eTMF BOOTCAMP
FROM TMF NOVICE TO EXPERT

Presented by
Fran Ross
Paul Fenton

Date
March 4th, 2021

Mastering & Integrating the TMF Reference Model in 2021

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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
- Please ask questions throughout today's session
- 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

eTMF BOOTCAMP
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Your speakers today

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Advanced Clinical

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Montrium is a leader in Electronic Trial Master File (eTMF) solutions for emerging life biotech and pharma. We specialize in helping small and medium sized organization optimize and evolve their processes through the Connect platform

OUR HISTORY

2005
Established

50+
Experienced Employees

11000
Life Science Users

Montreal, CA
Headquartered in

OUR STORY

Life Science Exclusive
Extensive Industry Experience

Focus on Emerging Orgs
Leader for Small-Medium Companies

250+ Tech Implementations
An experienced partner

Global Customer Base
In over 30+ countries

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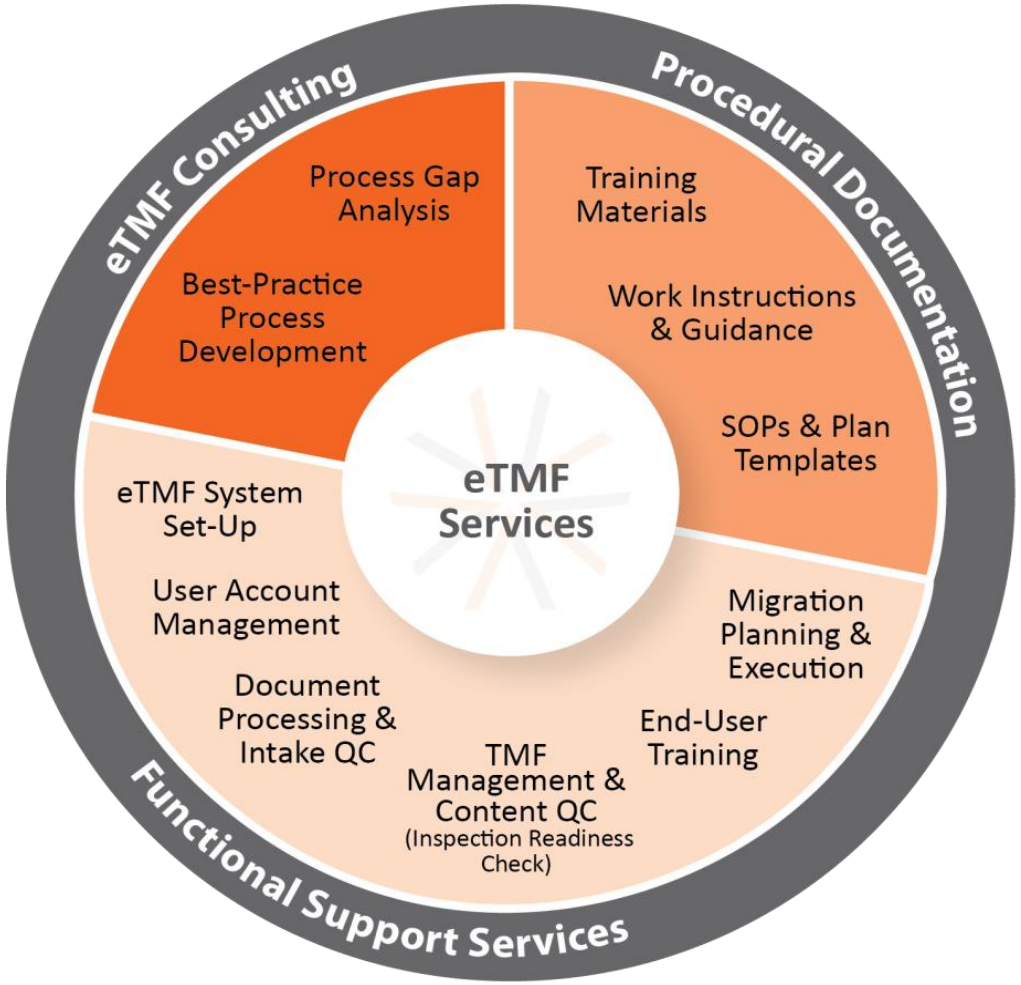
Advanced Clinical eTMF Services



Advanced Clinical offers *Strategic eTMF Services* as well as *eTMF Document Management* across the full TMF lifecycle

AC's eTMF philosophy
Compliance that works

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Agenda

- TMF Reference Model overview and organization
- Adapting the Model for any trial organization
- Applying the Model in eTMF
- Enabling the TMF Exchange Mechanism Standard

POLL

What is your highest priority TMF challenge today?

a) Leveraging the TMF Reference Model
b) Improving our eTMF system
c) Exchanging TMF records
d) Getting through an inspection
e) All of them!

