Recent Lessons

Clinical Trial Inspections – Sponsor Roles and Responsibilities → Data Integrity

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Documentation

- Document, document, document
- Key areas
  - Study documents (e.g., protocols, plans, manuals/guidelines)
  - Procedures/guidelines/instructions
  - CROs/Vendors
- Key Considerations
  - Document/Version Control (dates; required signatures)
  - Clarity (doc speaks for itself?)
  - Maintenance/Availability

Training

- Key Areas
  - Company-specific, including SOPs
  - Study-specific (e.g., protocol, monitoring guidelines, safety reporting)
  - Training after significant events/changes

- Key Considerations
  - Study personnel
    - Sponsor
    - CRO/vendor
    - Investigator/Site staff
  - Timeliness
    - Before study; after significant event/change; new personnel
  - Scope
  - current and relevant (to the study)
  - Retraining as needed (e.g., corrective actions, amendments,)
  - Documentation and tracking

Issue Management

- Identification
- Escalation
- Root Cause
- Resolution/Follow-up

Issue Management

- Identification
  - Key Areas
    - Safety (e.g., AEs, dosing, lab values, etc.)
    - Efficacy (e.g., drug handling/accountability, etc.)
    - Repeat problems (at site/across study)
  - Key Considerations:
    - Passive
      - Dependent on others and circumstances
    - Proactive
      - Study Planning and Development Robust
      - Training
        - Monitoring
        - Quality Monitoring (e.g., CRAs)
        - Co-monitoring
        - Risk Management Tools
    - Oversight & Accountability

Issue Management

- Escalation
  - Key Areas
    - Procedures
    - Documentation
  - Key Considerations
    - Criteria
    - To Whom
    - Implications/Scope
    - Minutes/Actions
    - Clarity
    - Accountability
    - Timeliness

Issue Management

- Root Cause
  - Thorough consideration
    - Breadth and depth
    - External input (experts/HAs)
- Resolution/Follow-up
  - Adequacy (per Root Cause)
    - Diligence
    - Corrective & Preventive Measures
      - Communication (timeliness, breadth)
      - Training
      - Embed (study/across studies)
        - Procedures
  - Timeliness
  - Documentation

CRO/Vendor Issues

- Key Areas
  - Selection
  - Written Agreements/Delegations
  - Training
  - Issue Management
  - Documentation
- Key Considerations
  - Regulatory Considerations
  - Scope of Activities
  - Qualification
    - Standards
    - Resources
  - Clarity
  - Adherence
  - Oversight & Accountability

Investigator/Site Issues

- Key Areas
  - Selection
  - Adherence to plans/protocols
    - Deviations/waivers
  - Delegations & Oversight
  - Secure GCP Compliance

- Key Considerations
  - Qualification
  - Documentation
    - Tracking
  - Termination
    - FDA notification
  - Proposed Rule –Falsification of Data

Miscellaneous

- Data Monitoring Committees/Data Safety Management Boards
  - Charters/Written Responsibilities
    - Document control (e.g, issuance, version control)
    - Membership
    - Minutes (Clarity and timeliness)
    - Adherence
    - Issue Management
- Clinicaltrials.gov
- Systems (electronic data capture, etc.)

Future?

- Quality Risk Management Tools
- Enhanced Monitoring
  - Co-Monitoring
  - Re-monitoring
  - IT solutions (database monitoring)
- Comprehensive Audits
  - Sponsor audits
  - Independent 3rd Party audits
- Tracking Quality
  - Patterns
  - Trends
  - Metrics
- Other (guidances?)