Make more out of your clinical data collection

Benefits of technical innovations within clinical trials

INTRODUCTION SPEAKER

Speaker

- Thomas Kissner, Chief Operating Officer
- Responsible for company data driven developments, consultation for EDC systems and data acquisition
- Oversees all CRO activities, focus on effective data management and client benefit

Company

- GCP-Service International
- EU-based, international full-service CRO, founded in 2004
- Conducts 30+ clinical trials per year with medical devices, IVDs and drugs (phase I-IV, pre- and post-market)

OUTLINE OF PRESENTATION

Outline

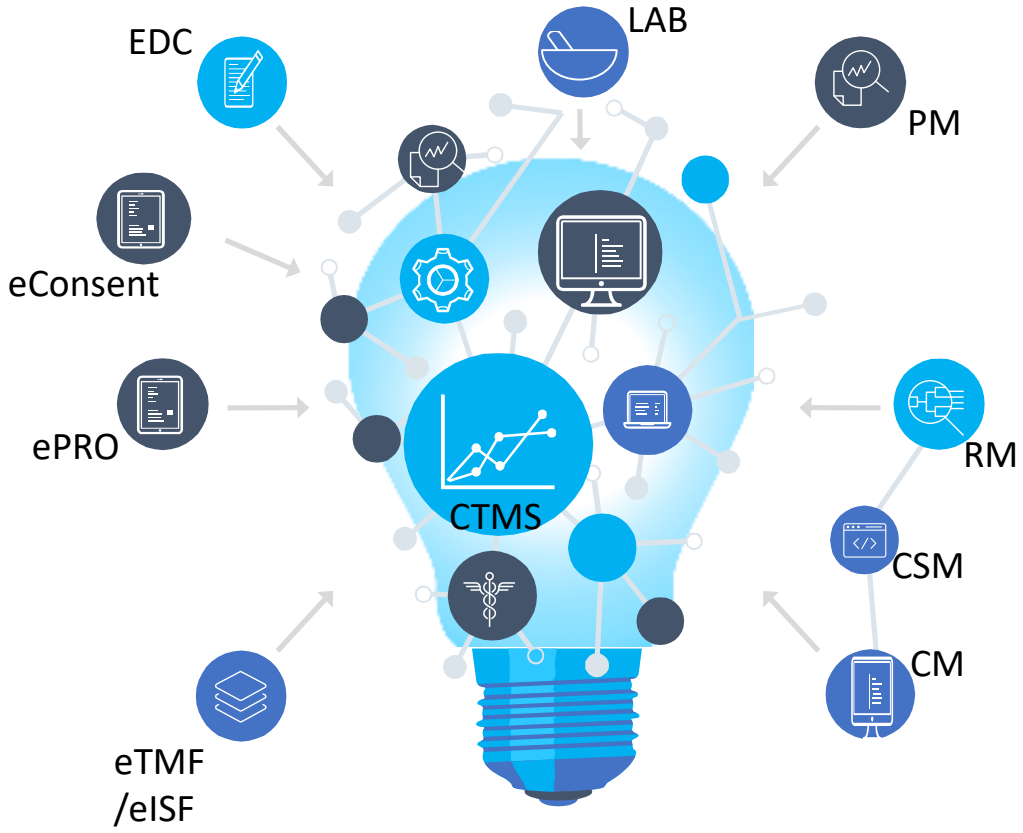
- Risk-based monitoring (RBM) and why do we need it?

- Which monitoring concepts does it entail and how can they be implemented?

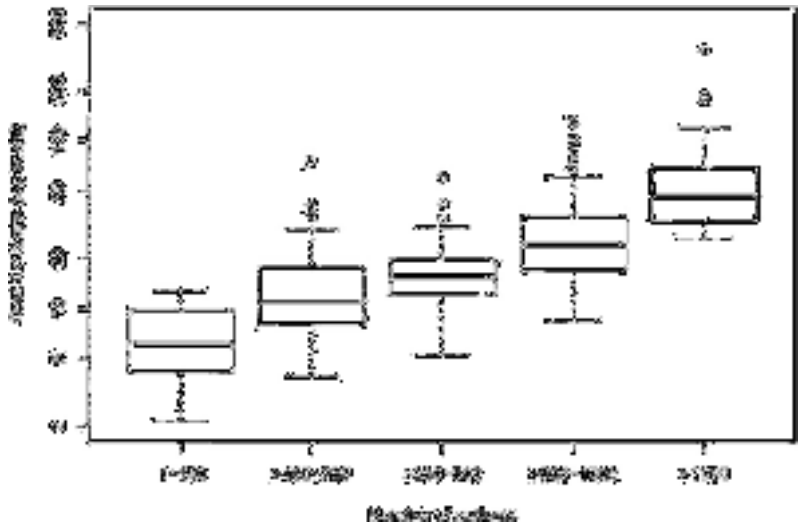
- Where are we and what does the future hold?

