Trial Master File Reference Model

General Meeting

12 November 2018

Agenda

- Welcome
- Membership Update
- Sub-group update
  - Non-interventional studies
  - Sub-artifacts
  - Devices
  - eTMF EMS
- Framework for destruction update
- MHRA Q&A from the TMF Summit
  - Full details to be posted to tmfrefmodel.com/resources
- MAGI eISF+eTMF initiative
- FDA-MHRA Data Integrity workshop
- Upcoming Industry meetings
- Meeting reminders (at back)

TRIAL MASTER FILE TMF REFERENCE MODEL

Since last meeting…

- 24 new project team members – current total 247
- 26 new Mailing List Subscribers – current total 764
- 11 new Yahoo!Group Forum members – current total 568
  - 11 new discussion topics posted
- LinkedIn group – 2,678 members
  - 5 new discussion topics posted

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

TRIAL MASTER FILE TMF REFERENCE MODEL

Activity of Subgroups

Group	Lead
Non-Interventional Studies	Russell Joyce
Sub-artifacts	Karin Schneider
Country specific artifacts	Eleanor Hewes
Device Studies	Melonie Warfel
Survey 2019	David Ives
J-GCP	Sub group
Framework for the Destruction of Paper	Lisa Mulcahy
Exchange Mechanism	Paul Fenton / Elvin Thalund / Ken Keefer
Change Control Board	Kelley Robinson / Joanne Malia

TRIAL MASTER FILE TMF REFERENCE MODEL

Non-Interventional Studies Update

- 6 regular participants in teleconferences
- 55 relevant artefacts identified from TMF Ref Mod v3.0
  - (38 essential, 17 desirable)
- Progress has decelerated over
  - complexity of- and variance in- global NIS regulations
  - inclusion of 127 “situation dependant” artefacts
  - eagerness to maintain alignment with TMF Ref Model definitions
- Currently revisiting definition of a NIS
  - to agree the specific type
  - to help define artefact requirements
  - Some preference for “NIS involving a medicinal product”
- New members always welcome!

TRIAL MASTER FILE TMF REFERENCE MODEL

Sub-artifacts Team Update

- **Finish Review of**
  - **Zone 10 Data Management**
- **Continue**
  - **Zone 04 IRB or IEC and other Approvals**
  - **Zone 05 Site Management**
- Trying to get this completed end of year.
- Small group only who are regularly participating – gentle reminder to contribute!!

- After that: consolidate into one excel deliverable
- Full subteam review – must have broad participation for that
- SC/Change control board review and approval

TRIAL MASTER FILE TMF REFERENCE MODEL

Devices

- 13 members with new members from Edwards Lifesciences and Medline since last meeting and continuing to add.
- Zones 1-9 reviewed with comments
- Zones 10 and 11 to be reviewed on Dec. 6th 1:00-2:30 EST
- Next steps:
  - Complete initial review on the 6th of Dec.
  - Re-review all Zones in January offline, add any other edits
  - Finalize suggested changes and submit to committee end of Jan /early Feb.
  - Determine approach for Device supporting asset - Best Practice, etc.
- If interested please join the group!

TRIAL MASTER FILE TMF REFERENCE MODEL

eTMF-EMS Webinars

- Bridging Regulatory Quality and Operational Efficiency with Open Standards (GoBalto, Aug 28)
- Technical Perspectives (Montrium, Oct 11)
- Getting Industry Engaged (IQVIA)
  - December 13, 10 AM EST
  - Survey
  - Panel discussion
  - If attending first eTMF-EMS webinar, submit form to RSVP https://tmfrefmodel.com/ems/
- More webinars to come…

TRIAL MASTER FILE TMF REFERENCE MODEL

Other eTMF-EMS Forums

- LinkedIn Group
  - Search “TMF Exchange Mechanism Standard”
  - Post questions and lessons learned
  - FAQs coming

