

SOP Title:	Unanticipated Problem Reporting		
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1.0 PURPOSE

The purpose of this standard operating procedure (SOP) is to describe the procedures for unanticipated problems and other events that must be reported to the SickKids Research Ethics Board (REB).

2.0 POLICY STATEMENT

The REB must receive and review unanticipated problems that may affect the safety, rights, and well-being of research participants. The REB may also receive other notifications such as protocol deviations, and complaints.

The SickKids Research Ethics Board (REB) has adopted the Canadian Association of Research Ethics Boards' Guidance on Reporting of Unanticipated Problems including Adverse Events to Research Ethics Boards in Canada guidance document issued in July 2010.

The purpose of this Standard Operating Procedure (SOP) is to describe the procedures for reporting unanticipated events including adverse events to the SickKids REB.

Unanticipated/Adverse Event reporting is the responsibility of the SickKids Principal Investigator (PI), who must complete the REB Adverse Event/Unanticipated Problem application, including information on the seriousness of the Event, assessing whether or not it is a direct consequence of the research intervention, and recommendations for any further action. The researcher is also responsible for reporting this information to other appropriate regulatory or advisory bodies including, but not limited to, the Data and Safety Monitoring Board (DSMB), safety monitoring committees, and external advisory boards.

The SickKids REB is available for consultation regarding non-reportable events.

3.0 DEFINITIONS

See Glossary of Terms

4.0 RESPONSIBILITY

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

5.0 PROCEDURES

5.1 Reportable Events

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

5.1.2 Local Adverse Events: The Researcher must report the following to the REB within a time frame specified by the REB:

- Any local adverse event 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 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 Researcher 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. 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;

5.1.3 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 REB reporting criteria:

- Non-local adverse event reports are reportable to the REB, 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 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, 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 REB within a time frame specified by the REB;

5.1.4 Other Reportable Events: The Researcher 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:
 - 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 REB 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 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;

5.1.5 Deviations to Previously Approved Research: The Researcher must report to the REB 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 informed consent form 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;

- 5.1.6 Privacy Breaches: The Researcher 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 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 REB,
 - The breach must be reported to the REB and, if applicable, to the appropriate Organizational Official as soon as the Researcher becomes aware of the breach;
- 5.1.7 Audit or Inspection Findings: The Researcher 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 quality assurance audit or other audits at the site;
- 5.1.8 Research Participant Complaint: The Researcher must report to the REB, 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.

5.2 Review of Reportable Events by the REB

- 5.2.1 The responsible REO Personnel will screen the reportable event submission for completeness;
- 5.2.2 Privacy breaches are reviewed by the REB 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 REB Chair or designee for review and final acknowledgement;
- 5.2.3 The REO Personnel may route the submission back to the Researcher to request clarifications, missing documents or additional information;
- 5.2.4 The REO Personnel will forward the submission to the REB Chair or designee;
- 5.2.5 The REB Chair or designee(s) will conduct a review of the report and determine if any action or follow-up is required;
- 5.2.6 The assigned REB Chair or designee(s) may request further information from the Researcher;
- 5.2.7 When reviewing a reportable event, the REB will:
- 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 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,

- 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;
- 5.2.8 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;
- 5.2.9 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, they may suspend ethics approval of the research pending review by the Full Board, providing the justification for such action is documented;
- 5.2.10 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;
- 5.2.11 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 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 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;
- 5.2.12 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 REB 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 REB may delegate regulatory authority reporting (as applicable) to the organization.

6.0 REFERENCES

See References