- There is more than RBM in clinical trials

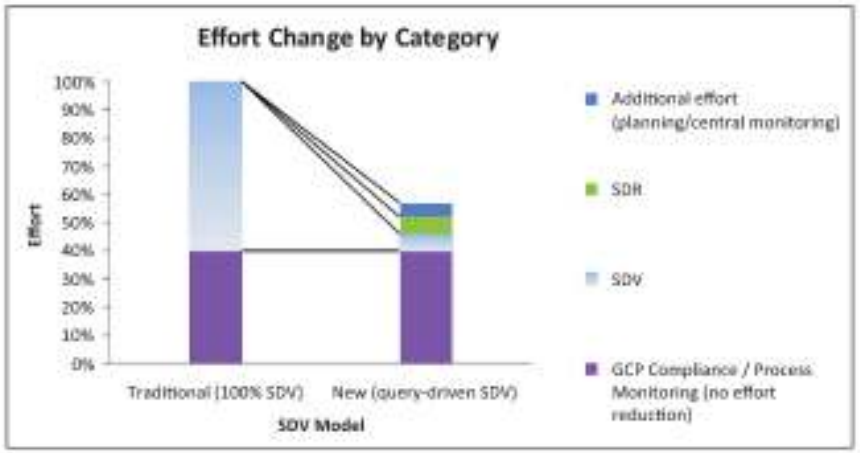
EVOLUTION OF CLINICAL TRIALS SYSTEMS



WHY RISK-BASED MONITORING?



Moore et al. (2020), BMJ Open



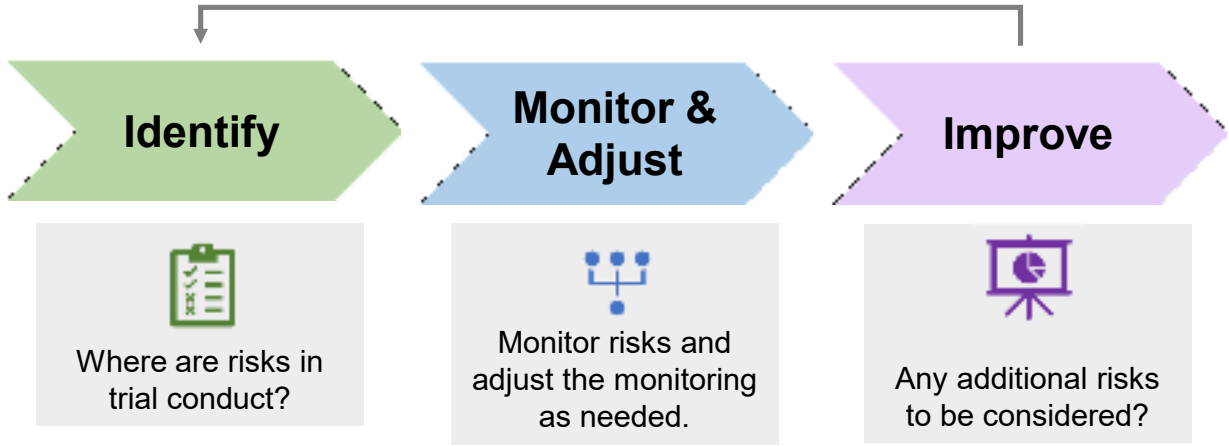
Tatsyura et al. (2016), Ther Innov Regul Sci

