Unleashing your eTMF with advanced TMF metrics and KPIs Framework

Presented by Franciska Darmer, Darmer LS Advisory

Meet the Speaker

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With more than 25 years of experience within the life science industry, Franciska has worked for numerous Life Science organizations and technology vendors, supporting customers on their strategic digitalization journeys across clinical operations and data management. Specialising in TMF Management and process optimisation, Franciska now works as an independent advisor providing TMF Management services to global Life Science organizations

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.*
- *The author(s) have no real or apparent conflicts of interest to report.*

Inspection Ready

Optimized

and…

Completeness

Quality

Time

Overall compliance

Risk Based eTMF Management

Long-term process optimization

Generating business Value

Foundational eTMF Metrics

Using data to ensure Inspection Readiness

Ensuring Inspection Readiness

In 2014 the MHRA updated their definition of a critical finding to include TMFs that are not readily available, Accessible or incomplete

Critical & major eTMF related inspection findings, are often the result of insufficient focus on business processes and oversight, with seemingly small omissions leading to significant compliance risks

> *Where provision of the TMF does not comply with Regulation 31A 1-3, as the TMF is not readily available or accessible, or the TMF is incomplete to such an extent that it cannot form the basis of inspection and therefore impedes or obstructs inspectors carrying out their duties in verifying compliance with the Regulations *https://www.gov.uk/guidance/good-clinical-practice-for-clinical-trials*

> The TMF was not adequately defined to ensure all relevant documentation for an SAE case could be located

> There were many documents missing from the eTMF, for example, signature sheets, correspondence, emails and previous versions of documents

> ⋯the TMF did not contain all the essential documents required to enable the reconstruction of trial events and demonstrate compliance⋯

> The eTMF was incomplete and unreliable with emails incomplete, duplicate documents, blank/ incomplete documents, the same name for many different documents, same document under different names and in different locations and missing documents.

> Where the TMF maintenance had been contracted out to a third-party contractor, there was limited information available in the organisation's own files to demonstrate effective oversight of clinical trial activities

eTMF Management Today

Average QC Management efforts – Phase III Trial

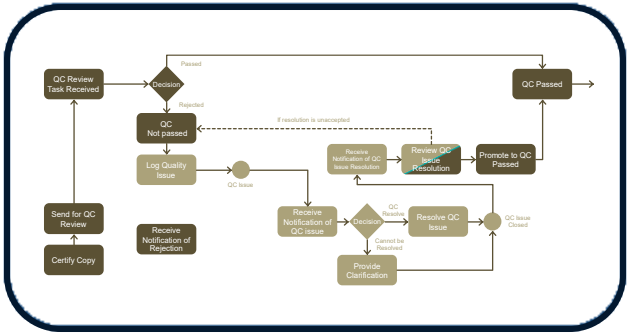
Average no. of documents in phase 3 trial	15.000
Minutes per document to scan, index and upload	4
Minutes to QC a TMF documents	2
Document Transfer Error Rate	20%
Average QI resolution time in minutes	4

Total efforts for basic TMF Management

15,000 x (4+2) + (15,000 x 20% x 4) = **1.700 hours**

The Data in Records Management

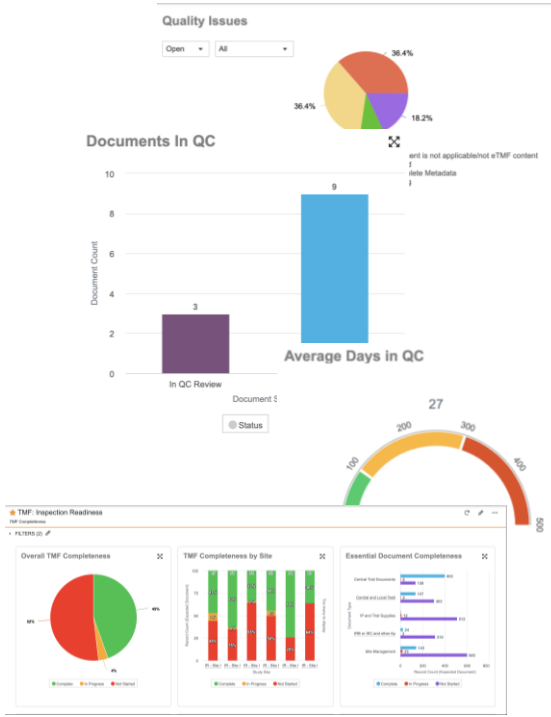
Purpose built eTMF systems drive data generation:



Sample QC workflow: Certfied copy → QC Review and Issue Resolution

+200 Data Points:

System users
Timestamps
Document classification
Document date
Document attributes
Associated vendor
Quality Issue (QI) type
QI details
QI resolution
Timeliness
QI ageing
Review cycle
Etc..