- eTMF-EMS Vendor Round Table
  - eTMF vendors
  - Open standard
  - Roadmap
  - Share information
  - Recognize compliance
  - Monthly conference calls start soon

TRIAL MASTER FILE TMF REFERENCE MODEL

eTMF-EMS Resources

- Published Specification
  - https://tmfrefmodel.files.wordpress.com/2018/06/etmf-ems-v1-0.pdf
- LinkedIn Group: “TMF Exchange Mechanism Standard (EMS)”
  - https://www.linkedin.com/groups/12136956/
- News About the Standard
  - https://tmfrefmodel.com/category/ems-news/
- Technical Resources
  - https://github.com/TmfRef/exchange-framework
- Latest Published XML Schema
  - https://github.com/TmfRef/exchange-framework/blob/1.0.01/TmfReferenceModelExchange.xsd

- **Get Involved or Submit Questions!**
  - https://tmfrefmodel.com/ems/

TRIAL MASTER FILE TMF REFERENCE MODEL

Framework for the Destruction of Paper >Approaching to the Finish Line

- Editing Team is preparing final document.
  - Target of **November 28, 2018** will be met!
- The Implementation Team is working on tools to support the Framework.
  - Tools will include template policy document, process maps, decision tree, and workbook format. Team will continue into 2019. Volunteers are still being accepted.
- Accessing v2.0 of the Framework
  - Authoritative location will be on DIA website; other locations TBD
  - Link will be communication to this team
- Thanks to each of the project's volunteers
  - Couldn't have done it without them

TRIAL MASTER FILE
TMF
REFERENCE MODEL

MHRA Q&A at the TMF Summit

User friendly eTMF features?

- Like to paper: tag documents, sort in date order, see documents in folders in the system (binder view), structured index, able to compare documents

Approach for training for inspectors?

- As short as possible. Recommend that the eTMF vendors keep records of inspector training and provide to Sponsors for subsequent inspections

TRIAL MASTER FILE TMF REFERENCE MODEL

MHRA Q&A at the TMF Summit

Audit trail requirements?

- Focus on data integrity – do you have all data from all electronic systems and do you review the data? E.g. workflow actions, who has accessed, when and what they looked at, did they delete anything, timeliness of uploads.
- Audit trail of eTMF is not as high priority of review vs. systems where subject data is collected.
- An actual report is the best way to view this information from the eTMF
- Format: Need to consider archiving for 25 years but analyzing a PDF format is problematic for review. Inspectors want the data, with ability to produces graphs, etc.
- Sponsors should receive the audit trail back with any eTMF, can be stored in most appropriate location

TRIAL MASTER FILE
TMF
REFERENCE MODEL

MHRA Q&A at the TMF Summit

eClinical vendors?

- MHRA focusing on eClinical vendors and majority had major findings for essential documents
- Define long term access to where their software validation documents are maintained, including testing records, failure fixing, helpdesk tickets
- Vendors should have a oversight approach to the sponsor's UAT

MHRA Q&A at the TMF Summit

Certified Copies?

- A certified scan process should be validated, with a level of ongoing QC to confirm the process and those doing the process must be trained. There is no need to sign and date a certified copy if a validated process was followed.
- A certified copy is not required if the original paper is kept.
- A certified copy can replace an original paper which can then be destroyed. If the original has not been destroyed, the MHRA may ask why.
- If paper has been destroyed and an issue is found, Inspectors would look to see if this is indicative of bigger problem and what the impact is.

MHRA Q&A at the TMF Summit

Draft docments?

- If drafts are the only way to demonstrate that the organization has followed an SOP process, then a draft may be required in the TMF.
- If a company has kept draft documents, the MHRA have the right to see these documents
- Drafts should be viewable in the system if they are in it.

TRIAL MASTER FILE
TMF
REFERENCE MODEL

MHRA Q&A at the TMF Summit

Signatures?

