Protocol Deviations on Subject Level[1,2]

Site Investigator name:	**Site name / number:**
Study Title (short name): ULTRA	
ABR number / Protocol ID: NL39577.018.12	
Subject Number: |__|__|__|__|__|	

Description of deviation[3]	Date deviation occurred	Reason for deviation	Corrective action taken[4]	Preventive action taken[4]	Increased risk for subject?[5]	Effect on data validity?[5]
	|__|__| |__|__|__| |__|__|__|__| d d m m m y y y y				O Yes O No	O Yes O No
	|__|__| |__|__|__| |__|__|__|__| d d m m m y y y y				O Yes O No	O Yes O No
	|__|__| |__|__|__| |__|__|__|__| d d m m m y y y y				O Yes O No	O Yes O No

[1]: To report protocol deviations on study level, please use Form METF01 Protocol Deviations on Study Level; [2]: Repeat this page if more deviations need to be reported;
[3]: Including timing to study product/intervention administration, protocol section that was deviated from, if applicable, outcome or consequences for subject/study;
[4]: If applicable; if not, please state NA; [5]: Must be completed by the (Coordinating) PI.

Signature Local Principal Investigator: _____ Date: |__|__| |__|__|__| |__|__|__|__| d d m m m y y y y

Signature Coordinating Principal Investigator: _____ Date: |__|__| |__|__|__| |__|__|__|__| d d m m m y y y y

Guidance notes to Protocol Deviations on Subject Level

Definition and classification of protocol deviations:

A protocol deviation is a failure to conduct all aspects of the study as described in the approved study protocol and GCP/ISO14155 (when applicable). These may be the result of human error when the deviation is investigator or trial management related or they could be subject related, where subjects misunderstand or ignore guidance given to them whilst they are on study.

Protocol deviations are classified as minor or major as outlined below:

Minor Protocol Deviations - any change, divergence, or departure from the study design or procedures of an accredited METC approved research protocol which does not have a major impact on the subjects' rights, safety or well-being, or the completeness, accuracy and reliability of the study data.

An example of minor protocol deviations would be a visit occurring outside the window defined in the protocol (e.g. + 3 days) because of holidays.

Major Protocol Deviations - a deviation from the accredited METC approved protocol that may affect the subject's rights, safety, or well-being and/or the completeness, accuracy and reliability of the study data.

Examples of major protocol deviations include but are not limited to the following*:

- Failure to obtain informed consent prior to initiation of study related procedures;
- Enrolment of a subject who did not meet all eligibility criteria;
- A subject received the wrong treatment or incorrect dose;
- A subject received an unallowable concomitant treatment;
- A subject met withdrawal criteria during the study but was not withdrawn;
- Failure to report a Serious Adverse Event;
- Failure to treat subjects per protocol, especially procedures that specifically relate to primary efficacy outcomes;

*: Please note that if the examples mentioned above occur more than once or if no adequate corrective and/or preventive action is undertaken, they are considered serious breaches of the GCP principle and should therefore be reported as such on form Serious Breach of GCP or Study Protocol (See AMC-CRU site, MET F02 Serious Breach of GCP or Study Protocol Form).

Reporting of protocol deviations

The investigator of the site where the protocol deviation occurred is responsible for maintaining and reporting of the protocol deviation. Study personnel or a study monitor may prepare a protocol deviation form, but this form should be signed by the Principal Investigator. For multicentre studies, a copy of the completed form should be kept in the Investigator File and the original sent to the Coordinating PI. For minor deviations the original should be sent periodically to the Coordinating PI at the time of the annual report to the accredited METC. For serious deviations, which may threaten the safety of a trial subject or impact the data validity, this form should be submitted within 24 hours of discovering of the deviation to the Coordinating PI.

Protocol deviations are summarized for Data Safety Monitoring Boards (DSMBs), if applicable, and an investigator may be required to report critical or major deviations to the accredited METC. The method of reporting protocol deviations should be described in the study protocol.

Note 1: You do not have to wait until you have all information, updates are acceptable. If the investigation or corrective and preventive action is ongoing at the time of reporting, it is acceptable to indicate your plans with projected timelines for completion. Follow-up reports should be clearly identified as such.

Note 2: There may be instances where because of the nature of the trial, it would be impractical to report all protocol deviations. For this reason, the site PI can use his/her discretion in deciding what deviations are reported, depending on the nature of the trial and the deviation.