TMF Reference Model Overview

Section #1

What is the TMF Reference Model?

- Industry consensus catalog of all TMF records
- ICH E6 Section 8 Essential Documents **plus** Adjudication, EDC, Data Mgmt, Statistics, etc.
- Drives clarity on the records to protect for clinical trial inspection
- Rigorous, extensive, collaborative and exhaustive life science community effort
- Positive feedback by Regulatory Authorities (not regulation nor requirement)
- Most recent version = TMF RM v3.2.1

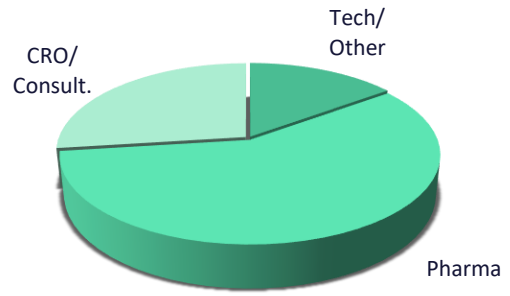
TMF Ref Model By the Numbers

- First version June 2010
- >400 members on team
- 60% US, 35% EU, 5% AP
- >400 Companies
  - Pharma
  - CRO
  - Vendor
- Regulatory agencies

  MHRA FDA

  EMA JPMA

Consortium Companies



TMF Reference Model Participation

- Community Meetings every other month
- Insights exchanged via LinkedIn and Yahoo groups
- Join (or start) community initiatives:
  - Change Control Board
  - eTMF-EMS

ALL WELCOME TO JOIN!

www.tmfrefmodel.com

How is the TMF Ref Model Structured?

Zone #	Zone Name	Typical Functions
Zone 1	Trial Management	Clinical Operations
Zone 2	Central Trial Documents	Clin Ops, Med Writing
Zone 3	Regulatory	Regulatory Affairs
Zone 4	IRB / IEC	Clin Operations
Zone 5	Site Management	Clin Operations
Zone 6	IP and Trial Supplies	Clin Operations, IP Supply
Zone 7	Safety Management	Safety
Zone 8	Central and Local Testing	Clin Operations, Bioanalytics
Zone 9	Third Parties	Legal, Procurement, Operations
Zone 10	Data Management	Data Management
Zone 11	Statistics	Statistics

POLL

Where are you on the TMF Reference Model continuum?

a) Using version 3.0 or later
b) Using version 2.0 or earlier
c) Working on TMF RM adoption
d) Thinking about adoption
e) Need more information

TMF Reference Model Benefits

Benefits of using the Model

- Tested and vetted by scores of life science organizations
- Industry Interoperability with trial third parties (CROs)
- Clinical partnerships and M&A
- OOTB alignment across the eTMF Vendor community

The Model is the START, not the FINISH

- Consensus, group-sourced Model = inherent compromise (record buckets, trial type records)
- Results should vary: your TMF needs specificity for your organization, your SOPs and your users
- Clarity in TMF structure drives excellence in eTMF management

Section #2

Adapting the Model for any trial organization

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TMF Information Architecture (IA)

- TMF IA = organization's baseline for:
  - Trial audits and inspections
  - eTMF configuration
  - SOPs
  - Clinical system interoperability

- IA is a crucial component of GCP inspection surety, and cornerstone for clinical trial technology initiatives

- Without a thorough TMF IA, organizations cannot transform TMF management from a burden to an asset

