Leveraging the TMF to Gain Insight into Clinical Quality Compliance

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Just in Time GCP®

Session Objectives

- ☑ Understand how **missing protocol training documentation** can indicate greater quality compliance issues in the study
- ☑ Examine **critical documents like site monitoring reports and oversight documentation** to evaluate possible risks and compliance concerns
- ☑ Discuss how **TMF content gaps** may signify data integrity issues within the study
- ☑ Use the **TMF as a strategic study asset** to ensure the study's success by proactively identifying risks

TMF Content Gaps as Indicators of Data Integrity Issues

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Maintaining & Managing Data Integrity

- Trackers & Logs
  - Authoritative sources, need all versions of trackers/logs filed in TMF
- Protocol Deviations
  - Easy access to what is going wrong
  - Easily track trends and identify outliers
  - Identify deviations impacting data integrity, subject safety, and human subject protection
- Data Oversight Documentation
  - Establish a process for providing medical and quality oversight of data
  - Can prevent long term issues with data integrity – trends in data queries
  - Window into subject safety
- Timeliness
  - If timeliness in the eTMF can't be achieved, it's unlikely to succeed elsewhere

Clues from your eTMF

- Document status
  - QC Rejected – analysis of trends to identify opportunities to process improve
  - In Progress – delays in finalizing records
  - Documents with Queries – delayed resolution; trends analysis
- Expected documents lists and other reporting tools
  - Do outcomes align with study expectations?
  - Are expected documents being updated as the story progresses?

What is an inspection ready TMF?

Complete

The TMF tells the entire story of the study

Timely

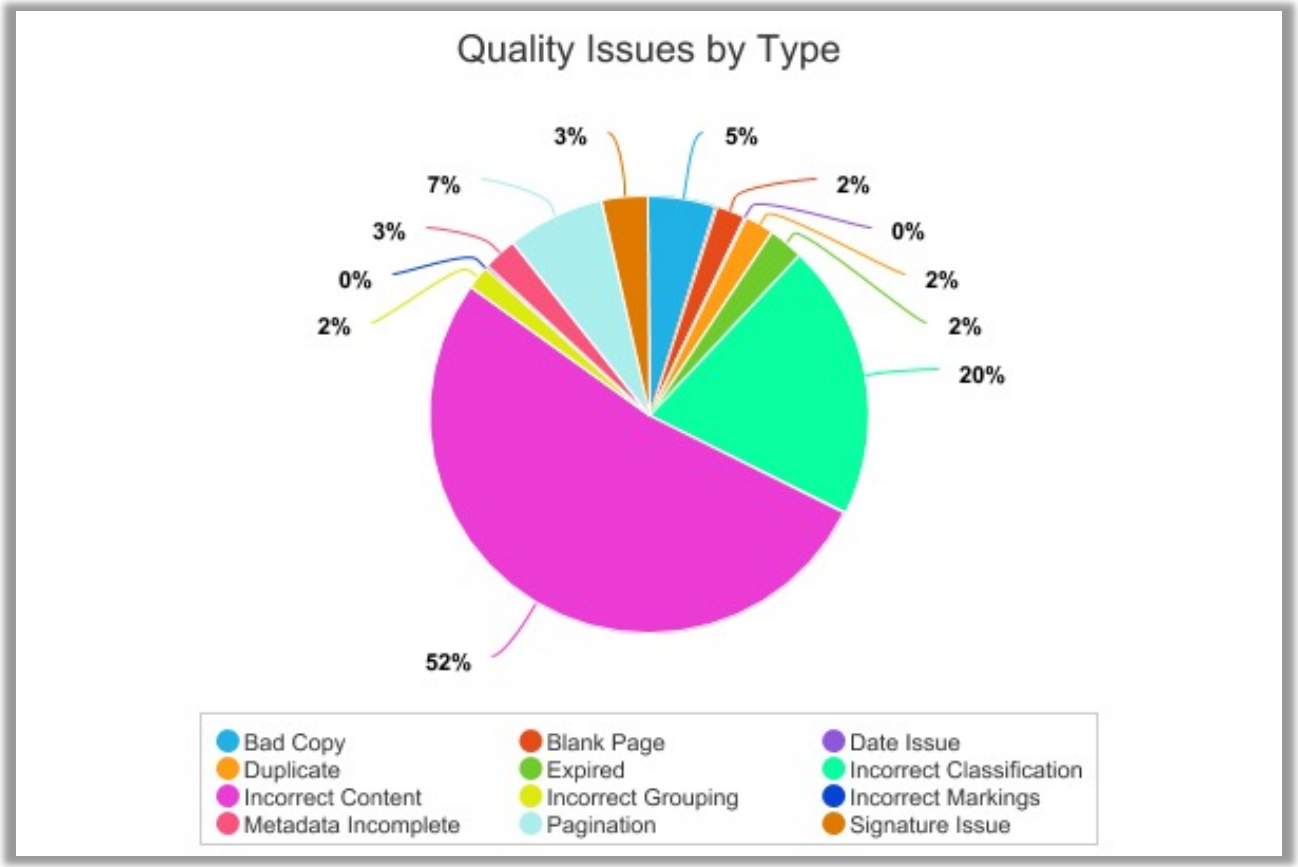
Content has been filed in TMF in a timely manner

