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Category: Study conduct

Title: Preparing for Monitoring and audit

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1. Purpose:

This standard operating procedure (SOP) describes the responsibilities of the Principal Investigator (PI) and the study team in its preparation for a monitoring and audit visit.

2. Scope:

This SOP is limited to the responsibilities of the study team in its preparation for a monitoring and audit visit.

3. Responsibilities:

PI, Co-investigator (Co-I), Study Co-ordinator, or any other appropriately qualified staff in the team, as delegated by the Principal Investigator, will be responsible for the implementation of this SOP.

4. Applicable rules, regulations and guidelines

- Indian GCP Guidelines 2001
  https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/download_file_division.jsp?num_id=MzM5NQ==

- National Ethical Guidelines for Biomedical and Health Research involving Human Participants ICMR, 2017
  https://www.indiascienceandtechnology.gov.in/sites/default/files/file-uploads/guidelineregulations/1527507675_ICMR_Ethical_Guidelines_2017.pdf

- ICH-GCP E6 (R3) Draft Guidelines dated 19th May 2023
  https://database.ich.org/sites/default/files/ICH_E6%28R3%29_DraftGuideline_2023_0519.pdf.

5. Refences to other SOPs:

- SOP No: D 18/06: Archiving documents

6. Detailed instructions

6.1. The purpose of study monitoring/audit is to verify that:

- The rights, safety and well-being of human participants are protected.
- Reported data are accurate, complete, and verifiable.
- The study is conducted in compliance with the protocol and applicable guidelines and regulations.

6.2. The PI must permit monitoring and auditing by Institutional Ethics Committee (IEC) members, regulators and/or sponsors at all times that is asked by the authorities.

6.3. At the same time the PI and study team should ensure that no document (original or copy) which allows the identification of a participant in the study is shared with the inspectors unless insisted upon by regulators and IEC members. Sponsor representatives should at no time be given access to documents that permit identification of a participant.

6.4. The PI should be available throughout the monitoring.

6.5. The study coordinator should ensure availability of a suitable location for monitoring.

6.6. The PI and study coordinator must ensure the availability of all team members for the monitoring.

6.7. The study coordinator must ensure that all relevant documents of the study (including but not limited to the following) are available for the monitor viz.

- Trial master file(s) [TMF(s)]
- Case Record Forms (CRFs) and Source documents
- Participant Informed Consent Forms (ICFs)
- Participant's medical files
- Documents related to the Investigational Product (IP).
- Documents related to the sample collection, storage, and shipment.
- All documentation related to Adverse Events (AEs) / Serious Adverse Events (SAEs)
- Documentation or correspondence with IEC

6.8. Study coordinator should ensure that all documentation (including lab reports) is complete including PI signatures, prior to monitoring/audit. The signature of PI should be obtained in real time.

6.9. The study coordinator should confirm the identity of monitors upon arrival by checking their identity cards.

6.10. Measures to ensure site preparedness for a monitoring visit or an audit are mentioned in Appendix 1 and 2.

7. Appendices

Appendix 1: Preparedness for monitoring by the sponsor [1]

	How to ensure site preparedness
Pre-Study monitoring/ visit	• Keep the SOPs of the site ready and ensure that all SOPs are current and valid. • Keep the IEC SOPs / URL where they can be found ready. • Ensure that all instruments relevant to the study e.g. refrigerators, centrifuges, Electrocardiogram (ECG) machine, weighing balance, sphygmomanometer, height measurement apparatus [as applicable to the study] are calibrated and the calibration certificates are ready for inspection by the monitor. • Ensure documentation for controlled access (Audio-Video consenting area, pharmacy room, document archival area, clinical pharmacology unit /outpatient department etc.) for all study areas is available for examination by the monitor. • Ensure documentation for updated emergency tray and all requisite instrumentation calibration and functioning (for example ECG, defibrillator, ventilator) so that these can be checked and verified by the monitor. • Ask for a report of the pre-study visit

