1. Purpose

To describe the Chong Hua Hospital Institutional Review Board (CHH IRB) review procedures for protocol violation/deviation.

2. Scope

This SOP provides instructions for taking action and maintaining records of various types of protocol deviation (Major or Minor) or violations:

It includes investigators who fail to comply with the procedures in the approved protocol or to comply with national/ international guidelines for the conduct of human research, including those who fail to respond to the CHH IRB's requests.

It also covers action taken by the CHH IRB related to protocol violation/ deviation reports submitted by the PI related to any event at the site that is not in compliance with the protocol documents previously approved by the CHH IRB.

3. Responsibility

It is the responsibility of the CHH IRB Secretariat to receive and record protocol violation/ deviation reports submitted to the CHH IRB. It is the responsibility of the CHH IRB Chair or Member-Secretary or Primary Reviewers to take action related to protocol violation/ deviation.

4. Flowchart

ACTIVITY	PERSON/S RESPONSIBLE	TIMELINE
Step 1: Received protocol Violation/Deviation	CHH IRB Secretariat	14 days
Step 2: Forward Protocol Violation/Deviation Report	CHH IRB Secretariat/Primary reviewer	
Step 3: Classification of protocol deviation and violation	CHH IRB Members	
Step 4: Board discussion and notification	Primary reviewer/CHH IRB Members	
Step 5: Communicate decision to PI	CHH IRB Secretariat/ chair	
Step 6: File documents in protocol file folder and update protocol database	CHH IRB Secretariat	

5. Procedures

Step 1- Receive Protocol Violation/Deviation Report

- Report 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 CHH IRB Site Visit team, or from related documents received by the CHH IRB.
- The CHH IRB 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.
- The PI submits to CHH IRB Staff the protocol deviation/violation form and the staff will check submitted documents for completeness and whether IRB Reference Number and form used are correct.

- The CHH IRB Staff records the report in the Communication log.

Step 2- Forward Protocol Violation/Deviation Report to Primary Reviewers

- The CHH IRB Staff records the report and forwards the package to the Primary Reviewer/s at least 7 days before the full board meeting.
- Primary Reviewer/s assess if the protocol violation/deviation impacts on patient safety or the integrity of the data.
- The following items must be assessed by the primary reviewer:
  - Description of reported deviation
  - Nature of report
  - Description of investigator preventive action
  - Description of investigator corrective action
  - Investigator's assessment on the impact of the deviation on the safety of participant/s
  - Impact or change in risk/benefit ratio
  - Investigator's assessment on the impact of the deviation on the credibility of data
  - Description of sponsor corrective action
  - Over-all assessment, including whether noncompliance have potentially serious consequences that could critically affect data integrity or put patients' safety at risk

- It is the responsibility of the Primary Reviewers to determine whether a protocol violation/deviation is major or minor.
- The assigned primary reviewer/s complete their review and recommend corrective actions, if any within 7 days after receipt.
- Their assessment is forwarded to the Secretariat.
- The result of the review decision is reported to full board for discussion.

- **Major protocol violation/deviation** is a persistent protocol noncompliance with potentially serious consequences that could put patients' safety at risk or critically affect data analysis
- **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

- Protocol violation in a research study should be discussed at Full Board meeting.
- The CHH IRB Secretariat includes the Protocol Violation/Deviation Report in the meeting agenda for the month.
- The CHH IRB Chair refers the Protocol Violation/Deviation Report to the Primary Reviewers at initial review.

Step 3- Classification of protocol deviation and violation: The primary reviewer will review the information available and classify the deviation according to the seriousness of the violation.

Protocol deviation. A protocol deviation occurs when, without significant consequences, the activities of a study diverge from the Institutional Review Board-approved protocol, e.g., missing a visit window because the subject is traveling. It is not as serious as a protocol violation.

Minor protocol deviation are the result of an unintentional deviation or omission from a protocol that CHH IRB has approved or determined to be exempt or the conduct of research without IRB review that would have qualified for an exemption. These deviations do not negatively affect the rights, safety, or welfare of the subjects.

Major protocol deviation is a deviation that adversely affects the rights or welfare of participants. Some examples are: the deviation has increased the risk and/or decreased the benefit to individual subjects; the non-exempt research has occurred without appropriate CHH IRB review and approval; when egregious or intentional deviation has occurred; and/or another situation exists in which the IRB has determined to be a major deviation.

