SOP 4 REVIEW PROCEDURES

Supersedes:	Version 04.1 dated 17 May 2019
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Approval Date:	31 October 2021

4. Review Procedures

4.1 Expedited Review
4.2 Full Committee Review
4.3 Exempt from Review
4.4 Review of Resubmission

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SOP 4.1 EXPEDITED REVIEW

1. Objective of the Activity

To describe the MDMRCI-ARMCI CRERC procedure for the review of protocols that qualify for expedited review *to ensure compliance with technical and ethical standards in the conduct of minimal risk study protocols thereby protecting the safety, rights and welfare of study participants and the integrity of research data.*

2. Scope

*This SOP applies to initial review and resubmissions, and post-approval submissions on protocols that have been classified as not involving more than minimal risk to study participants, or where the participants do not belong to vulnerable groups, or when study situation does not generate vulnerability to participants. This also applies to review of **a**) resubmission when the initial review was expedited, **b**) resubmission when the initial review was by Full Committee but CRERC-recommended revisions are minor, **c)** minor protocol amendment, **d)** progress/annual report when the initial review was expedited, and **e)** final report when the initial review was expedited.*

This SOP begins with the assignment of Primary Reviewers and Independent Consultant, if CRERC does not have the expertise given the nature of the protocol to be reviewed, and ends with the inclusion of approved protocols reviewed by expedited procedure in the agenda of the next meeting.

3. Responsibilities

The CRERC Chair or the Member-Secretary (if the former has conflict of interest) designates the Primary Reviewers and selects the Independent Consultant if CRERC does not have the required expertise given the nature of the study protocol.

The CRERC Member-Secretary reviews the assessment forms and checks for any disagreement in the recommendations and review decisions of the primary reviewers, and integrates the recommendations.

The medical/scientific Primary Reviewer reviews both the study protocol and the informed consent and/or assent forms while the lay person focuses on the recruitment procedure, informed consent and/or assent forms and informed consent process.

*The Administrative Secretary is responsible for: **a)** identifying and notifying the Primary Reviewers and Independent Consultant (if any) using Form 4.1 Request for Review for protocols for initial review, **b**) preparing Form 4.2 Notice of Review to the Researcher/PI of protocols for initial review, **c)** collating the recommendations of the Primary Reviewers and forwarding this to the Member-Secretary for review and finalization, **d)** preparing the communication to convey to the Researcher/PI the review decision of the CRERC using appropriate form, **e)** filing the documents in the protocol file folder, updating the protocol file index, and the e-protocol database, and **f)** identifying the submissions reviewed and approved by expedited review for inclusion in the meeting agenda of the upcoming meeting*.

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4. Workflow

No.	Activities	Person/s Responsible
1	Assign Primary Reviewers	CRERC Chair or Member-Secretary
2	Notify Primary Reviewers and Independent Consultant and send the protocol package to be reviewed	Administrative Secretary
3	Review the documents with the use of the assessment forms	Primary Reviewers
4	Review and collate the comments and recommendations in the assessment forms	Administrative Secretary, Member-Secretary
5	Communicate the CRERC decision to the Researcher/Principal Investigator (PI)	Administrative Secretary
6	File the protocol/protocol-related documents in the protocol file folder, and update the protocol file index and the protocol database	Administrative Secretary
7	Include protocols and protocol-related submissions approved by expedited review in the meeting agenda	Administrative Secretary

5. Detailed Instructions

5.1 Assign Primary Reviewers and Independent Consultant, if necessary

5.1.1 The Chair (or the Member-Secretary if the former has COI) assigns Primary Reviewers to do the review. For submissions with informed consent/assent, two Primary Reviewers are designated – a medical or scientific reviewer to review both the protocol and informed consent and/or assent, and a layperson to focus on the informed consent and/or assent and the informed consent process. The medical/scientific reviewer is responsible for the assessment of technical soundness and related ethical issues

For protocols that do not require informed consent/assent, resubmissions that do not involve revisions of the informed consent/assent, or minor protocol amendment only one medical or scientific reviewer is required.

5.1.2 If the CRERC does not have the necessary expertise required by the nature of the protocol to be reviewed, an Independent Consultant is selected by the Chair to assist the Primary Reviewer/s in the assessment of the submission. (Refer to SOP 2.2 – Selection and Appointment of Independent Consultants)

5.1.3 For initial review, the Administrative Secretary sends Form 4.1 Request for Review to the Primary Reviewers and Independent Consultant and follows up the return of said form to CRERC with their signed "conforme".

5.1.4 If the chosen Primary Reviewer/s is/are not available to do the initial review, the Chair/Member-Secretary is informed who will then designate other CRERC Member/s to do the review.

5.1.5 For review of resubmission and post-approval reviews, if the Primary Reviewer/s is/are not available the Chair/Member-Secretary may do the review.

5.2 Notify Primary Reviewers and Independent Consultant and send the protocol package to be reviewed

5.2.1 When the designated CRERC Members agree to do the review, the Administrative Secretary prepares the protocol/protocol related document package for review and the appropriate assessment form/s

5.2.2 The Administrative Secretary records the document package in the CRERC Form 9.2 Log of Outgoing Protocol Related Communications and forwards it to the Primary Reviewer/s and the Independent Consultant (if necessary) within seven (7) calendar days from the receipt of the document/s for review.

5.2.3 The Administrative Secretary prepares Form 4.2 Notification of CRERC Review to the Researcher/Principal Investigator (PI) to inform the latter on the initial review status of the protocol - the assigned CRERC Protocol No., and the type of review.