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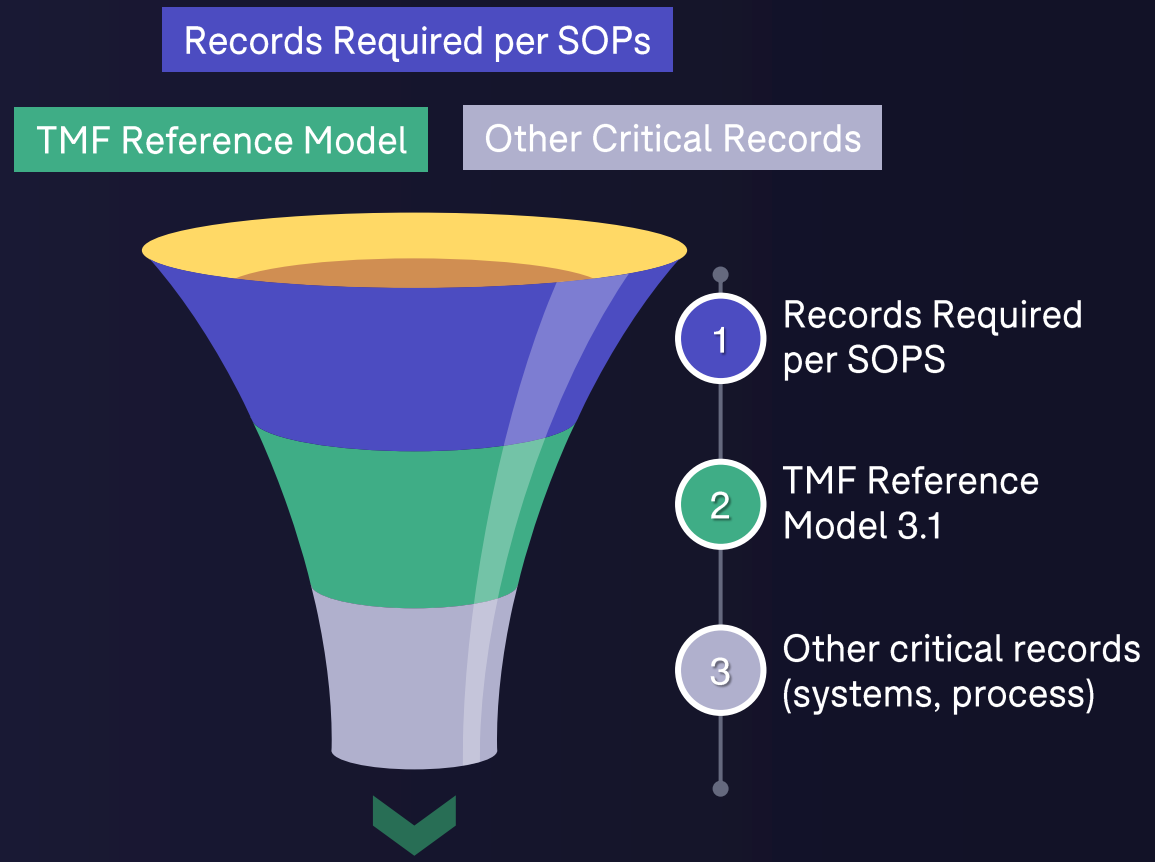
TMF Information Architecture (IA)

- Refine TMF Ref Model to **organization specificity**
- Drives enterprise transformation from “what's TMF?” to **"our own TMF"**
- Full transparency for clinical inspections



TMF Information Architecture

GOAL

TMFs autonomously demonstrate the full study story and prove compliance:

- Protocol followed
- Subjects protected
- Data solid

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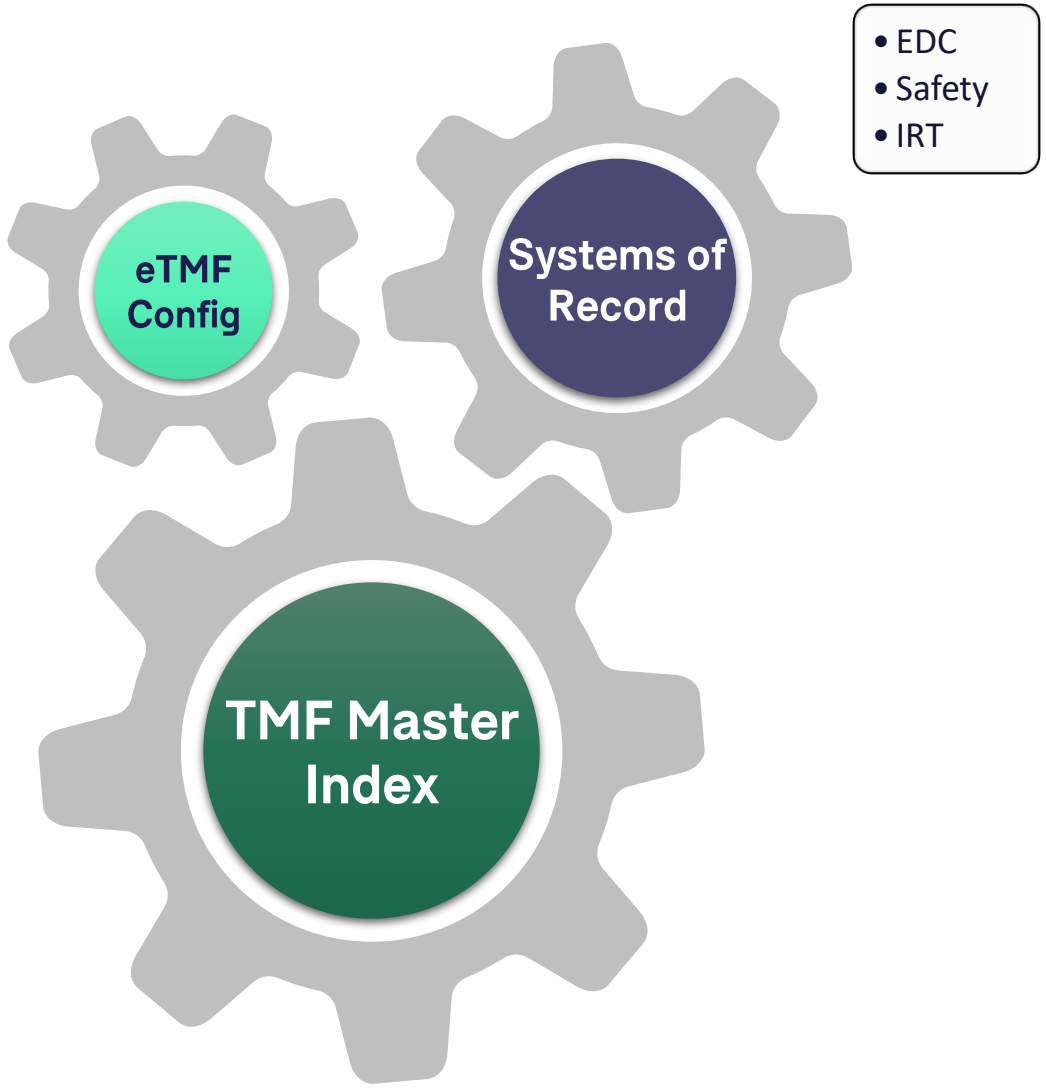
TMF Information Architecture (IA)

TMF IA is:

- Adopted from TMF Reference Model
- Global TMF baseline for all studies
- Clarifies standard “systems of record”
- Details eTMF config insights
- Used as starting point for each study’s TMF structure

TMF IA requires governance to stay aligned to:

- Health Authority changes
- New clinical practices
- Your SOP landscape
- TMF Reference Model updates
- eTMF Capabilities



How do you start it?

- **Prepare - do the ground work**
  - Join the TMF Reference Model community, understand the landscape
  - Know your TMF issues, find the applicable colleagues, ensure sponsorship

- **Clarify - differentiate the mission**
  - What will your TMF IA deliver, what will it not solve
  - Share “TMF Basics”, ensure common terms and language
  - Complete a current SOP gap analysis, create your baseline IA workbook = TMF Master

How do you finish it?

Gather – drive the discussion

- Set meeting norms, parking lot, expectations
- Conquer non-controversial records first (zone two before zone nine)
- Acknowledge gaps, track issues and move on
- Defer black holes – content creation complexity, third party differences, intra-department sore spots
- *Answer any question with an inspection view*
  "So fifteen years from now, the inspector…"

Accomplish – apply the results

- Celebrate the effort and the wins
- Inform everybody about everything
- Apply results –SOPs, change management, eTMF config, etc.
- **Safeguard the TMF Master –** updates will be needed

TMF Master – Example Column Types

Record Name	Expires (Y/N)	Signature (Y/N)	Restricted (Y/N)	System of record	Accountable
TMF Plan	N	N	N	eTMF	Clin Ops
Study Operations Manual	N	Y	N	eTMF	Clin Ops
Master Randomization List	N	N	Y	IRT	Biostats
Third Party Contracts	Y	Y	Y	eContract	Legal

TMF Master – Other Columns to Consider

Record Name	Level	Expected	Before (Milestone)	Version Required	Date Convention
TMF Plan	Trial	Y	First Site Initiated	Y	Version
Committee Charter	Country	N	First IRB Renewal	N	Approved
Lab Certification	Trial & Site	Y	Site Open	N	Effective
ICF	T/C/S	Y	Site Open	Y	Approved

