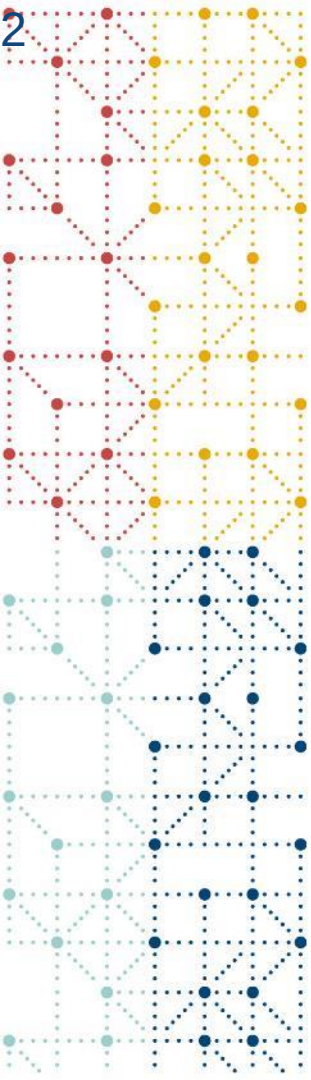
The TMF Reference Model
General Meeting September 2024

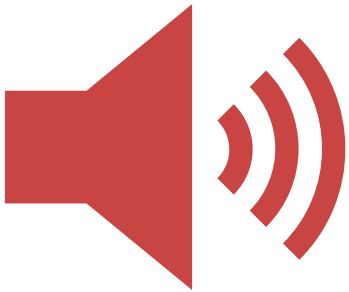
Presenters:

- Karen Roy, Consultant, CDISC; Chair, TMF Reference Model Steering Committee
- Dawn Niccum, EVP, QA & Compliance, inSeption Group, TMF RM SC Member
- Jamie Toth, Global Head, Trial Master File Management & Records, BeiGene; TMF RM SC Member
- Joanne Malia, Sr. Director, Development Records Mgmt, Regeneron, TMF RM SC Member
- Marisa Cole, Clinical Operations Manager, Technical Resources International
- Donna Dorozinsky, CEO, Just in Time, GCP, TMF Reference Model Steering Committee Member
- Paul Fenton, CEO, Montrium; TMF Reference Model Steering Committee Member



Housekeeping

Housekeeping

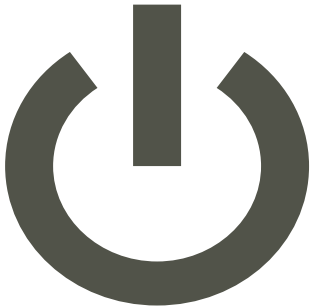


You will remain on **mute**

Housekeeping

Submit questions at any time via the Questions tool on your Zoom app

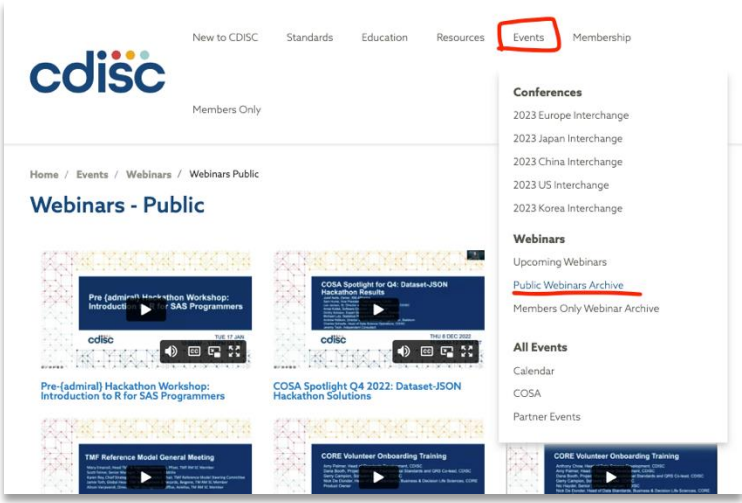
Housekeeping



Audio Issues?

First, close and restart your Zoom App
Second, check your local internet connection strength

Housekeeping



Webinar Recording

A recording of this webinar will be available in the Public Webinar Archive on the CDISC website.

https://www.cdisc.org/events/webinar/tmf-reference-model-general-meeting-q3

Agenda

- 2025 Steering Committee Changes
- Education Team
- ISF Initiative
- Risk Initiative
- CDISC TMF Interchange and other Events
- TMF RM Survey highlights
- The Road to Version 4

2024 Steering Committee

Steering Committee

A huge thank you to Kathie Clark for her many years of work on the Steering Committee!

