A Clinical Trials Transformation Initiative (CTTI)-Sponsored Meeting
October 13–14, 2010; Bethesda
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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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”

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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

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**Risk-Based Quality Management**

**Risk Assessment**

- What might go wrong?
- What is the likelihood (probability) it will go wrong?
- What are the consequences (severity)?

(source: ICH Q9)

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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
- SUSAR Reporting
- DSUR
- Delayed Audit Report
- Delayed Audit Closure
- No/ delayed Follow up
- Delayed Monitoring
- No/ delayed Follow up

Provide result reporting
- (S)AE Reporting
- Protocol deviations
- Late Data Entry

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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

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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
- ...

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?