- eSignature would need to be invalidated if document changes. Re-signature would be required or PDF of the corrected wet ink signed document should be upload into the eTMF.
- Electronic document and associated wet ink signature page scan can be filed separately as long as they can be seen as one complete document i.e. the signature page references the main document.

TRIAL MASTER FILE TMF REFERENCE MODEL

MHRA Q&A at the TMF Summit

TMF Index?

- Detailed index not required, just a topline index of where all of the documents are stored
- It is acceptable to see documents in different systems. Recommend to maximize the documents in the primary TMF
- Alternative systems need to meet all requirements for access as well as long term archiving

TRIAL MASTER FILE
TMF
REFERENCE MODEL

MHRA Q&A at the TMF Summit

eMails?

- Emails are important for reconstructing the story of a clinical trial
- Emails are hard to review if saved as PDF and uploaded to eTMF, as sometimes the PDFs are not searchable. Searching for words in title or text of emails themselves is key, not in one large non-searchable file dump
- It is often easier to review emails in the email software whilst the trial is ongoing, but need to consider long term storage after the trial is completed.

TRIAL MASTER FILE TMF REFERENCE MODEL

MHRA Q&A at the TMF Summit

Future Communications / Activities?

- The TMF guidance documents is still in draft. Was expected 1st November, is imminent, hopefully end of November
- MHRA blogs will not be formalised – they are used to communicate quickly and are there to potentially build future guidance
- eClinical system guidance being produced. Will include generic aspects e.g. electronic archiving, e-signatures, validation, certified copies. There will be sections on specific systems (IRT, ePRO, EDC) not eTMF
- FDA inspectors have shadowed MHRA inspectors – looking to develop joint inspections

TRIAL MASTER FILE TMF REFERENCE MODEL

MHRA Q&A at the TMF Summit

eISF?

- Sponsor/CRO personnel cannot remotely access an eISF (documents with patient identifiable information)
- Access when physically present on-site is acceptable
- Its all about Investigator control of access

TRIAL MASTER FILE
TMF
REFERENCE MODEL

MAGI eISF+eTMF Reference Model

- Draft MAGI ISF Reference Model is public
- Developed from “reg binder lists” (ICH, NIH, TMF RM, MAGI, and ACRP) for clinical research sites
- Created in partnership with MAGI, ACRP, and SoCRA
- MAGI request for review is posted
  - http://www.firstclinical.com/journal/2018/1811_ISF_Reference.pdf
- TMF Ref Model, as of v1.2 (Dec 2011) identified ISF records
- SC will ensure alignment of MAGI ISF to TMF RM
  - We are driven to reduce industry bifurcation
  - Enable record exchange under EMS
- Join us! TMF RM members, please review and send comments on the MAGI ISF draft

TRIAL MASTER FILE TMF REFERENCE MODEL

FDA & MHRA GCP Workshop
Data Integrity in Global Clinical Trials – Are We There Yet?

- Held October 23-24, 2018 in Silver Spring, MD
- Planned to be First in a Series
- 12 FDA Speakers; 3 MHRA Speakers
- Day 1 – Limited to 150 persons in person (3000 Connections, 68 countries)
- Day 2 – Restricted to in person participation only
  - Table Discussions on "Actual" Cases based on Realistic Situations
- Agenda, Slides (D1), Recordings (D1), Case Study Materials: http://sbiaevents.com/gcp2018/

FIRST EVER GCP Collaboration!

No Fee!