Monitoring is among the **most expensive** parts of clinical trials

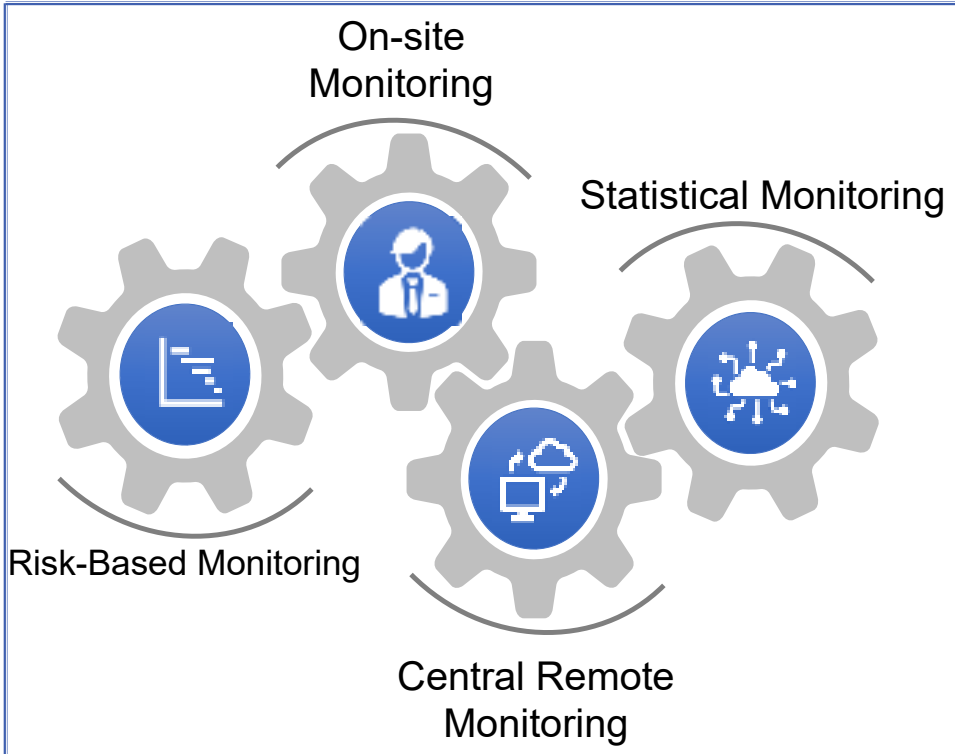
9-14% monitoring costs (U.S. Department HHS, 2014)
25% source data verification costs (Funning et al., 2009)

