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Developing Effective Quality Systems in Clinical Trials: An Enlightened Approach

Risk-Based Quality Management of Clinical Trials – A European Regulator’s View

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Disclaimer

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Quality Management

Frequent misconception

“We, as the clinical trial team care for scientific aspects,
budget and timelines...

whereas monitors
and auditors
will ensure GCP-compliance of trial conduct”

Gabriele Schwarz CTTI 2010, Bethesda

Risk-Based Quality Management

Quality in clinical trials

“Quality” is characterized by the ability to
• Effectively and efficiently answer the intended question about the benefits and risks of a medical product (therapeutic or diagnostic) or procedure while
• Ensuring protection of human subjects”

(source: CTTI website, https://www.trialstransformation.org/scope)
The basic idea of risked-based quality management of clinical trials is to collect and evaluate systematically any available data and information on the

• organisational (personnel, processes, IT etc.) level
• project/ trial level

in order

➢ to identify and assess potential risks
➢ to prioritize and mitigate these risks throughout the clinical trial course

(source: ICH Q9)
**Risk Assessment**

**Trial Design and Trial Initiation**

Potential risks in relation to e.g.

- IMP
- Trial related procedures
- Design of trial protocol, CRF and other trial documents
- Biometrical and statistical design
- Trial Organisation
- Planning of data collection and study tracking tools
- Planning of study-directed QA and QC activities

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**Risk Assessment**

**Trial Conduct**

**Leverage existing data**

- Inhouse data as well as data of CROs/ service provider

**Determine Areas with increased risk**

- Reg. Subm. Compliance
  - SUSAR Reporting
  - DSUR

- Audit Reporting
  - Delayed Audit Report
  - Delayed Audit Closure
  - No/ delayed Follow up

- Study monitoring
  - Delayed Monitoring
  - No/ delayed Follow up
  - -(S)AE Reporting
  - Protocol deviations
  - Late Data Entry

**Provide result reporting**

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Risk Assessment
Data Evaluation and Reporting

Potential risks in relation to e.g.

- Data management
- Data Quality Review
- Blinding
- Statistical analysis plan
- Data Freeze and data lock

Risk-Based Quality Management
Approach

Systematic risk identification and assessment as well as the definition of mitigation activities requires an interdisciplinary team, involving personnel from

- trial management
- preclinical and pharmaceutical development
- data management
- biometry and statistical analysis
- pharmacovigilance
- quality control and quality assurance

Source: http://pharmeng.engin.umi ch.edu/ourfocus.html
Risk-Based Quality Management

Risk Control

• Qualification of personnel of all involved parties (sponsor, CROs, other service provider, trial sites)
• General and trial-specific training
• Implementation of internal or (independent) external committees
• Prospective determination of ranges and thresholds (‘what is good enough?’)
• Developing benchmarks and reference data and/or asking for scientific advice
• Performance measurement of all involved parties
• ...

Risk-Based Quality Management

Conclusion

Risk-based quality management means

• A systematic and proactive risk assessment on an organisational and project/trial level
• A focused allocation of resources (monitoring, visits, audits, technical services, trainings, data quality checks) to the highest priority risks
• A close performance measurement focusing not only on timelines and budget, but also on quality in relation to pre-specified acceptance criteria or predefined ranges
• A timely escalation of any issues, implementation of risk mitigation actions and duly follow-up of agreed CAPAs
• A close collaboration and efficient communication between quality areas, functional services and business partners
Thank you for your attention!

Any questions?