Trial Master File Reference Model

General Meeting

22 June 2020

Agenda

- Welcome
- Update on Membership
- Update on Initiatives
- Change Control Board Update
- TMF RM turns 10! DIA Presentation
- Real World Studies
- CTTI meeting on ICH E6 (R3)
- Events
- Next Meeting

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Since last meeting*…

- 4 new project team members (groups.io) – current total 318
- 1086 Mailing List Subscribers** (tmfrefmodel.com)
  - 12 new discussion topics posted (13 responses, 2104 hits)
- LinkedIn group – 3,022 members (34 new members)
  - 4 new discussion topics posted
- For details on these different groups and how to get involved, see http://tmfrefmodel.com/join

** Make sure webadmin@tmfrefmodel.com is on your email whitelist

* 11 May 2020

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TMF RM Active Initiatives

Initiative	Deliverables / Activity
Sub-artifacts	• A super-set of sub-artifacts for Companies to select and customise • Removal of the 'Alternative Name' column – any unique names have been added as sub-artifacts • Gone to CCB
Devices	• Updated artifacts and sub-artifacts specific to Device studies
Real World Studies	• The TMF Reference Model artifacts that are required for Real World studies • Presented today
eMail	• Document best practices for handling email. Deliverables to include: defining relevant correspondence; best filing practices, handling attachments and links; archiving
J-GCP	• Bringing together JGCP and the TMF Reference Model
Exchange Mechanism	• An extension of the TMF RM which focuses on the transfer of content, metadata, audit trail and eSig information

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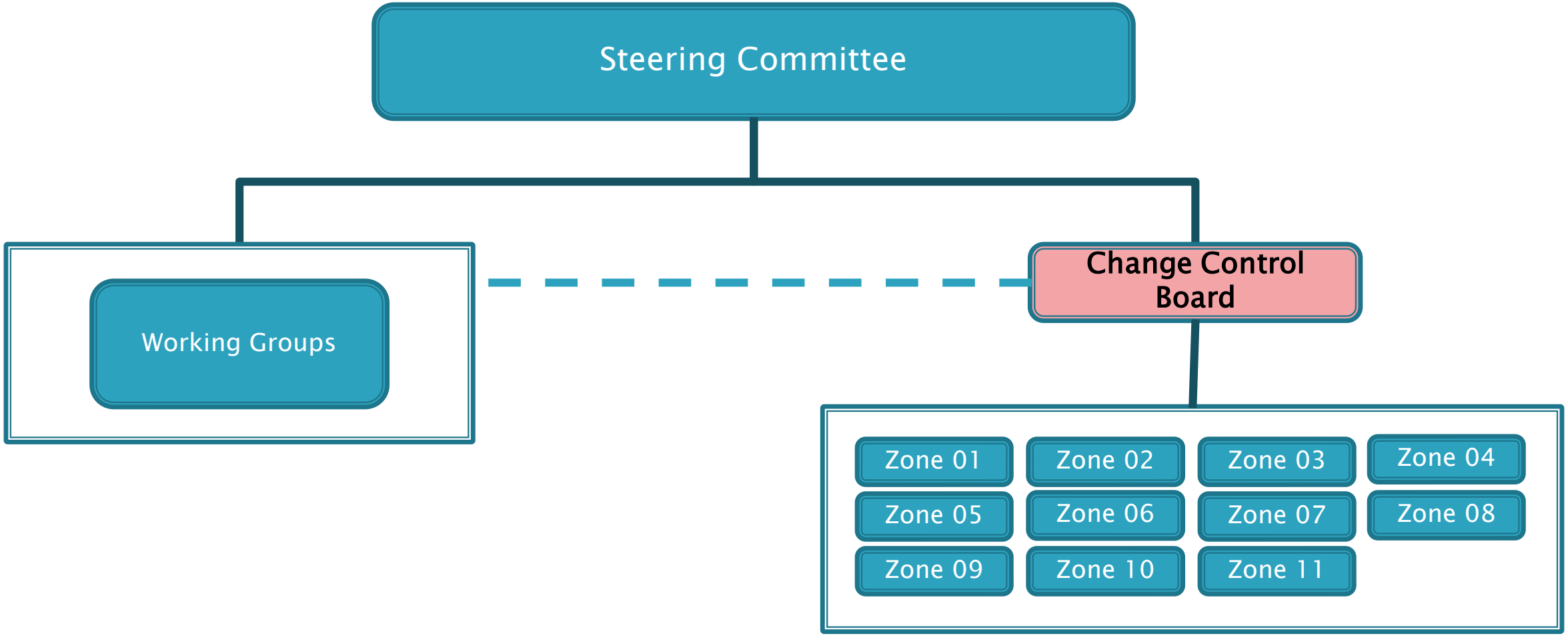
Change Control Board Charter

