

Standard Operating Procedure

Types of Audit

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1. ABBREVIATIONS

ASST-PG23:	Azienda Socio Sanitaria Territoriale – Papa Giovanni XIII
CAPA:	Corrective and Preventing Action
CRF:	Case Report Form
CSR:	Clinical Study Report
FROM:	Fondazione per la Ricerca Ospedale Di Bergamo
GCP:	Good Clinical Practice
ISF:	Investigator Site File
QAM:	Quality Assurance Manager
SOP:	Standard Operating Procedure
TMF:	Trial Master File

2. SCOPE

This SOP defines the types of audits to be carried-out to verify the compliance to SOPs, GCP and regulatory requirements when performing clinical trials and the suitability of processes applied and systems used for managing those trials.

3. FIELD OF APPLICATION

This SOP applies to clinical trials sponsored and/or supported by FROM or sponsored by ASST-PG23.

4. RESPONSIBILITIES

Operational Director

- Approves the trial audits to be performed upon QAM's proposal.

Quality Assurance Manager (QAM)

- Suggests the audits to be performed

Auditor

- Performs and manages the audit according to the SOP Audit Management (CQA01)

5. PROCEDURE

According to GCP regulation an audit is a systematic and independent examination of trial related activities and documents to determine whether the evaluated activities were conducted, and the data were recorded, analyzed and accurately reported according to the protocol (in case of clinical trial audit), SOPs, GCP, and applicable regulatory requirements.

Trial specific audits are those performed across a single trial regardless of the stage of development.

System audits are those conducted to verify the organization, the quality management system, and management of specific system to be applied in relation to clinical trials.

The audits to be performed are identified and suggested by QAM (e.g. Annual Audit Plan) and approved by the Operational Director. They are managed according to the SOP **Audit Management (CQA01)**.

According to the Determina n.809/2015 dated June 19th, 2015, at least one trial specific audit and one system audit must be performed on yearly basis at the Phase I units.

The Operational Director is also responsible for the auditor's identification and appointment with the support of the QAM who is responsible to verify the auditor's qualification according to the Italian Decree dated 15th November 2011 on the minimum requirements of a CRO.

5.1.1 Trial specific audit at an Investigational site

This type of audit is aimed to verify if an Investigational Site performs trial related activities in accordance with approved trial documentation, organization's SOPs, GCP and clinical trial regulations.

The date of the audit is agreed between the Auditor and the reference person of the organization to be audited. The audit duration is estimated by the auditor taking into consideration the type and the stage of the clinical trial and the number of patients enrolled.

The audit should be prepared by the auditor by means of reading the trial protocol/amendment, manuals, CRF, contract, monitoring visit reports and other documents pertinent to the type of audit.

At the investigational site the auditor is responsible for undertaking the following audit steps:

- Conduct an opening meeting with the auditee and the involved staff to discuss the purpose and the procedures of the audit, and to ascertain tasks and responsibilities delegated to each member of the staff.
- Interview the reference person of the auditee and the staff involved in the trial.
- Review the trial and quality system documentation.
- Visit the facilities.
- Conduct a closing meeting with the site staff.

Findings/observations noted during the audit will be communicated during the closing meeting and clarification could be sought by the auditor on any outstanding issue.

The auditee will be informed about the management of the Audit Report, the Audit Certificate and the CAPA plan.

On-Site audits should be conducted throughout the study period, usually prior to the database lock. All investigational sites participating in clinical trials may be audited.

Usually the On-Site audits are performed at the ASST-PG23 but also other sites involved in a trial sponsored by FROM or ASST-PG23 could be audited.

The selection of the investigational sites to be audited is mainly driven by the following criteria:

- higher/quicker recruitment than other participating sites;
- high rate of patient dropouts;
- greater/smaller number of SAE than other participating sites;
- greater number of protocol and GCP deviations;
- at random;
- "for cause" (in case a suspicion/evidence of malpractice).

The main activities to be performed by the auditor are:

- Interview the Principal Investigator and trial staff about the trial conduct, any critical issue and trial related procedures such as Informed Consent discussion with potential subjects/patients, drug accountability, biological sample management etc.
- Review of the ISF taking into consideration the SOP **Trial Files (CLI06)**.
- Check of all versions of the signed Informed Consent versus the hospital records.
- Check of data registered in the CRFs versus source documents (the percentage and the type of data to be verified is decided for each single trial).
- Check the timeframe of the SAEs notifications to the FROM/ASST-PG23 and/or delegate (as identified in the protocol) to verify if the SAEs have been reported in due time.
- Verify the management of the queries.
- Visit the facilities, including pharmacy and/or drug stockroom and laboratories to confirm their adequacy and performance.

5.1.2 System Audit

The purpose of this audit is to assess the performance of a complete system (e.g. laboratory, pharmacy) or a specific process within a system (e.g. training management, data management). Audits at GCP critical service providers are considered as system audits.

Depending on the system, and therefore on the facilities, to be audited different kinds of checks can be performed. As examples:

- Organization and staff qualification.
- Quality Management System and its application.
- Certification/accreditation.
- Facilities/equipment and relevant documentation.
- Document management/archive.
- Information Technology / Computer System Validation.

6. REFERENCES

- Guideline for good clinical practice E6(R2) (CPMP/ICH/135/95).
- Norma UNI EN ISO 13485:2003 Medical devices — Quality management systems — Requirements for regulatory purposes.
- Decree dated 15.11. 2011 Definition of the minimum requirements which CRO shall satisfy in order to work within clinical trials with medicinal product.
- Determina n.809/2015 dated June 19th, 2015 inerente i requisiti necessari per le strutture sanitarie che eseguono sperimentazioni di fase I di cui all'art.1 del decreto del Presidente della Repubblica 21 settembre 2001, n.439 e di cui all'art.31, comma 3 del decreto legislativo 6 novembre 2007, n.200.
- Q&A alle Determine AIFA n. 809/2015 e n. 451/2016 inerenti ai requisiti minimi necessari per le strutture che eseguono sperimentazioni di Fase I (08 luglio 2019).

7. TEMPLATES

None.

8. VERSION HISTORY

Version	Date	Reason for revision
1	30 Sept 2016	Starting document.
2	28 Feb 2020	<ul style="list-style-type: none"> • Deletion of the audit to be carried-out on trial specific documents. • Deletion of the audit to be carried-out at laboratories. • Inclusion of a general chapter regarding System Audits.