Title: Periodic and Continuing Review of Protocols

SOP Code: SOP10/v3

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Prepared by:

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Approved by:

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Notified by:

Registrar, Yenepoya deemed to be University	Signature with date: 3/10

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-1 (YEC-1)for periodic and continuing review of protocols approved by YEC-1 to ensure ethical and scientific conduct of research, beyond the approval process.
2. **Scope:** This SOP applies to all ongoing protocols approved by YEC-1 for which a periodic/continuing review of protocols is conducted at intervals as determined by YEC-1 based on
   - 2.1. The quantum of risk at the time of approval
     - 2.1.1. The risk:benefit analysis
     - 2.1.2. The type of the study
     - 2.1.3. Vulnerable nature of participants
   - 2.2. Post-approval events that may change the risk to the participants
     - 2.2.1. Amendments in the protocol
     - 2.2.2. Occurrence of adverse events or serious adverse events (on-site or off-site)
     - 2.2.3. Protocol deviations or violations
     - 2.2.4. New evidence published
     - 2.2.5. Other factors as determined by the YEC-1 members
3. **Definitions**
   - **3.1. Periodic review:** The review of the status of the study conducted during the validity period of the YEC-1 clearance at predetermined intervals.
   - **3.2. Continuing review:** The review of the status of the study conducted at the end of the validity period of the EC clearance when the PI requests for extension of YEC-1 approval (Ann07/SOP10/v3).
4. **Responsibilities:**
   - 4.1. **The YEC-1 Chairperson will**
     - 4.1.1. Ensure that periodic and continuing review of protocols is taking place as determined by the YEC-1.
     - 4.1.2. Recommend modifying the frequency of the periodic review based on the perceived change in risk-benefit for the participant.
     - 4.1.3. Approve the appointment of reviewers recommended by the Member-Secretary.

4.2. The YEC-1 Member-Secretary will

4.2.1. Ensure that the frequency of periodic and continuing review is determined and noted in the decision form for each protocol during the YEC-1 meeting.

4.2.2. Ensure that assessment of the periodic and continuing review application forms is done in a timely manner

4.2.3. Communicate with the PI, person reporting the deviation/violation, head of the institution of the study site, other relevant statutory authorities

4.2.4. Categorize the protocol as full review wherever the risk is perceived as more than minimal and recommend two reviewers.

4.2.5. Initiate appropriate action, with the approval of the Chairperson, if continuing review application 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-1 Secretariat will**

4.3.1. Maintain a calendar for periodic and continuing review of protocols as determined by the YEC-1 at the time of approval or subsequently based on post-approval events

4.3.2. Send one and if required two reminders to the Principal Investigators for submission of the periodic/continuing review application forms before the date by which the periodic or continuing review is scheduled for the protocol

4.3.3. Provide the list of protocols for which periodic and continuing review is scheduled every month

4.3.4. Provide a list of protocols to the Member-Secretary for which the periodic and continuing review application 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 full review protocols, the YEC-1 will determine the frequency of

periodic review of protocols at the time of approval of the protocol in the YEC-1 meeting based on the potential risk to the participants

5.1.2. For expedited review protocols, the YEC-1 Member-Secretary will determine the frequency of periodic review of protocols at the time of approval based on the potential risk to the participants

5.1.3. Protocols considered for exemption from review will generally not be considered for periodic review, except in cases where the Member-Secretary assesses the need for periodic review.

5.2. Determining the continuing review schedule at the time of approval of a protocol:

5.2.1. For all protocols, if the PI desires to renew the YEC-1 approval, the PI must initiate the process of continuing review in the last month of the validity of the protocol. For example, if the validity of the YEC-1 clearance is for 12 months, the PI should submit the continuing review request in the 11th month.

