Trial Master File Reference Model

General Meeting

11 February 2019

While we are waiting for attendees to join and the host to start the meeting, all lines will be muted. Please stay on the call. You can unmute yourself when you want to talk!

Agenda

- Welcome
- Membership Update
- Sub-group / Initiatives update
  - Investigator TMF Clarifications
  - Sub-artifacts
  - Observational Studies
  - Exchange Mechanism
- Framework for destruction RELEASED
- EMA Guideline on the content, management and archiving of the clinical trial master file – the draft to final changes
- The TMF Summit in Orlando – the key learnings!
- Upcoming Industry meetings
- Meeting reminders (instructions at the back)

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Since last meeting*…

- 10 new project team members – current total 257
- 28 new Mailing List Subscribers – current total 792
- 17 new Yahoo!Group Forum members – current total 585
  - 24 new discussion topics posted (60 messages)
- LinkedIn group – 2,730 members (52 new members)
  - 6 new discussion topics posted

- For details on all these different groups and how to get involved, see http://tmfrefmodel.com/join

* 12 Dec 2018

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TMF RM Active Initiatives

Initiative	Lead	Deliverables	Completion Goal
Investigator TMF Clarifications*	Fran Ross	• Investigator TMF terminology position paper • New column identifying holder of originals for each artifact • → Submit to Change Control Board	March 2019
Document Status	Scott McCulloch	• White Paper summarising/referencing current regulatory positions on: certified copies; filing of originals; management of document versions	March 2019
Devices	Melonie Warfel	• Enhancements/updates to the TMF Reference Model to facilitate easier adoption for medical device and diagnostics trials. • → Submit to Change Control Board	March 2019
Sub-artifacts*	Karin Schneider	• Comprehensive revision of the 'sub-artifact' examples in column I • → Submit to Change Control Board	June 2019

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TMF RM Active Initiatives

Initiative	Lead	Deliverables	Completion Goal
Annual Survey	David Ives	• Completed industry survey	September 2019
Observational Studies*	Russell Joyce	• Identify existing Reference Model artifacts that would be expected for observational studies and any additional artifacts not already included in the Reference Model • → Submit to Change Control Board	TBD
J-GCP	Jamie Toth	• To be confirmed, pending review/understanding of JPMA deliverable	TBD
Exchange Mechanism*	Paul Fenton	• Standard mechanism for the transfer of eTMF content	Ongoing

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Investigator TMF Clarifications

Issue:

While the term “Trial Master File” (TMF) has become a well-known industry term for a sponsor’s clinical trial records, there are several different terms used by regulators and by clinical research professionals to describe an investigator’s clinical trial records (Investigator Site File (quoted in the EMA Paper), Site Master File, Investigator TMF, etc). This variation introduces ambiguity, confusion and misunderstanding within the industry.

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Investigator TMF Clarifications

Position:

A complete Trial Master File includes two sets of records:

Sponsor Trial Master File = Records which serve to demonstrate the compliance of the *sponsor and monitor* with the standards of Good Clinical Practice and with all applicable regulatory requirements

Investigator Trial Master File = Records which serve to demonstrate the compliance of the *investigator* with the standards of Good Clinical Practice and with all applicable regulatory requirements.

The following terms are also used to refer to some or all of the clinical trial records at an investigator site: Investigator Site File, Regulatory Binder, Legal Binder, Subject Binder and Pharmacy Binder. While the Reference Model takes no position on definitions for these terms, we do suggest that all of the records referred to by these terms are part of the Investigator TMF. These sub-sets of the Investigator TMF may be held in different filing systems and may be electronic, paper or a hybrid of both.

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Investigator TMF Clarifications

Original records should remain in the TMF of the originating organization. Both the Sponsor TMF and Investigator TMF may hold copies of records generated by the originating organization (examples: sponsor provides a copy of investigator brochures to Investigator; investigator provides copies of curriculum vitae to sponsor). A revision to the TMF Reference Model has been proposed to identify the organization responsible for holding originals for each TMF artifact.