5.3 Review the documents with the use of the assessment forms:

5.3.1 The Primary Reviewer/s and the Independent Consultant complete the review using:

a) for the initial review: CRERC Form 4.3 Protocol Assessment Checklist and Form 4.4 Informed Consent Assessment Checklist (if the study protocol has an Informed Consent/Assent Form)
*Review decision can be anyone of the following: **i**) approval, **ii)** major revision, **iii)** minor revision, **iv)** disapproval and **v)** pending, for clarification*

*b) for resubmission: third column of Form 4.6 Protocol Resubmission Review decision can be anyone of the following: **i)** approval, **ii)** major revision, **iii)** minor revision, **iv)** disapproval, and **v)** pending, for clarification. (Refer to SOP 4.4 Review of Resubmission)*

c) for minor protocol amendment: CRERC Form 7.1 Application for Protocol Amendment (Box for CRERC Use) Review decision can be anyone of the following:
***i)** approval, **ii)** revision, **iii)** disapproval, and **iv)** pending, for clarification (Refer to SOP 7.1 Review of Protocol Amendment)*

d) for Progress/Annual Report when initial review is expedited review: CRERC Form 7.3 Progress/Annual Report (Box for CRERC Use) Review decision can be anyone of the following:
i) Renew approval
ii) Revise
iii) Request further information, specify
iv) Suspend:
- *enrollment of new subjects*
- *research procedures in currently enrolled subjects*
- *entire study*

v) Disapprove renewal
(Refer to SOP 7.2 Review of Progress/Annual Report)

*e) for final report when initial review is expedited review: CRERC Form 7.4 Final Report (Box for CRERC Use) Review decision can be anyone of the following: **i)** accepted, **ii)** revise, and **iii)** require action from the Researcher, iv) pending, for clarification (Refer to SOP 7.3 Review of Final Report)*

The review decision is major revision when the recommended revisions involve any of the following: study objectives, study design, recruitment of participants, exclusion/inclusion criteria, method of data collection, statistical analysis, mitigation of risks, protection of vulnerability, or other changes that impact on the potential risks to participants and on the integrity of the research data.

The review decision is minor revision when the recommended revisions of the study or related documents do not impact on potential risks to the participants and on the integrity of the research data, e.g. incomplete IC elements, use of appropriate words/phrase or improvement in sentence construction in the translation of English ICF to the local dialect, unsatisfactory IC format, or increase in reimbursable travel expenses per study visit.

5.3.2 *In addition to the review elements described in CRERC Form 4.3 Protocol Assessment and CRERC Form 4.4 Informed Consent Assessment, the primary reviewers should ensure that the study protocol comply with existing international and national guidelines and policies including, but not limited to the 2017 National Ethical Guidelines for Health and Health-related Research, and Data Privacy Act of 2012.*

*5.3.3 For research involving children and adolescents, the primary reviewers should ensure study protocol's compliance with the International Ethical Guidelines for Health and Health-related Research Involving Humans 2016, Guideline 17 such as in **(a)** obtaining consent for their continued participation if participants reach the legal age of maturity during the research, **(b)** special parental authority, **(c)** deliberate objection of children and adolescents who are too immature to give assent, or **(d)** observation of the study by a parent or guardian.*

5.3.4 The primary reviewers assess the competence of the Researchers/PIs by taking into consideration not only their scientific qualifications but also the number of other ongoing studies they have. Check the CV of the Researcher/Principal Investigator and other members of the Research Team. In an intervention study, ensure that they all have valid GCP Training.

5.3.5 *After the assessment is completed the Primary Reviewer/s and the Independent Consultant (if any) return all the documents including the completed assessment form/s to the CRERC within 7 calendar days from the date of their receipt of the protocol/protocol related documents.*

5.4 Review and collate the comments and recommendations in the assessment forms

5.4.1 The Administrative Secretary reviews the completed assessment forms to determine if there is agreement in the review decisions. The comments and decisions are consolidated using the appropriate form, (Refer to SOP 8.2 – Communicating CRERC Decision) and forwarded by e-mail to the Member-Secretary including the completed assessment forms of the Primary Reviewers. The Member-Secretary reviews and finalizes the list of recommendations.

5.4.2 If there are conflicting recommendations and/or disagreement in the review decisions between the Primary Reviewers, or between the Primary Reviewers and the Independent Consultant, or when the protocol is disapproved, the protocol is referred to the Full Committee for deliberation and decision. The Administrative Secretary includes the protocol in the Meeting Agenda of the upcoming Full Committee meeting.

5.5 Communicate the CRERC decision to the Researcher/Principal Investigator

5.5.1 The Administrative Secretary prepares the communication of CRERC decision to the Researcher/PI using the appropriate form within five (5) calendar days from the receipt of the results of the expedited review. (Refer to SOP 8.2 Communicating CRERC Decision)

5.6 File the protocol/protocol-related documents in the protocol file folder, and update the protocol file index and the protocol database

5.6.1 The Administrative Secretary adds the submissions and their corresponding completed assessment forms, duplicate copy of the Notification of CRERC Decision/Approval Letter to the protocol file folder and updates the protocol file index and the protocol data base accordingly. (Refer to the SOP 9.1 Management of Active Study Protocol Files)

5.7 Include protocols and protocol-related submissions approved by expedited review in the meeting agenda

5.7.1 The Administrative Secretary prepares a list of protocols approved by expedited review, and the Chair/Member Secretary reports them during the Full Committee meeting. This report is included in both the Meeting Agenda and the Minutes of the Meeting. (Refer to SOP 6.1 Preparation for CRERC Meeting Agenda and SOP 8.1 Preparation of Minutes of the Meeting)

