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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

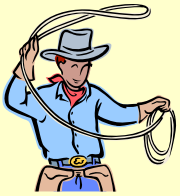
"We, as the clinical trial team care for

scientific aspects,

budget and timelines…

whereas monitors

and auditors



will ensure GCP- compliance of trial conduct"

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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)

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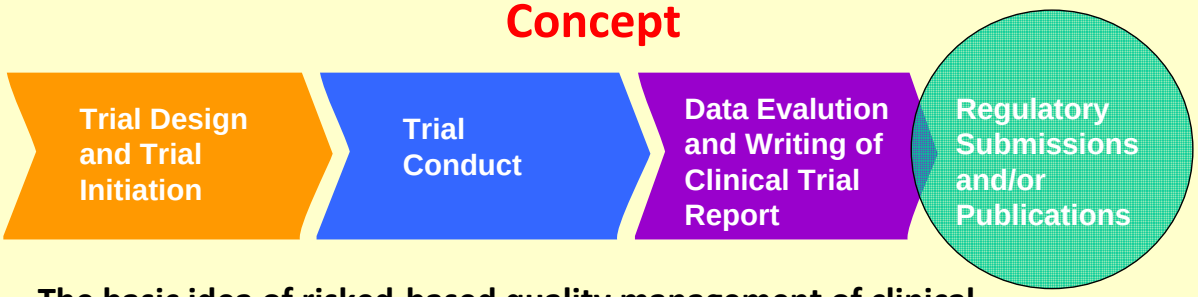
Risk-Based Quality Management
Concept



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)

Risk Assessment
Trial Design and Trial Initiation

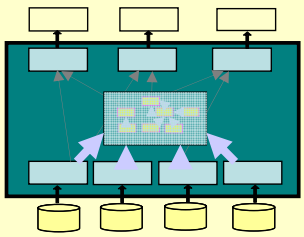
Potential risks in relation to e.g.

- **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**

Risk Assessment
Trial Conduct

Leverage existing data

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



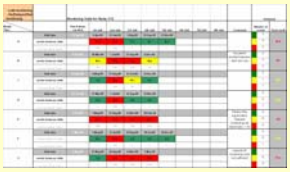
Determine Areas with increased risk

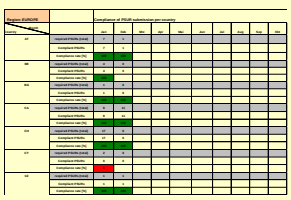
Reg. Subm. Compliance
- SUSAR Reporting
- DSUR

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





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 a 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.umich.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
- …

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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?