Accurate

The TMF holds quality records and accurate metadata

Study Level TMF Health

*Report Generated on 21Oct2022



Missing Document

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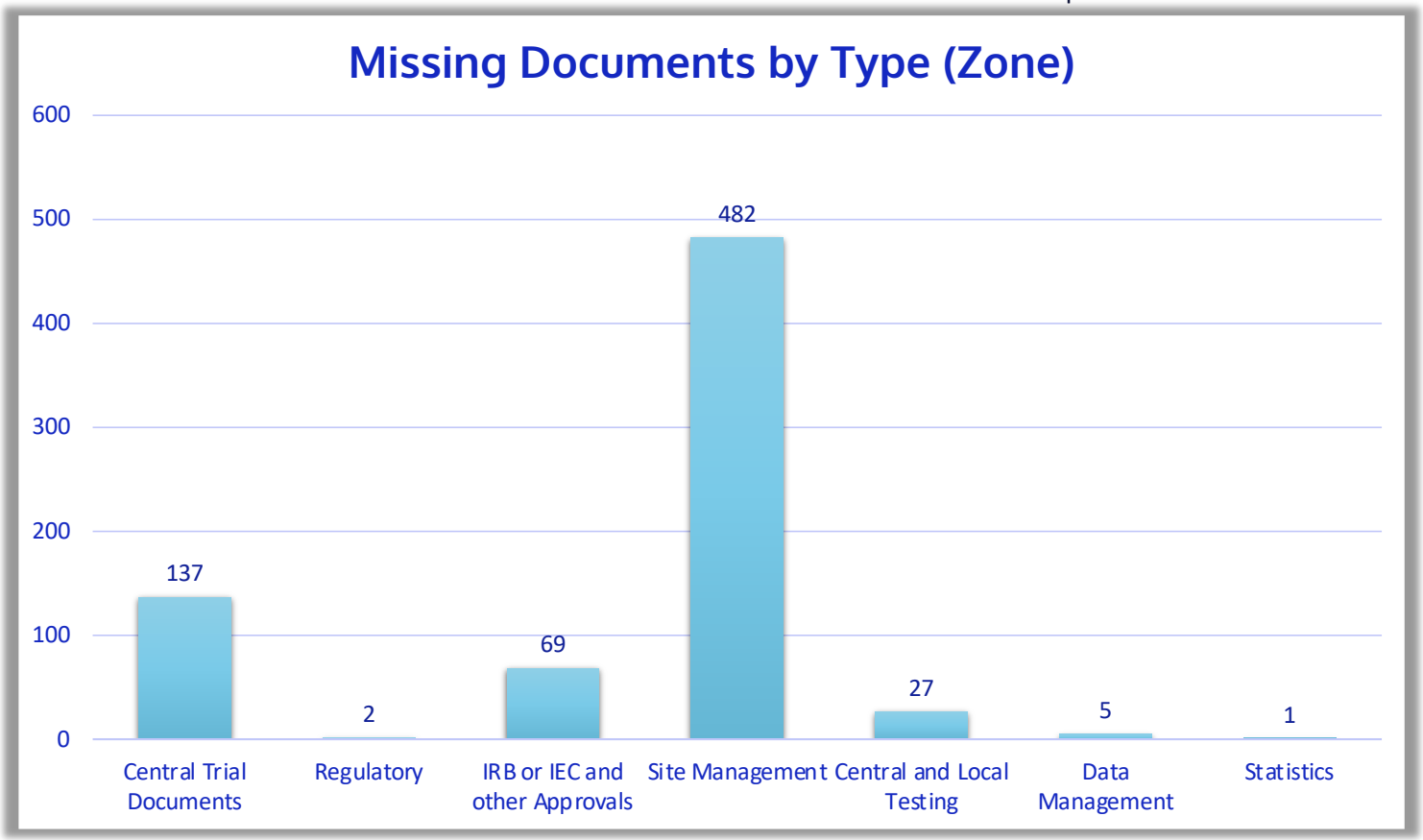

