Trial Master File Reference Model

General Meeting

12 June 2017

Agenda

- Welcome
- Steering Committee Update – Introductions from the new members
- Update on the new members
- Updated Project Charter
- Move to IO and MailChimp
- Update on MHRA workshop
- TMF RM survey results
- Exchange Mechanism Update
- Update on TMF Plan initiative
- ExL-Pharma Inspection Readiness conference
- Upcoming conferences

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Steering Committee Update

- Renewed Committee Members
  - Fran Ross, Paragon
  - Jamie Toth, Daiichi-Sankyo
  - Lisa Mulcahy, Mulcahy Consulting
  - Todd Tullis, Veeva
- New Committee Members
  - Dorte Frejwald Christiansen, NNIT
  - Scott McCulloch, Biomarin

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New members

Last name	First name	Company	Country	Type
Aquino	Lia	Science 37	USA	CRO
Bhimnathwala	Hema	ICON Clinical	USA	CRO
Cahill	Annette	Tetraphase	USA	Sponsor
Cahill	Kristen	Bioverativ	USA	Sponsor
Casey	Charliene	Agenus	USA	Sponsor
Chan	Eugenia	Penn Medicine - Uni. of Pennsylvania	USA	Non-profit
Creavin	Fay	Intercept Pharmaceuticals	UK	Sponsor
Culverwell	Todd	UCB	USA	Sponsor
Ferrell	Michael	Veeva	USA	System vendor
Galgano	Jessica	TherapeuticsMD	USA	Sponsor
Govindaraju	Vidhya	Amgen	USA	Sponsor
Hautzinger	Kelly	TherapeuticsMD	USA	Sponsor
Heuser	Renee	Abbvie	USA	Sponsor
Ibanez	Julia	Grifols	Spain	Sponsor
Isherwood	Tara	inVentiv Health	USA	CRO

New members

Last name	First name	Company	Country	Type
Kane	John	CTI Clinical Trial Consulting Services	USA	CRO
King-Andreini	Jason	BioMarin Pharmaceuticals	USA	Sponsor
Kroboth	Tim	Wingspan	USA	System vendor
Legrand	Linda	MeiraGTx	UK	Sponsor
Lopes	Hobson	Regeneron	USA	Sponsor
Manion	Barbara	Seattle Genetics	USA	Sponsor
McNeal	Lisa	Transition Therapeutics	USA	Sponsor
Pangaro	Eddie	Otsuka	USA	Sponsor
Patel	Dhara	LMK Clinical Research	USA	Consultant
Rajavel	Subash	OpenText	USA	System vendor
Rank	Meera	Icon Clinical	India	CRO
Sheikh	Raisha	Safedale Pharmacy	UK	CRO
Shore	Richard	Phlexglobal	UK	System vendor
Tsiflidis	Benjamin	GCP-Service International	Germany	CRO
Velazquez	Sammy	AbbVie	USA	Sponsor
Walter	Tanya	Medsource	USA	CRO

Project Charter v2 Approved

- Includes governance by a Steering Committee
- Allows for participation from non-DIA members but….
  - Steering Committee members to be DIA members
- Maintenance of membership information (data privacy)
- Maintenance of website (http://tmfrefmodel.com)
- Clarify scope – TMF Reference Model and its adoption / implementation only
- See http://tmfrefmodel.com/resources for revised Charter

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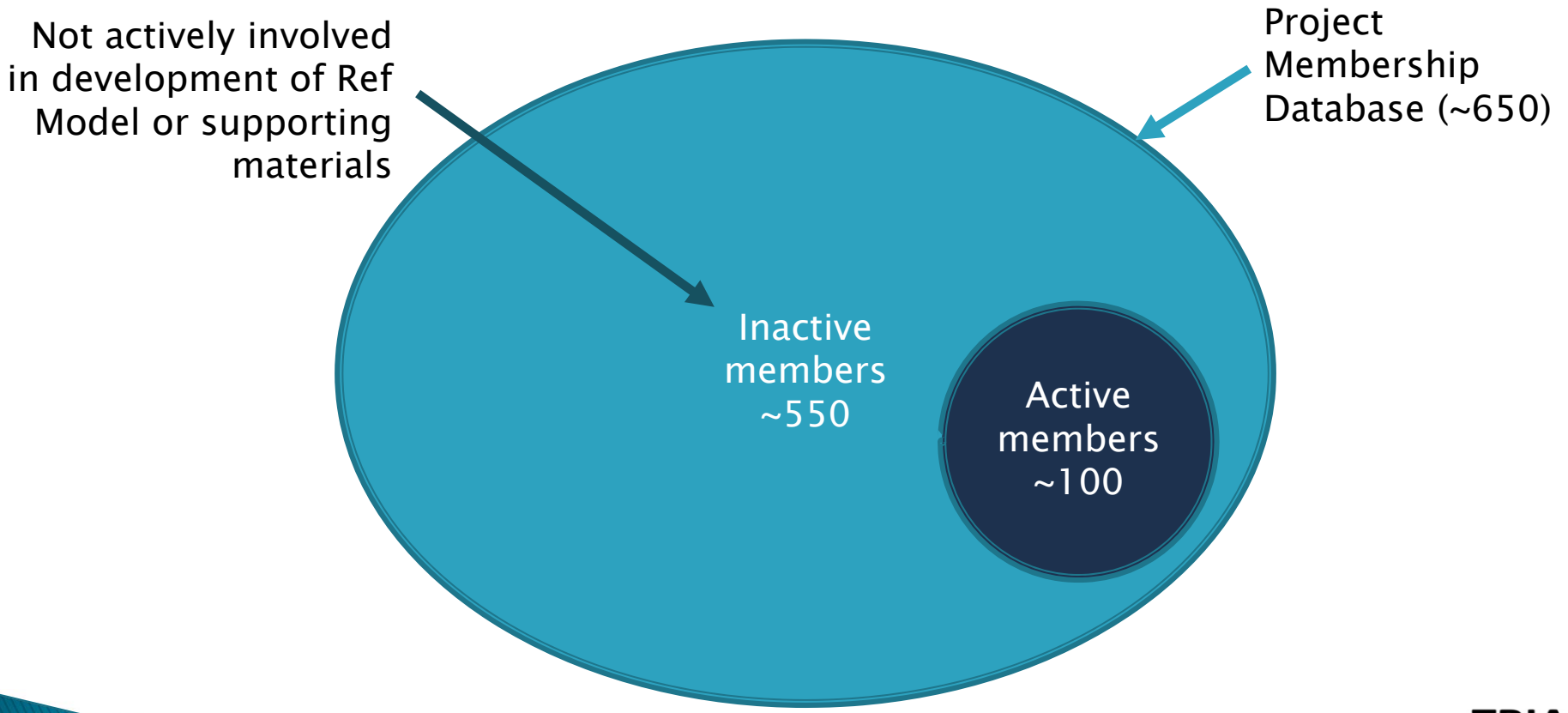
Current structure



