

Research & Performance Support
Regina Qu'Appelle Health Region
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Guidance Notes for Submitting Serious Adverse Event Reports to the RQHR Research Ethics Board

The RQHR Research Ethics Board (REB) requirements for submitting adverse event reports follow Health Canada's mandatory reporting requirements for 'serious and unexpected adverse drug reactions' and for incidents involving medical devices.

Investigator obligations for reporting adverse events falls under ICH GCP 4.11.1 which states **"ALL SERIOUS ADVERSE EVENTS (SAES) SHOULD BE REPORTED IMMEDIATELY TO THE SPONSOR EXCEPT FOR THOSE SAES THAT THE PROTOCOL OR OTHER DOCUMENT (E.G., INVESTIGATOR'S BROCHURE) IDENTIFIES AS NOT NEEDING IMMEDIATE REPORTING". IN ADDITION, "THE INVESTIGATOR SHOULD ALSO COMPLY WITH THE APPLICABLE REGULATORY REQUIREMENT(S) RELATED TO THE REPORTING OF UNEXPECTED SERIOUS ADVERSE DRUG REACTIONS TO THE REGULATORY AUTHORITY(IES) AND THE IRB/IEC". (Updated 10 June 2004)**

Introduction: It is the responsibility of the primary investigator conducting human research within and/or under the auspices of the Regina Qu'Appelle Health Region to report any serious and/or unexpected adverse events to the Research Ethics Board (REB). The following information is provided to assist investigators and others in determining which events to report and how to report them to the Research Ethics Board of the Regina Qu'Appelle Health Region.

The Adverse Event Acknowledgment Form is intended to apply to participants exclusively enrolled in research protocols within and/or under the auspices of the Regina Qu'Appelle Health Region. It is **not** intended to apply to all adverse events for the patients. The Adverse Event Acknowledgment Form is an addition to the normal adverse event reporting mechanisms within the Regina Qu'Appelle Health Region.

Serious Adverse Event Definition (SAE): A serious adverse event is any event that is fatal, immediately life threatening, persistently or significantly disabling/incapacitating, requires and/or prolongs inpatient hospitalization or results in a congenital anomaly/birth defect.

Instructions: An Adverse Event Report Form is to be submitted with each adverse event report. Please note that the form must be accompanied by the detailed serious adverse event report describing the actual incident (where applicable). The Adverse Event Report Form should be completed and signed by the principle investigator. Adverse effects which occur no more frequently than expected and which are discussed in the consent form need not be reported unless they result in death.

Reports of local serious adverse events require (19) copies of the serious adverse event report attached to the completed Adverse Event Report Form. Reports of adverse events which occur at another site of a multi-site study require (1) copy. The primary investigator must read the report(s) and fill out the Adverse Event Reporting Form accordingly.

Submit the original signed copy of the Adverse Event Report Acknowledgement Form and copies to the **Research Ethics Board, Research and Performance Support, 2180-23rd Ave., Regina, SK, S4S 0A5.**

Acknowledgment of Receipt: The chair of the REB will forward acknowledgment of receipt of adverse event reports following review of the Adverse Event Report Form to the primary investigator. Depending on the nature of the report, the following may result: no action may be taken, the consent form may need to be revised, study procedures may need to be modified, or approval of the study may be suspended, pending further inquiry.

REGULATORY REQUIREMENTS FOR CLINICAL TRIALS

1.1 SERIOUS AND UNEXPECTED ADVERSE DRUG REACTIONS

Reporting requirements for serious and unexpected adverse drug reactions are described in Section C.05.014 of the Health Canada 'Food and Drug Act' and Section 12.3 of the Food and Drug Act's "Guidance for Clinical Trial Sponsors: Clinical Applications" document (effective 2003/06/25).

Refer to the Regulations amending the Food and Drug Regulations (1024 - clinical trials) (effective 20 June 2001) at: http://www.hc-sc.gc.ca/hpfb/inspectorate/food_drug_reg_amend_1024_gcp_entire_e.html

Refer to the Guidance document at:

http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/ctd_cta_guidance_e.html#12.3

Refer to ICH Topic E2A: Clinical Safety Data Management: Definitions and Standards for Expedited Reporting (1995) for further information on definitions and timelines at:

http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/e2a_e.html

In addition, ICH GCP 5.17.1 states that *"The sponsor should expedite the reporting to all concerned investigators/institution(s), to the IRB(s)/IEC(s), where required, and to the regulatory authority(ies) of all adverse drug reactions that are both serious and unexpected"*.