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Sub-artifact Group

- Preparing deliverable to Steering Committee
  - Merged and reviewed previous sub-artifacts with new ones
  - Looking at alternate name column for overlap / requirement
  - Standardising names
- Steering Committee to review pre broad review
- Implementation guide to be updated
- Definitions to be reviewed for accuracy

TMF Reference Model					10-Sep-18			
Zone Name	Section #	Section Name	Artifact #	Artifact name	Sub-artifacts (examples of document types different from the artifact provided, overwrite with your company-specific records)	Sub-artifacts (Sub-ArtifactTeam QC Report) 28Jan2019	Core or Recommended for inclusion	ICH Code
Trial Management	01.01	Trial Oversight	01.01.01	Trial Master File Plan	Core Document List TMF Report TMF Transmittal Form TMF Setup Request	Trial Master File Index Trial Master File Inventory Trial Master File Report Document Transfer Documentation Filing & Archiving Plan	Recommended	5.5.7

Non-Interventional Studies Update

- Seven active members continue to contribute to the development of the NIS TMF
- Agreed that first iteration will apply only to “prospective non-interventional study involving a medicinal product prescribed in the in accordance with the terms of the marketing authorisation”.
- NIS group met face-to-face in December 2018 to agree NIS “Core” and “Recommended” artefacts from TMF Ref Model v3.0
- EU/EEA and US Country requirements applied to “Core” and “Recommended” artefacts
- “Core” artefacts reviewed in light of country requirements and now finalised (12 artefacts in total)
- Next TC meeting to
  - review EU/EEA & US country requirements for 119 “Recommended” artefacts to ensure that they are correct
  - agree definitions for the categories “Core” and “Recommended” in light of their allocation (whilst staying as close as possible to the original DIA TMF model)
  - review artefact / sub-artefact terminology to better reflect NIS vernacular / requirements (whilst staying as close as possible to the original DIA TMF model)
- Face-to-face meeting being scheduled for March 2019
- Aim to complete project by no later than May 2019

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Framework for the Destruction of Paper V2.0

Where can you find it??

