REVISION NO.	REVIEW DATE	AUTHORS	MAIN CHANGE
6	Sep 19, 2018	RERB Members	Added the following sections - Exempt from review - Designation of primary reviewers - Management of protocol withdrawal - Assent evaluation for researched involving minors - History of SOP Management of protocol resubmission was transferred from chapter 4 to this chapter Flowcharts were revised to have uniformity

2.1. Management of Initial Protocol Submission

2.1.1. Purpose

To describe the initial review procedures of the Research Ethics Review Board (RERB) from the time the RERB Secretariat receives the protocol and related documents until the approval letter is sent by the RERB to the Principal Investigator

2.1.2. Scope

The CGHMC RERB accepts the following protocols for review:

- CGHMC funded researches
- researches done in CGHMC by medical house staff
- research proposals submitted by CGHMC personnel for thesis defense
- industry sponsored researches to be conducted by CGHMC active/visiting medical staff to be conducted off-site (in the event that institution does not have an ethics review board in place). In consideration to multi-center trials or studies, each Center/trial site has to have an independent or its own RERB approval for the said protocol.

2.1.3. Responsibility

The following are the responsibility of the principal investigator or proponent:

- For protocols requiring a **full board review**:
  Make **at least 7 hard copies** (for RERB filing purposes and for use during RERB meeting) Place the original copies in a protocol file folder.
- For protocols that can undergo **expedited review**
  Make **at least 3 hard copies** (for RERB filing purposes and for use during RERB meeting). Place the original copy in a protocol file folder.
- For protocols for exempt of review
  Make **at least 2 hard copies**.

The RERB Secretariat manages all initial protocol submissions to the RERB. It covers the actions to be done from the time of submission to the filing of the original protocol package in the Active Study File cabinet and the preparation of copies of the documents for distribution to the reviewers.

It is the responsibility of the RERB Chair to determine the type of review – full board, expedited or exempt form review. The Chair is also responsible for assigning primary reviewers.

2.1.4 **Process Flow/Steps**

PROCESS/FLOW	RESPONSIBLE PERSON
receives and checks for completeness of protocol package	Secretariat
assigns permanent code to protocol package	Secretariat
logs the received protocol in the RERB database	Secretariat
determines the type of review: exempt, expedited or full	RERB Chair
assigns primary reviewers	RERB Chair
prepare the protocol package for distribution to the reviewers	Secretariat
files the original package in a properly coded protocol file folder & places in Active Folder	Secretariat

2.1.5 **Detailed Instructions**

2.1.5.1 Protocols submitted **on or before the 1st week of the month** will be included in the same month's RERB meeting, scheduled either on the **3rd or 4th Thursday of**

the month. In addition, the Chair or Vice-Chair reserves the right to call for a special meeting outside the regular meeting if necessary.

2.1.5.2. Trainee-initiated research

All protocols of CGHMC trainees to be conducted in the hospital need to be approved and signed by the respective Department's research technical review committee prior to submission to RERB for review. Co-authors need to affix their signatures in the cover letter stating they have read and likewise approved the conduct/content of the said study. However, the RERB may disapprove a research paper when there are clearly technical flaws in the conduct of the trial/study.

Researches of trainees done in relation to completion of training requirements will not be subject to institutional/review fees, unless these are externally funded (in whatever manner). Fees are dependent on the discretion of the Board.

Researches to be conducted by trainees that entail retrospective review of charts/medical records (with no actual participant/subject contact in whatever manner) will need to have a waiver of informed consent submitted to RERB (Form 11). A request letter addressed to the Medical Director or his designated authority/representative should likewise be sought prior to study implementation.

2.1.5.3. Industry/Sponsor initiated clinical trials

Corresponding review fees need to be settled by the investigator/sponsor prior to RERB board review. The sponsor or identified PI should submit the budget of the trial for the site for computation of the 10% institutional fee. This fee is computed as 10% of the total budget allocated for the number of committed subjects for the site, including, study team honoraria, and all other study related expenses (eg. procedural costs/fees, patient remuneration, on site laboratory/diagnostic costs, pharmacy fees, etc.), excluding the IRB review fee. The fee shall be settled by the sponsor within a month after the 1st subject is randomized into the trial. The Associate Director assisted by the RERB Secretariat is responsible for preparing the Statement of Account for each trial. There will be no refund of the institutional fees in case the committed number of participants for the site is not reached or early termination of trial for whatever reasons. Once

validity of RERB initial approval for the said study/trial has lapsed, renewal of approval is subject to a new fee.

Upon submission of the Application Form and Documents for Protocol Review (Forms 6A and 6B), the principal investigator or his/her representative should ensure that the protocol follows the standard protocol format and contains a Protocol Summary Sheet (Form 7).

All clinical study agreement (CSA) of externally supported studies/trials should undergo approval by the Legal Division of the Hospital prior to issuance of RERB approval letter. A parallel submission of CSA to the Legal Division of the Hospital for approval and protocol review to the RERB for approval is allowed.

2.1.6. **Receives and checks for completeness of initial protocol package**

2.1.6.1. The Secretariat checks the documents being submitted based on the RERB checklist.

A protocol package has to include the following:

i. Accomplished initial protocol submission form (Form
ii. Full protocol
iii. Executive summary that follows research project proposal format
iv. Declaration of conflict of interest (if applicable)
v. Data collection form/s
vi. Informed Consent form (English and Tagalog Version)
vii. Full study Budget
viii. CV of the trial team (incl. PI, co-investigators, research assistants/coordinators, etc.) and their updated (actual) GCP Certificate (Co-investigator should at least be in the same basic field of practice/specialization as the principal investigator)
ix. GANTT Chart (as necessary)
x. Ads for recruitment, if applicable
xi. Case report forms
xii. Questionnaires (English and Tagalog version)
xiii. Subject Worksheets/Patient Diary/Alert Cards (English and Tagalog versions)
xiv. Technical approval document (for trainee-initiated research)
xv. For multi-center trial, list of all the trial sites (local and/or international) together with their respective PIs

xvi. Phil FDA approval to conduct the trial (clinical trials)
xvii. Investigator's Brochure (if applicable)
xviii. Certificate of Insurance (if applicable)
xix. Certificate of Product Registration in the Philippines for Post Marketing Surveillance Studies (PMSS)

2.1.6.2. Incomplete and/or incorrect package will not be accepted, the secretariat will communicates with the concerned PI to return the package for modification.

