Trial Master File Reference Model

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Guidance for the Management of e-Mail Communications in Clinical Studies

WEBINAR
15-JAN-2021

Agenda

Welcome and Introductions

Objectives

About the Guidance Document

Regulations, Guidance and References

Ongoing e-Mail Communications Management

Archiving

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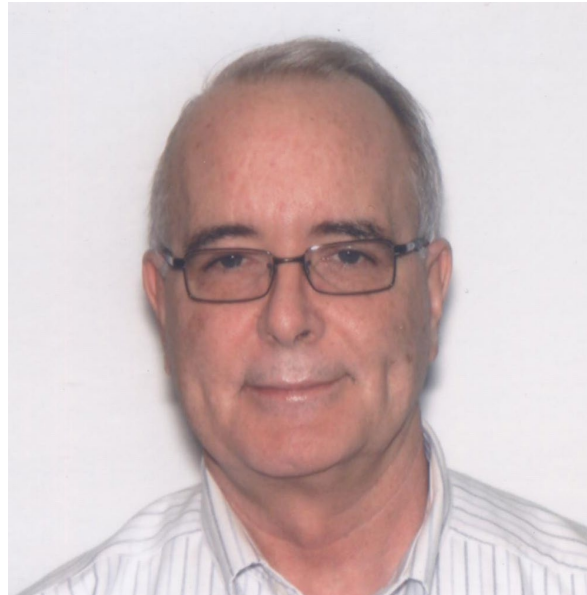**REFERENCE MODEL**

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Reference Model**

welcome

…and introductions

Meet the Presenters

Jamie Marie Toth
Sr. Director, Clinical Systems & Records
Daiichi Sankyo, Inc.
TMF Reference Model Steering Committee
Member
HSRAA Operations Committee Member
SAG Ltd., Board of Directors

Mark Mercer
Sr. Consultant CGI
Trial Master File SME

Russell Joyce
Director, Heath Barrowcliff Consulting Ltd
TMF Reference Model Steering Committee
Member
HSRAA Operations Committee Member
SAG Ltd., Board of Directors

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Objectives

Objectives for Today

To increase awareness of –and promote- the TMF Reference Model Guidance for the Management of e-Mail Communications in Clinical Studies

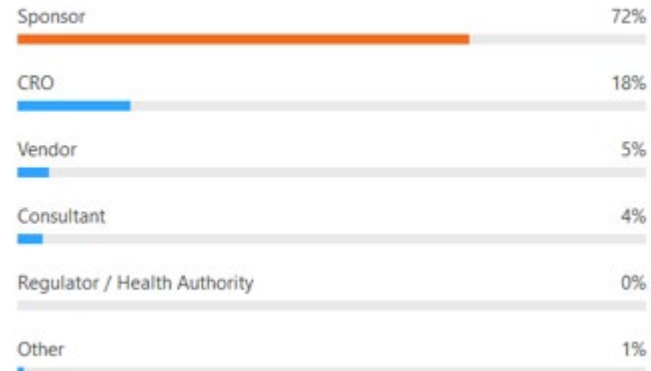To gain a greater understanding of how best to manage relevant communications in a clinical study

To encourage discussion of experiences in the management of relevant communications in clinical studies

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Poll

- For which type of organization do you work?

1. For which organization type do you work?

Organization	Percentage
Sponsor	72%
CRO	18%
Vendor	5%
Consultant	4%
Regulator / Health Authority	0%
Other	1%

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About the Guidance Document

Origin of the Guidance Document

Objective	**Across the industry, the issues associated with electronic mail (e-mail) are widespread. These include how we define and manage "relevant communications" for a trial/study; ensuring it is retained and appropriately managed in an authoritative system; and produced during a health authority inspection in a manner that is aligned with the expectations of regulatory authorities.**
Scope - In	Positions and recommendations for relevant electronic communications with a cross industry group ensuring that a wide range of viewpoints are incorporated (Sponsor, CRO, Vendor, Consultant).
Scope - Out	A technology tool for automation or specific technology tool(s) for managing e-mail.
Action Plan & Timeline	Kick off held October 2019; Four sub-teams (based on chapters in the text) met and then came back together.

