

GUIDELINES FOR REPORTING SERIOUS ADVERSE EVENTS/UNANTICIPATED PROBLEMS

1. Introduction

The Bruyère Continuing Care REB has broadly adopted the Canadian Association of Research Ethics Boards (CAREB) guidance document on “*Guidance on Reporting of Unanticipated Problems including Adverse Events to Research Ethics Boards in Canada*” (July 2010). The following guidance document outlines the requirements for reporting Unanticipated Problems, including certain Serious Adverse Events, to the REB. These reporting guidelines apply to all research conducted under the authority of the Bruyère REB.

In addition to these guidelines, the researcher should also adhere to the approved study protocol, sponsor requirements, REB study-specific requirements and regulatory requirements regarding the reporting of serious adverse events/unanticipated problems. In particular, investigators are required to comply with all applicable legal and regulatory provisions, including the *Food and Drugs Act* and Regulations, and ICH-GCP Guidelines E2A and related Health Canada Guidance.¹ Further, Investigators doing investigator-initiated clinical trials may have particular obligations, as a sponsor, to Health Canada under the *Food and Drugs Act* and Regulations.

2. Definitions

- 2.1 Adverse Event (AE):** any unfavourable or unintended occurrence in the health or well-being of a research participant who is administered an investigational product (drug, natural health product, or device) or who undergoes any other research procedure(s) and which does not necessarily have a causal relationship with the investigational product or any research procedure(s). An AE can therefore be any unfavourable and unintended event, occurrence, sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of an investigational product or other research procedure.
- 2.2 Investigator:** the Principal Investigator for the research site within the jurisdiction of the Bruyère REB, or delegate. For studies that qualify as Health Canada clinical trials, or for other biomedical research, the Investigator making a report shall be a physician or dentist (as applicable) in good standing with his or her provincial College.

¹ https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/dhp-mps/alt_formats/hpfb-dgpsa/pdf/prodpharma/e2a-eng.pdf

- 2.3 Periodic Safety Update Report (PSUR):** a summary report prepared by the Market Authorization Holder (MAH) that provides a periodic but comprehensive assessment of the worldwide safety data of a medicinal product. The PSUR can be an important source for the identification of new safety signals, a means of determining changes in the benefit-risk profile, an effective means of risk communication to regulatory authorities and an indicator for the need for risk management initiatives, as well as a tracking mechanism for monitoring the effectiveness of such initiatives.
- 2.4 REB of Record:** The REB with authority for the ethics review and oversight of a research study.
- 2.5 Serious Adverse Event/Experience (SAE):** any Adverse Event that:
- a) Results in death
 - b) Is life-threatening
 - c) Requires inpatient hospitalization or prolongation of existing hospitalization
 - d) Results in persistent or significant disability/incapacity
 - e) Results in a congenital anomaly/birth defect; or
 - f) 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.
- 2.6 Unanticipated Problem:** any incident, experience, or outcome (an event) that is:
- a) A Serious Adverse Event; or
 - b) Any other event, incident, experience, or outcome, meeting the conditions below, that in the opinion of the Investigator or sponsor, places research participants or others at a greater risk of physical or psychological harm than was previously anticipated, or have implications for the conduct of the study or the integrity of the research data;
- and** that meets **all** the following criteria:
- c) The event is **unexpected** (in terms of nature, severity, or frequency) given the research procedures that are described in the protocol-related documents (e.g. the REB-approved research protocol and informed consent document(s), Investigator's Brochure, Product Monograph); and/or the nature of the research participant population being studied; **and**
 - d) The event is **related or possibly related** to participation in the research (possibly related means there is a reasonable possibility that the event, experience, or outcome may have been caused by the investigational product(s) or procedures involved in the research); **and**
 - e) The event 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.

2.6.1 There are two categories of Unanticipated Problems, namely:

- a) External Unanticipated Problem: an Unanticipated Problem experienced by a research participant enrolled by investigator(s) at centres or institutions outside the jurisdiction of the Bruyère REB as REB of Record.
- b) Local Unanticipated Problem: An adverse event experienced by a research participant enrolled by the investigator(s) at one or more centres under the jurisdiction of the Bruyère REB as REB of Record.

3. Reporting Local Unanticipated Problems to the REB

3.1 The Investigator shall report any Local Unanticipated Problems to the REB for the duration of the study (i.e. until the study is closed at the REB).

3.2 For greater certainty, the following adverse events ordinarily should **NOT** be reported to the Bruyère REB:

- a) Events that are determined to be expected; or
- b) Events that are determined not to be related or possibly related to the investigational product or research procedures, whether the event is expected or not; or
- c) Events that do not suggest that the research places research participants or others at a greater risk of harm than was previously known or recognized.

4. Reporting External Unanticipated Problems to the REB

4.1 The Investigator shall report any External Unanticipated Problems to the REB for the duration of the study (i.e. until the study is closed with the REB) but shall report only if the unanticipated problem:

- a) is serious (see definition) or:
- b) requires a change to the Protocol and/or Consent Form(s); or
- c) requires immediate notification to research participants for safety reasons.

5. Unanticipated Problem Report Timing and Process

5.1 Unanticipated Problems shall be reported using the REB [Serious Adverse Event/Unanticipated Problem Reporting form](#);

5.2 Any report required under this SOP shall be made:
Within **3** business days of the occurrence of the event, or of an investigator becoming aware of it, if the death of a participant is involved; or otherwise;

5.3 Within **7** working days of the occurrence of the event, or of an investigator

becoming aware of it.

6. The form should include:

- 6.1** The REB protocol number, date of report, title of project, Site or Principal Investigator, and name of Sponsor;
- 6.2** Brief description of the serious adverse event/unanticipated problem;
- 6.3** Study status, number of participants enrolled at all sites, and total target number of participants;
- 6.4** Type of report, such as initial report or follow-up;
- 6.5** The unique coded study participant number, age at time of event, and gender;
- 6.6** A detailed description of the event including an assessment as to whether the event reaction was mild, moderate or severe. Provide all relevant information at the time of the report;
- 6.7** A description of the study team's response to the event;
- 6.8** A description of the research participant outcome of the event and the impact on their clinical care when the information becomes available;
- 6.9** An opinion expressed by the local investigator that the event is both serious and unexpected, and a justification of that opinion;
- 6.10** An opinion expressed by the local investigator that there is a reasonable possibility that the event is related to the investigational product(s) or procedures involved in the research, and an explanation of that opinion;
- 6.11** An opinion expressed by the local investigator respecting the impact of the event on the continuation of the study, and any further actions that may be required, such as changes to the study protocol and/or informed consent form, including the notification of present and/or past research participants.

7. Form Submission

If changes to the study are required, the relevant documents should be submitted to the REB using the [REB Amendment/Addendum Form](#).

8. Corrective Action

Upon review of the Report, the REB may require further corrective actions in follow-up of the Unanticipated Problem to ensure participant safety and/or study integrity. Such corrective actions or substantive changes may include:

- a)** Requiring changes to the research protocol to eliminate apparent immediate hazards to research participants;
- b)** Modification of inclusion or exclusion criteria to mitigate the newly identified risks;
- c)** Implementation of additional procedures for monitoring research participants;
- d)** Suspension of enrollment of new research participants;
- e)** Suspension of research procedures on currently enrolled research participants;
- f)** Modification of Informed Consent documents to include a description of newly recognized risks; and
- g)** Provision of additional information about newly recognized risks to previously enrolled research participants;
- h)** Such other corrective actions as may be determined necessary or desirable by the Bruyère REB.