Title: Protocol Deviations and Protocol Violations: Review and Management

SOP Code: SOP11/v4

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Prepared by:

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Approved by:

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Notified by:

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Details of superseded SOP11

Subcommittee convenor name	Version	Effective date (dd-mm-yyyy)	Describe the main change(s)
Dr. Vina Vaswani	v1.4	10-08-2015	Major revision
Dr. Ravi Vaswani	v2	01-08-2016	Major revision following FERCAP assessment (2016)
Dr. Uma Kulkarni	v3	03-10-2019	Major revision following introduction of NDCTR-19, FERCAP and NABH assessment

Details of current SOP11/v4

Subcommittee convenor name	Version	Effective date	Describe the main change(s)
Dr. Uma Kulkarni	v4	01-07-2023	1. Glossary section added in the SOP 2. Terminology on the decision on the protocol has been revised

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) in response to a non-compliance (NC), protocol deviation (PD) or violation (PV)

2. **Scope:** This SOP applies to research protocols

   2.1. Approved by the YEC-1 in which PD/PV has been identified by the YEC-1 or reported by any of the stakeholders: the PI/sponsor/participant/any other person.

   2.2. Approved by the YEC-1 in which NC by the investigators to regulations/rules/guidelines/YEC-1 terms and conditions has been identified

3. **Definitions:**

   3.1. **Non-compliance: A NC is noted** when the investigator or the trial site fails to

      3.1.1. Respond to YEC-1 requests

      3.1.2. Comply with the applicable national or international guidelines

      3.1.3. Comply with the national regulatory requirements

      3.1.4. Comply with the University/institutional rules and regulations

   3.2. **Protocol Deviation**: A PD is any change, divergence, or departure from the study team, design or procedures of a research protocol that is under the investigator's control and that has not been approved by YEC-1.

   3.3. **Protocol Violation:** A PV is a deviation from the YEC-1 approved protocol that may affect the subject's rights, safety, or well being and/or the completeness, accuracy and reliability of the study data. If a PD meets any of the following criteria, it is considered a PV.

      3.3.1. The deviation has harmed or posed a significant or substantial risk of harm to the research subject. For example

         3.3.1.1. A research subject received the wrong treatment or incorrect dose.

         3.3.1.2. A research subject met discontinuation criteria during the study but was not discontinued.

         3.3.1.3. A research subject received an excluded concomitant medication.

      3.3.2. The deviation compromises the scientific integrity of the data collected for the study. For example

         3.3.2.1. A research subject was enrolled despite not meeting the protocol's eligibility criteria (inclusion/exclusion criteria).

         3.3.2.2. Failure to treat research subjects as per protocol procedures that specifically relate to primary efficacy outcomes. (if it involves patient safety it meets the first category above)

         3.3.2.3. Inadvertent loss of samples or data.

      3.3.3. The deviation is a willful act and a breach of human subject protection regulations, policies, or procedures on the part of the investigator(s). For example

3.3.3.1. Failure to obtain a valid, informed consent prior to initiation of study-related procedures

3.3.3.2. Falsifying research or medical records.

3.3.3.3. Performing tests or procedures beyond the scope of the research question

3.3.4. The deviation involves a serious or continuing noncompliance with national, state, local or institutional human subject protection regulations, policies, or procedures. For example

3.3.4.1. Working under an expired professional license or certification

3.3.4.2. Failure to follow national regulations, and Yenepoya deemed to be University or YEC-1 policies.

3.3.4.3. Repeated deviations.

3.3.5. The deviation is inconsistent with the current national guidelines on research, medical, and ethical principles. For example

3.3.5.1. A breach of confidentiality.

3.3.5.2. Inadequate or improper informed consent procedure.

3.3.6. Any other act from any research team member that significantly increases the risk to participants, causes harm to participants, alters the reliability and credibility of the data

4. **Responsibility:**

4.1. **The YEC-1 Chairperson will**

4.1.1. Lead the discussion in the YEC-1 meeting so that suitable action is taken in case of NC/PD/PVs.

4.1.2. Approve Member-Secretary's recommendation to convene an emergency meeting and assign two or more members to attend the emergency meeting in cases where an urgent decision is required.