Steering Committee Changes

New Steering Committee Member:

Nick Hargaden, Moderna

New Charter:

Added Incoming Chair and Past Chair, so 2 new SC places

Effective January 2025

Chair has a maximum of two terms (6 years)

I will be stepping down (after 15 years!!)

Thank you for your support!

Nick Hargaden

Title: Director, Clinical Trial Systems and Operations

Organization: Clinical Development Operations, Moderna

Nick is the business owner for eTMF and CTMS applications at Moderna. He is the global head of TMF Operations managing in house and vendor teams. He has 25 years in application of computerized systems to speed drug development and improve quality including IRT, TMF, RBQM, eCOA.

https://www.linkedin.com/in/nickhargaden

Steering Committee Changes

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Education Team

Education Team

Still time to sign up for:

- Fundamentals of the TMF Reference Model
  - Scottsdale – 22 Oct 2024 with the CDISC+TMF Interchange
  - Virtual – 21-23 Jan 2025
  - 8 registrants
- The Critical Role of Data Managers, Biostatisticians, and Programmers in Achieving TMF Excellence
  - Scottsdale – 25 Oct 2024 with the CDISC+TMF Interchange
  - Virtual – 28 Jan 2025
  - 13 registrants

TMF Module 1: Introduction to the TMF Reference Model

- Free

- TMF QC Course – Coming Soon in 2025

ISF Initiative

ISF Initiative: Overview

TMF RM SC Liaisons:
Jamie Toth and Dawn Niccum

Co-leads:
Aryn Knight, Clinical Innovation and Research Institute, Memorial Hermann Health System
Matt Lowery, The Pathways Grp, LLC

Goal:
To develop an Investigator Site File (ISF) reference model for sites to use that supplements the TMF Reference Model with the intention of standardizing ISF structure, file naming conventions, and how/where site-level essential records are filed.

