

	<p style="text-align: center;">Peregrine Eye and Laser Institute Institutional Review Board</p>
<p>PELI-IRB-SOP-15-06-2026</p>	
<p>Version No. 6</p>	<p>SOP 15 Review of Protocol Violation/ Deviation</p>
<p>Approval Date: March 9, 2026</p>	
<p>Effective Date: March 9, 2026</p>	
<p>Supersedes: SOP 16 v. 5 July 16, 2022</p>	

SOP 15 Review of Protocol Violation/Deviation

I. Policy

All protocol deviations and violations shall undergo full board review regardless of classification to ensure comprehensive ethical oversight.

The Peregrine Eye and Laser Institute Institutional Review Board (PELI-IRB) shall review, assess, and take appropriate action on all reported protocol deviations, violations, and other forms of non-compliance related to IRB-approved research to ensure the continued protection of the rights, safety, and welfare of research participants and the integrity of research data.

All protocol deviations and violations shall be reported by investigators in a timely, accurate, and complete manner. The PELI-IRB shall evaluate each report using a structured, risk-based, and proportionate approach and shall determine the appropriate level of review and corresponding action in accordance with applicable ethical guidelines, regulatory requirements, and institutional policies.

II. Purpose

To describe the procedures and criteria for the review, assessment, documentation, and management of protocol deviations, violations, and non-compliance in IRB-approved research.

III. Scope

This SOP applies to all investigators and studies under the oversight of the PELI-IRB. It covers the receipt, review, assessment, documentation, and IRB actions related to protocol deviations or violations, including failure to comply with:

1. IRB-approved protocols and related documents; and
2. Applicable national and international ethical and regulatory guidelines for human research.

Protocol Deviation

A protocol deviation is any unplanned or unintended departure from the IRB-approved protocol, study procedures, or related documents that does not increase risk to research participants, does not adversely affect their rights, safety, or welfare, and does not materially affect the reliability, completeness, or integrity of study data.

Minor Protocol Violation

A minor protocol violation is a non-compliance that has minimal impact on participant **safety, rights**, welfare, or data integrity, whether occurring as a single or repeated event.

Major Protocol Violation

A major protocol violation is a significant divergence from the IRB-approved protocol, Good Clinical Practice, or applicable regulatory requirements that has affected or may reasonably be expected to affect one or more of the following:

1. the rights, safety, or welfare of research participants;
2. the validity, reliability, completeness, or integrity of study data;
3. the accuracy or legality of the informed consent process; or
4. compliance with ethical or regulatory standards.

Example of Major Protocol Violations are:

- a. Inadequate or delinquent informed consent
- b. Inclusion/exclusion criteria not met
- c. Unreported serious adverse events
- d. Improper breaking of the blind
- e. Use of prohibited medication
- f. Incorrect or missing tests
- g. Mishandled samples
- h. Multiple visits missed (5% of total participant population) or outside permissible windows
- i. Materially inadequate record keeping
- j. Intentional deviation from protocol, Good Clinical Practice, or regulations by study personnel
- k. Subject repeated non-compliance with study requirements

The SOP for review of protocol violations and deviations begins with the filing of protocol deviation /non-compliance report and ends with the filing of all related documents and update of the database.

IV. Responsibility

IRB Secretary

1. Receive, log, and track deviation/violation reports
2. Ensure completeness of submissions
3. Maintain an updated database of non-compliance
4. Support communication and documentation

PELI-IRB Chair and Members

1. Determine the level of review (expedited or full board)
2. Review findings **and** determine appropriate IRB action

V. Process Flow/Steps

STEP	ACTIVITY	PERSON RESPONSIBLE	TIMELINE
1	Receive and check completeness of submitted documents	Staff Secretary	1 calendar day
2	Notify Chair	Staff Secretary	1 calendar day
3	Distribute reports to reviewers	Staff Secretary	1 calendar day
4	Review and recommend action	Primary Reviewers	7 to 14 calendar days
5	Review recommendations	Chair	3 calendar days
6	Discuss at full board (if necessary)	Members	as scheduled
7	Communicate IRB decision	Staff Secretary	1-3 calendar days
8	File all related documents and update of protocol database	Staff Secretary	1 calendar day after decision

VI. Detailed Instructions

Step1 The Staff Secretary shall receive, log, and assess the completeness of protocol deviation/violation reports submitted by the Principal Investigator concerning non-compliance with the approved protocol and related documents.

