Title: Review of Protocol Deviations / Violations

SOP Code: SOP11/v2

Effective Date: 01/08/2016

Prepared by:

Dr. Uma Kulkarni Jt. Secretary, YUEC	Signature with date: 30/07/2016

Reviewed by:

Dr. Vina Vaswani Member-Secretary, YUEC	Signature with date: 30/07/2016

Approved by:

Dr. Sayeegeetha Hegde Chairperson, YUEC	Signature with date: 2/8/16

Notified by:

Registrar, Yenepoya University vide notification no. YUReg/ACA/YUEC/FERCAP/01/2016	Signature with date: 01/8/16 Dr. G. Shreekumar Menon Registrar Yenepoya University Mangaluru - 575 018

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Table of Contents:

1. Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe action to be taken by the YEC-1 when the investigator/ trial site fail to do any of the following:

1.1 Follow the procedures written in the approved protocol

1.2 Comply with national and/ or international guidelines, statutory provisions, institutional guidelines or rules or procedures mandated by the Yenepoya University Ethics Committee for the conduct of human research

1.3 Respond to the YEC-1 requests regarding statutory, ethical, scientific or administrative matter

2. Scope

2.1 This SOP applies to all research protocols involving human research participants approved by the YEC-1

2.2 The SOP applies to any deviation or violation of the protocol as reported by the principal investigator/ sponsor/ participant/ others

3. Responsibility:

3.1 The secretariat:

3.1.1 It is the responsibility of the secretariat to receive any report of deviation or violation of protocol by the principal investigator or any other person

3.1.2 The secretariat will ensure that the report is submitted in the prescribed format (Ann01/SOP11/v2)

3.1.3 It is the responsibility of the secretariat to bring this report to the notice of the Member-Secretary

3.2 The Member-Secretary:

3.2.1 It is the responsibility of the Member-Secretary to place the report of protocol deviation or violation in the agenda of the next YEC-1 meeting

3.2.2 It is the responsibility of the Member-Secretary to initiate the process of discussion and decision making on an urgent basis.

4. Definitions:

[National Institute of Health IRB Professional Administrators Committee Regulatory Process Workgroup Version 5.1,
11/18/2005 Available from
https://www.genome.gov/Pages/Research/Intramural/IRB/Deviation_Violation_examples8-07.pdf]

4.1 Protocol Deviation: A protocol deviation is any change, divergence, or departure from the study design or procedures of a research protocol that is under the investigator's control and that has not been approved by the Institutional Review Board.

4.2 Protocol Violation-A protocol violation is a deviation from the Institutional Review Board 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 the deviation meets any of the following criteria, it is considered a protocol violation. Example list is not exhaustive

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

- A research subject received the wrong treatment or incorrect dose.
- A research subject met withdrawal criteria during the study but was not withdrawn.
- A research subject received an excluded concomitant medication.

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

- A research subject was enrolled but does not meet the protocol's eligibility criteria.
- Failure to treat research subjects per protocol procedures that specifically relate to primary efficacy outcomes. (if it involves patient safety it meets the first category above)
- Changing the protocol without prior IRB approval.
- Inadvertent loss of samples or data.

c. The deviation is a will full or knowing breach of human subject protection regulations, policies, or procedures on the part of the investigator(s). For example

- Failure to obtain informed consent prior to initiation of study-related procedures
- Falsifying research or medical records.
- Performing tests or procedures beyond the individual's professional scope or privilege status (credentialing)

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

- Working under an expired professional license or certification
- Failure to follow federal and/or local regulations, and intramural research or CC policies
- Repeated minor deviations.

e. The deviation is inconsistent with the NIH Human Research Protection Program's research, medical, and ethical principles. For example

- A breach of confidentiality.
- Inadequate or improper informed consent procedure.

4.3 Minor Protocol Deviation: A minor protocol deviation is any change, divergence, or departure from the study design or procedures of a research protocol that has not been approved by the YEC-1 and which does not have a major impact on the subject's rights, safety or well-being, or the completeness, accuracy and reliability of the study data.

5. Detailed instructions:

5.1 Detection of Protocol deviation/ violation:

Protocol deviation/ violation may be detected in one the following ways (but not limited to those listed below):

5.1.1 Protocol deviation/ violation may be reported by Investigator/ study site/ sponsor/ Contract-Research Organization to the YEC-1.

5.1.2 The YEC-1 members performing monitoring of the project at trial site may detect protocol deviation/violation if the project is not been conducted as per protocol/ national/ international regulations.

5.1.3 The Secretariat may detect protocol deviation/ violation from failure to comply with statutory requirements/ failure to respond to requests from YEC-1 within reasonable time limit/ failure to respond to communication made by YEC-1.

5.1.4 The YEC-1 members may detect protocol deviation/ violation when scrutinizing annual/ periodic reports/ SAE reports/ any other communication received from the Investigator/ trial site/ sponsor/ study monitor/ contract research organization

5.1.5 The YEC-1 Secretariat and/ or YEC-1 members may become aware of a protocol deviation/ violation while reviewing study-related documents including reports filed in by the Principal Investigator (PI).

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

5.1.7 Any report/ communication brought to the notice of Member, Secretary/ Jt. Secretary/ Chairperson of YEC-1 by an independent person.

5.1.8 Communication received from the Head of the Institution informing YEC-1 about an alleged protocol violation/ protocol deviation.

