Title: Periodic Review of Protocols & Extension of validity

SOP Code: SOP10/v1

Effective date: 20/02/2025

Prepared by:

Mrs. Anju Ullas Member, YEC-3 SOP Subcommittee	Signature with date:

Reviewed by:

Dr. Asir John Samuel Convenor YEC-3 SOP Subcommittee	Signature with date:

Approved by:

Dr. Haripriya S, Chairperson, YEC-3	Signature with date:

Notified by:

Registrar, Yenepoya (deemed to be University)	Signature with date:

Table of Contents:

1. **Purpose:** The purpose of this Standard Operating Procedure (SOP) is to describe the procedure to be followed by Yenepoya Ethics Committee-3 (YEC-3) for periodic review of ongoing protocols approved by YEC-3 to ensure on-going ethical and scientific conduct of research, from the time of approval to completion of the study.
2. **Scope:** This SOP applies to all ongoing protocols approved by YEC-3 for which
   - 2.1. **A periodic review of protocols is conducted at intervals as determined by YEC-3 based on**
     - 2.1.1. The quantum of risk at the time of approval
       - 2.1.1.1. The type of the study
       - 2.1.1.2. The risk:benefit ratio
       - 2.1.1.3. Inclusion of vulnerable populations
     - 2.1.2. Post-approval events that may change the risk to the participants
       - 2.1.2.1. Amendments in the protocol
       - 2.1.2.2. Occurrence of adverse events or SAEs (on-site or off-site)
       - 2.1.2.3. Protocol deviations or violations
       - 2.1.2.4. New evidence published that may alter the risk
       - 2.1.2.5. Other factors as determined by the YEC-3 members
   - 2.2. **An extension of EC approval is requested**
     - 2.2.1. Before the end of the validity period if the study is not completed
3. **Definitions**
   - 3.1. **Periodic review:** The ongoing review of the status of the study conducted during the validity period of the YEC-3 clearance at predetermined intervals.
   - 3.2. **Extension of EC approval:** The PI requests extension of validity period of the EC approval if the study is not completed (Ann07/SOP10/v1).
4. **Responsibilities:**
   - 4.1. **The YEC-3 Chairperson will**
     - 4.1.1. Ensure that periodic review of protocols takes place as determined by the YEC-3.
     - 4.1.2. Recommend modifying the frequency of the periodic review, if required, based on the perceived change in risk-benefit for the participant in an ongoing study.
   - 4.2. **The YEC-3 Member-Secretary will**
     - 4.2.1. Ensure that the frequency of periodic review is determined and noted in the decision form for each protocol at the time of approval.
     - 4.2.2. Ensure that the assessment of periodic review forms is done as per schedule

and in a timely manner

4.2.3. Categorize the filled periodic review form of the ongoing protocol based on the risk as full review or expedited review

4.2.4. Assign reviewers for the periodic review

4.2.5. Initiate appropriate action, with the approval of the Chairperson, if periodic review forms are not submitted by the PI in a timely manner

4.2.6. Recommend modifying the frequency of the periodic review based on the perceived change in risk-benefit for the participant.

4.3. **The YEC-3 Secretariat will**

4.3.1. Maintain a calendar for periodic review of protocols as determined by the YEC-3 at the time of approval or subsequently based on post-approval events

4.3.2. Send an email reminder to the PI for submission of the periodic review forms one month before the scheduled date. If necessary, one or more reminders may be sent, if delayed.

4.3.3. Enter the list of protocols for which periodic review is scheduled every month in the meeting agenda

4.3.4. Provide a list of protocols to the Member-Secretary for which the periodic review form is not received as per the schedule.

5. **Detailed instructions:**

5.1. **Determining the periodic review schedule at the time of approval of a protocol:**

5.1.1. For clinical trials, the periodic review will occur as per the rules laid down by the Government of India, from time to time.

5.1.2. For other full review protocols, the YEC-3 will determine the frequency of periodic review at the time of approval, in the meeting.

5.1.3. For expedited review protocols, the YEC-3 Member-Secretary will determine the frequency of periodic review at the time of approval based on the decision of the reviewers.

