SAFETY INFORMATION AND UNANTICIPATED PROBLEMS REPORTING GUIDELINES

The following events/information must be reported to Island Health Research Ethics office within 10 business days.

REPORTABLE EVENTS THAT OCCUR AT THE LOCAL RESEARCH SITE or are ASSOCIATED WITH THE PRINCIPAL INVESTIGATOR

Event	Reporting Criteria (What to report)	Examples (not all-inclusive)	Form in Portal
Local Serious Adverse Event (SAE)	An adverse event that is: ✓ Documented at the local study site, ✓ Serious, ✓ Unanticipated, and ✓ Related	○ Pneumonia resulting from study drug administration ○ Significant allergic reaction resulting from study drug(s) ○ Cardiovascular event induced by study drug(s) or device ○ Complication from a study procedure	**Local Serious Adverse Event Report**
Major Protocol Deviation	Any change from REB-approved protocol that adversely affects the: ✓ risk/benefit ratio of the study, or ✓ rights, safety, or welfare of the participants or others, or ✓ integrity of the study	○ Failure to obtain informed consent ○ Omitting study procedure(s) required by-approved protocol ○ Drug dispensing/dosing error ○ Breach of participant confidentiality (e.g., breach of secured database) ○ Failure to securely control the study product ○ Deviation necessary to eliminate an apparent immediate hazard to a participant	**Protocol Deviation Report**
Protocol Waiver/ Exception	○ Any prospective request for an intentional deviation from the REB approved protocol except when necessary to eliminate immediate hazard to a participant.	○ Intentional deviation from the inclusion/ exclusion criteria set forth in the protocol	**Protocol Waiver Exception Request Form** **Attach copy of Sponsor approval**
Negative Inspection or Audit Finding or Enforcement Action	Any adverse finding issued to, or enforcement action taken against, the PI	○ Health Canada Compliance Notice or FDA Warning Letter ○ Adverse Sponsor audit results (critical observation) ○ Suspension or restriction of PI or Sub-PI medical license	**Local Unanticipated Problem Report** **Attach copy of the adverse audit results, enforcement action, etc.**
Other Unanticipated Problem	Unanticipated problem that adversely affects the: ✓ risk/benefit ratio of the study, or ✓ rights, safety, or welfare of the participants or others, or ✓ integrity of the study	○ Participant becomes incarcerated ○ Study personnel misconduct that adversely affects the study	**Local Unanticipated Problem Report**

REPORTABLE EVENTS THAT OCCUR EXTERNAL TO THE LOCAL RESEARCH SITE

Event/Report	Reporting Criteria (What to report)	Examples (not all-inclusive)	Form in Portal
Summary or Listings of External SAE Reports (e.g., IND Safety Reports)	ONLY Unanticipated problem that adversely affects the: ✓ risk/benefit ratio of the study, or ✓ rights, safety, or welfare of the participants or others, or ✓ integrity of the study	Summary or Listings of: ○ IND Safety Reports from other sites ○ MedWatch Reports from other sites ○ CIOMS Reports from other sites	**Non-Local Safety Information and Unanticipated Problem** **Attach copy of entire external SAE report for ONLY Unanticipated events**
Reports, publications, or interim results or findings	All reports, publications, or interim results or findings	○ DSMB reports and recommendations ○ Regulatory Agency Public Health Advisory ○ "Dear Healthcare Professional" Letter	**Non-Local Safety Information and Unanticipated Problem** **Attach copy of report, publication, interim finding, etc.**
New or updated study product safety information	**All new or updated study product safety information and a summary of changes.** ***For study product and comparator drugs**	○ Revised Investigator's Brochure ○ Revised label/ Package Insert ○ Device manual	**Non-Local Safety Information and Unanticipated Problem** **Attach copy of the new or updated study product safety information**

SAFETY INFORMATION AND UNANTICIPATED PROBLEMS REPORTING GUIDELINES

Event/Report	Reporting Criteria (What to report)	Examples (not all-inclusive)	Form in Portal
Recalls / Withdrawals	**Correspondence communicating a** Regulatory Agency **or Sponsor mandated marketing recall or withdrawal**	○ Regulatory Agency or Sponsor Marketing withdrawal	**Non-Local Safety Information and Unanticipated Problem** **Attach copy of the correspondence**

The following events/information are generally NOT required to be reported to Island Health Research Ethics office

NON- REPORTABLE EVENTS

Event	Examples (not all-inclusive)
Minor Protocol Deviations	○ Study visits performed slightly out of window ○ Change of contact information ○ A wording adjustment in questions
Individual Non-Local SAE Reports	○ SAE Reports from external sites not compiled into summary safety reports or listings
Minor Complaints Resolved by Research Staff	○ Minor research participant complaints resolved by the research staff

PROMPT REPORTING OF SAFETY INFORMATION AND UNANTICIPATED PROBLEMS

Island Health REB requires Principal Investigators (PI) to promptly report all events that may constitute ***unanticipated problems involving risk to research participants or others*** and new or updated safety information relating to study or study product. The following events/information must be reported to the research ethics office within 10 business days of their occurrence. Fatal or life-threatening events should be reported within five (5) business days.