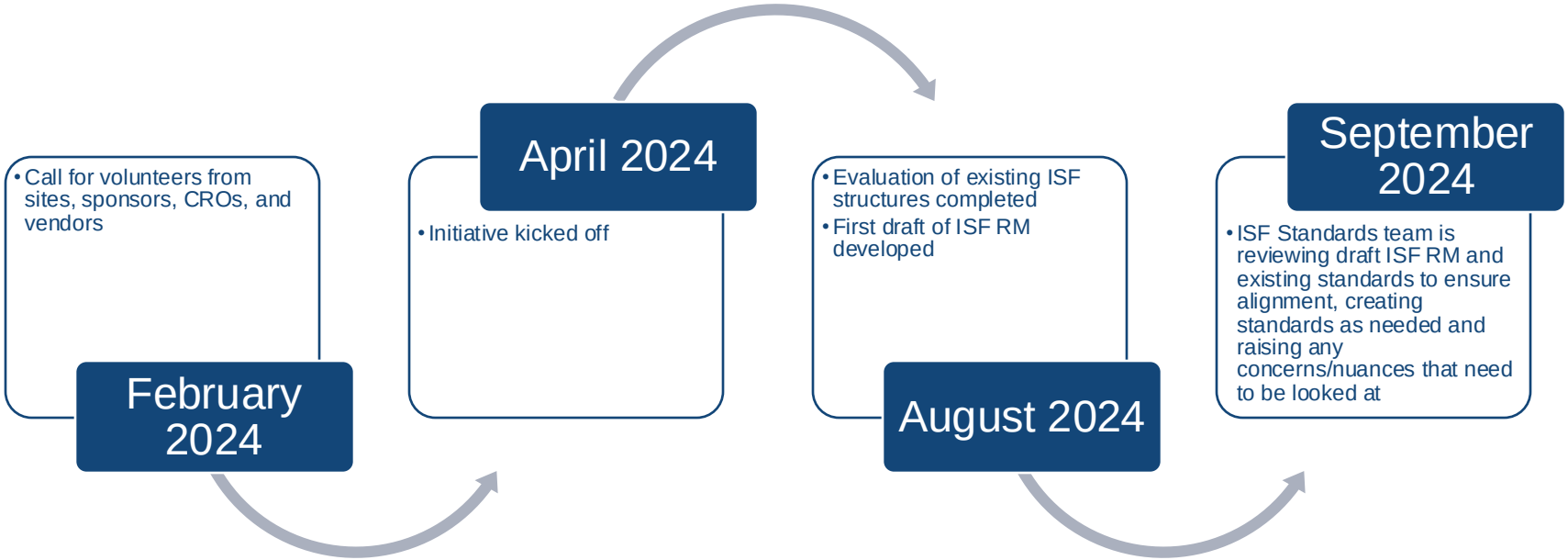
ISF Initiative: Overview

Committee: ~46 members across all aspects of the industry who have an interest ***in*** and experience ***with*** ISF/TMF/regulatory including sites, sponsors, CROs, service providers/vendors, consultants.

Sub teams:

1. **Evaluation**: Review of existing ISF structures
2. **Standards**: Setting standards
3. **Proofing**: Review of deliverables
4. **Outreach**: Presentations, publications, and white papers
5. **Training**: Training the industry on ISF RM

ISF Initiative: Progress to Date



Thank you to the entire ISF Team for the excellent progress made to date!

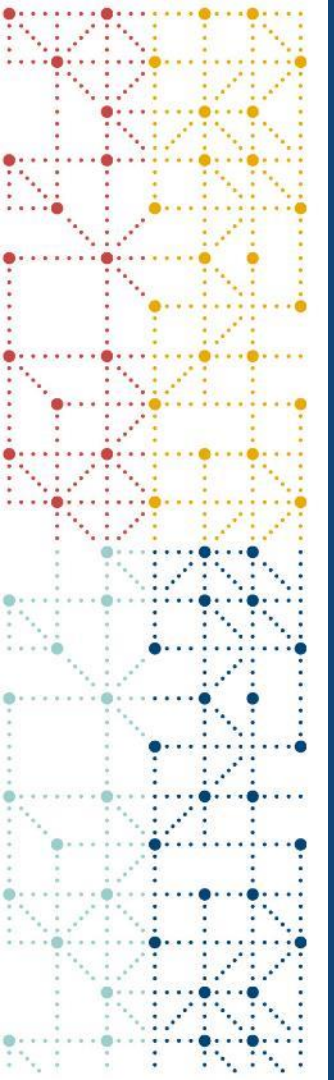
ISF Initiative: Ongoing and Future Activities

- First draft version of the ISF reference model expected to be completed in October 2024.
  - Formal CDISC internal review will be followed prior to public comment.
  - Alignment with TMF RM v4.0 activities will take place.
- Outreach is ongoing and will continue throughout the initiative.
- Training will be provided upon publication of the final ISF reference model.

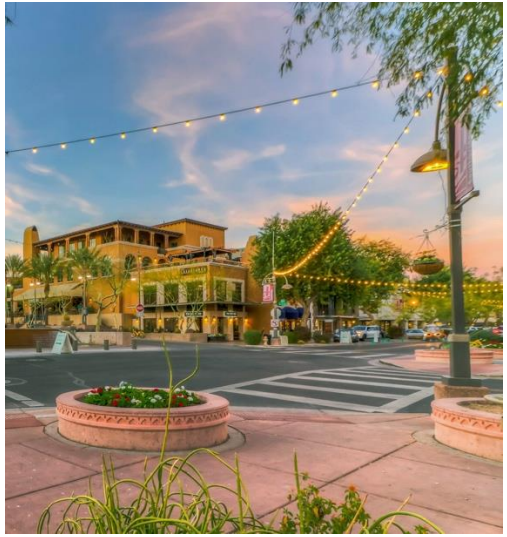
Risk Initiative

Risk Initiative

- Started in earnest in January 2024 with 3 workstreams:
  - White Paper
  - Tools
  - Training
- Workstream 1 has submitted paper for review (final?)
  - Tentative release by early January 2025
- Workstreams 2 has developed a workbook with a variety of tools
  - Checklists, assessments, etc. going through internal workstream review currently
  - Projected availability in November 2024
- Workstream 3 has begun a slide deck
  - Overview presentation in early 2025 and TMF General Meting
  - Dedicated TMF Risk webinar to follow
  - Determination to be made based on interest, if a training module will be developed