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E-Mail Communications Sub-Group Members

Name	organization
Jamie Toth	Daiichi Sankyo, Inc.
Jennifer Wilson	Syneos Health
Kathie Clark	Ennov
LoriAnn Verna	JustInTimeGCP
Mark Mercer	CGI
Mary Ann Brooks	Baxter
Russell Joyce	Heath Barrowcliff Consulting
Shah Ashraf	Transperfect
Tiffany Steward	Astellas
Cynthia Pinto	GSK
Dickson D'souza	IQVIA

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Overview of Guidance Document

- **This is guidance!**
- **21 pages includes:**
  - How to effectively file e-mail
  - Responsibility for filing e-mail
  - Subject lines
  - E-mail branching
  - Attachments
  - Use of embedded links
  - Unblinding e-mails
  - E-mail dates
  - Archiving
  - Regulations (17 citations)
  - Appendices (3) on repository options, preservation format options, and definitions
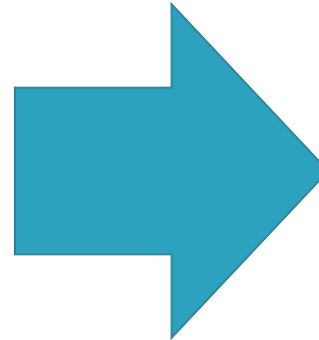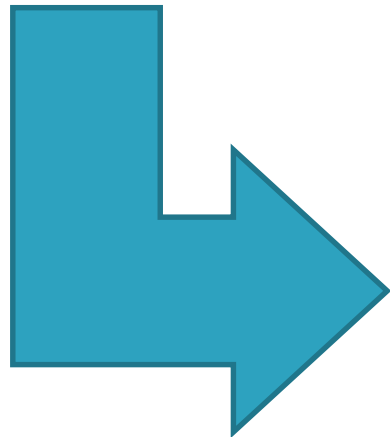
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Where To Find the Guidance Document

- Go to the TMF Reference Model website https://tmfrefmodel.com
- Click on **Resources**
- Scroll down to **TMF Tools**
- Select Industry Guidance: Electronic Communications

TMF Tools:

- Real-World Studies Document Index Provides a proposed Document Index for use on real-world studies, based on the TMF Reference Model for clinical trials (v1.0 Approved 29-July-2020) **NEW**
- Industry Guidance: Email Communications Guidance from the TMF Reference Model Project on the management of email communications in clinical studies (v1.0 Approved 29-July-2020) **NEW**
- TMF Reference Model User Guide: Introduction to the model, understanding its structure, and how to use it (v1.0 Approved 16-March-2018)
- TMF Reference Model Implementation Guidance: Provides a framework for implementing the model in your organization (v2.0 Approved 02-November-2020) **NEW**
- TMF Plan Template: Suggested structure and outline for a Trial Master File Plan (v1.0 Approved 23-February 2018)
- TMF Plan Template Feedback: Click on LINK to provide feedback on the TMF Plan
- Date Conventions Guidance: Guidance notes to be used with Date Conventions columns (Approved 15-Feb-2017)

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Regulations, Guidance and References

Regulations, Guidance, and References

Type	Title
Guidance	ICH GCP E6(R2)
Regulation	UK SI 2004/1031 Regulation 31A(9) and 31A(6)
Regulation	EU Directive 2005/28/EC
Guidance	MHRA GCP Guide 2012
Guidance	EMA/15975/2016 -Guideline on GCP compliance
Guidance	EMA/INS/GCP/856758/2018 Good Clinical Practice Inspectors Working Group Guideline on the content, management and archiving of the clinical trial master file (paper and/or electronic)
Regulation	Regulation EU 536/2014
Reference	MHRA Blog 30th Jul 2015
Reference	MHRA, TMF Q&A (Question 20) -ExL Events 7th TMF Summit, London, Oct 2018

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Ongoing e-Mail Communications Management

Disclaimer: It is for each organization to decide with established supporting guidance

Topics

M

- ❓ What is Relevant?
- 📧 E-Mail Formats
- 📍 Filing Locations
- 📁 Filing Responsibility
- ✉️ E-Mail Subject Lines & Matter
- 🔗 Attachments and Embedded Links
- 💬 Communications Containing Unblinding Information

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What is Relevant?

