

Policy on Reporting of Non-Local (External) Serious Adverse Events to UBC's

Research Ethics Boards

Effective Date: October 30th 2009

Background: This new policy was developed in response to the serious problem of over-reporting of non-local (external) serious adverse events to UBC's Research Ethics Boards, including submission of thousands of individual case reports which often included little or no information, explanation or analysis of the impact of the event on the study for which it was being reported. In response to this issue the European Commission, the US Food and Drug Administration and the Canadian Association of Research Ethics Boards have all developed Guidances endorsing summary reporting of non-local (external) SAE's, with some accompanying form of analysis of the events. The Guidances also confirm that single isolated adverse events rarely meet the requirements for reporting to REBs.

Definitions:

Adverse Reaction: Any response to a drug, biologic, or natural health product which is noxious and unintended, which occurs at doses normally used or tested for the diagnosis, treatment or prevention of a disease or the modification of an organic function. A reaction, as opposed to an adverse event, is characterized by the fact that a causal relationship between the product and the occurrence is suspected (i.e. judged to be at least a reasonable possibility).

Serious Adverse Event (SAE): Any untoward medical occurrence at any dose that:

- Results in death
- Is life-threatening
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity
- Is a congenital anomaly/birth defect
- Is an important medical event that may jeopardize the patient or may require medical intervention to prevent one of the outcomes listed above.

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

Medical Device Serious Adverse Event: An adverse event associated with a medical device complaint meets the criteria of a medical device SAE when both of the following are fulfilled:

- The event involves contact with the medical device **and**
- The event results in death or serious deterioration in state of health. This includes:
 - Life-threatening illness or injury

- Permanent impairment of a body function
- Permanent damage to a body structure
- A condition that requires medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to a body structure.

Local Serious Adverse Events: Local serious adverse events are all adverse drug reactions or adverse events which are **both** serious and unexpected and all unanticipated medical device SAE's, provided that the adverse drug reaction, adverse event or unanticipated medical device SAE occurs **at the UBC site for the study, and** provided that they are related or possibly related to the study drug or treatment.

Non-Local Serious Adverse Events: Non-local serious adverse events are all adverse drug reactions or adverse events which are **both** serious and unexpected, and all unanticipated medical device SAE's, that occur at **other (non-UBC) sites, and** that are related or possibly related to the study drug or treatment **and** (as articulated by the US Department of Health and Human Services and the U.S. Food and Drug Administration in the January 2009 "Guidance for Clinical Investigators, Sponsors, and IRBs Adverse Event Reporting" ([FDA Guidance](#)) that would have implications for the conduct of the study (e.g. requiring a significant, and usually safety-related change in the protocol such as revising inclusion/exclusion criteria or including a new monitoring requirement, informed consent or investigator's brochure. An individual adverse event occurrence very rarely constitutes such an event.

Policy:

Local serious adverse events should be reported to the REB promptly, but in any case no later than **seven (7)** days subsequent to the occurrence of the local event. Such events should be reported using the **REQUEST FOR ACKNOWLEDGEMENT FORM**, and should include:

- The status of the study and summary of participants enrolled
- A detailed description of the local event
- An opinion expressed by the local investigator that the event is both serious and unexpected and a justification of that opinion
- An opinion expressed by the local investigator that the event is related or potentially related to the study drug/procedure/device and an explanation of that opinion.
- An opinion expressed by the local investigator respecting the implications of the SAE on the continuation of the study and any further actions that may be required such as changes to the study procedure, informed consent or protocol.
- A statement of the study team response to the event and the patient outcome of the SAE

Non-local (external) serious adverse events should be reported to the REB **in the form of periodic summary reports**, accompanied by information that is meaningful and of use to the REB. The contents of the summary report(s) should ordinarily at a minimum, include a sponsor analysis of the significance of the adverse event or perhaps such an analysis from an independent Data Safety Monitoring Board (DSMB), with (where appropriate) a discussion of previous similar events. Such reports should be submitted using the **Request for Acknowledgement Form**.

UBC's REBs will ONLY accept individual case reports of non-local (external) SAE's in the exceptional circumstances noted in the FDA Guidance. Accordingly, such reports should only be submitted to the UBC REB if the individual non-local SAE is unexpected (not known to be associated with the underlying condition for which the experimental agent or device is being used and not previously associated with the experimental agent or device as described in the consent document(s)) and strongly associated with drug or device exposure. Similarly, one or a small number of serious adverse events that are associated with drug or device exposure, but that are otherwise uncommon in the study population (e.g. tendon rupture, progressive multifocal leukoencephalopathy) should be considered a reportable event. **Individual reports meeting these criteria are acceptable, but only if they contain a sponsor analysis of the significance of the event or perhaps such an analysis from an independent DSMB and if applicable a corrective action plan.** Such reports should be submitted using the Request for Acknowledgement Form.

The Request for Acknowledgement Form should be submitted using the RISE on-line system, with the following exception:

SAEs to be reported to the BC Cancer Agency REB must be submitted using the BCCA REB SAE database (refer to [BCCA SAE](#)) The RISE system may ONLY be used if either of the following applies;

- 1. If the Study is not yet "activated", then the RISE system may be used to submit these as a Request for Acknowledgment, (once the study is activated, you must use the BCCA REB SAE database).**
- 2. If the BCCA REB has granted permission to use RISE because you cannot be granted access to the BCCA SAE database. (To request access to the BCCA REB SAE database, contact the BCCA REB Administration: reb@bccancer.bc.ca**