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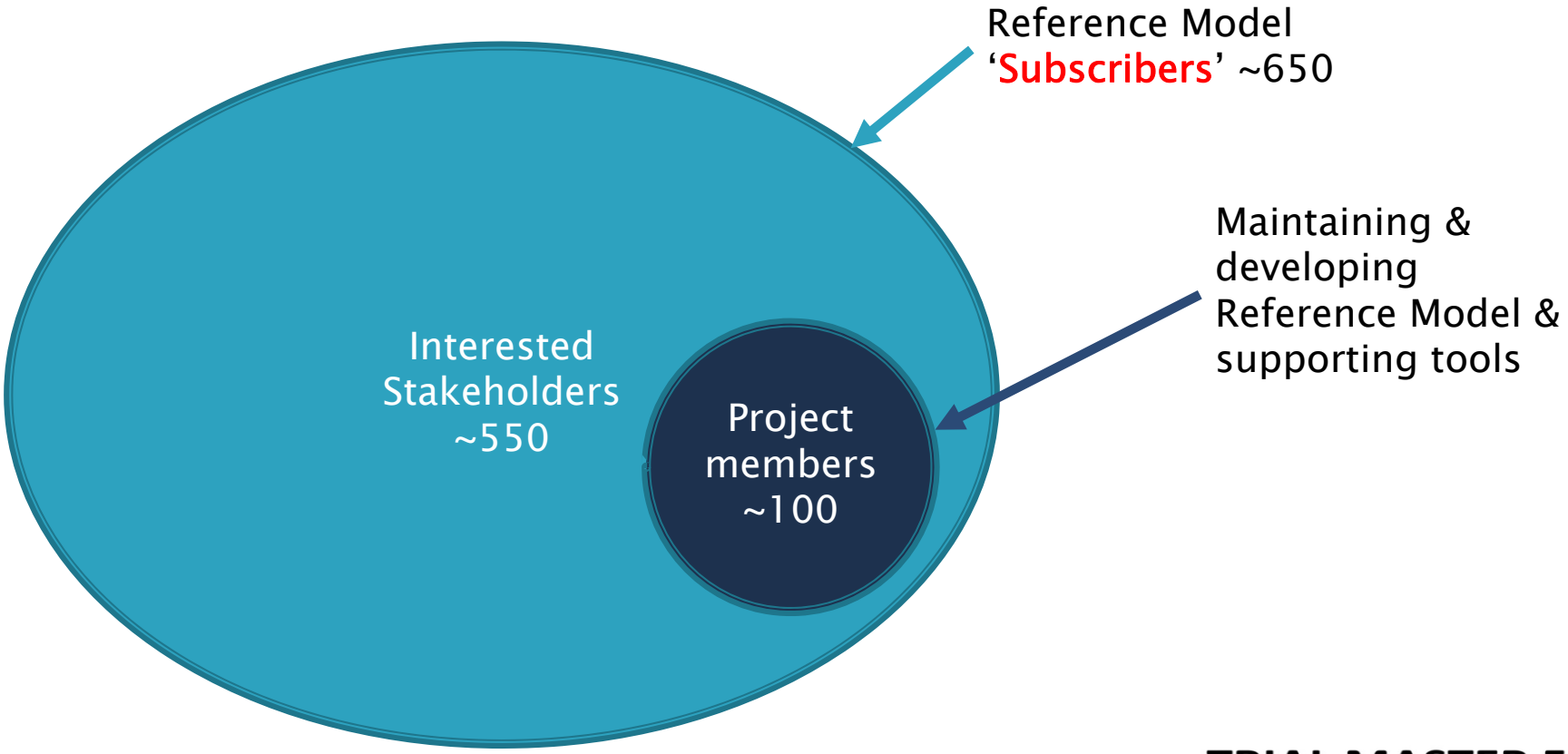
New structure aligned with Charter



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Subscribers

- Kept up-to-date with news
  - Notified of project update meetings
  - Materials available on website and notified of updates
  - Communication of important updates
  - Communication tool: MailChimp
    - Free
    - Easy for self-serve (subscribe link from website and update own profile)
    - All existing members have been added to MailChimp
  - Opt-in to Yahoo!Groups discussion tool (no change)
    - Will not be used for documents, sub-groups etc

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Project Members

- Only those participants on project working groups e.g.
  - zone groups
  - artifact sub-type group
  - dating conventions group
- New collaboration platform (groups.io)
  - Existing sub-group members will be added
    - Look out for invite from groups.io
  - New members will be asked which group they're joining
    - Project team is for ACTIVE participants ☺

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What about out-of-scope activities?