2.1.6.3. For protocols only awaiting approval from the FDA, the RERB can conduct a parallel review; however, the issuance of approval letter shall be withheld until completion of said requirement.

2.1.6.3. Only protocols with complete requirements (and payments as applicable) will be accepted and received by the Secretariat for RERB review.

2.1.7. If the package is complete, the Secretariat assigns a permanent code to the protocol package. All subsequent communications in relation to the protocol will utilize the code assigned.

2.1.7.1. A unique code shall be used to identify a specific protocol for efficient file management. The unique code known as CGHMC RERB Code shall be assigned to a specific protocol and shall bear the following:

CGHMC RERB					-		-		
		Year				Classification		Series No	

Classification: **R**- resident; **F** – fellows; **C** – consultant; **CT**-clinical trials/ sponsor-initiated protocol;

For example, the code CGHMCRERB2018-F-03 shall mean "Third (03) protocol received in 2018 is a resident submitted protocol.

2.1.8. The Secretariat logs the protocol in the RERB database.

2.1.9. The Chair shall determine the type of review – full board, expedited or exempt from review. The Secretariat shall prepare the appropriate communication as to the type of review.

2.1.10. The Chair shall assign two (2) RERB members to the primary reviewers of the protocol regardless of the type of review.

2.1.11. The secretariat prepares the copies of protocol package for distribution to the primary reviewers.

2.1.12 Filing of initial protocol package in a properly labelled protocol file folder and place in the Active Study File Cabinet.

2.1.12.1 Put the code of the protocol on the side of the file folder

2.1.12.2. File the folder in the Active Study Files cabinet under lock and key.

2.2. Designation of Primary Reviewers

2.2.1 Purpose

To describe the process of designating primary reviewers to study protocol

2.2.2. Scope

This SOP applies to the designation of primary reviewers until the review and prese

2.2.3. Responsibility

It is the responsibility of the RERB Chair to assign primary reviewers to protocols received

2.2.4. Process/ Flow

PROCESS/FLOW	RESPONSIBLE PERSON
assigns primary reviewers	RERB Chair
send the protocol pacakge to rhge assigned primary reviewers	Secretariat
review the protocol and related documents; accomplish study assessment forms	Primary Reviewers
discuss protocol and present actions and recomemndations during board meeting	Primary Reviewers

2.2.5. Detailed Instructions

2.2.5.1 The RERB Chair assigns one (1) scientific/ medical reviewer and one (1) non-medical as primary reviewers of the study protocol. Reviewers are selected on the basis of their expertise. The scientific/medical reviewer is tasked to review technical soundness and related ethical issues while the non-medical reviewer is tasked to review the informed consent process

and forms. In the case of clinical trials, a non-medical reviewer can be represented by a member who is not a medical doctor.

2.2.5.2. The secretariat sends the study protocol package to the assigned primary reviewers.

2.2.5.3. Primary Reviewers of study protocols for initial review should be present in the board meeting. In case of unavailability of the primary reviewers to attend the meeting, discussion of the study protocol may still proceed at the discretion of the RERB Chair. Said members are required to forward the completed assessment forms to the Secretariat Staff seven (7) days before the meeting. The findings summarized therein will be presented by the RERB Chair or his designee when the study protocol is deliberated on.

2.3. Expedited Review

2.3.1. Purpose

To describe the procedures for the review of protocols that qualify for expedited review

2.3.2 Scope

This SOP applies to the review and approval of study protocols or amendments with minimal risk to study participants and minor revisions in the protocol or informed consent. The submission procedures are the same as first time submission.

The following are types of protocols that can be subjected to expedited review after initial submission:

a. Protocols of a non-confidential nature (not of a private character, e.g. relate to sexual preference etc., or not about a sensitive issue that may cause social stigma), not likely to harm the status or interests of the study participants and not likely to offend the sensibilities nor cause psychological stress of the people involved.
b. Protocols not involving vulnerable subjects (individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation of benefits associated with participation or of a retaliatory response in case of refusal to participate, patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors and those incapable of giving consent).
c. Protocols that involve collection of anonymized biological specimens for research purposes by non-invasive means (e.g. collection of small amounts of blood, body fluids or excreta non-invasively, collection of hair or nail clippings in a non-disfiguring or non-threatening manner).
d. Research involving data, documents or specimens that have been already collected or will be collected for ongoing medical treatment or diagnosis
e. Proposed continuing reviews, protocol amendments and end of study reports that have minor modifications and no significant risk to study participants.

2.3.3. Responsibility

2.3.3.1 Expedited review is the responsibility of two (2) primary reviewers appointed to assess any protocol that qualifies for the expedited process. The same

assessment forms used for full board review should be used to evaluate the scientific and ethical merits of the protocol.

2.3.3.2. The Secretariat

- receives the documents submitted for initial review,
- receives the application documents submitted by investigators,
- checks items received using checklist as guide,
- signs a copy of the application form to acknowledge receipt of the documents, and
- returns a copy to the principal investigator or a duly designated representative.

2.3.4. Process/ Flow steps

PROCESS/FLOW	RESPONSIBLE PERSON
receipt and management protocol package	Secretariat
review the protocol and related documents using the study assessment forms	Primary reviewers
return duly accomplish assessment forms to secretariat	Primary Reviewers
discuss protocol and present actions and recomemndations during board meeting	Primary reviewers

2.3.5. Detailed Instruction

The Chair assigns two (2) RERB members as primary reviewers. An independent consultant may be invited to provide expert opinion about a protocol.

2.3.6. The members carry out the expedited review on the protocol and related documents (patient information sheet, consent form, advertisements, etc.) The review process should not take longer than 2 weeks upon distribution of protocol to primary reviewers.

2.3.7. If decision is reached by both primary reviewers, this will be discussed and reported during next full board meeting. Principal investigator is also invited to present the protocol and clarify all issues and comments.

