3.1 Review of Protocol Amendments
3.2 Continuing Review of Approved Protocols
3.3 Review of Serious Adverse Events
3.4 Review of Protocol Violation/Deviation/ Non-compliance
3.5 Responding to Participant Requests/Queries
3.6 Site Visits
3.7 Review of Early Protocol Termination
3.8 Review of Final Reports

REVISION NO.	REVIEW DATE	AUTHORS	MAIN CHANGE
6	Sep 19,2018	RERB Members	SOP on protocol resubmission was transferred to Chapter 2
6	Sep 19, 2018	RERB Members	Removed section on protocol deviation – sending of PD to national regulatory authorities and sponsor
6	Sep 19, 2018	RERB Members	Qualified representatives for site visit was removed – changed to Site Visit Team assigned by Chair
6	Sep 19, 2018	RERB Members	Classification of the type of review and assigning of primary reviewers are added in all the management of post-approval submission, (also included in the flowchart)
6	Sep 19, 2018	RERB Members	Basis for decision for termination of study was included
6	Sep 19, 2018	RERB Members	"secretariat" was removed as the authority responsible to initiate on-site evaluation of a study visit
6	Sep 19, 2018	RERB Members	Off-site SAEs/SUSARs are added in the process flow
6	Sep 19, 2018	RERB Members	SAE subcommittee was added to specify who reviews the SAE/SUSARs
6	Sep 19, 2018	RERB Members	Decision was clarified – voting
6	Sep 19, 2018	RERB Members	History of changes/ revisions was added

3.1. Review of Protocol Amendments

3.1.1. Purpose

To describe the RERB review procedures for amendments of the protocol and related documents

3.1.2. Scope

This SOP applies to previously approved study protocols and related documents that are being amended later and submitted for approval to the RERB. Any amendment of the study related documents may not be implemented until reviewed and approved by the RERB.

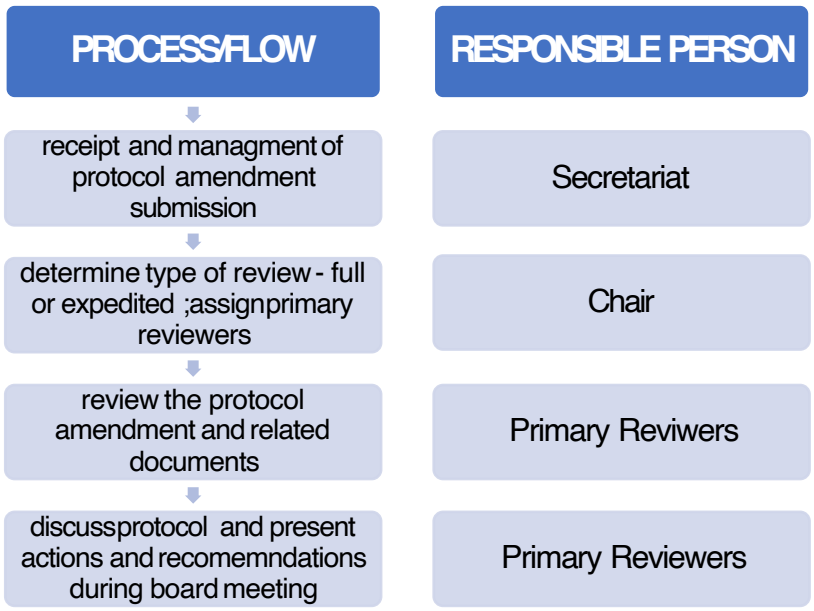
3.1.3. Responsibilities

It is the responsibility of the RERB Secretariat to manage protocol amendment package submitted by the PI.

It is the responsibility of the original primary reviewers of the protocol to review the amendments and recommend appropriate action.

It is the responsibility of either the RERB Chair to determine whether the amendment goes to expedited or full board review. The RERB approves the final decision for amendments submitted by the PI.

3.1.4. Process Flow/Steps



3.1.5. Detailed Instructions

3.1.5.1 The RERB should properly inform investigators to submit an amendment application whenever there is any change regarding the composition of the study team, the study site, and the protocol related documents and procedures previously granted by the RERB.

3.1.5.2 The RERB Secretariat checks the completeness of the amendment package submitted by the Investigator. (Form 19)

3.1.5.3 The RERB Secretariat refers the amendment package to the original primary reviewers of the protocol.

3.1.5.4 The original (initial) primary reviewers check the amended documents and compare them with the previously RERB approved documents in the protocol files. They check if the amendments would alter the risk/benefit ratio of the study to make appropriate recommendations using Form 16. Amendments that may potentially alter the risk/benefit ratio of a study are referred to full board for discussion.

If the initial reviewers are not available or have already resigned to do the review, the Chair designates qualified members to review the continuing review application and progress report.

3.1.5.5. Protocol amendment which increases risk to study participants may include, but is not limited to the following:

- A change in study design
- Additional treatments or the deletion of treatments
- Any change in the inclusion/exclusion criteria
- Change in method of drug intake or route of drug intake (e.g. oral changed to intravenous)
- Significant change in the number of subjects (increase or decrease in sample size that alters the fundamental characteristics of the study)
- Significant decrease or increase in dosage amount

3.1.5.6. If only **minor changes** are involved in the amendment, the reviewers' recommendation become the basis for the final decision of the RERB and a letter granting approval is prepared by the RERB Secretariat.

3.1.5.7. If **major changes** are involved in the amendment (alters the risk/benefit ratio of the study), the amendment is referred to full board after review by the primary reviewers. The members discuss the issues related to the amendments to arrive at a decision.

3.1.5.8. The RERB Secretariat prepares a communication letter (Form 28) to inform the investigators about the board decision. The Secretariat forwards the letter to the investigators for proper action.

3.1.5.9. The RERB Secretariat keeps a copy of all amendment related documents in the protocol files.

3.2. Continuing Review of Approved Protocols

3.2.1. Purpose

To describe the RERB procedures for the continuing review of approved protocols

3.2.2. Scope

This SOP provides instructions for the review of progress reports that are required by the RERB to be submitted by the PI to monitor the safety of participants enrolled in a study.

This SOP applies to the conduct of continuing review of study protocols involving human subjects at intervals appropriate to the degree of risk but not less than once a year. Depending upon the degree of risk to the participants, the nature of the studies, and the vulnerability of the study participants and duration of the study, the RERB may choose to review or monitor the protocols more frequently. The annual progress report serves as basis for continuing review of protocols whose approval needs to be renewed regularly.

This SOP describes the follow up of annual progress report and continuing review reports by the RERB Secretariat and the review of such reports submitted by the PI by designated members of the RERB in compliance with ICH-GCP requirements.