- Charter v2 clarifies scope of project (*the Ref Model*)
- Critical that out-of-scope TMF-related issues are addressed!
- DIA Document & Records Management (DRM) Community will establish project teams…. as originally intended ☺
  - http://bit.ly/2r05uxa
- Queries, ideas, volunteers?
  - Chair: Lisa Mulcahy

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Next steps summary

- All current members will receive information via MailChimp as ‘subscribers’
- New subscribers can join via link on http://tmfrefmodel.com
- All current sub-group members will be invited to join groups.io
  - Main Group: all project team members
  - Sub-groups: for individual sub-projects
- Website updated in line with this approach
- Projects to be established in DIA DRM Community if out-of-scope of Ref Model project

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MHRA Workshop – September

- 5th September, Leeds, UK
- To be advertised on MHRA website soon (email to be circulated)
- Target 100 attendees, May be limited to 1 per company
- 3 Stakeholder presentations:
  - Prep meeting this week – 13th, 14th or 16th June at 4pm
  - Sessions with multiple presenters and a lead
  - Interested? Contact Andy – Andrew.Fisher@mhra.gsi.gov.uk

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Activity Subgroups

Group	Lead
Metadata	Todd Tullis
Implementation toolkit / Upgrade User Guide	Mike Czaplicki Lisa Mulcahy **LOOKING FOR VOLUNTEERS!**
Dating conventions	Melissa Maberry ☑
Sub-artifacts	Karin Schneider
Inspection Preparation	Kathie Clark ☑
TMF Quality	Sholeh Ehdaivand ☑
Country specific artifacts	Eleanor Hewes
Milestones	Kathleen Kirby ☑
Single Site Structure	Karen McCarthy Shau
Survey	Jane Twitchen ☑

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2017 Reference Model Survey

Summary of Key Responses

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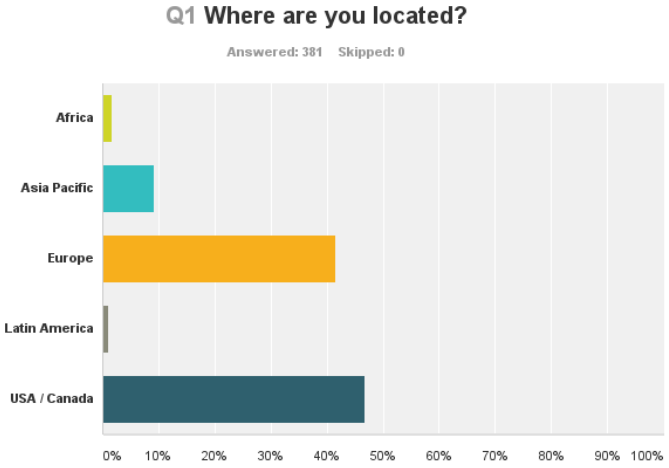
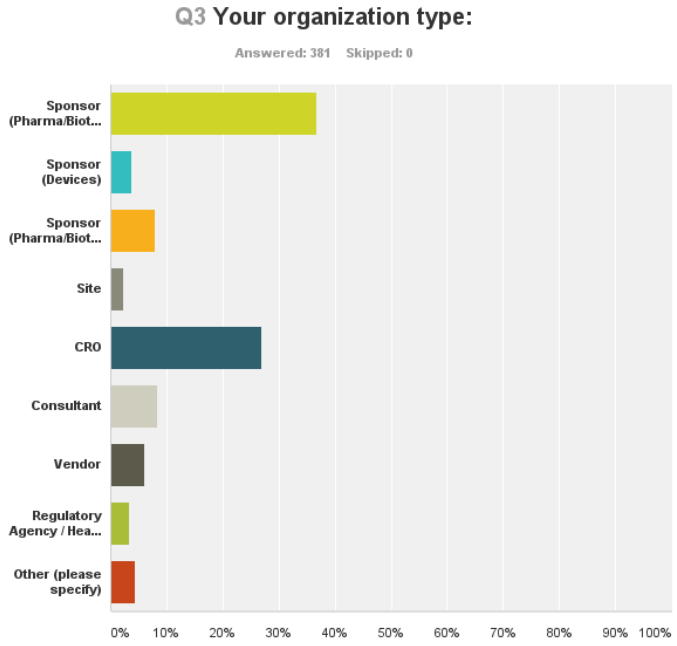
Who is our audience?

- 381 people took the survey
  - 205 took the 2015 (previous) survey
  - Highest before, 271 in 2013