6. Related Forms

CRERC Form 4.1 Request for Review (Primary Reviewer)
CRERC Form 4.2 Notice of CRERC Review (to the Researcher/PI)
CRERC Form 4.3 Protocol Assessment Checklist
CRERC Form 4.4 Informed Consent Assessment Checklist
CRERC Form 7.1 Application for Protocol Amendment
CRERC Form 7.3 Progress/Annual Report
CRERC Form 7.4 Final Report
CRERC Form 9.2 *Log of Outgoing Protocol Related Communications*

7. SOP Document History

Version No.	Version Date	Description of Changes
01	23 Jan 2015	Refer to SOP v. 01
02	21 May 2015	Refer to SOP v. 02
03	05 Feb 2016	Refer to SOP v. 03
04.1	17 May 2019	Refer to SOP v. 04.1
05	31 Oct 2021	▪ Changed Purpose to Objective, and Process Flow/Steps to Workflow to harmonize with PHREB's section titles. ▪ Changed the section on Scope, - included a description of submissions for expedited review, and the start and end tasks of the SOP ▪ Added the detailed responsibilities of the CRERC Chair, Member-Secretary, Primary Reviewers and those of the Administrative Secretary ▪ Removed Task #1 in version 4.0– "Determine that the submission qualifies for expedited review". This task is included in SOP 3.0 – Management of Submission. ▪ Added 5.1.2 – the possibility of calling in an Independent Consultant to assist in the review, and

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		5.1.3 - the possibility that the initially assigned Primary Reviewer/s may not be available and other CRERC members are then designated as reviewers. ▪ Added the assessment form to use (in 5.3.1 in current version), and categories of review decision appropriate to the kind of documents being reviewed; and other ethical assessment points to consider in the review (in 5.3.2, 5.3.3 & 5.3.4) ▪ Removed Task #5 in version 4.0 – "Return the accomplished assessment forms to the Secretariat". This task incorporated in Task #3 of the current version. ▪ Modify task #6 in version 4.0 – The Administrative Secretary collates the recommendations of the primary Reviewers and forwards this to the Member-Secretary who reviews and finalizes the communication of CRERC decision to the Researcher/PI ▪ Added timelines – from date of receipt of submission to forwarding of protocol/protocol related document to be reviewed to the Primary Reviewer/s; date of receipt of documents for review by the Primary Reviewers to the return of the completed assessment form to CRERC ▪ Cross-reference tasks in Detailed Instructions to related SOP ▪ Introduced new forms - CREC Form 4.1 Request for Review (for Primary Reviewer), CRERC Form 4.2 Notice of Review to PI, and CRERC Form 9.2 Log of *Outgoing Protocol Related Communications* ▪ Used Administrative Secretary instead of CRERC Secretariat where appropriate

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SOP 4.2 FULL COMMITTEE REVIEW

1. Objective of the Activity

To describe the MDMRCI-ARMCI CRERC procedure for the review of protocols that qualify for Full Committee review *to ensure compliance with technical and ethical standards in the conduct of more than minimal risk study protocols thereby protecting the safety, rights and welfare of study participants and the integrity of research data*.

2. Scope

This SOP applies to initial and post-approval submissions of protocols that are classified as more than minimal risk to study participants or involve study participants who belong to the vulnerable groups or whose study situation generates vulnerability to them. This also applies to review of: ***a)*** *resubmission when CRERC decision was major revision for protocol that was initially reviewed by Full Committee,* ***b)*** *major protocol amendment,* ***c)*** *Annual/Progress Report when the initial review was Full Committee review,* ***d)*** *Final Report when the initial review was Full Committee review,* ***e)*** *Early Termination Report,* ***f)*** *Protocol Violation Report,* ***g)*** *on-site SAE report,* ***h)*** *Study Site Visit Report, and* ***i)*** *complaints from study participant.*

This SOP begins with the assignment of Primary Reviewers and Independent Consultant, if CRERC does not have the have the expertise given the nature of the protocol to be reviewed and ends with the filing of the protocol or protocol-related documents in the protocol file folder, and updating the protocol file index, and protocol database.

3. Responsibilities

The CRERC Chair or the Member-Secretary (if the former has conflict of interest) designates the Primary Reviewers and selects the Independent Consultant if CRERC does not have the required expertise given the nature of the study.

The Administrative Secretary is responsible for: ***a)*** *informing the CRERC Chair and Member-Secretary of the submission;* ***b)*** *identifying and notifying the Primary Reviewers and Independent Consultant (if any) using CRERC Form 4.1 Request for Review for protocols for initial review, and sending the protocol package to be reviewed to them;* ***c)*** *preparing the communication to the Researcher/PI to inform him/her of the schedule of the Full Committee initial review of his/her protocol using CRERC Form 4.2 Notification of CRERC Review;* ***d)*** *reminding the Primary Reviewers and Independent Consultant (if any) three (3) calendar days before the due date for the submission to CRERC of the results of their assessment;* ***e)*** *preparing the communication of CRERC decision to the Researcher/PI; and* ***f)*** *filing the protocol or protocol-related documents in the protocol file folder, and updating the protocol file index and the protocol database*.