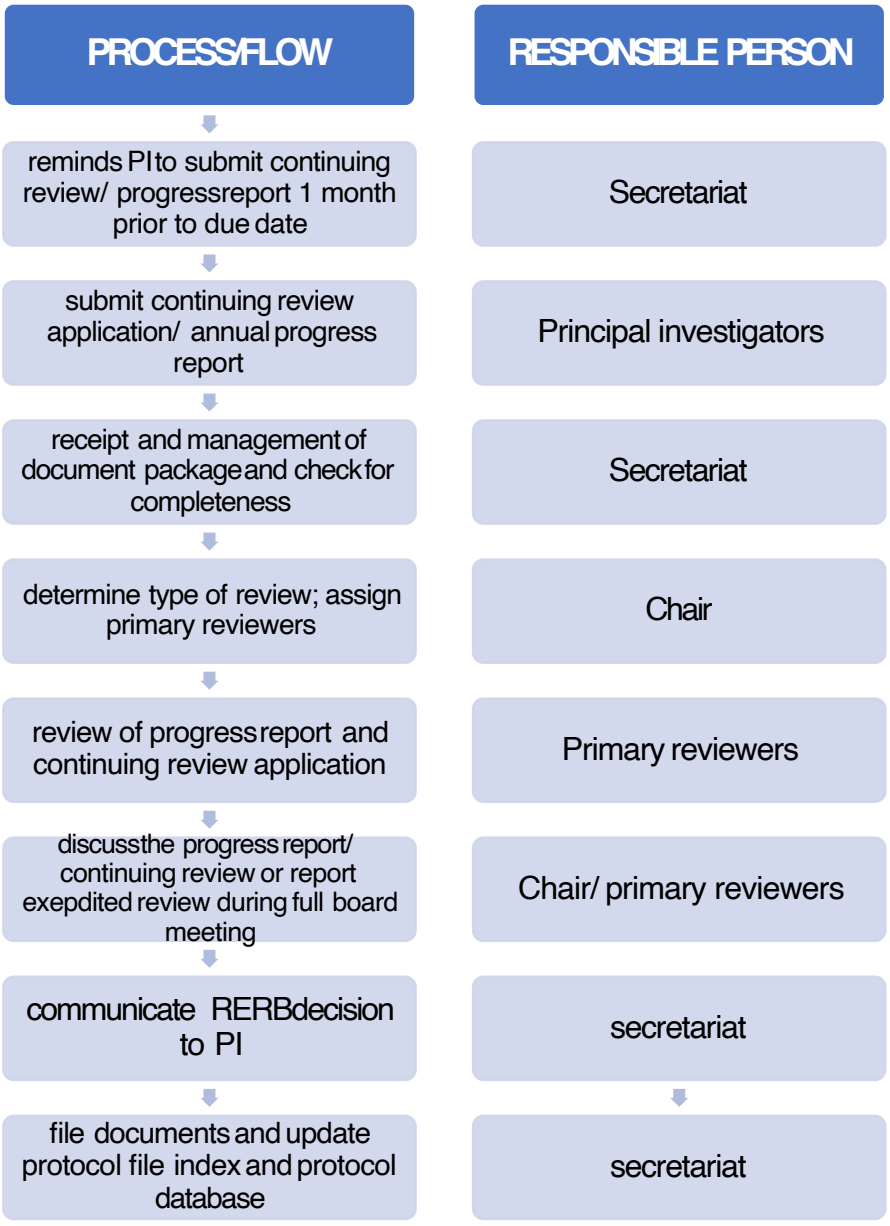
3.2.3. Responsibility

It is the responsibility of the RERB Secretariat to remind investigators to submit the continuing review application one (1) before due date of expiration of their protocol approval, to forward the reports to the primary reviewers for review and comments, and to communicate to the investigators the RERB decision.

It is the responsibility of the Chair to determine the type of review and assign primary reviewers.

It is the responsibility of the primary reviewers to review the reports to check completeness of information and ensure that the data are in accordance with the protocols and other related documents approved by the RERB.

3.2.4. Process Flow/Steps



3.2.5. Detailed Instructions

3.2.5.1. Submission and management of continuing review / progress report

- The Secretariat checks the database and tracks due dates of continuing and annual progress reports of study protocols approved by the RERB.
- The Secretariat prepares and sends reminder letter (Form 21) addressed to the PI one month before the due date of the report.
- The Secretariat checks the completeness of submitted report based on the items in Progress Report (Form 20) and Continuing Review Application Form (Form 22) and forwards the report to the Chair.

3.2.5.3. The Chair determines the type of review the progress report/ continuing review application should undergo and identify the primary reviewers.

3.2.5.4. The secretariat shall identify the initial primary reviewers of the protocol and forward the protocol package to them.

If the reviewers are not available to do the review, the Chair designates qualified members to review the continuing review application and progress report.

3.2.5.5. Continuing Review of Approved Protocols

3.2.5.5.1 The primary reviewers conduct review of continuing/annual reports if they are in accordance with the protocol and related documents approved by the RERB.

- For high-risk protocols, eg. randomized trials including investigational products, proponents have to submit continuing progress report every 6 months from time of approval and an annual report of the trial
- For low-risk protocols, eg. observational studies, cross-sectional studies, proponents have to submit continuing progress/annual report every 12 months from time of approval

3.2.5.5.2 The primary reviewers refer to the protocol file to check compliance with approval given by the RERB during initial review and upon submission of amendments.

3.2.5.5.3 The following are the key evaluation points in the review of progress report/ continuing review application:

- Risk assessment
  - The risks to the study participants are minimized

- The risks - benefit balance is reasonable, if any. What is important, is the knowledge that may be gained from the study.

- Adequacy of Informed Consent Forms. The different types of informed consent form should be provided, if applicable. It should be the most recently approved or currently in use. d) Appropriate and new significant findings should be provided to the study participants since these may be related to willingness to continue participation in the study (e.g. important toxicity or adverse event information).

• Local issues such as the following:
  - Changes in the PIs circumstances (e.g. suspension of hospital privileges or medical license, involvement in numerous clinical trials).
  - Evaluation, investigation and resolution of complaints related to the research, if any.
  - Changes in the acceptability of the research protocol in terms of institutional commitments such as personnel and financial resources, and adequacy of facilities. Changes in regulations, applicable national law or standards of professional conduct of practice. d) PI concerns about trial conduct at the site such as study coordinator ineffectiveness, inability of subjects to understand sections of the informed consent documents required by institutional policies, if any.

• Progress of the study:
  - Start date of the study and expected duration
  - Total subject enrollment
  - Expected enrollment
  - Actual enrollment
  - Enrollment issues
  - Withdrawal of participants:
    - number of participants who withdrew
    - lost to follow-up
    - Summary of reasons for withdrawal at local site

3.2.5.5.4. The primary reviewers shall give recommendations as follows:
  - RENEW APPROVAL: if assessment of the above evaluation points is satisfactory.