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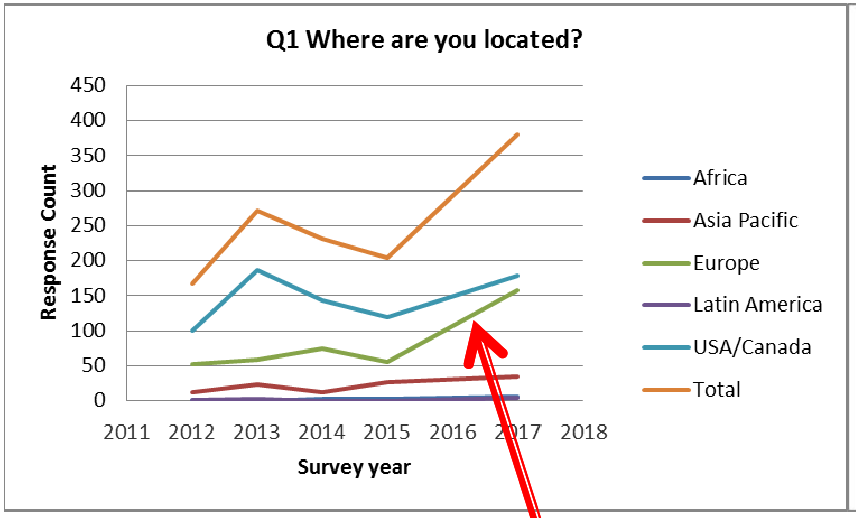
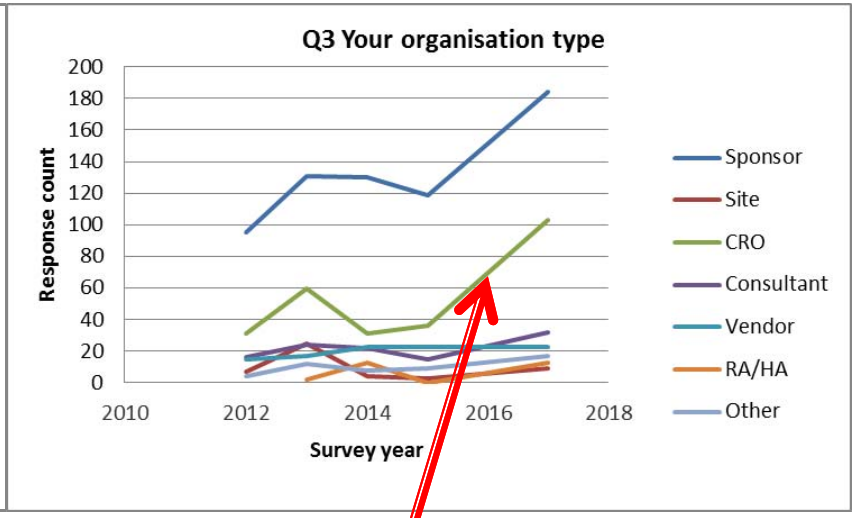
How has this Changed?





Really positive to see such an increase in European representation

Great to see significant growth in CRO contributors

SC Question: what can we do to promote awareness in Asia Pacific and Africa?

SC Question: What can we do to increase CRO 'active participation ' e.g. SC &/or subgroups?

Interesting Audience Comparisons:

	Africa	Asia Pacific	Europe	Latin America	USA / Canada	Total
Reference Model Total members	2	44	162	2	417	627
2017 Survey Data	6	35	158	4	178	381
Reference Model Committee			3		10	13

SC Question: How can we increase US contributions to the survey? (~30% took part)

	Africa	Asia Pacific	Europe	Latin America	USA / Canada
Reference Model Total members	0.32%	7.02%	25.84%	0.32%	66.51%
2017 Survey Data	1.57%	9.19%	41.47%	1.05%	46.72%
Reference Model Committee	0.00%	0.00%	23.08%	0.00%	76.92%

SC Question: the US is over-represented in our Steering Committee; SC to consider impact of this.

Note: further analysis to follow comparing Company demographics with Ref Model Members

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TMF Status – a few headlines (1)…

There has been a MASSIVE increase in Reference Model awareness with Inspectors between 2014 to 2017; with the figures reversing…

Question: Do you find the TMF Reference Model supports activities in clinical trial inspections?

	Yes	No	Not aware of the TMF Reference Model
2014	28.6%	0.0%	71.4%
2017	71.4%	0.0%	28.6%

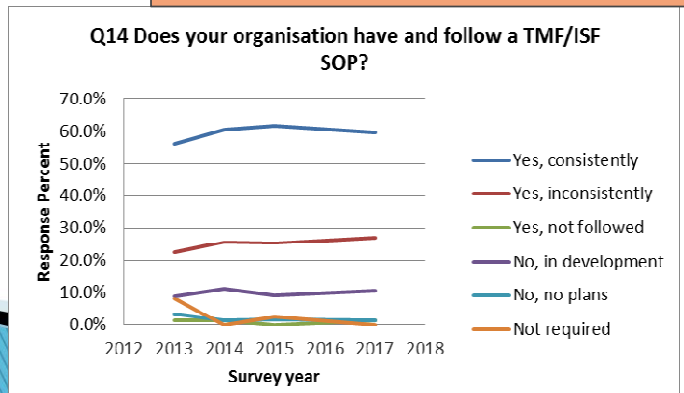
[new question]: There is currently a lack of consistency in how TMF is functionally organised. It will be interesting to track this from now onwards.

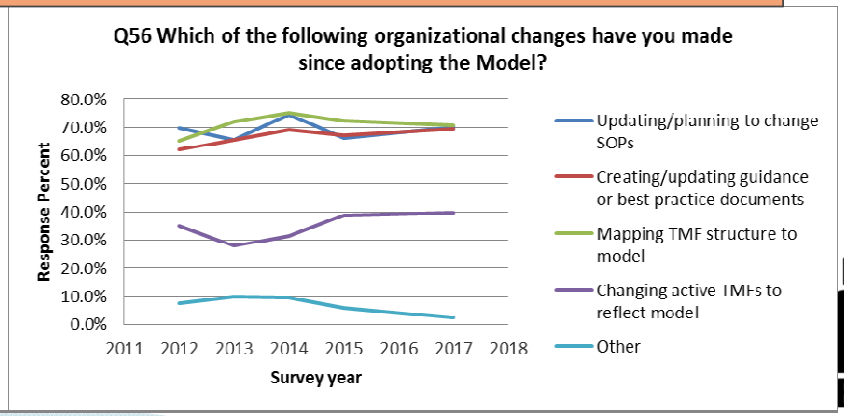
Is the TMF managed within your organization by a Central Group, or disparately across functions?