Site initiation visit	• Prepare specific questions related to operational aspects of the study which can be discussed with the sponsor at the time of site initiation. • Ensure that the entire team is present on the day of the site initiation. • Confirm supplies received [investigational product (IP), Trial master file (TMF), laboratory kits etc.] from the sponsor/CRO. • Ensure that any deficiencies identified during the pre-study visit have been addressed. • Ask for a report of the site initiation visit report. When received, file in the TMF
Routine monitoring visit	• Confirm a clear understanding among the team members of individual roles and responsibilities. • Ensure that all study team members are available. • Ensure a quiet area is available for monitoring. • Ensure proper documentation of Case Record Form (CRF) including signatures, updated TMF and other study related logs. • Arrange all case sheets, CRFs and TMFs clearly and sequentially. • Ensure that all documents are returned to their original place after monitoring. • Enquire regarding findings at the end of the visit. • Ensure that medical records and files are kept in a locked room if monitoring lasts for multiple days. • Discuss the findings in a formal interview and resolve as many findings as possible. • Tentative dates for the next visit may be discussed. • File the monitoring report/ follow up reports sent by the monitor in the TMF

Close out visit	• Ensure that all study team members are available. • Make necessary arrangements for retrieval of study related documents. • Provide secure area for archiving documents for a specific period as per sponsor's SOP. • In the case of hard copies, confirm that all case report forms are retrieved and submitted to sponsor and copies archived. • Ensure that all extra CRFs, study supplies and laboratory kits are returned to the sponsor/CRO. • Ensure that all biological samples have been shipped or back-up samples are destroyed as per site SOP and protocol. • Make sure that the final report provided by the monitor is placed in the TMF. • All electronic data should be archived as mentioned in the protocol and as per sponsor policy. • Send a copy of the final monitoring report to the IEC and close the study with IEC

Appendix 2: Site Preparedness for a sponsor or a regulatory audit

How to ensure preparedness
• Ensure a secure room and study team availability on the day of audit. • Ensure that the TMF is updated per site SOP. • Ensure subject screening/enrollment log and the duty delegation log are up to date. • Keep the initial IEC approval letter in the TMF and latest amendment approvals if changes have been made to the study. • Ensure that all correspondence (signed/dated applications, responses, e-mails) to and from the IEC and sponsor are filed.

- Ensure re-consenting [if applicable] has been completed and documented.
- Make sure protocol deviation/violation report has been submitted to the IEC and the IEC correspondence is filed in the TMF.
- Ensure all IEC correspondence of SAE report(s), if any, are available in the TMF.
- Ensure data collection, source documents and IP accountability log for each participant are up to date.
- Ensure that samples collection, storage and shipment logs are updated.
- Make sure that the audit log is up to date in case the site was audited previously.
- Keep all study hard copies in a cupboard with restricted access.
- Ensure that access to electronic study records and files are password protected.

Reference *[1]*. Ravi R, Bose D, Gogtay NJ, Thatte UM. Investigator preparedness for monitoring and audits. Perspect Clin Res 2018; 9:95-8

8. Glossary

a. Definition of Monitoring:

The act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, standard operating procedures (SOPs), GCP, and the applicable regulatory requirement(s).

b. Definition of Audit:

An audit is a systematic and independent examination of trial related activities and documents to determine whether the evaluated trial related activities were conducted, and the data were recorded, analyzed, and accurately reported according to the protocol, sponsor's SOPs, GCP, and the applicable regulatory requirement(s).

9. Abbreviations:

i.	AE	: Adverse Event
ii.	Co-I	: Co-Investigator
iii.	CRF	: Case Record Form
iv.	CRO	: Contract Research Organization
v.	ECG	: Electrocardiogram
vi.	GCP	: Good Clinical Practice
vii.	ICF	: Informed Consent Form
viii.	ICH	: International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use
ix.	ICMR	: Indian Council of Medical Research
x.	IEC	: Institutional Ethics Committee
xi.	IP	: Investigational Product
xii.	PI	: Principal investigator
xiii.	SAE	: Serious Adverse Event
xiv.	SOP	: Standard Operating Procedure
xv.	TMF	: Trial Master File
xvi.	URL	: Uniform Resource Locator

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