Approval of the progress report is necessary to renew approval of the protocol and allow the investigator to continue the conduct of research.

- PI to provide additional information or submit additional documents.
- Request modifications of the protocol or informed consent form if there is any change in the original risk-benefit assessment or any significant issues that may change risk-benefit balance.
- Suspend:
  - enrollment of new participants
  - research procedures in currently enrolled participants
  - entire study
- Disapprove renewal of continuing review

3.2.5.5.5. The primary reviewers must complete the review and accomplish Continuing Review Application/Progress Report Form, Section 2 (part to be filled-up by the reviewer) and shall be submitted to the secretariat

3.2.5.5.6. The recommendations and significant issues identified by the primary reviewers shall be included in the agenda for discussion during the full board meeting to arrive at a final decision and appropriate action.

3.2.5.5.7. For review of protocol progress reports under expedited review, RERB action is finalized at the level of the Chair and should be completed within fourteen (14) days

3.2.5.6. Discuss the continuing review/ progress report or report expedited review results to the RERB members during full board meeting.

3.2.5.6.1. The primary reviewers present to full board the results of the review, their recommendations and any significant issues identified in relation to the progress of the study.

3.2.5.6.2. The board deliberates and determines the need for the PI to elaborate, clarify or explain further any aspect of the progress report.

3.2.5.6.3. The following are possible review decisions of the board:

- Renew approval
- Request additional information
- Recommend further actions (i.e. modification in protocol / ICF, suspend study)
- Disapprove renewal

3.2.5.6.4. For progress reports approved under expedited review, approval is reported to the board by the Chair or Member-Secretary.

3.2.5.7. Communicate CGHMC RERB decisions to PI

3.2.5.7.1. The Secretariat takes note of the decision and/or discussion during the board meeting in the meeting minutes and communicates with the PI if further action is required.

3.2.5.7.2. The RERB Secretariat prepares the notification of RERB decision and sends the notification to the PI.

3.2.5.8. File documents and update protocol file index and protocol database

3.2.5.8.1. The RERB Secretariat keeps a copy of the progress report package together with the review comments of the primary reviewers in the protocol file folder and update the protocol file index.

3.2.5.8.2. The RERB Secretariat Staff files the protocol file folder in the active study file section of the cabinet under lock and key and updates the protocol database.

3.3. Review of Serious Adverse Events

3.3.1. **Purpose**

To describe the RERB review procedures for serious adverse events (SAE)

3.3.2. **Scope**

This SOP applies to the review of SAE and SUSAR reports submitted by investigators and sponsors to the RERB to comply with ICH GCP. The RERB 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

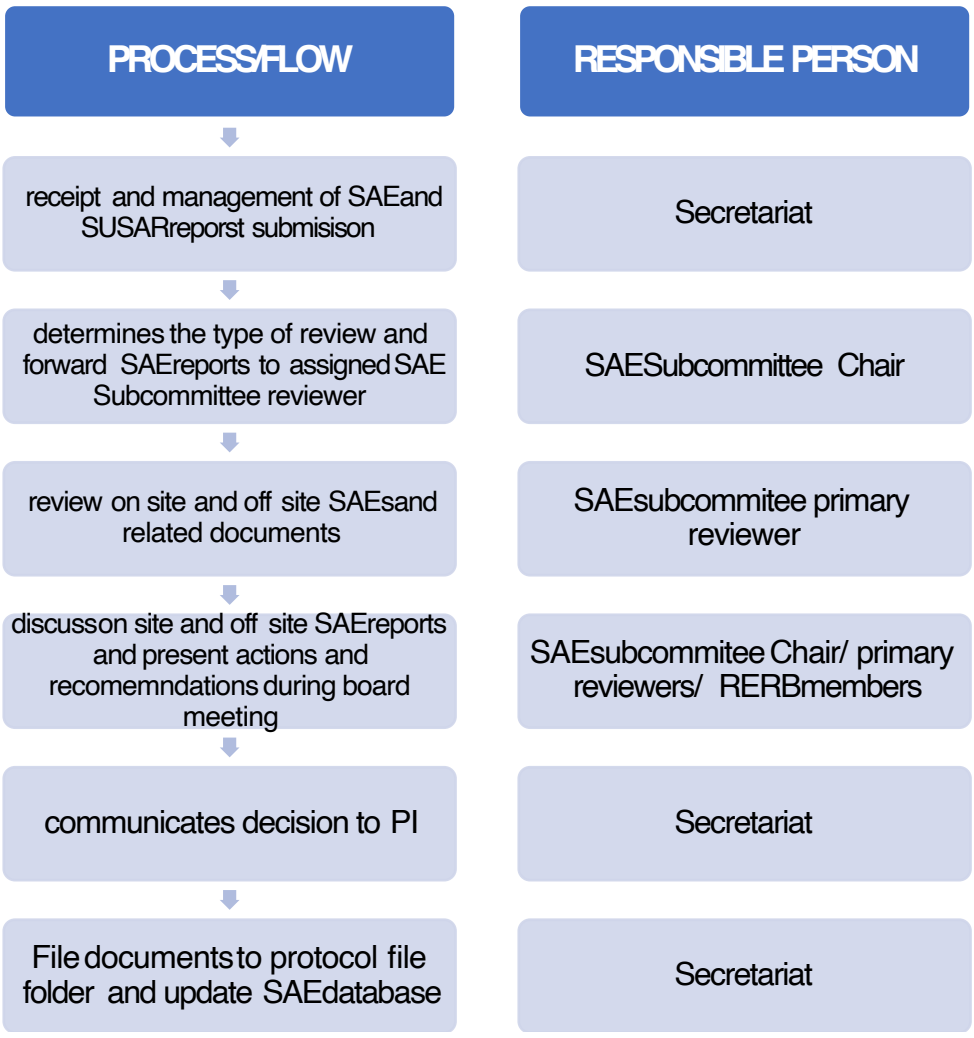
- Results in death,
- Is life threatening,
- Requires hospitalization or prolongation of existing hospitalization,
- Results in persistent or significant disability or incapacity, or
- Results in a congenital anomaly or birth defect.

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.