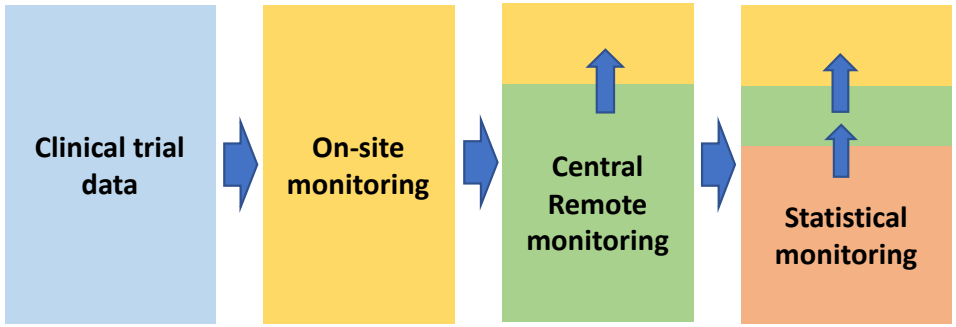
RISK-BASED MONITORING

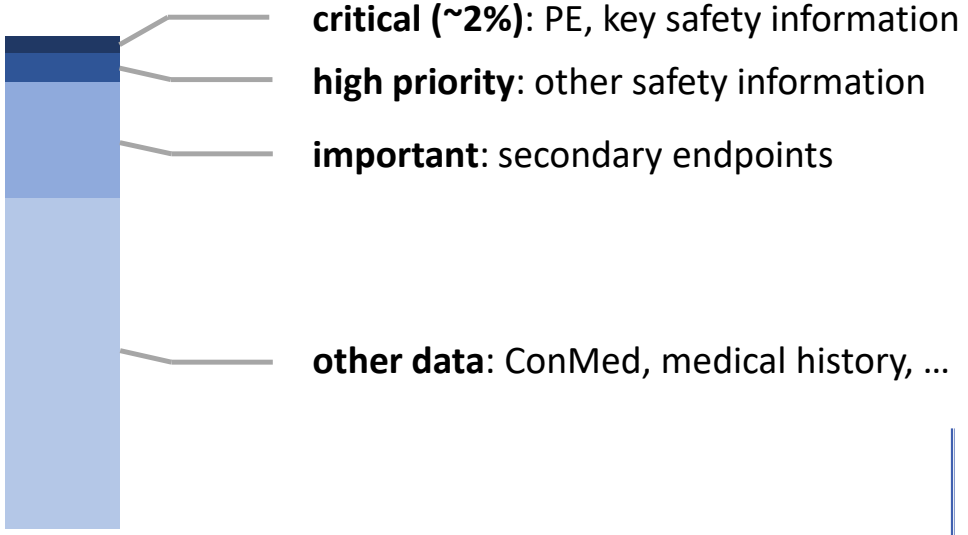
- Mixture of on-site, remote and statistical monitoring based on risk evaluation
- Monitoring frequency and intensity adjusted based on risk profile of study/site
- Supported (requested) by FDA and EMA