2.3.8. All expedited review will still undergo full board to facilitate timeliness of the review.

2.4. Full Board Review of Submitted Protocols

2.4.1. Purpose

To describe the procedures when protocol submissions are classified for full board review

2.4.2. Scope

This SOP applies to the review and approval of study protocols or amendments with medium to high risk to study participants and major revisions in the protocol or informed consent. The submission procedures are the same as first time submission.

2.4.3. Responsibility

The following are the responsibilities of the Secretariat:

- manages the document submission
- sends protocol documents to the primary reviewers
- refers the protocol to full board meeting for discussion and decision
- communicates the CGHMC RERB decision to the Principal Investigator
- files and keeps copies of the documents in the protocol files, and
- updates the protocol entry in the database.

It is the responsibility of the Chair to determine the type of review the protocol will undergo and assign appropriate primary reviewers and/ or independent consultant (if needed); review the summary of evaluation results and presiding over the convened full board meeting.

It is the responsibility of the primary reviewers to thoroughly review the protocol and related documents by using the assessment forms and make recommendation for appropriate action and submit the fully accomplished assessment forms to the secretariat. The primary reviewers shall actively lead the discussion during the full board review of the assigned study protocol.

2.4.4 Process/ Flow Step

PROCESS/FLOW	RESPONSIBLE PERSON
receipt and management protocol package	Secretariat
determine the type of review and assign primary reviewers	RERB Chair
send the protocol package to primary reviewers	Primary reviewers
review the protocol using the 2 study assessment forms	Primary Reviewers
returns the duly accomplished forms to the secretariat	Primary Reviewers
discuss and decide on the protocol and related documents during a convened board meeting	RERB Members
communicate CGHMC RERB decision to the PI	Secretariat
file copies of the documents in the protocol file folder and update protocol database	Secretariat

2.4.5 Detailed Instructions

2.4.5.1 The Secretariat

- Receives the protocol package
- Checks the completeness of the protocol package, includes putting check marks on document submitted part of Form 6
- Returns the signed acknowledgement form/receipt back to the representative of the principal investigators

2.4.5.2. Determine the type of review and assign primary reviewers

2.4.5.2.1. The Chair determines if the submitted protocols should undergo full board review.

2.4.5.2.2. The following are types of protocols that should undergo full board review after initial submission:

- Clinical trials about investigational new drugs, biologics or device in various phases (Phase 1,2,3)
- Phase 4 intervention involving drugs, biologics or device
- Protocols including questionnaires and social interventions that are confidential in nature (about private behavior, e.g. related to sexual preferences etc., or about sensitive issues that may cause social stigma) that may cause psychological, legal, economic and other social harm
- Protocols involving vulnerable subjects (individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation of benefits associated with participation or of a retaliatory response in case of refusal to retaliate, patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors and those incapable of giving consent) that require additional protection from the RERB during review
- Protocols that involve collection of identifiable biological specimens for research
- Major protocol violations
- Progress/Final reports that deviate from original approval given by the RERB

- Onsite SAEs or suspected unexpected serious adverse reactions (SUSARs) that may require protocol amendment or re-consent of participants

2.4.5.2.3. The Chair designate primary reviewers to review the protocol. with appropriate qualifications (medical member with expertise related to the protocol and a non-medical member to review the consent form. An independent consultant may be invited to provide expert opinion.

2.4.5.2.4. For study protocols classified for full board review, the Principal Investigator will be notified of the schedule of the review, the time slot of their study protocol and advised to be "on call" to answer any questions or make clarifications on issues raised by RERB members

2.4.5.3. Sends the protocol files together with the assessment forms to the primary reviewers/ independent consultant.

2.4.5.4. Review of the Protocol by the primary reviewers

- Use the Protocol Evaluation Form (Form 8) and the Informed Consent Evaluation Form (Form 9) to review the protocol and the consent form and write relevant comments
- Check the CV or information about the investigators (including actual GCP training), the study sites and other protocol related documents, including advertisements.
- Consider whether study and training background of the principal and/or sub-investigator/s are related to the study.
- Look for disclosure or declaration of potential conflicts of interest.
- Non-physician principal investigators should be advised by a physician when necessary.
- Determine if the facilities and infrastructure at study sites can accommodate the study.
- Check the "Child Assent Form" (Form 10) if the protocol involves children or other vulnerable groups as study participants based on PHREB guidelines. The

procedure for getting the assent of vulnerable participants should be clear (the objective of the study and the procedures to be done should be explained to the child or vulnerable participant separately).

- Children age under 7 years need not have a signed assent form,
- age 7 and under 12 need verbal assent,
- age 12 and under 15 need to sign a simplified child assent form,
- age 15 and under 18 should co-sign in the informed consent form with parents.

The primary reviewers are advised to note the following Review Guidelines:

- The protocol manifests scientific validity and contains all the standard sections to ensure scientific soundness.
- In assessing the degree of risks against the benefit, determine whether the risks are reasonable in relation to anticipated benefits; and/or if the risks can be minimized.
- Study participants are selected equitably especially if randomization is not to be used. Study participant's information sheet should be clear, complete and written in understandable language.
- There is voluntary, non-coercive recruitment of study participants.
- The informed consent is adequate, easy to understand and properly documented.
- There should be a translation of the Informed Consent document into the local dialect which should be comprehensible by the general public.
- The procedure for getting the Informed Consent is clear and unbiased.
- The persons who are responsible for getting the Informed Consent are named and they introduce themselves to the study participants.
- The research plan makes adequate provision for monitoring data collection to ensure the safety of study participants, where appropriate.
- There are adequate provisions to protect the privacy of study participants and to maintain the confidentiality of data, where appropriate.
- There is provision for compensation to study participants. There should be reasonable provision for medical/ psychosocial support; treatment for study related injuries, as well as compensation for participation to cover expenses like transport and lost wages because of participation.
- There are appropriate safeguards included to protect vulnerable study participants.
- There are provisions on steps to be taken when participants voluntarily withdraw during the course of study/trial, where appropriate.