Key Impacts to Data Integrity

- ❑ Vendor Selection
- ❑ Unblinding
- ❑ Audit Trail
- ❑ Data Management

TRIAL MASTER FILE TMF REFERENCE MODEL

eTMF Conferences coming up

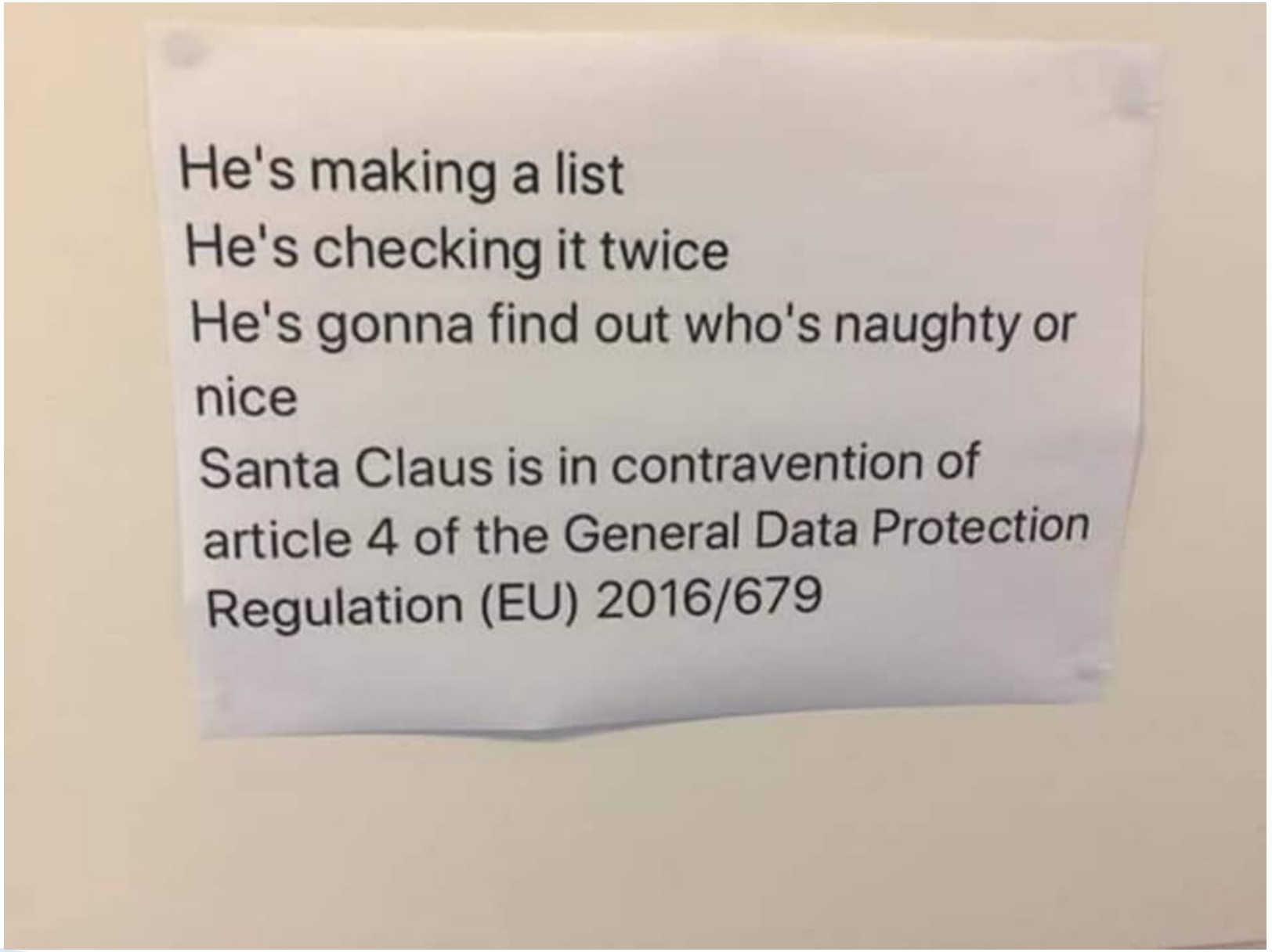
- IQPC, Inspection Readiness, 20th to 22nd November, Brussels https://gcpinspection.iqpc.com/
- DIA eDM – Clinical and Regulatory Operational Excellence, Barcelona, 28th to 29th November 2018 http://www.diaglobal.org/en/conference-listing/meetings/2018/11/edm-2018-clinical-and-regulatory-operational-excellence-forum
- ExL US TMF Summit, 22nd to 24th January, Orlando http://tmfsummit.com/us

TRIAL MASTER FILE TMF REFERENCE MODEL

TMF RM General Meetings

- 11 February 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

TRIAL MASTER FILE
TMF
REFERENCE MODEL



TRIAL MASTER FILE
TMF
REFERENCE MODEL

TRIAL MASTER FILE
TMF
REFERENCE MODEL

QUESTIONS?