Answer Options	Response Percent	Response Count
Centrally	53.7%	117
Disparately across functions	32.1%	70
Other/Combination (please comment)	14.2%	31

TMF SOP data was surprisingly static! (although these are still interpreted inconsistently…)

SC Question: does inability to write good SOPs hinder IR?





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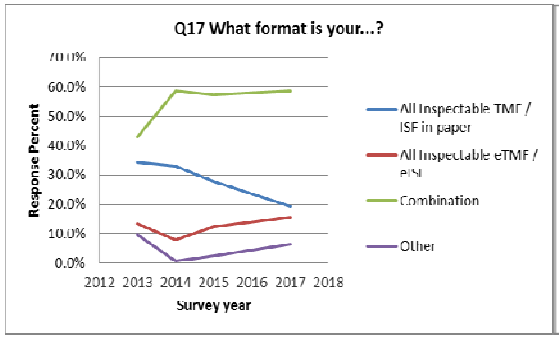
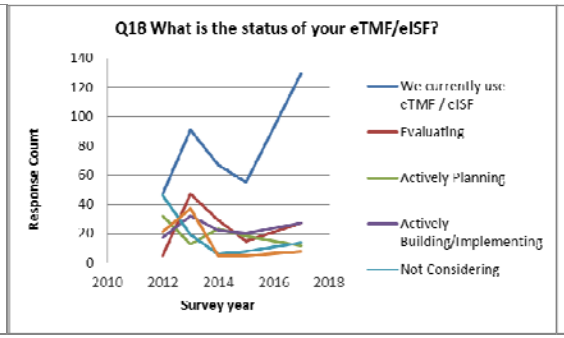
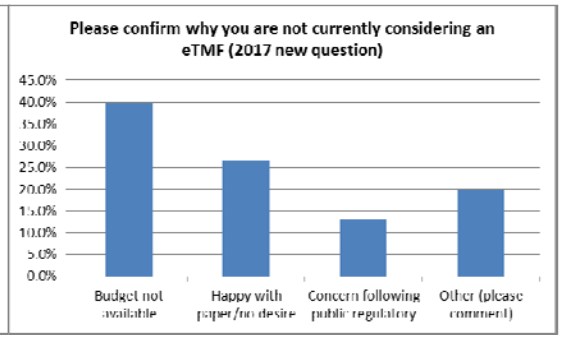
TMF Status – a few headlines (2)…

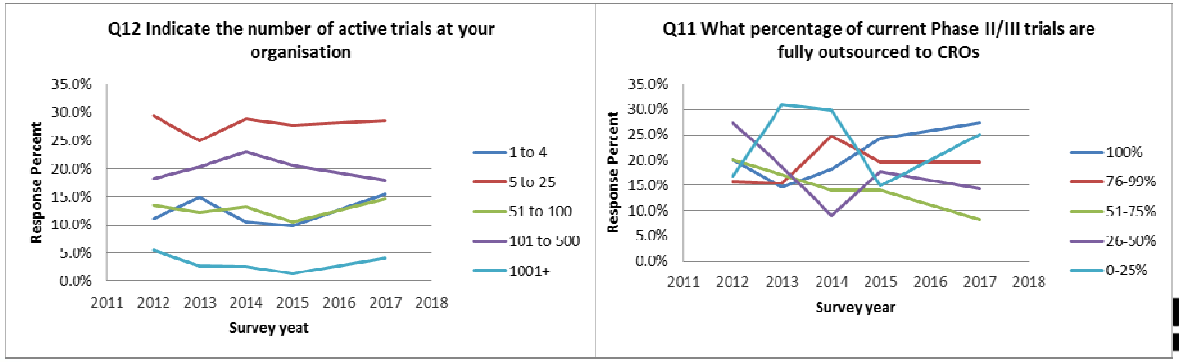
As expected, there's been a steady increase in the number of people using eTMF, but more are still considering this move and budget is the major rate-limiter…







The ratios of active trials are appearing to remain static, whilst we are seeing <u>huge amounts</u> of change, across all phases, in the outsourcing models..



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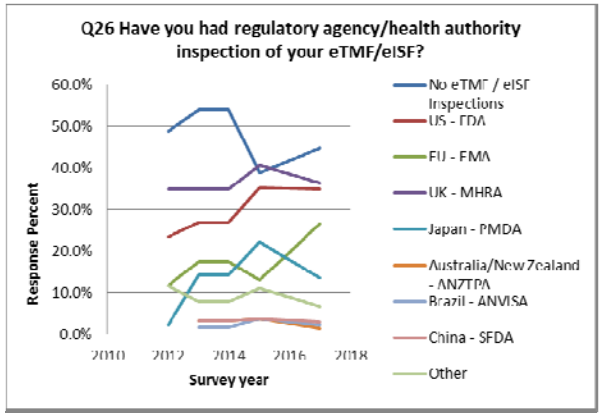
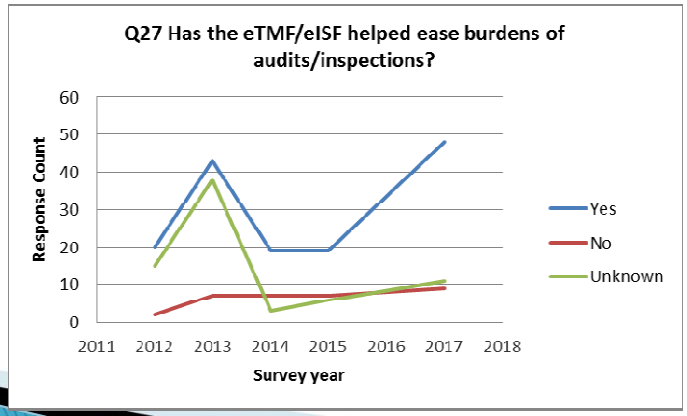
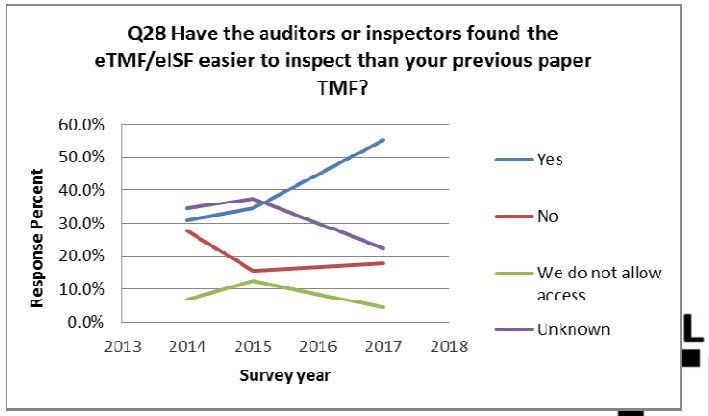
Inspection Experience (1)…

