eTMF BOOTCAMP
FROM TMF NOVICE TO EXPERT

Presented by
Katherine Cianciarelli
Mayeesha Rahim

Date
18-Feb-2021

TMF Fundamentals

An Introduction to better Trial Master File Management

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Housekeeping

- This session will be recorded and made available to all registrants
- All recordings will be available on demand via a link sent following each event
- The Certificate of Attendance will be provided at the conclusion of the eTMF Bootcamp series
- Registrants must attend at least 1 eTMF Bootcamp session to receive the certificate

Other Bootcamp Sessions

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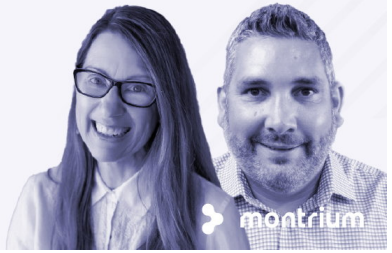
Session 2

Fran Ross, TMF Practice Director, Advanced Clinical

Paul Fenton, President & CEO, Montrium

Mastering & Integrating the TMF Reference Model in 2021.

March 4th @ 10am EST
(7am PST / 4pm CET)



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Session 3

Dawn Niccum, Sr. Director of QA & Compliance, InSeption Group

Improving the Quality of your TMF through Metrics & Technology.

March 31st @ 10am EST
(7am PST / 4pm CET)

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Session 4

Jamie O'Keefe, Vice President, Business & Technology Consulting, Just In Time GCP

Oliver Pearce, Commercialization Director, Montrium

How to Select & Implement an eTMF System in 90 Days.

April 14th @ 10am EST
(7am PST / 4pm CET)

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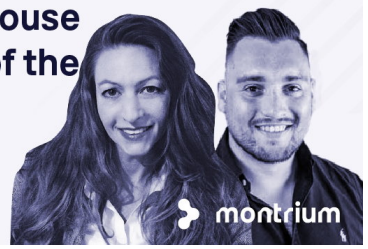
Session 5

Janine Penman, Managing Director, JPScientific

Oliver Pearce, Commercialization Director, Montrium

Bringing TMF Management In-House in 2021: The Year of the Sponsor eTMF

May 6th @ 10am EST
(7am PST / 4pm CET)



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Session 6

Stephanie Viscomi, Associate Director, TMF Operations, Alexion

Paul Fenton, President & CEO, Montrium

How to Manage a Multi-Vendor eTMF Ecosystem Effectively.

March 4th @ 10am EST
(7am PST / 4pm CET)

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Your speakers today

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Part 1

The Foundations of TMF Management

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What is a TMF?

- The Trial Master File (TMF) or its modern form, the Electronic Trial Master File (eTMF), is a collection of **essential documents** that are collected during the course of a **clinical trial.**

- This group of documents allows the conduct of a clinical trial to be **reconstructed and evaluated** at any point in time and provides **a story** of how the trial was managed and carried out. This collection of documents has to be updated regularly and the TMF completeness evaluated continuously.

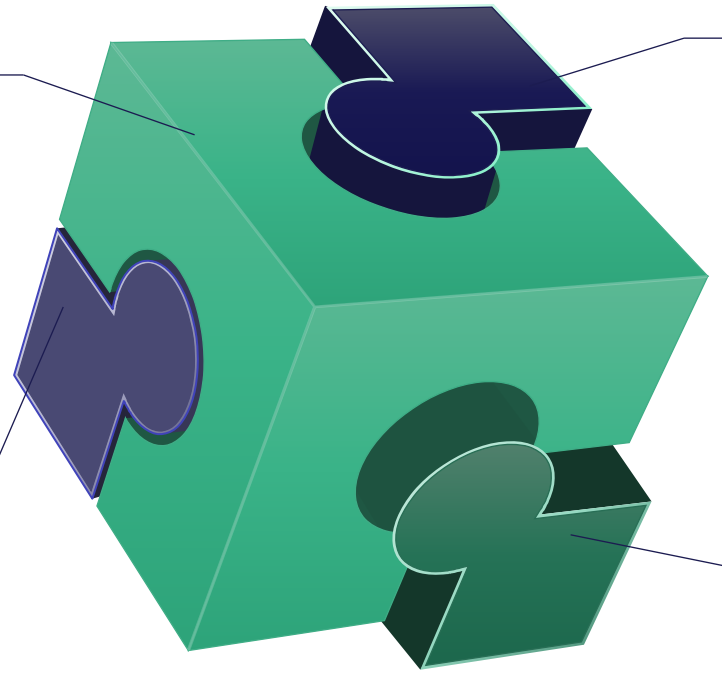
Foundations of TMF Management

1. Well defined TMF Plan
2. Standardized filing structure
3. Inspection Readiness framework
4. Contemporaneous use of basic metrics

Defining your TMF plan

1. Identify what you consider to be TMF content

2. Identify what content is being held in which systems



3. Identify metrics and KPIs for tracking TMF health

4. Identify who is responsible for your TMF content

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Internal Roles and the RACI Chart

RACI Charts can be used to establish the expectations of who will complete tasks associated to TMF Management