5.2.2. The date for initiation of the continuing review process will be stated in the YEC-1 approval letter.

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

5.3.1. For approved 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 of the periodic review schedule may be considered

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

5.3.3. The modification of the periodic review schedule may be called by the Member-Secretary/Chairperson/ concerned reviewers/YEC-1 meeting depending on the post-approval event

5.4. Assessment of the risk : The risk may be assessed by

5.4.1. The risk:benefit analysis (as provided in Ann01/SOP7A/v3)

5.4.2. The inclusion of vulnerable participants

5.4.3. The type of study

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

5.5.1. 6 monthly for protocols with minimal risk or those with SAEs/protocol deviations

5.5.2. 3 monthly for protocols with more than minimal risk or those with or those with multiple reports of SAEs/protocol deviations/violations

5.5.3. More frequently as decided by the YEC-1 on a case-to-case basis

5.5.4. Immediate submission on request by YEC-1 for protocols with complaints against the PI/site monitoring reports/for audits/any other observation by the YEC-1

5.5.5. On the recommendation of an external quality assurance body such as the central licensing authority, his/her representative or a Data Safety Monitoring Board.

5.6. Recording of the decision

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

5.6.2. The decision will be included in the YEC-1 approval letter

5.7. Maintaining the calendar for continuing review of protocols

5.7.1. The Secretariat will maintain a calendar for periodic and continuing review schedules of all the protocols in an excel sheet in the YEC-1 computer (Ann01/SOP10/v3)

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

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

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

5.8. Reminders to the PI:

5.8.1. The Secretariat will send notification to the Principal Investigator one

month before the scheduled date for periodic and continuing review.

5.8.2. The Secretariat will send a reminder by individual emails to the PIs of all the protocols which are due for periodic and continuing review in the subsequent month as per the format (Ann02/SOP10/v3)

5.8.3. A second reminder may be sent within 7 calendar days after the due date if the PI does not submit the period or continuing review application form in the scheduled month (Ann03/SOP10/v3)

5.9. Submission of periodic and continuing review report by the Principal Investigator:

5.9.1. The Principal Investigator will submit the periodic and continuing review application form as per the format (Ann04/SOP10/v3)

5.9.2. The Principal Investigator will send the report for periodic and continuing review before the scheduled date as mentioned in the approval letter.

5.10. Components of the periodic or continuing review application:

5.10.1. Protocol details (PI name and affiliation; Guide name - where applicable; protocol number; protocol title)

5.10.2. Date of initiation of the study

5.10.3. YEC-1 EC clearance validity

5.10.4. Protocol version followed

5.10.5. PIS version followed

5.10.6. ICF version followed

5.10.7. Sample size approved

5.10.8. Number of participants screened so far

5.10.9. Number of participants recruited so far

5.10.10. Number of participants who are ongoing

5.10.11. Number of participants who have completed the study

5.10.12. Number of participants who withdrew the consent

5.10.13. Reasons for withdrawal of each participant in detail

5.10.14. Number of participants who were discontinued from the study by the PI/Sponsor

5.10.15. Reasons for discontinuation of each participant from the study with detail

5.10.16. Number of participants with adverse events

5.10.17. Description of each adverse event in detail

5.10.18. Any SAEs reported:

5.10.19. If yes, provide details of the reports:

5.10.20. Any increase in the risk to the participants based on the findings of the study/new information in literature:

5.10.21. Any changes made in the selection criteria of participants

5.10.22. Any changes made in the protocol

5.10.23. Any changes made in the study team; any change in guide

5.10.24. Any changes in the sample size

5.10.25. Any difficulties/ events faced during the study

5.10.26. Has interim data analysis been done? If yes, provide the report.

5.10.27. Has the data safety and monitoring board reported? If yes, provide the report?

5.10.28. Any investigators have developed a conflict of interest during the conduct of the study

5.10.29. Compliance with the EC approval letter

5.11. Receipt of the submission for periodic and continuing review:

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

5.12. Categorization of the periodic and Continuing review application form:

5.12.1. Initial screening: The Member-Secretary will do an initial screening and decide on the review process based on the issues identified in the continuing review application form as in SOP07/v3.