4. Workflow

No.	Activities	Person/s Responsible
1	Assign Primary Reviewers and Independent Consultant, if necessary	CRERC Chair or Member-Secretary
2	Notify Primary Reviewers and Independent	Administrative Secretary

	Consultant, and send the protocol package to be reviewed	
3	Review the documents with the use of the assessment forms	Primary Reviewers, Independent Consultant
4	Discuss and deliberate on the protocol and related documents during a Full Committee meeting	CRERC Members
5	Communicate the CRERC decision to the Researcher/Principal Investigator (PI)	Admin Secretary, Member-Secretary, Chair
6	File the protocol or protocol-related documents in the protocol file folder, and update the protocol file index and protocol database	Administrative Secretary

5. Detailed Instructions

5.1 Assign Primary Reviewers and Independent Consultant, if necessary

5.1.1 The Chair or the Member-Secretary if the former has COI assigns Primary Reviewers to do the review. For submissions with informed consent/assent, two Primary Reviewers are designated – a medical/scientific reviewer to review both the protocol and informed consent/assent, and a layperson to focus on the informed consent/assent and the informed consent process. The medical/scientific reviewer is responsible for the assessment of technical soundness and related ethical issues.

For protocols that do not require an informed consent/assent, resubmissions or major protocol amendment that do not involve revisions of the informed consent/assent, Progress/Annual report, Closure/Final Report only one medical or scientific reviewer is required.

5.1.2 If the CRERC does not have the necessary expertise required by the nature of the protocol to be reviewed, an Independent Consultant is selected by the Chair to assist the Primary Reviewer/s in the assessment of the submission. (Refer to SOP 2.2 – Selection and Appointment of Independent Consultants)

5.1.3 For initial review, the Administrative Secretary sends Form 4.1 Request for Review to the Primary Reviewers and Independent Consultant and follows up the return of said form to CRERC with their signed "conforme".

5.1.4 If the chosen Primary Reviewer/s is/are not available to do the initial review, the Chair/Member-Secretary is informed who will then designate other CRERC Member/s to do the review.

5.1.5 For review of resubmission and post-approval reviews, if the Primary Reviewer/s is/are not available the Chair/Member-Secretary will do the review.

5.2 Notify Primary Reviewers and Independent Consultant (if any), and send the protocol package to be reviewed

5.2.1 When the designated CRERC Members agree to do the review, the Administrative Secretary prepares the protocol/protocol related document package for review and the appropriate assessment form/s.

5.2.2 The Administrative Secretary records the document package in CRERC Form 9.2 Log of Outgoing Protocol Related Communications, and forwards

to the Primary Reviewer/s and the Independent Consultant (if necessary) within seven (7) calendar days from the receipt of the document/s for review.

5.2.3 *For protocol submission for initial review, the Administrative Secretary prepares CRERC Form 4.2 Notification of CRERC Review to the Researcher/PI to inform the latter on the review status of the protocol - the assigned CRERC Protocol No., type of review, and date of Full Committee meeting in which the study protocol will be reviewed.*

5.3 Review the documents with the use of the assessment forms

5.3.1 *The Primary Reviewer/s and the Independent Consultant complete the review using:*

a) for Initial Review: CRERC Form 4.3 Protocol Assessment Checklist and CRERC Form 4.4 Informed Consent Assessment Checklist
Review decision can be any one of the following:
i) *Approval (when no further modification is required)*
ii) *Minor revision*
Revision is said to be minor when the recommended revision of the study or related documents do not impact on potential risks to the participants and on the integrity of the research data, e.g. incomplete informed consent (IC) elements, use of inappropriate words/phrase or improvement in sentence construction in the translation of English ICF to the local dialect, unsatisfactory IC format, or when allowable reimbursable travel expenses per study visit is inadequate. Resubmission is *subject to expedited review by the Primary Reviewer/s.*
iii) *Major revision*
Revision is said to be major when the recommended revision of significant aspects of the study involves any of the following: study objectives, recruitment of participants, exclusion or inclusion criteria, collection of data, statistical analysis, mitigation of risks, protection of vulnerability, etc. that impact on potential risks/harms to participants and on the integrity of the research data. Resubmission is subject to Full Committee review.
iv) *Disapproval* (due to ethical or legal concerns) Reasons for vote of disapproval should be noted in the minutes and communicated to the Researcher/PI.

b) for Resubmission: CRERC Form 4.6 Protocol Resubmission Form *(third column) Review decision can be any one of the following:*
i) Approval
ii) Minor revision
Another resubmission is subject to expedited review by the Primary Reviewer/s.
iii) Major revision
Another resubmission is subject to Full Committee review.
iv) Disapproval
Reasons for vote of disapproval should be noted in the minutes and communicated to the Researcher/PI.
v) pending, for clarification
(Refer to SOP 4.4 Review of Resubmission)

c) for major Protocol Amendment: CRERC Form 7.1 Protocol Amendment (Box for CRERC Use) Review decision can be any one of the following:
i) Approval
ii) Minor revision

Resubmission is subject to expedited review by the Primary Reviewer/s

iii) Major revision
Resubmission is subject to review by Full Committee
iv) Disapproval
v) Pending, for clarification
(Refer to SOP 7.1 Review of Protocol Amendment)

d) *<u>for Progress/Annual Report</u> of the study protocol that was initially reviewed by Full Committee review: CRERC Form 7.3 Progress/Annual Report (Box for CRERC Use) Review decision can be anyone of the following:*
i) Renew approval
ii) Revise
iii) Request further information
iv) Suspend:
- *enrollment of new subjects*
- *research procedures in currently enrolled subjects*
- *entire study*

v) Disapprove renewal
(Refer to SOP 7.2 – Review of Progress/Annual Report)

e) *<u>for Final/Closure Report</u> of the study protocol that was initially reviewed by Full Committee review:* CRERC Form 7.4 Final Report (Box for CRERC Use) *Review decision can be anyone of the following:*
i) Accepted
ii) Request for further information
iii) Require action from the Researcher/Principal Investigator
iv) Others, specify.
(Refer to SOP 7.3 Review of Final Report)

