2024 CDISC + TMF EUROPE INTERCHANGE — BERLIN

24-25 APRIL: CONFERENCE & EXPO | 22, 23, 26 APRIL: TRAININGS

Metrification of Your TMF Plan

Presented by Oli Cram, Product Director,
on behalf of Kathie Clark, Product Director CTMS and eTMF
Ennov - *Software for Life*

Meet the Speaker

Kathie Clark

Title: Product Director, eTMF and CTMS

Organization: Ennov - *Software for Life*

Kathie leads the design and development of Ennov's eTMF and CTMS solutions. She provides thought leadership for the industry and is the author of many white papers, journal articles and blog posts on eTMF, eClinical and regulatory topics. She is a member of the TMF Reference Model steering committee and has chaired or participated in a variety of working groups for the Reference Model. She has over 20 years of experience in regulated content management for Life Sciences and has worked with over 100 Life Sciences companies in the US, Europe, Japan, and Israel.

You can reach Kathie at kclark@ennov.com

Meet the 'stand-in' Speaker

Oli Cram

Title: Product Director

Organization: Ennov - *Software for Life*

Oli has over 16 years experience in the design and development of powerful EDC solutions for pharmaceutical companies, CROs, academic clinical trials units, and charitable organisations.

Oli works alongside Kathie delivering Ennov's eTMF and CTMS solutions, and together they are passionate about innovating to empower clinical research and improve patient outcomes.

You can reach Oli at ocram@ennov.com

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- *The author has no real or apparent conflicts of interest to report.*

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Agenda

1. The TMF Plan
2. Opportunities for Metrification
3. Conclusion

What is a TMF Plan?

- A TMF plan outlines the **procedures** and **guidelines** for **creating, maintaining, and organizing** the Trial Master File throughout the duration of the clinical trial.

- It details how documents will be managed, who is responsible for maintaining them, how they will be accessed, and how they will be stored securely to ensure compliance with regulatory requirements.

- Having a well-defined TMF plan is critical for ensuring the integrity, reliability, and regulatory compliance of clinical trial documentation
  - Streamlines processes
  - Mitigates risks
  - Facilitate efficient auditing and inspection by regulatory authorities

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TMF Reference Model TMF Plan Template

