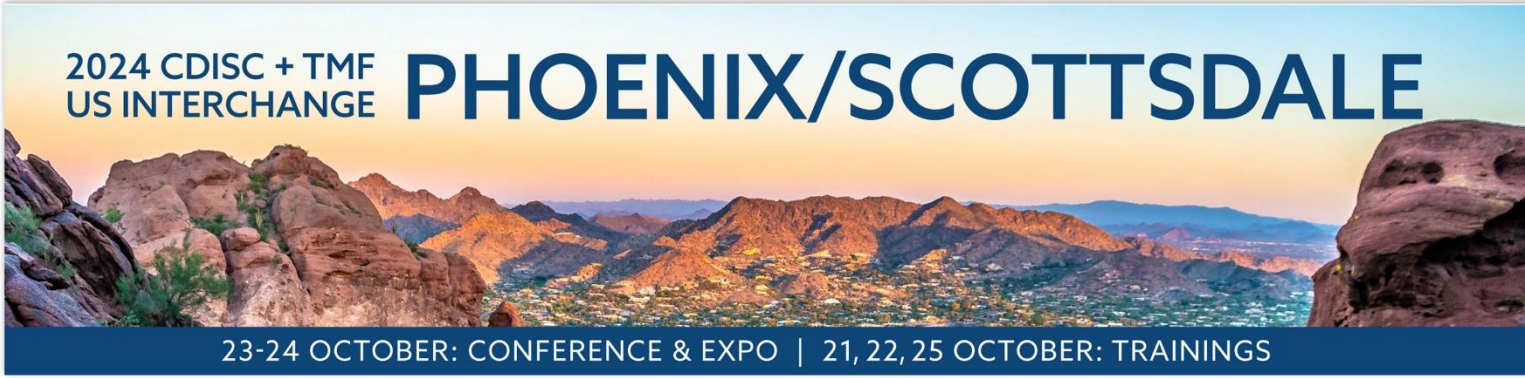


Using Reports to Address TMF Completeness – A Case Study

Jared Brooslin
Kate Santoro
Intellia Therapeutics

Meet the Speakers

Jared Brooslin

Title: Manager, Trial Master File

Organization: Intellia Therapeutics

- Began career managing paper Trial Master Files
- A maestro of building TMF departments for small pharma
- An advocate for improving TMF knowledge of functional leads

Kate Santoro

Title: Director, Operational Excellence

Organization: Intellia Therapeutics

- More than 20 years in Industry
- Implemented multiple eTMF systems + processes
- Co-lead CDISC-TMF Reference Model Change Control Board