- **NEW website launched**

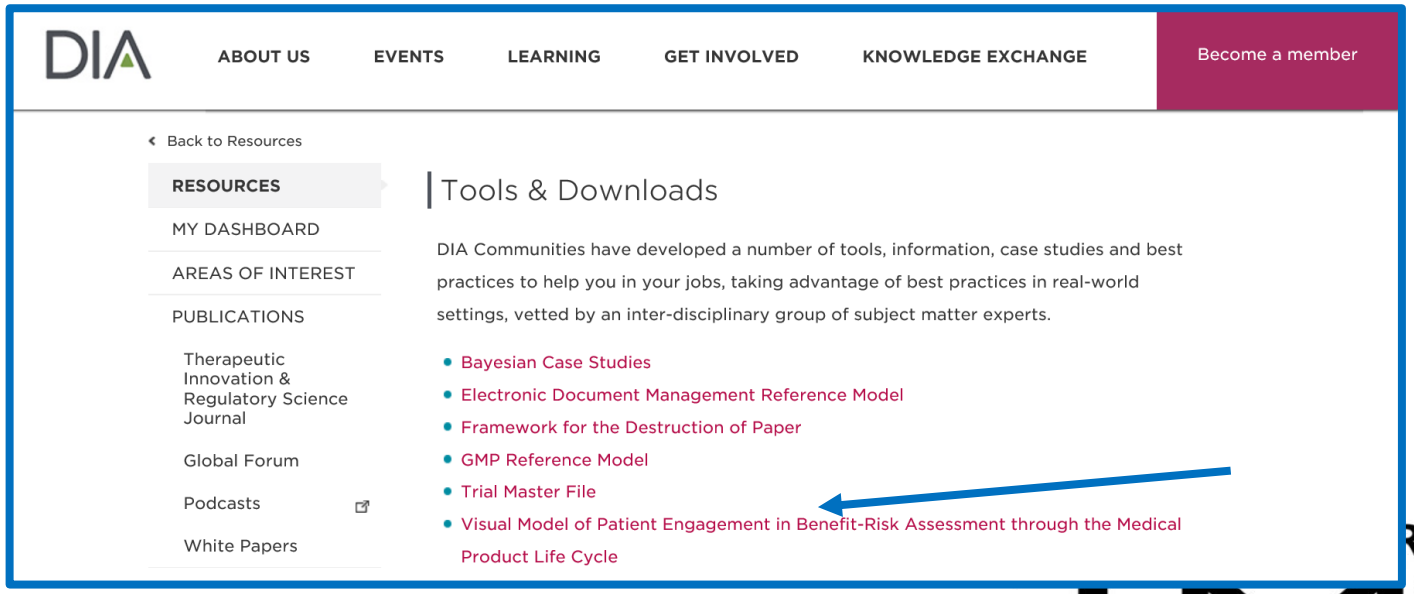
www.paperdestruction.org

Or

- **DIA website**

https://www.diaglobal.org/en/resources/tools-and-downloads#Destruction-of-Paper

(*Main Website → Knowledge Exchange → Tools & Downloads*)



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www.paperdestruction.org

- Dedicated Website for Framework and All Tools!
- Other items on the website:
  - **Surveys links and results**
  - **Feedback mechanism**

"Provision of a mechanism and acceptance of feedback is core to [the Framework mission]. The mechanism for feedback will be possible through a submission process posted on the website"

Mulcahy Consulting, LLC is independently providing support for the website

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What should I do now?

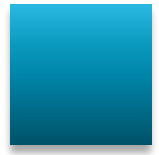
#1: Read the Framework

Adopt Paper destruction policies/procedures

Spread the word about the Framework

Participate in upcoming surveys

Provide Feedback on the Framework



Get Involved! Join Us

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EMA Guideline on the content, management and archiving of the clinical trial master file

Comparison of 2017 draft vs 2018 final – Main changes

Within Introduction

- Introduces concept of a “hybrid” TMF…. allows for TMF to comprise both paper and electronic components
- Includes the need for appropriate archiving to ensure accessibility
- Confirms TMF is not just “documents”…. includes records “containing information and data resulting from systems and procedures”

EMA Guideline on the content, management and archiving of the clinical trial master file

Comparison of 2017 draft vs 2018 final – Main changes

Section 3

- Confirms investigator TMF must be under investigator's control
- Allow for co-sponsorship of trials…. How will this be handled in relation to the TMF?
- Extended guidance on using CROs and third parties used by sites (moved from section 4)
- There should be a recognizable 'primary TMF'
- No need to duplicate documents covering multiple studies
- Extended list of documents that are not listed in ICH Section 8, including data management & statistics
- The need to retain evidence of following your review process specifically included (document reviews, quality reviews)

EMA Guideline on the content, management and archiving of the clinical trial master file

Comparison of 2017 draft vs 2018 final – Main changes

Sections 4-6

- Section 4: IT requirements apply to all systems holding TMF content, including electronic mail
- Section 5: Clarity on need for certified copies… only mandated if copies permanently replace originals (e.g. they've been destroyed)
- Section 6: Archive of TMF should include audit trails and maintain dynamic nature of records, where applicable
- Section 6: Improved guidance on use of contract archive services
- Inspection readiness section removed: just follow sections 1-6 

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TMF Summit Orlando – The Highlights

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TMF Summit Orlando – The Highlights

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US TMF Summit Take-aways

- More conversations about the TMF being comprised of data, including document content
  - Documents are collections of data items
  - Slow shift towards eTMF being a “Content Management System”?
- System integration highlighted still as a major issue
  - Root cause? Perhaps lack of exchange standards
- Higher industry expectations for OOTB functionality from eTMF systems
  - Security, role permissions, workflow, export, archiving