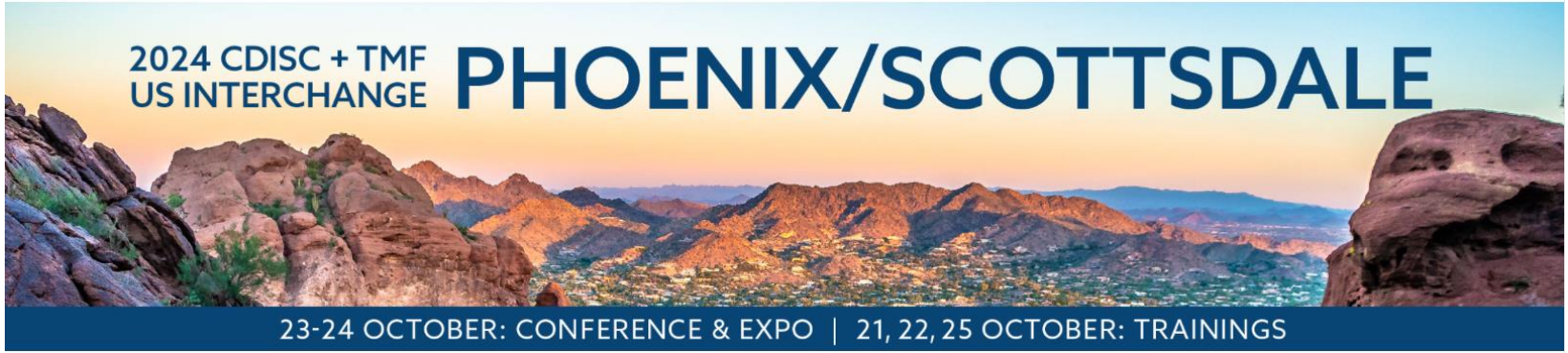
CDISC + TMF Interchange



2024 CDISC + TMF US Interchange

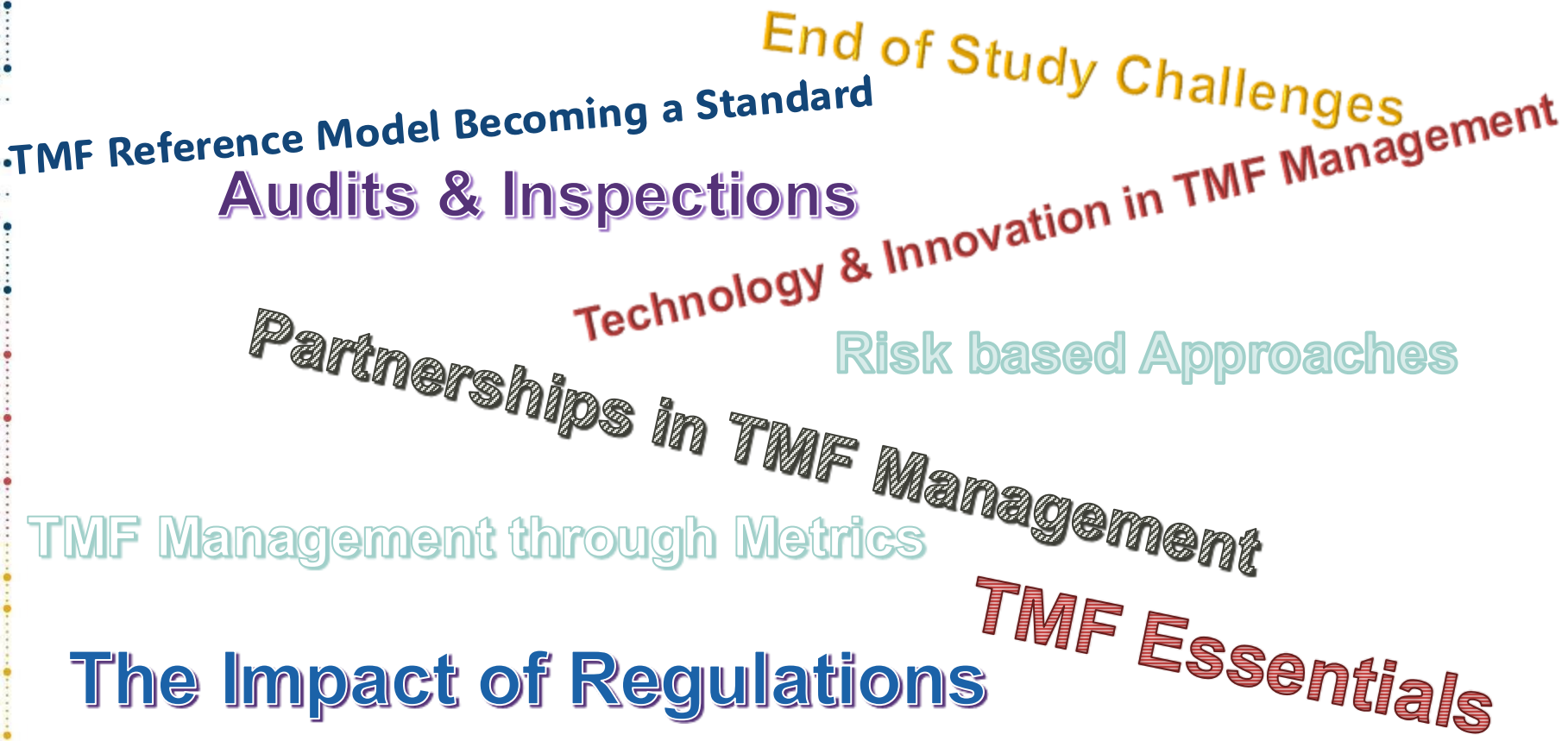
Scottsdale, Arizona
23 - 24 October 2024