A large proportion (over 40%) have still not had eTMF inspections, but many of us have had increased experience of MHRA/FDA/EMA inspections using eTMF,



There continues to be an overwhelming majority of people who agree that eTMF eases the burden of inspections (although those disagreeing is also slowly creeping up..)





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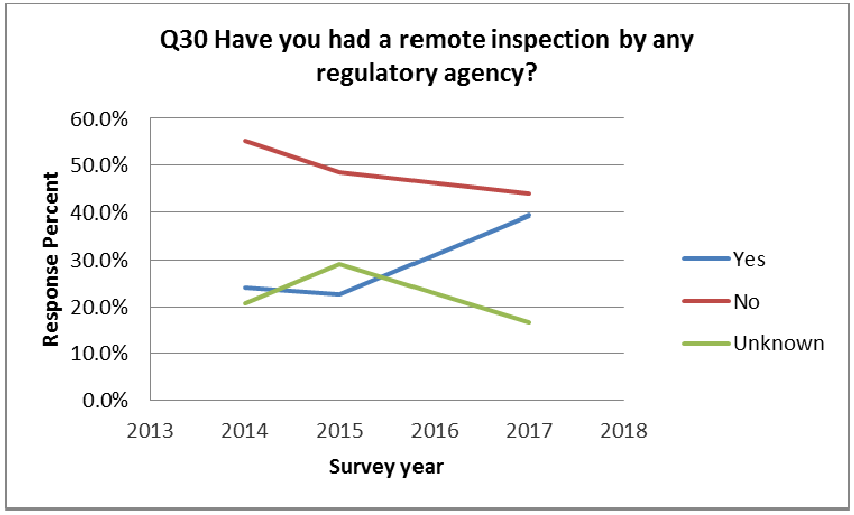
Inspection Experience (2)…

- There is an increase in the incidence of Remote inspections



- [new question] Passwords are most commonly supplied when onsite, for the duration of the inspection. It will be interesting to observe how this changes in years to come

When have you provided the Inspector/Auditor with their eTMF password?

Answer Options	Response Percent
Prior to the inspection, so they can start using straight away	15.4%
Prior to the inspection, but it only activates when they are onsite	13.8%
Once the inspection commences, but the password is only active whilst they're onsite	16.9%
Once the inspection commences, but the password is then active continually until the inspection is complete	35.4%
Other (please comment)	18.5%

Stay tuned….more to come….

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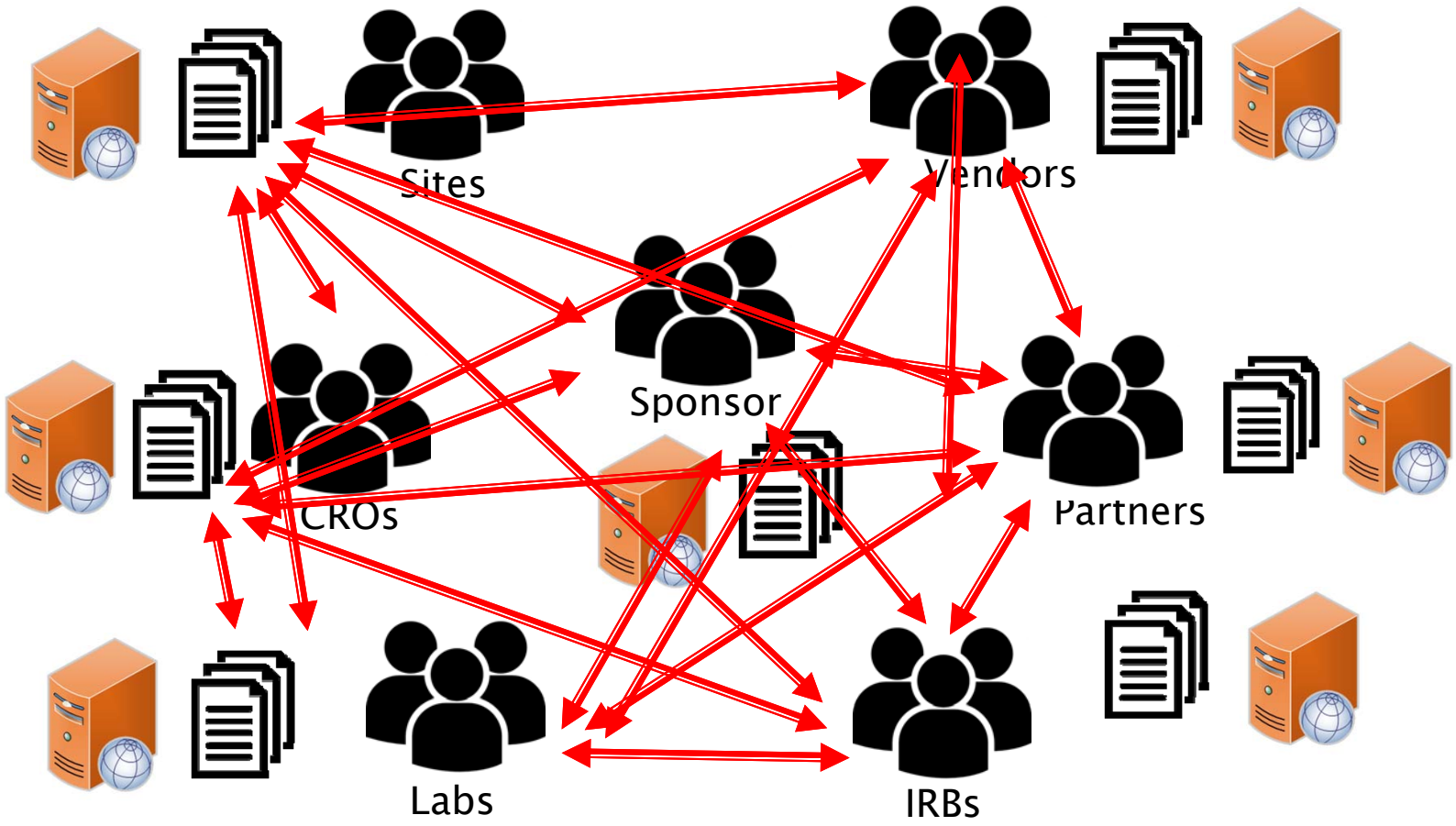
Trial Master File Reference Model

