

Guidance Document	Unanticipated Problem Reporting – Protocol Deviation/Violation
Effective Review	HSREB/NMREB
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As a Research Ethics Board (REB), Western University’s Health Sciences and Non-Medical REBs’ primary responsibility is to protect the safety and rights of human research participants, and therefore, the REB must be aware of situations that place research participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) that was previously known or recognized or as identified in the approved protocol.

The term ‘protocol deviation’ is not well defined by regulations or guidelines; however, deviations are generally identified as any unplanned or unforeseen change(s) to an REB approved protocol or procedure(s). Deviations differ from amendments in that they generally apply to a single occurrence or participant, and are not intended at the time to modify the entire protocol. Amendments are changes to the protocol (or protocol procedures) that are planned and that are approved by the REB prior to implementation.

There have been attempts to categorize protocol deviations as major versus minor and/or to distinguish between deviations and violations; however, there is no clear guidance on these distinctions. There are, however, guidelines and requirements for reporting protocol deviations. Examples of protocol deviations that should be reported to the REB include the following:

- Implementation of additional procedures for monitoring participants;
- Suspension of enrollment of new participants;
- Suspension of research procedures in currently enrolled participants

If an unanticipated deviation or divergence from the approved research protocol, consent process or study addenda **jeopardizes (a) participants’ informed consent, safety or privacy; (b) study efficacy; or (c) data integrity**, it must be promptly reported to the REB using the Protocol Deviation/Violation Form. Specific examples of reportable deviations (i.e., if they place participants at a greater risk) include the following:

- Informed consent improperly obtained or not obtained;
- Emergency deviations to the research protocol initiated by the investigator prior to obtaining REB approval to (e.g., eliminate apparent immediate hazards to participants);
- Major, non-emergent deviations without prior approval;
- Participant enrolment without meeting the eligibility criteria and without prior sponsor approval;
- **Eligibility Waiver: participant enrolment without the eligibility criteria with prior sponsor approval;**
- Study drug or dose not administered per protocol with increased risk of harm to participant.

If a protocol deviation meets the reportable criteria (i.e., **jeopardizes (a) study participants' informed consent, safety or privacy; (b) study efficacy; or (c) data integrity**), and has not otherwise been reported through an amendment to the protocol or consent form, it should be reported to the REB.

Protocol Deviations that lead to an SAE should be reported within 48 hours, otherwise within 10 working days.

NOTE: Research agreements may require the Principal Investigator (PI) to notify the sponsor of all unplanned deviations or departures from the REB approved protocol procedures. Sponsors reporting requirements for deviations may differ from the REB's reporting requirements. It is the PI's responsibility to comply with the reporting requirements outlined in the signed contract.

NOTE: Protocol deviations must meet reporting criteria to qualify for REB review.

Resources:

1. Office for Human research Protocols (OHRP) Guidelines on Reviewing and Reporting Unanticipated Problems Involving Risks to Participants or Others and Adverse Events www.hhs.gov/ohrp/policy/AdvEvtGuid.htm
2. ICH Good Clinical Practice Guidelines, Section 3.3.7 & Section 4.5.1-4.5.5
3. Goldfarb, Norman M. Directory of Protocol Deviation & Violation (PDV) Codes: A Lexicon for Understanding & Communicating Protocol Deviations & Violations, First Clinical Research www.firstclinical.com/resources/codes
4. Protocol Violations: Implications for Clinical Research" Clinical Research Focus, 12(7) Oct 2001

Western University's Research Ethics Boards operate in compliance with the Tri-Council Policy Statement 2: Ethical Conduct of Research Involving Humans; the International Conference on Harmonization of Good Clinical Practices; Part C Division 5 of the Food and Drug Regulations of Health Canada; and the applicable laws and regulations of Ontario.