https://www.cdisc.org/events/interchange/2024-cdisc-us-tmf-interchange



Not to be missed:

- Release of the Version 4 process, the road to standardization, the biggest change to the model in years!
- David Glasgow, Deputy Director, BIMO, FDA, on Inspections



The Future of the TMF Reference Model: The Next Version

Investigators and Inspectors

Other Upcoming Events

- 24-Sep to 26-Sep-2024, Edinburgh: HSRAA Conference
- 23-Oct to 24-Oct-2024, Phoenix: CDISC / TMF US Interchange US CDISC & TMF Interchange
- 14-May to 15-May-2025, Geneva: CDISC / TMF EU Interchange EU CDISC & TMF Interchange
- General Meetings:
  - Q4 - 3rd December

2024 Survey Highlights

Full results at TMF Interchange!

About the (323) Survey Respondents

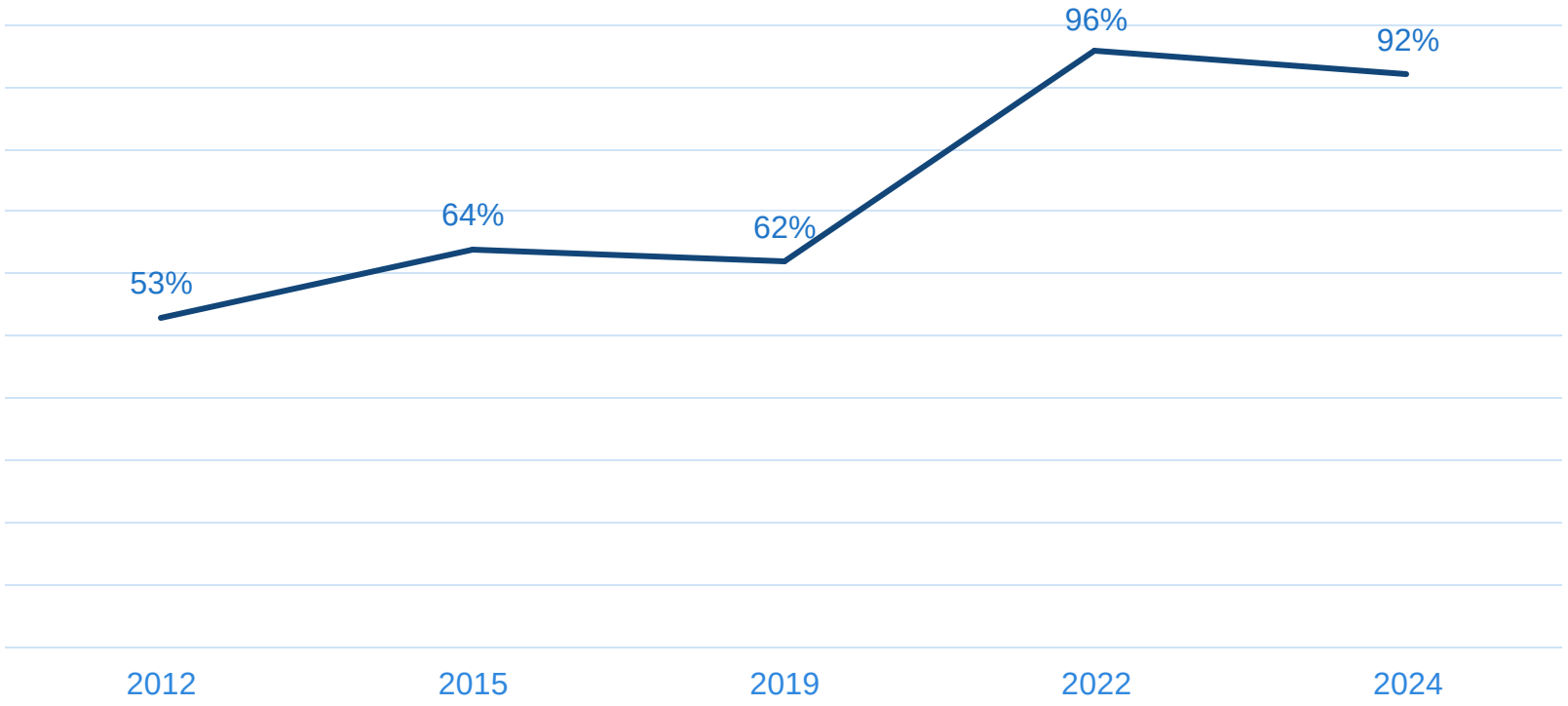
Your Region/Country		
North America	194	60%
Europe	94	29%
South-East Asia	22	7%
Western Pacific	8	2%
Africa	4	1%
South America	1	<1%

