William Osler Health System

Title	Guidelines for Reporting Protocol Deviations
Original Issue Date:	18-Oct-2019
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Approved By:	REB Chair

1.0 PURPOSE

The purpose of this guideline is to describe the requirements for reporting deviations to the Osler Research Ethics Board (REB). Teams are encouraged to read the Osler Policy on Ethical Conduct for Research Involving Humans and the Osler Responsible Conduct of Research.

2.0 POLICY STATEMENT

The Principal Investigator is responsible for conducting the study in compliance with the protocol that was approved by the REB. Should an unanticipated or unintentional deviation from the expected conduct of an approved study occur, the PI may be required to report it to the REB. The REB recognizes that deviations from the protocol can be both minor and major and distinguishes between those that must be reported to the REB and those that should not.

Major Protocol Deviations: All deviations that were implemented to eliminate immediate hazard(s) to a study subject(s) and/or that impacted the safety, welfare, comfort or rights of study subject(s), whether they were intentional or unintentional, are considered major and **must be reported** to the REB.

Minor Protocol Deviations: Deviations that involve only logistical or administrative aspects of the study are considered minor and **should not be reported to the REB** (e.g., study participant missed appointment, change in appointment date).

In accordance with ICH GCP E6(R3) Article 2.5.4, *"The investigator should follow the protocol and deviate only where necessary to eliminate an immediate hazard(s) to trial participants. In case of deviations undertaken to eliminate immediate hazard to trial participants, the investigator should inform the sponsor promptly."*

In addition, ICH GCP E6(R3) Article 2.5.5 states *"The investigator should report information on the immediate hazard, the implemented change and the subsequent proposed protocol amendment, if any, to the IRB/IEC and, where applicable, regulatory authorities"*

Lastly, ICH GCP E6(R3) Article 3.13.3 states *"The sponsor should take prompt action to address immediate hazards to participants. The sponsor should determine the causes of the hazard and based on this, take appropriate remedial actions. The sponsor should*

consider whether the protocol requires amendment in response to an immediate hazard. The information on the immediate hazard, if required, and any subsequent protocol amendment should be submitted to the IRB/IEC and/or regulatory authorities by the investigator/institution or sponsor (in accordance with applicable regulatory requirements).”

3.0 PROCEDURES

3.1 Reportable Protocol Deviations to the REB

The following are considered types of protocol deviations that meet the requirements of reporting to the REB:

- Changes to the study procedures(s) initiated to eliminate immediate hazards to research participants;
- Enrollment of a participant who did not meet the inclusion/exclusion criteria;
- Over-enrollment exceeding the number of participants approved by the REB;
- Deviation on the consent form (i.e., missing documentation on the ICF, failure of obtain consent, used an unapproved or wrong consent form, etc.);
- Performance of a study procedure not approved by the REB;
- Deviation on study procedure (i.e., failure to perform a study procedure that may affect patient safety, procedure or visit performed outside the time frame specified in the protocol, etc.);
- Study drug or intervention errors (i.e., incorrect dosing);
- Potential breach of confidentiality (i.e., missing documents, digital security breach, misplace of USB, etc.).
- Continuing to conduct research activities after the annual approval has expired and before the annual approval form was submitted or approved by the REB

3.1.1 Privacy Breach in Research

A Privacy Breach is when Personal Health or Personal Information has been accessed, used, disclosed or collected in a way which contravenes the provisions of PHIPA/FIPPA. Individuals must be notified if their PHI is:

- Lost, Stolen, Disposed
- Inappropriately accessed
- Duplicated, Modified

If a privacy breach occurs, please promptly follow the established workflow process outlined in the Privacy and Security Fundamentals for Research Training. If you require access to this information, please contact the Osler REB.

3.2 Submitting Protocol Deviations

All available information about the deviation must be reported to the REB within **15 calendar days** of the investigator becoming aware of the protocol deviation. Deviations should be reported to the Osler REB using the eREB Reportable Events Form. The eREB

Reportable Events Form directs the Principal Investigator to provide detail on:

- whether the protocol deviation affects the safety/increases the risk(s) to study subjects(s)
- whether corrective measures have been made to ensure that similar deviations do not occur
- whether the deviation affects the integrity of the study data
- whether a protocol amendment will be submitted to the REB for review and approval as a result of the deviation

The REB will not accept Protocol Deviation reports submitted through the eREB Reportable Events Form unless the PI has provided an e-signature in the eREB system. This signature attests that the PI is aware of the deviation and its safety implications and has assessed the impact of the deviation on the study procedures.

All protocol deviations should be documented in study files. The investigator is required to explain and sign off on all protocol deviations using the eREB Reportable Events Form. Further, the investigator must report all protocol deviations to the Sponsor, if applicable.

3.3 Review Process

The REB office will assess protocol deviations and will contact the PI when further information is needed. The REB may make recommendations to amend the protocol in order to eliminate such occurrences in future.

The REB will acknowledge receipt of the Protocol Deviation reports submitted through the eREB Reportable Events Form.

3.4 Protocol Deviations That Lead to Study Amendments

A protocol deviation may result in the need for an amendment to the study. In the event that a protocol deviation results in the need for an amendment, the deviation must be reported to the REB and an amendment must be submitted to the REB for review and approval through the eREB Amendment Form. If the amendment has already been implemented to eliminate an immediate hazard, indicate this by answering ‘Yes’ to the question that asks this in the eREB Amendment Form. The deviation and amendment must be submitted to the REB together to facilitate the review process.

3.5 Protocol Deviations That Are Also Serious Adverse Event(s)/Unanticipated Problem

If a protocol deviation resulted in an internal adverse event/unanticipated problem, this information should also be included in the same eREB Reportable Events Form.

4.0 REFERENCES

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 2022. https://ethics.gc.ca/eng/documents/tcps2-2022-en.pdf

Government of Canada, Food and Drug Regulations: Part C, Division 5, Drugs for Clinical Trials Involving Human Subjects, August 2022. https://lawslois.justice.gc.ca/PDF/C.R.C.,_c._870.pdf

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). *Clinical Safety Data Management: Definitions and Standards for Expedited Reporting E2A.* October 1994. https://www.ich.org/page/efficacy-guidelines

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). *ICH Harmonised Guideline: Good Clinical Practice E6(R3).* Final version, adopted on 06 January 2025. https://www.ich.org/page/efficacy-guidelines

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH).*E19 Guideline on Optimisation of Safety Data Collection.* November 2022. https://www.ich.org/page/efficacy-guidelines

5.0 REVISION HISTORY

Effective Date	Summary of Changes
18-Oct-2019	Original version
16-Jan-2026	Revised to include eREB updates and updated ICH GCP E6 (R3)