1. Purpose

To describe the Chong Hua Hospital Institutional Review Board (CHH IRB) review procedures for serious adverse events.

2. Scope

This SOP applies to the review of SAE and SUSARS reports submitted by investigators, Data Safety Monitoring Board (DSMB), sponsor, local safety monitor submitted to the CHH IRB to comply with ICH GCP. The IRB reviews such reports to determine appropriate action to protect the safety of participants in an approved study.

ICH-GCP E6 defines a serious adverse event (SAE) or a serious adverse drug reaction (ADR) as any untoward medical occurrence that at any dose:

- results in death,
- is life threatening,
- requires hospitalization or prolongation of existing hospitalization,
- results in persistent or significant disability or incapacity, or
- 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.

3. Responsibility

The primary responsibility of the CHH IRB is to review and address SAE and unexpected events involving risks to subjects or others as well as ethics complaints.

The primary responsibility of the IRB is to conduct an appropriate review of onsite SAE and SUSAR reports to ensure oversight over the safety of participants enrolled in the study. The IRB should also:

- Make sure that researchers are made aware of its policies and procedures concerning SAE reporting.
- Set up the necessary mechanisms to receive SAE and SUSAR reports from investigators of researches that it has approved.
- Review SAE and SUSAR reports from other sites within and outside the country to be updated about safety issues related to the protocols that it has approved.

4. Flowchart

ACTIVITY	PERSON/S RESPONSIBLE	TIMELINE
Step 1: Receive SAE/SUSAR Report	CHH IRB Staff	7 days
Step 2: Determine type of review and forward SAE Reports to appropriate reviewers	CHH IRB Chair/Member-Secretary/ CHH IRB Staff	7 days
Step 3: Review on-site and off-site SAEs	Designated IRB Medical Member/Member Secretary	During the full board meeting
Step 4: Discussion on-site SAE reports at full board to ensure patient safety	CHH IRB members/chair/Member Secretary	During the full board meeting
Step 5: Communicate decision to PI	CHH IRB Staff/Chair	7 days
Step 6: File documents in protocol file folder and update SAE database	CHH IRB Staff	7 days

5. Procedures

Step 1- Receive SAE/SUSAR Report

- The CHH IRB Staff checks submitted documents for completeness and whether IRB Reference Number and form used are correct (Form 2023-HRP-IRB-024-SERIOUS ADVERSE EVENT REPORT FORM).
- The CHH IRB Staff classifies the SAE/SUSAR reports according to their origin or sites where they happened: on-site or off-site (within or outside the country).
- Date of submission should be within the required timeline as mentioned in CHH IRB Guidelines.
- Record the submission in the logbook of received documents.

Step 2- Determine type of review and forward SAE Reports to appropriate reviewers

- On-site SAEs and SUSARs are reviewed by a medical member designated by the Chair.
- Off-site SAEs are reviewed through an expedited process by an IRB designated member.
- The CHH IRB Staff forwards the SAE Report to the member-secretary or a designated Member at least 7 days before the full board meeting.
- Designated members recommend appropriate action to be done by the CHH IRB.

Step 3- Review on-site and off-site SAEs: The CHH IRB adopts appropriate responses depending on the site where the SAE/SUSAR happened.
For SAEs that occur onsite, the CHH IRB analyzes the investigator/sponsor's assessment.

Assessment of the SAE is unlikely or unrelated to the study drug or article:

- The SAE is unlikely if the event abnormality with a time to drug intake makes relationships improbable but not impossible. (WHO-UMC causality categories).
- The report is forwarded to the Chair for review and determination if the report should be reviewed at the convened meeting by the full committee.

Assessment of the SAE is definitely, possibly, or probably related to the study drug or article:

- The SAE is certain if the event abnormality with plausible time relationship to drug intake, cannot be explained by disease or other drugs, and response to withdrawal is plausible. (WHO-UMC causality categories)
- The report is added to the agenda for review at a convened meeting by the full committee.

Assessment of the SAE is unexpected/ unanticipated and definitely, possibly, or probably related to the study drug or article:

- The SAE is probable if the event abnormality with reasonable time relationship to drug intake, unlikely to be attributed to disease or other drugs and response to withdrawal clinically reasonable. (WHO-UMC causality categories)
- The report is added to the agenda for review at a convened meeting by the full committee.
- For multicenter, international studies, the trend of occurrence of SAE/ SUSAR is noted in study sites in foreign countries and other local sites.
- For multicenter, national studies, note the nature (related or expected) of the SAE/ SUSAR.

Step 4- Discuss on-site SAE reports at full board to ensure patient safety

- Designated member/s presents the results of review to full-board by using the Template for IRB reporting of SAE and SUSARs (SAE PRESENTATION TEMPLATE).

- Full-board discusses on-site SAEs and its impact to patient safety.
- After deliberation CHH IRB decides on appropriate action as follows:
  - Request an amendment to the protocol or consent form
  - Request further information
  - Suspension of:
    - Enrollment of new research participants until further review by the CHH IRB
    - All trial-related procedures (except those intended for the safety and well-being of the participants) until further review by the CHH IRB
    - Termination of the study
- Take note and continue monitoring
- Conduct Study Site Visit.
- Designated members report trends in off-site SAEs for full board information. This will be reported on a quarterly basis to the full board.

Step 5- Communicate decision to PI: CHH IRB Staff prepares Notification of IRB Decision about SAE Report, for CHH IRB Chair's signature. The recommendations/actions will be communicated to the Principal Investigator/researcher.

Step 6- File documents in protocol file folder and update SAE database: CHH IRB Staff files the documents in the protocol file folder and updates the protocol file index. CHH IRB Staff encodes the SAE or updates the SAE Database.

6. History of SOP

Version No.	Date	Authors	Main Change
1	10 September 2010	Mr. Romel V. Cabazor	First draft
2	01 January 2014	Rev. Fr. Benedicto P. Tao	Change in the logo from CHH to CHH IRB logo Revised SOP and form numbering
3	01 September 2014	Rev. Fr. Benedicto P. Tao	Change Of IRB SOP in accordance to PHREB SOP format
4	01 October 2014	Rev. Fr. Benedicto P. Tao	Revised IRB SOP in accordance to PHREB SOP Format
5	01 January 2017	Dr. Elaine L. Gallardo	Revised CHH IRB SOP from version 04 to version 05
6	02 October 2017	Dr. Elaine L. Gallardo	Revised CHH IRB SOP in accordance to 2017 DOH-REC SOP ver02 Template Revised CHH Serious and Unexpected Adverse Event report form
7	04 January 2021	Dr. Elaine L. Gallardo	No change
8	04 January 2024	Atty. Dean Decal	Revised CHH IRB SOP in accordance with REC re-accreditation and Survey on 30 June 2023
9	21 August 2024	Atty. Dean Decal	Revised by designating member to review SUSARS, removing Member Secretary as SUSARS reviewer

7. References

- World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, 2000.
- International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996.
- National Ethical Guidelines for Health Research 2011 PNHRS
- Philippine Health Research Ethics Board, Workbook for Developing Standard Operating Procedures
- 2017 Department of Health – SOP Version No. 2
- World Health Organization-Uppsala Monitoring Center (WHO-UMC) causality categories