Disclaimer and Disclosures

- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.*

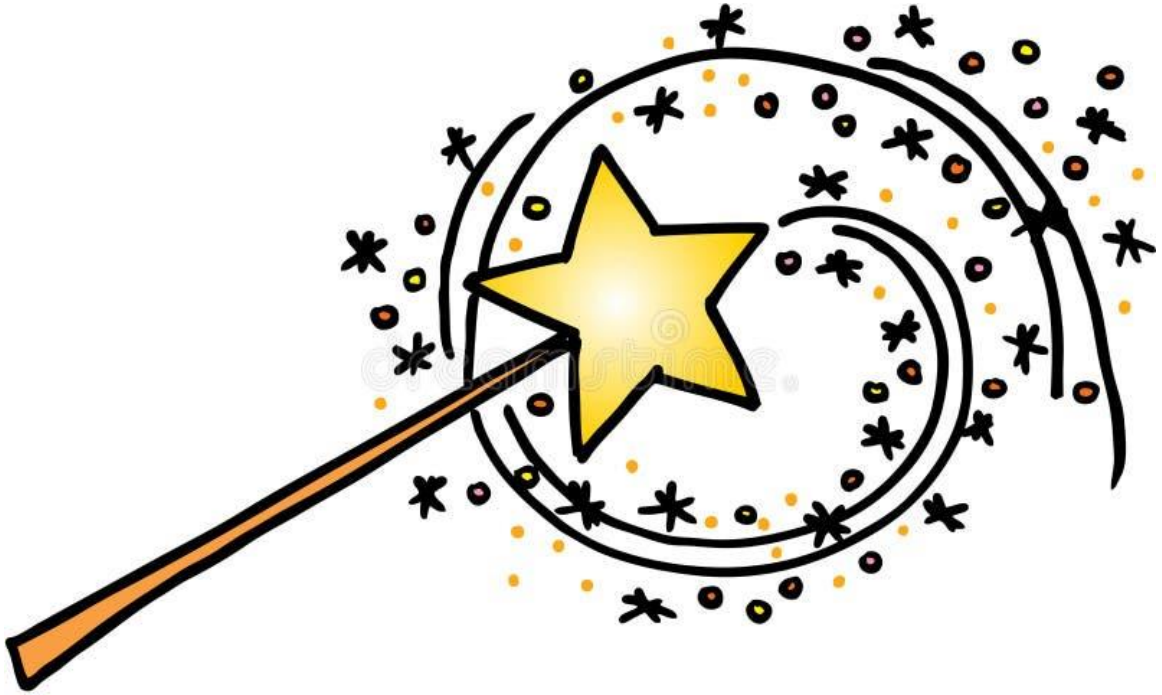
Agenda *(The Act)*

1. Background *(Setting the Stage)*
2. Standard Measures of Completeness *(The Pledge)*
3. Experienced Pitfalls *(The Turn)*
4. Specific Case Study *(The Prestige)*
5. Using Reports to Inform *(The Conclusion)*

Background

- Small-mid biotech company (~650 employees)
- Currently in start-up - 1st Phase 3 gene editing studies
  - We know we will be inspected!
- Need to manage this correctly from the start
  - Continuously monitor document quality
  - Understand completeness; measure at milestones
- TMF Health Measured Periodically
  - Individual document quality by 3rd party - queries issued for quality issues
  - Bi-annual TMF Quality Reviews (2x/yr) - completed by in-house team members
    - Confirm overall document quality
    - Assess completeness of artifacts
  - Monthly Metrics Reviews
    - Documents submitted per TMF Zone
    - Document status (final vs incomplete)
    - Query types
    - Outstanding queries

System Implementation



Ways of Managing Completeness

Managing Placeholders - Example

- Work with each study team's functional areas to determine estimated number of expected documents for each artifact based on study's protocol
- Provide monthly metrics showing the number of placeholders that remain for each File Level, Zone, and/or Artifact
- Create new placeholders when new events or milestones are planned or occur

Reality Check

- Placeholders not specific enough
  - Cover 15 MVRs, but which report is missing?
  - Which Investigator CV is missing?
- Standard process not followed
  - Not filing documents to the placeholders
- Heat maps not accurate

Completeness by Events

- Events show a connection between different types of documents

- The event of adding a site's new Sub-I CV to the eTMF will generate placeholders for other expected documents that are associated with that new Sub-I, such as:
  - Professional License
  - ICH-GCP Certificate
  - Financial Disclosure Form

- Review reports on specific events to verify that all documents expected for a particular event has been filed

A Broken “Process” for Managing 1572 Forms

- SOP: 1572 forms to be sent to FDA within 30 days
- Process:
  - Check SharePoint
    - Temporary repository for 1572 Forms and CVs
  - Ask for Updates
    - Rely on CRO or study team to inform on newly activated sites
  - Manual Comparison
    - Compare everything on SharePoint vs what was previously sent to identify new
- Issues:
  - Frequent late submissions to FDA
  - Duplication of efforts and filing
  - Relying on SharePoint as source rather than eTMF

Using System Reports to Inform

- Desire to have a more active TMF
  - Utilize reporting features to inform
- Build TMF Report
  - All 1572 Forms filed to-date
  - Move to 1572 Forms filed within last 30 days
- Initial report for 1572 Forms
  - 20 sites activated
  - 6 1572 forms filed in eTMF
- Result
  - 1572 forms being filed more regularly
  - Regulatory team ensuring completeness

Additional Examples of Managing Completeness with Reports

Site Documents

- Inform CRAs before monitoring visits
- Provide report of missing site documents

Event-based Reporting

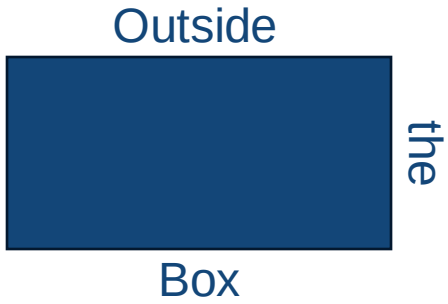
- Start-up activities
- Lock down TMF when complete

Artifact Reports

- Due and/or overdue artifacts

Conclusion

- Built-in System Functionality Can Be Great!
  - Carefully managed
  - Understand nuances & potential pitfalls
- May Require Additional Thinking
- Simple Reports Can Be Used to Inform
  - Completeness at a place in time
  - Documentation for specific events
  - Artifact-specific



Thank You!