Standard Operating Procedure
Clinical Research Secretariat (CRS)

Title: Preparing for Audit/ Inspection or Site inspection/audit readiness

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18.1. Purpose:

Aim of this Standard Operating Procedure is to guide the clinical team in its preparation for an audit and inspection.

18.2. Scope:

This Standard Operating Procedure is applicable to all institutional personnel working in clinical research study.

18.3. Procedure:

18.3.1 Information:

This SOP follows the principle inherent in Good Clinical Practice of the ICH concerning verification/audit and inspection of all aspects of a clinical study.

An audit is a systemic and independent examination of trial related activities and documents to determine whether the trial related activities were conducted, and the data were recorded, analyzed, and accurately reported according to the protocol, standard operating procedures, good clinical practice (GCP), and the applicable regulatory requirement(s).

Inspection is an official examination by regulatory authorities of documents, facilities, records, and any other resources that are deemed by the authorities to be related to the clinical trial and that may be located at the site of the trial, at the sponsor's and/or contract research organizations (CROs) facilities, or at other establishments deemed appropriate by the regulatory authorities.

No particular reason is needed to conduct an audit or an inspection directed towards the sponsor/sponsor-investigator or investigator's site.
There are two types of audits: routine audits and for-cause audits.

Routine audits are often performed by the sponsor, IRB, internal quality assurance department. The goal of an audit is to review, inspect and verify the ethical conduct of human subject research, integrity of previously reported data, adherence to the study protocol, and applicable institutional, state and federal regulations and guidance's. Most audits involve the review and inspection of informed consent forms, documentation of the consent process, reported data, regulatory records, source documents to ensure protocol compliance and drug accountability records. The auditors may also request to review the site's internal standard operating procedures (SOPs) for conducting human subjects research and copies of the research team's credentials and documentation of training to ensure appropriate delegation of specific research tasks.

For-cause audits may be conducted if during the monitoring process a sponsor has continual documented accounts of possible noncompliance, data discrepancies or concerns over the ethical conduct of the study by the investigator. The IRB or sponsor can themselves audit or can appoint third party for audit in such cases.

The criterion most cited for the selection of a site is the high number of research participants, who contribute to its result. An audit is an informal and planned process and can take place prior to, during or after the patient recruitment phase. A regulatory inspection is very often notified, however there are exceptions if the Competent Authority has concerns for patient safety or grounds to suspect that improper practices are occurring at a site. Under these circumstances, a "triggered" inspection will take place whereby inspectors have the legal right of entry to inspect premises at any time without notification.

18.3.2 Preparations for an audit or inspection visit:

- The following Personnel, where appropriate, should be available to answer questions and to attend the final meeting before the auditor/Inspector leaves the site:

  - Principal Investigator and research personnel
  - Personnel from other departments involved in the audit/inspection such as pharmacy, laboratory (departments should be intimated beforehand if the auditor/inspector intends to visit)

- The investigator will always get information in advance and in writing, of a planned visit for audit or inspection purposes.
- Investigator and Auditor/ Inspector both parties will agree on a date so that study team will get a sufficient period to prepare for the visit. But, in case of suspicion of fraud, inspector can arrive without notice.

18.3.2.1 Planning the visit Prior to an inspection:

Principal investigator should organize and plan the visit with the help of study team members. All records must be made available (direct access) for monitors, auditors and regulatory authorities. It is important to address the following

a. Logistic aspect of the visit:

- Establish the name(s) of the inspector(s), the scope of the inspection and agree all dates in advance.
- The study coordinator and other team members should be given a timetable of events and all roles and responsibilities agreed.
- For commercial trials sponsor and study monitors should be informed about the audit/inspection, they will act as a key liaison between the sponsor (if commercial company) and the Investigator's study team, providing support to ensure that the personnel and site are ready for an inspection.
- Identify and book suitable place/meeting room for the inspection, including space for all trial documents to be reviewed. Ensure that the room is tidy before the inspection
- Ensure that a photocopier and a telephone are available;
- Ensure, in case photocopies of study documents are made, entries of the same should be

made in Document tracking log and this log should be retained with the essential documentation of the study.

