Standard Operating Procedures of Institutional Ethics Committee

ICMR – NIRRCH Ethics Committee for Human Studies

Title: Intervention in Protocol Deviation/Violation /Non-compliance

SOP Code: 19/V1.5 Dated: 8th November 2024 Page Nos: 228 to 237

19.1. 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:

1. Follow the procedures written in the approved protocol
2. 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
3. Respond to the IEC requests regarding statutory, ethical, scientific, or administrative matters

19.2. Scope

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

19.3. Responsibility

The member Secretary/a designated member of the Secretariat is responsible for collecting the protocol deviation/violation/non-compliance report and placing it in the agenda of the full committee meeting (**AF/01/19/V1.4**).

19.4. Flow chart

Sr. No.	**Activity**	**Responsibility**
1	Noting protocol deviation / violation/non-compliance	IEC members and Chairperson
2	Determine action as protocol deviations/ violations/ non-compliance	IEC members and Chairperson
3	To review the protocol deviations	IEC members
4	Ethics Committee's discussion and decision	IEC members and Chairperson
5	Notify the investigator	IEC Secretariat and Chairperson
6	Keep records and follow up	IEC Secretariat

19.5. Detailed instructions

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

1. When IEC is informed about Protocol deviation/ violation/ non-compliance by
    a. Investigator/study site sponsor/ Contract-Research Organization
    b. Potential or enrolled participants submitting complaint/information

2. Detection by the Member Secretary/Secretariat when scrutinizing annual/periodic reports / SAE reports-
    a. when scrutinizing annual/periodic reports / SAE reports
    b. Failure to comply with statutory requirements
    c. Failure to respond to requests/communications made by the IEC within reasonable time limit.
    d. During site monitoring visit.
    e. Communication by research team/participant/third party

3. Communication/ complaint/ information received from research participant who has been enrolled or any individual who has been approached for enrolment Investigator herself/himself reports protocol deviation/ violation/non- compliance and waiver.

Note: The difference between protocol deviation and protocol waiver is that the latter is approval obtained from IEC prior to implementing departures from the protocol.

19.5.1 Definitions

a. Protocol non-compliance

Failure or refusal to comply with law/ national or international regulation or guidelines/ policies and requirements set by IEC. The following can fall under this category (refer to detailed instructions at 5 and this is not a comprehensive list).

i Recruitment administering only English consent forms when the participant is not well versed with English PIS & ICD
ii Delay in submitting Continuing Review Report/ Completion or Final Report
iii Delayed response to IEC minutes
iv A breach of confidentiality.
v Working under an expired professional license or certification

b. Protocol Deviation (Minor)

A protocol deviation is any change, divergence, or departure from the Study design or procedures of an IEC approved research protocol initiated by the investigator which is of a minor nature not increasing the risk. The Principal Investigator is responsible for reporting protocol deviations to the IEC using the standard reporting form. The following can fall under this category but may not be comprehensive list.

i Extending recruitment beyond the approval date
ii Follow up visit a day or two later than the fixed date (within permissible window).
iii Approvals of collaborating centers are lacking
iv Change in sample size/ methodology
v Change in study sites/ collaborators without informing EC

c. Protocol Violation (Major protocol deviations)

A protocol violation is accidental or intentional deviation or departure from the study design and procedures without approval of IEC and sponsor that may affect the participant's rights, safety, or wellbeing and/or the completeness, accuracy and study data integrity and has harmed or posed a significant or substantive risk of harm to the research participant. If the deviation meets any of the following criteria, it is considered a protocol violation. Examples given in the following list are not exhaustive.