Finalised May 2020

Joanne Malia

Project Structure – Change Control Board



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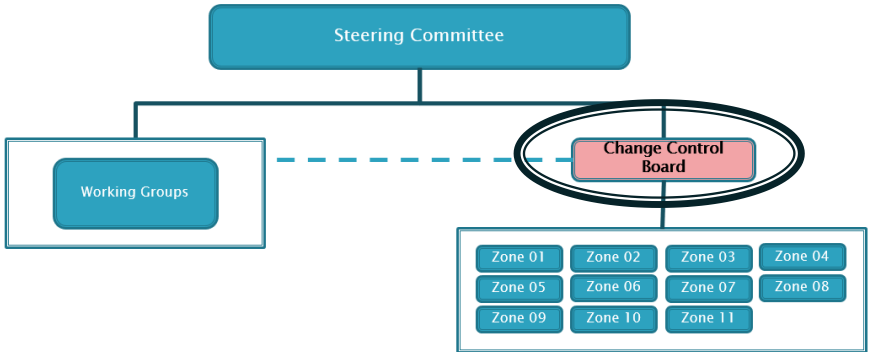
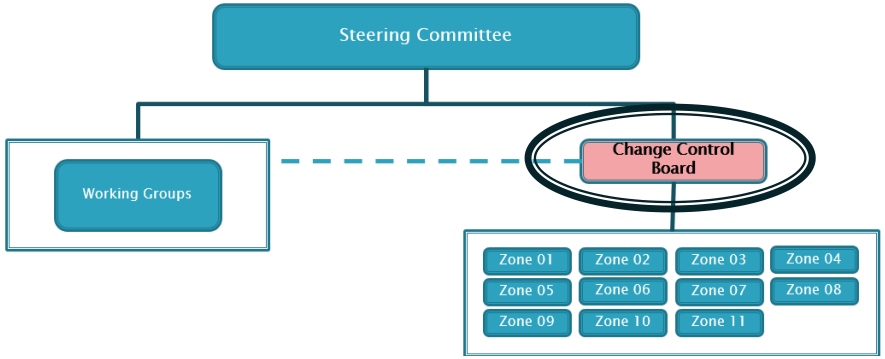
Project Structure – CCB



- **Change Control Board Structure**
  - Comprised of a variety of subject matter experts (no overlap with Zone Teams)
  - Includes CCB lead & Co-Lead (not a SC member, unless unavoidable)
  - Includes Steering Committee Liaison member (oversight)
- **Procedural Documentation**
  - Change Control Procedure v1.0 (01 Dec 2017)
  - Version Control Policy v1.1 (14 Feb 2018)

Role – CCB



- Meets on a **monthly basis** to review new changes submitted and feedback from the zones
- **Makes decisions** on new artifacts, redundant artifacts, or other changes to the Reference Model
- **Makes recommendation** to Steering Committee on categorisation of changes (major, minor, maintenance)
- Reviews any working group deliverable which will affect the structure of the TMF RM
- Any working group deliverable which does not affect the structure of the TMF RM (excel sheet) is not in the CCB remit
- **Prepares release notes** and guidance documentation

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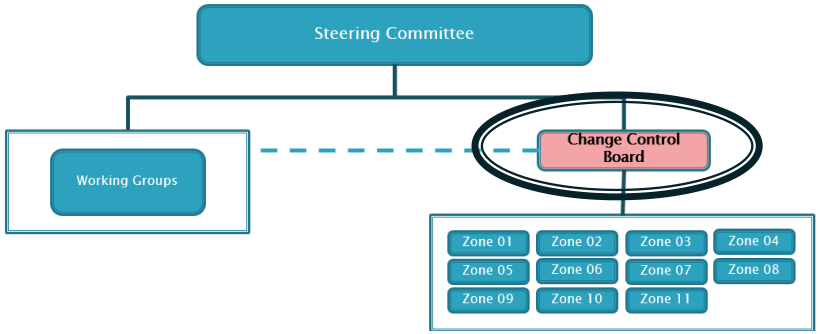
Benefits



- The CCB plays an **essential/critical role** by bringing **unbiased input** from a broader group of SMEs, and is **independent** from the Steering Committee
- Minimises the burden on the Steering Committee
  - Past experience shows workload regarding change control is too much for the SC alone
- Aligned with role of **Steering Committee as oversight** rather than making all the decisions for the project
- Provides significantly more **opportunities** for others to get involved without major time investment

CCB Recruitment

- Currently looking for new members

- Work in the TMF area
- Have 3-5 years experience
- A plus if from sponsor or CRO companies
- Like Too Much Fun!