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US TMF Summit Take-aways

- High interest in quality control and quality reviews
  - Several mentions of difficulties managing quality review processes using Excel (including root cause of an inspection finding!)
  - Development of a risk-based approach
- Increasing shift from paper (e.g. >20% of artifacts available electronically from other sponsor systems)
- Fabulous site panel!
  - Big appetite for using the Reference Model for investigator TMF
  - Sites would welcome greater use of electronic but sponsors keep pushing paper-based processes!
  - Need more dialog between industry & sites to understand each other's perspectives

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eTMF Conferences coming up

- HSRAA Conference, Cardiff, May 8 to 10
  - Andy Fisher speaking
- DIA Annual Conference, San Diego, 24 to 26 June – 10 years! Party??
- IQPC TMF Conference, Europe, September
- TMF Summit, London, 1st and 2nd October

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TMF RM General Meetings

- 1 April 2019
- Add to your calendar NOW or download the calendar file (.ics file) when you receive the meeting notification from MailChimp or from our homepage
- Outlook Meeting Request no longer distributed

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QUESTIONS?

Join the TMF Reference Model Yahoo! Discussion Group
https://groups.yahoo.com/neo/groups/tmfrefmodel/info

- Knowledge sharing
- Networking
- Too Much Fun!

Join the TMF Reference Model Project Team
(but be prepared to work!)
http://tmfrefmodel.com/join

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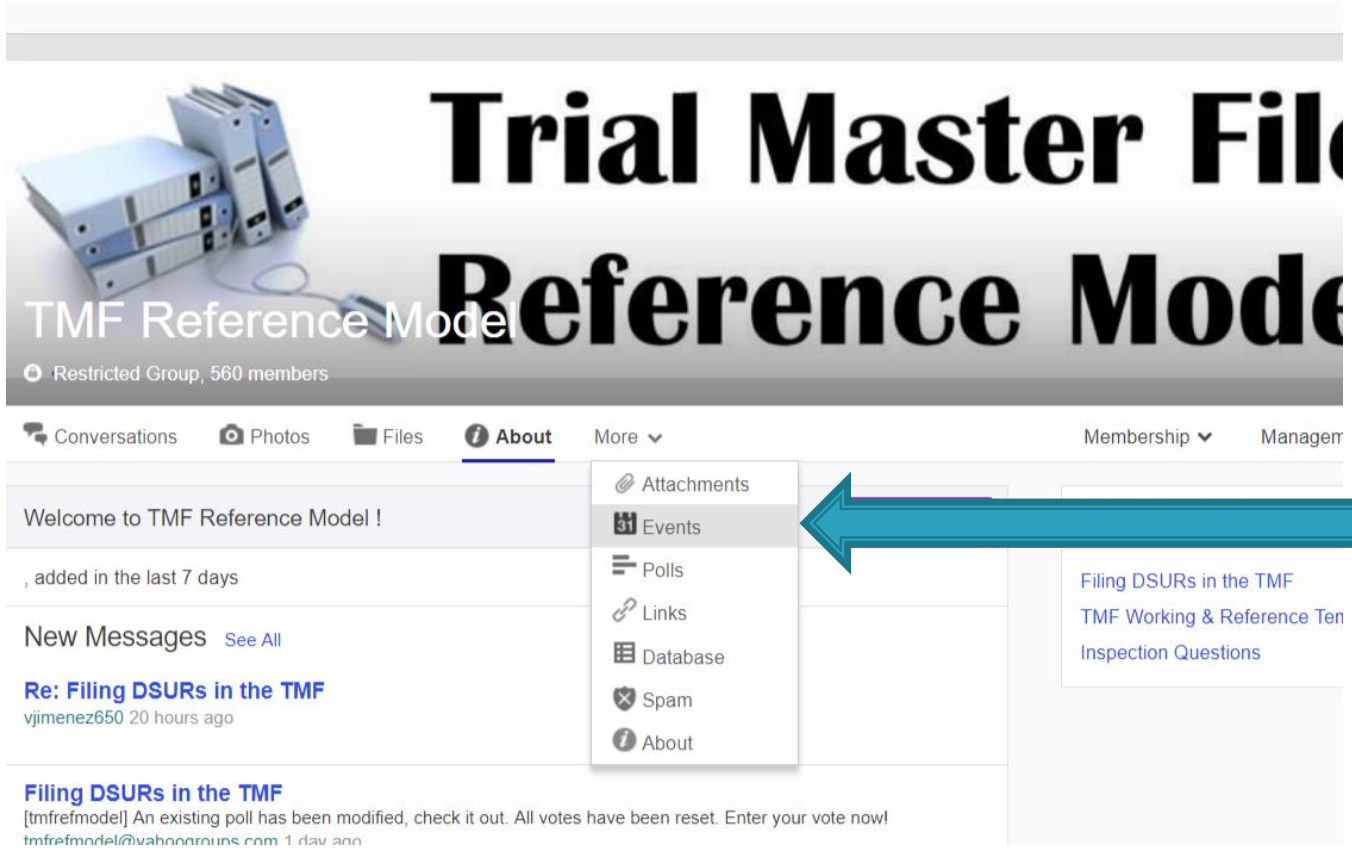
Meeting details