5.2 Receipt of protocol deviation / violation report by the Secretariat

5.2.1 The PI will report the protocol deviation/violation as per Ann01/SOP11/v2.

5.2.2 In case protocol deviation/violation is detected by any other person (See Section 5.1) and reported to the YEC-1 (there is no format for

this), the Member-Secretary will write to the PI to submit a protocol deviation/violation as per Ann01/SOP11/v2

5.2.3 The Secretariat will notify the Member-Secretary of any protocol deviation/violation report received from the PI/ from any source within 2 working days of receipt of the notification.

5.3 Actions to be taken:

5.3.1 The action of the YEC-1 will be based on:

- The nature and seriousness of the deviation / violation.
- Frequency of deviation/ violation in the study in the past.
- Frequency of deviation/ violation in previous studies conducted by the same
- PI/ Co-PI or in the same department.

5.3.2 Member-Secretary will decide on the impact of the protocol deviation / violation and act accordingly. Depending upon the seriousness, the YEC-1 shall do the following (not limited to these actions)

- Ask PI for written clarification as soon as the report of deviation is received
- If the impact is serious, this report will be shared with the Chairperson and two or more YEC-1 members designated by the Chairperson.
- If the impact of the protocol deviation is serious enough, the Member-Secretary will instruct the Secretariat to call for an emergency YEC-1 meeting specifically to discuss the issue within 7 working days of the initial scrutiny
- The Secretariat will put up the information and communication at the next YEC-1 meeting for discussion.

5.3.3 The Member-Secretary in consultation with YEC-1 members will review the information available and deliberate on it.

5.3.4 The Chairperson will take a final decision depending on the seriousness of the violation.

5.3.5 The decision will be taken to ensure that the safety and rights of the research participants are safeguarded. The decision will be taken by voting. A majority vote for approval, disapproval or request for modifications of a study suspension or termination of an ongoing study is defined as 2/3rd of the voting members present at the meeting.

5.3.6 The decision taken by YEC-1 could include one or more of the following:

- Determine that no further action is required, or take other actions as appropriate.
- Inform the PI that the YEC-1 has noted the violation / deviation, and instruct the PI to ensure that deviations/ violations do not occur in future and to follow YEC-1 recommendations.
- Enlist measures that the PI would undertake to ensure that such deviations / violations do not occur in future.
- Observe the research or consent process (depending on the nature and frequency of the deviation).
- Suggest modifications to the protocol
- Alter the interval for submission of the continuing review/ annual project status.
- Ask for additional training of the investigator and study team
- Reprimand the PI.
- Seek additional information from the PI.

- Conduct audit of trial by the YEC-1.
- Suspend the study till additional information is made available and scrutinized.
- Suspend the study till recommendations made by the YEC-1 are implemented by the PI and found to be satisfactory by the YEC-1.
- Suspend the study for a fixed duration of time.
- Suspension or termination of the study.
- Revoke approval of the current study.
- Inform DCGI/ other relevant regulatory authorities.
- Keep other research proposals from the PI/ Co-PI under abeyance. Review and/ or inspect other studies undertaken by PI/Co-PI.

5.3.7 This final decision will be recorded on Ann01/SOP11/v2 by the Member-Secretary

5.4 Procedure for notifying the PI and other concerned authorities

5.4.1 The Member-Secretary will draft the notification letter.

5.4.2 The notification signed letter by Member-Secretary will be sent to

- The PI
- The Department Head (if required on case to case basis)
- The Institutional Officials (if required on case to case basis).
- The relevant national authorities (if required on case to case basis)
- The other institutes (if required on case to case basis in case of multi-centric trials)

6. Records and follow up to be kept by YEC-1 secretariat:

6.1 The Secretariat will keep a copy of the notification letter in the respective project file

7. Annexures:

7.1 Ann01/SOP11/v2 - Deviation/ Violation Record

Ann01/SOP11/v2

Deviation / Violation Record

I. Deviation / Violation Report by the Principal Investigator
YEC-1 Protocol no.:
Study Title:
Principal Investigator:
Department:
☐ **Deviation from protocol** ☐ **Violation**
Description of deviation (s)/violation(s):
Corrective Actions Taken by the Principal Investigator (If any):
Reported by (Name of Principal Investigator/ Study Team Member):
Signature with date:

II. Provisional Decision by the Reviewer (Member-Secretary and/or Chairperson and/or YEC-1 Member/s)
□ Noted **□ Request the PI not to perform such deviations/ non compliances/ violations in future** **□ Specific recommendations state below to be followed (to be listed)** **□ Suspend the study till the YEC-1 recommendations are implemented** **□ Suspend the study till information available** **□Terminate approval of the current study (with reasons)** **□Refuse subsequent applications from PI** **□To discuss at the full Board meeting** **□Any other**
Reviewed by **Name/s:** **Signature/s with date:**
III. Final decision by the YEC-1
□ At the meeting on _____ **□ At the YEC-1 meeting on _____** **Final decision:** **Any recommendation:** **Signature of the Member-Secretary/Chairperson** **Date:**

8. Flow charts

No.	Activity	Responsibility
1	Detection and reporting of Protocol deviation/violation	YEC-1 members/ Secretariat/principal investigator
2	Receipt of protocol deviation / violation	Secretariat
3	Review, board discussion, decision and action	YEC-1 Members, Member-Secretary
4	Notify the Principal Investigator/ concerned authorities of YEC-1 action	Secretariat
5	Maintain records	Secretariat