- Contact persons (Principal Investigator and RERB Chair) with address and phone numbers are included in the Informed Consent.
- There is clear justification for the use of biological materials and a separate consent form for future use of biological specimens.
- Where applicable, provisions maybe made when investigational products will be made available to research participants after the trial at a reduced price.
- There are appropriate contracts or memoranda of understanding especially in collaborative studies.
- Examine community involvement and impact/benefit of the study to the community and/or the institution. If relevant, the reviewer looks for the following in the protocol:
- Community consultation
- Involvement of local researches and institution in the protocol design, analysis and publication of the results
- Contribution to development of local capacity for research and treatment in benefit to local communities
- Sharing of study results with the participants/community

2.4.5.5. After reviewing the protocol and the documents, the reviewer

- Recommends a decision.
- Records the decision by marking the appropriate block in the assessment form: Approved, Minor revision, Major revision for resubmission, or Disapproved.
- Includes comments and reasons for disapproval.
- Checks the completeness and correctness of marked items in the assessment forms.
- Indicates the date and affix his/her signature in the decision form.
- Returns the completed assessment forms to the Secretariat together with the protocol documents.

2.4.5.6. The secretariat checks the assessment forms for completeness and forwards them to the Chair to be included in the agenda for the next full board meeting.

2.4.5.7. Conduct a full board meeting to discuss and make decisions through majority vote about the protocol and related documents.

2.4.5.8. The members of the RERB attending the full board meeting shall arrive at a decision through majority vote on each issue in the protocol, with a final overall decision for: **APPROVED, MINOR REVISIONS, MAJOR REVISIONS or DISAPPROVED.**

For all protocols that have been recommended minor revision, a decision point to be voted upon by the Board should be made if approval maybe given at the level of the Chair upon recommendation of the Board once proponents fully comply with recommendations.

2.4.5.9. Communicating the CGHMC RERB decision to the principal investigator
For low-risk studies, if the study is approved, the RERB shall state the **validity that the initial approval is for 1 year** Request for renewal of approval of ongoing studies should be submitted one month before the expiration of the validity, together with an annual report for that year.

For high risk studies, if the study is approved, the RERB shall state the **validity that the initial approval for a year**. For studies longer than a year, subsequent approval needs to be sought pending the continuing/progress review (every 6 months) that the RERB conducts during the study. An annual progress report should be submitted by the principal investigator.

2.4.5.10. The Secretariat sends a decision letter (Notification of RERB Decision Form 15), with a list of approved documents to the principal investigator.

2.4.5.11. The letter contains identification of the document approved with version numbers and dates, validity of approval period, the frequency of continuing review and the responsibilities of the principal investigator throughout the course of the study.

2.4.5.12. If the principal investigator wishes to appeal the RERB decision, he/she may do so through a written request submitted to the RERB.

2.4.5.13. If the RERB requires modifications to any of the documents, the Secretariat prepares a letter to the Principal Investigator and identifies the necessary revisions to the documents before resubmission to the RERB.

2.4.5.14. If the protocol is approved, the Secretariat drafts the Approval Letter (Form 15), forwards it to the Chair to sign, then sends it to the principal investigator. There should be a file/receiving copy with specific date. All information regarding the date of the RERB decision such as the date when decision was written and signed by the Chair, and date when it was delivered to the principal investigator, are entered in the RERB database.

2.4.5.15. All meeting deliberations and decision regarding a protocol are noted in the meeting minutes, with relevant sections filed in the specific protocol file.

2.4.5.16. The RERB database is updated to record the decision. Copies of the assessment forms are kept in the protocol files.

2.4.5.17. The CGHMC RERB also allows, at the discretion of the Chair, guests (such as surveyors) or observers (such as trainees or students) to observe CGHMC full board meetings. Non-members who are attending any CGHGMC RERB meetings are required to sign the Confidentiality Agreement Form for Guest Attendees to RERB Meetings (Form 33).

2.5. Management of Exempt from Review

2.5.1. Purpose

To describe the procedure for the review of protocols that qualify for exemption from review

2.5.2. Scope

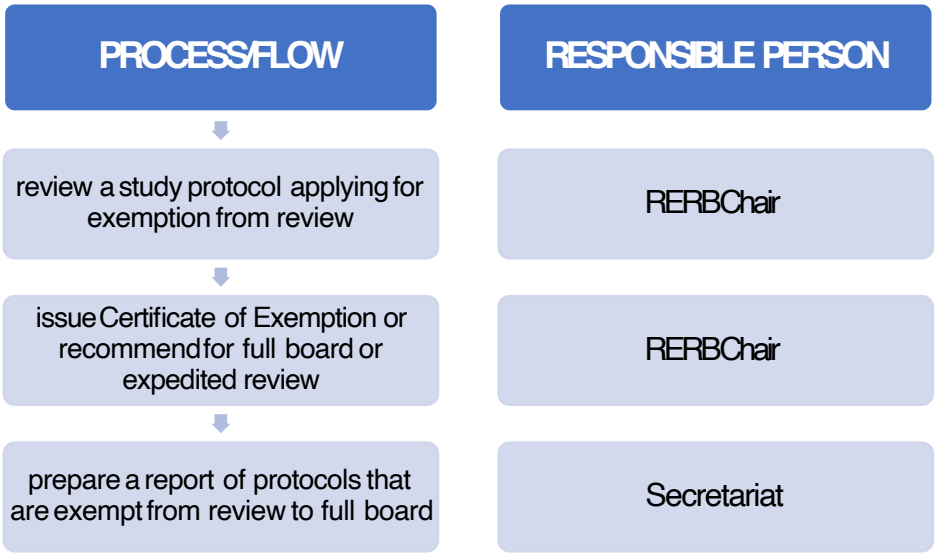
This SOP applies to the review of a study protocol submitted that qualifies for exemption from review

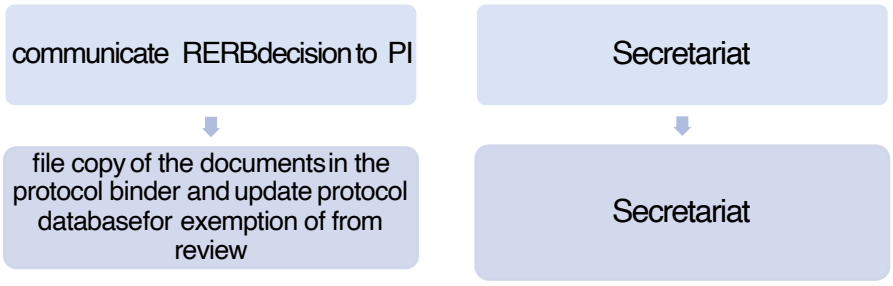
2.5.3. Responsibility

It is the responsibility of the RERB Secretariat to receive the application for Exemption from Review (Form 16) submitted to the RERB.