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

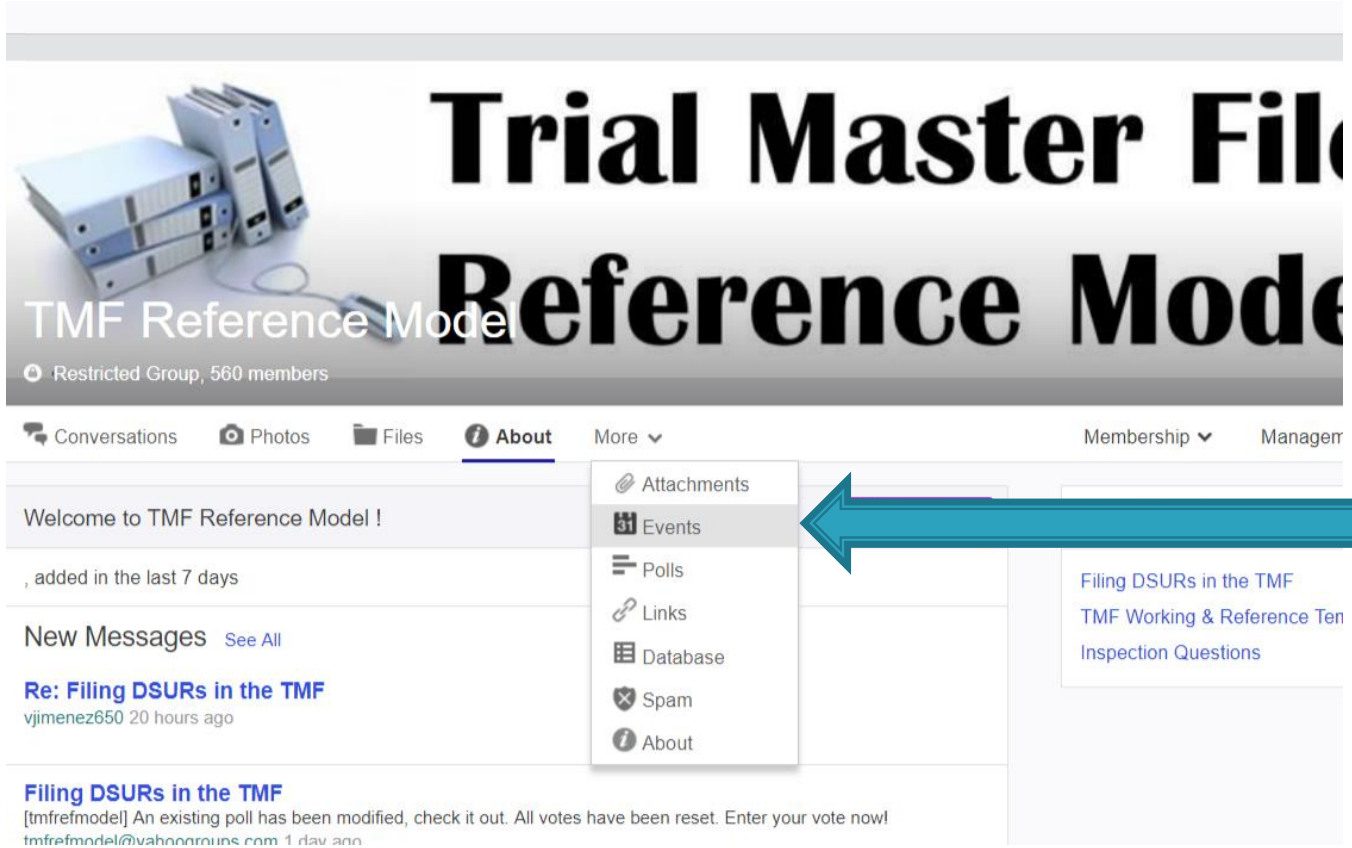
- Knowledge sharing
- Networking
- Too Much Fun!

