

Effective Monitoring and Auditing Clinical Trials

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Session Objectives

1. Describe regulatory and industry perspectives on quality clinical trials.
2. Identify key 483 observations related to inadequate sponsor oversight and monitoring practices.
3. Learn precision monitoring and auditing strategies and tools for efficient and effective clinical trial process.



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Monitoring and auditing are effective risk management tools



Discussion Points:

- Regulatory and Industry perspectives on effective monitoring and auditing of clinical trials
- The role of monitoring and auditing in risk management
- Essential monitoring and auditing tools for quality clinical trials



Definitions

- **Monitoring** – *The act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, standard operating procedures (SOPs), GCP, and the applicable regulatory requirement(s).*



Definitions

- **Auditing**– *a systematic and independent examination of trial-related activities and documents to determine whether the evaluated trial-related activities were conducted, and the data were recorded, analyzed, and accurately reported according to the protocol, sponsor’s standard operating procedures (SOPs), good clinical practice (GCP), and the applicable regulatory requirement(s).*



Regulatory Perspective

- Inadequate monitoring cited on Form FDA 483
- FDA Guidance Document on monitoring Clinical Investigators
- QA activities not a regulatory requirement for clinical trial operations BUT implied



Sponsor Perspective

- Responsible for ensuring proper monitoring of the investigation(s)
- Responsible for selecting monitors qualified by training and experience
- Monitor's responsibilities and monitoring procedures are described in ICHE6
- Responsible for implementing quality assurance (i.e. audits) as described in ICHE6



Investigator Perspective

- Responsible for receiving and responding to monitoring and auditing visits
- Responsible for managing the study in order to control risks and to ensure contingencies are in place for the occurrence of any adverse events



Strategic Imperatives

- Organizations must continue to increase efficiency, quality, compliance as they continue to decrease cost
- Management must proactively gather and analyze data to assess people, processes and technological effectiveness and efficiencies



Operational Imperatives

- Organizations has to be ready for increased scrutiny of all their operations and data
- Collaborative approach to identify key processes, quality goals and metrics
- Quality improvement plans provide quantitative data to support better communication within the organization



Monitoring Issues

- Monitoring visit issues not escalated or resolved in a timely manner
- Inadequate source data verification (SDV)
- Inadequate clinical supply chain management and investigational product (IP) reconciliation(i.e. expiry date , forecasting supply)
- Inadequate qualifications and training of monitors



Auditing Issues

- Ineffective audit plan
- Trend and root cause analysis not performed
- No defined process for escalation of significant findings and accountability for remediation
- Inadequate qualifications and training of auditors



Monitoring Strategies and Tools

Activity	Description
TMF creation and maintenance	Assists sponsor in maintaining required essential documents. Electronic TMF allows sponsor-CRO visibility
Clinical supply management	Develop procedures or clinical supply relabeling/expiry date management; develop automated tool for demand/supply forecasting/tracking/reconciliation (e.g. IVRS, EDC)
CRF-source verification	Direct method of verifying data transcribed on CRFs are consistent with source document by reviewing actual source data vs. photocopies
Source data verification (SDV)	SOP and or monitoring plan giving precise instructions on how the monitor should undertake SDV
Investigator compliance	Adopt an automated clinical trial management system (CTMS) and standard for site qualifications and training



Auditing Strategies and Tools

Activity	Description
Audit Strategy	Describes type of audits to be performed (e.g. system, site audit supplier) critical phase selection (i.e. pivotal phase III).
Audit Plan	Describes scope of a QA audit schedule, identifies audit team, outlines audit standards (e.g. FDA GCP/ICH, protocol)
Audit Technique	i.e. FDA CP, “Story Approach” links process with performance
Process Audits	Evidence QC performed at each operational stage of the study
Site Audits	Assures protocol and GCP compliance
Audit Report	Evaluate/categorize audit findings for trend analysis
CAPA process	Discrepancies are tracked/prioritized for root cause analysis/corrective action



Summary

- The manner in which we conduct clinical trials is under scrutiny by FDA
- Efficient and effective monitoring is key to assuring quality clinical trials
- FDA's inspectional approach appears to reflect principles of a QMS
- Regulatory compliance with GCP principles and best practices can be assured by adopting a risk management program



THANK YOU!

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