Scope of TMF Plan
BOLD = Opportunities for measurement

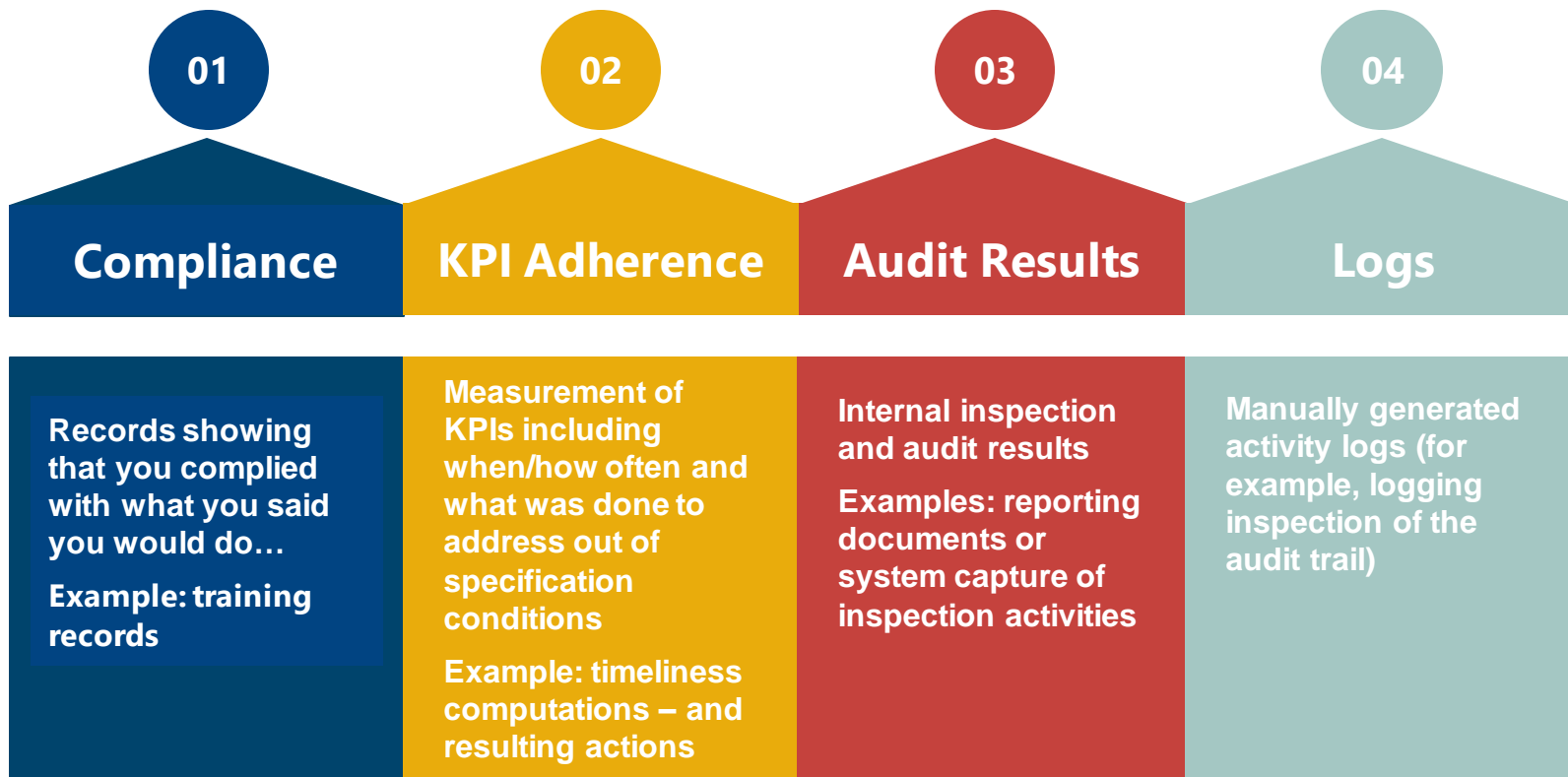|				
1	Approvals		7	Record and TMF Disposition
2	Document Version History		7.1	Destruction
3	Definitions and Abbreviations		7.2	Retention
4	Introduction		7.3	Archiving
5	TMF Oversight & Access Arrangements		7.3.1	Sponsor TMF
5.1	RACI Matrix		7.3.2	Investigator TMF
5.2	Access arrangements		7.4	Legal Hold
5.3	TMF Maintenance delegated to a CRO/Vendor		8	Applicable SOPs
5.4	For Inspections/Audits		9	**TMF Training**
6	TMF Content		10	**Conducting TMF Reviews**
6.1	TMF Format, Structure/Content Map/Specifications		10.1	**TMF Review Plan**
6.2	Authoritative Sources		10.2	**TMF Review Documentation**
6.2.1	**Originals, Wet Inks, and Raised Seals**		11	Transfers of TMF
6.2.2	**Relevant Correspondence**		12	Appendix
6.2.3	Unblinded Records			
6.2.4	**Translations**			

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Measuring the Process and Documenting Evidence

- As with most plans, Health Authority inspectors are likely to ask for evidence that you followed your plan

- In addition, organisations benefit from knowing if their plan is effective

- Examine your plan closely to identify areas where:
  - You make a commitment that you must prove you met
  - You define or reference a process that you must prove that you followed
  - You establish a KPI or threshold that can be measured

  ,,, and remove or modify those that don't add value

- Also define **who** will be responsible for measuring and analyzing, **what** standards must be met, and **how** deviations are addressed

TMF Plan

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Key recommendation: Define Evidence in Advance