5.1.4. Protocols considered for exemption from review will generally not be considered for periodic review

5.1.5. In addition, for all protocols, if the PI desires to renew the YEC-3 approval validity, the PI must initiate the process of periodic review in the last month of the validity of the protocol. For example, if the validity of the YEC-3 clearance is for 12 months, the PI should submit the periodic review request in the 11th month.

5.1.6. The date for initiation of planned periodic review process will be stated in the YEC-3 approval letter (one month before expiry of approval).

5.2. **Determining the periodic review schedule based on post-approval events of a protocol:**

5.2.1. For ongoing protocols in which SAEs, protocol deviations/violations are

reported or when the reports of site monitoring or audits or any other observation points out at an increased risk to the participant, or a complaint is received from any individual/party about a protocol, an initiation or modification in the frequency of the periodic review may be considered

5.2.2. The schedule previously determined may be modified by increasing or decreasing the frequency of periodic review or asking for an immediate submission of periodic review form.

5.2.3. Modification of the periodic review schedule may be called by the Member-Secretary/Chairperson/ concerned reviewers/YEC-3 meeting depending on the post-approval event

5.3. **Assessment of the risk: The risk may be assessed as per ICMR guidelines by considering the following**

5.3.1. The risk-benefit analysis (as provided in Ann01/SOP7A/v1)

5.3.2. The inclusion of vulnerable participants

5.3.3. The type of study

5.4. **Determination of the frequency of periodic review: This will be determined as**

	Initial risk assessment at the time of approval	**Post-approval SAEs/Protocol deviations**	**Frequency of periodic review**
5.4.1	Less than minimal risk or minimal risk	None	At the end of EC approval validity if study is extended (usually annual)
5.4.2	Minor increase over minimal risk particularly if involving vulnerable populations	No or occasional SAEs/ protocol deviations	6 monthly
5.4.3	More than minimal risk	SAEs/ Protocol deviations	3 monthly or more frequently
5.4.4	Any level of risk for any study	Recommendation of the site monitoring visit team, auditors, DSMB, or YEC-3 members or complaints received against PI	Immediate submission of periodic review

5.5. **Recording of the decision**

5.5.1. For those protocols where a periodic review is decided at the time of approval, the decision will be recorded in the decision form.

5.5.2. The decision will be included in the YEC-3 approval letter

5.6. **Maintaining the calendar for periodic review of protocols**

5.6.1. The Secretariat will maintain a calendar for periodic review schedules of all the protocols in an Excel spreadsheet in the YEC-3 computer (Ann01/SOP10/v1)

5.6.2. The Secretariat will update the calendar as and when protocols are approved

5.6.3. The Secretariat will identify all protocols which are due for periodic review in the coming month in order to send reminders to the PI

5.6.4. The Secretariat will identify all the protocols which are due for periodic review in the current month and inform the Member-Secretary

5.7. **Reminders to the PI:**

5.7.1. The Secretariat will send notification to the Principal Investigator and other research team members, one month before the scheduled date for periodic review.

5.7.2. The Secretariat will send a reminder by individual emails to the PIs of all the protocols which are due for periodic review in the subsequent month as per the format (Ann02/SOP10/v1)

5.7.3. A second reminder may be sent within 7 calendar days after the due date if the PI does not submit the period review application form in the scheduled month (Ann03/SOP10/v1)

5.8. **Submission of periodic review report by the Principal Investigator:**

5.8.1. The Principal Investigator will submit the filled, signed and dated periodic review form as per the format (Ann04/SOP10/v1)

5.8.2. The Principal Investigator will make the submission on or before the scheduled date as mentioned in the approval letter.

5.9. **Components of the periodic review:**

5.9.1. The components of the periodic review form will be as per annexure Ann04/SOP10/v1.

5.10. **Receipt of the submission for periodic review:**

5.10.1. The Secretariat will ensure that the contents of the periodic review form are complete with signature and date of the PI and any attachments, if applicable

5.11. **Categorization of the periodic review form:**

5.11.1. Initial screening: The Member-Secretary will do an initial screening and decide on the review process based on the issues identified in the periodic review application form as in SOP07/v1.

5.11.2. Full review: If serious ethical or scientific issues are identified, the Member-Secretary will categorize the form for full review. The submission for periodic review listed under full review will be managed as per SOP7A/v1.