4.2. **The YEC-1 Member Secretary will**

4.2.1. Communicate with the PI to seek any clarification or additional information regarding the report

4.2.2. Review the nature of the NC/PD/PV and assess risk

4.2.3. Convene an emergency meeting in cases where an urgent decision is required.

4.2.4. Assign one or more YEC-1 members to review the reports

4.2.5. Place the report of NC/PD/PV in the agenda of the next YEC-1 meeting

4.2.6. Communicate with the relevant authorities (wherever deemed necessary)

4.3. **The YEC-1 member(s) will:**

4.3.1. Review the NC/PD/PV report

4.3.2. Attend the emergency meeting, if nominated

4.3.3. Discuss and deliberate on the report in the YEC-1 meeting

4.4. **The YEC-1 Secretariat will**

4.4.1. Receive the report of NC/PD/PV by the PI or any other person

4.4.2. Ensure that the report is submitted in prescribed format (Ann01/SOP11/v2)

4.4.3. Forward the report to the Member-Secretary

4.4.4. File the PD/PV-related documents along with the concerned protocol files.

4.4.5. Prepare for the emergency meeting whenever needed.

5. **Detailed instructions:**

5.1. **Detection/identification of NC/PD/PV:** NC/PD/PV may be detected/identified in one of (but not limited to) the following ways :

5.1.1. Reported by the principal investigator/research team member/study site/sponsor/contract research organization to the YEC-1.

5.1.2. Reported by YEC-1 members during site monitoring visit/audits documents

5.1.3. Detected by the YEC-1 Member-Secretary or the Secretariat staff from failure of the PI to respond to requests or communications from YEC-1 within reasonable time limit or failure to comply with statutory requirements

5.1.4. Identified during review of annual/periodic reports/SAE reports/any other communication received from the investigator/trial site/sponsor/ study monitor/contract research organization.

5.1.5. Identified during review/audit of study-related documents including reports filed in by the investigator.

5.1.6. Communication/complaint/information/report received from a research participant who has been enrolled or his/her legal representative or any individual who has been approached for enrolment.

5.1.7. Communication brought to the notice of Member-Secretary/ Chairperson of YEC-1 by an independent person.

5.1.8. Communication received from the head of the institution/concerned department about an alleged PD/PV.

5.2. **Initial protocol deviation/violation reporting**

5.2.1. The initial protocol deviation/violation report is sent to the YEC-1 in the duly filled form (Ann01/SOP11/v4) by the person reporting it (PI or others)

5.2.2. The YEC-1 Member-Secretary will look for completeness of the form and request the PI to fill in the detailed response in Ann02/SOP11/v4

5.2.3. If the PI is reporting the PD/PV, they may fill both the initial and detailed protocol deviation reports together (Ann01 and Ann02/SOP11/v4).

5.2.4. In case protocol deviation/violation is detected by any other person (See

Section 5.1) and reported to the YEC-1 the Member-Secretary will write to the PI to submit a protocol deviation/violation as per Ann01/SOP11/v4

5.2.5. If the initial PD/PV is reported by participants/other individuals, YEC-1 may permit the reporting person not to disclose his/her name in the report, if so requested and the name of the individual will be kept confidential.

5.3. **Timelines for NC/PD/PV reporting:**

5.3.1. The investigators are expected to report any PD/PV to YEC-1 within 7 calendar days of noticing it.

5.3.2. The PI must submit the detailed PD/PV report to the YEC-1 within 15 calendar days of receipt of the YEC-1 communication of the initial PD/PV report.. Wherever the Member-Secretary/Chairperson perceives a high risk of harm to research participants, PI may be requested to respond even earlier.

5.3.3. If the PI is reporting the PD/PV, they may fill both the initial and detailed PD reports together (Ann01 and Ann02/SOP11/v4). For multiple PD/PVs, each deviation/violation must be filled in separate forms.

5.3.4. The Secretariat will inform the Member-Secretary of any initial or detailed PD/PV report within 2 calendar days of receipt.

5.4. **Review of the initial protocol deviation/violation report**

5.4.1. The Member-Secretary will scrutinize the initial PD/PV report

5.4.2. The Member-Secretary will communicate with the PI asking for additional information, if required

5.4.3. The Member-Secretary will inform the PI to submit the detailed PD/PV report within the stipulated time

5.5. **Review of the detailed protocol deviation/violation report**

5.5.1. The Member-Secretary will assign one or two members of the YEC-1 to review the report, based on the nature of deviations.