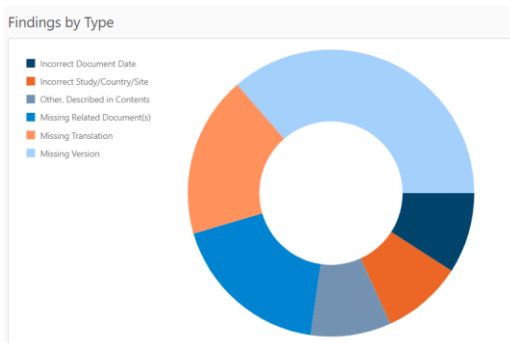| 01	02	03	04
Compliance	**KPI Adherence**	**Audit Results**	**Logs**
Records showing that you complied with what you said you would do… **Example: training records**	**Measurement of KPIs including when/how often and what was done to address out of specification conditions** **Example: timeliness computations – and resulting actions**	**Internal inspection and audit results** **Examples: reporting documents or system capture of inspection activities**	**Manually generated activity logs (for example, logging inspection of the audit trail)**

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the **Usual Suspects**

Your TMF plan may call out targets (KPIs) for TMF Completeness, Quality, and Timeliness. But… do you have:

- Clear **definitions** that are well-understood by all

- A defined **method** for automated or manual measurement

- Reporting requirements

- Clearly defined **escalations** and strategies for results that don't meet your KPI thresholds

QUALITY   TIMELINESS   COMPLETENESS

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Example: Measuring the TMF Review Process

- Plan recommendations: Describe the records expected to be generated, maintained and where filed to support the TMF review performed during the study. Plans for resolution should be included. If information exists in procedural documentation, refer to *Section 5, Applicable SOPs*

Top 5 Issues

REVIEW FINDING(S)

Missing Version

Missing Related Document(s)

Missing Translation

Incorrect Document Date

Incorrect Study/Country/Site

Findings by Type

- Incorrect Document Date
- Incorrect Study/Country/Site
- Other, Described in Contents
- Missing Related Document(s)
- Missing Translation
- Missing Version

- Reporting/metrics opportunities:
  - List of expected and actual records documenting review process; participants and roles
  - Confirmation that activities have been completed and records have been generated at expected times
  - Analysis of findings; evidence that findings have been addressed

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Example: Measuring the TMF Training Process

Plan recommendations: Describe how training will be handled both for internal and external users as appropriate. If necessary, append or embed training plans or other documents in this section or simply state the location of those documents.
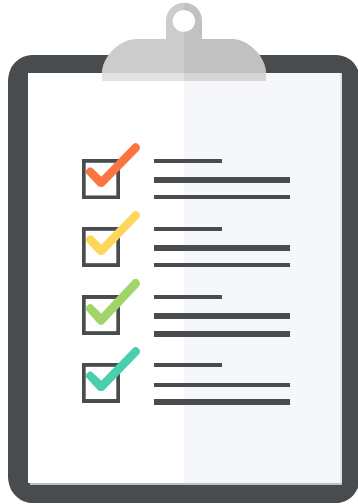
Reporting/metrics opportunities

1 List of expected and actual records documenting required and conducted training.

2 Review of training dates vs expected.

3 Review of identified need for / conduct of refresher or supplemental training.

4 Checks to confirm that regulated activities were not performed before required training was completed.

Vendor Performance

Service Level Agreements (SLAs)

- Fundamental component of vendor contracts. They define the specific services to be provided, performance expectations, and the metrics used to measure performance.

- SLAs can include criteria such as document processing times, quality standards, and responsiveness to inquiries or requests.

Quantitative analysis of vendor performance against the plan depends on mutually agreed, documented SLAs and KPIs.

Ideally, your eTMF can report agreed-upon metrics for **each specific vendor**.

Key Performance Indicators (KPIs)

- Quantitative measures used to evaluate the success of an organization or, in this case, a vendor in meeting its objectives.

- KPIs related to TMF management might include metrics such as document completeness, timeliness of submissions, accuracy of data entry, and adherence to regulatory requirements.

