UNIVERSITY OF SOUTHERN MAINE
Office of Research Integrity & Outreach

Procedure #:	HRPP-002
AAHRPP:	Element III.2.C.
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Reviewed By:	IRB; IRB Chair; ORIO; Research Integrity Officer
Procedure Title:	Protocol Violations

1.0 Objective

1.1. To describe the policies and procedures that the Institutional Review Board (IRB) and the Office of Research Integrity and Outreach (ORIO) follow for reviewing protocol violations.

2.0 General Description

2.1. The primary responsibility of the Institutional Review Board (IRB) is to ensure the protection of the rights and welfare of research subjects. 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.

3.0 Definitions

3.1. **Protocol Violation** is accidental or unintentional deviation involving a single subject that is not approved by the IRB prior to its initiation or implementation. Violations generally increase risk or decrease benefit, affects the subject's rights, safety, or welfare, or the integrity of the data. These protocol violations may be major or minor violations.

3.2. **Major Protocol Violation** is any protocol violation that may impact subject safety, make a substantial alteration to risks to subjects, or any factor determined by the IRB Chair or designee as warranting review of the violation by the convened IRB. Examples of violations that may be considered major include but are not limited to:

3.2.1. Failure to obtain informed consent, i.e., there is no documentation of informed consent, or informed consent is obtained after initiation of study procedures;

3.2.2. Enrollment of a subject who did not meet all inclusion/exclusion criteria;

3.2.3. Performing a study procedure not approved by the IRB;

3.2.4. Failure to report serious unanticipated problems or adverse events involving risks to subjects to the IRB and (if applicable), the sponsor;

3.2.5. Failure to perform a required lab test that, in the opinion of the Principal Investigator (PI), may affect subject safety or data integrity;

3.2.6. A drug or study medication dispensing or dosing error;

3.2.7. A study visit conducted outside of required time frame that, in the opinion of the PI or IRB, may affect subject safety;

3.2.8. Failure to follow safety monitoring plan.

3.2.9. Loss of portable data device or transfer of data across non-secured methods that contained identifiable, private information about subjects.

3.3. Minor Protocol Violation is any protocol violation that does NOT impact subject safety or does not substantially alter risks to subjects. Examples of violations which may be considered minor include but are not limited to:

3.1.1. Implementation of unapproved recruitment procedures;

3.3.2. Missing original signed and dated consent form (only a photocopy available);

3.3.3. Missing pages of executed consent form;

3.3.4. Inappropriate documentation of informed consent, including:

3.3.4.1. Missing subject signature;
3.3.4.2. Missing investigator signature;
3.3.4.3. Copy not given to the person signing the form;
3.3.4.4. Someone other than the subject dated the consent form;
3.3.4.5. Individual obtaining informed consent not listed on the IRB approved study personnel list.

3.3.5. Use of invalid consent form, i.e., consent form without IRB approval stamp or outdated/expired consent form;

3.3.6. Failure to follow the approved study procedure that, in the opinion of the PI, does not affect subject safety or data integrity:

3.3.6.1. Study procedure conducted out of sequence;
3.3.6.2. Omitting an approved portion of the protocol;
3.3.6.3. Failure to perform a required lab test;
3.3.6.4. Missing lab results;
3.3.6.5. Enrollment of ineligible subject (e.g., subject's age was 6 months above age limit);
3.3.6.6. Study visit conducted outside of required time frame;

3.3.7. Over-enrollment;

3.3.8. Enrollment of subjects after IRB-approval of study expired or lapsed;

3.3.9. Failure to submit a continuing review application to the IRB before study expiration.

3.4. Protocol Violations to eliminate apparent immediate hazards to subjects is a protocol violation that occurs because the investigator or research staff intentionally decided to deviate from the approved protocol to protect the welfare of the subject from an immediate hazard or risk. For example, reducing the dose of an investigational drug because of severe side effects.

4.0 Responsibility

4.1. Execution of SOP: IRB Chair, IRB Members, Office of Research Integrity and Outreach (ORIO) Staff, Research Compliance Administrator (RCA), Principal Investigator (PI), Study Personnel (SP).

5.0 Procedure

5.1. Submission of Protocol Violation

5.1.1. The PI submits any and all protocol violations that occur during the course of a study to the IRB immediately upon discovering them and within fourteen (14) calendar days of the occurrence.

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

5.2. Screening of Submissions

5.2.1. ORIO staff screen the protocol violation submission for completeness and accuracy. If the submission is incomplete, ORIO staff requests additional information from the PI, which they forward to the RCA upon receipt. The RCA initiates a fact-finding inquiry to gather additional information as needed.

5.2.2. The RCA screens submitted protocol violations to determine whether the violations involve vulnerable populations or require documentation of specific regulatory findings. If either of the above applies, then RCA advises the IRB of any regulatory requirements that the IRB should address in conducting the review. The IRB is responsible for applying the regulatory requirements.

5.2.3. The RCA screens submitted protocol violations for HIPAA concerns and follows the procedures outlined in the University of Maine System HIPAA Policy concerning noncompliance.

5.2.4. If the RCA believes that the protocol violation requires immediate action to protect subjects, the RCA will consult with the IRB Chair to determine what action is needed.

5.3. Determination of Seriousness

5.3.1. The RCA sends all information gathered regarding the protocol violation and the approved protocol to the IRB Chair or designee.

5.3.2. The RCA and IRB Chair analyze all information gathered and compare the information to the approved protocol. When necessary, the RCA and IRB Chair will consult with experts in a particular area of research.

5.3.3. The RCA and IRB Chair will make a determination regarding the seriousness of the violation as major or minor.

5.3.4. If the RCA and IRB Chair determine that no protocol violation has occurred, the investigation will be closed with no further action.

5.4. Review of Minor Protocol Violation

5.4.1. If the violation is minor, the IRB Chair and RCA will analyze the information gathered and determine what, if anything, must be done to correct the conditions creating the violation and what must be communicated to the research participants.

5.4.2. The RCA will notify the PI of the determination and corrective conditions in writing.

5.4.3. The RCA will present a summary of the violation at the next convened IRB meeting.

5.5. Review of Major Protocol Violation

5.5.1. If the violation is major, the RCA places the protocol violation on the agenda for discussion at the next convened IRB meeting. The RCA will send all protocol violation information gathered to each member for review.

5.5.2. The IRB Chair has the option to invite the PI to attend the meeting to answer any questions or concerns that the IRB may have concerning the protocol violation.

5.5.3. The convened IRB will analyze the information gathered and determine, what, if anything, must be done to correct the conditions creating the violation, what must be done to protect subjects, and what must be communicated to the research participants.

5.5.4. The RCA will notify the PI of the determination and any corrective conditions in writing.

5.5.5. The RCA will present a summary of the violation at the next convened IRB meeting.

5.6. Other Review Outcomes

5.6.1. The IRB may, if appropriate, make a determination that the protocol violation constitutes "serious" or "continuing noncompliance," or an "unanticipated problem involving risks to subjects or others" as defined in the *HRPP-004 NonCompliance*.

5.6.2. If the RCA determines that the violation is reportable to external agencies, the RCA follows procedures in accordance with *HRPP-034 Mandated Reporting to External Agencies*.

5.6.3. If the PI has concerns regarding the IRB decision, they may submit them to the IRB in a written document that includes justification for changing the IRB decision.

6.0 References

6.1. 45 CFR 46.103

6.2. 21 CFR 56.108