**FHS011hlp: Study exceptions and study deviations – pointers for researchers**

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| Instructions |
| * Forms to be downloaded from the Administrative Forms web page at <http://forms.uct.ac.za/forms.htm> |

What are study exceptions?

**Definition:**

A protocol or study exception is a one-time intentional action or process that departs from the HREC-approved protocol.

Occasionally investigators want to make a temporary change or a change which affects only one or a few participants. These temporary or limited changes are defined as ‘study exceptions’.

Examples of study exceptions include:

* Enrollment of a participant who does not meet the eligibility criteria, for instance a participant whose age slightly exceeds the age inclusion criterion
* Changing the dose of a study medication when justified
* Changing a visit date
* Adding an extra visit or omitting a visit

All study exceptions must receive HREC approval **prior** to initiation and must be listed in the subsequent progress report. Obtaining approval before implementing an exception avoids a protocol violation. Most study exceptions will apply only to individual participants. Such requests should be justified in terms of serving the best interests of the potential participant. The request will be reviewed by the Chairperson or designee using an expedited procedure. The PI should obtain additional approval from the sponsor for study exceptions.

What are study violations?

**Definition:**

A protocol deviation or violation is an unplanned or unforeseen failure of the principal investigator 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.

The PI must categorise a protocol deviation as major or minor.

Major protocol violations or deviations

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.

If a deviation meets any of the following criteria it should be classified as major (the list is not exhaustive):

* The deviation has harmed or posed a significant or substantive risk of harm to a participant:
* A participant received the wrong treatment or incorrect dose
* A participant met withdrawal criteria during a study but was not withdrawn
* The deviation compromises the scientific integrity of the study data:
* A participant was enrolled but does not meet the protocol’s eligibility criteria
* 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)
* Changing the protocol without Human Research Ethics Committee approval
* Inadvertent loss of samples or data
* The deviation is a willful or knowing breach of ethical or regulatory policies or guidelines:
* Failure to obtain informed consent
* Falsifying research or medical records
* Performing tests or procedures beyond the investigator’s professional scope
* Failure to follow the safety monitoring plan
* The deviation involves serious or continuing non-compliance with institutional or regulatory policies:
* Working under an expired professional license
* Repeated minor deviations

Minor protocol violations or deviations

Minor protocol deviations are deviations which do not affect a participant’s safety, compromise the integrity of study data or affect a participant’s willingness to continue taking part in the study.

Examples of minor deviations include:

* Missing pages of a completed consent form
* Inappropriate documentation of informed consent such as missing signatures
* Using an expired consent form that has not changed significantly
* Participant did not receive a copy of a signed consent form (but on discovery, a copy is given to participant)
* Study procedure conducted out of sequence

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 categorised 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.

The PI must report major protocol deviations to the Human Research Ethics Committee within seven calendar days of first hearing of the incident. 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 noncompliance 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 principal investigator.

If the principal investigator 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.

What are not considered protocol violations?

Changes, deviations or departures from the study design or procedures that are due to a participant’s non-adherence are not considered protocol violations e.g. a study participant did not return for a scheduled visit or a participant refused a blood draw.

What is the difference between a study exception and a study violation?

When the PI anticipates a one-time intentional action that departs from the HREC-approved protocol, he or she may request a one-time exception. Actions that fail to follow the approved protocol and are noted or detected after they occur are deviations.

Note: Submit ONE completed copy of the Study Exception or Study Deviation Form available on the HREC website to the HREC.