



Standard Operating Procedures
Research Ethics Committee (Human) (REC-H)

- **Deviations from approved study protocol**

1 DEVIATIONS FROM APPROVED STUDY PROTOCOL

1.1 POLICY

1. Research ethics and regulatory guidance requires that any changes to an approved protocol must receive prior HREC approval before implementation unless the change is to eliminate an immediate harm to a research participant. Sometimes changes are noted or recognized after they occur. All changes no matter how minor should be reported to the REC-H whether they are planned or noted after the fact.
2. Such incidences may result in the permanent suspension of the study.
3. Retrospective approval for deviations from approved study protocol is not possible.

1.2 PURPOSE

1. The purpose is to define protocol deviations and to outline procedures for reporting deviations to the HREC. Protocol deviations will also be distinguished from other protocol modifications.

1.3 DEFINITIONS

- a. Protocol amendment
 - i. A protocol amendment is a permanent, intentional action or process that amends or revises a previously approved protocol. There is documented approval from the Human Research Ethics Committee, and sponsor.
- b. Protocol or study exception
 - i. A protocol or study exception is a one-time intentional action or process that departs from the HREC approved protocol.
- c. Protocol deviation
 - i. A protocol deviation is an unplanned or unforeseen failure of the PI or other study personnel to follow the specified procedures approved by the HREC. Protocol deviations differ from amendments because they usually apply to a single incident or participant and are not intended at the time to change the study.
 - ii. It is the PI's responsibility to categorise a protocol deviation as major or minor.

1.4 MAJOR PROTOCOL DEVIATIONS

1. Major protocol deviations are deviations which affect a participant's safety, condition or status, the integrity of the study data, pose a significant risk of harm and change the balance of risks and benefits and a participant's willingness to continue participation.
2. If a deviation meets any of the following criteria it should be classified as major (the list is not exhaustive):
 - a. The deviation has harmed or posed a significant or substantive risk of harm to a participant:
 - i. A participant received the wrong treatment or incorrect dose.
 - ii. A participant met withdrawal criteria during a study but was not withdrawn.
 - iii. A participant received an excluded related medicine.
 - b. The deviation compromises the scientific integrity of the study data:
 - i. A participant was enrolled but does not meet the protocol's eligibility criteria.
 - ii. Failure to treat participants per protocol procedures that specifically relate to primary efficacy outcomes (if it involves participant's safety, it meets the category above).
 - iii. Changing the protocol without HREC approval.
 - iv. Inadvertent loss of samples or data.
 - c. The deviation is willful or knowing breach of ethical or regulatory policies or guidelines:
 - i. Failure to obtain informed consent

- ii. Falsifying research or medical records
- iii. Performing tests or procedures beyond the investigator's professional scope
- iv. Failure to follow the safety monitoring plan
- d. The deviation involves serious or continuing non-compliance with institutional or regulatory policies:
 - i. Working under an expired professional license.
 - ii. Repeated minor deviations.

1.5 MINOR PROTOCOL DEVIATIONS

1. Minor protocol deviations are deviations which do not affect a participant's safety, compromise the integrity of the study data or affect a participant's willingness to continue taking part in the study.
2. Examples of minor deviations include:
 - a. Missing pages of a completed consent form
 - b. Inappropriate documentation of informed consent such as missing signatures
 - c. Using an expired consent form that has not changed significantly
 - d. Participant did not receive a copy of the signed consent form (but on discovery, a copy is given to the participant)
 - e. Study procedure conducted out of sequence.
3. Often making a distinction between major and minor deviations is a matter of degree; for example, signing an expired/invalid consent form that has not changed significantly is likely to be categorized as a minor deviation, whereas signing an expired/invalid consent form which has since added or deleted study procedures to a new consent form would be considered a major deviation.

1.6 DOCUMENTING AND REPORTING PROTOCOL DEVIATIONS

1. As soon as a protocol deviation is identified in a study, it must be reviewed, documented and categorized by the PI. Documentation must include the following:
 - a. PI's name and study title
 - b. Date deviation occurred
 - c. |Date deviation identified
 - d. Has sponsor been notified, where applicable.
 - e. Has sponsor agreed to allow participant to remain in the study, where applicable
 - f. Description of deviation
 - g. Explanation of why deviation occurred
 - h. Corrective follow-up action taken
 - i. Preventative measures implemented, where applicable.
 - j. Investigator's assessment of whether deviation is major or minor, with reasons.
 - k. PI's signature and date
2. Deviations may be recorded as a summary log or a note in the study records.
3. The PI of currently active studies making use of human participants who deviate from the approved study protocol are required to immediately suspend data collection activities and report major protocol deviations within seven calendar days of first hearing of the incident to Imtiaz.Khan@mandela.ac.za for advice on the required procedure to follow.
4. The Chair or a designee will review all protocol deviations. As part of the review the Chair will determine whether the deviation constitutes an unanticipated problem that involves risks to participants or others, or serious or continuing non-compliance which requires further action. Once the review is complete and the Chair is satisfied that appropriate follow-up action has occurred, an official acknowledgement will be sent to the PI.

5. If the PI determines the deviation is minor and has no impact on the study or welfare of participants, no further action is necessary, and the deviation can be reported in the next annual progress report.