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

TRIAL MASTER FILE
TMF
REFERENCE MODEL

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

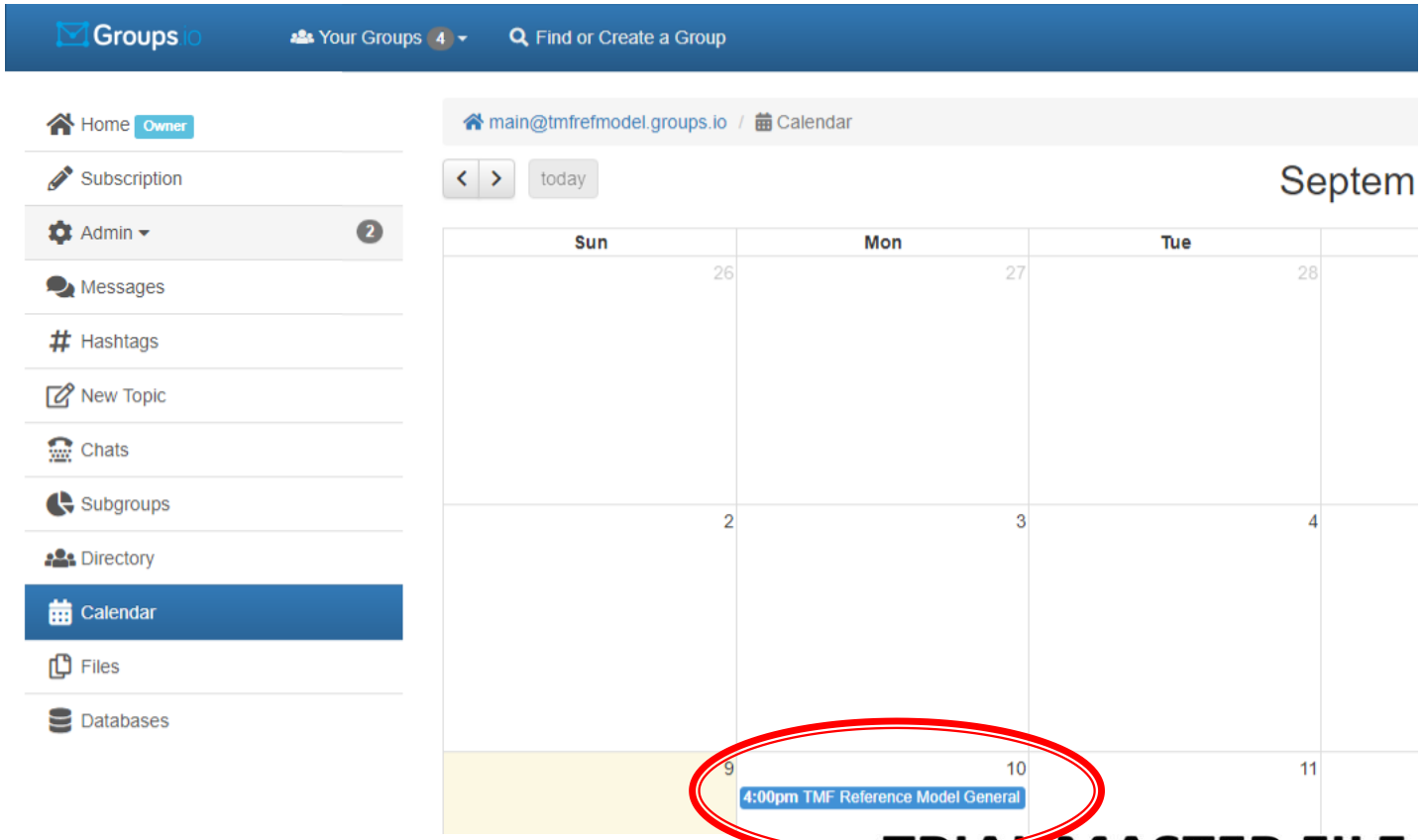
TRIAL MASTER FILE TMF REFERENCE MODEL

Meeting details

