

Purpose of the audit program

- Verify study data that could affect the interpretation of primary study endpoints by checking compliance to protocol and regulatory requirements and accuracy of submitted data
- Assessment of trial related activities and documents for adherence to Good Clinical Practice (GCP)
- Provide educational support for data quality and data management practices

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Scheduling of Audits



- New LAPS, Members, NCORPs within 18 months of first patient registration
- New affiliates, components at next parent institution audit
- Institutions audited at least once every three years but remain at risk for more frequent audits
- FDA registration studies more frequent monitoring

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FDA Registration Study Site Visits



- LungMAP initial audit at three months after first registration to a sub-study, then every six months
- \$1418, \$1806, \$1914 initial audit at six to nine months after first registration, additional site visits dependent on accrual
- S2302 (Pragmatica) will be audited on same schedule as treatment audits

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On-Site Versus Off-Site Audits



On-site

- LAPS / Main Member / NCORP
- Component / affiliate with large accrual
- FDA registration study site visits for sites requesting onsite audits

Off-site

- Most NCORP components and Main Member affiliates audited off site with parent institution
- Most FDA registration study site audits can be audited off site

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Notification Process



- Scheduled three to four months prior to the audit.
- Formal notification/case list by email four to six weeks prior to the audit.
- Includes detailed instructions on how to prepare for the audit and Site Questionnaire for audit planning.

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The Audit Team • QA representative • One or more Nurse or CRA auditors • NCI-CTMB observer occasionally in attendance XSWOG → NCI-CTMB

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Audit Process Regulatory review (IRB, consent form content and Delegation of Task Log/Site Authority Log) Investigational drug accountability (drug accountability,

pharmacy visit)Patient case review

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Regulatory Audit



- IRB: Regulatory documents for all protocols on the case list
- Informed consent content: minimum of four consents
- Delegation of Task Log (DTL) and Site Authority Log
- Trial Master File (TMF): FDA registration studies

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IRB Audit - Local IRB

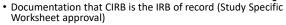


- Approvals: initial and continuing reviews, protocol updates
- Reportable external Safety Reports and internal SAEs
- All versions of IRB-approved consent forms or a comprehensive list
- SOPs for alternative procedures (e.g., submission of unanticipated events only)

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IRB Audit - CIRB



- Approved boilerplate language for ICFs
- Date of local implementation of protocol updates and consent versions
- Submission of unanticipated events (e.g., reportable local SAFs)
- NO COPIES OF CIRB APPROVAL DOCUMENTS REQUIRED

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Consent Form Content



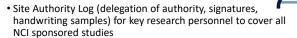
- Compared to model consent
- Contains all elements required by federal regulations
- Updated by protocol modifications
- Specimen banking/optional studies questions same as model
- CIRB sites: identical to approved boilerplate merged with model

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Delegation of Task Log



- Delegation of Task Log (CTSU website)
 - o All registration studies (S1418, S1806, S1914)
 - o LungMAP sub-studies
 - All new studies that use investigational agents (since August 2020 for Ph III studies/since October 2020 for Ph I/II studies)

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Trial Master File



- Protocol
- Regulatory documents
- CLIA Certificates and list of normal lab values/range
- List of local SOPs
- Site training documents (GCP, protocol specific, etc.)
- Placeholder for centrally filed documents (e.g., CVs, 1572s)





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Investigational Drug Accountability



- Review of Drug Accountability Record Forms: NCI DARF or NCI Oral DARF required for all studies using investigational agents
 - Control and satellite records
 - Complete and timely entries
 - Good documentation practices
 - Patient returns documented on Oral DARF

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Investigational Drug Accountability



- Shipping receipts, transfer and return forms
 - Unused or expired drug returned or destroyed within 90 days of end of use
 - \bullet No substitution of commercial drug for investigational agent

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Investigational Drug Accountability



- Cross reference DARFs against patient records to verify dose and dates of dispensing
- SOP for authorized prescriptions (ordering investigator must have active CTEP account)
- On-site audits: Tour of pharmacy
 - Assess security and storage conditions
 - Verify physical inventory
- Off-site audits: Tour of pharmacy conducted via Teams, FaceTime, WebEx, etc.





