RR0900 – SAFETY AND ADVERSE EVENTS REPORTING

1.0 PURPOSE

To provide direction for the responsibility of reporting and review of safety information and serious adverse events related to research involving human participants previously approved by the Interior Health (IH) Research Ethics Board (REB).

2.0 DEFINITIONS[1]

TERM	DEFINITION
Adverse Drug Reaction (ADR)	In the pre-approval clinical experience with a new medicinal or natural health product or its new usages, particularly as the therapeutic doses may not be established: all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug or natural health product reactions. The phrase "responses to a medicinal product" means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility; i.e., the relationship cannot be ruled out. In marketed medicinal or natural health products: a response to a drug or natural health product which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of diseases or for modification of physiological function.
Adverse Event (AE)	Any untoward medical occurrence in a research participant administered an investigational product and which does not necessarily have a causal relationship with this treatment. An adverse event (AE) can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of an investigational product, whether or not related to the investigational product.
Clinical Trial	Any investigation in human participants intended to discover or verify the clinical, pharmacological and/or other pharmacodynamics effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy. Note: A clinical trial may also involve a device, observation, questionnaires, interviews or diagnostic tests

[1] All definitions in this section have been adapted N2 Network of Networks Glossary of Terms.

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TERM	DEFINITION
Data Safety Monitoring Board (DSMB)	An expert advisory group established by a research sponsor, that is responsible for assessing at intervals the progress of a clinical trial, the safety data and critical efficacy endpoints, and to recommend to the sponsor whether to continue, modify, or stop a trial.
Local Adverse Event	An adverse event occurring at a site under the jurisdiction of the IH REB.
Serious Adverse Event	An adverse drug, device, or natural health product reaction that requires in-patient hospitalization or prolongation of existing hospitalization; that causes congenital malformation; that results in persistent or significant disability or incapacity; that is life threatening; or that results in death.
Suspected Unexpected Serious Adverse Reaction (SUSAR)	A serious adverse drug, device, or natural health product reaction that is not identified in nature, severity or frequency in the risk information set out in the Investigator's Brochure or on the label of the drug or natural health product.
Sponsor	An individual, company, institution, or organization that takes responsibility for the initiation, management, and/or financing of a clinical trial.
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 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 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 [investigational product(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. *Unexpected: an event is “unexpected” when its specificity and severity are not accurately reflected in (a) the protocol-related documents such as the REB approved research protocol, the Investigator Brochure, or the current REB approved informed consent document, or (b) other relevant sources of information such as

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	product labelling and package inserts; 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.
Unexpected Adverse Drug Reaction	An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g. Investigator's Brochure for an unapproved investigational product or package insert for an approved product).

3.0 POLICY

3.1 Safety Reporting

3.1.1 The REB will 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:

3.1.1.1 Reports of unanticipated problems involving risks to participants or others;

3.1.1.2 Reports of any serious or continuing non-compliance;

3.1.1.3 Reports of any changes significantly affecting the conduct of the research or increasing the risk to research participants;

3.1.1.4 Results of any interim analysis or Data and Safety Monitoring Board (DSMB) assessments;

3.1.1.5 Local adverse events that meet the reporting criteria as provided in the protocol for the study associated with the SAE;

3.1.1.6 Summary reports of any audits and inspections; or

3.1.1.7 Any other new information that may affect adversely the safety of the research participants or the conduct of the research.

3.1.2 Researchers and the REB are not appropriately situated to assess the significance of individual adverse events occurring at sites outside their jurisdiction. The REB respects that the sponsor and/or DMSB are responsible to analyze safety and adverse event information for multi-jurisdictional studies and will accept their reports.

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The researcher will report a non-local adverse event to the REB if the event meets the definition of an unanticipated problem and requires a change to the research procedures and/or the research documents; or if it requires immediate notification to participants for safety reasons.

3.1.3 If a safety report represents a significant change to the level of risk to participants full Board review will take place at the next scheduled REB meeting.

3.1.4 For safety events reviewed at a full Board meeting, the REB will determine whether further action is required. Possible actions the REB may take include, but are not limited to:

3.1.4.1 Placing a hold on the research pending receipt of further information from the researcher;

3.1.4.2 Requesting modifications to the research;

3.1.4.3 Requesting modifications to the study documents shared with participants;

3.1.4.4 Providing additional information to past participants;

3.1.4.5 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;

3.1.4.6 Altering the frequency of continuing review;

3.1.4.7 Termination or suspension of the research;

3.1.4.8 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.

3.1.5 When action is taken to ensure the protection of the rights, safety, and wellbeing of participants (e.g., for an unanticipated problem involving risks to participants or others) the REB Chair or designee is responsible for notifying the researcher. The Chair will also report to the Chief Nursing Officer and Professional Practice Lead, who in turn will report to the Vice President, Clinical Operations North. The VP Clinical Operations North has the authority to notify the sponsor and the appropriate regulatory authorities (as applicable).