- Wondering where to find details of the next meeting?



On Yahoo!Groups, click on Events to show group calendar. Click on an event to see dial-in details

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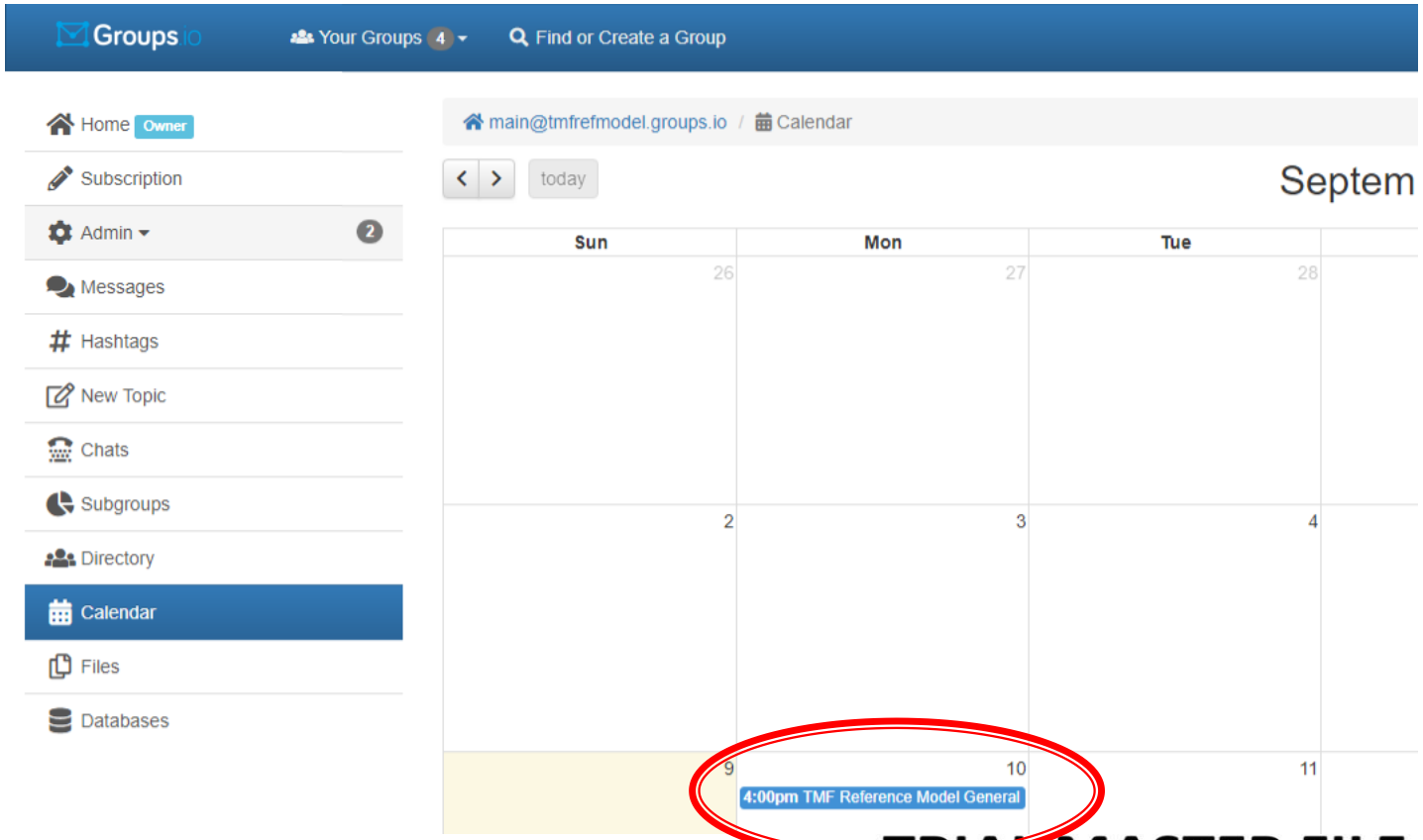
https://tmfrefmodel.groups.io/g/**main**/