3.3.3. **Responsibilities**

- The primary responsibility of the RERB is to conduct an appropriate review of SAE and SUSAR reports to ensure oversight over the safety of participants enrolled in the study.
- The RERB should also make sure that researchers are made aware of its policies and procedures concerning SAE reporting.
- The RERB setsup the necessary mechanisms to receive SAE and SUSAR reports from investigators and sponsors of researches that it has approved.
- The primary responsibility of the RERB is to receive and review SAE and SUSAR reports from its own site and to take the necessary action to ensure the safety of participants in the study.
- In multicenter studies, The RERB also receives SAE and SUSAR reports from other sites within and outside the country. It is the responsibility of the RERB to be updated about safety issues related to studies that it has approved.
- The RERB has the authority to suspend or terminate approval of research at its site when the safety of participants is no longer assured. When RERB takes such action, it is required to provide the reasons for its action and to promptly report such decision to the investigator, the sponsor, the institution and relevant regulatory authorities.

3.3.4. **Process Flow/Steps**



3.3.5. Detailed Instructions

3.2.5.1. The RERB should inform investigators that they are required to report SAEs and SUSARs to the RERB for all studies approved by the RERB. They should use (Form 18) to report SAEs.

3.3.5.2. For on-site SAEs and SUSARs, the PI/study team should report the incident within 24 hours from the time/day the team is notified to the sponsor. A similar submission should be done within 7 days to the RERB.

3.3.5.3. For off-site SAEs and SUSARs, the PI/study team should submit a cumulative notification to RERB every month.

3.3.5.4. The RERB Secretariat shall be responsible for forwarding the reports to the SAE subcommittee Chair at least 7 days before full board meeting.

3.3.5.5. The SAE subcommittee Chair determines the type of review of SAE reports

3.3.5.5. On-site SAE and SUSAR reports shall be reviewed by a SAE subcommittee member who is assigned by the SAE subcommittee Chair

3.3.5.6 Off-site SAEs are reviewed through expedited process by the SAE subcommittee Chair to note the trends in SAE occurrences.

3.3.5.6. Criteria for the review

To review SAE reports, SAE subcommittee members should use the same form (Form 18) filled up by the principal investigator and fill up Section 2 that recommends appropriate action to be done by the RERB. The review procedures are as follows:

- If assessment of the SAE is **unlikely or unrelated to the study drug or article**: The subcommittee chair determines if the report should be reviewed and discussed at full board or expedited at the level of the SAE subcommittee Chair.
- If 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.
- 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.
- For multi-center, international studies, note the trend of occurrence of SAE/SUSAR in study sites in foreign countries and local sites
- For multi-center, national studies, note the nature of SAE/SUSAR whether related or suspected

- For SAEs that occur onsite, members should analyze the investigator/sponsor assessment (related, unexpected) and may need to recommend some form of action to the investigator to ensure the safety of participants.

3.3.5.8. Discuss on-site SAE reports and recommendations of SAE subcommittee to full board to ensure participants' safety.
The SAE subcommittee Chair/ primary reviewer shall present the results of SAE subcommittee's review and recommendation to full board.
After reviewing the report and the recommendations by the SAE subcommittee, the Chair calls for a vote on any of the following actions:

- No further action, SAE report on file
- Take note and continue monitoring
- Request further information from the PI
- Conduct site visit
- Request an amendment to the protocol or the informed consent form
- Suspend enrolment of new research participants until further review of the RERB
- Suspend all trial related procedures (except those intended for the safety and well-being of the participant) until further review by the RERB
- Termination of the study

The RERB shall make a decision to terminate a previously approved clinical trial based on the following considerations:

- Safety reports that indicate that continuing the study will worsen the condition of, as well as increase the risks to the study participants
- Recommendation by the Principal Investigator or the sponsor
- Other considerations that impact on the risk/benefit ratio.

3.3.5.9. Communicate CGHMC RERB decision to PI.

3.3.5.9.1. The RERB Secretariat notifies the investigator of the action taken by the RERB.

3.3.5.9.2. The RERB Member Secretary drafts a formal letter duly signed and dated by the Chair to the investigator to notify them of the action they should take according to the RERB decision.

3.3.5.10. File documents in protocol file folder and update SAE database

3.3.5.10.1. The secretariat files the documents in the protocol file folder and update protocol file index

3.3.5.10.2. The secretariat updates the SAE data

3.4 Review of Protocol Violation/Protocol Deviation/ non-compliance

3.4.1. **Purpose**

To describe the RERB review procedures for protocol violation/ deviation

3.4.2. **Scope**

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

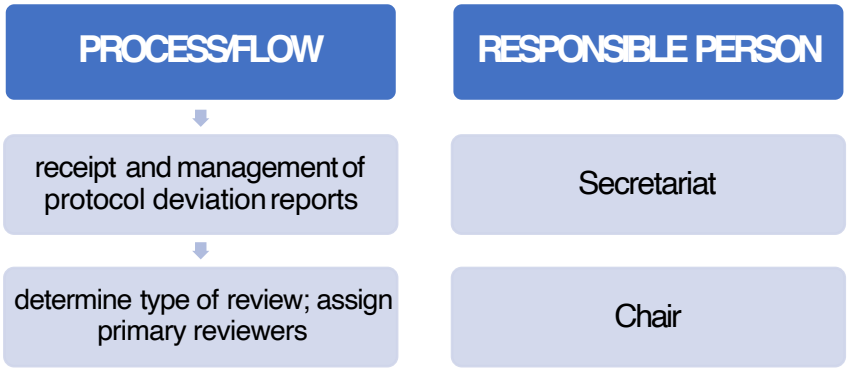
- It includes investigators who fail to comply with the procedures in the approved protocol or to comply with national/ international guidelines for the conduct of human research, including those who fail to respond to the RERB's requests.
- It also covers action taken by the RERB related to protocol 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 RERB.

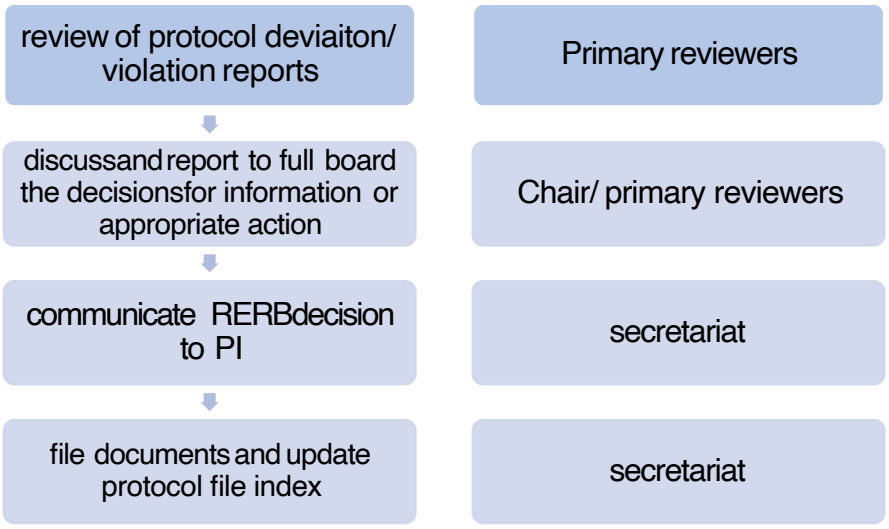
3.4.3. **Responsibility**

It is the responsibility of the RERB Secretariat to receive protocol violation/ deviation reports (Form 21) submitted to the RERB.

