Title: Review of Protocol Deviations / Violations

SOP Code: SOP 11/V2

Effective Date: 21-10-2019

SOP Constitution and Approval:

Prepared by:	Signature and Date:
Dr. Lokesh. S, IHEC Member	21/10/19
Dr. Siva Ranganathan Green, Member Secretary, IHEC	21/10/19
Dr. Uma Narayanamurthy, Additional Member Secretary, IHEC	Uma. N 21/10/19.
Reviewed by:	**Signature and Date:**
Dr. Ananthakrishnan. N, IHEC Member	21/10/19
Dr. Sivagnanam G, IHEC Co-Chairperson	
Approved by:	**Signature and Date:**
Dr. Jambulingam, P IHEC Chairperson	21.10.19
Dr. Adithan C, Dean Research, SBV	21/10/19
Dr. Ravishankar M, Dean, MGMCRI	21/10

1. Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe action(s) to be taken by the IHEC 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 Human Ethics Committee (IHEC) for the conduct of human research,
- respond to the IHEC requests regarding statutory, ethical, scientific or administrative matters.

2. Scope

This SOP applies to all IHEC approved research protocols involving human research participants

3. Responsibility

The IHEC Secretariat is responsible for receiving deviation/ violation reports as per (AX 01/SOP 11/V2) 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 IHEC members should review and take action on such reports.

4. Definitions

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

Protocol Violation- A protocol violation is a deviation from the IHEC 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.

I. 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.

II. 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 IHEC approval.

• Inadvertent loss of samples or data.

III. The deviation is a willful 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).

IV. 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 policies

• Repeated minor deviations.

V. 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.

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 IHEC 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):

a. Protocol deviation/ violation may be reported by Investigator/ study site/ sponsor/ Contract-Research Organization to the IHEC.
b. The IHEC 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.
c. The Secretariat may detect protocol deviation/ violation from failure to comply with statutory requirements/ failure to respond to requests from IHEC within reasonable time limit/ failure to respond to communication made by IHEC.
d. The IHEC 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 IHEC Secretariat and/ or IHEC 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/ Additional

Member Secretary/ Chairperson of IHEC by an independent person.

h. Communication received from the Head of the Institution informing IHEC 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 as per Annexure 1 AX01/ SOP 11/V2.
2. In case protocol deviation/violation is detected by any other person (See Section 5.1) and reported to the IHEC (there is no format for this), the Member Secretary/Additional Member Secretary will write to the PI to submit a protocol deviation/violation as per Annexure 1 AX01/ SOP 11/V2.
3. The Secretariat will notify the Member Secretary/ Additional 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 IHEC 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/ Additional Member Secretary will decide on the impact of the protocol deviation / violation and act accordingly. Depending upon the seriousness, the IHEC 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 IHEC members designated by the Chairperson.
   - If the impact of the protocol deviation is serious enough, the Member Secretary/ Additional 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 board meeting for discussion.

3. The Member Secretary/ Additional Member Secretary in consultation with IHEC 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. 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 by consensus.
5. The decision taken by IHEC 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 IHEC has noted the violation / deviation, and instruct the PI to ensure that deviations/ violations do not occur in future and to follow IHEC 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 interval for submission of the continuing review/ annual project status.
   - Ask for additional training of investigator and study team.
   - Reprimand the PI.
   - Seek additional information from the PI.
   - Conduct audit of trial by the IHEC.
   - Suspend the study till additional information is made available and scrutinized.
   - Suspend the study till recommendations made by the IHEC are implemented by the PI and found to be satisfactory by the IHEC.
   - 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.

6. This final decision will be recorded on AX01/ SOP 11/V2 by the Member Secretary/ Additional Member Secretary.

5.4 Procedure for notifying the PI and other concerned authorities

- The Member Secretary/ Additional Member Secretary will draft a notification letter.
- The signed letter by Member Secretary/ Additional 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 IHEC 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).