- R = RESPONSIBLE
- A = ACCOUNTABLE
- C = CONSULT
- I = INFORM

Example of RACI chart

	Director of Clinical	CRA	Project Manager	CTA	Data Manager	Pharmacovigilance Specialist	Statistician
Authoring Documents	C,I	R	A	I	R	R	R
Filing and Indexing	I	R	A	R	A	A	A
QC	I	R	A	R	R	R	R
Maintaining Quality, Timeliness and Completeness	A	I	A	I	I	I	I

POLL

Do you know who is responsible for the day-to-day TMF management in your organization for a particular study?

a) Yes, it's clearly defined

b) No, I'm not sure

c) Not currently managing the TMF at my organization

Part 3

Putting in place a standardized TMF structure

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Why is a structure important?

- Standardized filing and nomenclature across the team
- Improved efficiency of work processes
- Enforcing a standard facilitates exchange of information between stakeholders

The TMF Reference Model

The TMF Reference Model
The TMF Reference Model
The TMF Reference Model
The TMF Reference Model

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What is the TMF Reference Model?

The TMF Reference Model provides standardized taxonomy and metadata and outlines a reference definition of TMF content using standard nomenclature.

Zone #	Zone Name	Section #	Section Name	Artifact #	Artifact name	Definition / Purpose	Recommended Subartifacts - Documents/documentation recommended to be filed to the artifact.	Core or Recommended for inclusion
01	Trial Management	01.01	Trial Oversight	01.01.01	Trial Master File Plan	To describe how records for the trial will be managed and stored during and after the trial, including study-specific processes and documentation for archiving and destruction. To include TMF filing structure to be used. May include TMF content list, filing structure and chain of custody records. Artifact can include any evidence of plan execution including, but not limited to: plan, reports, checklists, etc.	Document Transfer Documentation Evidence of Quality Review Request to Lock TMF Trial Master File Plan Trial Master File Index Trial Master File Report	Recommended
01	Trial Management	01.01	Trial Oversight	01.01.02	Trial Management Plan	To describe overall strategy for timelines, management and conduct of the trial and typically makes reference to other artifacts. Artifact can include details on contingency plan covering details for site start up planning.	Clinical Development Plan Project Management Plan Trial Management Plan	Recommended
01	Trial Management	01.01	Trial Oversight	01.01.03	Quality Plan	To describe the operational techniques and activities undertaken within the quality management system to verify that the requirements for quality of the trial-related activities have been fulfilled. Relevant parts may include, but not be limited to, a plan written for internal oversight of study quality management, an audit plan, data verification steps; also includes escalation in the event of a quality issue being identified and all corrective and preventative actions determined. Artifact can include any evidence of plan execution including, but not limited to: plan, reports,	Quality Documentation Quality Plan Quality Report	Recommended

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POLL

Are you currently using the DIA TMF Reference Model?

a) Yes, version 3.1

b) Yes, version 3.2

c) A hybrid

d) No

Putting in place an inspection readiness framework

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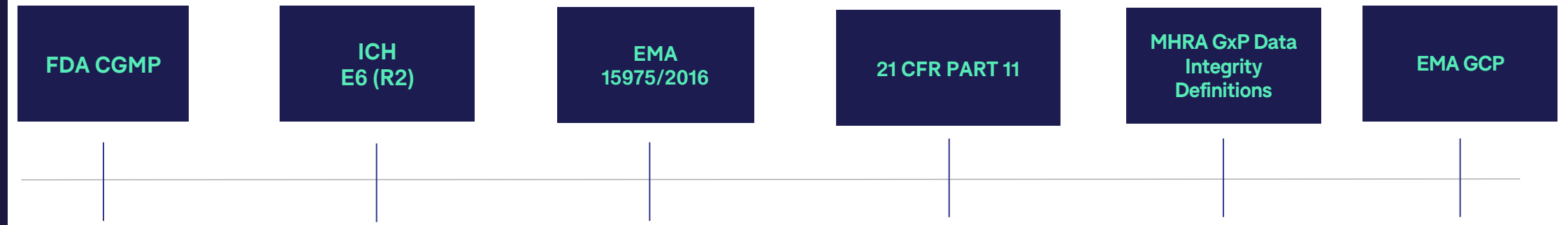
The Regulatory Landscape



FDA Data Integrity and **Compliance with CGMP (April 2016)**

Integrated addendum to **ICH E6(R1):** Guideline for Good Clinical Practice **E6(R2) (November 2016)**

Guideline on GCP compliance in relation to trial master file (paper and/or electronic) for content, management, archiving, audit and inspection of clinical **trials**

FDA Use of Electronic Records and Electronic Signatures in Clinical Investigations Under 21 CFR Part 11 Questions & Answers' **(June 2017)**

MHRA GxP Data Integrity Guidance and Definitions, Revision 1 **(March 2018)**

Guidance on remote GCP inspections during the COVID-19 pandemic (June 2020)

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What is an inspection?

- A trial master file inspection refers to “the act by a regulatory authority, in conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority to be related to the clinical trial and that may be located at the site of the trial, sponsor’s and/or CRO’s facilities, and other establishments deemed appropriate by the regulatory authority” (ICH GCP Sec 1.29).