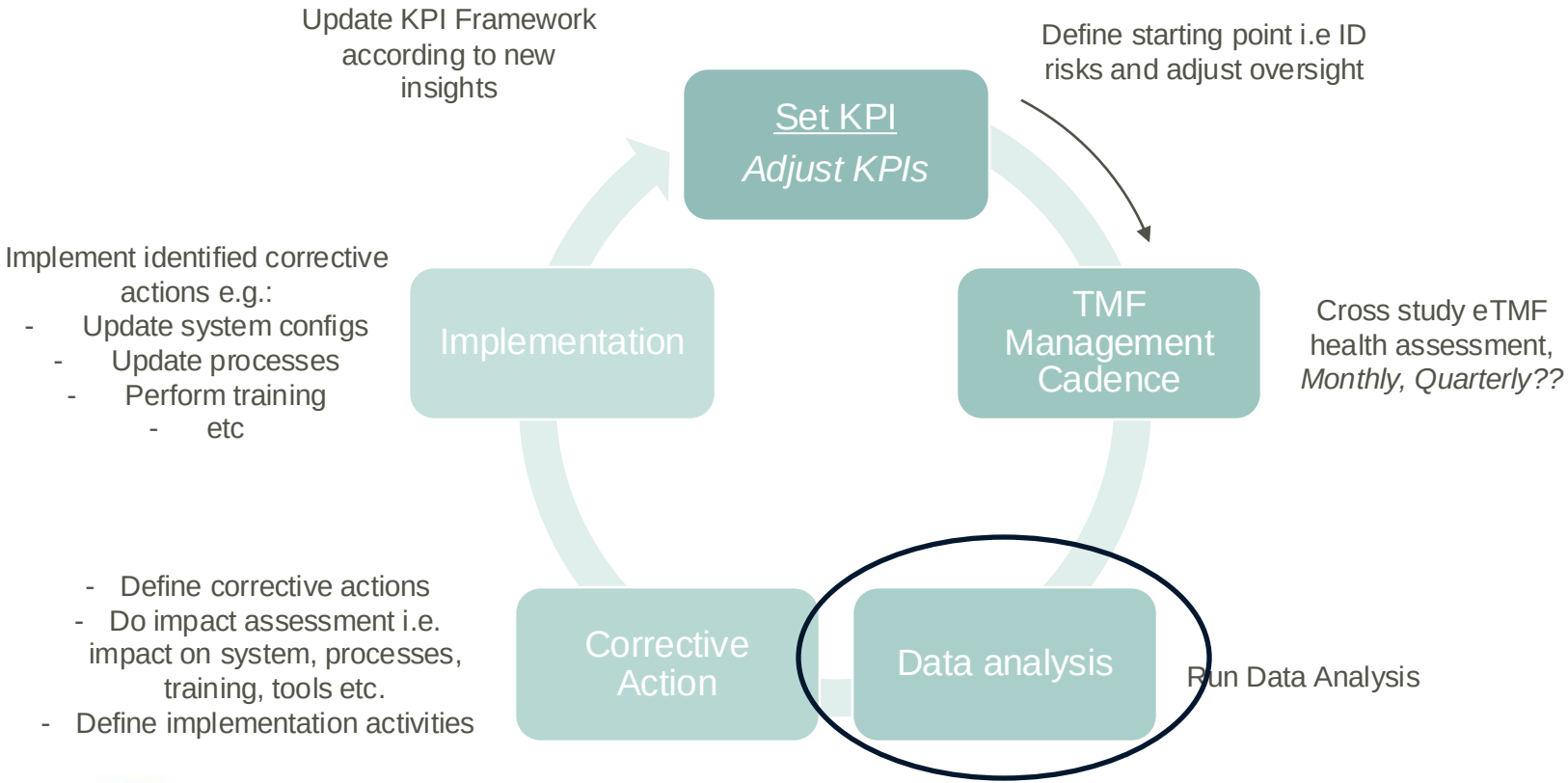


Understanding your data maturity…

What is your QI Rate?

- Do you have a QI threshold defined?
- What happens when you exceed your QI threshold?
- Which corrective actions might be performed?
- Do you track QI rates over time?