- Mostly North America & Europe
- Mostly Sponsors & CROs
- Mostly 4+ years of TMF RM awareness

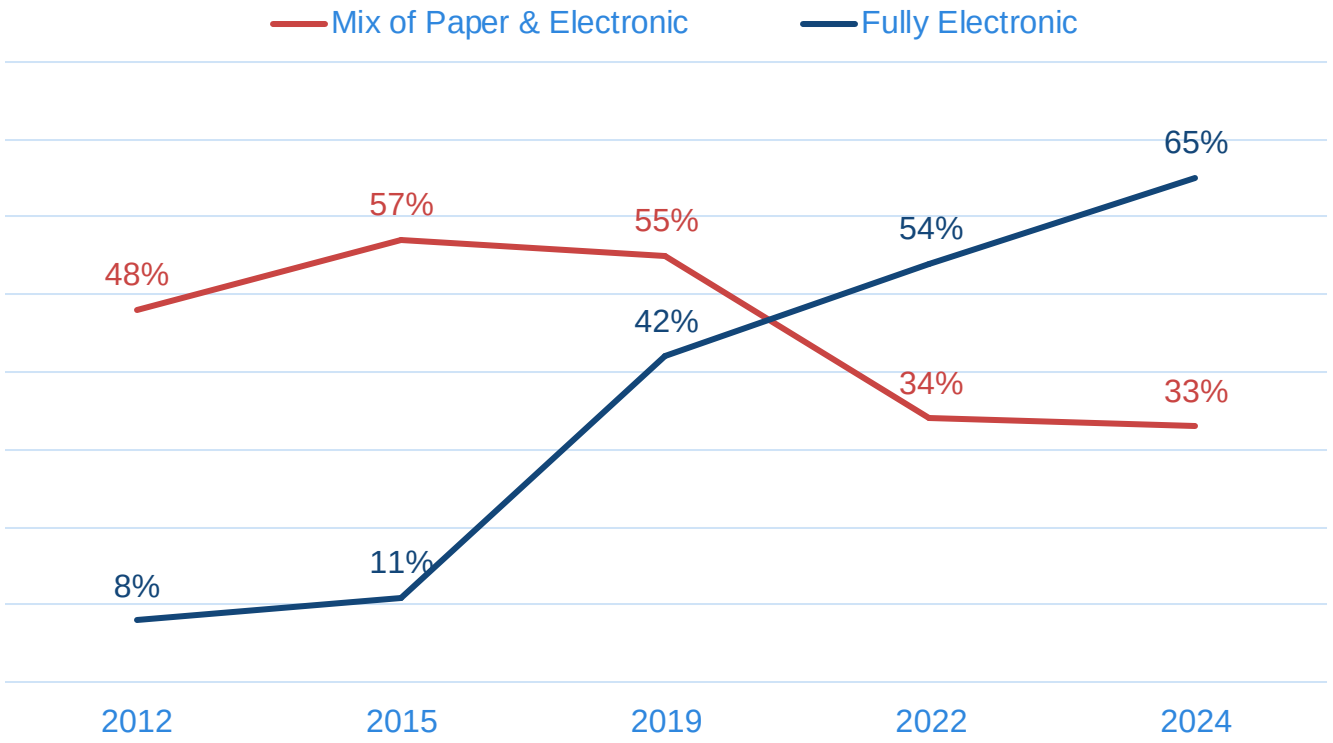
Your Organization Type		
Sponsor	164	51%
CRO	77	24%
Consultant	42	13%
Vendor	21	7%
Research Site/Institution	18	6%
Regulatory Agency/Health Authority	1	<1%