- It should be recalled that no document (original or copy) identifying a research participant (nominative data) should leave the institution. If a photocopy of such documents is provided to any stakeholders outside the hospital premises on demand, the participant identifiers must be masked and not visible.
- Ensure that all the documents will be available promptly, in response to any possible request during the visit.
- Ensure that research team personnel, including the investigator, will be available to provide explanations or to answer questions for at least a part of the visit.
- If applicable, ensure that other departments involved in the study will be informed of this visit and their concerned authority should be available, if need, example: pharmacy, laboratory, ward etc.
- If applicable, ensure that arrangements will be made to translate documents or to facilitate communication during the visit;
- Organize refreshments such as tea/coffee/biscuits but no lunch or extras as this can be viewed as an enticement? so to be avoided?
- Principal Investigator should provide inspection training/mock interviews for staff to prepare for an inspection and document in their training records.

b. Preparation for Inspection/Audit visit

An inspector will be looking for a number of things during the inspection process including:

- Verify that the original documents are available
- Essential documentation of the study as described in annexure 8,
- Medical files and other source documents with adherence to following defined measures:

  - Records should be accurate, complete, legible, attributable, original and timely
  - Data should be consistent with the source documents, or discrepancies explained.
  - Document explaining all deviations from protocol and explain.
  - Any changes should be initialed, dated and signed
  - Document all dose/therapy modifications, visits and tests not conducted
  - Data verification will check CRF's for completeness, looking at data queries, lab results, ECG's, X-rays etc., protocol details/ number in notes, concomitant medication, adverse events, adherence to study specific procedures, bio-sample storage temperature log.

- Case Report Forms (CRFs).
- Informed Consent Forms for all research participants, Investigator notes regarding verbal consents (if applicable), Consent notes and Consent comprehension notes
- Pharmacy log (management of investigational products), dispensing log, temperature log, document regarding drug shipments if applicable, and any other document related to the study.
- Standard Operating Procedures of clinical trial site.
- Any other log as described by the sponsor.
- Site Master File/ Investigator Master File

- Approval and correspondence- ethics approval with all correspondence with ethics committee,
- Laboratory – manual, reference normal ranges, reports, accreditation records and procedures
- Protocol and amendments (signed and dated), Information leaflet and consent form (all current updated versions), previous version of protocols, indemnity and all correspondence between sponsor and investigator, sample CRF, study safety reports.
- Personnel – CV's (signed and dated) of those working on study, training record (such as GCP), duty delegation log
- Drugs – Shipping record, drug receipt (possibly held in pharmacy), sample of labels, accountability, security and dispensing log
- Patient Details – Screening/enrolment/identity logs, randomization log, SAE reports Interim or annual reports/ Continue review applications submitted to Ethics Committee
- Any monitoring documentation
- Data collection training documentation, eCRF completion guideline

Above mentioned document list is commonly inspected for any study inspection. You may refer to Annexure 8 for a comprehensive list as required.

- It is the responsibility of PI/CO-I and study team members to check the information contained in all these documents is complete, up-to- date and in agreement with the data or source documents.

- It is important that:
  - Documents are up to date, reviewed and that staff are familiar with location and content
  - There is a clear Audit trail o Relevant documents bear dates and version numbers
  - A Tracking log is kept, if documents are updated (evidence of distribution and receipt)
  - Patient hospital notes should include up to date annotations, copy of consent form, laboratory results, X-ray results etc. related to participation in the clinical trial
  - Staff delegation logs are kept up to date for any change of personnel

8.3.2.2 Conduct of an audit or inspection:

Verify the identity of the auditors or inspectors from the regulatory agency at the time of arrival.

- For reasons of confidentiality, while they are in the institution, auditors or inspectors should always be accompanied by a member of the research team.
- Inspection by a regulatory agency can extend from a few days to a week or more if necessary.
- Inspection visits normally start with an introductory meeting prepared by the auditors or inspectors.
- The meeting is followed by the evaluations of conduct of the study.
- Review of the study documentation is carried out during this type of visit. Auditor/ Inspector

will review documentation as stated in point A

- The auditors or the inspectors can ask to visit locations where study procedures are carried out; consequently, it is important to notify the affected departments before this visit.
- At the end of the visit, the auditors or inspectors often hold a meeting with the research team and the investigator. Auditors/ inspector will provide verbal feedback of the findings, followed by a detailed written inspection report. Each finding is referred to the particular regulation/guideline to which it is attributed. A reply to the report is required.
- This meeting allows for the clarification of elements or the correction of deficiencies noted during the visit.

8.3.3 Audit Report:

- Following inspection by a regulatory agency, a written report is submitted to the sponsor and follow-up communication to the investigator listing the observations or deviations noted during the inspection.
- All the deficiencies should be addressed with the proper corrective measures. These measures should be documented and transmitted in writing to the regulatory agency within the allotted time frame.
- In case of Sponsored trials, investigator should immediately contact the sponsor or the sponsor-investigator who will assist with the drafting of the required corrective measures, and their implementation.

8.4. Applicable Staff:

- All the study team members