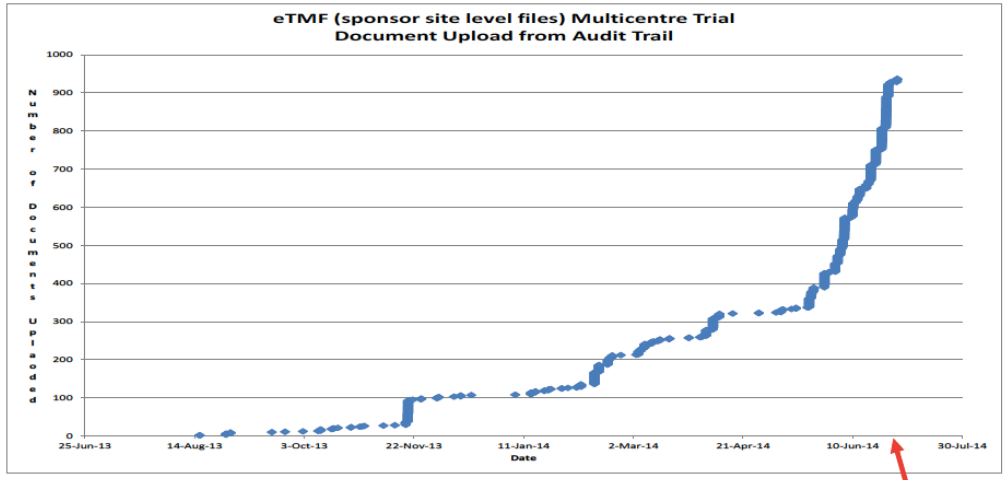
What is inspection readiness?

- Inspection readiness is a quality objective - the objective being to operate at a level that is always ready for inspection, without requiring much preparation in the days or hours leading up to the inspection.

- Inspection readiness starts by understanding the regulatory expectations for your TMF.

What they don't want to see

Document Uploading (audit trail)



What are the regulators looking for?
(in inspections)

1. To receive some form of access to the TMF, whether direct or assisted
2. To be able to review TMF related metrics that tell the story of how the study has been conducted and how the TMF has been managed
3. To easily access TMF relevant content that is not primarily stored in the TMF
4. That the sponsor ensures oversight of any outsourced activities including TMF management

Remote Inspection Requirements

- Adequate access to systems containing TMF Management
- Adequate communication tools including video conferencing, chat and inspector viewing tool
- Ability view audit trails, activity logs and metadata in order to reconstruct trial management
- Ability to download & save records
- Use of Electronic document request form and ability to track questions
- Ability to connect to all systems that hold TMF relevant information

Part 4

3 Pillars of Great TMF Management

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3 Pillars of Great TMF Management

Completeness

Timeliness

Quality

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Completeness

The TMF is considered complete when all the documentation collected over the course of a clinical trial are available in the TMF in an organized and auditable way that ensures that the trial can be reconstructed.

Completeness
Practical Considerations

- Start with the easiest attribute – milestones
- Build eTMF plans based on specific study designs
- Identify study events which would require artifacts e. protocol amendment, safety case
- Evaluate data needs to identify and calculate completeness of artifacts contained outside of the primary system

Timeliness

EMA:

- "Article 57 states "*the clinical trial master file shall at all times contain the essential documents relating to that clinical trial.*" The requirement "*at all times*" means that the TMF should be updated, and completed in a timely manner."
- "[…] it is important, therefore, to keep the TMF up to date, with documents placed in the TMF in a timely manner as this greatly assists the successful management of a trial by the investigator and sponsor (or party to whom the sponsor has delegated its duties)."

ICH E6:

- "Filing essential documents at the investigator/institution and sponsor sites in a timely manner can greatly assist in the successful management of a trial by the investigator, sponsor and monitor."

Timeliness

Practical Considerations

- Establish methods for measuring timeliness and standards around dates
- Consider a process to define when TMF artifacts need to be in a TMF
- Establish a mechanism for detecting missing artifacts
  - Most documents can be tied to a milestone e.g. Site Selected -> Site Initiated
  - Compliance with protocol timelines, study plans established at trial start
  - Workflows

Quality

The Trial Master File Reference Model Quality Group's (TMF RM QG) Recommendations for TMF quality review specifies a two step process for the review of the TMF, including firstly quality control of each of the individual documents as well as the entire TMF.

Quality

Practical Considerations

- Define a plan for risk-based TMF review, consider:
  - Study design and complexity
  - Number of vendors
  - Number of systems used containing TMF records
  - Assigning risk scores to document types based on process risk and other factors

- Think about how you can better organize information to better tell the story of what happened and leverage this information to assess risk

In conclusion

- A comprehensive TMF Plan is critical for setting yourself up for success
- A well defined structure allows for easy retrieval and exchange of documents and data
- Contemporaneous filing and defined scope and location of your content will help with inspection readiness
- Use of completeness, timeliness and quality will help you track and maintain the health of your TMF

CONTACT DETAILS

Get in touch

Thank You!

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