When did you first become aware of the TMF RM?		
4-10 years ago	174	54%
10 or more years ago	92	28%
1-3 years ago	49	15%
Within the past year	8	2%

YES, my organization uses the TMF RM



My organization's TMFs/ISFs are …

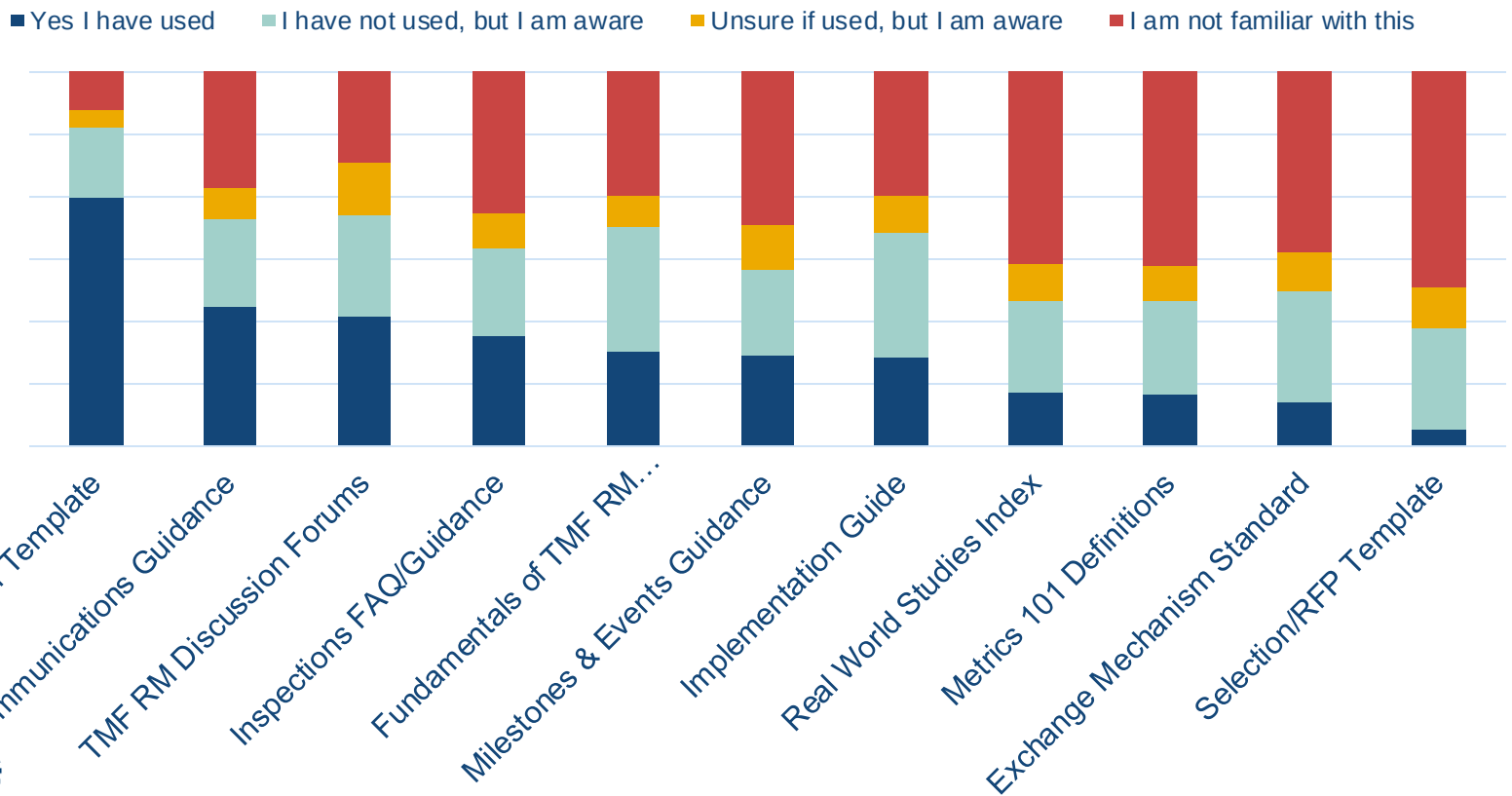


TMF/ISF Inspection Experiences* (within past 2 years)

- 48% have had an **on-premise** inspection
- 41% have had a **remote** inspection
  - 10% from an agency other than FDA, EMA, MHRA, PMDA
- The most common inspection findings received:
  - **65% Completeness**