The Chair is responsible for the assessment whether the submitted protocol qualifies for exemption from review.

2.5.4 Process Flow/Steps





2.5.5 Detailed Instructions

2.5.5.1 The Chair shall review and evaluate the study protocol applying for review exemption if the protocol meets the criteria for exemption. The exemption from review may be seen in following situations:

- Research on educational practices such as instructional strategies or effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods
  Exceptions:
  - When research on use of educational tests, survey or interview procedures, or observation of public behavior can identify the human participant directly or through identifiers, and the disclosure of information outside research could subject the participant to the risk of civil or criminal or financial liability or psychosocial harm
  - When interviews involve direct approach or access to private papers

- The research proposals which do not involve live human participants or data derived from them are exempt from ethics review. For example,
  - Audits of educational practices
  - Research on microbes cultured in the laboratory
  - Research on immortalized cell lines
  - Research on cadavers or death certificates provided such research reveals no identifying personal data
  - Analysis of data freely available in public domain

- In some circumstances research which appears to meet low risk criteria may need to be reviewed by the ERC. This might be because of requirements of:
  - The publisher of the research
  - An organization which is providing funding resources, existing data, access to participants etc.

2.5.5.2. Issue Certificate of Exemption (Form 17) or recommend for full board or expedited review

If the protocol and related documents satisfy the criteria as listed in above, a Certificate of Exemption from review will be prepared by the Secretariat and forward to the Chair for signing.

If the protocol does not meet the criteria for exemption, the protocol shall be recommended for full board or expedited review.

2.5.5.3. The secretariat shall prepare a report of all protocols exempted from review and this will be presented during full-board meeting.

2.5.5.4. The secretariat will communicate RERB decision to the principal investigator by preparing the Certificate of Exemption from Review duly signed and dated by the Chair and issues the certificate to the principal investigator.

2.5.5.5. The secretariat files copy of the documents in the protocol file binder and update protocol database for exemption from review.

2.6 Use of Study Assessment Forms

2.6.1. **Purpose**

To describe the procedures related to the use of study assessment forms in ethics review

2.2.2. **Scope**

This SOP applies to the use of the Study Assessment Forms in the review and assessment of protocols and related documents submitted to RERB for initial review and approval. The RERB uses two study assessment forms. The two assessment forms are accomplished by individual reviewers. Any comments, evaluation, recommendations and the initial decision of each reviewer regarding a protocol are all noted in these two forms.

The Study Assessment Forms are designed to standardize the review process and to facilitate reporting of recommendation and comments given to each individual protocol and related documents.

There are two (2) CGHMC RERB Assessment Forms for protocol review (see Appendix):

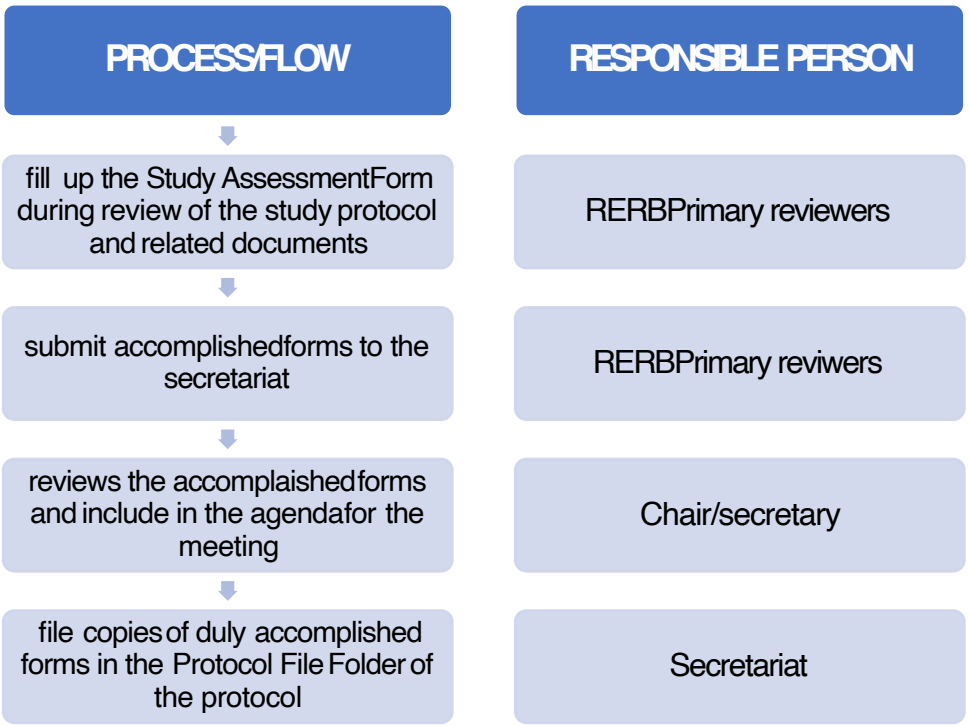
a. Protocol Evaluation Form (Form 8)
b. Informed Consent Evaluation Form (Form 9)

2.2.3. **Responsibility**

It is the responsibility of the RERB reviewers to individually fill up the assessment forms after reviewing each study protocol and submit to the secretariat.

The Secretariat is responsible for recording and filing the RERB action, relevant points and deliberation about a particular protocol, including the comments for specific action. The final decision of the Board will be reflected in the Minutes of the Meeting.

2.2.4. **Process Flow/Steps**



2.2.5 Detailed Instructions

2.2.5.1. The CGHMC RERB reviewer checks if the two study assessment forms (Protocol Evaluation Form and Informed Consent Evaluation Form) are attached with each protocol package received for review.