It is the responsibility of the primary reviewers to assess protocol deviation/ non-compliance/ violation and make appropriate recommendations/actions related to protocol violation/ deviation.

3.4.4. **Process Flow/ Steps**





3.4.5. Detailed instructions

3.4.5.1. Receipt and management of protocol Noncompliance / violation / deviation reports.

3.4.5.1.1. Reports of protocol noncompliance/violation/deviation may come from the investigators and other parties related to any event in the site that is not in compliance with the previous approved protocol and related documents. (Form 24)

3.4.5.1.2. The PI should document, explain and report to CGHMC RERB any noncompliance from approved protocol whether minor or major and the PI may implement a deviation from the protocol to eliminate an immediate hazard(s) to study participants without prior approval by CGHMC RERB, but must submit as soon as possible, a report of deviation, the reason for it and if appropriate, an appropriate study protocol amendment(s).

3.4.5.1.3. Reports of noncompliance/violation/deviation shall be facilitated thru submission of Non-Compliance/ violation/ deviation package (Form 24) together with the documents necessary to clarify and or justify the noncompliance.

3.4.5.1.4. The secretariat staff checks for completeness of noncompliance report package.

3.4.5.2. Determine type of review and assign primary reviewers

3.4.5.2.1. The Chair classifies the submission whether it should be subjected to full board or expedited review.

3.4.5.2.2. Submissions subjected to Expedited Review shall include minor protocol deviation which is a non-systematic protocol noncompliance with minor consequences, in terms of its effect on the participants rights, safety or welfare, or does not affect the scientific soundness of the study protocol. This also includes deviations that are administrative in nature.

3.4.5.2.3. Major protocol violation/deviation consist a persistent protocol noncompliance with potentially serious consequences that could put participants safety at risk or critically affect data analysis. These reports shall be subjected to full board review. The secretariat includes the protocol noncompliance in the meeting agenda for the month.

3.4.5.2.4 The secretariat shall identify the initial primary reviewers of the protocol and forward the protocol package to them.

If the initial reviewers are not available or have already resigned to do the review, the Chair designates qualified members to review the continuing review application and progress report.

3.4.5.3. The Secretariat forwards the protocol non-compliance report to the primary reviewers who shall do the review and make recommendations to the board.

3.4.5.4. Review of noncompliance/ violation / deviation reports by primary reviewers

3.4.5.4.1. The primary reviewer assesses the reports. Assessment shall focus on whether the protocol violation/deviation impacts on the safety and rights of the participants or the integrity of the data.

They shall recommend corrective and preventive actions depending on the degree of seriousness of the noncompliance/violation/deviation.

3.4.5.4.2 The decision can be any of the following:

- Noted/Acknowledged - no further information or action required
- Request additional information from the PI to properly evaluate the noncompliance (i.e. safety measures taken by PI after prohibited drugs are taken)
- Recommend further actions (i.e. request PI to attend full board meeting to explain frequent violations)
- Corrective actions are required – the subcommittee should specify the corrective measures to prevent harm to current and future research participants.
- Site visit needed

3.4.5.5. Discuss or report to full board the SAE subcommittee decisions for information or appropriate action.

3.4.5.5.1. The primary reviewers present their results during full board meeting.

3.4.5.5.2. After reviewing the report and with due consideration to the recommendations by the primary reviewers, the RERB Chair calls for a vote on any of the following actions:

- Inform PI that CGHMC RERB noted the non-compliance/violation/ /deviation and inform that the non-compliance/violation/deviation do not occur in the future and follow the RERB recommendations.

- Request the PI to attend full board meeting for additional information.
- Suspend the study until additional information is made available.
- Suspend the study until recommendations by the RERB are implemented by the PI and found satisfactory by the RERB.

- Revoke approval of current study when there is fraud or unresolved serious safety issues.
- Keep other research proposal of the PI or CO under abeyance.
- Conduct site visit

Suspension and termination shall be based on serious violations and repeated major violations. Such decision is recorded in the minutes of meeting. The decision will be taken to ensure that the safety and rights of the research participants are protected.

3.4.5.6. Communicate RERB's decision to the PI

3.4.5.6.1. The RERB Secretariat notifies the PI of RERB decision (Form 28): Action letter to Continuing Review Application/Final Report/Non-compliance/SAE/Site Visit signed and dated by the Chair and sends to the PI.

3.4.5.6.2. If the CGHMC RERB decision is No Further Action, the secretariat prepares a notification letter addressed to the PI signed and dated by the Chair.

3.4.5.6.3. If corrections or corrective actions are required from the PI, the PI shall provide the information within two weeks.

3.4.5.7. Keep records and follow-up

3.4.5.7.1. Keep the copy of the notification letter in the "noncompliance" file.

3.4.5.7.2. Store the file in the shelf with an appropriate label.

3.4.5.7.3. Follow up the action after a reasonable time.

3.4.5.7.4. Maintain a file that identifies investigators who are found to be noncompliant with national/international regulations or who fail to follow protocol approval stipulations or fail to respond to the CGHMC RERB's request for information/action.

3.5. Responding to Participant's Requests/Queries

3.5.1. Purpose

To describe the RERB procedures related to participant requests and queries

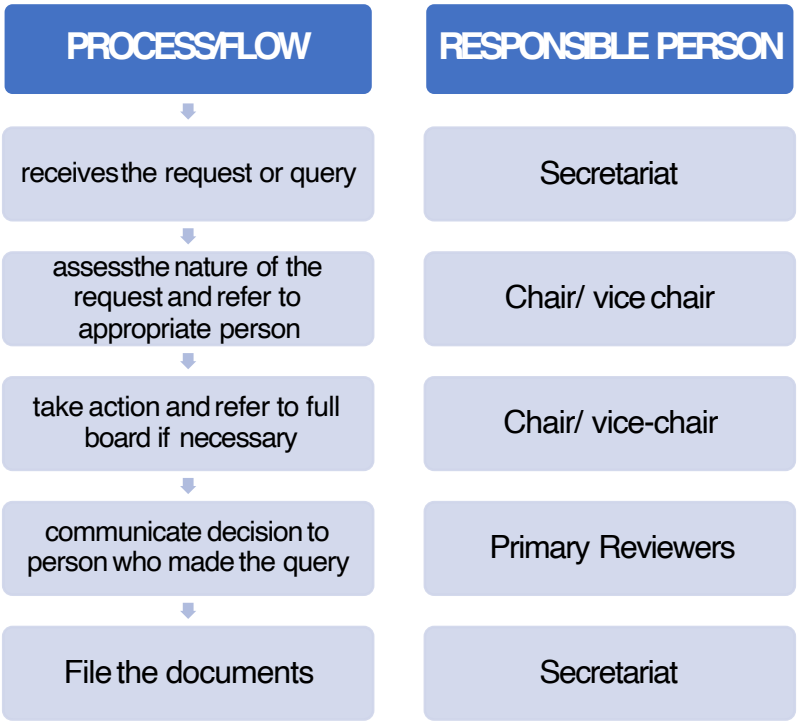
3.5.2. Scope

This SOP applies to all queries and requests related to the rights and well-being of the research participants in studies approved by the RERB.