Using eTMF data to accelerate Inspection Readiness



Performing Data Analysis on eTMF Data

1 Extract eTMF data

ualification)	#QI
	18240
vestigator Brochure	108
02 Product Risk Language	77
00.01.03 Investigator Brochure Review Form	72
00.01.03.G01 Substantial Amendment Determination Form	24
00.01.04 Investigator Brochure Summary of Changes	17
00.01.05 Investigator Brochure Local Language Translation Documents	107
00.01.06 Investigator Brochure Other	27
00.02.01 Investigational Medicinal Product Dossier (IMPD)	10
00.02.02 Investigational Medicinal Product Dossier (IMPD) Translation Documents	2
00.04.01 Governance Committee Meeting Materials	26
00.05.01 Restricted Development Safety Update Report (DSUR)	25
00.05.01.G01 Restricted Six-Monthly Line Listing (SLL)	25
00.05.01.G02 Unrestricted Blinded Line Listing (BLL)	37
00.05.01.G03 Unrestricted Suspected Unexpected Serious Adverse Reaction (SUSAR)	124
00.05.01.G04 Restricted Suspected Unexpected Serious Adverse Reaction (SUSAR) Submission to IRB and IEC	609
00.05.01.G05 Unrestricted Suspected Unexpected Serious Adverse Reaction (SUSAR) Submission to IRB and IEC	21
00.05.01.G07 Unrestricted Suspected Unexpected Serious Adverse Reaction (SUSAR) Listing	3
00.05.01.G09 Restricted Country Specific Listing	10
00.05.01.G12 Unrestricted Six-Monthly Line Listing (SLL)	1
00.05.01.G13 Restricted Suspected Unexpected Serious Adverse Reaction (SUSAR)	2
00.05.02 Correspondence	46
00.05.02.G01 Unrestricted Urgent Safety Measure (USM) Letter	9
00.05.03 Tracking Information	15
00.05.04 Meeting Material	27
00.05.05 Minute	50
01.01.01 Trial Master File (TMF) Management Plan	124
01.01.01.G01 Trial Master File (TMF) Review Form	1713
01.01.01.G02 Trial Master File (TMF) Transfer Form	2
01.01.01.G03 TMF Study Lock Request Form	2
01.01.01.G05 TMF Oversight Plan	5
01.01.01.G06 TMF Startup or Update Form	3
01.01.01.G07 TMF Migration Related Documents	13
01.01.02 Project Management Plan	144
01.01.02.G01 Regulatory Affairs Management Plan	39
01.01.02.G02 Other Plans	346
01.01.05 Study Quality and Risk Management Documents	155
01.01.05.G01 Study Data Quality and Risk Management Documents	24
01.01.04 List of SOPs Current During Trial	70
01.01.04.G01 SOP Waivers	127
01.01.05 Operational Procedure Manual	172

2 Identify Repeating Patterns

	#QIs	QIs %
05 Site Management	167792	47%
04 IRB or IEC and other Approvals	45376	13%
02 Central Trial Documents	37742	10%
01 Trial Management	26323	7%
06 IP and Trial Supplies	19827	6%

QI Type 'Other' – QC Comment Based Breakdown	Approximately #QIs
Incorrect Title	15513
Incorrect or Missing Language	9155
Incorrect Date	4344
Incorrect or Missing Version	2666
Incorrect or Missing Metadata	2643

Title Incorrect or Incomplete	Data Incorrect	Classification Incorrect
05.02.07 Site Staff Qualification Supporting Information	05.02.07 Site Staff Qualification Supporting Information	05.05.01 Correspondence
05.02.10 Financial Disclosure Form	02.02.03.G02 Site Specific Informed Consent Form	05.04.05 Additional Monitoring Activity
04.01.02 IRB or IEC Approval	05.05.01 Correspondence	01.05.03.G01 CRO Meeting Material
05.04.03 Interim Monitoring Visit Report	04.01.02 IRB or IEC Approval	05.02.03 Protocol Amendment Signature Page
05.04.03.G01 Interim Monitoring Visit Confirmation Letter	05.04.03.G01 Interim Monitoring Visit Confirmation Letter	04.01.02 IRB or IEC Approval
05.04.03.G02 Interim Monitoring Visit Follow-up Letter	05.03.03 Site Evidence of Training	04.03.02 IRB or IEC Progress Report
05.02.05 Sub-Investigator Curriculum Vitae	05.04.03 Interim Monitoring Visit Report	05.03.03 Site Evidence of Training
04.01.01 IRB or IEC Submission	05.04.03.G02 Interim Monitoring Visit Follow-up Letter	02.02.03.G02 Site Specific Informed Consent Form
05.02.11 Data Privacy Agreement	05.04.06 Important Protocol Deviation (IPD) Form	02.02.03.G01 Country Specific Informed Consent Form
02.02.03.G02 Site Specific Informed Consent Form	08.01.01 Certification or Accreditation	05.02.07 Site Staff Qualification Supporting Information

Performing Data Analysis on eTMF Data

3 Do Root Cause Analysis

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4 Identify most impactfull cause for error

Ask why!