1. A research participant has received the wrong treatment (medication or dose)
2. A research participant had met withdrawal criteria during the study but was not withdrawn.
3. A research participant received an excluded concomitant medication.
4. A research participant is not recruited as per eligibility criteria.
5. Sample size more than the approved number.
6. Failure to obtain informed consent and/or assent prior to initiation of study-related procedures
7. Inadequate or improper informed consent procedure.
8. Changing the protocol without prior IEC approval.
9. Inadvertent loss of samples or data.
10. Falsifying research or medical records.
11. Performing tests or procedures beyond the individual's professional scope or privilege
12. Status (credentialing)
13. Incorrect or missing tests
14. Mishandled samples
15. Recruiting participants without or before EC approving the protocol
16. Not reporting AE/SAEs as per prescribed timelines
17. Multiple visits missed or outside permissible window
18. Publications not within the approved sample size/study sites/ methodology
19. Repeated or too many minor deviations

19.5.2 Noting the protocol deviation /violation/non-compliance reports

The Secretariat will receive 1 copy (soft and hard) of Protocol deviation/violation/non-compliance Report filled as per the format – AF/EC/01/19/V1.4 with covering letter from the Principal Investigator.

It is the responsibility of the IEC Secretariat to review the report for completeness. If necessary, the IEC secretariat will retrieve the master file from the archives with permission of the Member Secretary. The Secretariat shall forward the Report along with protocol deviation Form AF/EC/01/19/V1.4 and covering letter to the Member secretary.

19.5.3 Categorize the protocol deviations

The member secretary will categorize the issues as protocol deviations as minor or major (violations) and non-compliance and place it in the agenda of next IEC meeting.

The PI/Member Secretary will present a brief oral summary of the protocol deviations/violations/non-compliance and the comments of the IEC members/Chairperson in the IEC Full committee meeting.

19.5.4 Review process

The Chairperson / member secretary / primary reviewers will review the submitted protocol deviations/violations/non-compliance issues and assess the impact of the deviation on the safety wellbeing of the participants and data integrity of the study along with risk benefit analysis.

The Chairperson/member secretary / IEC members will review the available information and take a decision depending on the seriousness of the matter.

The decision will be taken to ensure that the safety and rights of the research participants are safeguarded. The decision will be taken by consensus / voting if there is no consensus. The actions taken by IEC could include one or more of the following:

1. Inform the Principal Investigator (PI) that IEC has noted the non-compliance /deviation /violation
2. Call for detailed additional information from PI if EC cannot come to a decision .
3. Reprimand and warn the PI to ensure that non-compliance/deviations/violations do not occur in future and follow IEC recommendations
4. Enlist measures that the PI would undertake to ensure that non-compliance/ deviations/violations do not occur in future. This could include refresher GCP training.
5. If PI is still non-compliant then submission of new projects from PI will not be accepted for two consecutive meetings or 4 months whichever is earlier
6. Suspend the study until additional information is made available and recommendations made by the IEC are reviewed and found satisfactory by IEC before being implemented by the PI .
7. Inform the Institutional Head/Director/Dean.
8. Revoke approval of the current study.
9. Inform DCGI/ Other relevant regulatory authorities.
10. Keep other research proposals from the PI/ Co-PI under abeyance till reviewed and audited by IEC (inspection is by regulator).
11. 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 decision of the IEC will be based on:

[1] The nature and seriousness of the non-compliance /deviation /violation

[2] Frequency of non-compliance /deviation / violation in the study in the past

[3] Frequency of non-compliance /deviation / violation in previous studies conducted by the same PI/ Co-PI or in the same department.

This action will be recorded by the Member Secretary.

19.5.5 Record and communicate the decision to the PI.

1. The decision will be communicated to the PI within 14 days except if the decision is project suspension/termination, which will be communicated to the Principal Investigator within 1 working day of the meeting.
2. The Secretariat will record the decision reached on the protocol deviation / violation in the minutes of the meeting.

