Ontario Shores
Centre for Mental Health Sciences

REB STANDARD OPERATING PROCEDURES MANUAL

Name of SOP: Reportable Events to the REB
REB SOP # 015

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

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

Description:
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 REB 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 (see REB SOP # 013, Amendments Review)
- 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 my 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 REB review and approval except where necessary to eliminate apparent immediate hazards to human participants. If changes are made to eliminate immediate hazards, the investigator must notify the REB immediately

Procedure:
The Investigator is responsible for submitting reportable events that meet the REB's reporting criteria according to CAREB procedures;

1) Local Serious Adverse Events (Local SAEs):

The Investigator must report the following to the REB within a time frame specified by the REB (2 days):

- Any local adverse event that in the opinion of the Investigator meets the definition of an unanticipated problem

- The completed sponsor's serious adverse event (SAE) form (if applicable) must be appended to the local SAE reportable event form
- All reports submitted to the REB 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 Investigator or medical designee
- Once a local SAE is acknowledged by the REB, 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 Investigator 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 by the REB office

2) External Serious Adverse Events (External SAEs):

Upon receipt of an External SAE or a periodic safety update or safety summary report, the Investigator must determine if it meets the REB reporting criteria:

External adverse event reports are reportable to the REB, if in the opinion of the Investigator, 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 REB 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
- 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 adverse event reports or periodic safety updates or safety summary reports that meet the reporting criteria must be submitted to the REB within a time frame specified by the REB

3) Other Reportable Events:

The Investigator is responsible for reporting to the REB 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 REB to ensure protection of research participants
- Any changes to the risks or potential benefits of the research, such as a) An interim analysis indicates that participants have a lower rate of response to treatment than initially expected b) Safety monitoring indicates that a particular side effect is more severe, or more frequent than initially expected c) Information is published from another research project that shows that an arm of the research is of no therapeutic value d) 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 Investigator is also responsible for submitting to the REB other types of reportable events, such as a) DSMB reports b) Interim analysis results C) Any unanticipated problems or other events that could significantly impact the overall conduct of the research or alter the REB's approval or favorable opinion to continue the research
- A change to the research that was initiated without prior REB 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 REB within a time frame specified by the REB

4) Deviations to Previously Approved Research:

The Investigator must report to the REB any deviations that meet the following reporting criteria:

- Deviations that in the opinion of the Investigator 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 REB; deviations that lead to an SAE should be reported within a time frame specified by the REB

5) Privacy Breaches:

The Investigator must report to the REB any unauthorized collection, use, or disclosure of personal information (PI) including, but not limited to:

- The collection, use and disclosure of Personal Information that is not in compliance with the jurisdictional legislation or its regulation
- Circumstances where Personal Information is stolen, lost or subject to unauthorized use or disclosure or where records of Personal Information are subjected to unauthorized copying, modifications or disposal
- In the Investigator context, any unauthorized collection, use or disclosure of Personal Information that was not authorized under the research and approved in the plan that was submitted to the REB
- The breach must be reported to the REB and to the Leader, Privacy & Access at Ontario Shore's as soon as the Investigator becomes aware of the breach

6) Audit or Inspection Findings:

The Investigator must report to the REB 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

7) Research Participant Complaint:

The Investigator must report to the REB, 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

8) Review of Reportable Events by the REB:

- The responsible REB Office Personnel will screen the reportable event submission for completeness
- Privacy breaches are reviewed by the REB Chair or designee, and any recommendations including remedial actions are determined in consultation with the Leader, Privacy & Access at Ontario Shores
- The privacy breach report is forwarded to the REB Chair or designee for review and final acknowledgement
- The REB Office Personnel may route the submission back to the Investigator to request clarifications, missing documents or additional information
- The REB Office Personnel will forward the submission to the designated REB reviewer(s)
- The assigned REB reviewer(s) will conduct a review of the report and determine if any action or follow-up is required
- The assigned reviewer(s) may request further information from the Investigator;
- When reviewing a reportable event, the REB should a) assess the appropriateness of any proposed corrective or preventative measures by the sponsor and/or Investigator b) consider any additional appropriate measures that may or may not have been identified or proposed by the sponsor and/or Investigator c) consider whether the affected research still satisfies the requirements for REB 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 d) 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 e) consider whether suspension or termination of the ethics approval of the research is warranted

- If the event does not raise concerns and does not appear to involve risks to research participants or others, the REB Chair or designee acknowledges the report, and no further action is required
- If the REB 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
- If the event raises concerns or involves risk to research participants such that REB action may be required, the item is added to the agenda of the next Full Board meeting
- For reportable events reviewed at a Full Board meeting, the REB determines whether further action is Required; Possible actions that could be taken by the REB include, but are not limited to:

    - Placing a hold on the research pending receipt of further information from the Investigator
    - 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 Investigator and research staff
    - Termination or suspension of the research
    - If the REB determines that the event does not raise concerns about risks to research participants, the REB may decide that no further action needs to be taken

- 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 REB chair or designee is responsible for reporting to the Investigator and Ontario Shore's Official(s) and has the authority to notify the sponsor and the appropriate regulatory authorities (as applicable). The REB may delegate regulatory authority reporting (as applicable) to the organization

Responsibility:

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

The Investigator is responsible for reporting to the REB 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 Investigator is responsible for reporting to the REB 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 REB is responsible for reporting to the Investigator and Ontario Shore's 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 REB may delegate regulatory

authority reporting (as applicable) to the organization.

The REB Chair or designee is responsible for reviewing all reportable events submitted to the REB 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 REB 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.

References:

1) N2 CAREB REB SOPs v1 *SOP 404.001* (September 2014) https://oicronca.box.com/s/95k7ydj574579ajvbe06

2) Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, and Social Sciences and Humanities Research Council of Canada, Tri-Council Policy Statement: Ethical conduct for Research Involving Humans, December 2010: (short name: TCPS 2) http://www.pre.ethics.gc.ca/eng/policy-politique/initiatives/tcps2-eptc2/Default/

3) ICH: E6 - Guidance for industry: Good Clinical Practices (GCP): (April 1996) http://www.fda.gov/downloads/Drugs/Guidances/ucm073122.pdf

4) U.S. Department of Health and Human Services (HHS): Code of Federal Regulations (CFR), Title 45 Part 46.103, Part 46.108 http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html

5) U.S. Department of Health and Human Services (HHS): Office for Human Research Protections (OHRP) Policy & Guidance Library http://www.hhs.gov/ohrp/policy/index.html

6) Ontario Shores Research Ethics Board Terms of Reference, Functions and Responsibilities (2009)