5.5.2. **The reviewers will look at the following:**

5.5.2.1. Nature and seriousness of PD/PV

5.5.2.2. Nature, seriousness and frequency of PD/PVs in this study reported in the past.

5.5.2.3. Nature, seriousness and frequency of PD/PVs in previous/ similar studies conducted by the PI/ Co-PI or in the same department.

5.5.3. The reviewers may recommend one of the following based on the seriousness, impact and urgency:

5.5.3.1. Discussion in emergency meeting of 2 or more members of YEC-1

5.5.3.2. Discussion in the regular YEC-1 meeting

5.6. **Emergency meeting:**

5.6.1. The Chairperson/Member-Secretary will nominate 2 or more YEC-1 members to take part in the emergency meeting.

5.6.2. Emergency meeting will be conducted within 2 calendar days of the decision

5.6.3. Members will deliberate and decide on the action to be taken in case of each PD/PV

5.6.4. The decision/recommendation of the emergency meeting will be communicated to the PI. If additional information/clarification is required from the PI, the same is communicated by the Member-Secretary.

5.6.5. The minutes of the meeting will be tabled for the next YEC-1 meeting

5.7. **YEC-1 meeting:**

5.7.1. **In case where PD/PVs are tabled for discussion in the YEC-1 meeting**

5.7.1.1. The details of the protocol deviations/violations are presented by the YEC-1 Member-Secretary to the members

5.7.1.2. YEC-1 members will deliberate and decide - by majority vote - on the action to be taken in case of each of the NC/PD/PVs

5.7.1.3. If additional information/clarification is required from the PI, the same is noted in the minutes by the Member-Secretary.

5.7.1.4. The decision and recommendation of the YEC-1 is noted in the minutes and communicated to the PI

5.7.2. **In case where minutes of emergency meeting are forwarded to YEC-1**

5.7.2.1. Member-Secretary will summarise the PD/PVs and read out the minutes of the Emergency meeting before the YEC-1 members

5.7.2.2. The decision on the protocol deviation/violation report is ratified

5.7.2.3. If YEC-1 has any further recommendations on the protocol deviation/violation report, the same will be included in the minutes and communicated to the PI.

5.8. **Decision making:**

5.8.1. The decision may be taken in the emergency meeting or in the YEC-1 meeting on the protocol deviation /violation report

5.8.2. The decision will be taken keeping in mind the safety and protection of the participants and their rights and the scientific integrity of the protocol.

5.8.3. The decision will include at least the four following components:

5.8.3.1. Decision on the future of the protocol

5.8.3.2. Recommendation to the PI/ research team

5.8.3.3. Recommendation for the safety of the participants

5.8.3.4. Communications to relevant authorities (if deemed necessary)

5.8.4. **The Decision on the protocol:**

5.8.4.1. No further action required

5.8.4.2. Request information

5.8.4.3. Recommend further action

5.8.5. **Recommendation to the researcher/research team**

5.8.5.1. Recommend deletion/discard of the data (wherever required)

5.8.5.2. Take necessary precautionary steps to prevent PD/PVs in future

5.8.5.3. Undertake training of concerned research team members

5.8.5.4. Reprimand or warn the PI

5.8.5.5. Keep other research protocols from the PI/ Co-PI under abeyance

5.8.5.6. Audit other studies undertaken by PI/Co-PI/department

5.8.5.7. Disallow subsequent applications of research protocols for a specified period of time

5.8.6. **Recommendation for the affected participants/samples**

5.8.6.1. Follow-up participants for as long as the harm potential exists

5.8.6.2. Revisit/re-consent may be taken from the participant (if necessary)

5.8.7. **Communications (whichever deemed necessary)**

5.8.7.1. To the DCGI/ other relevant regulatory authorities

5.8.7.2. To the Sponsor

5.8.7.3. To the Department/ Institution /University

5.8.7.4. To the community

5.9. **Communication of the decision to the PI**

5.9.1. The Member-Secretary will draft the notification letter with the above mentioned decision and recommendation to the PI

