Rochester Regional Health Clinical Investigation Committee
Major Protocol Deviations Guidelines – November 2016

Purpose: This guideline provides information intended to clarify what events are considered major deviations from approved research, what needs to be reported to the Rochester Regional Health (RRH) Clinical Investigation Committee (CIC), what information is needed by the CIC to review the deviation, and how the study team should provide that information in a timely manner to ensure compliance with current CIC policy.

Audience: Researchers, study coordinators, and CIC committee members.

Definition: Major Deviation means any alteration/modification to the CIC-approved research that has the potential to negatively impact subject safety or integrity of study data (ability to draw conclusions from the study data), or affect the subject's willingness to participate in the study.

Investigators are responsible for conducting human-subjects research in accordance with all applicable federal, state, and local laws and regulations as well as all RRH CIC policies and procedures. Federal regulations specifically require the CIC to review proposed changes in a research study, and to ensure that such changes in approved research are not initiated without CIC review and approval except when necessary to eliminate immediate hazards to the participant(s) or others [45CFR46.103(b)(4)(iii) and 21CFR56.108(a)(4)]. Planned changes to the CIC-approved protocol are to be submitted to the CIC and must be approved prior to initiation or implementation of the change.

Deviations

1) Major deviations should be reported to the CIC within 48 hours of the occurrence of the event or notification to the principal investigator of the event.
2) Major deviations should be submitted using the major deviation form.
3) Follow the major deviations/violation report form for proper documentation of the deviation. An example of an appropriate summary would include description of the major protocol deviation, explanation of the reason for the major deviation, and description and corrective action that will be implemented to prevent recurrence.
4) Researchers are responsible for monitoring their studies throughout the year for adherence to the CIC approved protocol. The purpose of this monitoring is to identify major deviations and to look for trends in minor deviations that may indicate a systemic issue in how the study is being conducted that could potentially negatively impact the rights, safety, or welfare of participants or the study's ability to produce scientifically valid results.

Examples of Major Deviations

These lists are not all-inclusive.

1) Failing to obtain legally effective consent prior to initiating research procedures. This includes:
    a. failure to obtained signed consent when required

b. failure to re-consent when required
c. use of an unapproved consent form

2) Medication errors such as:
   a. administering the wrong study drug to a participant
   b. administering the wrong dose of the right study drug
   c. failure to control the study product (secure storage)
3) Failing to conduct a study procedure or administer a study assessment that was meant to assess the safety of the individual's continuation in the study.
4) Changes necessary to eliminate apparent immediate hazards to a participant or others.
5) Informed consent obtained by someone other than individuals authorized by the CIC to obtain informed consent.
6) Enrollment of a participant who did not meet all inclusion/exclusion criteria after screening
7) Performing a study procedure that has not been approved by the CIC.
8) Study visit conducted outside the required timeframe that, in the opinion of the investigator, may impact the safety of the participant.
9) Failure to follow the CIC-approved safety monitoring plan.
10) Implementation of recruitment procedures that have not been CIC-approved.
11) Failure to report serious adverse event to the CIC and/or sponsor

Procedures

Unplanned or unintentional deviations in CIC-approved research may occur during the conduct of a research study or be discovered during routine data monitoring activities of the sponsor or investigator. When an investigator discovers or is made aware of an unapproved major deviation, s/he must report the major deviation to the CIC within 48 hours of the date the investigator becomes aware of the unapproved deviation.

Unapproved minor deviations should be reported to the sponsor as outlined in the sponsor's protocol or research or investigative plan of such deviations. The Principal Investigator is responsible for reviewing the Minor Deviations periodically to monitor compliance with the approved research.

It is the responsibility of the Principal Investigator (PI) to determine whether an unapproved deviation from the CIC-approved protocol is major or minor deviation and to ensure proper reporting to the CIC. When making the determination of whether the unapproved deviation is major or minor, the Principal Investigator should consider whether the deviation negatively affected any of the following:

1) The rights or welfare of the subject
2) Risk benefit assessment
3) Accuracy of results