PCMC IR-EC SOP 18.0: Review of Protocol Violation / Protocol Deviation

Supersedes:	PCMC IRB-EC SOP 01.0, V. 3.0
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18.0 REVIEW OF PROTOCOL VIOLATION / PROTOCOL DEVIATION

18.1 Policy Statement

The IR-EC shall require submission of protocol violation and protocol deviation within 14 days upon awareness.

A protocol violation is a major issue as it might affect methodology and ethical concerns to human participants.

A protocol deviation may be a minor issue that will not affect the methodology or ethical concerns but must nevertheless be reported.

18.2 Purpose of the Activity

To ensure that the conduct of the research adheres to an approved protocol and maintains the safety and protection of the particpants.

18.3 Scope

This SOP includes the procedures for the review of progress reports that begins from the receipt of the protocol violation/deviation report and ends with filing of documents in protocol file and updating protocol database.

18.4 Process Flow/Steps for Review of Protocol Violation / Protocol Deviation

NO.	ACTIVITY	PERSON/S RESPONSIBLE
1	Receipt of Protocol Violation/Deviation Report	IR-EC Secretariat
2	Forwarding Protocol Violation/Deviation Report to Chair	IR-EC Secretariat, Chair
3	Forwarding Protocol Violation / Deviation Report to Reviewers	IR-EC Secretariat, Chair / Primary reviewers
4	Discussing / reporting during full board meeting for decision/information	IR-EC Members, Chair
5	Communicating the decision to PI	IR-EC Secretariat, Chair
6	Filing documents in protocol file folder and updating protocol database	IR-EC Secretariat

18.5 Detailed Instructions

18.5.1 Receipt of the Protocol Violation/Deviation Report

18.5.1.1 Reports of protocol deviation/violation may come directly from the PI, or as a result of study site monitoring by the Clinical Monitor / Sponsor or the IR-EC Site Visit Team, or from related documents received by the IR-EC.

18.5.1.2 The IR-EC members performing monitoring of the research study at the trial site may detect protocol violation / deviation if the implementation of the research is not conducted as per approved protocol or institutional, national or international standards.

18.5.1.3 It shall be the responsibility of the Principal Investigator to determine whether a protocol violation/deviation is major or minor, and ensure proper recording to IR-EC. If the PI is unsure whether the variance is a violation or deviation s/he should seek advice from the sponsor to ensure appropriate action is taken.

18.5.1.4 The IR-EC Secretariat shall check the submitted documents for completeness and whether Protocol Code number and Protocol Deviation / Violation Form used (Form 18.1) are correct.

18.5.1.5 The IR-EC Secretariat shall record the report in the Log of Incoming Documents.

18.5.2 Forwarding Protocol Violation/Deviation Report to Chair

18.5.2.1 The Secretariat shall forward the report to the Chair to classify and recommend appropriate actions:

a. **Major protocol violation/deviation** is a persistent protocol noncompliance with potentially serious consequences that could put the patient's safety at risk or critically affect data analysis.
   Examples of protocol violations:
   i. Failure to obtain valid informed consent (e.g. obtained informed consent on a non-dated stamped form
   ii. Loss of laptop computer that contained identifiable, private information about subjects
   iii. Accidental distribution of incorrect study medication or drugs
   iv. Not following inclusion/exclusion criteria

b. **Minor protocol deviation** is a nonsystematic protocol noncompliance with minor consequences, in terms of its effect on the participant's / subject's rights, safety or welfare, or the integrity of study data; includes deviations that are administrative in nature. Examples of protocol deviations:
   i. A rescheduled study visit

ii. Failure to collect an ancillary self-report questionnaire
iii. Subject's refusal to complete scheduled research activities

18.5.2.2 Protocol violation in a research study should be discussed at Full Board meeting

18.5.2.3 The IR-EC Secretariat shall include the Protocol Violation / Deviation Report in the meeting agenda for the month

18.5.2.4 The IR-EC Chair shall refer the Protocol Violation / Deviation Report to the Primary Reviewers for initial review or shall review the report himself/herself.

18.5.3 Forwarding Protocol Violation / Deviation Report to Reviewers

18.5.3.1 The IR-EC Secretariat shall record the report and shall forward the package to the Primary Reviewer / Chair at least 7 days before the full board meeting.

18.5.3.2 Primary Reviewer/s or Chair shall assess if the protocol violation / deviation impacts on patient safety or the integrity of the data.

18.5.3.3 The assigned Primary Reviewer/s or Chair shall complete their review and shall recommend corrective actions, if any, within 7 days after receipt.

18.5.3.4 The Primary Reviewer/s or Chair shall forward their assessment to the Secretariat.

18.5.3.5 The result of the review decision shall be reported to full board for Discussion.

18.5.4 Discussing / reporting during full board meeting for decision/information

18.5.4.1 The Primary reviewer/s or Chair shall present the result of their assessment to full board. The full board shall deliberate on effects of the protocol violation / deviation on the rights and safety of research participants or integrity of data.

18.5.4.2 Possible decisions are as follows:

a. Acknowledged – no further information or action required
b. Additional information required – additional information is needed in order to properly evaluate the violation
c. Correction and/or corrective actions are required. The IR-EC must specify the corrective measures to prevent harm to current and future research participants. Examples are:
    i. Require revisions to the currently approved protocol;
    ii. Place restrictions on the PI, coordinator or any research personnel that may have been responsible for the deviation / violation;
    iii. Increase the frequency of the continuing review period for the study;

iv. Require changes in the procedures to eliminate or reduce deviations that are occurring consistently and with risk to the participant;
v. Audit investigator's site

d. Suspend or terminate approval of current studies.
Prior approval may be withdrawn for the following reasons:
i. SAE directly or indirectly attributed to the research;
ii. Breach of previously approved conduct of the research;
iii. Major changes, violations or amendments to the approved protocol without another approval by the PCMC IR-EC;
iv. Revisions in the informed consent form without another approval from PCMC IR-EC

18.5.5 Communicating IR-EC decision to PI

18.5.5.1 IR-EC Secretariat shall prepare the Notification Letter for signature of the IR-EC Chair.

18.5.5.2 If correction and/or corrective action shall be required from the PI, the PI is requested to provide the information within two weeks.

18.5.5.3 The IR-EC Secretariat shall follow up the action required after a reasonable time.

18.5.5.4 A site visit may also be required by the IR-EC.

18.5.6 Filing documents in protocol file folder and updating protocol database

18.5.6.1 The IR-EC Secretariat shall check if Protocol Violation / Deviation Report is completely accomplished (Form 18.1), signed and dated by Primary Reviewers / Chair and shall file the document in the protocol file folder, and update the protocol file index

18.5.6.2 Filed documents shall also include the Study Site Monitoring Visit Report, if a post-review study site visit was conducted.

18.5.6.3 The Secretariat shall record the protocol violation / deviation in the protocol violation / deviation database to facilitate tracking of repetitive violations / deviations of the same nature or who fail to follow protocol approval stipulations or fail to respond to the PCMC IR-EC's request for information / action.

18.6 Forms

Form 18.1 V.3.0 Protocol Violation / Deviation Report

18.7 Glossary