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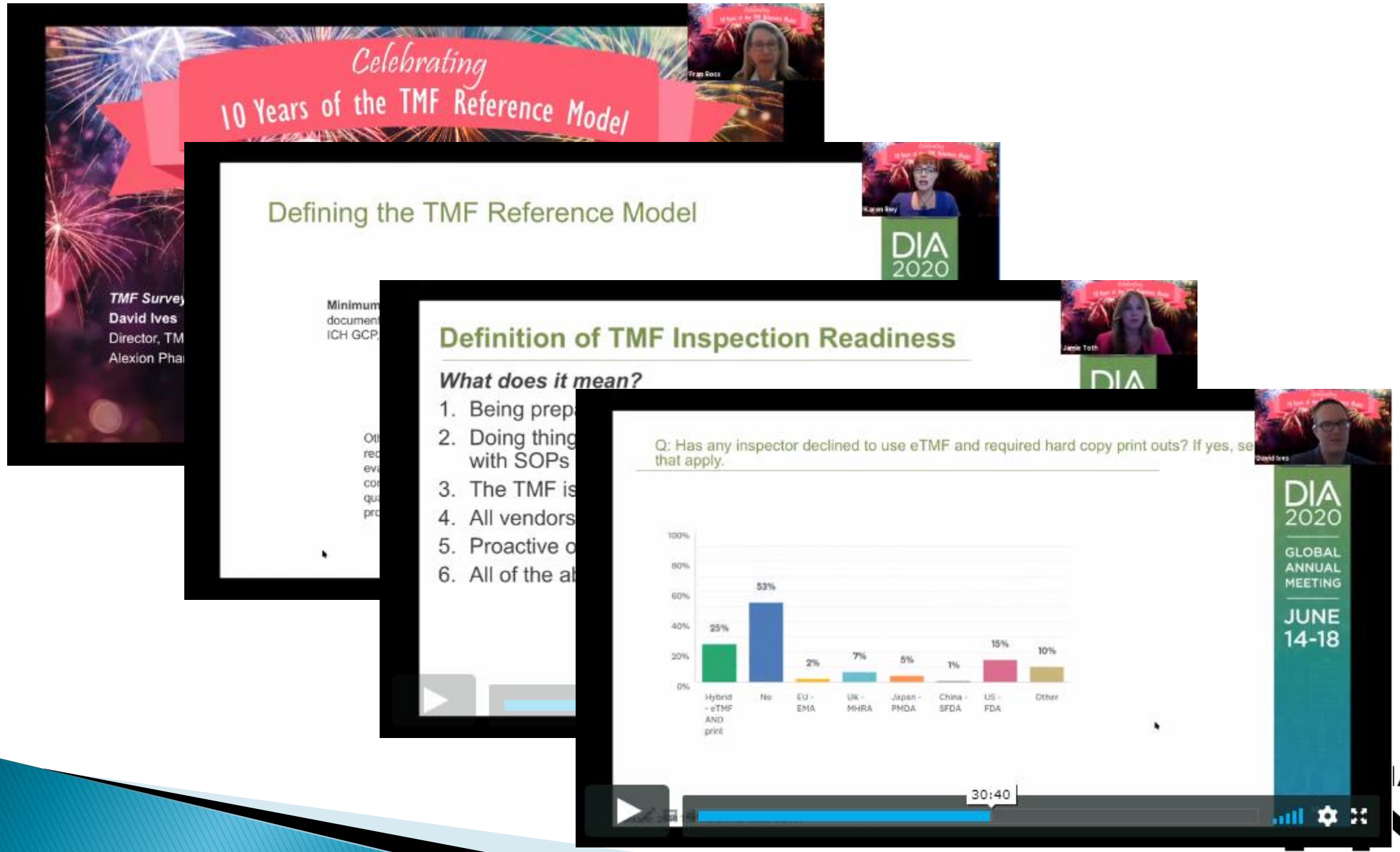

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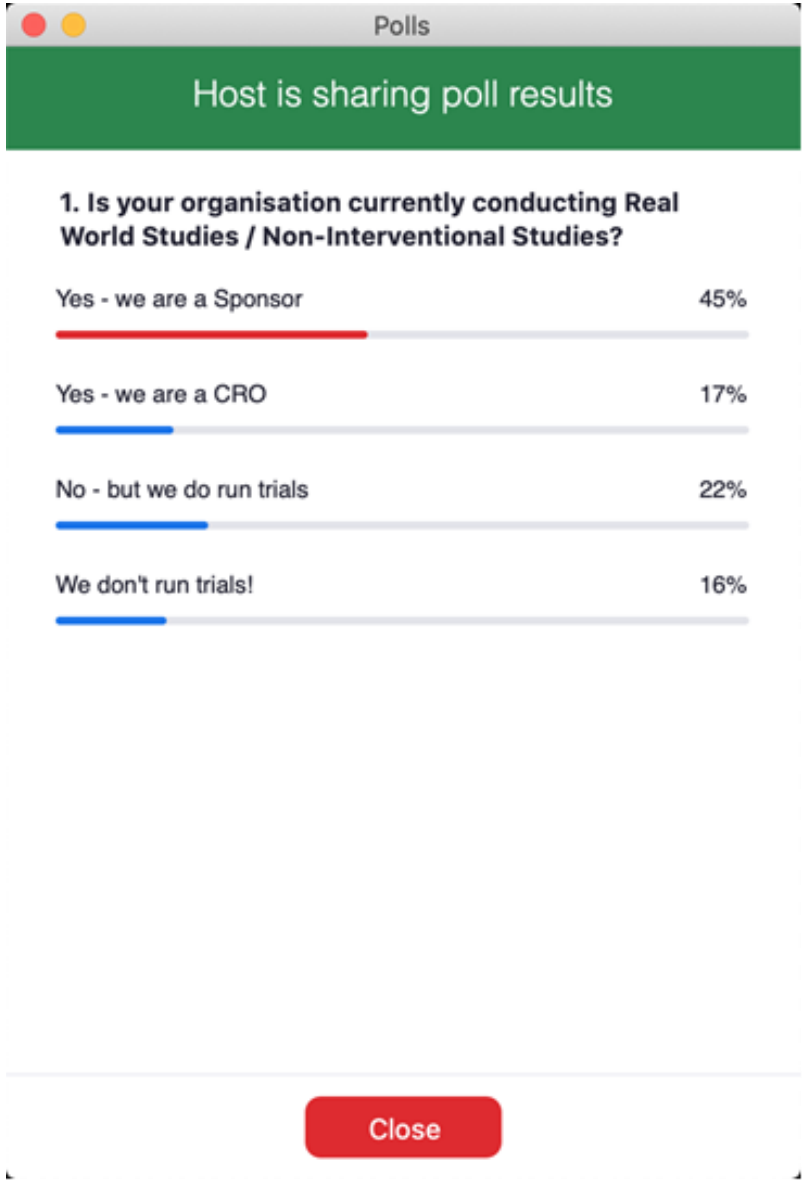
Real World Study – Document Index (RWS-DI)