5.12.2. Full review: If serious ethical or scientific issues are identified, the Member- Secretary will categorize the form for full review by identifying two reviewers and table it for deliberation in the subsequent YEC-1 meeting. The submission for periodic and continuing review listed under full review will be managed as per SOP7A/v3.

5.12.3. Expedited review: If no serious ethical or scientific issues are identified, the Member-Secretary may categorize it for expedited review and inform the YEC-1 members in the subsequent YEC-1

meeting. The submission for periodic and continuing review listed under expedited review will be managed as per SOP7B/v3.

5.13. Review of the periodic and Continuing review application form:

5.13.1. The reviewers will review the contents of the continuing review application form (Ann05/SOP10/v3)

5.13.2. Any clarifications/ responses from the PI following YEC-1 communication following the review of periodic and continuing review application form will also be reviewed as above.

5.14. The provisional decision by the reviewers:

5.14.1. Noted and the study can continue without any changes

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

5.14.3. Decision in the full review meeting

5.15. The final decision on periodic or continuing review: The final decision in the YEC-1 can be recorded in one of the following (Ann06/SOP10/v3):

5.15.1. Noted and the study can continue without any changes

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

5.15.3. The study can continue but YEC-1 Audit or Site Monitoring for the protocol is warranted

5.15.4. The study can continue after amendments are made in the protocol and are approved by YEC-1

5.15.5. The study is suspended until audit report/ site-monitoring report/ other clarification/communications are made satisfactorily

5.15.6. The study is terminated.

5.15.7. 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. The decision will be communicated to the PI within 7 calendar days after the final decision

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 continuing review application as per the

schedule or if the PI does not respond to the queries by the YEC-1 within 30 calendar days, then the same will be considered as protocol deviation/ violation and action will be initiated as per SOP11/v3

5.16.4. If any other protocol deviations/violations are identified action will be taken as per SOP11/v3

5.16.5. If audit/site monitoring is planned, action will be initiated as per SOP20/v3.

5.16.6. If amendment in protocol is recommended, action will be initiated as per SOP09/v3.

5.16.7. If suspension/ termination of the study is recommended, action will be initiated as per SOP14/v3.

5.16.8. If change in frequency of continuing review is recommended, the same will be done as per SOP10/v3.

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 or continuing review:

5.17.1. The PI is expected to submit the periodic or continuing review application form at the scheduled time as determined by the YEC-1 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 or continuing 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-1 approval letter.

5.17.4. The PI is expected to submit the periodic and continuing review application 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 or continuing review application as per the schedule or if the PI does not respond to the queries by the YEC-1 within 30 calendar days, then the same is considered as protocol deviation/ violation and action is initiated as per SOP11/v3

5.17.6. If the PI fails to submit the continuing review application form, at least one month before the end of the validity period of the EC clearance,

the PI must not include the data collected within the interim period between expiry of the initial approval and commencement of the continuation of approval.

5.17.7. The Member-Secretary may include failure to submit continuing review form of the protocol, for discussion in the YEC-1 meeting and YEC-1 can decide regarding the status of the ethics committee approval and future submissions by the Principal Investigator

6. **Annexures:**

6.1.1. Ann01/SOP10/v3: Calendar for periodic and continuing review schedule

6.1.2. Ann02/SOP10/v3: Reminder to the Principal Investigator to submit periodic / continuing review application form

6.1.3. Ann03/SOP10/v3: Second reminder to the Principal Investigator to submit the periodic / continuing review application form

6.1.4. Ann04/SOP10/v3: Periodic/ Continuing Review Application Form

6.1.5. Ann05/SOP10/v3: Assessment form for Periodic / Continuing Review Application

6.1.6. Ann06/SOP10/v3: Final Decision form for Periodic/ Continuing review

6.1.7. Ann07/SOP10/v3: Application for extension of the study.

6.1.8. Ann08/SOP10/v3: Approval letter for extension of the study

Ann01/SOP10/v3:

Calendar for Periodic and Continuing review schedule

S. No	Protocol Number	Title of the study	Name of the PI	Date of YEC- 1 Approval	Frequency of continuing review	Submitted on	Date of first continuing review	Reminder sent on	Submitted on

Ann02/SOP10/v3

Reminder to the Principal Investigator to submit periodic and continuing review application form

Date:

Name of the Principal Investigator:

Department:

Reference:

Protocol Number:

Protocol title:

Date of YEC-1 approval:

Date of YEC-1 approval validity:

Frequency of Periodic review:

Subject: Reminder to submit periodic / Continuing review application form

Dear Dr./Mr./Ms. _____

You are requested to submit the duly filled and signed periodic/ continuing review application form to YEC-1 on or before_____.

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

If you are submitting the continuing 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/Jt Secretary/Chairperson, YEC-1

Ann03/SOP10/v3:

Second reminder to the Principal Investigator to submit Periodic / Continuing review application form

Date:

Name of the Principal Investigator:

Department:

Reference:

Protocol Number:

Protocol title:

Date of YEC-1 approval:

Date of YEC-1 approval validity:

Frequency of Periodic/ Continuing review:

Subject: Second reminder to submit Periodic / Continuing review application form

Dear Dr./Mr./Ms. _____

We have not received the Periodic/ continuing 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 / continuing review application form to YEC-1 within 7 calendar days failing which, this will be considered as protocol deviation/violation, and will be suitably dealt with as outlined in SOP11/v3..

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/Jt Secretary/Chairperson, YEC-1

Ann04/SOP10/v3:

Periodic/ Continuing Review Application Form

A. Protocol details

a. Protocol No. _____
b. Title: _____
c. Name of the Principal Investigator:
d. Name of the guide (wherever applicable):
e. Department:

B. Timelines of the protocol:

a. Approved by YEC-1 on _____. Valid until: _____
b. Extension of EC clearance if any: From_____ valid until: _____
c. Amendment approved by YEC-1 if any on _____. Valid until: _____
d. Date of initiation of the study:
e. Date of the last recruitment:
f. Due date for periodic/ continuing review;

C. Version followed

a. Protocol version followed
b. PIS version followed
c. ICF version followed
d. Case record form version followed

B. Sample size details

a. Sample size approved at this site:
b. Number of participants screened so far
c. Number of participants recruited so far
d. Number of participants who are ongoing
e. Number of participants who have completed the study

C. **Withdrawal and discontinuation details**

a. Number of participants who withdrew the consent
b. Reasons for withdrawal of each participant in detail
c. Number of participants who were discontinued from the study by the PI/Sponsor
d. Reasons for discontinuation of each participant from the study with detail

D. Adverse events details

a. Number of participants with adverse events
b. Description of each adverse event in detail
c. Any SAEs reported:
d. If yes, provide details of the reports:

E. Changes in the protocol/ risk to participants:

a. Any changes made in the selection criteria of participants
b. Any changes made in the protocol
c. Any changes made in the study team; any change in guide
d. Any changes in the sample size
e. Any changes in the funding status
f. Any increase in the risk to the participants based on the findings of the current study/new information in literature:

F. Monitoring/ data analysis

a. Has interim data analysis been done? If yes, provide the report.
b. Has the data safety and monitoring board reported? If yes, provide the report?
c. Has YEC-1/ regulatory authorities conducted a site monitoring/ audit? If yes, provide the report

G. Any other:

a. Any investigator(s) have developed a conflict of interest during the conduct of the study
b. Any difficulties/ events faced during the study

Signature of the PI:
Date:

Signature of the Guide if applicable:
Date:

Ann05/SOP10/v3:

Assessment form for Periodic / Continuing Review Application

Categorization of the Periodic/ Continuing 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/v3:

Final Decision form for Periodic/ Continuing review

Protocol Number:

Title of the protocol:

Name of the Principal Investigator:

Department:

Validity of EC clearance: From_____ to _____

Extended validity: From: _____ to _____

Final decision:

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. The study can continue but YEC-1 Audit or Site Monitoring for the protocol is warranted
D. The study can continue after amendments are made in the protocol and are approved by YEC-1
E. The study is suspended until audit report/ site-monitoring report/ other clarification/communications are made satisfactorily
F. The study is terminated.