RISK-BASED MONITORING







RISK-BASED MONITORING

Risk-based Monitoring

✓ Adjust frequency and intensity

✓ Rational based on risk factors

✓ Combine different monitoring approaches

On-site Monitoring

✓ Source data verification

✓ Identification of unreported issues

✓ Site support and motivation

Remote Monitoring

✓ Remote (source) data review

✓ Standardized comparison across sites

✓ More time and cost efficient

STATISTICAL MONITORING

Investigators, Study Nurses

Investigators conduct the study, collect clinical data

Automated Processing

Tool to process and analyze collected study data, generates statistical summary

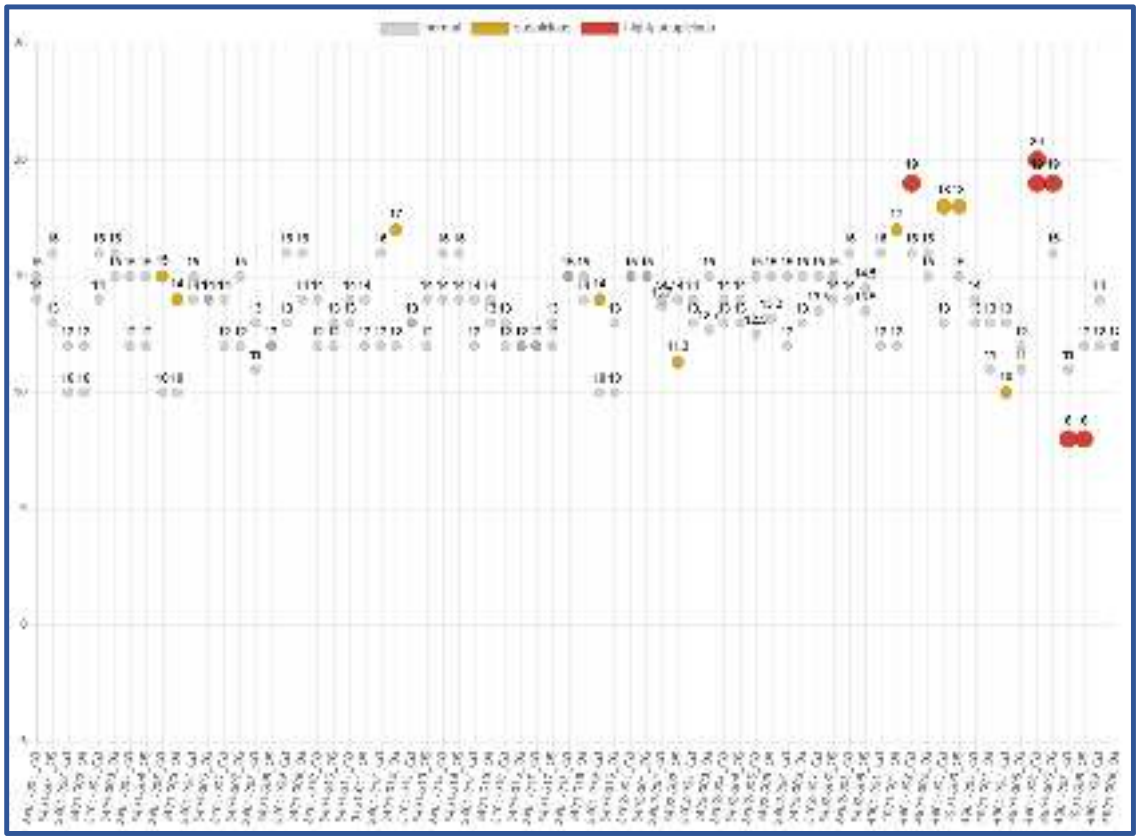
Biostatistician

Expert who manages analyzed and raw data, identify issues and clarify them with monitors.

Clinical Research Associate (CRA)

Expert who oversees and reviews study data, visits study site, reports to sponsor/CRO