Events that occur at the PI's research site or are associated with the PI	**Study, protocol, or product related events that occur external to the PI's research site**
Serious Adverse Events	Unanticipated External SAE Reports (Summary Reports or Listings only)
Major Protocol Deviations or Protocol Waivers	Reports, publications, or interim results or findings
Research Participant Complaints	New or updated study product information
Adverse Audit or Enforcement Action	Recalls / Withdrawals / Clinical Holds
Other Unanticipated Problems	DSMB report summary

REPORTING OF IND SAFETY REPORTS, MEDWATCH REPORTS AND CIOMS REPORTS

The vast majority of individual CIOMS Reports, IND Safety Reports, and MedWatch Reports ("Reports") ***do not need to be reported*** to Island Health Research Ethics office. The only Reports that must be reported are those reports that reveal an unanticipated problem involving risk to participants or others. Please submit form *Non-local Safety Information and Unanticipated Problem* form with summary safety reports or listings that include such information.

NOT REPORTABLE EVENTS

Typically, a number of events occur during the course of a study that do not meet VIHA REBs reporting requirements. Examples of such events may include:

- Adverse events that, in the PI's judgment, are not related to the study;
- Adverse events that are anticipated or expected as part of the study;

- External serious adverse event reports (e.g., IND Safety Reports) that, in the PI's judgment, do not adversely affect the conduct of the PI's study at his/her research facility;
- Minor protocol deviations (such as study visits performed slightly out of window);
- Minor research participant complaints that are adequately resolved by the research staff.

The occurrence of events that do not satisfy Island Health's reporting requirements (e.g. adverse events, minor protocol deviation or other unanticipated problems) do not need to be reported to the REB. However, if in the PI's judgment, any adverse events, minor protocol deviations or other unanticipated problems when considered together indicate that changes to the research plan and/or consent form should be made, then the PI should provide an analysis of the events and any rationale for suggested changes at the time of continuing review and/or site closure. This includes any minor deviations that the Sponsor may have requested be reported to the REB.

Definitions

Adverse event – *"Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An adverse event (AE) can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporarily associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product."* ICH Topic E6, Health Canada GCP Guidance for Industry

Serious Adverse Event – an undesirable event experienced by a research participant that is serious in nature, unanticipated, and at least possibly related to the study product.

- ❑ Related – a reasonable possibility that the adverse event may have been caused by the study product or study procedures (e.g. "possibly related", "probably related", and "definitely related")
- ❑ Serious – results in death, is life-threatening, results in persistent or significant disability/incapacity (a substantial disruption of the participant's ability to conduct normal life functions), results in or prolongs inpatient hospitalization, is a congenital anomaly/birth defect, or jeopardizes the participant or requires intervention to prevent one of the outcomes listed above.
- ❑ Unanticipated - not identified in nature, severity, or frequency in the relevant safety documents(s) for the study product or is not identified as a possible risk in the study protocol or the informed consent form for the study.

Protocol Deviation/Violation – A protocol deviation is any change, divergence, or departure from the design or procedures of a research project protocol that is under the Investigator's control and that has not been approved by the REB.

Major Protocol Deviation/Violation –
An unanticipated or unintentional divergence or departure from the expected conduct of an approved study that is not consistent with the current research protocol, consent document or study addenda. Examples of protocol major deviations include:

1) changes in procedures initiated to eliminate immediate hazards to study subjects;
2) enrolment of subjects outside protocol inclusion/exclusion criteria, whether agreed to or not by the sponsor;
3) medication/intervention errors [i.e. incorrect drug/intervention, incorrect dosage of the drug];
4) inadvertent deviation in specific research intervention procedures or timing of the research intervention which could impact upon the safety or efficacy of the study-related intervention or upon the experimental design [n.b. this would not include appointment deviations usually];
5) breach of confidentiality or privacy whereby confidential information about a subject is revealed in inappropriate settings, or to persons without a need to know, or by data exposure (computer security breach, documents left unsecured), and;
6) significant deviation from the consenting process.

Minor Protocol Deviation/Violation –
A protocol deviation where ALL of the following are true:

1) has no substantive effect on the risks or benefits for the individual research subject;
2) has no substantive effect on the value of the data collected;
3) has no effect on the rights, safety or welfare of participants; and
4) does not result from willing or knowing misconduct on the part of an investigator or study staff.

Examples of protocol minor deviations include:

a) change of monitor(s);
b) change of telephone number(s);
c) visits outside of window identified in protocol; and/or
d) a wording adjustment on a question.

Protocol Waiver – Documented approval from the research project sponsor that a specific participant, who may not meet all specific inclusion/exclusion criteria within a research project protocol can be enrolled into a trial, or in the case of studies that have a second set of criteria prior to randomization, can be randomized. Protocol waivers may also pertain to requested changes in the treatment or dosage plan.

Unanticipated problem involving risk to participants or others –

Any incident, experience or outcome that meets all of the following criteria:

a) Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the REB-approved research protocol and informed consent document, or the Investigator Brochure; and (b) the characteristics of the research participant population being studies; and
b) 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 investigational product(s) or procedures involves in the research); and
c) 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.