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PCMC IR-EC SOP 15.0: Review of SAE

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15.0 REVIEW OF SAE

15.1 Policy Statement

The IR-EC shall require reporting of SAE (SUSAR, UE/UR) within 14 days upon awareness of such events.

This-SOP shall apply to the review of SAE and SUSAR reports submitted by Investigators and Sponsors to the PCMC IRB-EC to comply with ICH-GCP. The PCMC IR-EC shall review such reports to determine appropriate action to protect the safety of participants in an approved study.

ICH-GCP E6(R2) defines a Serious Adverse Event (SAE) or a serious Adverse Drug Reaction (ADR) as any untoward medical occurrence that at any dose

a. results in death,
b. is life threatening,
c. requires hospitalization or prolongation of existing hospitalization,
d. results in persistent or significant disability or incapacity, or
e. results in a congenital anomaly or birth defect.

A **suspected unexpected serious adverse reaction (SUSAR)** is a serious event the nature and severity of which is not consistent with the applicable product information. In the case of an unapproved investigational product, the event is not consistent with the Investigator's Brochure (IB). In the case of a licensed product, the event is not consistent with the approved package insert or summary of product characteristics.

Unexpected Event/Unanticipated Risk (UE/UR) are sometimes discovered during the course of the studies, it includes any event that in the investigator's opinion may adversely affect the rights, welfare and safety of the study participants.

The primary responsibility of the PCMC IR-EC shall be to conduct an appropriate review of AE, SAE, and SUSAR reports to ensure oversight over the safety of participants enrolled in the study.

The PCMC IR-EC shall also:

a. Make sure that researchers are made aware of its policies and procedures concerning AE, SAE, SUSAR reporting (See Form 10.3: Approval Form)
    i. Adverse Events of special interest (AESI) – The IR-EC should be notified of any local site AESI which the sponsor deems reportable within two (2) working weeks but not later than 1 (one) month from its occurrence/site

notification. These initial reports should be followed by detailed written report one (1) month after its occurrence/site notification.

ii. All SAEs, SUSARs and UEs/URs should be reported by the Investigators to the PCMC IR-EC within ten (10) working days of occurrence/notification. These initial reports should be followed up by detailed written reports one (1) month after the incident occurrence/notification occurred. The follow-up reports should identify subjects by unique code numbers assigned to the trial subjects rather than by the subjects' name, personal identification numbers, and/or addresses.

b. Set up the necessary mechanisms to receive AE, SAE, and SUSAR reports from Investigators of researches that it has approved.
c. Receive and review AE, SAE, and SUSAR reports from its own site and to take the necessary action to ensure the safety of participants in the study.
d. In multicenter studies, review SAE and SUSAR reports from other sites within and outside the country to be updated about safety issues related to studies that it has approved.

The SAE Reviewer shall be the member of the PCMC IR-EC who is a medical doctor / toxicologist / pharmacist designated by the IR-EC Chair to review the AE, SAE, SUSAR and recommend appropriate actions to prevent further harm to subjects.

15.2 Purpose of the Activity

To ensure safety and protection of participants from harm through vigilant monitoring for SAE and prompt reporting to the IR-EC as well as to determine risk and promote development of possible interventions to improve care by observing for trends.

15.3 Scope

This SOP includes the procedures for the review of SAE that begins from the receipt of the SAE/SUSAR report and ends with filing of documents in protocol folder and updating SAE database.

15.4 Process Flow/Steps for Review of SAE

NO.	ACTIVITY	PERSON/S RESPONSIBLE
1	Receipt of SAE/SUSAR Report	IR-EC Secretariat
2	Determining type of review and forwarding SAE Reports to appropriate reviewers	IR-EC Chair IR-EC Secretariat
3	Reviewing on-site and off-site SAEs	SAE Reviewer / IRB-EC Chair /

		Primary reviewer
4	Discussing on-site SAE reports at full board to ensure patient safety	IR-EC Members, IR-EC Chair
5	Communicating decision to PI	IR-EC Secretariat, IR-EC Chair
6	Filing documents in protocol file folder and updating SAE database	IR-EC Secretariat

15.5 Detailed Instructions

15.5.1 Receipt of the SAE/SUSAR Report

15.5.1.1 The PI shall report the SAE using PCMC IR-EC Form 15.1 (SAE Report Form) and PCMC IR-EC Form 15.2 (SUSAR Report Form) for reporting SUSARs.

15.5.1.2 The IR-EC Secretariat shall check submitted documents for completeness and whether the Protocol code number and form used are correct.

