,
 - In the Researcher context, any unauthorized collection, use or disclosure of PI that was not authorized under the research and approved in the plan that was submitted to the HREB,

The breach must be reported to the HREB and, if applicable, to the appropriate Organizational Official as soon as the Researcher becomes aware of the breach;

- 5.2.7 Audit or Inspection Findings: The Researcher must report to the HREB a summary of any relevant audit or inspection findings following a Health Canada inspection, an FDA or other regulatory audit, an internal QA audit or other audits at the site;
- 5.2.8 Research Participant Complaint: The Researcher must report to the HREB, and to the organization if required by local procedures, a complaint from a participant when the participant reports concerns about their rights as a research participant or about ethical issues related to the research.

5.3 Review of Reportable Events by the HREB

- 5.3.1 The responsible HREB Office Personnel will screen the reportable event submission for completeness;
- 5.3.2 Privacy breaches are reviewed by the HREB Chair or designee, and any recommendations including remedial action are determined in consultation with the organization's privacy office. The privacy breach report is forwarded to the HREB Chair or designee for review and final acknowledgement;

- 5.3.3 The HREB Office Personnel may route the submission back to the Researcher to request clarifications, missing documents or additional information;
- 5.3.4 The HREB Office Personnel will forward the submission to the designated HREB reviewer(s);
- 5.3.5 The assigned HREB reviewer(s) will conduct a review of the report and determine if any action or follow-up is required;
- 5.3.6 The assigned reviewer(s) may request further information from the Researcher;
- 5.3.7 When reviewing a reportable event, the HREB should:
 - Assess the appropriateness of any proposed corrective or preventative measures by the sponsor and/or Researcher,
 - Consider any additional appropriate measures that may or may not have been identified or proposed by the sponsor and/or Researcher,
 - Consider whether the affected research still satisfies the requirements for HREB approval; in particular whether risks to research participants are still minimized and reasonable in relation to the anticipated benefits, if any, to the research participants and the importance of the knowledge that may reasonably be expected to result,
 - Consider whether some or all of the research participants should be notified of the events (i.e., if it may affect the participant's willingness to continue participation in the research), and
 - Consider whether suspension or termination of the ethics approval of the research is warranted;
- 5.3.8 If the event does not raise concerns and does not appear to involve risks to research participants or others, the HREB Chair or designee acknowledges the report, and no further action is required;
- 5.3.9 If the HREB Chair or designee determines that the event meets the criteria for an unanticipated problem, and if immediate action is required to protect the safety of research participants, he/she may suspend ethics approval of the research pending review by the Full Board, providing the justification for such action is documented;
- 5.3.10 If the event raises concerns or involves risk to research participants such that HREB action may be required, the item is added to the agenda of the next Full Board meeting;
- 5.3.11 For reportable events reviewed at a Full Board meeting, the HREB determines whether further action is required. Possible actions that could be taken by the HREB 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 of continuing review,
- Observing the research or the consent process,
- Requiring additional training of the Researcher and research staff,
- Termination or suspension of the research,
- If the HREB determines that the event does not raise concerns about risks to research participants, the HREB may decide that no further action needs to be taken;

5.3.12 When action is taken to ensure the protection of the rights, safety, and well-being of participants (e.g., for an unanticipated problem involving risks to participants or others) the HREB chair or designee is responsible for reporting to the Researcher and the Organizational Official(s) and has the authority to notify the sponsor and the appropriate regulatory authorities (as applicable). The HREB may delegate regulatory authority reporting (as applicable) to the organization.

6.0 REFERENCES

See References.

7.0 REVISION HISTORY

SOP Code	Effective Date	Summary of Changes
SOP 404	November 14, 2019	Original version