5.11.3. Expedited review: If no serious ethical or scientific issues are identified, the Member-Secretary may categorize it for expedited review. The submission

for periodic review listed under expedited review will be managed as per SOP7B/v1.

5.12. **Review of the periodic review form:**

5.12.1. The Member-Secretary will identify reviewers for the periodic review depending on the categorisation

5.12.2. For expedited review, one YEC-3 member/Member-Secretary will be assigned to review

5.12.3. For full review, two YEC-3 members will be assigned to review the periodic review

5.12.4. The reviewers will review the contents of the periodic review application form (Ann05/SOP10/v1)

5.12.5. Any subsequent clarifications/ responses from the PI following YEC-3 communication after the periodic review will also be reviewed as above.

5.13. **The provisional decision by the reviewers:**

5.13.1. Noted and the study can continue without any changes

5.13.2. Noted and the PI has to provide more details/ provide clarifications within 30 calendar days.

5.13.3. Decision in the full review meeting

5.14. **The final decision on periodic or periodic review:** The final decision in the YEC-3 can be recorded in one of the following (Ann06/SOP10/v1):

5.14.1. Approved

5.14.2. Request information

5.14.3. Further action recommended which may include Audit or Site Monitoring, amendment, suspension or termination of the study.

5.15. The decision letter is signed and dated by the Chairperson/ Member-Secretary

5.16. **The follow-up action after the final decision**

5.16.1. Decision will be communicated to PI within 7 calendar days

5.16.2. The decision will be communicated to the Head of the Institution/ Sponsor/ Regulatory bodies if required

5.16.3. If the PI does not submit periodic review application as per the schedule or if the PI does not respond to the queries by the YEC-3 within 30 calendar days, then the same will be considered as protocol deviation/ violation and action will be initiated as per SOP11/v1

5.16.4. If any other protocol deviations/violations are identified action will be taken as per SOP11/v1

5.16.5. If audit/site monitoring is planned, action will be initiated as per SOP20/v1.

5.16.6. If amendment in protocol is recommended, action will be initiated as per

SOP09/v1.

5.16.7. If suspension/ termination of the study is recommended, action will be initiated as per SOP14/v1.

5.16.8. If change in frequency of periodic review is recommended, the same will be done as per SOP10/v1.

5.16.9. A copy of the submitted from, review forms and the decision letter will be filed in the respective protocol file

5.17. **Non submission of report for periodic review:**

5.17.1. The PI is expected to submit the periodic review form at the scheduled time as determined by the YEC-3 at the time of approval or after approval following a post-approval decision.

5.17.2. The PI will be reminded by email one month before the scheduled date for periodic review.

5.17.3. A second reminder will be sent if the deadline is missed within 7 calendar days of expiry of the validity of the YEC-3 approval letter.

5.17.4. The PI is expected to submit the periodic review form as per the schedule with a grace period of one week extended to a maximum of one month on the written request by the PI.

5.17.5. If the PI does not submit periodic review application as per the schedule or if the PI does not respond to the queries by the YEC-3 within 30 calendar days, then the same is considered as protocol deviation/ violation and action is initiated as per SOP11/v1

5.17.6. If the PI fails to submit the periodic review application form, one month before the end of the validity period of the EC approval, the PI must not include the data collected in the interim period between expiry of the initial approval and commencement of the continuation of approval.

5.17.7. Any data collected in this interim period will constitute a protocol deviation/ violation and will be treated as such as per SOP11/v1. Moreover, such data will need to be discarded and not included in the analysis.

5.17.8. The Member-Secretary may include failure to submit a periodic review form of the protocol, for discussion in the YEC-3 meeting and YEC-3 can decide regarding the status of the ethics committee approval and future submissions by the Principal Investigator.