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Other Types of Audits against TMF Plan

TMF Plan Section	Type of Audit
6.2.1 Originals, Wet Inks, and Raised Seals	**Signature** audits: which records require signatures, and whether all final records have required signatures
6.2.1 Originals, Wet Inks, and Raised Seals	**Hardcopy** audits: which records require retention of paper, and confirmation that paper has been retained and cataloged
---	**Living document** audits: for any documents where TMF Plan/SOPs require periodic update of current version to TMF, checks that this was done
6.2.2 Relevant Correspondence	**Relevant Correspondence** audits: compliance with defined rules for relevant correspondence (also see TMF Reference Model Guidance for the Management of e-Mail Communications in Clinical Studies)
8 Applicable SOPs	**Applicable SOP** audits: compliance with SOPs listed in Section 8 (or your equivalent) of TMF Plan, including evidence of compliance
6.2.4 Translations	**Translation** audits: compliance with translation requirements established in your TMF Plan and/or Translation Plan

Effectiveness Check Ideas

01 USER SATISFACTION SURVEYS

Are the consumers of the TMF satisfied with their ability to find what they need quickly and reliably?

02 DOCUMENT RETRIEVAL TIME

Measure the time it takes to retrieve specific documents from the TMF when needed. Efficient document retrieval is crucial for responding to regulatory queries, audits, and inspections promptly
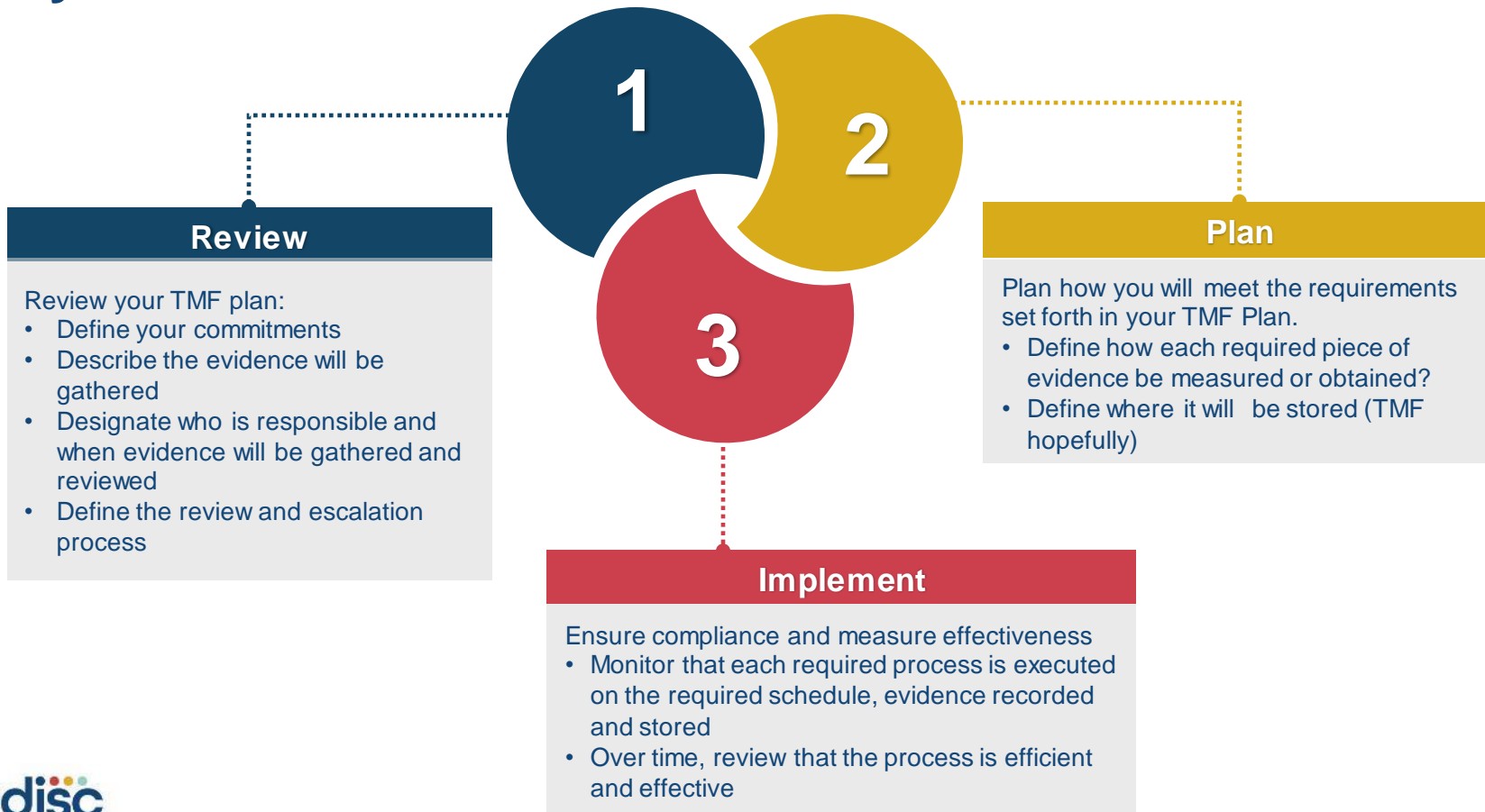
04 AUDIT FINDINGS AND CORRECTIVE ACTIONS

