Ontario Cancer Research Ethics Board
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Guidance

To: All Ontario Oncology Trial Centres Using OCREB

From: Ontario Cancer Research Ethics Board

Date: September 25, 2018 (previous version March 7, 2012)

RE: Protocol Deviation Reporting Criteria

Protocol deviations must meet the reporting criteria to be reported.

As a research ethics board, OCREB's primary responsibility is to protect the safety and rights of human research participants, and therefore OCREB must be aware of situations that place research participants at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized or as identified in the protocol, or that jeopardizes the integrity of the data or the efficacy of the study.
The term protocol deviation is not well defined by regulations or guidelines but deviations are identified as any unplanned or unforeseen change to a REB approved protocol or protocol procedures. Deviations are different from amendment in that they generally apply to a single occurrence or participants 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 must be reported to OCREB include the following:

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

If an unanticipated deviation or divergence from the approved research protocol, consent document(s) or study jeopardizes participants' safety, or jeopardizes study efficacy or data integrity, it must be promptly reported to OCREB. Specific examples of reportable deviations include:

- Informed consent improperly obtained or not obtained;
- Emergency deviations to the research protocol initiated by the investigator prior to obtaining OCREB approval (e.g., to eliminate an immediate hazard";
- An eligibility waiver that was provided by the sponsor;
- If the study drug or dose were not administered as per protocol, resulting in an increased risk of harm to the participant.

If the protocol deviation meets the reportable criteria and has not otherwise been reported through an amendment to the protocol or to the consent form, it should be reported to OCREB through the submission of a Centre Reportable Events Form.
Protocol deviations that lead to a local serious adverse event should be reported within 7 days of becoming aware of the event.

Note: research agreements may require the investigator to notify the sponsor of all unplanned deviations or departures from REB approved protocol procedures. Sponsor reporting requirements for deviations may differ from OCREB's reporting requirements. It is the investigator's responsibility to comply also to comply with the reporting requirements as outlined in the contract with the sponsor.

Resources:

1. OHRP Guidance on Unanticipated Problems Involving Risks & Adverse Events Guidance (2007)
2. ICH GCP Guidelines, Section 3.3.7 & Section 4.5.1-4.5.5.
3. Protocol Violations: Implications for Clinical Research: Clinical Research Focus, 12(7) Oct 2001.
4. 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

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