2.2.5.2. The RERB primary reviewers read the protocol and related documents and individually fill up both forms for each protocol. Complete all relevant items in the study assessment forms and make comments.

2.2.5.3. The primary medical reviewer accomplishes the Protocol Document Evaluation Form and Informed Consent Evaluation Form while the primary non-medical reviewer focuses on the ICF only.

2.2.5.4. The study Protocol Evaluation Forms ensure assessment of the scientific and ethical aspects of the protocol.

- Rationale and significance of the study
- Objectives of the study
- Review of literature
- Sample size
- Methodology and data management
- Inclusion/exclusion criteria
- Control arms (placebo, if any)
- Withdrawal or discontinuation criteria
- Vulnerability determination
- Risk/benefit assessment
- Full disclosure of information, including risks
- Benefits and risks that may be derived from the study
- Use of understandable language
- Voluntary participation
- Remuneration
- Confidentiality
- Legally Authorized representative to sign the consent form
- Contact details of RERB Chair and office for ethical concerns and those of the principal proponent and his/her team for protocol related issues

2.2.5.5. The primary reviewer signs and submits the evaluation forms together with the reviewed protocol back to the Secretariat.

2.2.5.6. The Secretariat checks whether the forms are complete, compiles the assessment forms and submits these to the Member-Secretary and/or Chair.

2.2.5.7. The member-Secretary and/or Chair reviews the complied assessment forms and includes the recommendation and action of the primary reviewers and include them in the agenda in the next full board meeting.

2.2.5.8 The Secretariat files the accomplished forms in the Protocol File Folder of the protocol

2.6. Review of a Medical Device Protocol

2.6.1 Purpose

To describe procedures in the review of medical device protocols submitted to the RERB

2.6.2. Scope

This SOP provides instructions for review and approval of medical device protocols intended for human participants submitted to the RERB.

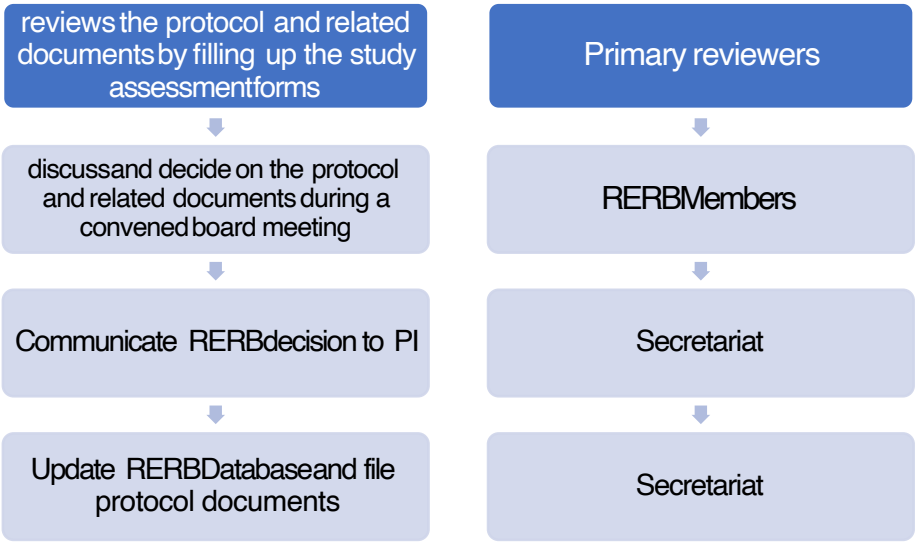
2.6.3. Medical device protocols are reviewed through the same expedited or full board procedures depending on the level of risks involved in the study. An investigational new device is given a Significant Risk (SR) or Non Significant Risk (NSR) classification by the regulators in the sponsor country. This information should be provided by the sponsor to the RERB. The RERB should make provisions to minimize the risks to human participants during review of the protocol and related documents.

2.6.4. Responsibility

It is the responsibility of the RERB members to review medical device protocols in accordance with international and national guidelines and regulations.

2.6.5. Process Flow/Steps

PROCESS/FLOW	RESPONSIBLE PERSON
receipt and management of protocol submission	Secretariat
determine type of review and assign appropriate primary reviewers	RERB Chair



2.6.6. Detailed Instructions

2.6.6.1. The same procedures are followed when the protocol is submitted for initial review. When reviewing a medical device protocol, the reviewer should consider the following:

- Proposed investigational plan
- Informed consent form
- Description of the device/Product information
- Description of study participant selection criteria
- Safety monitoring procedures
- Reports of prior investigations conducted with the device
- Principal investigator's curriculum vitae
- Risk assessment determination for new investigational device (Significant Risk or Non Significant Risk)
- Statistical plan and analysis
- Copies of all labeling for investigational use

2.6.6.2. The Secretariat checks the information/communication from the principal investigator related to the Significant Risk (SR) or Non Significant Risk (NSR) determination by regulators (FDA) from the sponsor country. The protocol is assigned to expedited or full board review depending on the risk assessment.

2.6.6.3. Primary reviewers with appropriate expertise are assigned to review the protocol related documents. It is advisable that a bioengineer with appropriate experience related to the medical device together with a medical doctor with related clinical experience are assigned to review the protocol while a lay person/ non medical member reviews the consent form.

2.6.6.4 The same RERB assessment forms are used for review and the primary reviewers make a decision in expedited review or make a recommendation for discussion during the next full board meeting.

2.6.6.5. For full board review, a decision is made after discussion. If the protocols are for revision, they are sent back to the principal investigator for modification. The documents are resubmitted and reviewed through expedited channel for minor revision and sent to full board for review of major revisions.

2.6.6.6. Once an approval decision is reached, the approval letter is prepared, signed by the Chair and communicated to the principal investigator. The frequency of continuing review is indicated in the approval letter.

2.6.6.7. The relevant documents are kept in the protocol file and the RERB entry about the protocol is updated.

2.8 Review of Resubmitted protocols

2.8.1 Purpose

To describe the review procedures of the CGHMC RERB in relation to resubmission of protocols with revisions after initial review.