6. **References:**

6.1. ICMR's National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017

7. **Annexures:**

7.1.1. Ann01/SOP10/v1: Calendar for periodic review schedule

7.1.2. Ann02/SOP10/v1: Reminder to the Principal Investigator to submit periodic review form

7.1.3. Ann03/SOP10/v1: Second reminder to the Principal Investigator to submit the periodic review form

7.1.4. Ann04/SOP10/v1: Application for periodic review/extension of the study

7.1.5. Ann05/SOP10/v1: Assessment form for periodic review

7.1.6. Ann06/SOP10/v1: Final Decision form for periodic review

7.1.7. Ann07/SOP10/v1: Approval letter for extension of the study

Ann01/SOP10/v1:

Calendar for periodic review schedule

S. No	Protocol Number	Title of the study	Name of the PI	Date of YEC- 3 Approval	Frequency of periodic review	Submitted on	Date of first periodic review	Reminder sent on	Submitted on

Ann02/SOP10/v1

Reminder to the Principal Investigator to submit periodic review form

Date:

Name of the Principal Investigator:

Department:

Reference:

Protocol Number:

Protocol title:

Date of YEC-3 approval:

Date of YEC-3 approval validity:

Frequency of Periodic review:

Subject: Reminder to submit periodic review form

Dear Dr./Mr./Ms. _____

You are requested to submit the duly filled and signed periodic review application form to YEC-3 on or before_____.

Any lapse or delay in submission of the periodic review application form will be considered as protocol deviation/violation.

If you are submitting the periodic review application form and requesting for extension of the EC clearance validity, then delay will result in a lapse of ethics committee approval. Please note that data

collected in the interim period where the ethics committee approval is not renewed, cannot be included in your final analysis. and if done, will constitute a protocol violation.

Thank you,

Yours sincerely,

Member-Secretary/Chairperson, YEC-3

Ann03/SOP10/v1:

Second reminder to the Principal Investigator to submit periodic review form

Date:

Name of the Principal Investigator:

Department:

Reference:

Protocol Number:

Protocol title:

Date of YEC-3 approval:

Date of YEC-3 approval validity:

Frequency of Periodic review:

Subject: Second reminder to submit periodic review form

Dear Dr./Mr./Ms. _____

We have not received the periodic review application form from you despite the reminder sent to you by email on _____.

You are requested to submit the duly filled and signed periodic review form to YEC-3 within 7 calendar days failing which, this will be considered as protocol deviation/violation, and will be suitably dealt with as outlined in SOP11/v1.

If you are requesting for extension of the EC approval, then delay will result in a lapse of a seamless ethics committee approval. Please note that data collected in the interim period where the ethics committee approval is not renewed, cannot be included in your final analysis. and if done, will be considered as a protocol violation.

Thank you,

Yours sincerely,

Member-Secretary/Chairperson, YEC-3

Yenepoya Ethics Committee - 3
Ann04/SOP10/v1
Periodic/Continuing Review Application Form

Periodic / Continuing Review

Yenepoya Ethics Committee-3 (YEC-3)

EC Ref. No. *(For office use)*

Title of study: .....

.....

.....

Principal Investigator (Name, Designation and Affiliation): .....

.....

.....

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

   Period of Continuing Report: dd mm yy ---- to ------ dd mm yy
3. Does the study involve recruitment of participants? Yes ☐ No ☐

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

   Number Completed:..... Number on followup:.....

   (b) Enrolment status – ongoing / completed/ stopped

   (c) Report of DSMB[1] Yes ☐ No ☐ NA ☐

   (d) Any other remark.....

   .....

   (e) Have any participants withdrawn from this study since the last approval? Yes ☐ No ☐ NA ☐

   If yes, total number withdrawn and reasons: .....

   .....

   .....
4. Is the study likely to extend beyond the stated period ?[2] Yes ☐ No ☐

   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: dd mm yy

   (b) In case of amendments in the research protocol/ICD, was re-consent sought from participants? Yes ☐ No ☐

   If yes, when / how: .....

   .....

   .....

Note: ICD - informed consent document

[1] *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.*
[2] *Problems encountered since the last continuing review application with respect to implementation of the protocol as cleared by the EC*

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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: ..... dd mm yy

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Ann05/SOP10/v1:

Assessment form for periodic review

Categorization of the periodic review application form:

Protocol No:

Title:

Principal investigator:

Full review /Expedited review:

Assignment of reviewers with dates of communication

Name of the reviewer 1:

Name of the reviewer 2:

Signature with date:

Chairperson/ Member-Secretary

Reviewer's assessment:

Protocol No:

Title:

Principal investigator:

A. Any clarifications required?
    a. If yes, provide details
B. Assessment by the reviewer:
    a. Any ethical issues noted?
    b. If yes, provide details:
C. Are there any scientific issues noted?
    a. If yes, provide details:
D. Are there any protocol deviations?
    a. If yes, provide details
E. Are there any unreported serious adverse events?
    a. If yes, provide details:

F. Recommendation of the reviewer:
    a. Noted and the study can continue without any changes
    b. Noted and the PI has to provide more details/ provide clarifications within 30 calendar days.
    c. Decision in the full review meeting

Signature of the reviewer

Date:

Ann06/SOP10/v1:

Final Decision form for periodic review

Protocol Number:

Title of the protocol:

Name of the Principal Investigator:

Department:

Validity of EC clearance: From_____ to _____

Extended validity: From: _____ to _____

Lapsed periods (if any): From _____ to _____

Final decision:

A. Approved
B. Request information
C. Further action recommended

Signature of Chairperson/Member-Secretary with date

Ann07/SOP10/v1:

Approval letter for extension of the study

Subject: YEC-3 Approval Letter for extension of the study

Ref: Protocol no. YEC-3/ titled, " "

Names of all research team members *(including Guides)*

No	Name	Role in the research team	Designation/ Affiliation
		Principal investigator	
		Guide/ Co-PI	

(Insert rows to add more names)

The YEC-3 has reviewed the periodic review application form dated (DD/MM/YY)

YEC-3 hereby approves extension of the study for the protocol no. YEC-3/_____/20___ and related documents as listed in the approval letter dated DD/MM/YY and amendment of the protocol approved, if any, on DD/MM/YY.

This extension is valid from: DD/MM/YY to DD/MM/YY. Any data collected before or beyond the validity period shall be considered as protocol deviation and liable to action.

It is the responsibility of the Principal Investigator to:

1. Provide correct, updated contact details and respond to YEC-3 communications without delay.
2. Adhere to the current regulatory guidelines.
3. Adhere to the undertaking signed by the PI.
4. Adhere to the approved version of the protocol (and related documents)
5. Adhere to the compensation plan as per the approved protocol
6. Restrict recruitment to the approved sample size of _____*(approved sample size)*
7. Inform the YEC-3 at the time of recruitment of the first participant.
8. Obtain written approval of YEC-3 before any proposed change in the protocol (amendment) is implemented in the prescribed format **(Ann01/SOP9B/v1)**
9. Report to YEC-3 any deviation from the guidelines/approved version of the protocol without delay (including change in research team members) in the prescribed format **(Ann01/SOP11/v1** - Initial report and **Ann02/SOP11/v1 -** Detailed report**)**
10. As per the current regulatory guidelines, report to YEC-3 all serious adverse events in the prescribed format **(Ann01/SOP12 v1** - Onsite SAE and **Ann02/SOP12/v1** - Offsite SAE**)** and their follow-up actions.
11. Submit the periodic review as specified by YEC-3 in the prescribed format **(Ann04/SOP10/v1)**
12. Submit periodic review form one month before the end of validity of this approval **(Ann04/SOP10/v1)**
13. Report to YEC-3 an adverse event/change in risk to participants (excluding SAEs) that may occur during the study in the periodic review
14. Submit a completion report to YEC-3 when the data/sample collection is completed in the prescribed format **(Ann01/SOP13/v1)**

15. Submit a summary of the study when the data analysis is completed.
16. Maintain the privacy of the participants/ samples and confidentiality of data.
17. Securely retain the original of YEC-3 approval letter, as issuing duplicate approval letter is liable to a fee
18. Respond to any communication from YEC-3 pertaining to the study auditing/site monitoring/etc .

All communications with YEC-3 should be by email to yec3@yenepoya.edu.in

YEC-3 functions in accordance with (insert names of the current regulations and guidelines).

YEC-3 is registered with (insert names of the currently approved regulatory authorities, letter number and validity) and recognized by (insert names of the recognizing bodies with validity).

