Quality Assurance Program

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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

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

FDA Registration Study Site Visits

- LungMAP – sub-studies with FDA registration potential - initial audit at three months after first registration to a sub-study, then every six months
- LungMAP – sub-studies that do not have FDA registration potential will be audited on the same schedule as treatment audits by the group to whom they are credited
- S2302 (Pragmatica) – will be audited on same schedule as treatment audits

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

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.

The Audit Team

- QA Auditor/Nurse Auditor as Lead Auditor
- One or more Nurse or CRA auditors
- NCI-CTMB observer occasionally in attendance

Site Representatives

- ORPs
- Research Nurses
- Principal Investigator or designate
- Regulatory Representative
- Pharmacy staff

Audit Process

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

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

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)

IRB Audit – CIRB

- Documentation that CIRB is the IRB of record (Study Specific Worksheet approval)
- Approved boilerplate language for ICFs
- Date of local implementation of protocol updates and consent versions
- Submission of unanticipated events (e.g., reportable local SAEs)
- NO COPIES OF CIRB APPROVAL DOCUMENTS REQUIRED

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

Delegation of Task Log

- Site Authority Log (delegation of authority, signatures, handwriting samples) for key research personnel to cover all NCI sponsored studies
- Delegation of Task Log (CTSU website)
  - All registration studies (S1806, S2302)
  - 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)

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)

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

Investigational Drug Accountability

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

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.

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

Patient Case Review: Categories

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

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

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

Eligibility

- Verify diagnosis by review of pathology or other diagnostic reports
- 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

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

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

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

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

Exit Interview

- Meet with PI and staff
- Summarize findings
- Clear up any questions
- Preliminary Report indicating any major deficiencies submitted within one working day to the NCI

Audit Ratings

- Acceptable
  - See you in three years
- Acceptable, Follow-up Needed
  - A written response including a corrective and preventive action plan must be submitted

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

Some Helpful Hints

- Take lots of notes, sign and date them
- No white out
- Keep records on a real-time basis
- Document height and weight and performance status
- Keep logs for tracking adverse events, concomitant medications

Some Helpful Hints

- Conduct secondary review of eligibility prior to registration
- Look at an audit as a "Positive Learning Experience"
- Include Affiliate/Component staff in the audit process
- Conduct internal audits, training
- Use reports on CRA Workbench

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

Additional Resource on SWOG website

- Guidance on record retention
- Internal QA audits
- Site Authority Log
- Links to NCI and PMB
- TMF requirements for FDA registration trials

Questions?

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