Dr Stuart McCully



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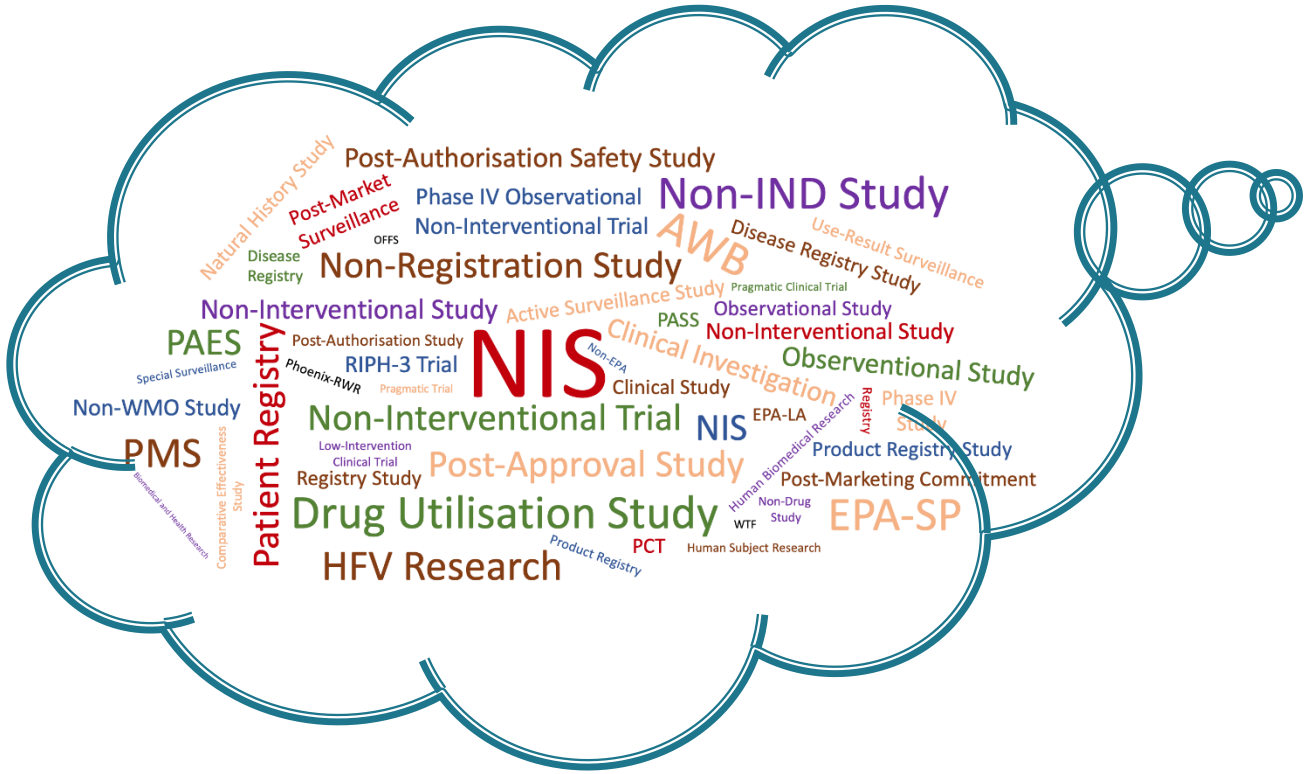
Rationale for RWS-DI



- DIA TMF Reference Model was designed for **CLINICAL TRIALS**
- What if your clinical study isn't a clinical trial?
  - >40% of the artifacts aren't relevant
  - Need to 're-invent the wheel' with every study
  - Extra (unnecessary!) effort involved in documenting what isn't relevant
  - Penalised in audits for missing documents…that you don't have because your study isn't a clinical trial
  - Increasing need for 'regulatory grade' RWE driving need for robust and credible TMF document index for real world studies

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Method

- Working group of RWS experts convened in March 2018
- Aim
  - Develop a TMF framework for real world studies based on the long-established and widely-adopted Clinical Trial Master File Reference Model (CTMF-RM)
  - Remain as consistent as possible with the CTMF-RM format and structure, adapting where necessary
- Scope
  - Clinical studies that are not clinical trials
  - Based on a prospective study design to provide maximum coverage of the potential document or artifact types across the range of non-interventional study designs, from retrospective chart reviews to prospective product registry studies

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Differences between CT TMF and RWS-DI

	Standard TMF Model	RWS-DI
Applicability	Clinical Trials	Clinical Studies that are not Clinical Trials*
Zones	11	10
Sections	40	23
Artifacts	249	130
…of which "core"	197	11
…of which "Recommended"	52	119
Terminology	Trial	Study
Terminology	Subjects	Patients
Terminology	Safety Reporting	Pharmacovigilance

* Examples: Non-interventional studies, non-IND studies, observational studies, disease registry studies, PASS, retrospective chart reviews etc