Member-Secretary/Chairperson, YEC-3 Date:

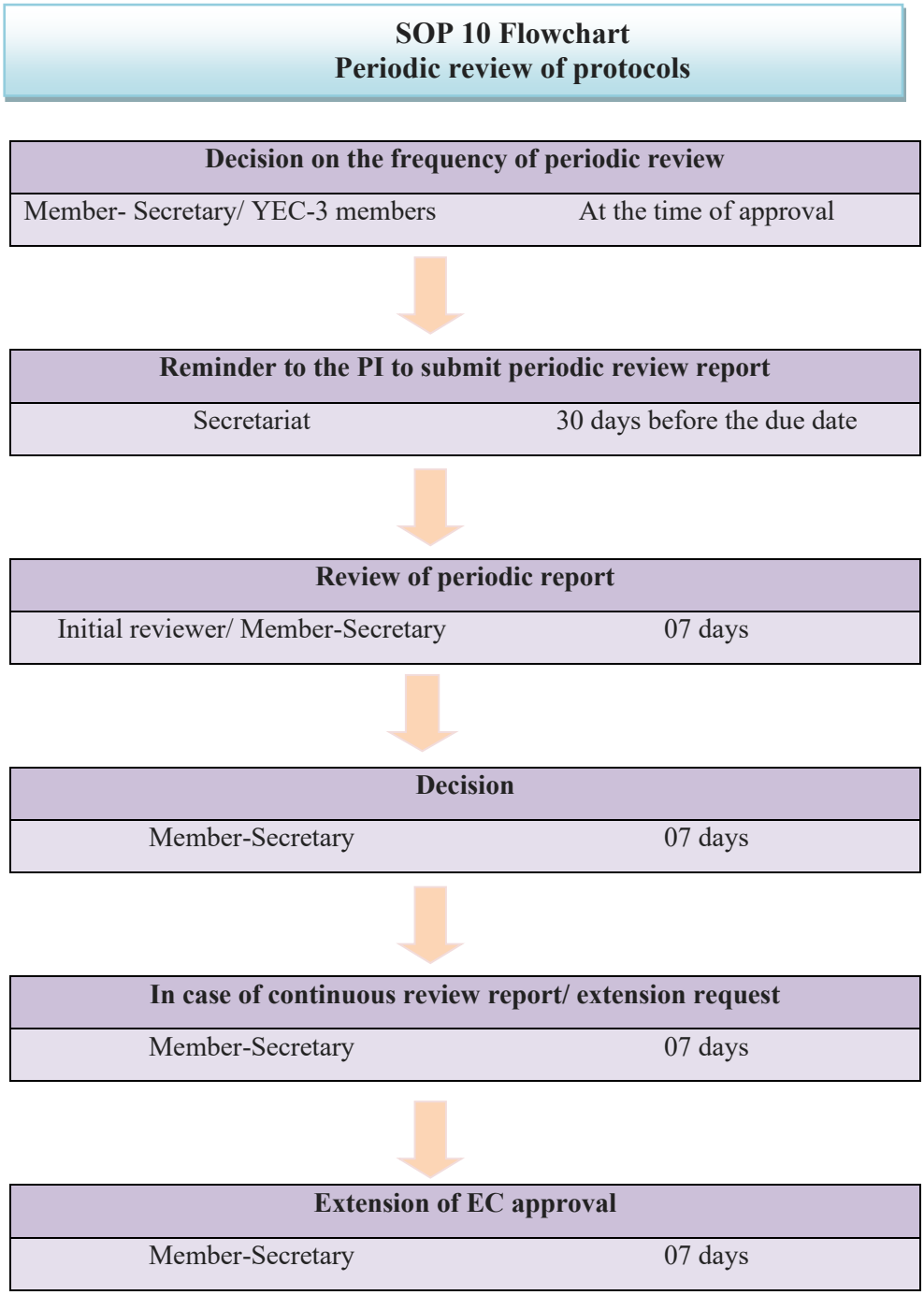
Important Dates:

Date of YEC-3 approval: *XX/XX/20XX*

Date of expiry of the validity of YEC-3 approval: *YY/YY/20YY*

Date for initiation of periodic review (if needed): *(write date a month prior to YY/YY/20YY)*

8. **Flowchart:**



1. 9. **Glossary:**

ICF: Informed Consent Form

PI: Principal Investigator

PIS: Participant Information Sheet

Protocol: A set of documents that contain the detailed components of the proposed study

SAE: Serious Adverse Event