5.10. **Records and follow up by YEC-1 secretariat:**

5.10.1. The Secretariat will maintain a copy of the reports, minutes and decision letter in the respective protocol file

5.10.2. As per the decision further action will be initiated as per the respective SOPs by the Member-Secretary

5.10.2.1. Amendment (SOP 09)

5.10.2.2. Audit/ site monitoring visit (SOP 16)

5.10.2.3. Increased frequency of continuing review (SOP 10)

5.10.2.4. Suspension/termination (SOP14)

5.10.2.5. Other actions are recommended.

6. **References:**

6.1. New Drugs and Clinical Trials Rules, 2019 of the Drugs and Cosmetics Act 1940

7. **Annexures:**

7.1. Ann01/SOP11/v4: Protocol Deviation/ Violation Initial Report

7.2. Ann02/SOP11/v4: Protocol Deviation/ Violation Detailed Report

7.3. Ann03/SOP11/v4: Review and decision making on the protocol deviation/violation report

Ann01/SOP11/v4: Deviation/Violation Initial Report

1.	**YEC-1 Protocol no.:**	
2.	**Study Title:**	
3.	**Principal Investigator:**	
4.	**Department:**	
5.	☐ **Protocol Deviation** ☐ **Protocol Violation**	
6.	**Detected/identified by:**	
7.	**Identified/ detected on:**	
8.	**Description of deviation (s)/violation(s):** **(Please use separate form for each deviation/violation and attach supporting documents, if available)**	
9.	**Name of the person reporting the deviation/violation:** **(YEC-1 may keep this confidential if so requested by the reporting person as described in 5.2.5)**	
10.	**Signature with date:**	
11.	**Signature of the Member-Secretary with date**	

Ann02/SOP11/v4: Protocol Deviation / Violation Detailed Report

(To be filled by the Principal Investigator)

1.	**YEC-1 Protocol no.:**	
2.	**Protocol deviation/ violation No: (please fill one form for**	

	each deviation/violation)	
3.	**Study Title:**	
4.	**Principal Investigator:**	
5.	**Department:**	
6.	☐ **Protocol Deviation** ☐ **Protocol Violation**	
7.	**Initial report by:**	
8.	**Date of initial report:**	
9.	**Reported to YEC-1 by:**	
10.	**Description of deviation (s)/violation(s):**	
11.	**Reason (s) for the protocol deviation/violation:**	
12.	**Number of participants/samples affected:**	
13.	**Corrective action already taken:**	
14.	**Corrective action planned:**	
15.	**Number of deviations/violations previously reported with dates**	
16.	**Whether corrective action taken for the same**	
17.	**Signature with date:**	

Ann03/SOP11/v4: Protocol deviation/ violation review and decision form

1.	**YEC-1 Protocol no.:**	
2.	**Protocol deviation Number:**	
3.	**Study Title:**	
4.	**Principal Investigator:**	
5.	**Department:**	
6.	☐ **Protocol Deviation**	

	☐ **Protocol Violation**	
7.	**Name of the reviewer:**	
8.	**Reviewer's comments**	
9.	**Whether there has been an increase in the risk of harm to the participants/ participant rights have been affected**	**Yes:** **No:** **Description:**
10.	**Whether there is a possible impact on the scientific integrity of the study**	**Yes:** **No:** **Description:**
11.	**Provisional Decision by the Reviewer**	
	1.	
	2.	
	3.	
12.	**Final decision by YEC-1**	
	• At the emergency meeting on _____ **• At the YEC-1 meeting on _____** **Final decision:** **Any recommendation:** **Signature of the Member-Secretary/Chairperson** **Date:**	1. No further action required 2. Request information 3. Recommend further action

