UNIVERSITY OF MANITOBA

Bannatyne Campus Research Ethics Boards
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Submission Procedures for Submitting Protocol Deviations

1.0 Introduction

As per 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/favorable 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)).

The following guideline outlines:

- Requirements for submitting information concerning a protocol deviation that had not received prior approval by a Bannatyne Campus Research Ethics Board, as required under ICH GCP 4.5.2, because the deviation was necessary in order to ensure subject safety, was of an inadvertent nature, or was administrative in nature.

2.0 Definitions

Protocol deviation - is any action or inaction that does not correspond to the approved protocol. A protocol deviation may include accidental/unintentional or intentional changes, including changes made to eliminate an immediate hazard to subjects or others. Protocol deviations may be major or minor.

Major protocol deviation - adversely affects the rights and welfare of subjects, the safety of subjects, the integrity of the study data and/or the subject's willingness to continue study participation.

Examples of major protocol deviations may include, but are not limited to:

- Intentional deviation from the protocol to eliminate immediate hazard to subjects or others
- Enrollment deviations
    - Enrollment of a subject who did not meet all inclusion/exclusion criteria
    - Enrollment of a minor as an adult
    - Enrollment of subjects after suspension or expiration of the project
    - Over-enrollment (exceeding the maximum approved by the REB)
    - Implementation of unapproved recruitment procedures
- Consent Deviations
    - Failure to obtain informed consent, written or verbal, as per REB approval, i.e. there is no documentation of informed consent or informed consent obtained after initiation of study procedures
    - Failure to obtain child assent, when required by REB
    - Informed consent obtained by someone other than individuals authorized to obtain consent
    - Use of invalid consent form, i.e. consent form not approved by REB, or outdated/expired.
    - Inappropriate documentation of informed consent, including
        - Missing subject signature
        - Missing investigator signature
        - Missing the date of consent
        - Copy not given to the person signing the form
- Procedural deviations
    - Performing study procedure not approved by REB
    - Increasing the number of procedures without REB approval

    - Procedures performed by unapproved personnel or at unapproved locations
    - Incorrect randomization
    - Failure to perform a required lab test or other procedure that, in the opinion of the Principal Investigator, may affect subject safety or data integrity
    - Study visit conducted outside of required timeframe that, in the opinion of the Principal Investigator, may affect subject safety
- Drug/Device Administration
    - Drug/study medication dispensing or dosing error
    - Use of expired drug
    - Use of commercial inventory instead of study inventory
    - Implant of incorrect device
    - Implant by unapproved study personnel
- Failure to report adverse event and/or follow the safety monitoring plan
- Major breach of confidentiality i.e. unauthorized release of personal information, failure to de-identify documents leaving study site
- Findings of multiple minor deviations

Minor protocol deviation - does not impact subjects' rights and welfare, subject safety, the integrity of the study data and/or the subject's willingness to continue study participation.

Examples of minor protocol deviations may include, but are not limited to:

- Missing original signed and dated consent form (only a photocopy available)
- Sponsor-approved deviation from enrollment criteria
- Failure to follow the approved study procedure that, in the opinion of the Principal Investigator, does not affect subject safety or data integrity
    - Study procedure conducted out of sequence
    - Omitting an approved portion of the protocol
    - Failure to perform a required lab test
    - Study visit conducted outside of required timeframe that does not create risk
- Failure of subject to return study medication

3.0 Procedures for submitting protocol deviations to the REB:

The Principal Investigator is responsible for submitting any and all protocol deviations that occur during the course of the study.

a) **Major protocol deviations** - Complete the ***Bannatyne Campus Major Protocol Form*** and submit the form to the REB no later than 7 days of discovering them. If the deviation has potential to affect patient safety it must be reported immediately.

b) **Minor protocol deviations** –These deviations should be documented in the study file. Enter the minor protocol deviations as they occur on the ***Bannatyne Campus Research Ethics Board Minor Protocol Deviation Log Form*** and attach it to the annual study status report at the time the site is requesting REB annual renewal and at final study closure. They do not need to be submitted to the REB as they occur.

4.0 Acknowledgement

If required by the sponsor, the REB office will acknowledge **receipt** of protocol deviations provided the Bannatyne Campus Protocol Deviation Form is completed and submitted in duplicate to the REB office along with a self addressed return envelope. Other documentation **will not** be given an acknowledgement of receipt.

The duplicate copy will be stamped dated by the REB office staff and placed in the addressed return envelope.

It should be noted, there is no regulatory requirement for acknowledgement of notices re protocol deviations.