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Audit trail reviews, a regulatory requirement?

How to take an RBQM approach

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Tanya Du Plessis
Chief Data Strategist & Solutions Officer

Tony Hewer
Founder & Director, Cepheus Consultancy

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Speakers

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Tanya Du Plessis

Chief Data Strategist & Solutions Officer

Tanya du Plessis has more than 18 years of experience as a manager of various data management operational teams, and she is a certified clinical data manager and project management professional. She holds a M.Med.Sc in Hematology and Cell Biology from University of the Free State.

Tony Hewer

Director & Founder, Cepheus Consultancy

Tony's IT career spans over 30 years with the past 20 years in the clinical research space. He's had experience in software development, program management and quality, security and regulatory disciplines. He has a BSc and PhD in astrophysics from University College London.

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AGENDA

- What do guidance documents say about audit trail reviews?
- What is the purpose of the audit trail reviews?
- How to do audit trail reviews **meaningfully, quickly and effectively**.
- How to prove you align with guidance
- Q&A - please use the Q&A tab

Audit Trail Reviews…

Where did this come from?

- A **valid** belief that audit trails [pluralized] provide a rich record of trial history.
- ***Reviewing*** audit trails is not, in of itself, of much value!
- The nature of "audit trails" has "expanded" with time.

What objectives are we really trying to address

- The overall scientific integrity of a clinical trial - robust, quality data outcomes facilitated by robust, quality planning and execution by all stakeholders

Planning & Executing

- Use a RBQM framework - driven by trial protocol and DM plan
- Use common *general* approaches and techniques, but aligned to the trials' identified – but changeable - risk profiles
- Avoid replication of activities (across multiple functional disciplines)
- Ask: how can audit trails help?

Guidance Documents…*Implying* but not *defining*

FDA: 21 CFR Part 11

- Electronic records and electronic signatures
- ***Implies*** need for review and verification of the audit trails

ICH E6 (R2)

- Importance of maintaining accurate and complete records of the trial
- The requirement for accurate and complete records ***implies*** the need to review and verification

(EMA) Annex 11

- There should be appropriate controls in place to ensure the integrity, security, and accuracy of the trial data.
- Emphasizes the need for system-generated audit trails to be available for review during inspections

Guidance Documents…"Defining"?

EMA: Guideline on computerised systems and electronic data in clinical trials (Section 6.2.2)

- "Instructions" (!) on audit trail reviews
- Came into effect Sep-2023

But there's also a plethora of material which touch – vividly or otherwise - upon ATR in wider contexts

SCDM: The Evolution of Clinical Data Management to Clinical Data Science A Reflection Paper on the impact of the Clinical Research industry trends on Clinical Data Management. (2019).

eClinical Forum & SCDM: Audit Trail Review: A Key Tool To Ensure Data Integrity - An Industry Position Paper (2021).

FDA: Data Integrity and Compliance With Drug CGMP Questions and Answers Guidance for Industry. (2016).

MHRA: GxP Data Integrity Guidance and Definitions. (2018).

Guidance Documents…

EMA: Guideline on computerised systems and electronic data in clinical trials (Section 6.2.2)

- "Instructions" on audit trail reviews

- Data review should focus on ***critical*** **data.**
- Data review should **be proactive and ongoing**
- Manual review as well as review by the use of **technologies to facilitate the review of larger datasets** should be considered.

- Procedures should be **in place**
- Performance of data review **should be documented**.

In addition to audit trail review, metadata review could also include (among others) **review of access logs, event logs, queries, etc.**

Audit trail review can also be used to detect situations **where direct data capture has been defined in the protocol but where this is not taking place as described**

Data review can be used to (among others):

- Identify **missing data**
- Detect signs of **data manipulation**
- Identify **abnormal data/outliers** and data entered at **unexpected or inconsistent hours and dates** (individual data points, trial participants, sites)
- Identify **incorrect processing of data** (e.g. non-automatic calculations)
- Detect **unauthorised accesses**
- Detect **device or system malfunction** and to **detect if additional training is needed** for trial participants / site staff et al.
- Not limited to….