Similarities between CT TMF and RWS-DI…

Term	Definition
Zone	Zones are akin to the processes required to conduct a clinical study. Zones provide the first level structure by grouping related activities.
Section	Sections are akin to the range of activities relevant to a specific process. Sections therefore aid understanding of the process and are helpful for classification and searching.
Artifact	Artifacts are information that is captured during the conduct of a clinical study as evidence of the conduct of those activities and are directly related to the purpose or definition described in the Real World Study Document Index. An artifact should not be considered as a stand-alone document but rather a collection of information, records, documents, and data that fulfil a specific purpose.
Core	An artifact that is created or collected for an applicable RWS as dictated by local regulations, local guidance, contractual obligations, or considered essential based on the consensus of the Real World Study Documentation Index Working Group and must be in the RWS-DI.
Recommended	An artifact that does not have to be produced for an applicable RWS but if created or collected is recommended to be in the RWS-DI (if not retained elsewhere) based on consensus of the Real World Study Documentation Index Working Group.

…with just some very slight modifications to the wording!

Next Steps

- Publication
- Peer review
- Modification

The RWS-DI Team

All team members work within the real world study environment.

Jeff Kirsch	– Senior Director, Quality & Risk Management and Governance, GSK
Kath Firth	– Head of Quality Operations, GSK
Linda Rudolph	– Principal Consultant, Quality Werx LLC
Russell Joyce	– Director and Principal Consultant, Heath Barrowcliff Consulting
Shelley Brigstock	– Study Project Manager, Novo Nordisk
Stuart McCully	– Founder, Phoenix-RWR
Tara Isherwood	– Senior Director, Regulatory Advice and Delivery, Syneos Health

Questions

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Trial Master File Reference Model

ICH E6 (R3) – CTTI Stakeholder Engagement Session (4-5 June 2020)

Marie-Christine Poisson

What is CTTI?

CLINICAL TRIALS **TRANSFORMATION** INITIATIVE

Multi-stakeholder,
public-private partnership
co-founded by Duke University & FDA

Participation of 500+ more orgs and ± 80 member organizations

MISSION: To develop and drive adoption of practices that will increase the quality and efficiency of clinical trials

CTTI

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Who participated and what was discussed?

- The web conference was to inform the discussions of the ICH Expert Working Group (EWG), which is tasked with the revision or the guideline to integrate advances in clinical trial design and conduct and make it more agile and inclusive.
- During the conference, members of the EWG (23 members in total) provided an overview of the ongoing work and invited multiple stakeholders to share their perspectives: EWG members, Clinical investigators, Patient organizations.

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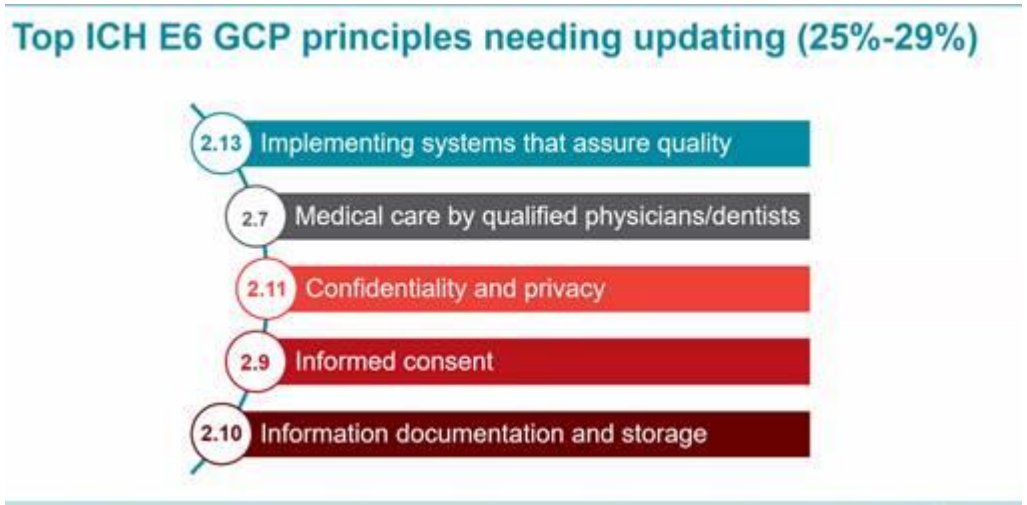
CTTI Survey

- 327 people across 39 countries responded to the Survey
- 60% Europe and Asia, 30% USA
- Pharma, CRO and Academia

- Sections needing most updating:
  - Section 4: Investigator
  - Section 5: Sponsor
- Most frequent update required:
  - Monitoring (45%)



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Key Themes for Revision

- Modernization, renovation, total rewriting
- Flexibility & Simplification
  - Specific on what is required for which type of research
  - Clarity on what is optional based on a particular study
  - Provide framework for all types of studies and their location (e.g., lower and middle-income countries)
  - Remove complexity where possible especially for investigators
- Updates to incorporate
  - New study designs (e.g., master protocol)
  - New technologies (e.g, eConsent, ePro, remote monitoring, telemedicine, direct to patient)

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Key Themes for Revision (Cont'd)

- Align with and reference ICH E8 (R1) and other relevant guidelines (e.g., Q9)
- Clarify terms and concepts
  - Critical to quality factors
  - Quality management using risk based approach
  - Quality tolerance limits
- Clarity on sponsor and investigator allocation of responsibilities; especially monitoring, investigator staff, resources

