University of Kentucky Office of Research Integrity and Institutional Review Board Standard Operating Procedures			
Revision #6	**TITLE: Protocol Violations**		**Page 1 of 5**
Approved By: ORI Director	Signature	Date	Date First Effective: 07-08-05
Approved By: Nonmedical IRB Chair	Signature	Date	
Approved By: Medical IRB Chair	Signature	Date	Revision Date: 05-09-19

OBJECTIVE

To describe the policies and procedures for reviewing a protocol violation

GENERAL DESCRIPTION

Federal regulations require the Institutional Review Board (IRB) to review proposed changes in any research activity and to ensure that the investigator does not initiate such changes in approved research without IRB review and approval except when necessary to eliminate apparent immediate hazards/risks to the subject [45 CFR 46.108(a)(3)(iii) and 21 CFR 56.108(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.) and all of the information outlined in the IRB application/protocol reviewed and approved by the IRB.

Definitions

A *protocol violation* is any exception or deviation involving a single subject that is not approved by the IRB prior to its initiation or implementation. These protocol violations may be major or minor violations. (See Modification, Deviation and Exception SOP for definitions of *exception* and *deviation*.)

A *major violation* is one that may impact subject safety, make a substantial alteration to risks to subjects, or any factor determined by the IRB Chair or an IRB member to warrant a review of the violation by the convened IRB. Examples of major violations may include, but are not limited to:

- Failure to obtain informed consent (i.e., there is no documentation of informed consent, or informed consent is obtained after initiation of study procedures);
- Enrollment of a subject who did not meet all inclusion/exclusion criteria;
- Performing a study procedure not approved by the IRB;
- Failure to report serious unanticipated problems/adverse events involving risks to subjects to the IRB and (if applicable), the 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 time frame that, in the opinion of the PI or IRB, may affect subject safety;
- Failure to follow the safety monitoring plan.

A *minor violation* is a violation that does not impact subject safety or does not substantially alter risks to subjects. Examples of minor violations may include, but are not limited to:

- Implementation of unapproved recruitment procedures;
- Missing signed and dated consent form;
- 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;
    - Individual obtaining informed consent not listed on IRB approved study personnel list.
- 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.
- Over-enrollment.

RESPONSIBILITY

Execution of SOP: Principal Investigator (PI)/Study Personnel, IRB Chair, IRB, Office of Research Integrity (ORI) Research Compliance Officer (RCO), ORI Staff

PROCEDURES

Submission of Protocol Violations

1. The PI submits all protocol violations that occur during the course of a study to the IRB immediately upon discovering them and/or within fourteen (14) calendar days of the occurrence. The PI or designee completes and submits the IRB Protocol Violation Report with required attachments to the ORI.

2. The PI also reports all protocol violations to the sponsor, if applicable, following the sponsor's requirements.

Screening of Submissions

1. ORI staff screen the IRB Protocol Violation Report for completeness and accuracy. If the submission is incomplete or inaccurate, ORI staff either return it to the PI or continue to process the submission but request additional information from the PI, which they forward to the IRB.

2. If UK is the reviewing IRB for a reliance study, ORI staff contact the Reliance Team to determine if the reliance agreement/communication plan stipulates reporting requirements for the protocol violation.

3. ORI staff screen submitted protocol violations to determine whether the violations involve vulnerable populations or require documentation of specific regulatory findings. If either of the above applies, ORI staff advise the IRB of any regulatory requirements the IRB should address in conducting the review. The IRB is responsible for applying the regulatory requirements.

4. ORI staff screen submitted protocol violations for HIPAA concerns and follow the procedures outlined in the HIPAA in Research SOP regarding noncompliance. Investigators working in a UK covered entity must comply with the UK Medical Center's HIPAA policies and procedures.

Determining Mechanism of Review (i.e., Expedited vs. Convened)

1. ORI staff send the IRB Protocol Violation Report, including any applicable attachments, to the IRB Chair. If the IRB Chair is not available, ORI staff may send the report to another member of the IRB.

2. The IRB Chair or IRB member makes a determination regarding whether the violation is major or minor and whether to review the violation using convened or expedited review

procedures, respectively. If the violation is minor, the IRB Chair or IRB member conducts the review using expedited procedures.

3. If the sponsor or the PI specifically requests convened review procedures for a protocol violation which the IRB Chair has determined to be minor, ORI staff place the protocol report on an agenda for full review following procedures outlined in the Initial Full Review SOP.

Expedited/Full Review Procedures

1. The IRB Chair or a designated IRB member conducts expedited review using standard expedited review procedures. (See Expedited Initial Review SOP)

2. If the protocol violation report undergoes full review, the IRB Chair or designated IRB member has the option to invite the investigator to attend the meeting to answer any questions or concerns that the IRB may have regarding the protocol violation.

3. ORI staff notify the PI in writing if he/she must attend an IRB meeting. ORI staff schedule the submission for review and provide the IRB Protocol Violation Report to the IRB. The full committee reviews the protocol violation using the procedures outlined in the Initial Full Review SOP.

4. If the IRB determines that the violation is reportable to external agencies, ORI staff notify the ORI Research Compliance Officer (RCO). The ORI RCO or designee prepares a report to the applicable federal agency and maintains records as outlined in the Mandated Reporting to External Agencies SOP.

Review Outcome(s)

1. The IRB/ORI staff handle the review and outcome of review as outlined in the Modification--IRB Review of Changes SOP and Deviation and Exceptions--IRB Review of Changes SOP and/or, if applicable, the Termination or Suspension of Research by the IRB SOP.

2. The convened IRB may, if appropriate, make a determination that the protocol violation(s) constitute “serious” or “continuing noncompliance,” or an “unanticipated problem involving risks to subjects or others” as defined in the Noncompliance SOP.

3. If the PI has concerns regarding the IRB’s decision, he/she may submit an appeal that includes justification for changing the IRB decision. The PI sends the request to the ORI. The IRB Chair or the convened IRB reviews the appeal. The IRB determination of the review of the appeal is final.

REFERENCES

21 CFR 56.108(a)(4)
45 CFR 46.108(a)(3)(iii)