Title: Continuing Review of Study Protocols

1. Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe how continuing review of previously approved protocols should be managed by the Institutional Ethics Committee (EC). The purpose of the continuing review is to periodically monitor the progress of the study, to ensure continuous protection of the rights and welfare of research participants.

2. Scope

This SOP applies to conducting any continuing review of already approved study protocols at pre-specified intervals. All the projects approved by the EC will be reviewed at least once a year or completion of the proposal whichever is earlier. Depending upon the degree of risk to the participants, the nature of the studies, the vulnerability of the study participants and duration of the study, the EC may choose to review or monitor the protocols more frequently.

3. Responsibility

It is the responsibility of the EC Secretariat to remind the PIs and Member Secretary regarding continued review of protocols at the correct interval. All the approved protocols will be reviewed annually. It is the responsibility of the Member Secretary to ensure a decision regarding whether the project needs to be reviewed more frequently is taken during the EC meeting in which the project is finally approved. This must be recorded in the minutes. A fresh decision to increase review may be taken if required based on the SAE reports [As per ICMR 2017 guidelines, SAEs must be reported for all trials and if applicable timelines as specified by regulators to be followed (within 24 hours to the sponsor, EC and regulator, if applicable, followed by a due analysis report in 14 days)], monitoring reports, or safety concerns. This is responsibility of the SAE subcommittee and Member Secretary.

The EC is responsible for reviewing the progress made in the protocol (number of patients recruited, dropped out, reasons for drop-out), the occurrence of unexpected events or problems, and compliance of the investigator regarding EC communication.

4. Detailed instructions

4.1 Determining the date of continuing review

- The date of the continuing review will always be at least once in the year or completion of the proposal whichever is earlier. The EC also should examine the means taken for medical management of SAE's.
- The EC may recommend more reviews during the approval process depending on the level of risk ("for cause" monitoring). This will be documented in the minutes.
- The following situations may justify "for cause" monitoring:
  - ✓ high number of protocol violations/deviations;
  - ✓ large number of proposals carried out at the study site or by the same researcher;
  - ✓ large number of SAE reports;
  - ✓ high recruitment rate;
  - ✓ complaints received from any adverse media report;
  - ✓ adverse information received from any other source;
  - ✓ non-compliance with EC directions;
  - ✓ misconduct by the researcher; and any other cause as decided by the EC.
- The Secretariat will inspect the minutes of meeting to set a timetable for continuing review.
- The Secretariat will identify and record the due dates for each project

4.2 Notifying the PI or the study team

The Secretariat will send a reminder to the PI as per the format *AX 01/SOP 10/V4* two months prior (if an annual review) or less as appropriate (if any special additional reviews are required) to the due date of continuing review.

4.3 Managing the continuing review package upon receipt

- The Secretariat will receive a package (soft and hard copy) submitted by the PI for continuing review of each approved protocol. Only one set (soft and hard copy) of continuing review report shall be submitted by the PI to the EC as per the format Continuing Review Application Form (*AX 02/SOP 10/V4)*.

4.4 Verifying the contents of the package

- The Secretariat will ensure that the contents of the package include the following documents:
    - Continuing Review Application Form (*AX 02/SOP 10/V4)*
    - The Continuing Review Application Form duly filled with an explanation for any "yes" (ticked on the Continuing Review Application Form (*AX 02/SOP 10/V4)*

      answers on the application form and a discussion of scientific developments, either through the conduct of this study or similar research that may alter risks to research participants. The changes in the selection criteria of participants, protocol/Informed consent Document amendments, changes in the study team, any unexpected complications etc. must have been discussed in the attached narrative.

- The Secretariat will confirm complete information is appended and for the presence of the required signatures of the Principal Investigator in the Continuing Review Application Form (*AX 02/SOP 10/V4*).

4.5 Review process

- The Continuing review submission may undergo expedited review (as per the procedure described in SOP7B/V4) or full board review (as per the procedure described in SOP7A/V4) as deemed appropriate by the EC Chairman/ Member Secretary
- The EC Chairman/ Member Secretary/ Member/s will use the Continuing Review Application Form (*AX 02/SOP 10/V4)* to guide the review and deliberation process.
- The Secretariat will send the Continuing Review Application Form (*AX 02/SOP 10/V4)* to the designated EC members.
- The EC Chairman/ Member Secretary/ Member/s could reach one of the following decisions after review:
    1. Noted - The EC approves the continuation of the project without any modifications.
    2. Modifications recommended: The study protocols that have been suggested modifications by the EC may not proceed until the conditions set by the EC in the

decision have been met. The amendments and the required documents should be amended and submitted to the EC within one month for re-review.

3. The project cannot be continued: The reasons for discontinuation of the project should be mentioned in the letter notifying the decision to the Principal Investigator. This decision shall be recorded by the Member Secretary on *AX 02/SOP 10/V4.*

- The EC Chairman will sign and date the EC decision on Continuing Review Report after a decision has been reached.
- The decision on continuing review taken by the Chairman/ Member Secretary/ Member/s will be informed to all EC members at the next full board meeting
- The continuing review report may be discussed at full board if deemed necessary by Chairman/Member Secretary.
- The EC Secretariat will maintain and keep the EC Decision forms and minutes of the meeting relevant to the continuing review as part of the official record of the review process in the project file.