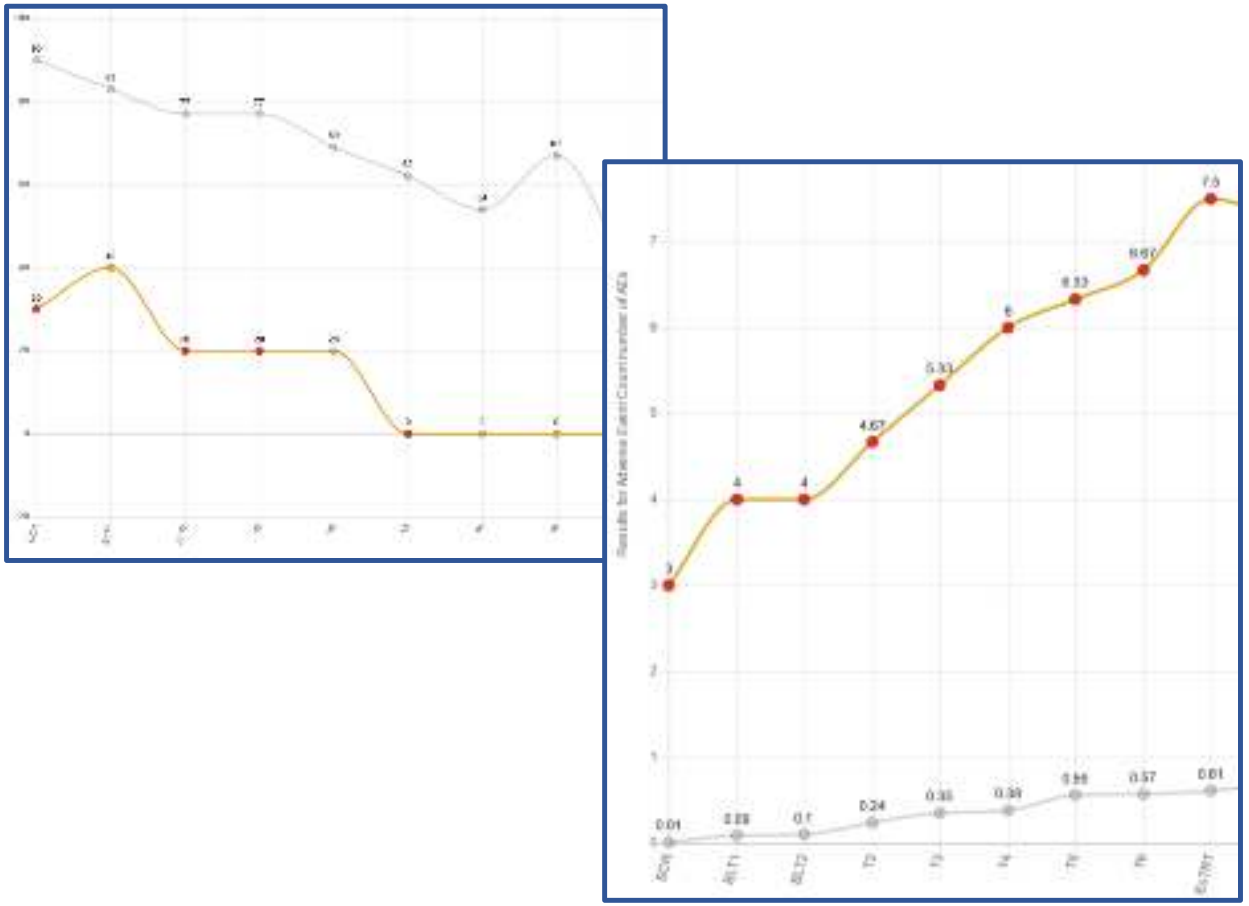
STATISTICAL MONITORING



Assessment of **outliers** by comparing across data sources and assessing changes. Enables **targeted investigation** of expected outcome.

Patient-Level

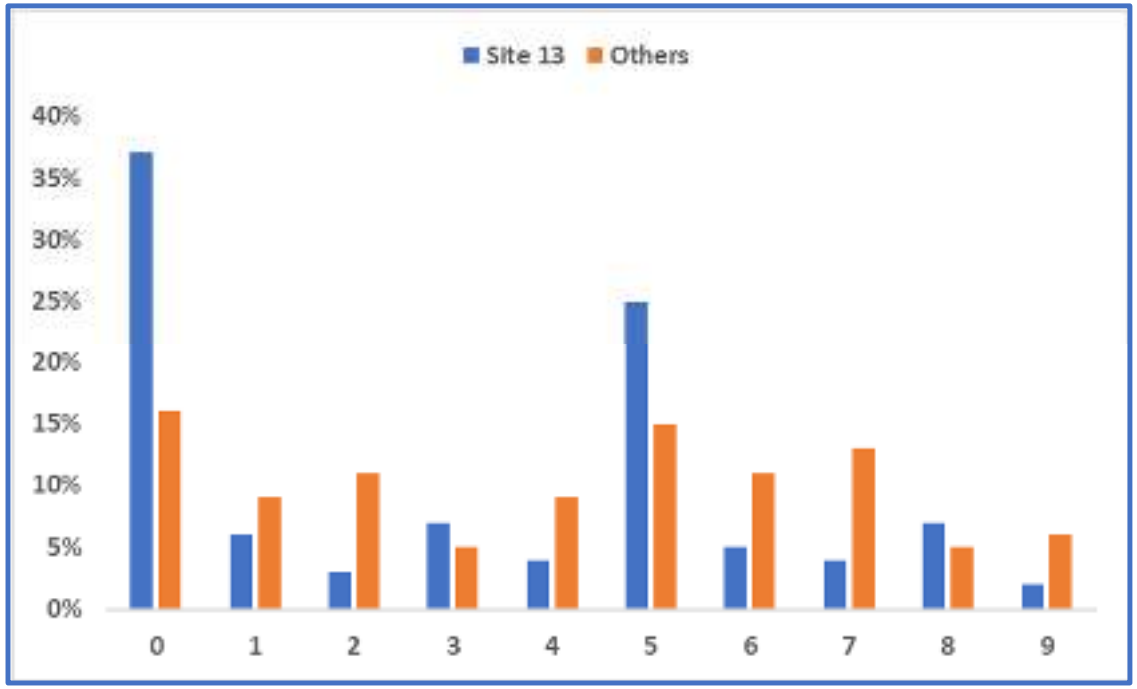
STATISTICAL MONITORING



Assessment of **systematic differences** between data sources.
Enables proactive identification of **analysis risks**.

Site-Level

STATISTICAL MONITORING



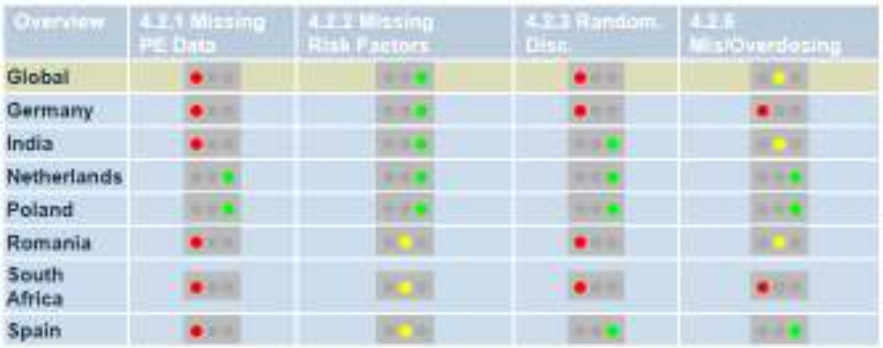
Assessment of **number preferences, inliers, suspicious dates, identical patient profiles**, etc. to identify **fraudulent data**.