80:20 - Identify 20% cause for 80% effect:
Example:

- Limited use of Autonaming
- Limited guidance material available
- High turnover at CRO

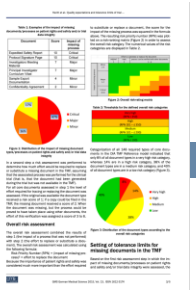
Risk Based Approach to TMF Management

When good enough is good enough

Risk Based Approach – An industry perspective

Applying a Risk Based Approach (RBA) to TMF Management to improve quality, ensure safety and overall data integrity…. and **reduce effort?**

ICH E6 (R2) – Public review June 2015, Published Nov 2016



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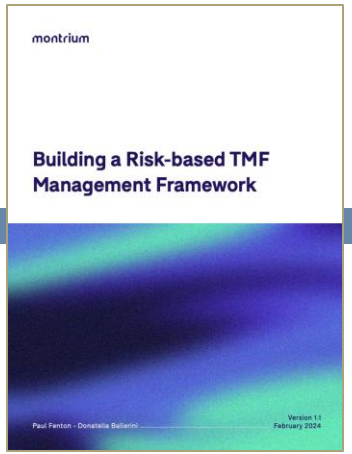
Vendor Presentation



V1.1. February 2024

CDISC TMF Risk Based working group - Adoption of Montrium Risk-based TMF Management Framework

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4

Realizing Business Benefits of RBA

Document Applicabilitty /Outsourced	Impact on Patient Safety/Data Integrity TBD	Primary QC (Indexer)	Secondary QC (via QC workflow)	Inspection Readiness /Additional Periodic Reviews (Post-approval QC)
Core /Outsourced	Critical Major Minor No Impact	100% 100% 100% 100%	100% 100% 0% 0%	10% 10% 10% 0%
Core /In-house	Critical Major Minor No Impact	100% 100% 100% 100%	100% 100% 0% 0%	10% 10% 10% 0%
Recommended /Outsourced	Critical Major Minor No Impact	100% 100% 100% 100%	100% 100% 0% 0%	10% 10% 10% 0%
Recommended /In-house	Critical Major Minor No Impact	100% 100% 100% 100%	100% 100% 0% 0%	10% 10% 10% 0%

Realizing Business Value with eTMF Data

Example of impact of RBA to eTMF on Quality Management

Average no. of documents in phase 3 trial	15.000
Minutes per document to scan, index and upload	4
Minutes to QC a TMF documents	2
Document Transfer Error Rate	20%
Average QI resolution time in minutes	4

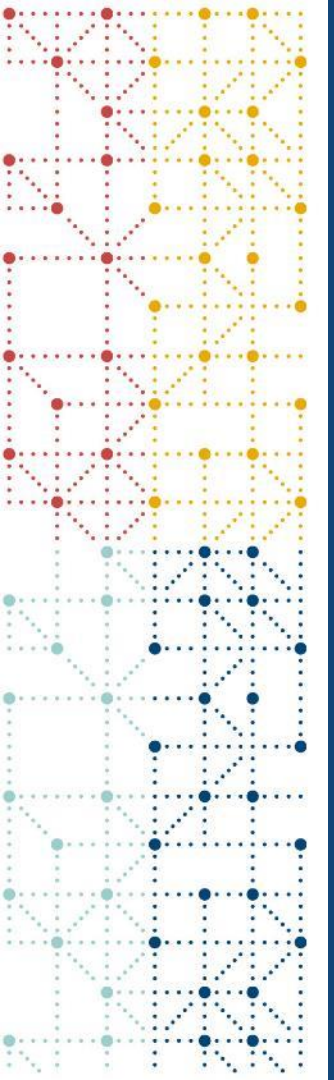
Total efforts for basic TMF Management
15,000 x (4+2) + (15,000 x 20% x 4) = **1.700 hours**

=

15-20% reduction in effort

1700h → 1445h

Impact of descoping all Minimal and No Impact artifacts



Thank you!

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Thank You!