4.6 Communicating EC Decision to the PI

- The Secretariat will notify the PI of the decision within 14 days of the meeting at which the report was discussed or of the date of review by the Chairman/ Member Secretary/ EC Member/s.

4.7 Non-submission of continuing review report by principal investigator before or on due date.

- If a PI fails to submit the continuing review report before or on due date, the Secretariat will send a email reminder within 15 days after due date of review.
  If there is no response, the EC secretariat will put up the matter for discussion at the forthcoming full board meeting for appropriate action which may consist of but not limited to sending:

  a) A reminder letter again

  b) A letter asking explanation for non-submission

  c) A letter asking the PI to put recruitment of new participants on hold till report is submitted

d) Any other action as deemed appropriate by EC

5. References to other applicable SOP/s - nil

6. Annexures

Annexure 1 *AX 01/SOP 10/V4*- Reminder letter by the EC to principal investigator Annexure 2 *AX 02/SOP 10/V4*- Continuing Review / Annual report format

Annexure 1: AX 01/SOP 10/V4

Reminder letter by the EC to principal investigator

Date:-

Name of Principal Investigator:-

Department:-

Ref: - Project no. Title: XXXXXX

The above referenced project was approved by the EC on XXXXXXX and is due for Continuing Annual/ Periodic Review by the EC. You are requested to submit an Annual/ Periodic status report in the prescribed format which is enclosed (Continuing Review Application Form *AX 02/SOP 07*) at the earliest, on or before XXXXX. (1 month period)

Signature with date _____

Member Secretary/ Chairman _____

Project No.:	**Date of EC approval:**
Project Title:	
Principal Investigator : **Department :**	

Annexure 2: AX 02/SOP 10/V4

Continuing Review / Annual report format

SMVMCH-EC Ref. No. (for office use):

Title of study:

Principal Investigator (Name, Designation and Affiliation):

1. Date of EC Approval: Validity of approval:
2. Date of Start of study: Proposed date of Completion:

   Period of Continuing Report: - to -
3. Does the study involve recruitment of participants?

a. If yes, Total number expected..... Number Screened: ..... Number Enrolled: .....

   Number Completed:..... Number on follow up:.....

b. Enrolment status – ongoing / completed/ stopped

c. Report of DSMB Yes☐ No☐ NA ☐

(In case there is a Data Safety Monitoring Board (DSMB) for the study provide a copy of the report from the DSMB. If not write NA)

d. Any other remark

e. Have any participants withdrawn from this study since the last approval?
   If yes, total number withdrawn and reasons:

4. Is the study likely to extend beyond the stated period? *(Problems encountered since the last continuing review application with respect to implementation of the protocol as cleared by the EC)*
   If yes, please provide reasons for the extension

5. Have there been any amendments in the research protocol/Informed Consent Document (ICD) during the past approval period?
   If No, skip to item no. 6 Yes☐ No☐
   a. If yes, date of approval for protocol and ICD :
   b. In case of amendments in the research protocol/ICD, was re-consent sought from participants? Yes☐ No☐
      If yes, when / how

6. Is any new information available that changes the benefit - risk analysis of human participants involved in this study? Yes ☐ No ☐
   If yes, discuss in detail:

7. Have any ethical concerns occurred during this period? Yes☐ No☐
   If yes, give details:

8. a. Have any adverse events been noted since the last review? Yes☐ No☐

Describe in brief:

b. Have any SAE's occurred since last review? Yes☐ No☐
If yes, number of SAE's:…… Type of SAE's: ……..

c. Is the SAE related to the study? Yes ☐ No ☐
Have you reported the SAE to EC? If no, state reasons Yes ☐ No ☐

9. Has there been any protocol deviations/violations that occurred during this period?
If yes, number of deviations ……
Have you reported the deviations to EC? If no, state reasons Yes ☐ No ☐

10. In case of multicenteric trials, have reports of off-site SAEs been submitted to the EC ?
Yes☐ No☐ NA ☐

11. Are there any publications or presentations during this period? If yes give details Yes☐ No☐

Any other comments:

Signature of PI with date:

7. Flow Chart

No.	Activity	Responsibility
1	Determine the date of continuing review	Administrative Officer / Secretariat
2	Notify the Principal Investigator or study team	EC Secretariat
3	Manage continuing review package upon receipt and verifying its contents	EC Secretariat
4	Notify the members of the EC	EC Secretariat
5	Review of Continuing review report	EC Secretariat, Members and Chairman
6	Prepare meeting agenda	EC Secretariat
7	Communicate the EC decision to the Principal Investigator	EC Secretariat

8. References

1. Forum for Ethics review Committees in India (FERCI). Standard Operating Procedures of Institutional Ethics Committee (cited 22nd October 2018). Available from: http:// www.ferci.org/sops/.
2. Ethical guidelines for biomedical research on human participants. (2017). Indian Council of Medical Research. Available from: http://www.icmr.nic.in/guidelines/ICMR _Ethical_ Guidelines _2017.pdf
3. Ministry of Health and Family Welfare. New Drugs and Clinical Trials Rules, 2019. Available from: https://cdsco.gov.in/opencms/export/sites/CDSCO_WEB/Pdf-documents/NewDrugs_CTRules_2019.pdf

	Name	Designation	Signature
Prepared	Dr. Girija. S	Member	
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Approved	Dr. Thiagarajan. T	Chairman	
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