11.1 Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe action(s) to be taken by the IEC when investigator(s)/ trial site(s) fail(s) to:

- follow the procedures written in the approved protocol,
- comply with national and/ or international guidelines, statutory provisions, institutional guidelines or rules or procedures mandated by the Institutional Ethics Committee (IEC) for the conduct of human research,
- Respond to the IEC requests regarding statutory, ethical, scientific or administrative matters.

11.2 Scope

This SOP applies to all IEC approved research protocols involving human research participants.

11.3 Responsibility

The IEC Secretariat is responsible for receiving deviation/ violation reports as per request submitted by the Principal Investigator (PI) /others and placing it on the agenda of the meeting. Reporting of deviation/ violation in any other reporting format will not be accepted.

The IEC members should review and take action on such reports.

11.4 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.pdfAccessed on 3rd June2015]

Protocol Deviation and Protocol Violation:

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 IEC. Upon discovery, the Principal Investigator is responsible for reporting protocol deviations to the IEC using the standard reporting form.

Protocol Violation- A protocol violation is a deviation from the IEC approved protocol that may affect the subject's rights, safety, or wellbeing 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.

I. The deviation has harmed or posed a significant or substantive risk of harm to the research participant. For example,
   - Receiving the wrong treatment or incorrect dose.
   - Withdrawal criteria met during the study but were not withdrawn.
   - Receiving an excluded concomitant medication.

II. The deviation compromises the scientific integrity of the data collected for the study. For example,
   - A research participant who was enrolled does not meet the protocol's eligibility criteria.
   - Failure to treat research participants as 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 IEC approval.
   - Inadvertent loss of samples or data.

III. The deviation is a wilful breach of human participant 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 (credentials)

IV. The deviation involves a serious or continuing noncompliance with central, state, local, or institutional human participant protection regulations, policies, or procedures. For example,

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

V. The deviation is inconsistent with the Human Research Protection requirements in research ethics principles. For example,

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

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 IEC 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.

11.5. Detailed instructions

11.5.1 Detection of Protocol deviation/ violation

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

a. Protocol deviation/ violation may be reported by Investigator/ study site/ sponsor/ Contract-Research Organization to the IEC.
b. The IEC members performing monitoring of the project at trial site may detect protocol deviation/violation if the project has not been conducted as per protocol/ national/ international regulations.
c. The Secretariat may detect protocol deviation/ violation from failure to comply with statutory requirements/ failure to respond to requests from IEC

within reasonable time limit/ failure to respond to communication made by IEC.

d. The IEC 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.

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

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

g. Any report/ communication brought to the notice of Member, Secretary/ Jt. Secretary/ Chairperson of IEC by an independent person.

h. Communication received from the Head of the Institution informing IEC about an alleged protocol violation/ protocol deviation.

5.2 Receipt of protocol deviation / violation report by the Secretariat

1. The PI will report the protocol deviation/violation in the prescribed form.
2. In case protocol deviation/violation is detected by any other person (See Section 5.1) and reported to the IEC (there is no format for this), the Member Secretary will write to the PI to submit a protocol deviation/violation in the prescribed form.
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

1. The action of the IEC 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.

2. Member Secretary will decide on the impact of the protocol deviation / violation and act accordingly. Depending upon the seriousness, the IEC shall do the following (not limited to these actions):
   - Ask PI for written clarification as soon as the deviation is received
   - If the impact is serious, this report will be shared with the Chairperson and two or more IEC 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 and schedule a full-board 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 full committee meeting for discussion.
3. The Member Secretary in consultation with IEC members will review the information available and deliberate on it.
4. The Chairperson will take a final decision depending on the seriousness of the violation. 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 if there is no consensus.

   The decision taken by IEC 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 IEC has noted the violation / deviation, and instruct the PI to ensure that deviations/ violations do not occur in future and to follow IEC 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 IEC.
- Suspend the study till additional information is made available and scrutinized.
- Suspend the study till recommendations made by the IEC are implemented by the PI and found to be satisfactory by the IEC.
- 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.

  This final decision will be recorded by the Member Secretary.

11.5.4 Procedure for notifying the PI and other concerned authorities

The Member Secretary will draft a notification letter.

- The signed letter by Member Secretary will be sent to the PI and Department Head(s) (if required on case to case basis) and Institutional Officials (if required on case to case basis).
- The IEC secretariat will send a copy of the notification to the relevant national authorities (if required on case to case basis) and institutes (if required on case to case basis in case of multi-centric trials).

11.5.5.5Records and follow up to be kept by IEC secretariat

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

6. Annexure 1

Annexure1:AXO1/SOP 11/V1 - Deviation/ Violation Record

Annexure 1AXO1/SOP 11/V1

Deviation / Violation Record

IEC Protocol no.:
Study Title:
Principal Investigator:
Department:
□ Deviation from protocol □ Violation
Description of deviation (s)/violation(s) Corrective Actions Taken by the Principal Investigator: _____ _____ _____

Discussion of the protocol deviation/violation at the

Emergency meeting on _____

Next Scheduled full board meeting on _____

Final decision at the full board meeting held on

_____

Signature with date IEC Member Secretary

7. Flow Chart

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