The Vice-Chair shall ensure that all reported non-compliance issues and relevant details are appropriately included in the IRB meeting agenda for review and deliberation.

The Principal Investigator shall accomplish and submit Form 15: Non-Compliance Report within seven (7) calendar days from the occurrence of the violation. For minor protocol deviations, the accomplished form may alternatively be submitted as an attachment to the next Progress Report, Continuing Review, or Final Report, as applicable.

Step 2 The Staff Secretary refers the submission to the Chair within 1 **calendar** day upon receipt of the reports and awaits further instructions.

Step 3 **The Staff Secretary** shall distribute all necessary documents to their respective reviewers **within 1 calendar** day upon being **instruction from the Chair**.

Step 5 Reviewers shall evaluate each submission using the assessment elements described in this section and shall classify the event based on its nature, severity, frequency, and impact on participant protection and data integrity. Reviewers will fill out their assigned section on Form 15 and submit to the Staff Secretary within 7 calendar days.

ASSESSMENT OF PROTOCOL DEVIATIONS AND VIOLATIONS

In reviewing reported protocol deviations and violations, the PELI-IRB shall conduct a structured, risk-based, and proportionate assessment. Reviewers shall evaluate each submission using the assessment elements described in this section and shall classify the event based on its nature, severity, frequency, and impact on participant protection and data integrity.

For consistency of review and documentation, reviewers shall refer to the Protocol Deviation and Violation Classification Guide when determining whether an event constitutes a protocol deviation, minor protocol violation, or major protocol violation, and when recommending appropriate IRB actions.

Protocol Deviation and Violation Classification Guide

Review Element	Protocol Deviation (Minor)	Minor Protocol Violation	Major Protocol Violation
Nature of Event	Unplanned and isolated departure from the approved protocol.	Repeated or cumulative deviations from the approved protocol.	Significant divergence from the protocol, GCP, or regulatory requirements.
Risk to Participants	No increase in risk to participants.	Minimal risk, but the issue occurs repeatedly.	Increased or potential risk to participant rights, safety, or welfare.

Impact on Informed Consent	Consent process unaffected.	Consent obtained but administratively incomplete or technically deficient.	Consent absent, invalid, outdated, or misleading.
Impact on Data Integrity	No material impact on study data.	Possible cumulative impact on data if repeated.	Data integrity, validity, or completeness compromised.
Frequency / Pattern	Isolated occurrence.	Recurrent or patterned issue.	May be isolated or repeated but considered serious.
Examples	Minor visit window delay • Late report submission	Repeated missed visits Recurrent documentation lapses	Enrollment without informed consent • Inclusion/exclusion criteria violation Unreported Serious Adverse Event (SAE)
IRB Action	Documentation and acknowledgment by the IRB.	Corrective and Preventive Action Plan (CAPA) and enhanced monitoring.	CAPA, protocol amendment, investigator clarification/interview, possible suspension or termination of study.
Level of Review	Administrative review or expedited review (if applicable).	Expedited or Full Board review, depending on severity.	Full Board review required.

CAPA- Corrective and Preventive Action

Description and Documentation

The review shall confirm that reports clearly describe:

- a. protocol identification and approved version
- b. what occurred and how it diverged from the approved protocol
- c. date, duration, frequency, and setting of the event
- d. number and type of participants affected
- e. immediate actions taken by the investigator
- f. impact on participant safety, rights, informed consent, and data integrity
- g. supporting source documents or explanations

Incomplete reports may require additional information prior to determination.

Assessment of Severity

- a. Severity shall be assessed based on the following considerations:
- b. actual or potential risk to participants

- c. impact on participant rights, welfare, or confidentiality
- d. validity of the informed consent process
- e. integrity and interpretability of study data
- f. whether the event is isolated or reflects a pattern of noncompliance

Step 6 The Chair reviews recommendations and notes any repeated non-compliance or intentional violations.

Step 7 **protocol deviations/violations** are discussed at full board **meeting**.

Adequacy of root cause analysis (RCA) and corrective and preventive action (CAPA) is determined.

The IRB shall review the investigator's root cause analysis addressing:

- a. human factors (training, supervision);
- b. procedural or system gaps;
- c. protocol feasibility issues;
- d. institutional or logistical constraints; and
- e. participant-related factors (without removing investigator accountability).