TMF Master – other columns to consider

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ICF	T/C/S	Y	Site Open	Y	Approved

TMF Master - Additional Considerations

- **Keep all the TMF RM rows**
  - If artifact is not used note as N/A, or if solved by another record, note relationship
    - "Communication Plan N/A, component of Project Plan”
- **Don't delete the Artifact Number nor the Unique ID Code columns**
  - Artifact Numbers could change – Unique ID is forever
- **Judiciously add additional rows as required to ensure TMF completeness**
  - Critical records mandated in your SOPs or record buckets that require specificity
- **Judiciously rename records for user clarity**
  - "Other meeting material" = Trial Team Meeting Material
- **Leverage Sub-artifacts re-engineered in TMF RM Version 3.2.**

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TMF RM 3.2 – Sub-artifacts

- Sub-artifacts are records related to the main artifact
- Intended to give more options for TMF management specificity
- Sub-artifacts can be very useful, but need to be tailored
- Sub-artifacts fall into different categories
  - Alternative Names – different names for the main artifact
  - Related Records – documents in addition to the main artifact
  - Record LOVs – different types of the main artifact

TMF RM Name	TMF RM Subartifacts	Alternative Records	Related Records	Record LOVs
TMF Plan	Document Transfer Evidence of Quality Review Request to Lock TMF Trial Master File Plan Trial Master File Index Trial Master File Report		TMF Index TMF Review Certificate eTMF Access Log	
Trial Mgmt Plan	Clinical Development Plan Project Management Plan Trial Management Plan	Clinical Dev Plan Project Mgmt Plan		
Meeting Material	Agenda Attendance Sheet Minutes Presentation Materials			Agenda Minutes Materials Other
IP Site Release Documentation	IP Site Release Checklist IP Site Release Documentation IP Site Release Notification	IP Release Form Site Greenlight Form IP Release Checklist		
Close Out Monitoring Report	COV Confirmation Letter COV Follow-Up Letter COV Waiver Final Trial Close Out Mon Report	COV Waiver	COV Confirmation Ltr COV Follow-Up Ltr	

How long does a TMF IA take?

Good enough is great!

- Complete v1.0 mastery can take 4 to 12+ months
- Achieve as much specificity as possible
  - Expect clarity on the majority of critical record decisions
  - Defer items needing future attention
- Drive just over the speed limit
  - Request forbearance, appreciate cooperation
- Keep the laser focus on inspection

"So twelve years from now, the inspector would find …."

Section #5

Applying the Model in eTMF

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Have you implemented an eTMF which integrates the TMF Reference Model?

a) Yes, we implemented an eTMF which uses the Model as is without any modifications

b) Yes, but we made some changes to the RM

c) No, it was impossible to implement the RM in our eTMF

d) We don’t current have an eTMF

The reference model was designed for both paper and electronic systems...

Implementing the model in an eTMF

There are certain considerations that need to be taken in to account when implementing it in an electronic system:

- **Compliance** – Does the vendor of the system already provide a configuration which is aligned with the TMF RM
- **Document types** – there could be many more than the artifacts within the model, use of sub-artifact names could be useful
- **Versioning** – how to manage/update RM versions within your system
- **Completeness calculations** – using the core or recommended column to define what is required

Implementing the model in an eTMF (cont.)

- **Referencing** – Use the artifact number and unique ID
- **Structure** – leverage the process zone and section structure to facilitate navigation
- **Date conventions** – leverage the date conventions in the model to provide a basis for calculating timeliness
- **Import/Export** – The RM can provide a baseline to facilitate the identification of TMF content that needs to be exported/imported between 2 parties – eTMF-EMS takes this further
- **Metadata** – align with the eTMF-EMS where possible

What is the eTMF-EMS

Electronic Trial Master File – Exchange Mechanism Standard

- An extension of the TMF RM which focuses on the transfer of content, metadata, audit trail and eSig information
- A TMF metadata standard
- A mechanism for exchanging TMF content between systems
- A method for describing TMF artifacts which is comprehensible by both humans and machines

Current and future scope of eTMF-EMS

- Current focus is on the transfer of documents and associated metadata
- Scope will be extended in the future to provide for more use cases
- V1 already released and working groups about to start up for next version
- Speak with your vendor and ask if they currently or plan to support it
- Get involved with one of the EMS working groups (contact me…)

Questions?

CONTACT DETAILS

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Thank You!

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