f) *<u>for on-site SAE Report</u>:* CRERC Form 7.5 Onsite Serious Adverse Event *Report (*Box for CRERC Use*) Review decision can be anyone of the following:*
i) Request an amendment to the protocol or informed consent form
ii) Request further information, specify
iii) Suspend:
- *enrollment of new research participants until further review by the CRERC*
- *all trial-related procedures (except those intended for the safety and well-being of the participants) until further review by the CRERC*

iv) Terminate the study
v) Take note and continue monitoring
vi) Conduct study site visit
(Refer to SOP 7.4 Review of SAE Report)

g) *<u>for Protocol Violation/Deviation Report</u>:* CRERC Form 7.6 Protocol Violation/Deviation Report (Box for CRERC Use) *Review decision can be anyone of the following:*
i) Take note and continue monitoring
ii) Request further information
iii) Suspend:
- *enrollment of new research participants until further review by the CRERC*

- *all trial-related procedures (except those intended for the safety and well-being of the participants) until further review by the CRERC*

iv) Require correction and/or corrective actions
iv) Conduct study site visit
(Refer to SOP 7.5 Review of Protocol Violation/Deviation Report)

h) for Early Study Termination: CRERC Form 7.7 Early Study Termination (Box for CRERC Use) *Review decision can be anyone of the following:*
i) Approve
ii) Request for further information
iii) Request for action from PI
(Refer to SOP 7.6 Review of the Early Termination of Study Report)

5.3.2 *In addition to the review elements described in CRERC Form 4.3 Protocol Assessment and CRERC Form 4.4 Informed Consent Assessment, the primary reviewers should ensure that the study protocol comply with international and national guidelines and policies including, but not limited to, the 2017 National Ethical Guidelines for Health and Health-related Research and Data Privacy Act of 2012.*

5.3.3 *For research involving children and adolescents, the primary reviewers should ensure study protocol compliance with the International Ethical Guidelines for Health and Health-related Research Involving Humans 2016, Guideline 17 such as in (1) obtaining consent for their continued participation if participants reach the legal age of maturity during the research, (2) special parental authority, (3) deliberate objection of children and adolescents who are too immature to give assent, or (4) observation of the study by a parent or guardian.*

5.3.4 *The primary reviewers assess the competence of the Researchers/Principal Investigators by taking into consideration not only their scientific qualifications but also the number of other ongoing studies they have.* They must check the CV of the Researcher/Principal Investigator and other members of the Research Team as well as their disclosure or declaration of conflict of interest. In an intervention study, a valid GCP Training is required.

5.3.5 Review the appropriateness of the sites where the study will be conducted.

5.3.6 After the assessment is completed the Primary Reviewer/s and the Independent Consultant (if any) return all the documents including the completed assessment form/s to the CRERC *at least seven (7) calendar days before the date of the Full Committee meeting.*

5.3.7 The Administrative Secretary reminds the Primary Reviewer/s and the Independent Consultant (if any) to submit their assessment report three (3) calendar days before their due date, and then checks completeness of the assessment forms.

5.3.8 The Administrative Secretary includes the protocol in the agenda of the upcoming Full Committee meeting.

5.4 Discuss and deliberate on the protocol and related documents during a Full Committee meeting

5.4.1 Deliberate on the technical and ethical merits of the protocol or protocol-related documents during a Full Committee meeting. (Refer to SOP 6.2 Conduct of CRERC Review Meeting).

5.4.2 The members of the CRERC attending the Full Committee meeting must approve the following:

i) Competence of Principal and Co-Investigators (if any) and members of the Research Team
ii) Protocol
iii) Informed Consent Form/s
iv) Advertisements or recruitment materials
v) Study sites covered by the application

5.4.3 The CRERC members vote on specific items to arrive at a decision. (Refer to 5.3.1 above for possible review decisions depending on the kind of documents reviewed.)

5.4.4 Letter of appeal for reconsideration of CRERC review decision especially disapproval may be made. (Refer to SOP 5 Management of Appeal of CRERC Decision based on CIOMS 2016, Guidelines 23)

5.4.5 If the study protocol is approved, the CRERC determines the frequency of continuing review.

The resubmission of a study protocol for major revision is reviewed by Full Committee while that of a study protocol for minor revision is reviewed by expedited procedure by the Primary Reviewers or by the Member-Secretary or Chair if the Primary Reviewers are not available.

5.4.6 All meeting deliberations and decision regarding a protocol are noted in the meeting minutes (Refer to SOP 8.1 on Preparation of Meeting Minutes).

5.5 Communicate the CRERC decision to the Researcher/Principal Investigator

5.5.1 The Administrative Secretary prepares the communication of CRERC Decision to the Researcher/PI using the appropriate form within 5 days from the date of the Full Committee meeting. (Refer to SOP 8.2 Communicating CRERC Decision)

5.6 File the protocol or protocol-related documents in the protocol file folder, and update the protocol file index and protocol database

5.6.1 The Administrative Secretary files the submitted documents and their corresponding completed assessment forms, excerpt of the minutes of the meeting where the protocol was deliberated, duplicate copy of Notification of CRERC Decision/Approval Letter in the protocol file folder; updates the protocol file index, and the protocol database accordingly. (Refer to the SOP 9.1 Management of Active Study Protocol Files)