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Patient Case Review



- 10% of SWOG and CTSU accrual
- 10% of treatment and cancer control cases
- Minimum of one case for each non-SWOG FDA registration study
- Minimum of three cases
- One unannounced case for on-site audits





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Patient Case Review: Categories



- Informed consent
- Eligibility
- Treatment administration
- Disease / endpoint assessment
- Toxicity assessment
- General data quality

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Case Review: Categories Chart preparation

- Shadow chart is acceptable
- Recommended chart organization: Consent and screening/eligibility, then chronological by cycle / reporting period - H&P, labs, disease assessments, etc.
- Color coded flagging
- Specimen submission documents flagged (print out of specimen tracking documents)
- If auditor will review records in EMR, EMR Source Documentation Locator Form must be completed prior to the audit





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Informed Consent



- Most current version signed prior to registration
- Contains all required signatures
- Informed of new findings in a timely manner
- Specimen banking/optional studies offered and intent reported correctly in OPEN at time of registration
- HIPAA authorization signed

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Eligibility



- Verify diagnosis by review of pathology or other diagnostic
- Review medical history for exclusion criteria.
- Verify pre-study assessments meet protocol requirements and performed within specified time limits.
- Eligibility affirmation signed.
- NO EXCEPTIONS GRANTED.

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Treatment Administration



- BSA / dose calculations verified
- Verification of both drug orders and drug administration
- Appropriate dose modifications
- Patient diaries or other supporting documentation of compliance to oral medications
- Documentation to support delays or deviations in treatment

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Endpoint Assessment



- Disease/endpoint assessments performed per protocol
- Review of radiology reports, pathology reports, lab reports, records of physical examinations, etc.
- Same method of measuring the disease at baseline and at each assessment
- Tumor measurements documented
- Off treatment follow-up conducted per protocol

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Adverse Event Assessment



- Required baseline and follow-up studies performed
- Grade and attribution of AEs documented, signed off by investigator/qualified practitioner
- Documentation of immune-related status, if applicable
- Adverse events reported appropriately.
- Serious Adverse Events (SAEs) reported in a timely manner

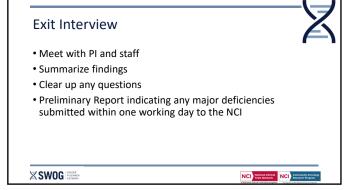
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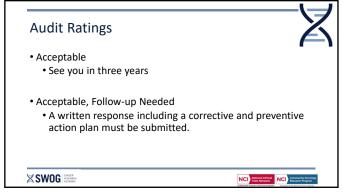


General Data Quality Adequate source documentation Data accurately reported on the data collection forms Timely submission of data Specimens/images/questionnaires submitted per protocol Good documentation practices

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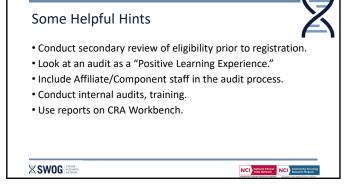


Audit Ratings Unacceptable • A written response including a corrective and preventive action plan must be submitted. • Repeat audit within 6 - 12 months. • If repeat offender: Site Improvement Plan required / possible suspension of registration privileges.

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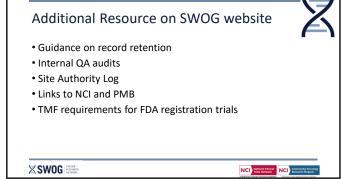




Additional Resources SWOG website (https://swog.org.: > Clinical Trials > Quality Assurance & Audits) • Site Preparation for an Audit • Best Practices guidance document • SWOG regulatory guidance • Patient chart review guidance • Investigational drug videos / PMB policies

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