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GUIDANCE NOTE FOR SUBMITTING PROTOCOL DEVIATIONS TO THE FHREB

1. PURPOSE

The purpose of this Guidance Note is to instruct investigators on the FHREB requirements for submitting information concerning a protocol deviation that had not received prior approval by the FHREB, as required under ICH GCP 4.5.2, [1] because the deviation was necessary in order to ensure subject safety, was of an inadvertent nature, or was administrative in nature. This document has been adopted with permission from the University of British Columbia.

2. DEFINITION OF PROTOCOL DEVIATION

A protocol deviation is an unanticipated or unintentional divergence or departure from the expected conduct of an approved study that is not consistent with the current research protocol, consent document or study addenda. Examples of protocol deviations include:

- changes in procedures initiated to eliminate immediate hazards to study subjects;
- enrolment of participants outside protocol inclusion/exclusion criteria, whether agreed to or not by the sponsor;
- medication/intervention errors [i.e. incorrect drug/intervention, incorrect dosage of the drug];
- inadvertent deviation in specific research intervention procedures or timing of the research intervention which could impact upon the safety or efficacy of the study-related intervention or upon the experimental design [n.b. this would not typically include participant visits/appointments that fall outside the scheduled window];
- breach of confidentiality or privacy whereby confidential information about a participant is revealed in inappropriate settings, or to persons without a need to know, or by data exposure (computer security breach, documents left unsecured), and;
- significant deviation from the consenting process.

3. ICH GCP REQUIREMENTS

Article 4.5.4:

"The investigator may implement a deviation from, or a change of, the protocol to eliminate an immediate hazard(s) to trial subjects without prior IRB/IEC approval/favourable opinion. As soon as possible, the implemented deviation or change, the reasons for it, and, if appropriate, the proposed protocol amendment(s) should be submitted:
to the IRB/IEC for review and approval/favourable opinion,
to the sponsor for agreement and, if required,
to the regulatory authority (ies)."

Article 4.5.2: [See footnote #1]

This article permits changes which involve only logistical or administrative aspects of the trial (e.g. change in monitor(s), change of telephone number(s) to be implemented prior to obtaining REB approval.

[1] ICH GCP 4.5.2 "The investigator should not implement any deviation from, or changes of the protocol without agreement by the sponsor and prior review and documented approval/favourable opinion from the IRB/IEC of an amendment, except where necessary to eliminate an immediate hazard(s) to trial subjects, or when the change(s) involves only logistical or administrative aspects of the trial (e.g. change in monitor(s), change of telephone number(s)).

4. OBLIGATIONS OF PRINCIPAL INVESTIGATORS

It is the responsibility of the Principal Investigator to notify the FHREB of all protocol deviations that: 1) expose participants to potential increased risk; 2) compromise the integrity of the study; 3) are repetitive in nature; 4) alter participant eligibility, or 5) affect the privacy of the participant.

The Principal Investigator, or person designated by the investigator, must complete and sign a report [See Section 6 for guidelines] that documents the protocol deviation that occurred and submit it to the FHREB according to the FHREB Standard Operating Procedure described in Section 5.

5. FHREB STANDARD OPERATING PROCEDURE FOR REPORTING PROTOCOL DEVIATIONS.

Refer to Section 6 for guidelines for completing a report on a protocol deviation.

A deviation from, or change of, the protocol to eliminate immediate hazards to the study participants must be reported to the FHREB within 7 days of its discovery.

All other deviations must be reported to the FHREB within 15 days of their discovery.

If appropriate, amendments to the protocol must also be submitted to the FHREB at the time that the protocol deviation report is submitted.

Notification of protocol deviations will be acknowledged. Depending on the circumstances of the specific deviation, a request for further information may be sent to the investigator by the FHREB Chair/designate. The FHREB does not approve deviations from the protocol that are reported after the fact.

6. GUIDELINES FOR COMPLETING A PROTOCOL DEVIATION REPORT

The protocol deviation report must be completed and signed by the Principal Investigator/designated representative for the study concerned. The report must include the following content:

- describe the deviation that occurred with an explanation of the circumstances that lead to the deviation and the resulting problem;
- explain how the deviation did/did not compromise the scientific integrity of the study;
- explain how the deviation did/did not increase the risk or the possibility of risk for the research participant;
- describe steps taken or that will be taken to correct/address the problem resulting from the deviation, and;
- describe a plan for ensuring that a similar deviation does not occur in the future.