Title: Protocol Deviation/Non-Compliance/Violation

SOP Code: SOP 12/V1 dated 18th February 2017

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1. Purpose

The purpose of this Standard Operating Procedure (SOP) is to provide instructions for taking action(s) 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

2. Scope

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

3. Responsibility

It is the responsibility of the IEC Secretary /Chairperson to bring to the notice of the Full Board if it is brought to their notice that investigators have failed 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 IEC for the conduct of human research
- respond to the IEC requests regarding statutory, ethical, scientific or administrative matters

The Secretariat is responsible for collecting the Deviation/Non-compliance/Violation Form *AX 01/SOP 12/V1* and recording the decision of the IEC in the form.

4. Flow chart

No.	Activity	Responsibility
1	Detection of Protocol deviation/ non-compliance/ violation	IEC members / Secretariat
2	Noting protocol deviation/ non-compliance/ violation	IEC members / Secretariat
3	Board discussion, decision and action	IEC members, Member Secretary and Chairperson
4	Notify the Principal Investigator	IEC Secretariat,
5	Keep records and follow up	IEC Secretariat

5. Detailed instructions

5.1 Detection of Protocol deviation/ non-compliance/ violation

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

1. Protocol deviation/ non-compliance/ violation may be reported by Investigator/ study site/ sponsor/ Contract-Research Organization to the IEC
2. The IEC members performing monitoring of the project at trial site may detect protocol deviation/non-compliance/violation if the project is not been conducted as per protocol/ national/international regulations.
3. The Secretariat may detect protocol deviation/non-compliance/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.
4. The IEC members may detect protocol deviation/non-compliance/violation when scrutinizing annual/ periodic reports/ SAE reports/ any other communication received from the Investigator/ trial site/ sponsor/ study monitor/ contract research organization.
5. The IEC secretariat and/ or IEC members may become aware of a protocol deviation/ non-compliance/ violation while reviewing study-related documents including reports filed in by the Principal Investigator.
6. Communication/ complaint/ information received from research participant who has been enrolled or any individual who has been approached for enrollment
7. Any report/ communication brought to the notice of Member, Secretary/ Jt. Secretary/ Chairperson of IEC by an independent person
8. Communication received from the Head of the Institution informing IEC about an alleged protocol violation/ non-compliance/ protocol deviation

5.2 Noting protocol deviation / non-compliance / violation by the Secretariat

1. The IEC members who have performed monitoring of a particular trial site and detect protocol violation will inform the Secretariat in writing within 2 working days.
2. The Secretariat will notify the Chairperson of any protocol deviation/non-compliance/violation from the project files/protocol deviation/non-compliance/violation letters (soft copy and hard copy) forwarded by the Principal Investigator/ from any source within 7 working days of receipt of the notification from principal investigator (PI) depending upon the seriousness of non-compliance. Whenever protocol violation has been observed, the Chairperson and/ or Member Secretary and /or two or more IEC members designated by the Chairperson of IEC will scrutinize (initial scrutiny) the violation/ non-compliance/ deviation for gravity and implications. This scrutiny could be conducted jointly/ individually at a meeting/ through telephone/ email/ any other mode of communication. The findings shall be documented individually or in the form of report by the IEC Secretary. Depending upon their judgment the IEC shall:

a. Ask PI for written clarification as soon as the deviation is received OR

b. The Secretariat will call for and schedule a full-board meeting specifically to discuss the issue within 7 working days of the initial scrutiny OR

c. The Secretariat will put up the information and communication at the next full board meeting

5.3 Board discussion, Decision and Action

- If the protocol deviation / non-compliance / violation is detected by IEC member during monitoring visit he/she will present the protocol deviation / non-compliance / violation information.
- If detected by Secretariat/forwarded by Principal Investigator, the Member Secretary will present the protocol deviation / non-compliance / violation information.
- The Chairperson/IEC members will review the information available and take a 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. The actions taken by IEC could include one or more of the following:
  - ✓ Inform the Principal Investigator that IEC has noted the violation/ non-compliance/ deviation and;
  - ✓ Direct the PI to ensure that deviations/non-compliances/violations do not occur in future and follow IEC recommendations.
  - ✓ Enlist measures that the PI would undertake to ensure that deviations/non-compliances/violations do not occur in future
  - ✓ Reprimand the PI.
  - ✓ Call for additional information.
  - ✓ Suspend the study till additional information is made available and is 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.
  - ✓ Inform the Institutional Head/ Director/Dean.
  - ✓ 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.
  - ✓ Refuse to review subsequent applications from an investigator cited for non-compliance for a specified duration of time.
  - ✓ Any other action considered appropriate by the IEC for safeguarding the interests of the research participants participating in the current trial or in future trials.

- The action that the IEC will be based on:
  - [1] The nature and seriousness of the deviation / non-compliance/violation
  - [2] Frequency of deviation / non-compliance/violation in the study in the past
  - [3] Frequency of deviation / non-compliance/violation in previous studies conducted by the same PI/ Co-PI or in the same department
- This action will be recorded on *AX 01/SOP 12/V1* by the Member Secretary.

5.4 Notifying the Principal Investigator

- The Secretariat will send a notification signed by the IEC Chairperson to the Principal Investigator **within 14 days of the meeting,** if the decision was 'request the Principal Investigator not to perform such deviations/non-compliances/violations in future'.
- The Secretariat will send a project suspension/termination letter signed by the IEC Chairperson to the Principal Investigator **within 1 working day of the meeting,** if the decision was 'suspend the study till further information available/terminate approval of the current study'
- If the decision was 'refusal of subsequent project applications from the Principal Investigator, this notification letter signed by IEC Chairperson will be sent to the Principal Investigator **within 14 days of the meeting**.
- One copy of all letters shall be kept in the project file by the Secretariat.

6. Glossary

Non-compliance / Violation	The IEC monitors whether investigators do not perform the study in compliance with the approved protocol, ICH GCP, FDA regulations and/or fail to respond to the IEC request for information/action.

7. References

[1] World Health Organization, Operational Guidelines for Ethics Committees that Review Biomedical Research, (Geneva 2000) - *www.who.int/tdr/publications/publications/* (last accessed 31st August 2013)

[2] International Conference on Harmonization, Guidance on Good Clinical Practice (ICH GCP) 1996- *http://www.ich.org/LOB/media/MEDIA482.pdf* (last accessed 31st August 2013)

8. Annexure

Annexure 1 *AX 01/SOP 12/V1* Deviation/Non-Compliance/Violation Record

Annexure1

AX 01/SOP 12/V1

Deviation / Non-Compliance / Violation Record

IEC Protocol no.:	
Study Title:	
Principal Investigator:	
Department:	
☐ Deviation from protocol ☐ Violation	☐ Non-Compliance
Description of deviation (s)/violation(s) Corrective Actions Taken by the Principal Investigator:	
Reported by (Name of Principal Investigator/ Study Team Member): Signature with date:	

Provisional Decision by the Reviewer (Member Secretary and/or Chairperson and/or IEC Member)

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

_____

_____

- ☐ Suspend the study till the IEC recommendations are implemented
- ☐ Suspend the study till information available
- ☐ Terminate approval of the current study
  Reasons for termination

_____

_____

- ☐ Refuse subsequent applications from an investigator cited for non-compliance.
- ☐ To discuss at the full Board meeting
- ☐ Any other _____

Reviewed by
Name:
Signature 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
Chairperson / Member Secretary