19.6. ANNEX

ANNEX 1	AF/01/19/V1.4	Protocol Deviation/ violation/ non-compliance Reporting Form (Reporting by case)
ANNEX 2	AF/02/19/V1.4	Document History

ANNEX 1 **AF/01/19/V1.4**

Protocol Deviation/ Violation/ Non-compliance /
Reporting Form (Reporting by case)

	Protocol /Deviation/ Violation /Non-compliance Reporting Form (Reporting by case) **ICMR-NIRRCH Ethics Committee for Human Studies**

Project No. …… Duration of the study:.....
Title of study:……
……

Principal Investigator (Name, Designation and Affiliation): …… ……..
Co-PIs/Collaborators (Name, Designation and Affiliation): ……

……

1.Date of EC approval : ……

2.Date of start of study: ……

3.Participant ID: ……

4.Tick the correct option:

a. Non-compliance b. Deviation c. Violation

Sr. No.	Option	Definition with example
1	Non compliance	Failure or refusal to comply with law/ national or international regulation or guidelines/ requirements set by IEC. 1. Recruitment administering only English consent forms when the participant is not well versed with English PIS & ICD 2. Delay in submitting Continuing Review Report/ Completion or Final Report 3. Delayed response to EC minutes
2	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. 1. Extending recruitment beyond approval date 2. Recruitment without consent 3. No consent with assent 4. Approvals of collaborating centers are lacking 5. Change in sample size/ methodology 6. Change in study sites/ collaborators without informing EC

3	Violation	A protocol violation is a deviation from the IEC approved protocol that may affect the participant's rights, safety, or wellbeing and/or the completeness, accuracy and reliability of the study data. 1. A enrolled research participant does not meet the protocol's eligibility criteria. 2. Change in the protocol without prior IEC approval. 3. Loss of samples or data inadvertently. 4. Failure to obtain informed consent prior to initiation of study-related procedures 5. Falsifying research or medical records. 6. Performing tests or procedures beyond the individual's professional scope or privilege 7. Status (credentialing) 8. Recruiting participants without EC approving the protocol 9. A breach of confidentiality. 10. Inadequate or improper informed consent procedure. 11. A research participant has received the wrong treatment 12. A research participant had met withdrawal criteria during the study but was not withdrawn. 13. A research participant received an excluded concomitant medication. 14. Failure to treat research participants per protocol procedures that specifically relate to primary efficacy outcomes. 15. Working under an expired professional license or certification 16. Failure to follow federal and/or local regulations, and intramural research policies 17. Repeated minor deviations

5. Date of occurrence:. ……

6. Total number of non-compliance/ deviations /violations reported till date in the study:

……

7. Non-compliance /Deviation/Violation identified by:
    a. Principal Investigator/study team
    b. Sponsor/Monitor
    c. SAE Sub Committee/EC
8. Is the deviation related to (Tick the appropriate):
    a. Consenting
    b. Source documentation
    c. Enrolment

d. Staff/Sites
e. Laboratory assessment
f. Participant non-compliance
g. Investigational Product
h. Safety Reporting
i. Publication
j. Others *(specify)*.....

9. Provide details of Non-compliance/ Deviation/Violation:

……

……

10. Corrective action taken by PI/Co-PI: ……

……

……..

11. Impact on (if any): Study participant/ Quality of data

12. Are any changes to the study/protocol required? Yes/ No

If yes, give details**……**

……

Signature of PI with date : ……

ANNEX 2 **AF/02/19/V1.4**

Document History

Author	Version	Date	Description of the Change
Dr. Ragini Kulkarni	Version 1.0	20th March 2013	First approved copy
Dr. Ragini Kulkarni	Version 1.1	24th September 2014	SOP no. changed from SOP 11 to SOP 16
Dr. Ragini Kulkarni	Version 1.2	7th November 2017	Added the line in 5.2 'Retraining of the study team members may be recommended if required'. Added in ANNEX 1 'Impact of the deviation on patient safety/data credibility'
Dr. Beena Joshi	Version 1.3	1st May 2019	SOP no. changed from 16 to 19 ICMR Common Ethical Review form for Protocol Violation/Deviation Reporting Form (Reporting by case) added as Annex 1
Dr. Vikrant Bhor	Version 1.4	8th November 2024	All bullets are numbered. ● Extensive modifications done in description