- An e-mail is relevant if it contains agreements or significant discussions and key decisions regarding

| study administration and conduct | protocol instructions, clarifications, and violations | safety information and reporting | awareness of issues arising during the study, especially exceptional or critical circumstances | study committees or boards and regulatory authorities | processes or decisions made where there is no SOP or policy to support that process or decision |

Poll

- How do you store e-mails in your eTMF?

Polling 2: eMail Formats ⌄ Edit

Polling is closed   209 voted

1. How do you store emails in your eTMF?

Native format (e.g. *.msg, *.eml, etc.)   (99) 47%

Rendered PDF   (93) 44%

Other, please specify in Chat   (17) 8%

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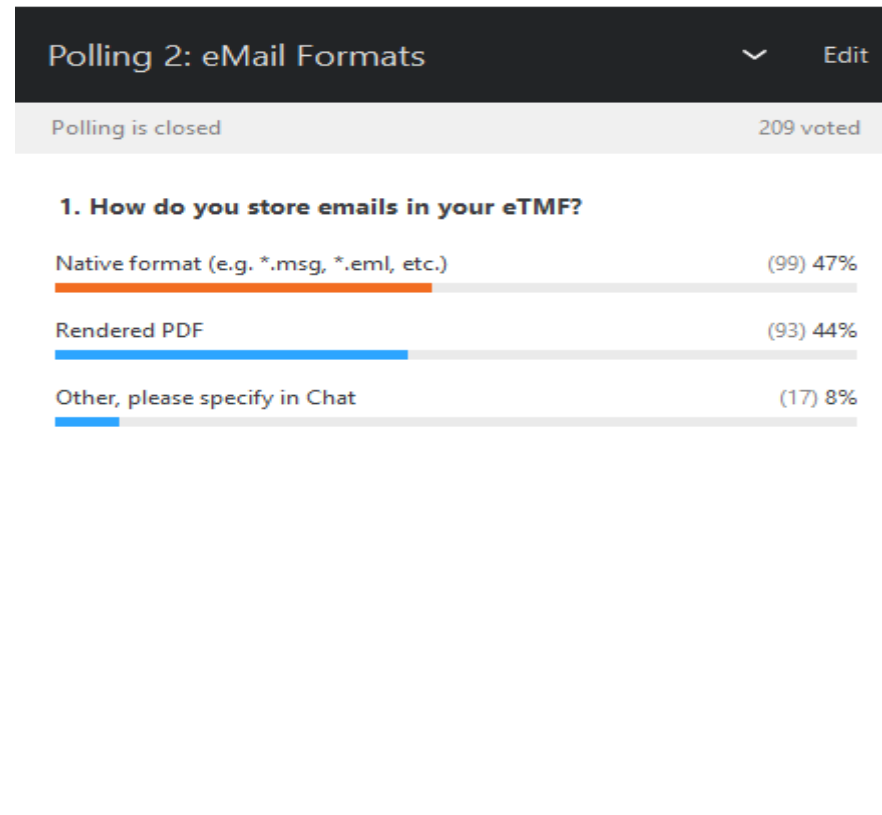
File Formats

- Native format best…
  - …with all metadata to preserve provenance, authenticity, integrity, and evidential value
  - …true for the initial e-mail and each response to prevent "after-the-fact" modifications

- Non-native format acceptable…
  - …from a regulatory perspective

- Consider longevity and (re-)usability of the format

- If working with third parties
  - …e-mail format should be agreed in TMF Plan
  - Include handling, storage, management, and transfer

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Filing Locations/Classifications

- Consider the purpose of the e-mail
  - …as it relates to reconstruction of clinical study events
  - Does e-mail align to an artifact, process, decisions, course of action
  - Relation to zone, section, or artifact

- Regulations do not stipulate the location
  - Take care to ensure that e-mails remain complete and legible
  - Must be able to be made available upon request

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Poll

- What is the frequency of TMF e-mails being filed?