3.2 Researcher Responsibilities

3.2.1 The researcher shall provide the REB with an acceptable plan for monitoring the safety of participants.

3.2.2 The researcher is responsible and accountable for the safety of participants for the duration of the research project including ongoing evaluation of risk of harm related to adverse events. The researcher will evaluate all local adverse events during the study and determine whether the events are considered serious against the following criteria:

3.2.2.1 Results in death;

3.2.2.2 Is life-threatening;

3.2.2.3 Requires hospitalization or prolongation of existing hospitalization;

3.2.2.4 Results in persistent or significant disability or incapacity;

3.2.2.5 Results in a congenital anomaly; or

3.2.2.6 Jeopardizes the participant or requires intervention to prevent one of the outcomes listed above.

3.2.3 The researcher shall promptly report any new information that may affect the welfare or consent of participants to the REB, and to other appropriate regulatory or advisory bodies. Events that may increase the level of risk to participants, or have other ethical implications that may affect participants' welfare must be reported within **14 calendar days.** Local serious events, where there is real harm to participants, must be reported to the REB at the earliest opportunity and no later than **7 calendar days** from the time of the event.

3.2.4 For local adverse events, drug reactions, and unanticipated problems the researcher should include the following information in the report of the event:

3.2.4.1 A description of the event including severity, with participant identifiers removed (use participant's research ID only);

3.2.4.2 Attached copy of the completed serious adverse event form and signed by the researcher or medical designee;

3.2.4.3 The proposed research changes, study document changes or other corrective actions to be taken by the sponsor or the site in response to the event(s);

3.2.4.4 Once a local serious event is acknowledged by the REB, subsequent important follow-up reports related to the event should be submitted when available, as update(s).

3.2.5 When new information is relevant to the participants' welfare, the researchers shall promptly inform all participants to whom the information applies (including former participants).In certain circumstances, e.g. when there is a privacy breach, the researcher will work with the REB to determine which participants must be informed and how the information should be conveyed.

4 PROCEDURES

4.1 Research Ethics Board Coordinator

4.1.1 Receives all safety information and reports and responds as follows:

4.1.1.1 For reports that present no risk to participants, sends an Acknowledgement of Receipt e.g. CIOMS reports, Dear Investigator Letters, periodic line listings, DSMB reports.

4.1.1.2 For local events that are serious but expected, are not related to the investigational product or research procedures, or are not serious, forwards to the Chair for review.

4.1.1.3 For local, Serious and Unexpected Adverse Events, notify the Chair and add to the REB agenda for full board review.

4.1.2 For studies not housed on the RISe platform, adds all safety reports and related documents to the project file.

4.1.3 Maintains tracking tool on all safety events and reports these to the REB at the next scheduled meeting.

4.2 REB

4.2.1 Reviews all safety events that require full Board review.

4.2.2 Reviews the Safety Report and discusses safety events as required.

4.2.3 Issues provisos as required in the event that a Safety Report as submitted requires additional information in order for a decision to be reached.

4.3 REB Chair

4.3.1 Reviews all safety information and reports and determines the level of risk. This may be delegated to the Research Ethics Board Coordinator.

4.3.2 Sends acknowledgment to the researcher indicating;

4.3.2.1 The event has been reviewed and acknowledged; or

4.3.2.2 Further action is required by the researcher; or

4.3.2.3 The event requires review by the full Board.

4.3.3 Informs the researcher, in writing, of the decision of the full Board.

4.3.4 Reports any serious events posing immediate potential or real harm to participants to the Chief Nursing Officer and Professional Practice Lead, who in turn reports to the Vice President, Clinical Operations North. .

5 REFERENCES

- Canadian Association of Research Ethics Boards. (2010). *Guidance on Reporting of Unanticipated Problems including Adverse Events to Research Ethics Boards in Canada.*
- Canadian Association of Research Ethics Boards and N2 Network of Networks. (2019). Standard Operating Procedure 404.003: *Ongoing REB Review Activities.*

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- 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 2018-4.
- Interior Health. (2019). Research Policy Manual: *RR1200 Suspensions and Terminations of REB Approval.*
- International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), ICH Harmonized Guideline, Integrated Addendum to ICH E6(R1); Guideline for Good Clinical Practice, E6(R2), November 9, 2016.
- UBC Office of Research Ethics. (2018). Standard Operating Procedure 408: *Reportable Events and Reporting*.
- US Department of Health and Human Services, Code of Federal Regulations, Title 45, Part 46, Protection of Human Subjects (45CFR46, subsection 46.113).
    - US Food and Drug Administration Code of Federal Regulations, Title 21, Chapter 1 Part 56, Institutional Review Boards, (21CFR56).

**This policy replaces the following policies:
IH REB Policy: *Serious and Unexpected Adverse Events, Management Of* approved March 6, 2008
IH REB Policy: *Safety Monitoring Log* approved December 6, 2007