6. Related Forms

CRERC Form 4.1 Acknowledgement and Notice of Review to the Researcher
CRERC Form 4.2 Request for Review (Primary Reviewer)
CRERC Form 4.3 Protocol Assessment Checklist
CRERC Form 4.4 Informed Consent Assessment Checklist
CRERC Form 4.6 Protocol Resubmission Form
CRERC Form 7.1 Protocol Amendment
CRERC Form 7.3 Progress/Annual Report
CRERC Form 7.4 Final Report
CRERC Form 7.5 Onsite Serious Adverse Event Report
CRERC Form 7.6 Protocol Violation/Deviation Report
CRERC Form 7.7 Early Study Termination
CRERC Form 9.2 Log of Outgoing Protocol Related Communications

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7. SOP Document History

Version No.	Version Date	Description of Changes
1	23 Jan 2015	Refer to SOP
2	21 May 2015	Refer to SOP
3	05 Feb 2016	Refer to SOP
4.1	17 May 2019	Refer to SOP
5	31 Oct 2021	▪ Changed Purpose to Objective, and Process Flow/Steps to Workflow to harmonize with PHREB's section titles ▪ Changed the section on Scope, - included a description of submissions for Full Committee review, and the start and end tasks of the SOP ▪ Added the detailed responsibilities of the CRERC Chair/Member-Secretary, and those of the Administrative Secretary ▪ Removed Task #1 – Determine that the submission qualifies for Full Committee review. This task is included in SOP 3.0 – Management of Submission. ▪ Added 5.1.2 possibility of calling in an Independent Consultant to assist in the review; 5.1.3 – selection of other CRERC Members if the initially assigned Primary Reviewer/s is/are not available ▪ Removed Task #5 of version 4.0 - Return the accomplished assessment forms to the Secretariat. This task incorporated in Task #3 of the current version. ▪ Added the assessment form to use (in 5.3.1 in current version) and possible review decision appropriate to the kind of documents being reviewed. ▪ Added timelines – from date of receipt to forwarding of protocol/protocol related document to be reviewed to the Primary Reviewer/s; Change timeline of completion of review from 14 days date of receipt to the return of the completed assessment form to CRERC to at least one week before the date of the Full Committee meeting. ▪ Introduced new forms - Form 4.1 Acknowledgement and Notice of Review to PI, Form 4.2 Request for Review (for Primary Reviewer) and CRERC Form 9.2 Log Outgoing Protocol Related Communications ▪ Cross referenced tasks with related SOPs ▪ Used Administrative Secretary instead of CRERC Secretariat

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SOP 4.3 EXEMPT FROM ETHICAL REVIEW

1. Objective of the Activity

To describe the procedures for the review of protocols which qualify for exemption from review *to ensure that no protocol is inappropriately exempted from review.*

2. Scope

This SOP applies to the management of a study protocol submitted to the MDMRCI-ARMCI CRERC that requests exemption from ethical review according to the criteria set in section 5.4.1A of SOP 3.0 Management of Protocol Submissions. *The SOP starts with the review of the study protocol applying for exemption from review and ends with the inclusion of the protocol exempted from review in the meeting agenda for reporting to the CRERC en banc.*

3. Responsibilities

The CRERC Chair or Member-Secretary is responsible for the assessment whether the submitted protocol qualifies for exemption from review. The Chair designates a Member to do the assessment if s/he and the Member-Secretary have conflict of interest.

The Administrative Secretary is responsible for **a)** informing the CRERC Chair and Member-Secretary of the submission and request for exemption from review, **b)** preparing the communication of CRERC decision to the Researcher, **c)** filing the protocol and related documents in the protocol file folder and updating the protocol file index and protocol data base, and **d)** sending the reminder letter to the Researcher a month before the expiry date of the ethical approval for the submission of the Final Report, or Annual Report if the study is still ongoing.

4. Workflow

No.	Activity	Person Responsible
1	Review the study protocol applying for exemption from review	CRERC Chair or Member-Secretary
2	Communicate the CRERC decision to the Researcher	Administrative Secretary
3	Monitor the completion of the study	CRERC Chair
4	File the protocol and protocol-related document in the protocol file folder, and update the protocol file index and the protocol database	Administrative Secretary
5	Include protocol exempted from review in the meeting agenda	Administrative Secretary

5. Detailed Instructions

5.1 Review the study protocol applying for exemption from review

The Chair or Member-Secretary shall then evaluate the study protocol using CRERC Form 4.5 Checklist for Exemption from Ethical Review within a week from the date of complete submission of the protocol package. If both the Chair and

Member-Secretary have conflict of interest, the former designates a Member to do the review.

If the assessment of the Reviewer shows that the protocol is not for exempt, s/he makes a decision together with the Chair to reclassify the type of review as expedited or Full Committee. (Refer to SOP 4.1 for Expedited Review or SOP 4.2 for Full Committee Review)

5.2 Communicate the CRERC decision to the Researcher

5.2.1 If the protocol qualifies for exemption from review, the Reviewer submits the results of the assessment to the CRERC Administrative Secretary who prepares CRERC *Form 8.12 Certificate of Exemption from Ethical Review*. (Refer to SOP 8.2 Communicating CRERC Decision)

5.3 *Monitor the completion of the study*

5.3.1 The duration of ethical approval is only one year and the Researcher is required to submit the Final Report. An Annual/Progress Report is required if renewal of ethical approval is requested, and the study is still ongoing to ensure that the implementation of the study did not deviate from the original protocol that was submitted.

5.3.2. The Administrative Secretary shall send a letter of reminder (CRERC Form 7.2 Reminder Letter for Submission of Annual/Final Report) to the Researcher 60 days prior to expiry date of the ethical approval to submit the Final or Annual/Progress Report if the study is still on-going to ensure that it still meets the criteria for exempt from review.