Polling 3: Filing Frequency   ⌄   Edit

Polling is closed   210 voted

1. What is the frequency of TMF e-mails being filed?

Contemporaneously throughout the duration of the study   (114) 54%

Periodically during the conduct of the study   (70) 33%

At study closure   (26) 12%

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Poll

- Who is responsible for filing e-mails into the TMF?

Polling 4: Filing Responsibility ∨ Edit

Polling is closed — 200 voted

1. Who is responsible for filing e-mails into the TMF?

Originator of the communication	(76) 38%
Primary recipient of the communication	(27) 14%
Central group or individuals responsible for filing all communications	(82) 41%
Other, please specify in Chat	(15) 8%

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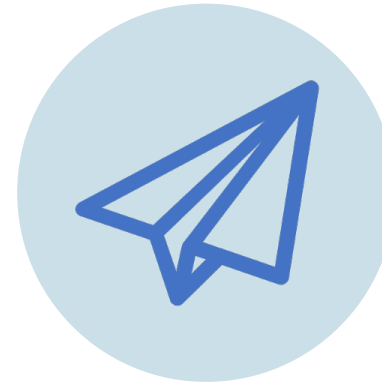
Filing Responsibility

Contemporaneously throughout the duration of the study

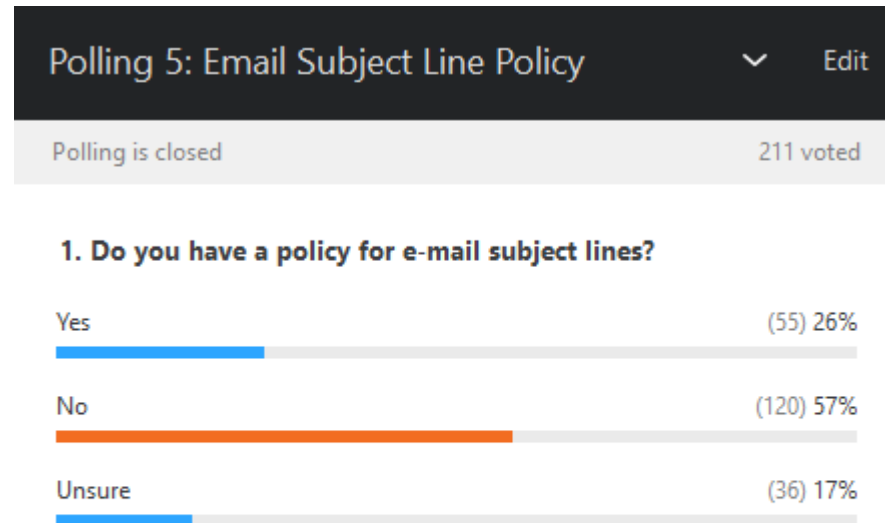Periodically during the conduct of the study

At study closure

Originator of the communication

Primary recipient of the communication

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M

Poll

- Do you have a policy for e-mail subject lines?

Polling 5: Email Subject Line Policy ⌄ Edit

Polling is closed   211 voted

1. Do you have a policy for e-mail subject lines?

Yes   (55) 26%

No   (120) 57%

Unsure   (36) 17%

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e-Mail Subject Matter

eMail lines problematic if …
…subject matter changes
…the e-mail branches

Where necessary to change the subject matter…
…start a new e-mail with a subject line related to the new subject matter.