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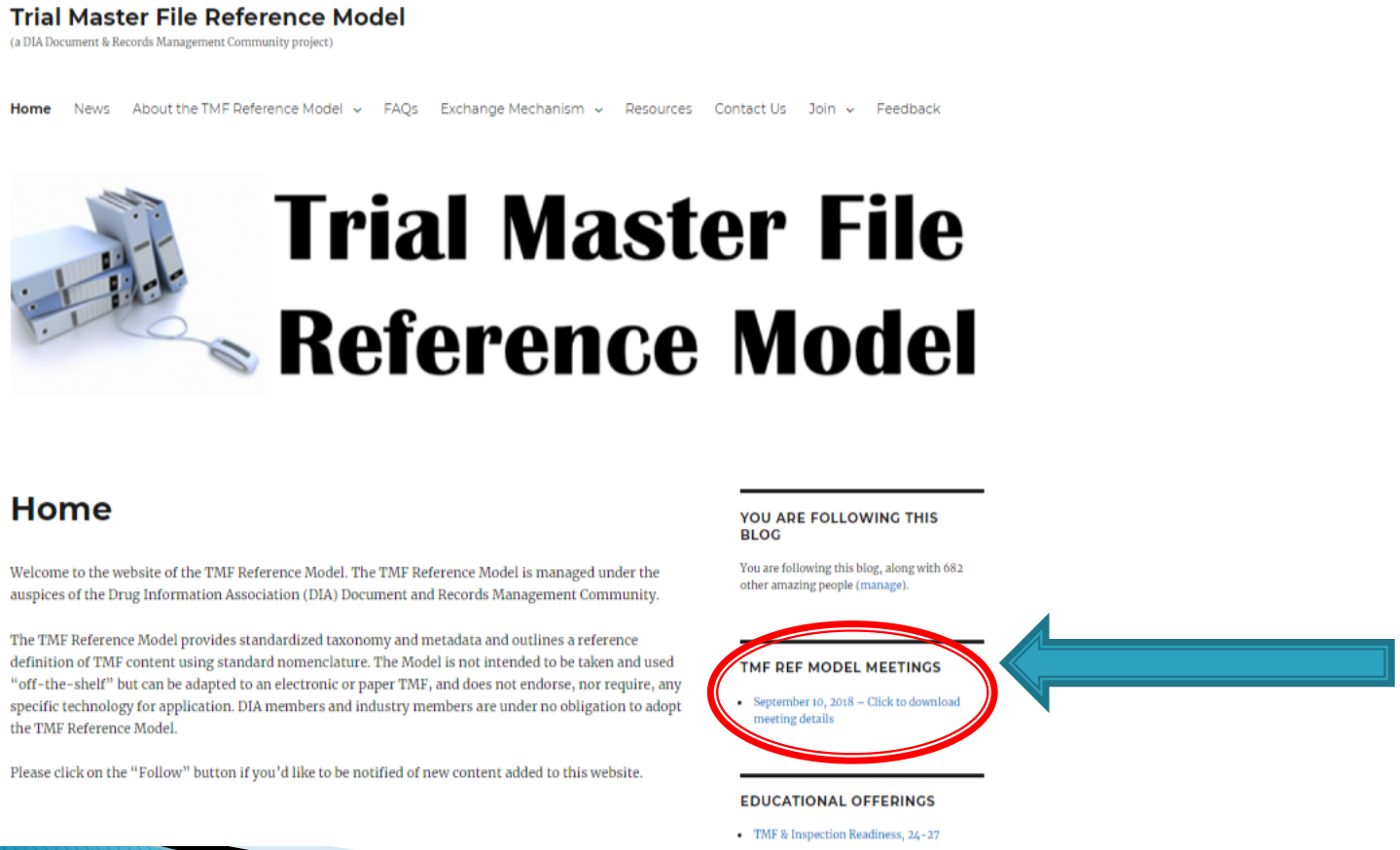