eTMF Exchange Mechanism

Challenge of eTMF Transfer



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Commonality is Key

- Uniform criteria are vital in Life Sciences
  - ICH eCTD and MedDRA
  - CDISC STDM and AdAM
  - ISO 9001
  - CDC ICD10

- eTMF Exchange Mechanism!

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eTMF Exchange Mechanism

What is it?

- XML-based exchange mechanism
- Works with any version of TMF RM
- Exchanges between any eTMF solution

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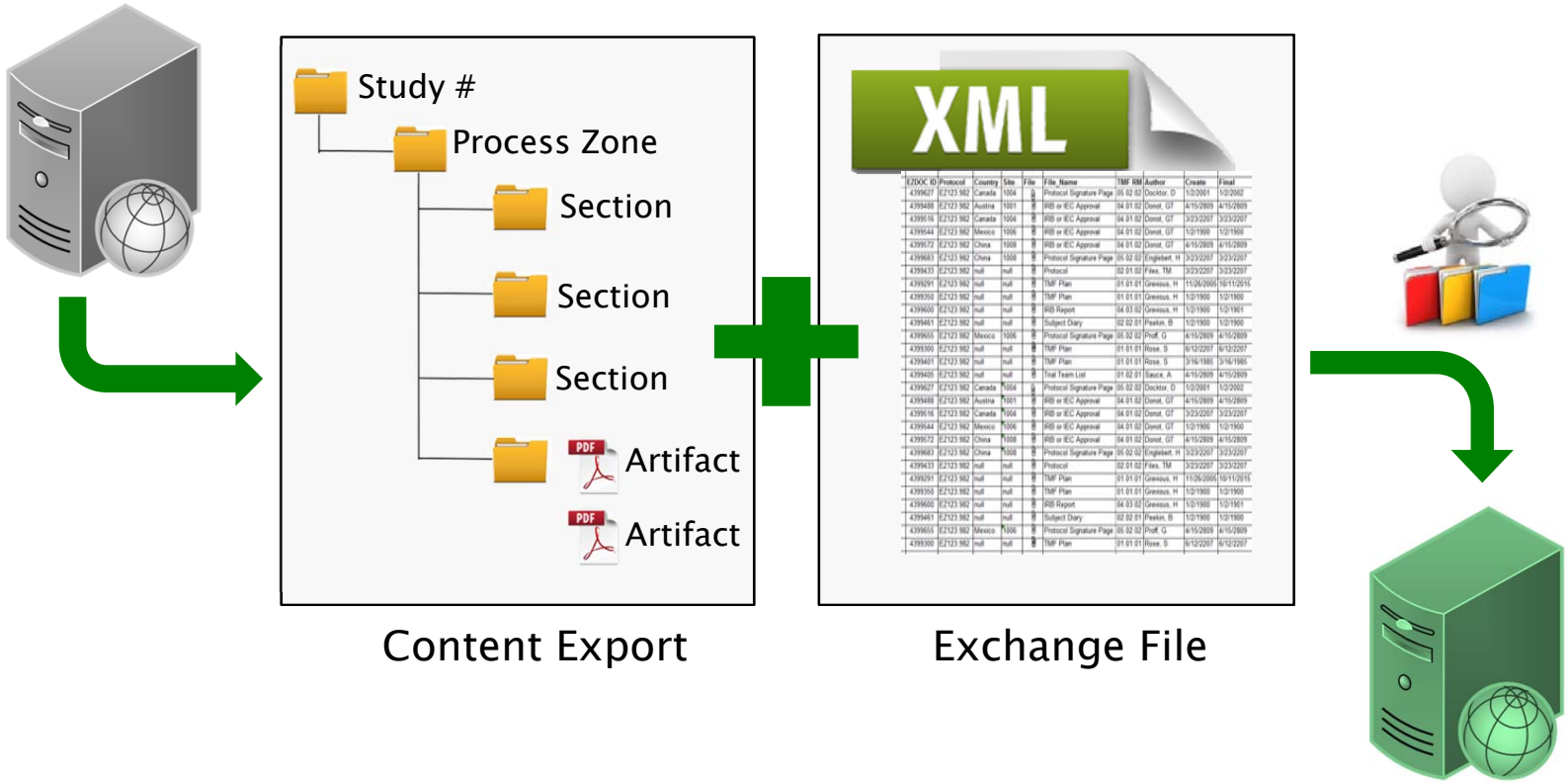
How it works


Study #
Process Zone
Section
Section
Section
Artifact
Artifact
XML
Content Export
Exchange File

Why eTMF Exchange Mechanism?