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e-Mail Subject Lines
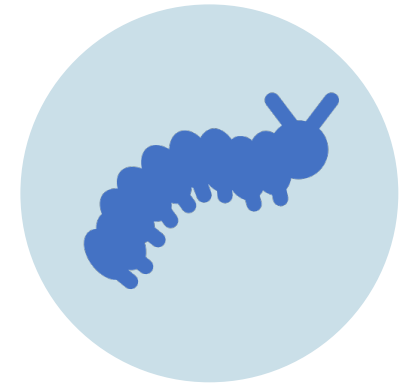
Concise and focused?

Repetitious?

Meaningful?

Relatable to one topic?

Unambiguous?

Poll

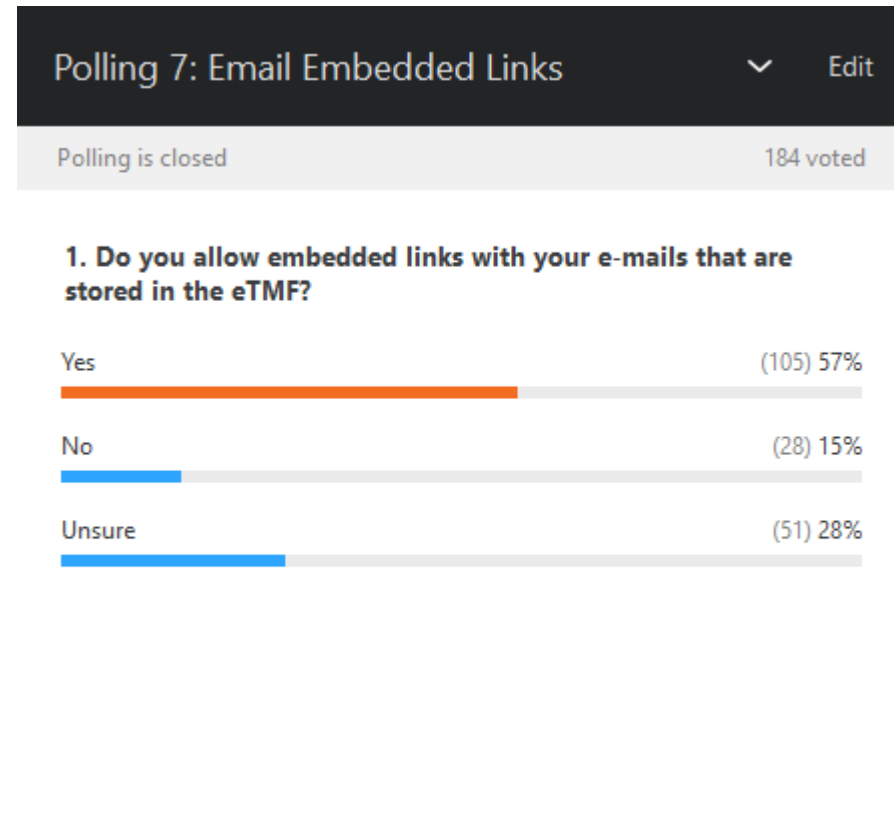- Do you store your e-mails with attachments?

1. Do you store your e-mails with attachments?

Yes	74%
No	17%
Unsure	9%

Poll

- Do you allow embedded links with your e-mails that are stored in the eTMF?

Polling 7: Email Embedded Links   ⌄   Edit

Polling is closed   184 voted

1. Do you allow embedded links with your e-mails that are stored in the eTMF?

Yes   (105) 57%

No   (28) 15%

Unsure   (51) 28%
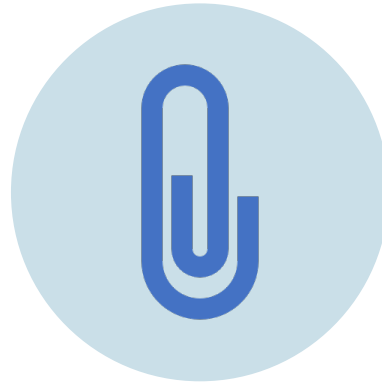
Attachments and Embedded Links
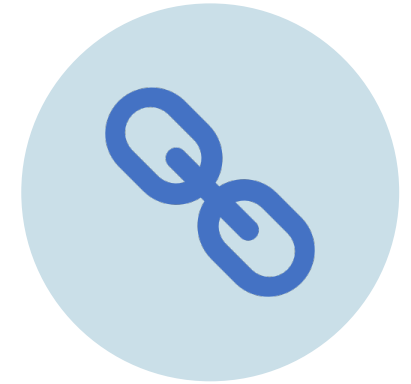
Considerations