The IRB shall assess whether proposed CAPA are adequate and proportionate, including:

- a. corrective actions to address the immediate event
- b. preventive actions to avoid recurrence;
- c. assigned responsibility and timelines; and
- d. methods to verify effectiveness.

Possible IRB actions for protocol deviations are:

- a. Notation with no further action
- b. Request for explanation or clarification
- c. Monitoring during continuing review

For protocol violations, based on assessment, the IRB may require:

- a. additional information;
- b. CAPA submission or modification;
- c. clarificatory interview;
- d. protocol amendment;
- e. site visit;
- f. suspension of recruitment; or

g. withdrawal or termination of ethical clearance.

Step 8 All decisions shall be documented in the minutes and formally communicated to the investigator

Step 9 All reports, assessments, decisions, and correspondence shall be filed in the study record and reflected in the IRB deviation database in accordance with SOP on management of active study files.

VII. Forms

1. Form 15 Deviation/Non-compliance/ Violation Report
2. Form 4.9 Request Information for Post-Approval Procedures
3. Form 4.8 Approval Letter for Post Approval Procedure

VIII. References

1. Journal of Clinical Research Best Practices Nov 2005 Norman M. Goldfarb
2. 2020 PHREB SOP Workbook
3. Philippine Health Research Ethics Board (PHREB) National Ethical Guidelines for Health and Health-Related Research in Human Participants
4. World Health Organization (WHO)
5. ICH-GCP E6 (R2) and E6 (R3)
6. Council for International Organizations of Medical Sciences (CIOMS)

IX. Revision Index

Version	Date	Reasons For Revision
01	August 8, 2013	Patterned SOP after the SOP drafted by the DOH SOP Team (based on the FERCAP template)
02	February 3, 2014	Revised section 3.7 (additional requirements from the PI for premature suspension or termination of a research study), added section 3.8 suspension or termination of IRB approval, added Form 3.11 (Reminder Letter), added section 3.9 continuing review, added Form 3.12 Application for Continuing Review
03	January 26, 2016	Changed logo of “Pacific Eye and Laser Institute” to “Peregrine Eye and Laser Institute” in the document header and in the header of forms 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.11, 3.12
04	June 15, 2017	The following major revisions of both SOP and forms 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.11, 3.12 made in compliance with PHREB recommendations of official finding report last June 8, 2017: <ul style="list-style-type: none">• State in the SOP 3 that the IRB reviews by full board reports of onsite SAE/SUSARs and indicate timelines for reporting (SOP 3.1.5.2 SAE reporting timelines should comply with the ICH-GCP guidelines)• Ensure that Protocol violations and deviations are categorized accordingly• Define major and minor violations

		<p>Organize the sequence of discussion of the protocol (i.e. Scientific, then ethical issues, ICF; include the PDPVs and reasons for that)</p> <p>Ensure appropriate timelines for SAE reporting are incorporated in the SOP AND communicated to the PI</p> <ul style="list-style-type: none"> ● Ensure timely review of the continuing reports ● Indicate reviewers of SAEs in the minutes ● Ensure that SAE reviewer is a medical doctor ● Categorize protocol deviations into major or minor and how deviations will affect risk ● Reflect recommended actions required of PI on deviations/violations in the meeting minutes ● Consistently require Final reports for all studies <p>Communicate to the PI the results of review of final report.</p> <p>Ensure consistency of the flow chart with the detailed instructions (e.g. person responsible for a particular process).</p>
5	July 16, 2022	<p>Reformat numbering to conform to 2020 PHREB SOP workbook</p> <p>Refer to SOP 3.4 of version 4 of PELI IRB</p> <p>Add references within the SOP</p> <p>Rewrite process flow and steps for more consistency</p> <p>Add “forms” to include forms used in the SOP</p>
6	March 9, 2026	<p>Revised and reclassified as SOP 14 to align with the PHREB Accreditation Policy 2024 for Specialty Clinics</p> <p>Added a Policy section to define the governing principles and general guidelines of the SOP.</p> <p>Convert all timelines to calendar days</p> <p>Forms were re-numbered to correspond with the SOP in which they are used to ensure consistency, traceability, and proper document control. All form numbers mentioned in the SOP were updated accordingly to align with the revised numbering system</p> <p>Provide guidance on how PDs are reviewed</p> <p>Add table for Protocol Deviation and Violation Classification Guide</p> <p>Include in the Scope the start and the end of activities covered by the SOP</p> <p>Included correct the definition of minor and major deviations</p>