Signature of Chairperson/Member-Secretary with date

Ann07/SOP10/v3:

Application for extension of the study.

Date:

Name of the Principal Investigator:

Department:

Reference:

Protocol Number:

Protocol title:

Subject: Request for extension of the YEC-1 clearance

Protocol timelines:

a. Date of YEC-1 approval:
b. Dates of Approval of amendments if any:
c. Dates of previous extension of EC clearance if any
d. Date of submission of the last continuing review application form:
e. Any lapse in YEC-1 clearance validity:

Sample size details:

f. Sample size approved at this site:
g. Number of participants screened so far
h. Number of participants recruited so far
i. Number of participants who are ongoing
j. Number of participants who have completed the study

Study duration details:

k. Projected duration of study at the time of first YEC-1 approval:
l. Duration of study completed so far:
m. Expected duration in months to complete the study:

Signature of the PI

Date:

Ann08/SOP10/v3: Approval letter for extension of the study

Subject: YEC-1 Approval Letter for extension of the study

Ref: Protocol no. YEC-1/ titled, " "

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

N	Name	Role in the research team	Designation/ Affiliation
		Principal investigator	
		Guide/ Co-PI	

(Insert rows to add more names)

The YEC-1 has reviewed the continuing review application form dated (DD/MM/YY)

YEC-1 hereby approves the extension of the study for the protocol no. YEC-1/_____/20___ and the related documents as listed in the approval letter dated DD/MM/YY and amendment of the protocol approved, if any, on DD/MM/YY.

The extension of the study 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-1 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-1 at the time of recruitment of the first participant.
8. Obtain written approval of YEC-1 before any proposed change in the protocol (amendment) is implemented in the prescribed format **(Ann01/SOP9B/v3)**
9. Report to YEC-1 any deviation from the guidelines/approved version of the protocol without delay (including change in research team members) in the prescribed format **(Ann01/SOP11/v3** - Initial report and **Ann02/SOP11/v3 -** Detailed report**)**
10. As per the current regulatory guidelines, report to YEC-1 all serious adverse events in the prescribed format **(Ann01/SOP12 v3** - Onsite SAE and **Ann02/SOP12/v3** - Offsite SAE**)** and their follow-up actions.

11. Submit the periodic review as specified by YEC-1 in the prescribed format **(Ann04/SOP10/v3)**
12. Submit continuing review form one month before the end of validity of this approval **(Ann04/SOP10/v3)**
13. Report to YEC-1 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-1 when the data/sample collection is completed in the prescribed format **(Ann01/SOP13/v3)**
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-1 approval letter, as issuing duplicate approval letter is liable to a fee
18. Respond to any communication from YEC-1 pertaining to the study/ auditing/ site monitoring/ others.

