1. Purpose

The audit processes followed by the Office of Sponsor and Regulatory Oversight (OSRO) for ensuring that target organizations follow Good Clinical Practices (GCP), current Good Manufacturing Practices (cGMP) and Good Laboratory Practices (GLP) regulations are outlined.

2. Scope

2.1. This standard operating procedure defines the procedures for planning, conducting, and reporting of compliance audits of

2.1.1. OSRO Quality Management System and ancillary programs (Quality, Operations, Safety, Regulatory and Pharmaceutical Management).

2.1.2. Facilities that manufacture investigational products for which OSRO holds the Investigational New Drug Application (IND), Investigational Device Exemption (IDE) submission or Non-Significant Risk Device Study (NSR).

2.1.3. Commercial partners that manufacture investigational products for Center for Cancer Research (CCR) clinical trials and hold the INDs or IDEs for these products.

2.1.4. CCR clinical trials for which OSRO is the sponsor.

2.1.5. Contract research organizations, pharmaceutical companies, institutions, service providers and other collaborators affiliated with CCR clinical trials for which OSRO is the sponsor.

2.1.6. Facilities used to support CCR clinical trials for which OSRO is the sponsor including clinical research facilities, investigational product storage or preparation, human subject specimen storage or testing, and/or endpoint data generation or collection.

2.2. Limitation

2.2.1. This procedure does not apply to clinical study-specific monitoring that are described within a study protocol.

3. Responsibilities

3.1. OSRO Quality manages the audit system.

3.1.1. The OSRO Sponsor and Regulatory Oversight Support (SROS) Contractor assists OSRO Quality as needed.

3.2. OSRO personnel shall participate in audits of their Functional Groups.

3.3. The OSRO Director approves audit schedules, plans and reports.

4. References

4.1. 102 Audit Policy

4.2. 104-S01 Corrective and Preventive Action (CAPA) System

4.3. ICH E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1) Guidance for Industry (FDA), March 2018

4.4. ISO 19011:2018 Guidelines for Auditing Management Systems

4.5. All applicable Codes of Federal Regulations for GCP, cGMP and GLP based upon the audit scope

5. Definitions

Refer to the OSRO Lexicon.

6. Procedure

6.1. Any one of the following audit types will be used depending on the audit scope and objective.

6.1.1. System audit

6.1.1.1. The system audit verifies that a management system is appropriate and effective.

6.1.2. Process audit

6.1.2.1. The process audit verifies that processes are working within established limits. For example:

- Process parameters are met
- Resources are adequate for process performance
- Written procedures exist and are followed

6.1.3. Product audit

6.1.3.1. The product audit examines a product or service to evaluate whether it conforms to requirements and specifications.

6.2. Audits may use any one or more of the following methods depending on scope, risk and history.

6.2.1. On-site visit,

6.2.2. Remote via video conferencing (e-audit), or

6.2.3. Questionnaire.

6.3. The OSRO audit program will focus on three (3) units.

6.3.1. OSRO systems,

6.3.2. CCR clinical trials for which OSRO serves as sponsor, and

6.3.3. Suppliers and vendors who support these CCR clinical trials.

6.4. OSRO Quality maintains the audit schedule.

6.4.1. The schedule may be used to provide evidence to regulatory agency inspectors that audits are scheduled and performed per procedure.

6.4.2. Audits should be scheduled with sufficient advance notification to the Auditee.

6.4.2.1. For Cause audits should be scheduled with little advance notification to the Auditee.

6.4.3. The audit schedule for OSRO Functional Groups is set with input from other OSRO members.

6.4.3.1. Each Functional Group should be audited once per year.

6.4.4. The audit schedule for suppliers/vendors is set with input from OSRO Operations, Safety and Pharmaceutical Management.

6.4.4.1. Each supplier/vendor should be audited once per year via a questionnaire.

6.4.4.2. More in-depth audits by e-audit or on-site audit are recommended to occur every 2 years.

6.4.4.3. If any product quality issues arise, then a For Cause audit is warranted (see Step 6.9).

6.5. Internal OSRO Audits

6.5.1. The audit focus will be the effectiveness of the links between the Functional Group's procedures and the major quality systems, e.g., training, deviation system, and CAPAs.

6.5.1.1. Compliance with procedures will be assessed.

6.5.2. Internal audit reports will not be provided to regulatory agency inspectors.

6.6. Supplier/Vendor Audits

6.6.1. Material, product, or service will be evaluated based upon the risks to the clinical trial.

6.6.2. Compliance with written specifications, written procedures and government regulations will be assessed.

6.6.3. An audit may be scheduled for numerous reasons, including but not limited to:

- Initial qualification of a supplier/vendor,
- Routine scheduled audit,
- Non-conformance of material received from a supplier, or
- A change in product, service, or manufacturing facility.