Track audit findings related to the TMF, including deficiencies or non-compliance issues. Measure the effectiveness and timeliness of corrective actions taken to address audit findings and prevent recurrence.

03 LOGS OF PROBLEM REPORTS

Check reports around "missing" documents (whether actually missing or not), misfiled documents, etc.

05 TRAINING AND COMPETENCY

Evaluate the training and competency of personnel responsible for TMF management. Monitor training completion rates and assess the proficiency of staff in document management procedures and regulatory requirements
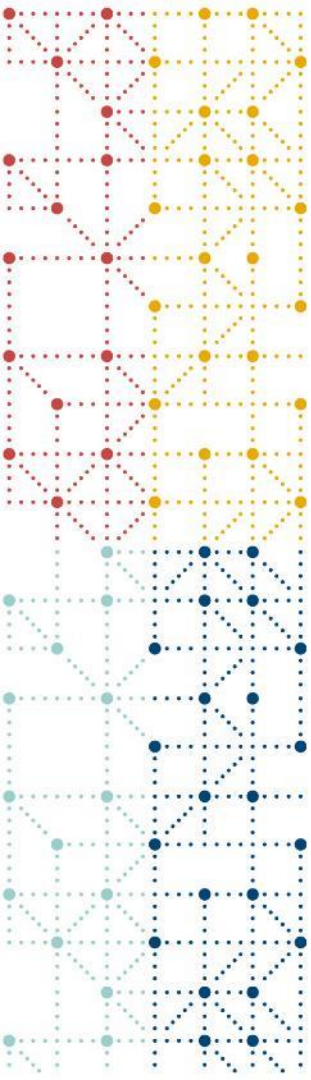
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Key Recommendations

1

Review

Review your TMF plan:
- Define your commitments
- Describe the evidence will be gathered
- Designate who is responsible and when evidence will be gathered and reviewed
- Define the review and escalation process

2

Plan

Plan how you will meet the requirements set forth in your TMF Plan.
- Define how each required piece of evidence be measured or obtained?
- Define where it will be stored (TMF hopefully)

3

Implement

Ensure compliance and measure effectiveness
- Monitor that each required process is executed on the required schedule, evidence recorded and stored
- Over time, review that the process is efficient and effective

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Conclusion

- By applying metrics to a TMF plan, organizations can monitor the effectiveness of their document management processes, identify areas for improvement, and ensure the integrity and compliance of clinical trial documentation throughout the trial lifecycle.

- Adding details of required evidence and associated metrics as part of your TMF plan can provide significant clarity, but keep in mind that this also results in establishing internal (management) and external (regulator) expectations

Thank You!

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