Protocol violation. A divergence from the protocol that materially (a) reduces the quality or completeness of the data, (b) makes the Informed Consent Form

inaccurate, or (c) impacts a subject's safety, rights, or welfare. Examples of protocol violations may include but not limited to the following:

- Inadequate or delinquent informed consent
- Inclusion/exclusion criteria not met
- Unreported serious adverse events
- Improper breaking of the blind
- Use of prohibited medication
- Incorrect or missing tests
- Mishandled samples
- Multiple visits missed or outside permissible windows
- Materially inadequate record keeping
- Intentional deviation from protocol, Good Clinical Practice, or regulations by study personnel
- Subject repeated non-compliance with study requirements

- The issues as well as the details of deviation involving research investigators are included in the agenda of the CHH IRB meeting.

- A file is maintained that identifies investigators who are found to be non-compliant with national/international regulations or who fail to follow protocol approval stipulations or fail to respond to the CHH IRB request for information/action.

Note: The Board may elect to suspend or terminate approval of current studies or refuse subsequent applications from the investigators cited. Such decisions are recorded in the minutes.

Step 4- Board Discussion and notification: The Primary Reviewers present the result of their assessment to full board that deliberates on effects of the protocol violation/deviation on the rights and safety of research participants or integrity of data.

Possible decisions are as follows:

- Acknowledged-no further information or action required
- Additional information required-additional information is needed in order to properly evaluate the violation
- Preventive actions to prevent harm to current research participants
    - Suspension of enrollment until further review
    - suspension of procedures except those that guarantee safety of subjects
- Correction and/or corrective actions are required. The CHH IRB must specify the corrective measures to prevent harm to current and future research participants which may include the following
    - Suspension or
    - Termination of approval of a current study or
    - Refusal of subsequent applications from an investigator cited for non-compliance.

Recommendation

- Approved
- Noted
- Corrective action/ Preventive action required (Specify below)
- Site visit needed

Required Corrective/ Preventive action:

- Suspension of enrollment until further review
- suspension of procedures except those that guarantee safety of subjects
- Suspension of approval
- Termination of approval of a current study
- Refusal of subsequent applications from an investigator cited for non-compliance.

Step 5- Communicate decision to PI

- The CHH IRB Staff recorded the CHH IRB's decision during a full board meeting.
- CHH IRB Staff prepares the Notification Letter for signature of the CHH IRB Chair.
- If preventive and/or corrective action are required from the PI, the PI is requested to provide the information within 4 weeks upon receipt of the communication letter.
- A site visit may also be required by the CHH IRB.

Step 6- File documents in protocol file folder and update protocol database

- CHH IRB Staff checks if the Protocol Violation/Deviation Report is completely accomplished, signed and dated by Primary Reviewers and files the document in the protocol file folder, and updates the protocol file index.
- Filed documents should also include the Study Site Monitoring Visit Report, if a post-review study site visit was conducted.
- Record the protocol violation/deviation in the protocol violation/ deviation database to facilitate tracking of repetitive violations/deviations of the same nature.

6. History of SOP

Version No.	Date	Authors	Main Change
1	10 September 2010	Mr. Romel V. Cabazor	First Draft
2	01 January 2014	Dr. Manuel Emerson S. Donaldo	Change in the logo from CHH to CHH IRB logo Revised SOP and form numbering
3	01 September 2014	Dr. Manuel Emerson S. Donaldo	Change of IRB SOP in accordance to PHREB SOP Format
4	01 October 2014	Dr. Manuel Emerson S. Donaldo	Revised IRB SOP in accordance to PHREB SOP format
5	01 January 2017	Dr. Omid U. Etemadi	Revised CHH IRB SOP from version 04 to version 05
6	02 October 2017	Dr. Omid U. Etemadi	Revised CHH IRB SOP in accordance to 2017 DOH-REC SOP ver02 Template Revised CHH IRB protocol violation/Deviation report form
7	04 January 2023	Dr. Omid U. Etemadi	No change
8	04 January 2024	Atty. Dean G. Decal	Revised CHH IRB SOP in accordance with REC re-accreditation and Survey on 30 June 2023
9	21 August 2024	Atty. Dean G. Decal	No Change

7. References

- Arun Bhatt, what is the difference between protocol deviation and protocol violation Perspect Clin Res. 2012 Jul-Sep; 3(3): 117.
- 2017 Department of Health – SOP Version No. 2
- 2020 PHREB SOP Workbook