On TMF Reference Model website, click on calendar link. This downloads a .ics file that you can import into your Outlook/Google calendar

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Meeting details

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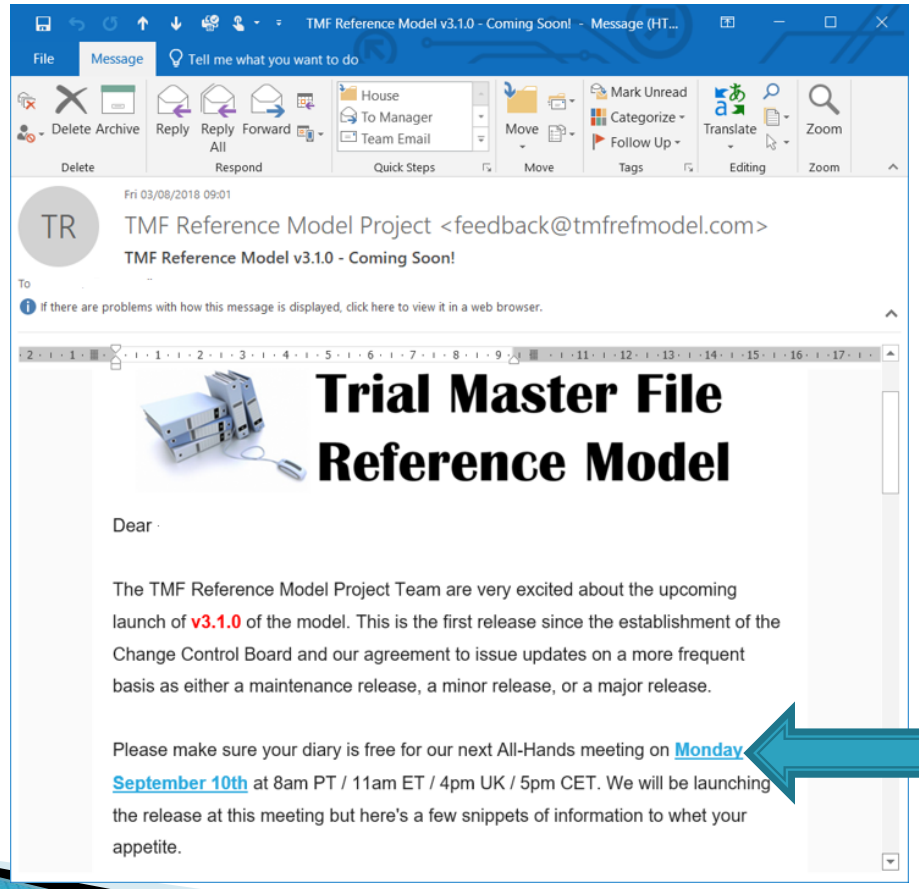

In Reference Model emails, click to download calendar file (.ics) for import into your Outlook/Google calendar

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