

Protocol Deviations, Exceptions, and Violations

Protocol Deviations/Exceptions

Deviations are unplanned or unforeseen changes to an IRB-approved protocol. They are different from amendments in that they generally apply to a single occurrence or subject (e.g. modification of study procedures for 1 subject; allowance of subject entry into a study when not meeting the protocol eligibility criteria) and are not intended at the time to modify the entire protocol.

All **significant protocol deviations** must be reported promptly when the site becomes aware of the study event, and IRB concurrence should be obtained prior to implementation, except where an immediate hazard to a subject is being eliminated. The IRB does not require reporting of non-significant deviations to the IRB (e.g. when the change(s) involves only logistical or administrative aspects of the trial such as a change in monitor, or telephone number)

The Mount Sinai IRB defines **significant deviations** as those that:

- 1) affect the rights, safety or welfare of study subjects;
- 2) change the risk/benefit ratio;
- 3) affect the scientific design of the study; or
- 4) violate an ethical principle.

A **request for deviation** should include:

- 1) an explanation of what protocol rule is being altered and why;
- 2) a description of the net effect on risk/benefit; and
- 3) indication of whether a protocol amendment will be submitted or not, and why.

For **protocol exceptions** in order to enroll an individual subject, a request should be submitted to the IRB in order to obtain IRB concurrence prior to subject enrollment. The request should include:

- 1) explanation of why this protocol is the best choice for this individual,
- 2) description of the criteria that makes this person ineligible to enroll in this trial,
- 3) documentation of approval by the trial sponsor (if there is one) to provide an exception;
- 4) indication of whether the data collected from this individual will be kept separate from the data analysis;
- 5) indication of whether an amendment to the protocol is intended to follow or not.

Protocol Violations

Investigators are responsible for conducting human subject research in compliance with federal and state laws and regulations, institutional policy, and standards of professional conduct and practice. Failure to remain in compliance can result in loss of funding or permission for an investigator to do human subject research, as well as affecting the conduct of research at the entire institution.

Protocol violations are unintentional changes to an IRB-approved protocol that often represent non-compliance (such as performance of an unapproved study procedure (where no immediate hazard to a subject exists), failure to adhere to an approved protocol; failure to obtain informed consent). Such events are often noted after the fact, or based on a technical error resulting in the protocol or standard operating procedure not being followed.

Mount Sinai IRB requires that all **significant** protocol violations are to be reported promptly when the site becomes aware of the event. **Any violation resulting in harm to the subject must be reported to the IRB within 24 hours of becoming aware of the event, along with an adverse event report form. A corrective action plan is also needed to prevent such future occurrences.**

The Mount Sinai IRB defines **significant violations** as those that:

- 1) affect the rights, safety or welfare of study subjects;
- 2) change the risk/benefit ratio;
- 3) affect the scientific design of the study; or
- 4) violate an ethical principle.

The IRB does not require reporting of non-significant violations to the IRB.