

INSTRUCTIONS FOR REPORTING OF LOCAL and NON-LOCAL ADVERSE EVENTS

DEFINITIONS

- A. Investigational Product:** Any drug, biologic, radiopharmaceutical, vaccine, natural health product, medical device or placebo being given to a research participant
- B. Adverse Event (AE):** Any untoward medical occurrence in a research participant, administered investigational product, including an occurrence which does not have a causal relationship with the product. An AE can be any unfavourable and unintended sign, symptom, or disease temporally associated with the use of an investigational product, whether or not related to the investigational product
- C. Serious Adverse Event (SAE):** Is any adverse occurrence or response to a drug/intervention that:
- Results in death
 - Is life-threatening
 - Requires inpatient hospitalization or prolongation of existing hospitalization
 - Results in persistent or significant disability/incapacity
 - Results in a congenital anomaly/birth defect
 - Based upon appropriate medical judgment, is an important medical event that may jeopardize the health of the research participant or may require medical intervention to prevent one of the outcomes listed above
- D. Unanticipated Problem:** any incident, experience, or outcome (including an adverse event) that meets **ALL** of the following criteria:
- ***Unexpected** (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the HiREB-approved research protocol, informed consent document, and/or the Investigator Brochure; and (b) the characteristics of the research participant population being studied; **AND**
 - **+Related or possibly related** to participation in the research, (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the [intervention(s)] or procedures involved in the research); **AND**
 - Suggests that the research **places research participants or others at a greater risk of harm** (including physical, psychological, economic, or social harm) than was previously known or recognized.

Note:

***Unexpected:** an event is “unexpected” when its specificity and severity are not accurately reflected in the HiREB-approved research protocol, the current HiREB-approved informed consent document, the Investigator Brochure, and/or other relevant sources of information; or when the event is not associated with the expected natural progression of any underlying disease, disorder, predisposing risk factor, or condition of the participant(s) experiencing the adverse event.

+Related to the research procedures: an event is “related to the research procedures” if in the opinion of the Researcher or sponsor, the event was more likely than not to be caused by the research procedures.

REPORTING LOCAL ADVERSE EVENTS

- Any **local serious adverse event** that in the opinion of Local Principal Investigator (LPI) is **both unexpected and related or possibly related to**, the study intervention or research procedures, must be reported to the HiREB. Please see definitions under “Unanticipated Problem” above. *In the case of sponsored multi-site clinical trials, the LPI is unlikely to know if the SAE may pose a threat to other research participants at other sites; thus a local SAE must be reported if it satisfies the first 2 criteria of being unexpected and related/possibly related to, the study intervention.*
- Use the **Local Serious Adverse Event Report Form**
- Report **within 7 business days** of becoming aware of the event
- All reports submitted to the HiREB must have all research participant identifiers removed (i.e., participant research ID number only)
- Once a local adverse event is acknowledged by the HiREB, subsequent important follow-up reports related to the adverse event should be submitted when available, as update(s)
- The reporting of SAEs may not be deferred to the Annual Progress Report
- Local SAEs must be reported by the LPI to the study sponsor and/or appropriate federal government agencies (eg. Health Canada)
- If the local site is part of a multi-centre study, the LPI must also append the most recent Data Safety Monitoring Board (DSMB) or a Sponsor-generated safety Report summarizing SAEs to date and any implications for the risk/benefit ratio, as described below

NOTE: The following local adverse events need NOT be reported to the HiREB:

- SAE that is expected and considered related to the investigational product or research procedures
- SAE that is expected and considered not related to the investigational product or research procedures
- SAE that is unexpected and is considered not related to the investigational product or research procedures
- Non-serious AE which is expected
- Non-serious AE which is unexpected

REPORTING OF LOCAL SERIOUS ADVERSE EVENT TO HiREB

LOCAL SAE				ACTION
Unexpected	Expected	Not Related	Related	
X			X	Report to HiREB
X		X		No Report to HiREB
	X		X	No Report to HiREB
	X	X		No Report to HiREB

REPORTING NON-LOCAL SERIOUS ADVERSE EVENTS

- Upon receipt of a non-local adverse event, a periodic safety update, or safety summary report, the Local Principal Investigator must determine if it meets the HiREB reporting criteria:

A Non-local Adverse Event is reportable to the HiREB, if in the opinion of the Local Principal 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. Please see definitions under “Unanticipated Problem” above.

- Use the **Non-Local Serious Adverse Event Report Form**
- The report submitted to the HiREB must include all of the following information:
 - a. The description of the unanticipated event(s)
 - b. All previous safety reports concerning similar adverse events
 - c. An analysis of the significance of the current unanticipated event(s) in light of the previous reports
 - d. 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 non-local individual SAE reports, periodic safety updates, or safety summary reports that meet the reporting criteria must be submitted to the HiREB **within 15 business days** of the Local Principal Investigator becoming aware of the event/report(s)
- Reports not meeting these requirements will be returned to the Local Principal Investigator

DSMB and SPONSOR-GENERATED SAFETY REPORTS

- All DSMB Reports must be forwarded to the HiREB **within 15 business days** of the Local Principal Investigator becoming aware of them
- The DSMB report must be accompanied by a letter from the Local Principal Investigator indicating his/her acceptance of the findings and recommendations of the DSMB