- Subgroup of TMF Reference Model
- Extensive and diverse TMF expertise
  - eTMF Vendors, Sponsors and CROs
  - Expertise in trials, records and technology
- Unified mission
  - Flexible and simple components
  - Easy to maintain

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Progress To Date

- ExMech subgroup meets weekly
- Initial components in draft
- Alignment / initial reviews
  - eTMF vendors, Sponsor and CRO business users
  - TMF RM SC and Metadata Subgroup
- Planning for solution vendor assessment
  - Need warriors for beta testing
- We need YOU!

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Exchange Mechanism Subgroup

Role	Duties	Lead	Backup
Co-Chair*	Oversee all leads and general strategy for the standard.	Paul Fenton	Elvin
Co-Chair*	Oversee all leads and general strategy for the standard.	Elvin Thalund	Paul
TMF RM SC Liaison*	Liaise with the TMF RM SC. Consult with SC to define and manage governance rules and charter.	Kathie Clark	Fran
Project Management Lead*	Manage schedule. Coordinate subgroup activities.	Ken Keefer	**TBD**
Change Control Lead*	Coordinate all change activities and chairs change control and comments review meetings.	Kristen Cahill	Gift Chareka
Technical Lead (XML Standard)*	Maintain the XML. Participate in comments review and change control meetings.	Martin Snyder	**TBD**
Technical Lead (Metadata)*	Maintain the ExMech metadata. Participate in comments review and change control meetings.	**TBD**	**TBD**
Vendor Coordination Lead*	Coordinate vendors input and participation. Participate in comments review meetings.	Richard Shore	**TBD**
Business Coordination Lead*	Coordinate Sponsors, CROs and other business users input and participation. Participate in comments review meetings.	Fran Ross	**TBD**
Technical Lead (Implementation Process)	Help define guidance and rules for implementation.	TBD	TBD
Communications Lead	Promote through press releases, presentations, webinars and other channels. Address any external communications.	Subash Rajavel	TBD
Training Lead	Promote training, manage the compilation and maintenance of user guides.	TBD	TBD

Call for Support

- Help us keep the momentum going
- ExMech subgroup members needed!
  - Both technical and business experts
  - Take a primary or back-up role
  - Commitment: weekly meeting plus review sessions
  - Interested? email Ken Keefer KKeefer@keeferconsulting.com

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TMF Plan Template Group – To become a DRM Initiative?

Working Group Lead: Jamie Toth
Co-Lead: Lorna Patrick
Team Members: See next slide

Brief description of project & objectives	Objective: Develop a cross-industry usable, simplistic TMF Management Plan template.. Guidance provided on how to deal with variations depending on study size, phase, type.
Scope - In:	Template to be used for studies that are Early Phase I - Phase IV, Investigational Drug and Medical Device, Biologics.
Scope - Out:	Development of an SOP. Processes already created within a given company around the TMF.
Desired deliverables	• A simplistic Plan template that can be used within any company, where company specifics can be added. • Guidance on Plan usage and any variations and how to adapt Plan.
Target end date	Early January 2018
Status / Issues	• First meeting held on 31-Mar-2017 • Biweekly meetings scheduled through January 2018

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Team

Name	Company
Deborah Castellana	Celgene
Elaine Berry	The Emmes Corporation
Etienne Hinton	Duke Clinical Research Institute
Jamie Toth	Daiichi Sankyo, Inc.
Jennifer Eberhardt	Shire
Kelly Hautzinger	Therapeutics MD
Lisa Mulcahy	Mulcahy Consulting
Marion Mays	Quintiles
Menzi Reed	Pharma Consulting Group
Tyler Prater	Eli Lilly
Tony Nguyen	Ultragenyx Pharmaceutical
Mike Czaplicki	GSK
Dina Antonacci	Mallinckrodt Pharmaceuticals
Subash Ravel	OpenText
Marie Christine Poisson-carvajal	Pfizer
Anne-Mette Varney	Novo Nordisk
Sarah Curno	Hedian Records Management
Linda Hoppe	UCB
Lorna Patrick	Quotient Clinical
Dr. Mujib Khan	Biorasi
Luisa Monica	LMK Clinical Research Consulting

Inspection Readiness conference London, May 22-23 2017

- Kath Meely, MHRA (main take-away)
  - Data integrity
  - Oversight of how data is managed
  - System maps, flow diagrams are helpful
  - Have system validation documentation ready up-front
  - Planning of the inspection – discuss and plan up-front, e.g. if teleconference is needed for interviews
- When you file TMF documents, it should be easy for QA/inspectors to find the documents again

eTMF Conferences coming up

- DIA Chicago, June
- DIA Operational Excellence Forum, Berlin 12 to 14 September
- EXL TMF Summit, Japan, September
- IQPC TMF Conference, September, Amsterdam
- EXL TMF Summit, London, October

- Plus Inspection Readiness, Quality forums etc.

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TMF RM General Meetings

- 11-Sep
- 6 – Nov

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QUESTIONS?

Keep up to date & join our meetings:
SUBSCRIBE to our mailing list

Participate in our working teams:

http://tmfrefmodel.com/join

- Knowledge sharing
- Networking
- Too Much Fun!

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