5.3.3. The Chair or the Member-Secretary or the exempt-Reviewer will then assess any of the following responses of the Researcher and take the corresponding action:
a) If the Researcher submits Annual/Progress Report using CRERC Form 7.3 Continuing Review Application, and there are no changes in the protocol, the ethical approval for the exemption from review will be renewed.
b) If the Researcher submits the Final Report using CRERC Form 7.4 Final Report, and there are no changes in the protocol, the report is accepted, and the protocol is declared inactive and archived (Refer to SOP 9.3 Archiving of Inactive Study Files), and the Researcher is informed.

5.4 File the protocol and protocol-related document in the protocol file folder, and update the protocol file index and the protocol database

5.4.1 The Administrative Secretary includes Certificate of Exemption and any additional submissions to the protocol file folder, and updates the protocol file index and the protocol data base. (Refer to SOP 9.1 Management of Active Study Protocol and Administrative Files)

5.5 Include protocol exempted from review in the meeting agenda

5.5.1 The Administrative Secretary includes the protocol exempted from review in the agenda of the forthcoming meeting, and the Chair/Member Secretary reports this during the Full Committee meeting. This report is included in both the Meeting Agenda and the Minutes of the Meeting. (Refer to SOP

6.1 Preparation for CRERC Meeting and SOP 8.1 Preparation of Minutes of Meeting)

6. Related Forms

CRERC Form 4.5 Checklist for Exemption from Ethical Review
CRERC Form 7.2 Reminder Letter for Submission of Annual/Final Report
CRERC Form 7.3 Continuing Review Application
CRERC Form 7.4 Final Report
CRERC Form 8.12 Certificate of Exemption from Ethical Review

7. SOP Document History

Version No.	Version Date	Description of Changes
01	23 Jan 2015	Refer to SOP v. 01
02	21 May 2015	Refer to SOP v. 02
03	05 Feb 2016	Refer to SOP v. 03
04.1	17 May 2019	Refer to SOP v. 04.1
05	31 Oct 2021	▪ Changed Purpose to Objective, and Process Flow/Steps to Workflow to harmonize with PHREB's section titles. ▪ Added in the section on Scope, a description of the start and end tasks of the SOP ▪ Added the detailed responsibilities of the CRERC Chair, and those of the Administrative Secretary ▪ Remove Task #1 in version 4.0 – "Issue Certificate of Exemption". This is incorporated in Task #2 in current version "Communicate decision to the Researcher" ▪ Renumber Certificate of Exemption from Form 4.1 to Form 8.12 and transfer to SOP 8.2 - Communicating CRERC Decision ▪ Added Task # 3 of the current version – Reminding the Researcher to submit either a Final Report or Progress Report a month before the expiry date of the ethical approval ▪ Introduced new form – CRERC Form 4.5 Checklist for Exemption from Ethical Review ▪ Added Task #5 – Inclusion of the protocol that was exempted from review in the agenda of the upcoming Full Committee meeting ▪ Used Administrative Secretary instead of CRERC Secretariat

SOP 4 REVIEW PROCEDURES

SOP 4.4 REVIEW OF RESUBMISSION

1. Objective of the Activity

To describe the procedures for the review of revised protocol or protocol-related documents *to ensure that revisions are in accordance with the recommendations*.

2. Scope

This SOP applies to all protocol/protocol-related submissions after initial review or reviews by CRERC before approval regardless of the type of review. It covers all CRERC activities during the review of the revised protocol that had been initially reviewed by CRERC. *This SOP starts with the receipt of the revised protocol and ends with the filing of the protocol and related documents and the updating of the protocol file index and the protocol data base.*

3. Responsibilities

*The CRERC Administrative Secretary is responsible for: **a)** receiving the revised protocol with CRERC Form 4.6 Protocol Resubmission, and verifying that the document package is complete; **b**) forwarding the revised protocol to the Primary Reviewer/s who did the initial review; **c)** following up the results of the review, **d)** preparing the communication of CRERC decision to the Researcher/PI within the specified timeline; **e)** filing the documents in the protocol file folder, and updating the protocol file index and protocol data base*.

The Primary Reviewer is responsible for **a)** assessing the revisions if these are in accordance with the recommendations, *and **b)** returning the protocol and the CRERC Form 4.6 Protocol Resubmission Form with the review notations to the CRERC Administrative Secretary within the specified timeline.*

4. Work Flow

No.	Activities	Person/s Responsible
1	Receive and manage the resubmission document package	Administrative Secretary
2	Notify Primary Reviewer/s and send the resubmission document package to be reviewed	Administrative Secretary
3	Review if the resubmission complied with the required modifications	Primary Reviewers
4	Return the resubmission document package with the results of the review to CRERC	Primary Reviewer/s
5	Communicate the CRERC decision to the Researcher/Principal Investigator (PI)	Administrative Secretary
6	File the revised protocol and related documents in the protocol file folder, and update the protocol file index and protocol database	Administrative Secretary

SOP 4 REVIEW PROCEDURES

5. **Detailed Instructions**

5.1 Receive and manage the resubmission document package

5.1.1 The Administrative Secretary receives the resubmitted protocol package, and checks its completeness, the accuracy of the version no. and date indicated in CRERC Form 4.6 Protocol Resubmission Form and in the footer of the revised protocol/protocol related document/s and whether the changes are highlighted.

*The resubmission is said to be complete if **a)** it has the revised protocol or protocol-related document, **b)** it has the CRERC Form 4.6 Protocol Resubmission where the 1st and 2nd columns are filled, **c)** the revised document has the correct version no. and date in the footer, **d)** the changes as stated in CRERC Form 4.6 Protocol Resubmission are highlighted and their location in the protocol document is correctly identified.*

5.1.2 If submission is found to be in order, the Administrative Secretary stamps "Received" and the date of receipt on the document package and properly records the documents in CRERC Form 9.1 Log of Protocol Related Submissions and in the protocol database.