5.5 Records and follow up to be kept by IHEC secretariat

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

6. Annexure

Annexure 1: AX01/ SOP 11/V2 - Deviation/ Violation Record

Annexure 1: AX01/ SOP011/V2

Deviation/ Violation Record

IHEC Protocol no:

Study Title:

Principal Investigator:

Department:

1. Deviation from protocol:
2. Protocol violation:
3. Description of deviation (s)/violation(s):
4. Corrective Actions Taken by the Principal Investigator:

5. Reported by (Name of Principal Investigator/ Study Team Member):

Signature with date:_____

Provisional Decision by Reviewer (Member Secretary/ Additional Member Secretary and/or Chairperson and/or IHEC Member/s)

- Noted
- Request the PI not to perform such deviations/ non compliances/ violations in future
- Specific recommendations stated below to be followed

Specific recommendations stated below to be followed

- Suspend the study till the IHEC recommendations are implemented
- Suspend the study till information available
- Terminate approval of the current study

  Reasons for termination
- Refuse subsequent applications from PI
- To discuss at the full board meeting
- Any other

Reviewed by

Name/s:

Signature/s with date:

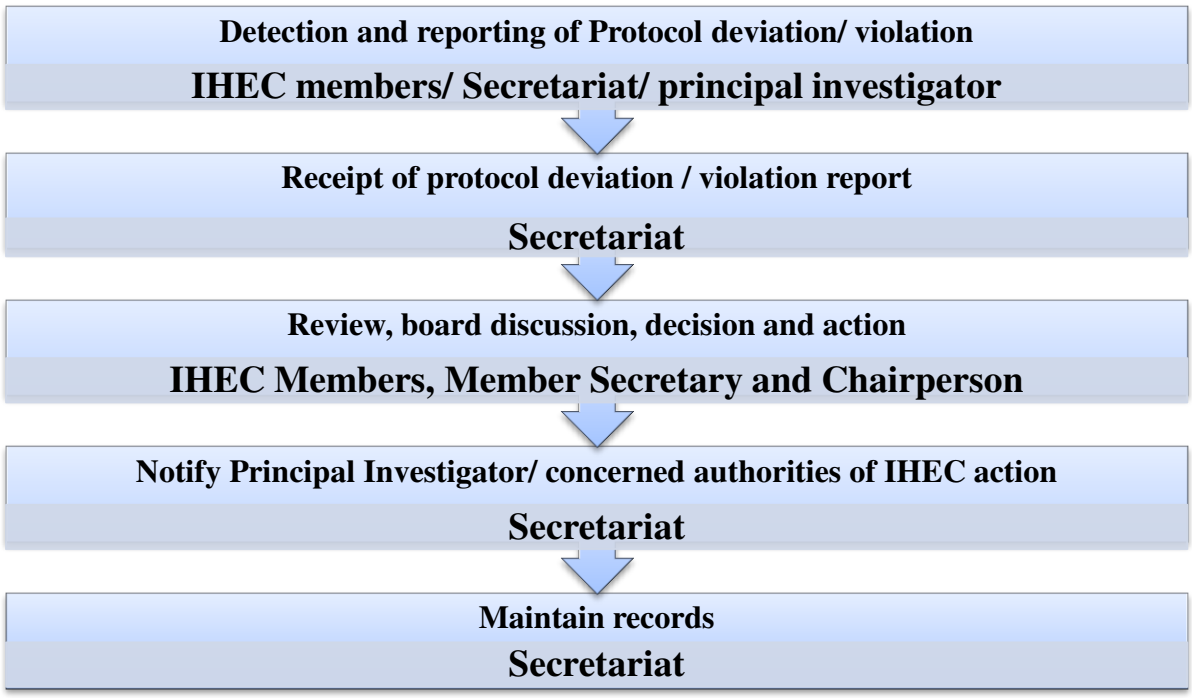
Discussion of the protocol deviation/violation at the

- Emergency meeting on
- Next Scheduled full board meeting on
- Final decision at the full board meeting held on

Signature with date

IHEC Member Secretary

7. Flow Chart



8. References

- *Forum for Ethics review Committees in India (FERCI). Standard Operating Procedures of Institutional Ethics Committee (cited 5th October 2019). Available from: http://www.ferci.org/sops/*
- *Indian Council of Medical Research (ICMR). National Ethical guidelines for biomedical and health research involving human participants, October 2017 (cited 6th October 2019) available from: http://www.icmr.nic.in/guidelines/ICMR_Ethical_Guidelines_2017.pdf*
- *National Institute of Health IRB Professional Administrators Committee Regulatory Process Workgroup, Version5.1,11/18/2005. Available from: https://www.genome.gov/Pages/Research/Intramural/IRB/Deviation_Violation_examples8-07.pdf*