- Wondering where to find details of the next meeting?

On Groups.io, click on Calendar to show group calendar. Click on an event to see dial-in details

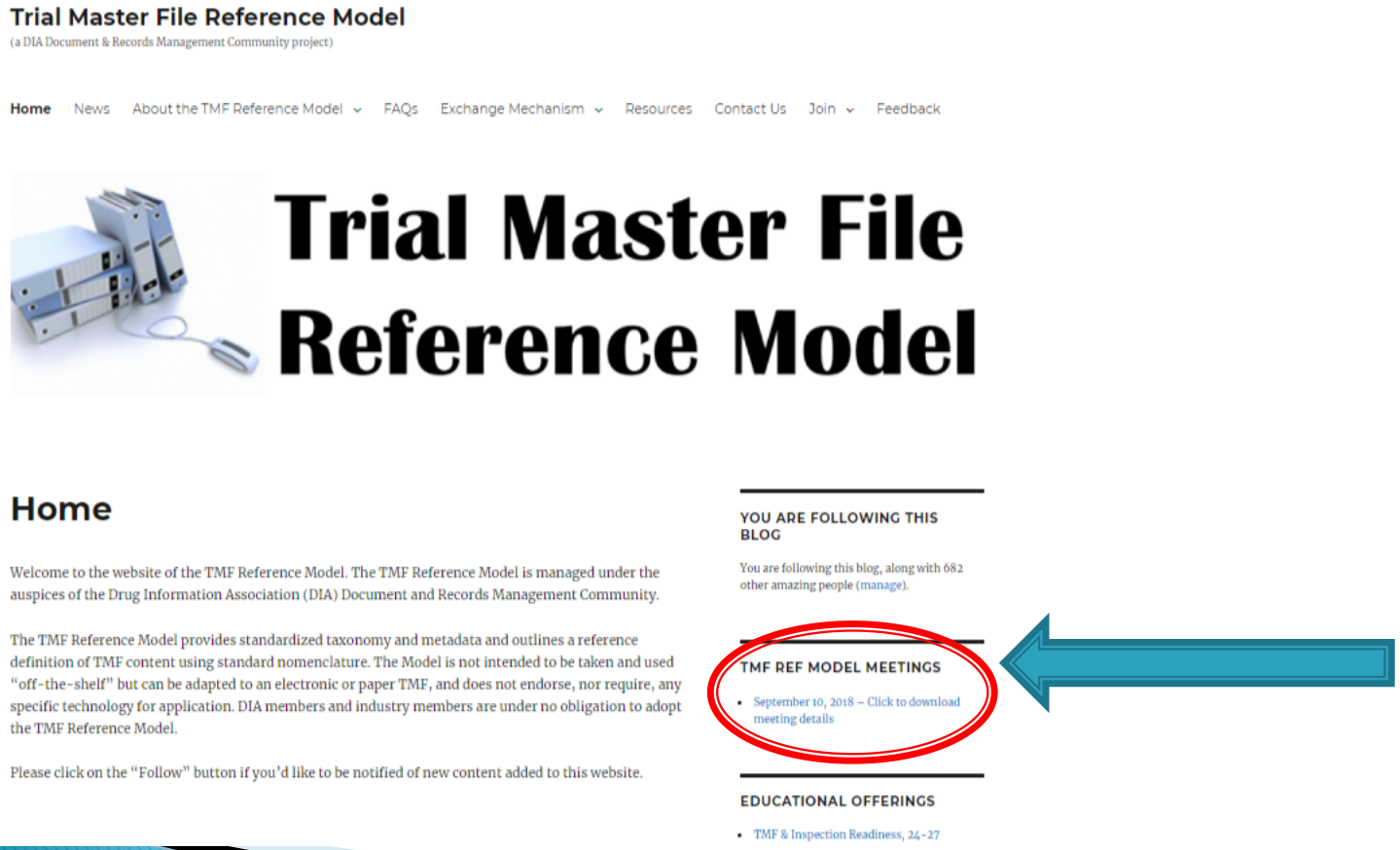
https://tmfrefmodel.groups.io/g/**main**/