3.5.3. Responsibility

A designated member of the secretariat is responsible for receiving participant queries and requests related to their participation, refers relevant issues to the RERB Chair or members for the RERB to take appropriate action. The Secretariat keeps records of all actions taken by the RERB.

3.5.4. Process Flow/Steps



3.5.5. Detailed Instructions

3.5.5.1. **Receive the request or query.**

- The RERB Secretariat receives the inquiry or requests from research participants/patients or the community through various forms of communication (email, telephone call, letter, etc.)
- Reply to the request or query, if it is within the authority of the secretariat or refer to the Chair or RERB member for appropriate action.
- Record the request and information in the Request Record Form (Form 25) and keep a copy in the files.

3.5.5.2. Take action

A designated RERB member takes appropriate action.

- Investigate the fact
- Record information and any action or follow-up taken in the Form 18
- Sign and date the form and forward to the Secretariat for filing.
- Report to the RERB about the action taken and the outcomes.

3.5.5.3. File the request document

- Keep the record form in the "response" file.
- Keep a copy in the study file.
- Store the file in the appropriately labeled shelf.

3.6 Site Visits

3.6.1. Purpose

To describe the RERB procedures related to the conduct of site visits

3.6.2. Scope

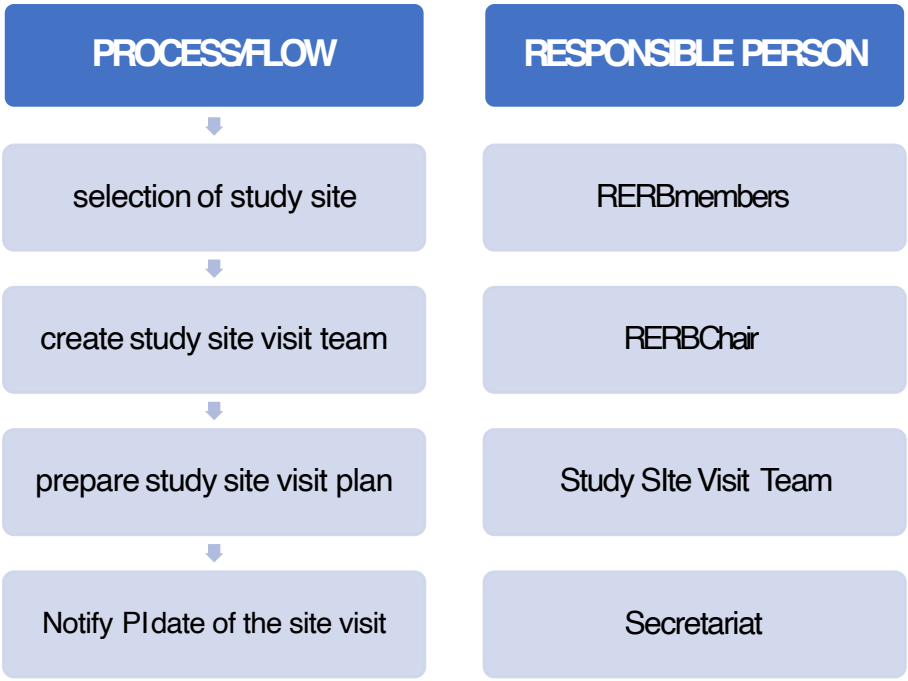
This SOP applies to any visit made in CGHMC study sites to check compliance with GCP and RERB approved protocol and related documents.

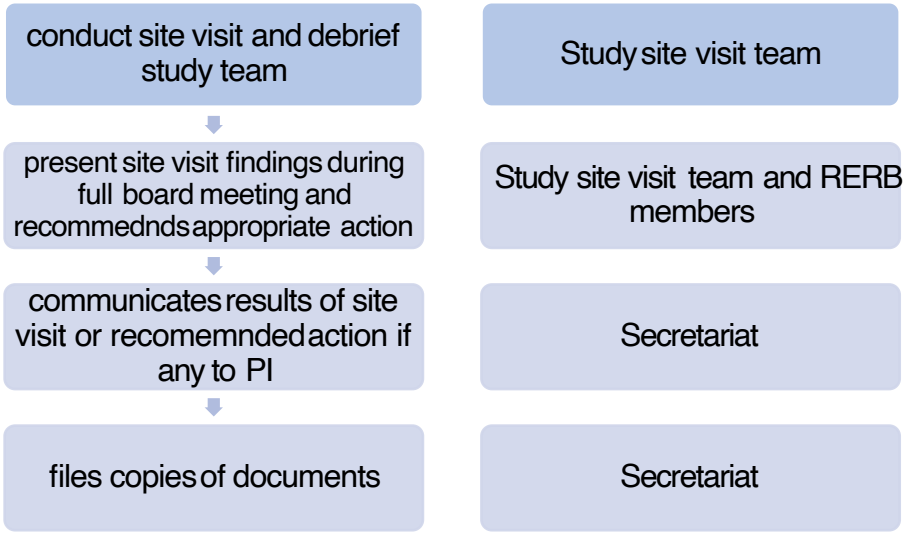
3.6.3. Responsibility

It is the responsibility of the RERB Chair and designated RERB members to perform on its behalf on-site visit of the research projects it has approved.

The RERB members, in consultation with the Chair may initiate an on-site evaluation of a study site for cause or for a routine audit.

3.6.4. Process Flow/Steps





3.6.5. Detailed Instructions

3.6.5.1. **Selection of study**

- Review periodically the database files of the submitted/approved study protocols.
- Select study needed to be monitored based on the following criteria:
  - New study or new PIs
  - Reports of remarkable serious adverse events
  - Big number of studies carried out by the same PI
  - Frequent protocol submission for IRB review
  - Non-compliance or suspicious conduct
  - Frequently fail to submit final reports
  - Frequent protocol violations

3.6.5.2. **Create study site visit team**

The Chair shall select members of the study site visit team and designates the team leader. Members should include the primary reviewers.
The Site Visit Team members are informed of their assignment.

