



1. Purpose

The purpose of this operating procedure is to outline the process the Methods Centre (MC) follows for identifying and processing serious adverse event (SAE) information reported during the conduct of a research study.

2. Responsibilities

Research Site: The research site is responsible for reporting all SAEs as soon as possible after being made aware of the occurrence of an event and following the procedures outlined below regarding follow-up.

Methods Centre: The MC is responsible for processing the SAE report information and following up with the research site and governing regulators as necessary.

3. Procedures

3.1 A Serious Adverse Event (SAE) is defined as any untoward medical occurrence that at any dose:

- 3.1.1 Results in death
- 3.1.2 Is life-threatening (refers to an event in which the study participant was, in the opinion of the qualified investigator (QI), at risk of death from the event if medical intervention had not occurred. NOTE: This does not include an event that hypothetically had it occurred in a more serious form, might have caused death).
- 3.1.3 Requires in patient hospitalization or prolongation of existing hospitalization
- 3.1.4 Results in persistent or significant disability/incapacity (i.e. a substantial disruption in an individual's ability to conduct normal life functions)
- 3.1.5 Is a congenital anomaly or birth defect
- 3.1.6 Other medically important condition (Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious events when, based on medical judgment, they may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed above).

3.2 The study protocol should outline any other criteria that should be used to determine SAEs for a specific study.

3.3 The research site should report a new SAE to the MC as soon as they are able following knowledge of the occurrence of the event.

3.4 Unless otherwise noted in a study specific work instruction, the research site will complete a study specific SAE Report Form, and fax the information to the MC.

3.5 The SAE Report Form will contain, at a minimum, the following fields:

- 3.5.1 Study ID
- 3.5.2 Participant ID (enrolment number or randomization number)
- 3.5.3 Participant age
- 3.5.4 Participant sex
- 3.5.5 Name of event being reported
- 3.5.6 Reason for reporting the event (i.e. SAE criteria)
- 3.5.7 Date/time of onset
- 3.5.8 Expectedness of the event
- 3.5.9 Relationship to investigational product



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- 3.5.10 Study treatment code (if unblinded)
- 3.5.11 Treatment for the event
- 3.5.12 Cause attributed to the event
- 3.5.13 Participant status in study
- 3.5.14 Outcome

3.6 The research site should also report the SAE to their local Research Ethics Board (REB) using established forms and policies at the local institution.

3.7 Upon receipt of the SAE information, the MC will review the information on the SAE report for completeness and medical coherency.

3.8 The MC will communicate with the research site to resolve any outstanding SAE report information and to discuss any ambiguities in the information provided.

3.9 All SAEs must have an assessment concerning the relationship to investigational product.

- 3.9.1 Definitions for research sites to use to determine the relationship to investigational product will be provided by the MC.
- 3.9.2 Definitions will be split into two groups: related and unrelated.
- 3.9.3 In the absence of a relationship to investigational product determination, or if there is any doubt concerning the relationship assessment, the relationship should be considered “related” to the investigational product.

3.10 The MC will track individual SAE reports and forward onto the Data Safety Monitoring Committee as per study specific procedures.

3.11 Unless otherwise specified, in accordance with regulations, the MC will determine whether expedited reporting to Health Canada and other governing regulators is required in the following manner:

- 3.11.1 The event must meet the criteria for a “serious” adverse event.
- 3.11.2 There must be a suspicion of a relationship with the investigational product.
- 3.11.3 The reported event must be an unexpected adverse event (i.e. not consistent with information found in the current Investigator’s Brochure or Product Monograph)

3.12 Expedited SAEs are considered supplemental information to the existing product monograph. For expedited SAEs, reports will be forwarded to all research sites for notification to their respective REBs.

3.13 In the event that the study participant treatment code must be revealed for safety reasons, study specific procedures should be followed in addition to SOP # 304 Study Treatment Code Unblinding.

- 3.13.1 In the event that an SAE deemed to be expeditable is unblinded, the study treatment code information should be forwarded to Health Canada and other governing regulators, as applicable, with the SAE report.

3.14 Any study participant who experiences an SAE should be followed by the research site until the first of the following occurs:

- 3.14.1 The event resolves.
- 3.14.2 An outcome is reached.
- 3.14.3 The event is otherwise explained or stabilized.

3.15 The research site should provide the MC with follow-up SAE Reports until one of the criteria in 3.14 is fulfilled.



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4. References

- 4.1 ICH GCP topic E2A Clinical Safety Data Management : Definitions and Standards for Expedited Reporting
- 4.2 Food and Drug Regulations Division 5: Drugs for Clinical Trials Involving Human Subjects Section C.05.014.
- 4.3 SOP 304: Study Treatment Code Unblinding