TRIAL MASTER FILE TMF REFERENCE MODEL

Meeting details

- Wondering where to find details of the next meeting?

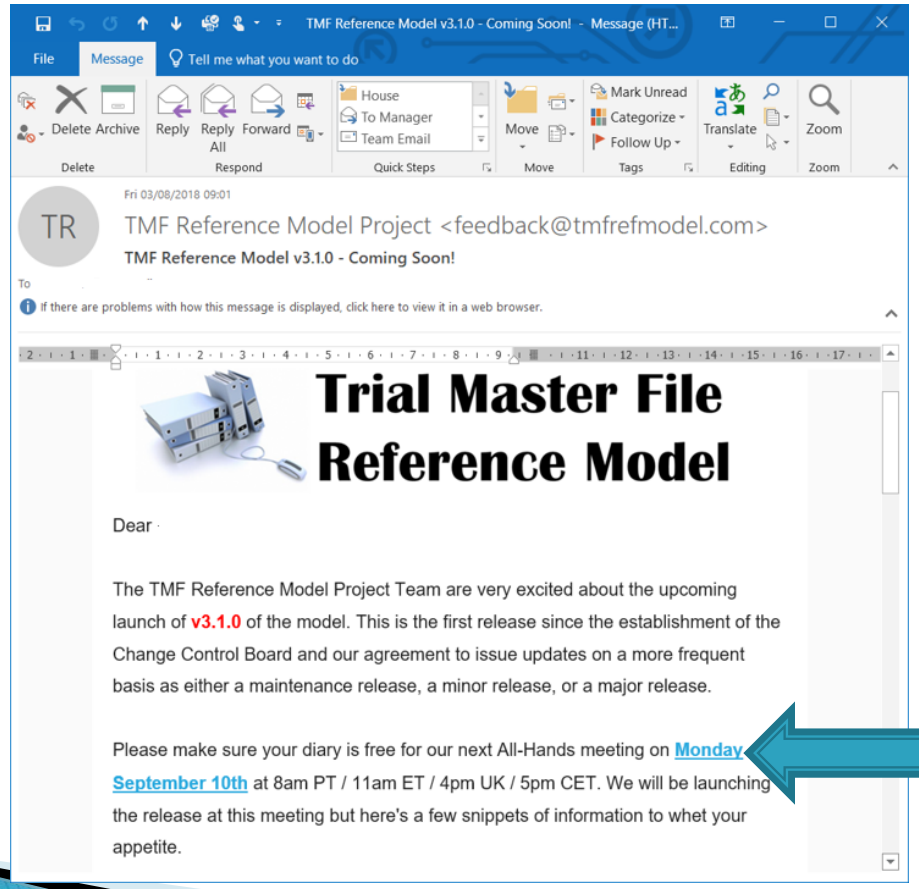


On TMF Reference Model website, click on calendar link. This downloads a .ics file that you can import into your Outlook/Google calendar

TRIAL MASTER FILE TMF REFERENCE MODEL

Meeting details

- Wondering where to find details of the next meeting?



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

TRIAL MASTER FILE
TMF
REFERENCE MODEL