3.6.5.3. The secretariat staff prepares the study site visit package consisting of the following:

- Latest version of the approved protocol and informed consent documents
- Other relevant documents such as: protocol deviation reports, on-site SAEs/SUSAR reports
- Copy of Site Visit Report Form

3.6.5.4. Prepare Study Site Visit Plan

The Study Site Visit Team prepares the study site visit plan that includes the following:

- Date and time of the planned visit
- Members of the study site visit team
- Objectives of the visit
- Documents to be reviewed
- Persons to be interviewed

3.6.5.5. The study site visit team, in consultation with the Chair, is given access to documents in the protocol file folder of a study for monitoring. The team may also photocopy some parts of the files (like advertisement materials, the informed consent form (ICF), case report form) for comparison with the documents used in the study sites.

3.6.5.5. Notify PI of date of site visit

3.6.5.4.1. The secretariat staff contacts the study site or PI and coordinate the date and time for the site visit.

3.6.5.4.2. The PI shall be given at least four (4) weeks' notice to ensure their active participation.

3.6.5.4.3. The secretariat staff prepares and sends letter to the PI, formally informing them of the planned study site visit. Attach to the letter the study site visit plan and report form

3.6.5.6. Conduct site visit and debrief study team

3.6.5.5.1. The study site visit team conducts the site visit as per the study site visit plan and additional guidance from Site Visit Report Form (Form 26).

3.6.5.5.2. The CGHMC RERB study site visit team will:

- Review filled up informed consent documents to make sure that the site is using the most recent version.
- Review randomly the subject files to ensure that subjects are signing the correct informed consent.
- Observe consent process, it possible.
- Check if the files are orderly and confidentiality is maintained.
- Interview members of the research team.
- Debrief the PI about site visit findings and comments.
- Get immediate feedback.

3.6.5.5.3. After the visit, the CGHMC RERB study site visit team will :

Write a report using Site Visit Report Form within 2 weeks, describing the findings during the audit

Forward a copy of the site visit report to the secretariat for inclusion in the next board meeting.

Send a copy of the report to the study site for their file.

File the site visit report in the protocol file.

3.6.5.6. Present the site visit findings during the Full Board meeting.

3.6.5.6.1. The study site visit team presents the report during the full board meeting.

3.6.5.6.2. The Board decides whether the rights, safety and welfare of the research participants are compromised and recommends appropriate action.

3.6.5.6.3. Decision/Recommended action of the board can be any of the following:

NO FURTHER ACTION

REQUEST ADDITIONAL INFORMATION

RECOMMEND FURTHER ACTION

3.6.5.7. Communicate results of site visit and the recommended actions, if any to the PI.

The secretariat staff communicates the board decision to the PI as follows:

3.6.5.7.1. If no further action is required, notify PI

3.6.5.7.2. If additional information or further action is required, notify the PI. The PI must comply with the recommendations and submits response to the RERB.

3.6.5.7.3. Secretariat staff prepares the report of action taken by the PI and the member-secretary reports it to the board.

3.6.5.8. File copies of documents

3.6.5.8.1. The secretariat staff files the study site visit report, excerpt of the minutes of the meeting when report was discussed and the notification letter (including the response of the PI, if any) in the protocol file folder and update the protocol file index and protocol database.

3.7. Early Protocol Termination

3.7.1. Purpose

To describe the RERB procedures related to early termination of protocol implementation

3.7.2. Scope

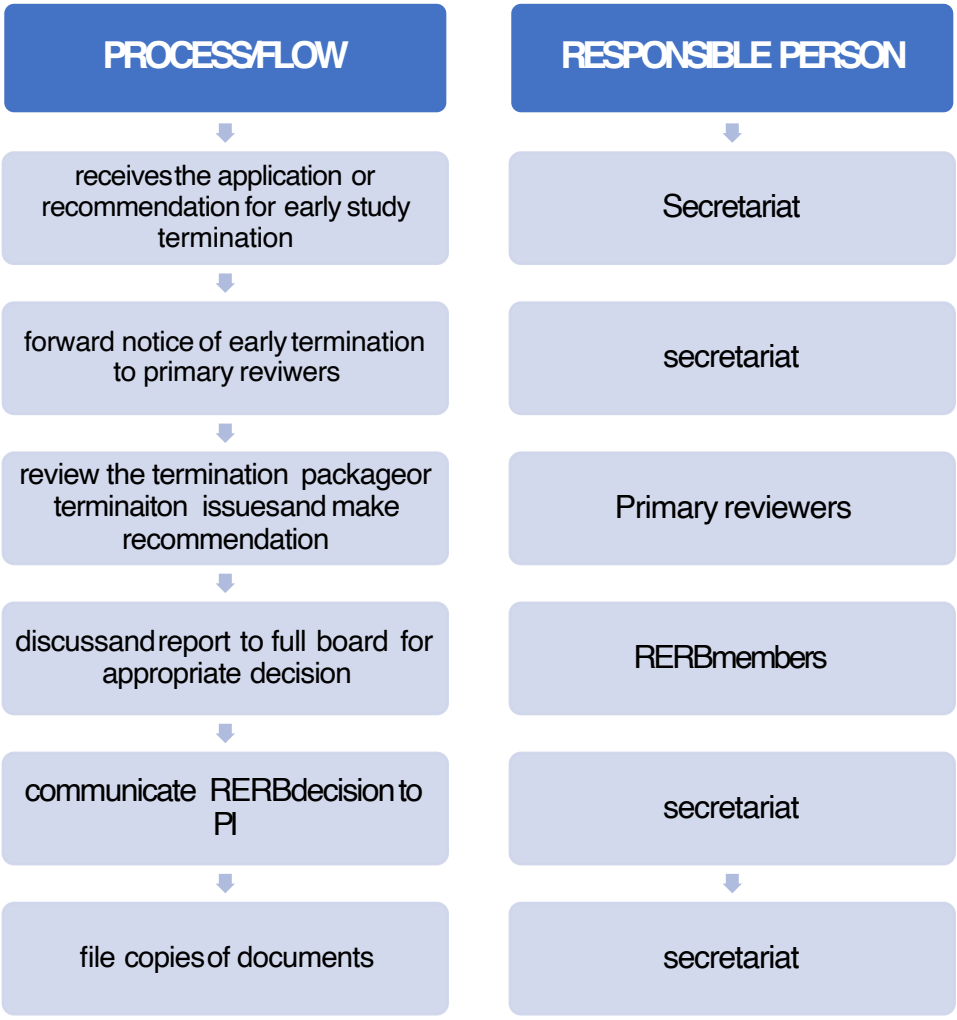
This procedure describes how the RERB proceeds and manages the premature or early termination of a protocol when subject enrollment is discontinued before the scheduled end of the study. Protocols are usually terminated at the recommendation of the Data Safety Monitoring Board (DSMB), the Scientific Director, sponsor, PI, by the RERB itself or other authorized bodies. This is done when the safety of the study participants is doubtful or at risk.