2.8.2. Scope

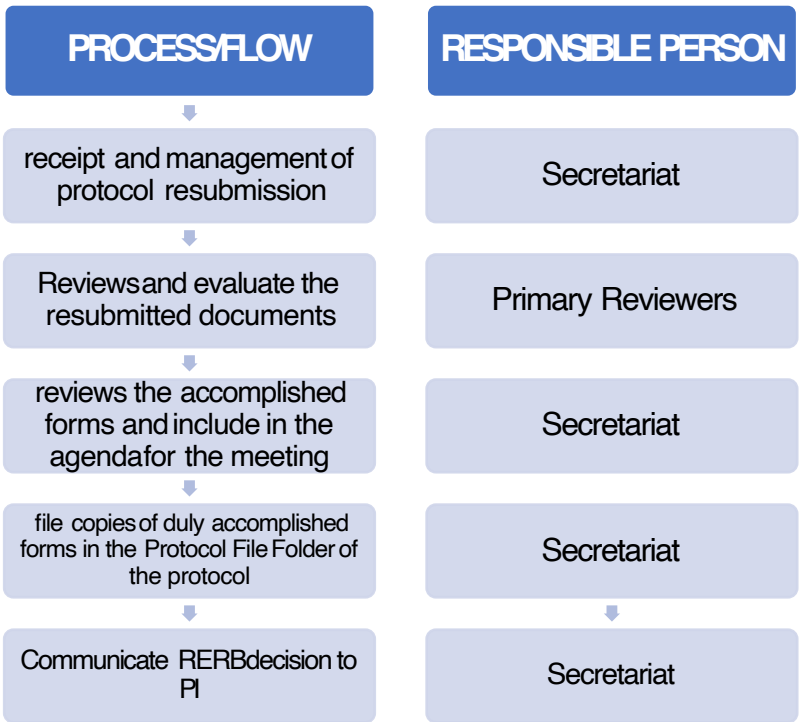
This SOP applies to the study protocols submitted by investigators and sponsors that have been reviewed earlier with recommendations for revisions in the initial review process.

2.8.3. Responsibilities

It is the responsibility of the RERB Secretariat to receive the resubmitted protocol package (Form 12) submitted to the RERB.

It is the responsibility of the board members or designated members to make appropriate recommendations/actions related to the resubmitted protocol

2.8.4. Process Flow/Steps



2.8.5 **Detailed Instructions**

2.8.5.1. The secretariat receives the resubmitted protocol package and checks the completeness of the resubmitted protocol package

- resubmitted protocol form (Form 12) addressing the revisions
- revised version of the protocol and related documents
- revisions made to the documents should be highlighted or underlined

2.8.5.2. The secretariat notifies the Chair of a resubmitted protocol package

2.8.5.3. The Chair determines how resubmitted protocol package be managed

Protocol with minor revisions may pass through expedited review

Protocol with major revisions shall pass through another review

- the primary reviewers/ secretary will present the protocol and the major revisions
- the RERB shall deliberate on the revision and decide by majority vote as **APPROVED, MINOR REVISIONS, OR DISAPPROVED**

2.8.5.4. Written communication of the decision

The secretariat notifies the principal investigator of the decision of the RERB through hard copy

If the RERB requires revisions of any of the documents, the secretariat sends a written request of the specific revisions to the investigator to make the necessary changes and resubmit the documents to the RERB

2.9. Withdrawal of Study Protocol Submission

2.9.1. Purpose

To describe the RERB procedures related to withdrawal of study protocol submission

3.8.2. Scope

This procedure describes how the RERB proceeds and manages the withdrawal of study protocol submission

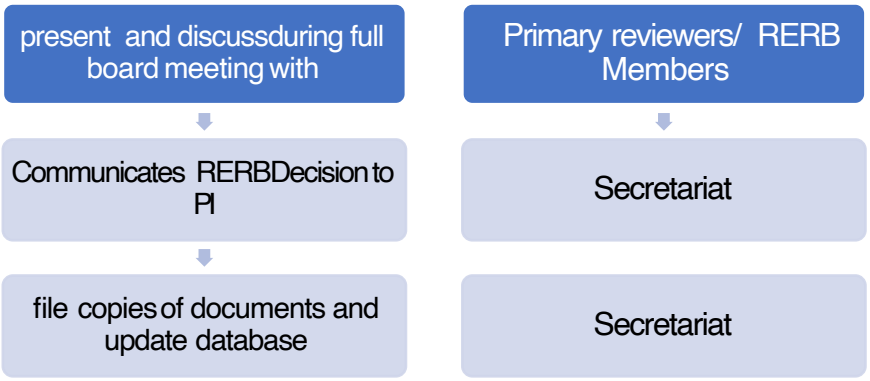
3.8.3. Responsibility

It is the responsibility of the RERB to act on any withdrawal of study protocol submission application. All applications are reviewed during full board meeting to decide on appropriate action.

The Secretariat is responsible for the receipt and management of the withdrawal of study protocol submission application and documents (Form 13). The primary reviewers review the reasons for the withdrawal and make a recommendation to full board.

3.8.4. Process Flow/Steps

PROCESS/FLOW	RESPONSIBLE PERSON
receipt and management of protocol withdrawal submission	Secretariat
forward application to Primary reviewers for evaluation	Secretariat
review the withdrawal application and make appropriate actions	RERB Primary Reviewers



3.8.5. Detailed Instructions

3.8.5.1. RERB Secretariat

- Receives application of withdrawal for study protocol submission (Form 13).
- Receives the study protocol termination package prepared and submitted by the principal investigator.
- Checks the completeness of the contents of the package to include the application for withdrawal of protocol submission. The request for the withdrawal should contain a brief written summary of the reason for the withdrawal of the protocol submission

3.8.5.2. RERB Primary reviewers review and evaluates the reason for the withdrawal of the protocol submission and make appropriate action
Discusses during full board meeting on appropriate decision.