Trial Master File (TMF) as a Window into Trial Quality Gaps

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Gaps in Training Content

Collection

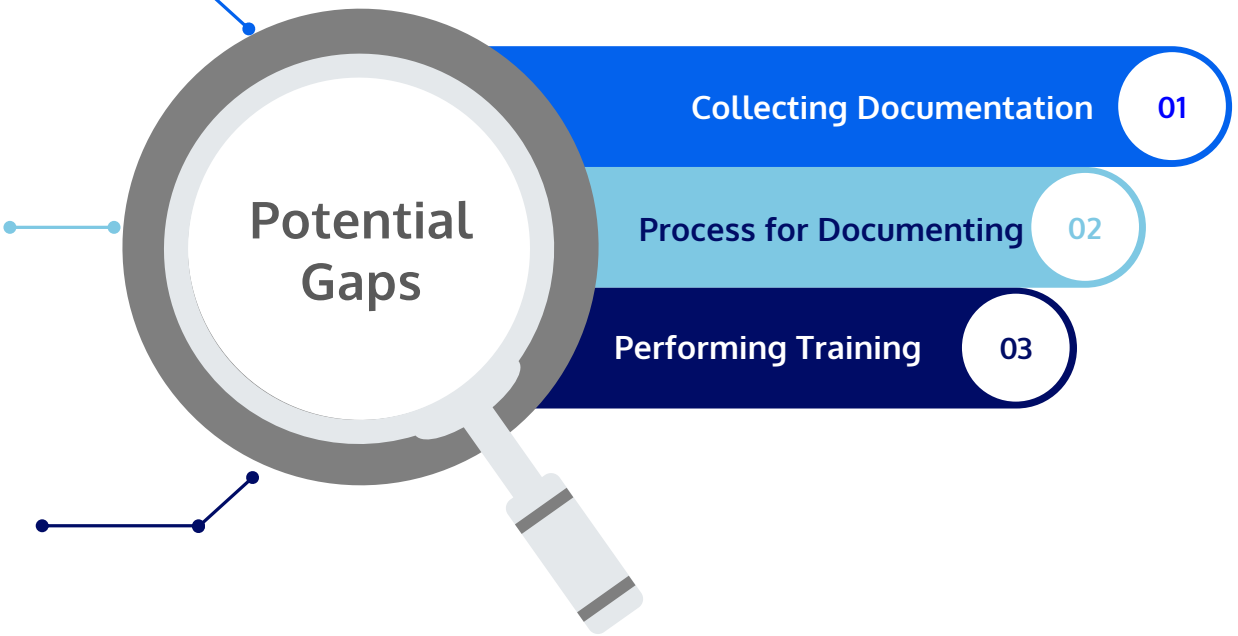
The training was performed & documented, but not collected.

Documentation

The training was performed, but not documented or collected.

Training

The training was not developed and/or delivered.

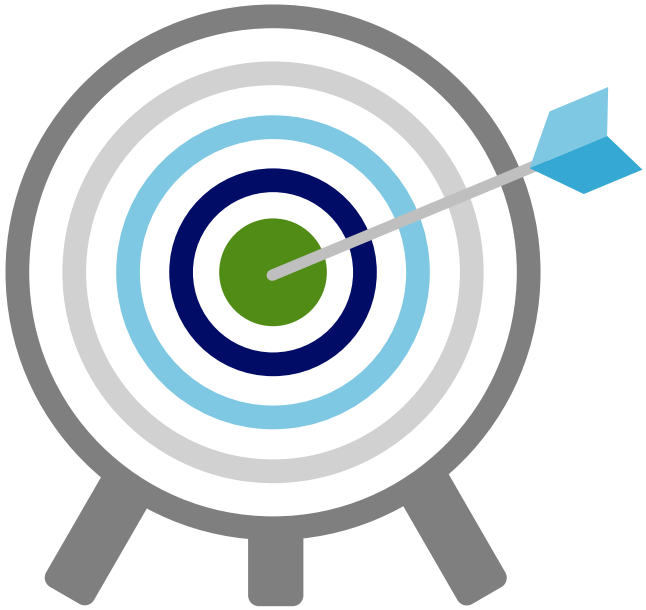


Impact on Quality

What do gaps in training content tell you about quality of the trial?