5.1.3 In the event that the Researcher/PI fails to submit the revised protocol/protocol-related document within ninety (90) calendar days from the date of the Notification of CRERC decision of the last review (with or without letter of request to withdraw from the review process), the study protocol is deemed inactive and transferred to the file storage cabinet for inactive files. (Refer to SOP 9.3 Archiving of Inactive Study Files) The Researcher/Principal Investigator is informed accordingly.

5.2 Notify Primary Reviewers and send the resubmission document package to be reviewed

5.2.1 *The Administrative Secretary informs the Primary Reviewers about the submission and follows up the response. If the chosen Primary Reviewer/s is/are not available, the Chair/Member-Secretary is informed who will then do the review or designate other CRERC Member/s to do the review.*

5.2.2 If the Primary Reviewers are available to do the review, the Administrative Secretary sends the document package to the Primary Reviewers within seven (7) calendar days from the date of receipt after it is logged in CRERC Form 9.2 Log of Outgoing Protocol Related Communications.

5.2.3 *For protocols initially reviewed by Full Committee, the type of review of the resubmission is determined after the review – usually back to Full Committee if the review decision is major revision, expedited review by the Primary Reviewer/s or by the Member Secretary or Chair if the review decision is minor revision. For protocols initially reviewed by expedited procedure, the type of review of resubmitted protocol is the same except if there is a disagreement in the review decisions of the Primary Reviewers. In this case, the resubmitted protocol is referred to the Full Committee.*

If the resubmission is reviewed by expedited procedure, refer to SOP 4.1 Expedited Review. If the resubmission is reviewed by Full Committee, refer to SOP 4.2 Full Committee Review.

SOP 4 REVIEW PROCEDURES

5.3 Review if the resubmission complied with the required modification/s

5.3.1 Using CRERC Form 4.6 Protocol Resubmission, the Primary Reviewers verify if the recommended revisions are complied. *The Primary Reviewers write the results of their assessment in the third column of the accompanying filled CRERC Form 4.6 Protocol Resubmission.*

5.3.2 *Review decision can be any one of the following:*

i) Approval,
ii) Minor revision,
iii) Major revision,
iv) Disapproval
v) Pending, if major clarifications are required or more information (specify information to be requested) is needed before a decision can be made.

5.4 Return the resubmission document package with the results of the review to CRERC

5.4.1 The Primary Reviewers return the reviewed documents together with the completed CRERC Form 4.6 Protocol Resubmission *within 7 days from date of receipt of the document package.*

5.4.2 The Administrative Secretary records the returned resubmission package in CRERC Form 9.1 Log of Protocol Related Submissions.

5.4.3 If the protocol was initially reviewed by Full Committee and the revision was classified as major, the medical/scientific Primary Reviewer presents the results of their assessment to CRERC *en banc*. (Refer to SOP 4.2 Full Committee Review)

5.5 Communicate the CRERC decision to the Researcher/PI

5.5.1 The Administrative Secretary prepares the communication of CRERC Decision to the Researcher/PI using the appropriate form within 5 days from the receipt of the results of the expedited review, or within 5 days from the date of the Full Committee meeting. (Refer to SOP 8.2 Communicating CRERC Decision)

5.6 File the revised protocol and related documents in the protocol file folder, and update the protocol file index and the protocol data base

5.6.1 The Administrative Secretary files the documents in the protocol file folder, and updates the protocol file index of the protocol file folder. The Administrative Secretary also updates the Resubmission columns of the protocol database. (Refer to SOP 9.1 Management of Active Study Protocol Files)

6. **Related Forms**

CRERC Form 4.6 Protocol Resubmission
CRERC Form 9.1 Log of Protocol Related Submissions
CRERC Form 9.2 Log of Outgoing Protocol Related Communications

7. **SOP Document History** (Changes in previous versions cannot be tracked)

Version No.	Version Date	Description of Changes
01	23 Jan 2015	Refer to SOP v. 01

SOP 4 REVIEW PROCEDURES

02	21 May 2015	Refer to SOP v. 02
03	05 Feb 2016	Refer to SOP v. 03
04.1	17 May 2018	Refer to SOP v. 04.1
05	31 Oct 2021	▪ Changed Purpose to Objective, and Process Flow/Steps to Workflow to harmonize with PHREB's section titles ▪ Changed the section on Scope, - included a description of the start and end tasks of the SOP ▪ Added the detailed responsibilities of the Administrative Secretary • Added to Task #1 – description of complete resubmission package, the recording of resubmitted document in the Log of Protocol Related Submissions and in the protocol data base, when the study protocol is dropped from the review if the Researcher fails to resubmit revised protocol/protocol-related document. • Added to Task #3 – categories of review decisions • Change the turn-around-time for the review of the resubmission to 7 days instead of 14 days. • Subsumed Task #5 of version 4.0 (discuss and decide major modification in FB meeting) in Task #4 of current version, and revised Task #6 of version 4.0 • Added cross references to related SOPs • Added another column in CRERC Form 4.5 Protocol Resubmission for the Primary Reviewers comments/notes • Introduced new forms in the SOP: CRERC Form 4.2 Request for Review, CRERC Form 9.1 Log of Protocol Related Submissions, and CRERC Form 9.2 Log of Outgoing Protocol Related Documents • Revised CRERC Form 4.6 Protocol Resubmission – adding a third column where primary Reviewer documents his/her assessment • Change CRERC Secretariat to Administrative Secretary

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