8. **Glossary:**

DCGI: Drugs Controller General of India

PD: Protocol deviation

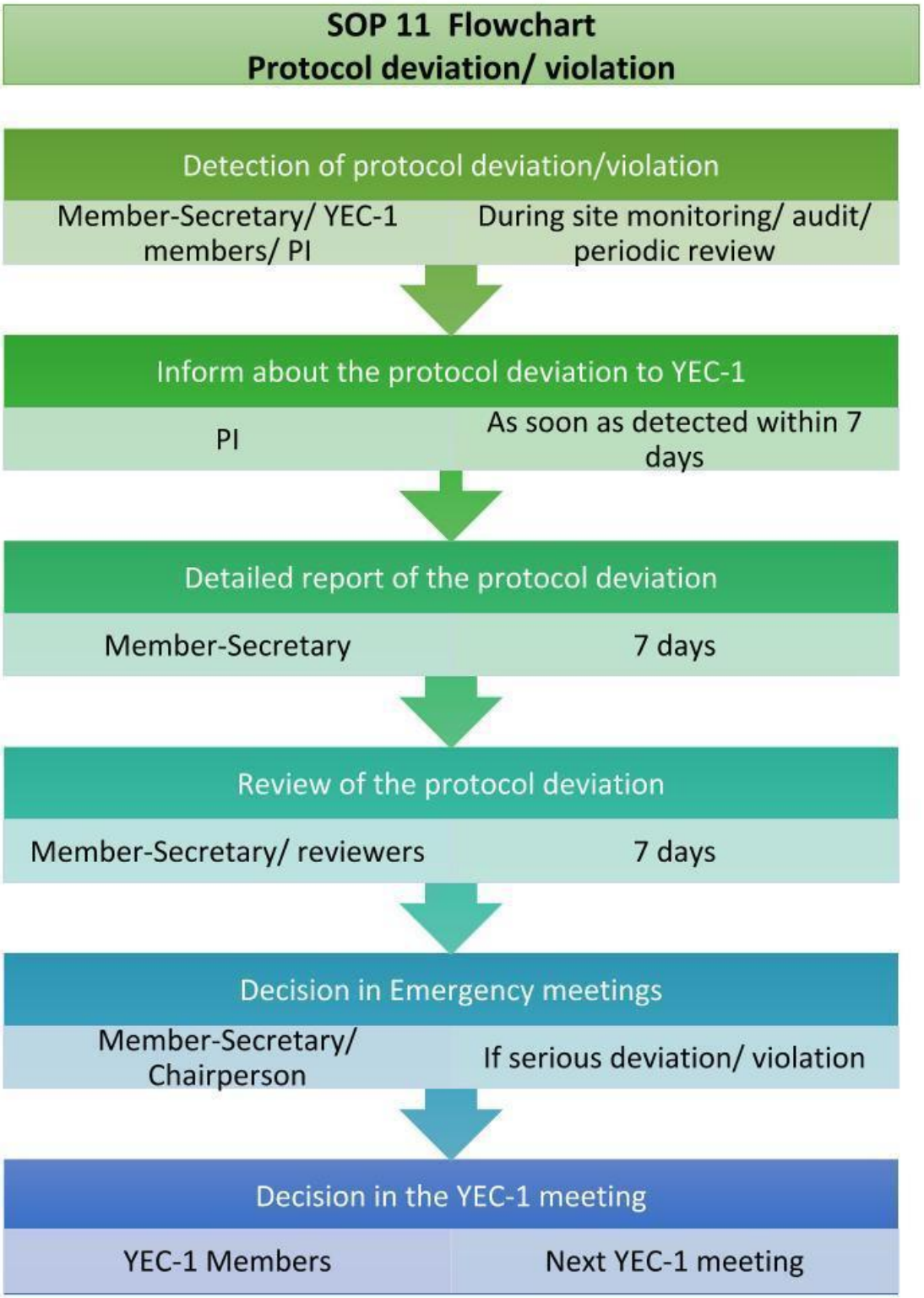
PI: Principal Investigator

Protocol: Refers to a set of documents that contain the detailed components of the proposed study

PV: Protocol violation

NDCTR: New Drugs and Clinical Trials Rules, 2019

9. **Flowchart:**


SOP 11 Flowchart
Protocol deviation/ violation
Detection of protocol deviation/violation
Member-Secretary/ YEC-1 members/ PI
During site monitoring/ audit/ periodic review
Inform about the protocol deviation to YEC-1
PI
As soon as detected within 7 days
Detailed report of the protocol deviation
Member-Secretary
7 days
Review of the protocol deviation
Member-Secretary/ reviewers
7 days
Decision in Emergency meetings
Member-Secretary/ Chairperson
If serious deviation/ violation
Decision in the YEC-1 meeting
YEC-1 Members
Next YEC-1 meeting