Category : Study conduct-All studies (Government funded/NGO funded/Regulatory)

Title : Dealing with protocol deviations and violations in any clinical study

SOP No / Version No. : 20/08

Date first effective: 01 Jan 2026 Review date: 31 Dec 2026

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SOP No / Version No.: 20/08 **Total pages:** 10

Date first effective: 01 Jan 2026 **Next Review date:** 31 Dec 2026

Version: 08

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1. Table of Contents

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1. **Purpose:**

This standard operating procedure (SOP) describes the responsibilities of the research team towards procedures to be followed in the event of protocol deviations and violations in investigator initiated or pharma sponsored studies.

2. **Scope**

This SOP is limited to describing procedures while dealing with protocol deviations and violations in any clinical study.

3. **Responsibilities:**

Principal investigator, Co-investigator, Study Coordinator or any other appropriately qualified staff in the team, as delegated by the Principal Investigator, will be responsible for proper documentation and reporting of all study related protocol deviations and violations.

4. **Applicable rules, regulations and guidelines**

- National Ethical Guidelines for Biomedical and Health Research involving Human Participants (2017), https://ethics.ncdirindia.org/ICMR_Ethical_Guidelines.aspx, last accessed on 1st Jan2026.
- New Drugs and Clinical Trials Rules (2019), https://cdsco.gov.in/opencms/opencms/en/Acts-and-rules/New-Drugs/, last accessed on 1st Jan2026.
- ICH HARMONISED GUIDELINE GOOD CLINICAL PRACTICE (GCP) E6(R3), https://database.ich.org/sites/default/files/ICH_E6%28R3%29_DraftGuideline_2023_0519.pdf, last accessed on 1st Jan2026.
- India GCP guidelines (Draft, September 2024), https://ethics.ncdirindia.org/asset/pdf/Indian_GCP_guideline.pdf, last accessed on 1st Jan2026.

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- National Ethical Guidelines for Biomedical Research Involving Children.https://ethics.ncdirindia.org//asset/pdf/National_Ethical_Guidelines_for_BioMedical_Research_Involving_Children.pdf last accessed on 1st Jan2026.
- Standard-Operating-Procedures of Institutional Ethics Committee, Seth GS Medical College and KEM Hospital, Mumbai https://www.kem.edu/wp-content/uploads/2025/03/SOPs_V7_effective_from_9th_Dec_2024_Seth_GSMC_&_KEMH_Mumbai.pdf V7-effective-from-9th-Dec-2024_.pdf (last accessed 10th Dec, 2025)

5. Reference to other applicable SOPs

SOP No / Version No: 03/08: Responsibilities of the study team

SOP No / Version No: 05/08: Administering and documenting informed consent

SOP No / Version No. 17/08: Continued communication with Ethics Committee

SOP No / Version No 21/08: Contact and communication with sponsor

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6. Detailed instructions

1. During the conduct of the research, there may be either planned or unplanned changes made to the approved research protocol. Amendments are changes to the approved research protocol. As a rule usually any planned change(s) in the planned protocol must be reviewed and approved by the Institutional Ethics Committee prior to implementation (Refer SOP No / Version No. 17/08: Continued communication with Ethics Committee), except when necessary to eliminate apparent immediate hazards to the participant.
2. If a planned change is made to eliminate apparent immediate harm to the participant, then this type of change can be initiated without prior Institutional Ethics Committee approval. However, the Institutional Ethics Committee must be notified in writing within 24 hours giving specific justification for such an occurrence (SOP No / Version No. 17/08 Continued communication with Ethics Committee).
3. **Case Definitions:-**

   A **protocol deviation** is defined as any unplanned or unintentional departure from the protocol, Investigator's Brochure, approved informed consent process, or applicable regulatory requirements, occurring after Institutional Ethics Committee (IEC)/Independent Ethics Committee (IEC/IRB) approval. Such deviations are generally not implemented prospectively and typically do not have a significant impact on participant rights, safety, or well-being, nor on the reliability of study data. In accordance with ICH GCP E6(R3), all protocol deviations must be documented, evaluated for their impact on participant safety and data integrity, and managed through appropriate corrective and preventive actions (CAPA), as applicable.

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A **protocol violation** is defined as a significant or serious non-compliance with the approved protocol, Good Clinical Practice (GCP), or applicable regulatory requirements that may affect the rights, safety, or well-being of trial participants, or compromise the integrity and reliability of study data. Protocol violations may arise from failure to adhere to protocol-specified procedures, inadequate oversight, or systemic non-compliance. In line with ICH GCP E6(R3), such violations require prompt identification, documentation, root cause analysis, and implementation of corrective and preventive actions (CAPA). Reporting to the sponsor and IEC/IRB must be performed within defined timelines, especially for violations that meet criteria for serious non-compliance.

A **protocol exception** is defined as a prospectively planned and approved departure from the protocol for an individual participant or a specific situation, granted prior approval by the IEC/IRB (and sponsor, where applicable), in accordance with ICH GCP E6(R3). Protocol exceptions are implemented when strict adherence to the protocol is not feasible but where participant safety, rights, and data integrity are not compromised. These exceptions are not considered protocol amendments and do not constitute permanent changes to the protocol. All protocol exceptions must be justified, documented, and approved prior to implementation, except where necessary to eliminate immediate hazards to participants, in which case the deviation must be reported promptly to the IEC/IRB.

4. If the study is a sponsored study, prior approval of the sponsor is also required for a protocol exception except in an emergency situation to eliminate immediate harm (SOP No / Version No 21/08: Contact and communication with sponsor)
    a. Protocol violations represent instances of non-compliance implemented without prior IEC/IRB approval, contrary to the requirement for prospective review and approval of protocol changes, except where necessary to

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eliminate immediate hazards to trial participants. Such violations may arise due to unintentional human error, inadequate oversight, or systemic process deficiencies, or may reflect willful or deliberate non-compliance by the Principal Investigator or study team. In alignment with ICH GCP E6(R3), all such occurrences must be promptly identified, documented, and evaluated to determine their impact on participant safety, rights, and data integrity. A root cause analysis should be undertaken, and appropriate corrective and preventive actions (CAPA) must be implemented to prevent recurrence. Serious or persistent non-compliance should be reported to the IEC/IRB and sponsor in accordance with applicable regulatory timelines and may warrant further actions, including increased oversight, suspension, or termination of study activities

5. The study team should attempt to minimize these occurrences. Protocol violations may be:
   - **Major violations**: An act that may impact the participant's safety or posed a significant risk/harm to a research participant and/or compromised the scientific integrity of the data collected or confounded the scientific analysis of the study results which can affect the participant's willingness to participate in the study.
   - **Minor violations**:

     An act that represents a less significant non-compliance with the approved protocol, which does not have a meaningful impact on the participant's safety, rights, or well-being, and does not compromise the scientific integrity or reliability of the study data. These do not affect the overall risk–benefit assessment of the study or the participant's willingness to continue participation but should be documented, monitored, and reviewed periodically to ensure they do not recur or indicate systemic issues.

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Reviewer as appropriate:

Signature with date

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