OBJECTIVE

To define 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)]. 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.

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;
- 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, ORI Staff, ORI Director, Provost and Senior Vice President for Academic Affairs, Vice Provost for Research, Economic Development and Innovation (VPREDI), Office of Sponsored Programs

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 (3) days of the occurrence. The PI completes and submits a Protocol Violation Form through the electronic Research Administration (eRA) software system.

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

Screening of Submissions

1. ORI staff screens the Protocol Violation Form for completeness and accuracy. If the submission is incomplete or inaccurate, ORI staff will return it to the PI requesting additional information from the PI.

2. 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.

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

1. ORI staff send the Protocol Violation Form, including any applicable attachments, to the IRB Chair or designee through eRA.

2. The IRB Chair or designee 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.

Expedited/Full Review Procedures

1. The IRB Chair or designee conducts expedited review using standard expedited review procedures.

2. If the protocol violation report undergoes full review, the IRB Chair or designee 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 they must attend an IRB meeting. ORI staff schedule the submission for review and provide the Protocol Violation Form to the IRB.

4. If the IRB determines that the violation is reportable to external agencies, the ORI Director will notify the Provost and Senior Vice President for Academic Affairs, VPREDI, and OSP, if external funding is involved. The ORI Director 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 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.

2. If the PI has concerns regarding the IRB's decision, they 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.

REVISION HISTORY

Version No.	Brief Description of Changes	Created on Date
00	Creation of SOP	11/8/2019
01	Updated title of Vice Provost for Research, Economic Development and Innovation (VPREDI) and hyperlinks	9/22/2023

SIGNATURE HISTORY

Name and Title	Signature	Date

REFERENCES

45 CFR 46.108(a)(3)(iii)
JMU Policy # 1104