Quality Assurance Program

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Purpose of the audit program

- Verify accuracy of submitted data
- Verify compliance with protocol and regulatory requirements
- Provide educational support

Scheduling of Audits

- New LAPS, Members, NCORPs – within 18 months of first patient registration
- New affiliates, components – at next parent audit
- Institutions audited at least once every three years
- Pilot study for multigroup audits (every 2 years)
- FDA registration studies – more frequent monitoring

Monitoring Visits

FDA registration studies

- S1400 (LUNG-MAP) – initial audit at three months after first registration to a new sub-study, then every six months
- S1404, S1418, S1605 – initial audit at six to nine months after first registration, additional site visits dependent on accrual
- S1806 – activating soon

On-Site Versus Off-Site Audits

On-site

- LAPS / Main Member / NCORP
- NCORP component / affiliate with large accrual
- Monitoring visits for sites using investigational agents

Notification Process

- Scheduled three to four months prior to the audit.
- Formal notification/case list by email four 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 representative
- One or more Nurse or CRA auditors
- NCI observer

Site Representatives

- CRAs
- Research Nurses
- Principal Investigator
- Regulatory Representative
- Pharmacist

Audit Process

Audit Process

- Regulatory review (IRB, consent form content and DTL)
- Investigational drug accountability (drug accountability, pharmacy visit)
- Patient case review

Regulatory Audit

- IRB: Regulatory documents for all protocols on the case list and one to two long term follow-up protocols
- Informed consent content: three to five 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)

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
- Delegation of Task Log (CTSU)
  - S1418
  - S1605
  - S1806 – coming soon
- Other groups' 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
  - 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
- On-site audits: Tour of pharmacy
  - Assess security and storage conditions
  - Verify physical inventory

Patient Case Review

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

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
- Chronological by cycle / reporting period - H&P, labs, assessments, etc.
- Color coded flagging
- Specimens flagged
- If review of EMR, a summary of treatment cycles and disease assessments is helpful

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
- HIPAA authorization signed

Eligibility

- Verify diagnosis by review of pathology or other diagnostic reports.
- Review medical history for exclusion criteria.
- Verify pre-study tests 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
- 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.
- 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
- AEs reported appropriately.
- 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 submitted per protocol
- Good documentation practices

Exit Interview

- Meet with PI and staff
- Summarize findings
- Clear up any questions

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 12 months.
- If repeat offender: Site Improvement Plan required / possible suspension of registration privileges.

Some Helpful Hints

- Take notes, sign and date them
- No white out
- Keep records on a real-time basis
- Document height and weight and performance status

Some Helpful Hints

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

Additional Resources

- SWOG website (https://swog.org : QA/Audits)
- Best Practices document
- SWOG regulatory guidance
- Patient chart review guidance
- Investigational drug video / PMB policies

Additional Resources

- Record retention guidance
- Internal QA audits
- Site Authority Log
- Links to NCI and PMB
- TMF requirements for FDA registration trials