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Key Themes for Revision (Cont'd)

- Section 6 – Needs guidance to make protocol simpler and more feasible, and incorporate new protocol design
- Section 8 – Revisit the concept of "essential documents", clarify "certified copies", clarify terms and definitions, incorporate elements from EMA, MHRA regulations.
- Alignment with regulators on expectations

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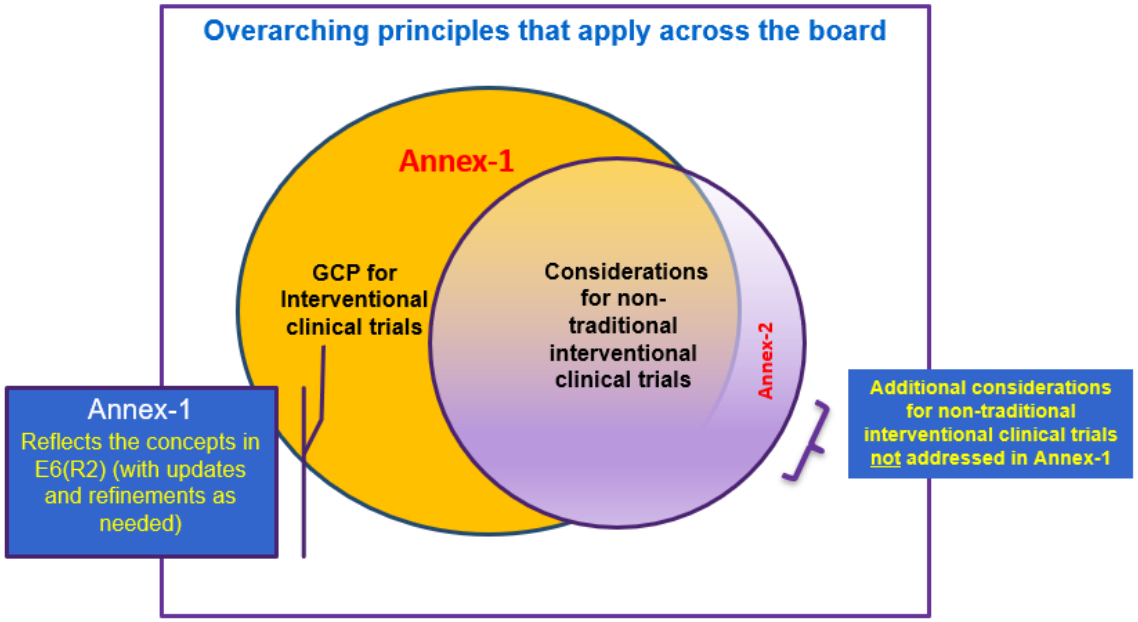
The Approach to ICH E6 Revision

ICH E6: An Important Global Standard

Preliminary Conceptual Representation of the Approach to ICH E6(R3)



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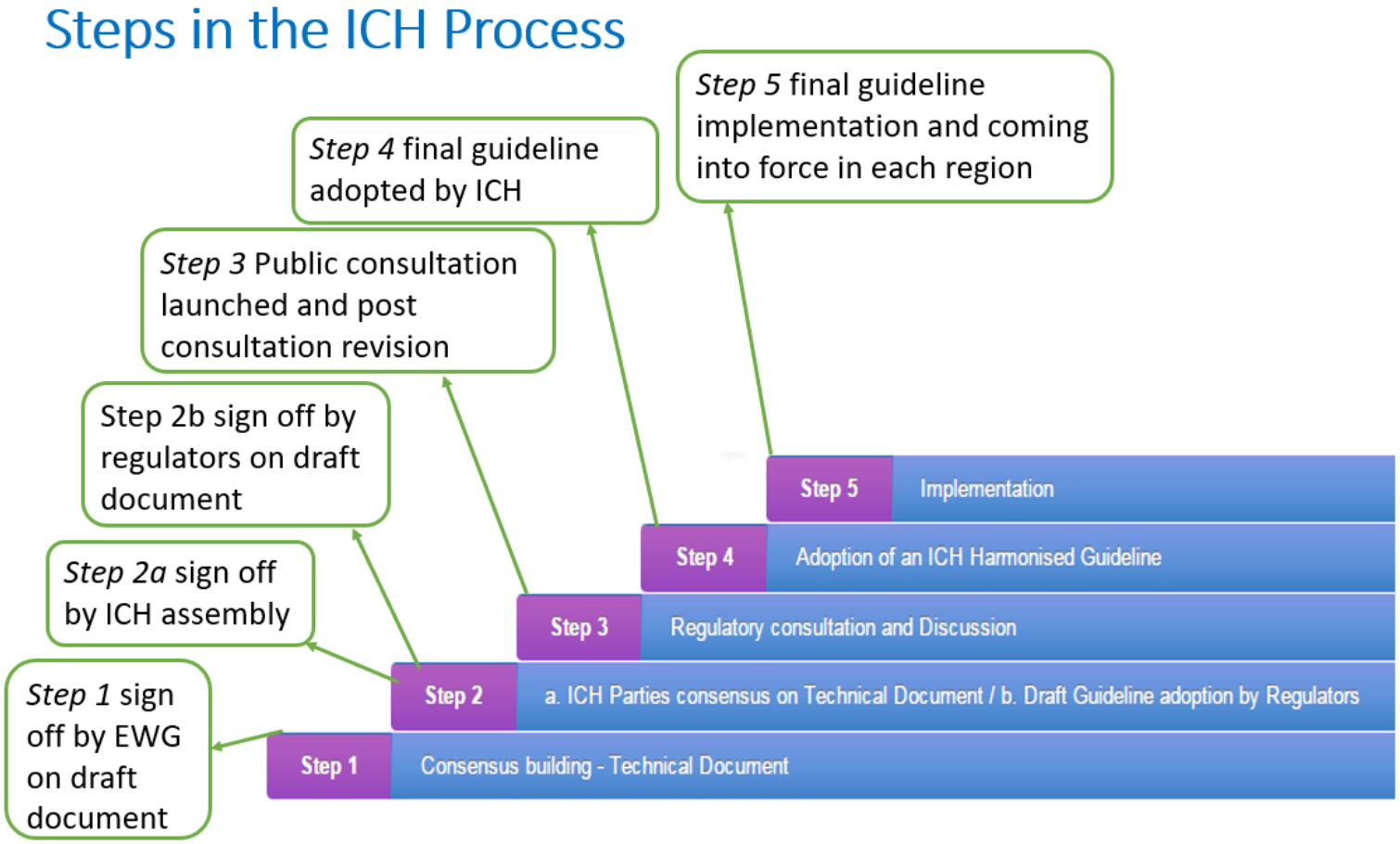
What Next?