Already filed with TMF

Content of e-Mail is relevant

Contains an attachment not filed within the eTMF

Risk to attachment lost during rendering

Avoid the use of embedded links

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Communications with Unblinding Information

- **File in (e)TMF with the relevant artifact**
  - but access should be strictly controlled and restricted
  - at study, country and site level as applicable
  - should not be accessible by blinded users until study blind is lifted

- **If not filed contemporaneously…**
  - …establish process to file after blind is lifted
  - …and before (e)TMF is archived.

- **Once the study blind is lifted,**
  - controls must be in place to capture and maintain audit trails

- **For each organization to decide**
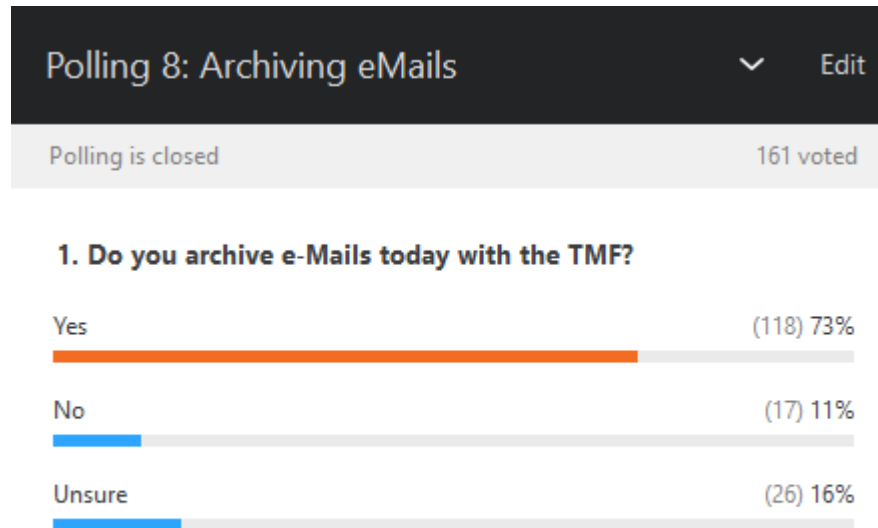 - …but must establish supporting guidance

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Archiving

Poll

- Do you archive e-Mails with the TMF?

Polling 8: Archiving eMails   ⌄   Edit

Polling is closed   161 voted

1. Do you archive e-Mails today with the TMF?

Yes   (118) 73%

No   (17) 11%

Unsure   (26) 16%

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Archiving

Ensure that archived records remain:

- ✔ available on request
- ✔ non-modifiable, complete, and legible
- ✔ for duration of the required retention period

GCP Archivist should have custody of all archived communications

Provide signpost in TMF index to show archive location

Consider [impact of] preservation format options*

*Note: No regulations mandate format for archived e-mails

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Questions and Answers

Questions/Comments

email@tmfrefmodel.groups.io

Or

Post on the tmfrefmodel.com at https://tmfrefmodel.com/forums look for the *e-mail communications* topic

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About the TMF Reference Model

- Website: https://tmfrefmodel.com

- Join the TMF Reference Model Discussion Group
  https://tmfrefmodel.com/register

  - ✔ Knowledge sharing
  - ✔ Networking
  - ✔ Too Much Fun!

- Join the TMF Reference Model Project Team
  - but be prepared to work!)
- https://tmfrefmodel.groups.io/g/main

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