Refer to <http://www.ncehr-cnerh.org/english/gcp/> for this document.

1.2 MEDICAL DEVICES

The Health Canada "Medical Devices Regulations" Sections 59 to 62 (effective 7 May 1998) require adverse incidents or problems experienced with medical devices to be reported to the Health Product and Food Branch Inspectorate.

Mandatory reporting requirements for medical devices are described in the Health Canada Guidance document "Mandatory and Voluntary Problem Reporting for Medical Devices" (6 July 2001).

Refer to the Regulations at:

<http://laws.justice.gc.ca/en/f-27/sor-98-282/128343.html>

Refer to the Guidance document at:

http://www.hc-sc.gc.ca/hpfb/inspectorate/man_vol_pro_rep_md_entire_e.html#2_1

2. REB SUBMISSION REQUIREMENTS FOR ADVERSE EVENTS

2.1 CRITERIA FOR LOCAL INITIAL SERIOUS AND UNEXPECTED ADVERSE DRUG REACTIONS

2.1.1 Criteria

Report an adverse event ONLY if the adverse drug reaction is BOTH serious and unexpected AND related/possibly related to the study treatment.

Some sponsors request that the investigator submit adverse drug reaction reports according to the local 'IRB's policies and procedures'. Ensure that these reports are submitted ONLY if they meet the criteria in 2.1.1, as this is the RQHR Research Ethics Board policy.

Do not report adverse drug reactions to the RQHR REB if they are:

- serious but expected, OR
- serious but unrelated to the study product (expected or not).

2.1.2 Exceptions

a. Other adverse event reports may be submitted **ONLY** if the sponsor's protocol has specific stipulations for the submission of these reports to the REB.

b. The ICH Topic E2A Guidance (Section 3 A (2)) includes a provision for submitting a serious and expected adverse event report if there is an increase in the rate of occurrence, which is judged to be clinically important.

2.1.3 Criteria For International Safety Reports

Submit International Safety Reports (i.e. CIOMS reports, Medwatch letters, Dear Investigator letters) **ONLY** if the adverse drug reaction meets the criterion in 2.1.1.

2.1.4 Criteria For Follow-Up Reports

Submit follow up reports to a serious and unexpected adverse drug reaction **ONLY** if the subject's condition worsened **AND/OR** the relationship of the adverse event to the study drug changed.

Follow up reports that do *not* meet these criteria will be returned to the investigator.

2.2 CRITERIA FOR LOCAL SERIOUS AND UNEXPECTED MEDICAL DEVICE INCIDENTS

Report an adverse event **ONLY** if the event relates to a failure of the device or a deterioration in its effectiveness **AND** has led to the death or a serious deterioration in the state of health of a patient, user or other person, or could do so if it were to recur.

3. SUBMISSION TIMELINES

Submission to the REB for local events should coincide with the timelines required by Health Canada, if at all possible.

4. REB ACKNOWLEDGEMENT OF SAE REPORTS

4.1 REB ACKNOWLEDGEMENT POLICY

There is no regulatory requirement for acknowledgement of serious and unexpected SAE's by REB's. However in order to provide evidence to investigators of their submission to the REB, the REB office will now acknowledge receipt of all REB SAE forms and reports within 5 business days.

4.2 ACKNOWLEDGEMENT PROCESS

The SAE form has been redesigned. REB staff will sign and date the first page of the form when it is received in the office. The first page will then be faxed back to the contact person identified on the form. This process is being adopted to ensure that investigators have an accurate record of their submissions to the REB office as quickly as possible.

4.3 REVIEW PROCESS

The REB SAE reviewers will continue to review the SAE forms as part of the REB administrative process. However, a verification of the completion of the review will not be sent to investigators, as this is not a regulatory requirement. Submitted SAE reports will be kept on file with the relevant study documents in the REB office after the review is completed.

5. UPDATED INVESTIGATOR BROCHURES

Updated Investigator Brochures and any addendums to Investigator Brochures should be submitted as an amendment for acknowledgement only using the REB 'Request for Amendment of a Previously Approved Project' at <http://www.rqhr-rps.ca/assets/rps/files/Application%20requesting%20amendment.pdf>.

Updated Investigator Brochures are acknowledged by 'Acknowledgement Memo' only. Certificates of approval are not issued for updated IB's, unless a summary of the new information in the IB is provided in the amendment application.

6. CUMULATIVE LISTING OF EXPEDITED REPORTS

A "Cumulative Listing of Expedited Reports" is not required by the REB. Please do *not* submit.