15.5.1.3 The Chair/IR-EC Secretariat shall classify the SAE/SUSAR reports according to their origin or sites where they happened: on-site or off-site (within or outside the country).

a. Onsite – from the perspective of one particular institution engaged in a multicenter study, refers to events experienced by subjects enrolled by the investigator(s) at the institution. In the context of a single-center study, all SAE / SUSAR should be considered on-site. It also includes SAE / SUSAR events occurring on all PCMC approved sites.

b. Offsite – from the perspective of one particular institution engaged in a multicenter study, refers to SAEs/SUSARs experienced by subjects enrolled by investigators at other institutions engaged in the study.

15.5.2 Determining type of review and forwarding SAE Reports to appropriate reviewers

15.5.2.1 On-site SAE and SUSARS shall be reviewed by the SAE Reviewer. If they are not available to do the review, the Chair shall designate a suitable member to do the review (preferably, a pharmacist or a pharmacologist).

15.5.2.2 Off-site SAEs and SUSARs shall be reviewed through expedited process by the SAE reviewer to note the trends in SAE occurrence

15.5.2.3 The IR-EC Secretariat shall forward the SAE / SUSAR Report to the SAE Reviewer at least 7 days before the full board meeting.

15.5.2.4 The SAE Reviewer shall recommend appropriate action to be done to the IR-EC.

15.5.3 Reviewing on-site and off-site SAEs

15.5.3.1 The IR-EC shall adopt appropriate response depending on the site where the SAE/SUSAR happened.

15.5.3.2 For **SAEs/SUSARs that occurred onsite**, the IR-EC should analyze the investigator's assessment (related, unexpected):

a. Assessment of the SAE is unlikely or unrelated to the study drug or article. The report is forwarded to the Chair for review and determination if the report shall be reviewed at the convened meeting by the full board.
b. Assessment of the SAE is definitely, possibly, or probably related to the study drug or article. The report is added to the agenda for review at a convened meeting by full board.
c. Assessment of the SAE is unexpected/unanticipated and definitely, possibly, or probably related to the study drug or article. The report is added to the agenda for review at a convened meeting by full board. The IRB-EC may need to recommend some form of action to the PI to ensure the safety of the participants.

15.5.3.3 For multicenter, international studies, note the trend of occurrence of SAE/SUSAR in study sites in foreign countries and other local sites. For multicenter, national studies, note the nature (related or expected) of the SAE/SUSAR.

15.5.3.4 The SAE reviewer or Primary reviewer or Chair shall forward the assessment to the Secretariat. The Secretariat shall schedule SAE/SUSAR, report for full board on advise of Chair.

15.5.4 Discussing on-site SAE reports at full board to ensure patient safety

15.5.4.1 The Chair or SAE reviewer or primary reviewer shall present the results of the review to full board.

15.5.4.2 The full board shall discuss on-site SAEs and its impact on patient safety.

15.5.4.3 After deliberation, the IR-EC shall decide on the appropriate action as follows:

a. Take note, no further action needed and continue monitoring
b. Request further information
c. Request an amendment to protocol or consent form. This may include:
    i. changes in the protocol to eliminate apparent immediate hazards to the subject;
    ii. modification in the inclusion and exclusion criteria to mitigate the newly identified risks;
    iii. implementation of additional procedures for monitoring subjects; or

iv. modification in the ICF documents to include a description of newly recognized risks

d. Suspension of:
   i. Enrollment of new subjects until further review by the IR-EC
   ii. All trial-related procedures in currently enrolled subjects (except those intended for the safety and well-being of the participants) until further review by the IR-EC.
e. Termination of the study
f. Conduct a Study Site Visit

15.5.4.4 Chair or SAE Reviewer, Chair or Primary Reviewer shall report trends in off-site SAEs for full board information. This shall be reported on a quarterly basis to full board.

15.5.5 Communicating decision to PI

15.5.5.1 The IR-EC Secretariat shall prepare Notification of IR-EC Decision about the SAE Report, for the IR-EC Chair's signature.

15.5.5.2 The IR-EC shall forward the notice to the PI.

15.5.6 Filing documents in protocol file folder and updating SAE database

15.5.6.1 The IR-EC Secretariat shall file the documents in the protocol file folder and shall update the protocol file index.

15.5.6.2 The IR-EC Secretariat shall encode the SAE or updates the SAE Database.

15.6 Forms

Form 15.1 V3.0 Serious Adverse Event (SAE) Report
Form 15.2 V.3.0 Unexpected Event and Unanticipated Risk Report

15.7 Glossary