3.7.3. Responsibility

It is the responsibility of the RERB to act on any early protocol termination application. It is also the responsibility of the RERB to withdraw approval for any previously approved protocol when the safety or benefit of the study participants is doubtful or at risk. All applications are reviewed during full board meeting to decide on appropriate action.

The Secretariat is responsible for the receipt and management of the termination documentation. The primary reviewers review the reasons for early termination and make a recommendation to full board.

3.7.4. Process Flow/Steps



3.7.5. Detailed Instructions

3.7.5.1. RERB Secretariat

3.7.5.1.1. Receives application or recommendation for early study termination.

3.7.5.1.2. Receives recommendation and comments from the Sponsor, DSMB, RERB members, Scientific Director, or other authorized bodies for study protocol termination.

3.7.5.1.3. Informs the principal investigator to prepare and submit a protocol termination package.

3.7.5.1.4. Receives the study protocol termination package prepared and submitted by the principal investigator.

3.7.5.1.5. Checks the completeness of the contents of the package to include the Study Termination (Form 27). The request for termination memorandum should contain a brief written summary of the protocol, its results, and accrual data.

3.7.5.2. Review the submission

3.7.5.2.1 The primary reviewers assess the termination issue, review safety data and make recommendation.
*it is important to note if the Termination Package contains a plan of how the participants who are still active in the study will be followed up. If no plan is noted, the CGHMC RERB should recommend to the PI that such plan should be included.

3.7.5.2.1. The secretariat shall include the submission for early termination in the agenda for full board review.

3.7.5.3. Discuss at full board for appropriate action

3.7.5.3.1. The RERB deliberates on the effects of early study termination on the safety and welfare of study participants.

3.7.5.3.2. Final decision of the application are as follows:
APPROVAL/ NO FURTHER ACTION
RECOMMEND FURTHER ACTION
FURTHER INFORMATION REQUIRED/ CLARIFICATION FROM PI

3.7.5.4. Communicates the RERB decision to PI

3.7.5.4.1. The RERB secretariat prepares letter of notification signed and dated by the Chair.
The PI may be requested to provide additional information or documents or implemented actions to ensure the safety and welfare of subjects still active in the study.

3.7.5.5. File pertinent documents and update protocol database

3.7.5.5.1. The secretariat files the pertinent documents, excerpt of the minutes of the meeting when it was discussed, and the Notification Letter (Form 28), including the response from the PI, if any, in the protocol file folder and update the protocol file index.

3.7.5.5.2. Upon approval of the Early Study Termination Application, the study protocol is classified as inactive, the protocol code no. is updated and the protocol file folder re-labelled and transferred to storage for inactive files.

3.7.5.5.3. The secretariat staff updates the protocol database and labels the protocol "inactive-early termination."

3.8 Review of Final Report

3.8.1. **Purpose**

To describe the RERB review procedures for follow-up and review of final reports for any study previously approved by the RERB

3.8.2. **Scope**

This SOP aims to provide instructions for the review of final reports that are submitted by the PI after completion of subject enrollment and all follow up procedures.

This SOP describes the review of final reports submitted by the PI by designated members of the RERB in compliance with ICH-GCP requirements.

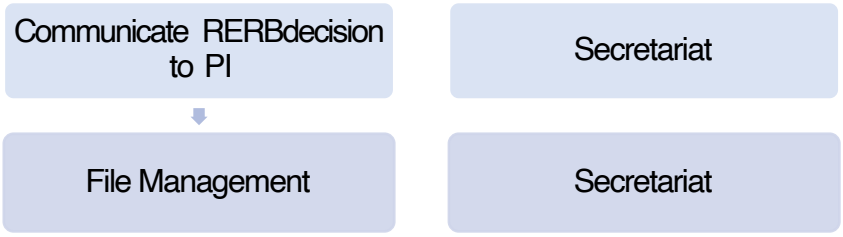
3.8.3. **Responsibility**

It is the responsibility of the RERB Secretariat to identify study protocols whose final reports are due. The secretariat checks for the completeness of the final report form (Form 20).

It is the responsibility of the primary reviewers to review and present the final report during the meeting

3.8.4. **Process Flow/Steps**

PROCESS/FLOW	RESPONSIBLE PERSON
Receive the Final Report package and check its completeness	Secretariat
determine the type of review and assign primary reviewers	RERB Chair
Forward final or closure report to primary reviewers for review	Secretariat
Review final report, render decision and report to full board	Primary Reviewers



3.8.5. Detailed Instructions

3.8.5.1. Submission and management of Final Reports

- The Secretariat checks the database.
- The Secretariat reviews the completeness of submitted report based on the items in Final Report Form (Form 23) and forwards the report to the primary reviewers for review.

3.8.5.2. The Chair determines the type of review the progress report/ continuing review application should undergo and identify the primary reviewers.

The secretariat shall identify the initial primary reviewers of the protocol and forward the protocol package to them.

If the reviewers are not available to do the review, the Chair designates qualified members to review the continuing review application and progress report.

3.9.5.3. The secretariat staff shall forward the Final report or Closure report package to the primary reviewers.
The secretariat includes the final report submission on the agenda for the next RERB meeting for discussion and final decision.

3.9.5.4. Review of Final Reports, render decision and report to full board
The primary reviewers present the final report during the full board meeting

The RERB decision can be any of the following:
APPROVE (Acknowledged/Accepted)
Request for additional information, specify
Recommend further action, specify

3.8.5.5. Communicate result of RERB decision to PI

3.8.5.6. PI is notified by the secretariat staff of the RERB decision
PI may be requested to provide additional information or submit additional documents, in which case the final report maybe accepted, but action regarding archiving maybe deferred depending on the submission of requested additional information or documents

If the final report is approved, the PI is informed of the following:

The study protocol is now classified as INACTIVE; Study protocol record will be made available for three (3) years in the archives after the expiration date.

3.8.5.7. File Management

3.8.5.7.1. The RERB Chair signs the Final Report Form.

3.8.5.7.2. The secretariat staff stores the signed Final Report documents in the study protocol file folder upon approval of the final report, and when no further action is expected from the PI.

3.8.5.7.3. The secretariat staff enters relevant study protocol data into the study protocol Database to signify the end of the study.

3.8.5.7.4. The secretariat Staff transfers the study protocol folder to the Inactive Files.