Timeframe for Steps 1-2:
Principles & Annex 1: 24 months
Annex 2: 12-18 months



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Information on the ICH E6 revision efforts

- ICH E6 main page (www.ich.org)
  - ICH E6(R3) Concept Paper
  - Summary of the ICH E6 engagement proposal

- •CTTI's ICH E6 Renovation Work (https://www.ctti-clinicaltrials.org)
  - Webinar Recording
  - Powerpoint Slides
  - Executive Summary
  - Survey Findings
  - In-Depth Interview Findings
  - Open Comment Opportunity Findings

- Meeting details also available on FDA's website.

TMF-related events coming up*

NEW Events page on website (under Resources menu)

- Clinical Document World, Virtual Event, 8-11 September
- FierceLive / Questex / Exl European TMF Summit, London, UK 19-21 October
- Electronic Trial Master File Forum, New Jersey & Virtual, 20-21 Oct
- AGxP San Antonio, TX - 8-11 November
- IQPC TMF & GCP Inspection Readiness, Bruges, Belgium RE-SCHEDULED TO APRIL 2021

* COVID-19 dependent

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TMF RM General Meetings

- <27th July>
- Add to your calendar NOW or download the calendar file (.ics file) from our homepage
- Outlook Meeting Request no longer distributed

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QUESTIONS?

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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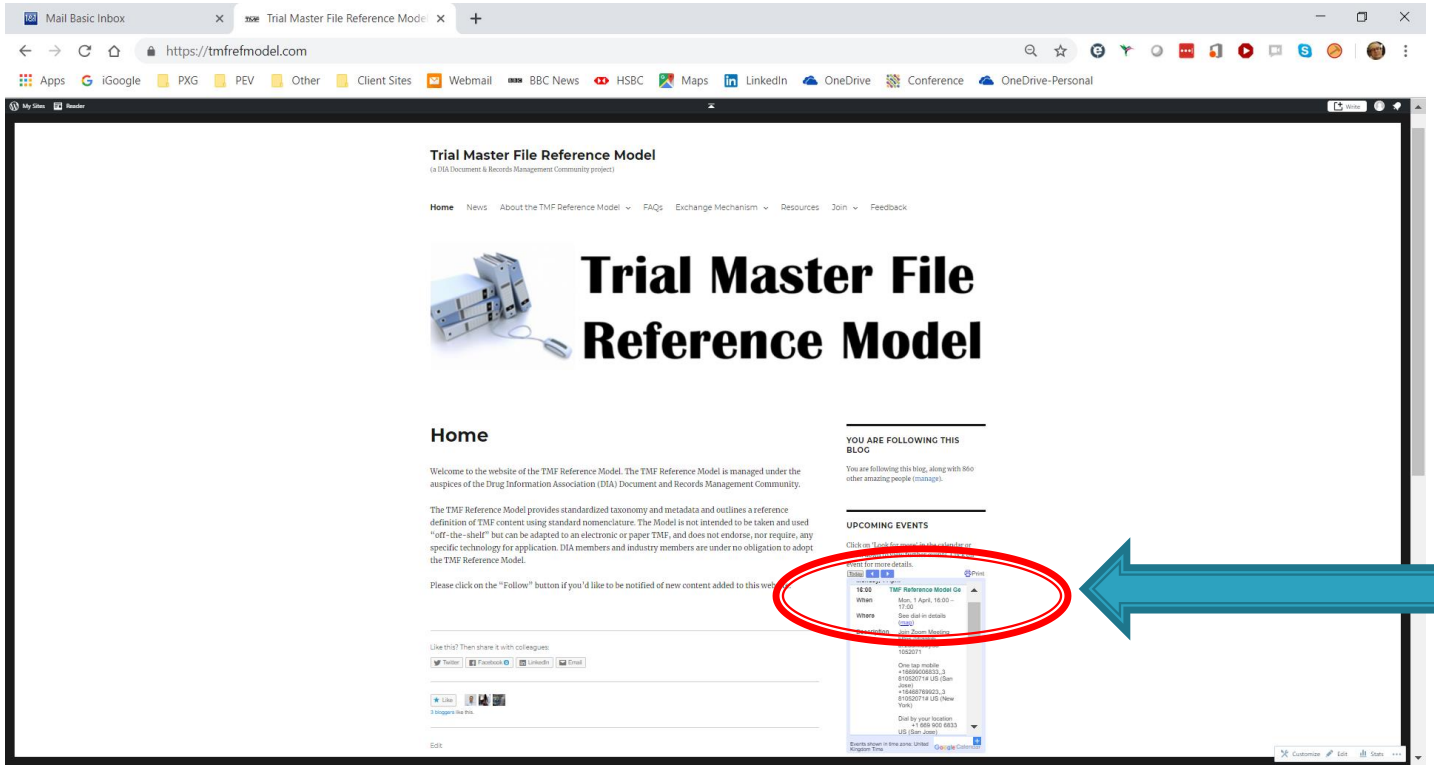
Meeting details