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CURRENT CHALLENGES
AUDIT TRAIL REVIEWS

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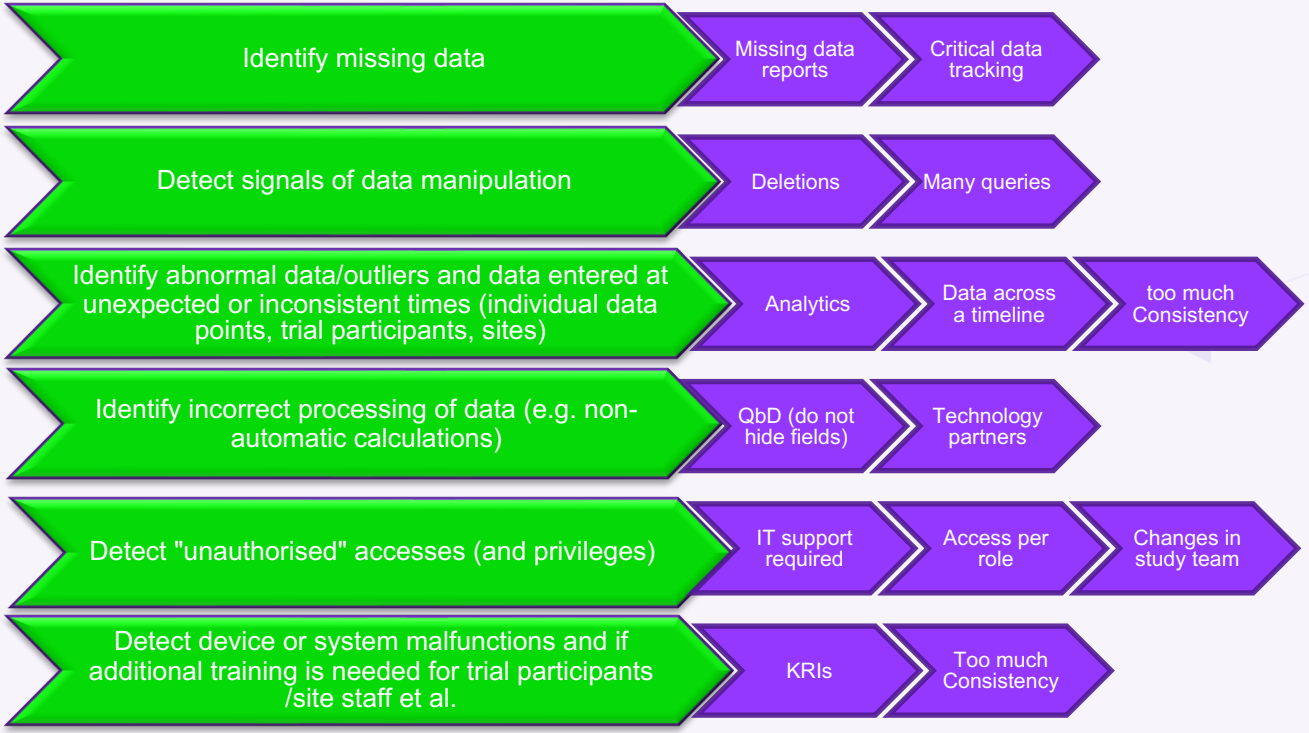
Performing [audit trail] reviews to…

…include, but not limited to…



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RBQM: Efficient and effective

EMA: Guideline on computerised systems and electronic data in clinical trials (section 6.2.2):

"Procedures for risk-based trial specific audit trail reviews should be in place and performance of review should be documented."

- Starting high and diving down/slice-dice as needed - follow the data!
- Detect signals
- Define starting points
- Reviewer must have insight
- Track discrepancies and concerns

Use tech-based tools to help simplify – and automate - the mechanisms

Record – and learn from - the outcomes

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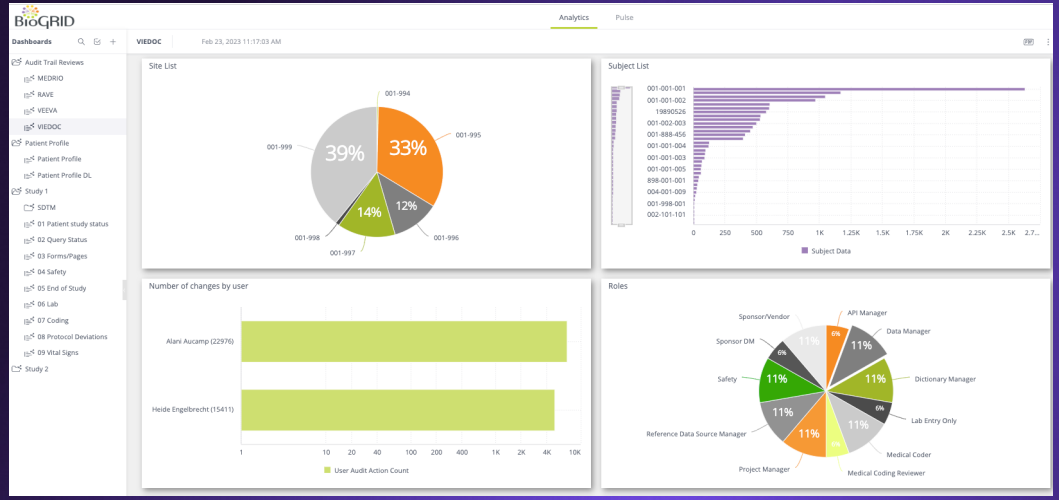