All communications with YEC-1 should be by email to ethcom@yenepoya.edu.in

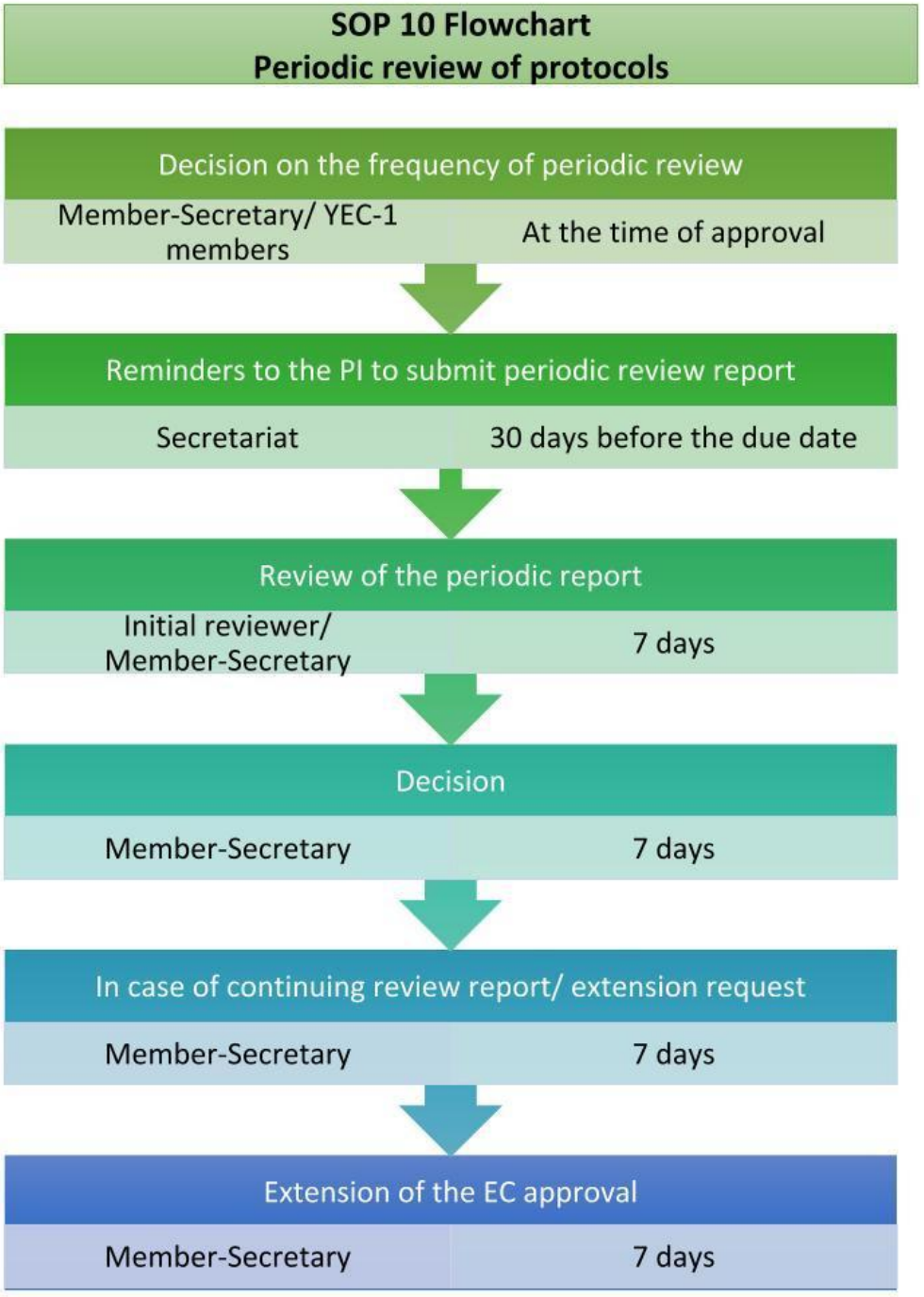
YEC-1 functions in accordance with *(insert names of the current regulations and guidelines)*.

YEC-1 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/Jt Secretary/Chairperson, YEC-1 Date:

Important Dates:
Date of YEC-1 approval: *XX/XX/20XX*
Date of expiry of the validity of YEC-1 approval: *YY/YY/20YY*
Date for initiation of continuing review (if needed): *(write date a month prior to YY/YY/20YY)*

7. **Flowchart:**


SOP 10 Flowchart
Periodic review of protocols
Decision on the frequency of periodic review
Member-Secretary/ YEC-1 members
At the time of approval
Reminders to the PI to submit periodic review report
Secretariat
30 days before the due date
Review of the periodic report
Initial reviewer/ Member-Secretary
7 days
Decision
Member-Secretary
7 days
In case of continuing review report/ extension request
Member-Secretary
7 days
Extension of the EC approval
Member-Secretary
7 days