- Is documentation being collected and filed in the TMF?
- Who is responsible for training the trial team? Investigator sites?
- Does responsible party have a process for conducting & documenting training?
- Is the team relying on the site's process for documenting training? Is this an adequate process? Beware of inconsistent process – inspector can pick what they like and expect it across the trial.
- Have there been delays in ethics approval and therefore amendment has not been implemented at the site(s) and therefore no training.

Fixing the Gap – **Training Content**



Establish Requirements

Establish training requirements for study team and investigator sites.

Define Processes

Define the process for drafting training materials, performing, documenting, and collecting training documentation.

Clarify Expectations

Establish expectations in study plans and/or procedural documents.

Sustain Oversight

Continue to assess for completeness.

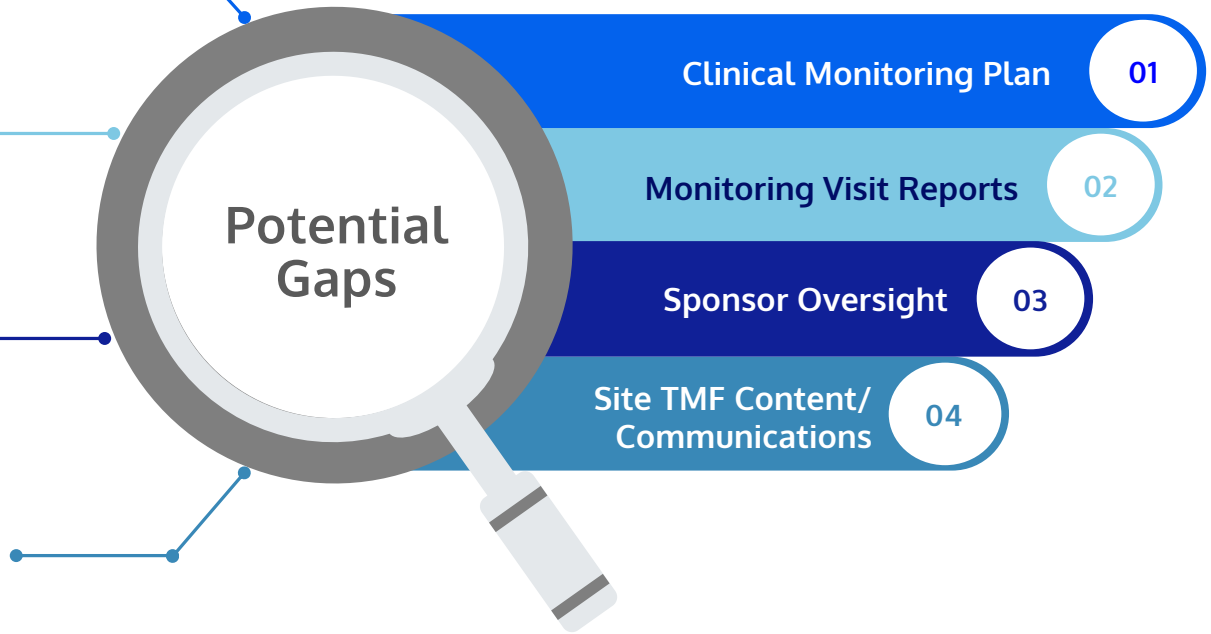
Gaps in Clinical Monitoring Content

Clinical Monitoring Plan
Missing Clinical Monitoring Plans could indicate deeper issues between the Sponsor/CRO.

Monitoring Visit Reports
Missing Monitoring Visit Reports could indicate process or logistics issue with the CRO.

Sponsor Oversight
Sponsors must document oversight of Monitoring Visit Reports, including all versions of trackers/logs.

Site TMF Content/Communications
CRAs generally collect content as part of routine monitoring visits. Is there an appropriate process for getting this content into the TMF?