The RERB deliberates on the reason for the withdrawal of protocol submission.
Final decision of the application are as follows:
APPROVAL/ NO FURTHER ACTION
FURTHER INFORMATION REQUIRED/ CLARIFICATION FROM PI

3.8.5.3. Communicates the RERB decision to PI

3.7.5.4.1. The RERB secretariat prepares letter of notification signed and dated by the Chair.

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, 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 withdrawal of protocol submission 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- protocol withdrawal."

2.10. Assent Evaluation for Researches involving Minors

2.10.1 Purpose

To describe the procedures related to assent evaluation forms for researches involving Minors

2.10.2. Scope

This SOP applies to the assent forms submitted by PI in researches involving minors until the evaluation of these forms by the primary reviewers.

"Minors" refers to persons under 18 years of age and the term may be used interchangeably with the term "children".

Age of majority, placed at 18 years of age based on RA No. 6809 is the age the person is emancipated from parental authority, and is considered "qualified and responsible for all acts of civil life", and can enter into contracts on their own, or sign the ICF.

In pediatric practice (by the Philippine Pediatric Society) however, pediatric age group is under 19 years of age, in which case, in pediatric research, some participants can already sign the ICF without requiring parental consent.

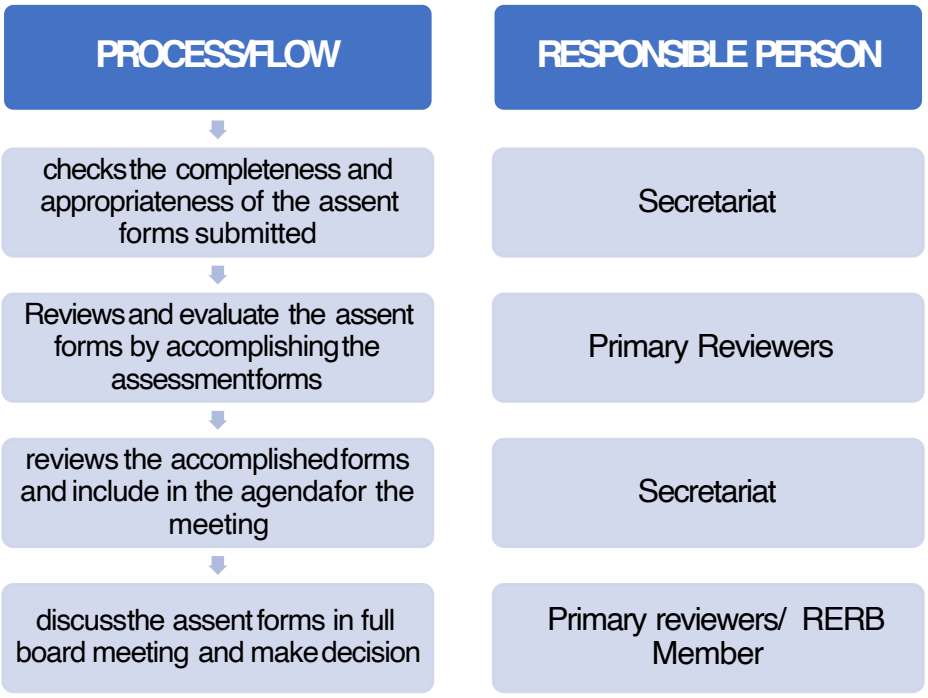
2.10.3. Responsibility

It is the responsibility of the PI to submit appropriate assent forms in their protocol package.

The Secretariat is responsible for receiving and checking the completeness and appropriateness of the assent forms submitted and also forwarding these forms together with the protocol package to the primary reviewers for evaluation.

It is the responsibility of the primary reviewers to read and evaluate the assent forma submitted and make recommendation during full board meeting.

2.10.4. Flow Chart/ Process



2.10.5. Detailed Instructions

The CGHMC RERB is guided in its review by Guideline 17 "Research Involving Children and Adolescents" of the International Guidelines for Biomedical Research (CIOMS, 2016) in research protocols involving children.

For minors or children, additional informed consent forms are required such as Assent Forms, and participants legally authorized representative (LAR). Assent is the manifestation of the agreement of a minor to participate in a research or clinical trial. The assent may be in oral or written form.

2.10.5.1. The PI before undertaking the research involving children must ensure that:

- The research might not equally well be carried out in adults.
- The purpose of the research is to obtain knowledge relevant to the needs of children.

- A parent or legal representative of the child has given permission.
- The agreement (assent) of the children has been obtain to the extent of the child's capabilities.
- A refusal of the child to participate or continue in the research will be respected.

2.10.5.2 Requirement for permission from a legally authorized representative (LAR)

2.10.5.2.1. A parent or legally authorized representative (LAR) of each child shall provide the necessary consent for participation of the minor.
In default of parents or judicially declared guardians, this order of authority shall be followed:
- Grandparents
- Oldest sibling over 21 years of age, unless unfit or disqualified
- Actual custodian over 21 years of age, unless unfit or disqualified

2.10.5.2.2. Where the parents are both minors or incapacitated to enter contracts, or give consent to their child's participation in the research, the guidelines on medical treatment of such a child may be followed whereby a third party may give the consent (i.e., the child's grandparents, physician, or the hospital administrator, as in emergency cases).

2.10.5.2.3. Requirement for assent
Aside from the informed consent being required from LARs, assent from minors must also be obtained. Thus, the protocol must include the procedure for obtaining the minor's assent and this assent must be obtained without coercion.

2.10.5.2.4. At any age, any sign of dissent shall be observed, and children who dissent must not be recruited to the study.

2.10.5.2.5. The manner and form by which a minor provides his or her assent shall be as follows:

- Minors under 7 years of age: No formal assent, verbal or written, unless there is manifestation of dissent

- Minors 7 years of age - under 12 years of age: Verbal assent is acceptable, but there must be documentation of the verbal assent. Documentation may be in the form of a written description of the process and witnessed.

- Minors 12 – 15 years of age: Shall sign a simplified Assent Form that is different from the ICF which the parents or guardians sign.

- Minors 15 -18 years of age: Can sign on the same ICF document signed by the parents.

- If children reach the age of maturity during the research, their consent to continue participation should be obtained.

2.10.5.3. Review and evaluation of assent forms submitted CGHMC RERB must have at least one member who is a pediatrician to review a pediatric research.