

# PARTNERS HUMAN RESEARCH COMMITTEE POLICIES AND PROCEDURES

## PROTOCOL DEVIATIONS, EXCEPTIONS AND VIOLATIONS

### 1.0 POLICY

Investigators are responsible for conducting human-subjects research in accordance with all applicable federal and state regulations, Partners and Partners Human Research Committee (PHRC) policies and procedures, and the specific requirements of the PHRC panel (the IRB) that reviewed the research study. During the conduct of the study, changes to the protocol may be proposed or unintentional changes may be discovered. Changes to the IRB-approved protocol, planned or otherwise, are governed by federal regulations and PHRC policies and procedures.

The federal regulations specifically require the IRB to review proposed changes in a research activity, and to ensure that such changes in approved research are not initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject [45CFR46.103(b)(4)(iii) and 21CFR56.108(a)(4)]. Research activity includes all aspects of the conduct of the research study, e.g., recruitment methods, consent process, procedures used to protect privacy and confidentiality, etc. – all of the information outlined in the protocol submission and reviewed and approved by the IRB. Non-compliance with these regulations, PHRC policies and procedures, or PHRC requirements during the conduct of a research study results in a protocol violation, and as such must be reported to the IRB.

Planned changes to the IRB-approved protocol, i.e., protocol deviations and protocol exceptions, must be submitted as formal protocol amendments or protocol exceptions to the IRB and must be approved prior to initiation or implementation of the change. Any protocol deviation that is not approved by the IRB prior to initiation is a protocol violation and must be reported to the IRB as outlined below.

### 2.0 DEFINITIONS

The following definitions apply throughout this guidance document:

*PROTOCOL DEVIATION:* Any alteration/modification to the IRB-approved protocol. The protocol includes the detailed protocol, protocol summary, consent form, recruitment materials, questionnaires, and any other information relating to the research study.

*PROTOCOL EXCEPTION:* Any temporary protocol deviation that is approved by the IRB prior to its initiation, e.g., enrollment of a subject who does not meet the eligibility criteria.  
Note: Any permanent change to the protocol constitutes an amendment that must be submitted to the IRB for approval prior to initiation.

*PROTOCOL VIOLATION:* Any protocol deviation that is not approved by the IRB prior to its initiation or implementation.

*MAJOR VIOLATION:* a violation that may impact subject safety, affect the integrity of study data and/or affect subject's willingness to participate in the study.

*MINOR VIOLATION:* a violation that does not impact subject safety, compromise the integrity of study data and/or affect subject's willingness to participate in the study.

### 3.0 REPORTING REQUIREMENTS

All major protocol violations must be reported to the IRB within ten (10) working days of discovery using Insight/ eIRB to complete and submit the 'Other Event' form (Note: the principal investigator must review and sign off in eIRB before the submission can be routed to the IRB). Minor violations are to be reported at continuing review. It is the responsibility of the Principal Investigator (PI) to determine whether a violation is major or minor and to ensure proper reporting to the IRB. Reports of protocol violations should be submitted to the sponsor as outlined in the sponsor's protocol.

#### MAJOR VIOLATIONS

Examples (the list of examples is intended as a guide and is not all-inclusive)

- Failure to obtain informed consent, i.e., there is no documentation of informed consent§  
Informed consent obtained after initiation of study procedures
- Informed consent for IND/IDE studies obtained by someone other than individuals authorized by IRB to obtain consent, e.g. someone other than a licensed physician investigator
- Enrollment of a subject who did not meet all inclusion/exclusion criteria
- Performing study procedure not approved by the IRB
- Failure to report serious adverse event to the IRB and/or sponsor
- Failure to perform a required lab test that, in the opinion of the PI, may affect subject safety or data integrity
- Drug/study medication dispensing or dosing error
- Study visit conducted outside of required timeframe that, in the opinion of the PI, may affect subject safety
- Failure to follow safety monitoring plan

## MINOR VIOLATIONS

Examples (the list of examples is intended as a guide and is not all-inclusive)

- Implementation of unapproved recruitment procedures
- Missing original signed and dated consent form (only a photocopy available)
- Missing pages of executed consent form
- Inappropriate documentation of informed consent, including
  - missing subject signature
  - missing investigator signature
  - copy not given to the person signing the form
  - someone other than the subject dated the consent form
- Use of invalid consent form, i.e. consent form without IRB approval stamp, or outdated/expired consent form
- Failure to follow the approved study procedure that, in the opinion of the PI, does not affect subject safety or data integrity
  - Study procedure conducted out of sequence
  - Omitting an approved portion of the protocol
  - Failure to perform a required lab test
  - Missing lab results
  - Enrollment of ineligible subject (e.g., subject's age was 6 months above age limit)
  - Study visit conducted outside of required timeframe
- Failure of subject to return study medication
- Over-enrollment
- Enrollment of subjects after IRB-approval of study expired
- Failure to submit continuing review application to the IRB before study expiration