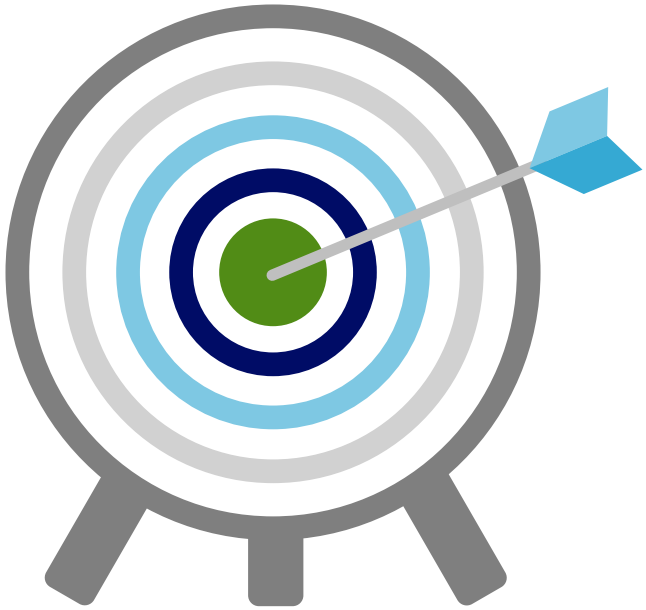


Impact on Quality

What do gaps in clinical site monitoring content tell you about quality of the trial?

- Missing Clinical Monitoring Plan
  - Gap in content? Gap in process?
  - Not finalized? Conflict between CRO and Sponsor?
- Missing Monitoring Visit Documentation
  - Gaps in monitoring visits?
  - Delays in finalizing report?
- Sponsor Oversight of Monitoring Visit Reports
  - Missing versions?
  - Escalations/follow ups documented?
- Missing Site TMF content / Site Communications
  - Is it being collected? Or is it not being submitted?
  - What are requirements from the CMP?
  - Telephone contact reports?

Fixing the Gap – Clinical Monitoring Content



Approve Plans

Finalized Clinical Monitoring Plan filed.

Define Processes

Establish oversight standards for reviewing Monitoring Visit Reports – document reviews.

Collect Content

Ensure site content is collected and filed.

File Content

Process for filing site communications.

Where there is smoke, there is fire.....

Overall Quality
If there are issues in the quality of the TMF, most likely there are issues in the quality of the study.

Time for Remediation
Early identification of quality issues allows time for remediation.

Root Cause Analysis
When reviewing the TMF, look beyond TMF quality issues to determine if it is an issue with quality documentation or an issue with quality process.

Questions?

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30 years experience in drug development and clinical compliance

Founded Just in Time GCP in 2005

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Lead Editor of the Barnett GCP Question & Answer Guide

Let Us Help You Answer...

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- Are Your **Partners Doing What They Say** They Are Doing**?**
- **What Don't You Know** About Your Study's Quality?
- Is Your **TMF GCP Inspection Ready**?

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- **TMF Story of the Study**
- **eTMF Current State/ Future State Roadmap**
- **TMF Health Assessment**
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A Question & Answer Guide

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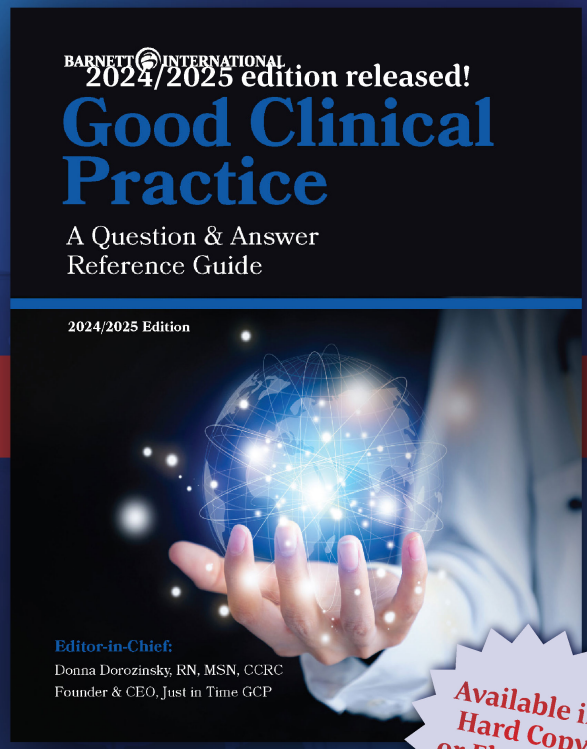

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