Site-/Trial-Level

MONITORING IMPLEMENTATION

Implementing Risk-based Monitoring

- ✓ **Establish SOPs**
  - ➢ Establish necessary **tools**
  - ➢ Establish **reporting paths**
- ✓ **Train staff on new processes**
- ✓ **Assess study risks**
  - ➢ Add risk-based rational to monitoring
- ✓ Inform and train **sites** (if necessary)
- ✓ Perform monitoring
- ✓ **Continue monitoring risks**



MOVING FORWARD

Status Quo

- ✓ **Scientific foundation**
  - ➢ Off-site monitoring is more efficient
  - ➢ Preparedness part of risk-mitigation

- ✓ **Current practice**
  - ➢ More frequent adoption during COVID-19 pandemic

- ✓ **Perceived limitations**
  - ➢ Some remaining insecurity around regulatory compliance
  - ➢ Data protection limitations to remote source data review/verification

Outlook

- ✓ **Regulators!**
  - ➢ To provide guidance
  - ➢ To given insurance

- ✓ **Sponsors!**
  - ➢ To embrace risk-based monitoring

- ✓ **CROs!**
  - ➢ To support employees and sites
  - ➢ To support Sponsors

SUMMARY RBM

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Adjusting monitoring **frequency** and **intensity** based on **risk-factors**.

RBM Definition

Start implementation by **identifying risks** to **assessments** and **processes**. Identify **data sources** to gain **oversight**.

Start With Risks

Based on the **risk profile**, find a corresponding **rational** to **combine different monitoring techniques**.

Implement RBM

RBM lives from **continuous adaptations.** Continuously **review risks**, and **adjust** monitoring **intensity** and **frequency**.

Adapt During Trial

GENERATING OVERSIGHT

Key Sources

- ✓ Available data in EDC system
- ✓ Consent / Randomization status
- ✓ (Remote and on-site) Monitoring reports
- ✓ eTMF and eISF status
- ✓ Protocol deviations
- ✓ ePRO compliance

Overview	4.2.1 Missing / Non-evaluable PE	4.2.2 Missing / Non-evaluable Confounder	4.2.3 Data Query Rate	4.2.4 Visit Window Compliance
Global				
Austria				
Czech Republic				
Spain				
3401				

EXPLOSION DATA SOURCES AND VOLUME

Electronic Case Report Forms (**eCRF**),
Interactive Web/Voice Response Systems (**IxRS**)

Central Labs

Imaging &
Genomics

Monitoring
Reports

VARIETY

Wide range of **data sources** and data **formats**

eTFM/eISF

Sensors &
Wearables

Electronic Clinical Outcome Assessment (**eCOA**),
electronic Patient Reported Outcomes (**ePRO**)

Electronic Health
Records (**EHR**)

PURPOSE-BUILT PLATFORM

Data Integration

Central data platform

diverse data **integration** and **interoperability**

Image source: Systems Ltd

PURPOSE-BUILT PLATFORM

Cost intensive and Complex

Monitoring is among the **most expensive** parts of clinical trials

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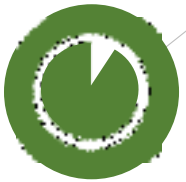
25% source data verification costs (Funning et al., 2009)

eSystem cost ranges in the **lower expensive** parts of clinical trials overall costs



2-5 % eSystem costs. (Examination of Clinical Trial Costs and Barriers for Drug Development – ASPA)

RBQM IN CLINICAL TRIALS

GCP-Service International

Review of **accuracy** and **completeness** (quality control) can be performed in a risk-based manner.

TMF and ISF

Query processing can be performed in a risk-based manner. Identifying **highly queried parts of the EDC** system can increase oversight.

Data Management

Risk-based approach to **program validation** for the final statistical output helps focus resources.

Biostatistics

Thank you for your attention!

Questions?

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