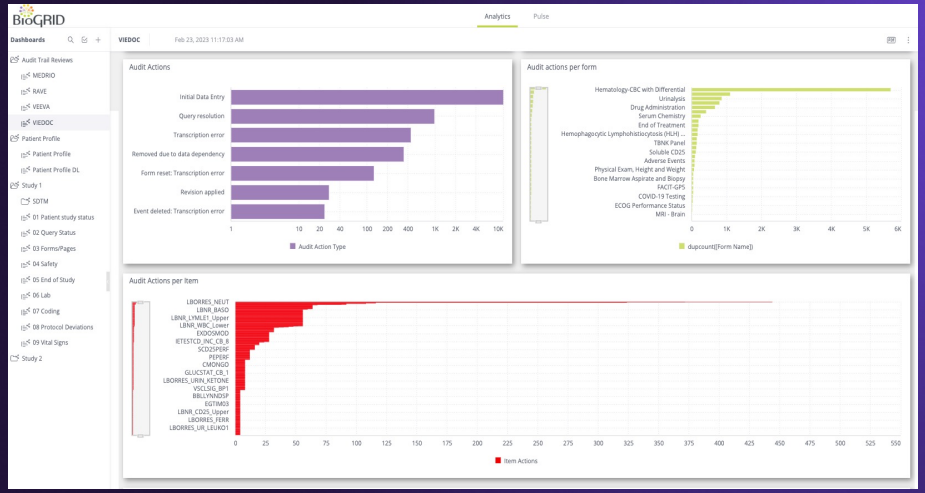

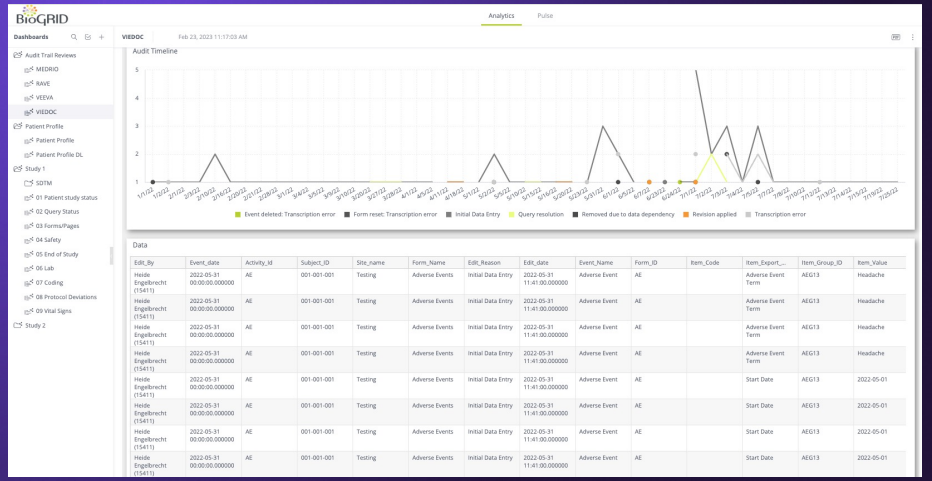

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Evidence of compliance to guidance?

If it isn't documented, it didn’t happen!

- **SOP/WI:** Define process (ie: from identification – results - actions)
- **Evidence:**
  - Report – and retain - audit trails reviews outcomes -
  - Document outcomes in a workflows/tracker (electronic/manual)
- Include **names/roles** of [attributable] team members addressing and managing the identified risks
- Ensure **traceability back you your risk log is visible** (and KRIs)
  - Risk management plan (to protocol)

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CLOSING THOUGHTS

- Guidance is ambiguous/limiting and overly complex – so, do what you can to assure the overall scientific integrity of a trial
- Focus on the need to *reproduce* trial history and detect anomalies **quickly**
- Do audit trail reviews **meaningfully, quickly and effectively** within a wider risk-based approach to data integrity and trial management
- There is no one-size-fits-all approach.
- ATR is NOT a checkbox exercise.
- What does the future hold?

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THANK YOU!

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Audience Q&A Session

ⓘ Start presenting to display the audience questions on this slide.