- Wondering where to find details of the next meeting?



On TMF Reference Model website, click on calendar to see meeting details. Click 'Copy to my calendar' to add to your Outlook / Google calendar.

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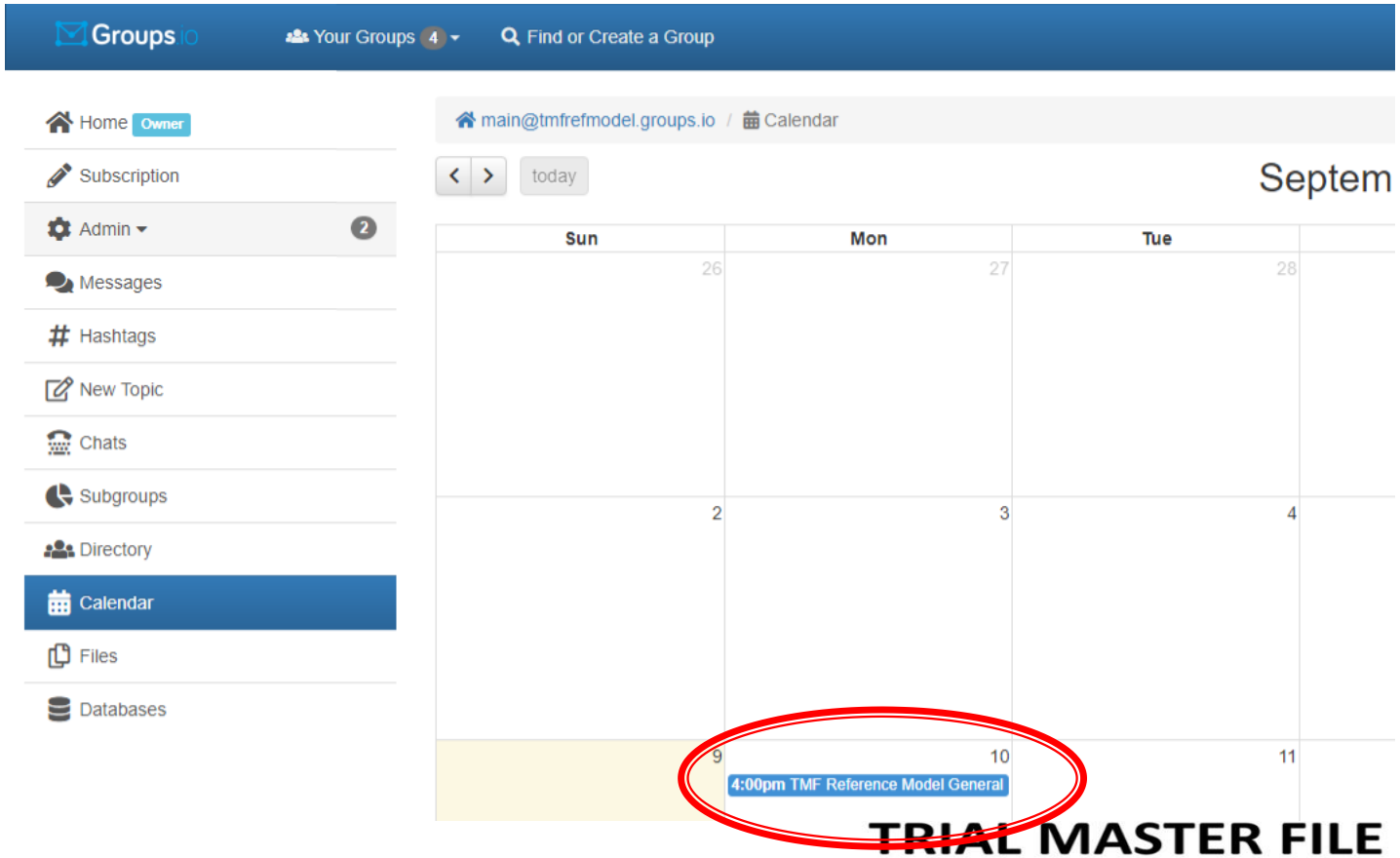
Meeting details

- 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**/



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