6.6.4. Vendors are classified as one of the following:

6.6.4.1. Approved – a supplier who has been audited and deemed capable of consistently meeting required standards.

6.6.4.2. Approvable – a supplier who has been audited and deemed capable of consistently meeting required standards after initiating appropriate corrective actions.

6.6.4.3. Disqualified – a supplier who has been audited and found to have deficiencies in consistently meeting standards.

6.7. Clinical Trial Audits

6.7.1. A clinical trial audit will only occur for cause when a significant GCP violation has been observed.

6.7.2. The audit focus will be the assessment of overall GCP compliance.

6.7.2.1. Operational methods used by the site will be evaluated.

6.7.3. The audit process will emphasize the Food and Drug Administration's (FDA's) ALCOA standard: Attributable, Legible, Contemporaneous and Complete, Original and Accurate.

6.7.4. The audit is divided into the following components:

6.7.4.1. Facility tour

6.7.4.2. Data review

6.7.4.3. Staff Interviews

6.7.4.4. Pharmacy

6.7.4.5. Laboratory

6.7.4.6. Cold-chain and storage

6.7.4.7. Regulatory binder

6.7.4.8. Electronic records

6.8. The Audit Process

6.8.1. Audits can be conducted by internal OSRO resources or utilizing resources of the OSRO support contract.

6.8.2. Before the Audit

6.8.2.1. The Auditor creates the audit plan detailing the audit's scope, audit type (Step 6.1), audit method (Step 6.2), and when the audit will occur and the duration.

6.8.2.1.1. The OSRO Quality Head and OSRO Director approve the audit plan.

6.8.2.2. The audit agenda is sent to the Auditee.

6.8.3. During the Audit

6.8.3.1. The audit is initiated by the Auditor holding an opening meeting which states the purpose of the audit, briefly describes the audit process, reviews the agenda, and finalizes the logistics.

6.8.3.2. Depending on the audit type and method, the Auditor may request to view operations, tour areas, interview personnel, and/or review documentation.

6.8.3.3. The Auditee ensures that key personnel are available during the audit.

6.8.3.4. The Auditee ensures all requests are fulfilled, and if one cannot be, provides justification.

6.8.3.5. If the Auditee was audited previously by OSRO, then any observations found in the last audit should be reviewed.

6.8.3.6. If an audit extends over multiple days, then each day, the Auditor provides an end of day verbal summary to the Auditee, detailing any areas of concern that might be listed as an observation.

6.8.3.7. At the end of the audit, a closeout meeting to discuss the findings of the audit will be conducted with the Auditee.

6.8.4. The Audit Report

6.8.4.1. The Auditor drafts the audit report.

6.8.4.2. The OSRO Quality Head and OSRO Director approve the audit report.

6.8.4.3. After approval, the Auditor sends the audit report to the Auditee and relevant site management.

6.8.5. Audit Responses

6.8.5.1. A written response addressing observations will be required from the Auditee.

6.8.5.2. Responses should include a statement of the corrective action(s) completed or planned and the date by which the corrective action(s) was or will be completed.

6.8.5.3. Verification that corrective actions have been implemented shall be documented after one or both of the following:

6.8.5.3.1. Next routine audit.

6.8.5.3.2. Additional follow-up measures depending on the severity of the issues (i.e. requiring further evidence of corrective action, moving up the next scheduled audit date, etc.).

6.8.6. Audit Closure

6.8.6.1. If no observations are identified during the audit, then the audit is considered closed when the audit report is approved and the Auditee confirms report receipt.

6.8.6.2. If observations are identified during the audit, then the Auditee should create a CAPA per its internal procedure. Once the CAPA is executed and completed, the audit is closed.

6.9. For Cause Audits

6.9.1. A For Cause audit is requested by the OSRO Director when a failure to implement quality systems or repetitive failure is suspected or is found.

6.9.1.1. The audit should occur with little or no advance warning to the Auditee.

6.9.2. The OSRO Director instructs OSRO Quality to perform the For Cause audit and provides the information needed to create an audit plan.

6.9.3. The OSRO Director determines if reporting to a regulatory body, e.g., the FDA, is warranted.

6.10. OSRO Quality archives the audit report and audit-related documents.

7. Associated Documents

7.1. 102-S01-W01 Conducting Internal OSRO Audits

7.2. 102-S01-W02 Conducting Vendor Audits

7.3. 102-S01-W03 Conducting CCR Clinical Trial Audits

8. Change Summary

Revision Number	Effective Date	Description of Change
1	29JUN2021	New Document
2	16NOV2021	Added Steps 3.1.1 and 4.5. Step 2.1.2. – added "or Non-Significant Risk Device Study (NSR)" Step 6.8.6 – added "and the Auditee confirms report receipt" Corrected spelling and semantic errors. General updates to procedure.
3	06SEP2023	Biennial review Step 4 – added hyperlinks Updated document language as required