  - **61% Timeliness (i.e., non contemporaneous)**
  - 44% CRO / Site Oversight

* Only Sponsors, CROs, and Research Institutions were able to respond to these questions

Within the past 18 months, have you or your organization used any of these TMF RM resources?



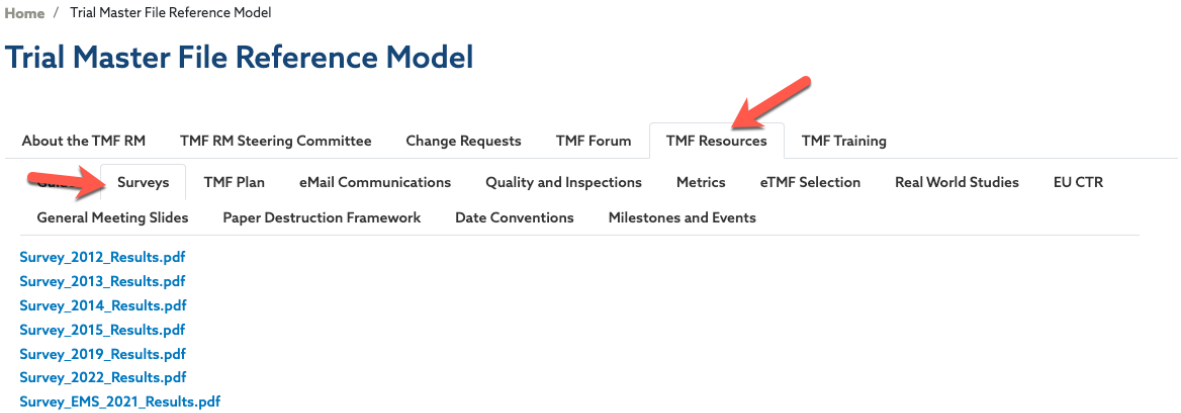
In which ways could the CDISC TMF Reference Model be MOST improved?

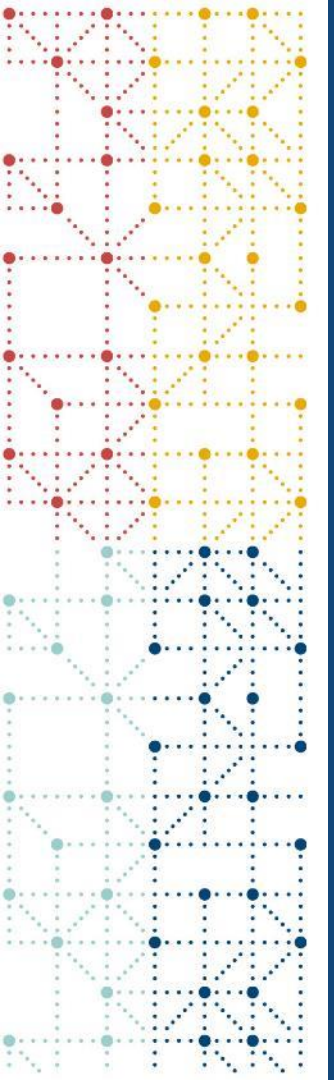
	Examples (NOT exhaustive):
Simplification	“There are too many artifacts and sub-artifacts.”
Flexibility	“Address evolving regulatory requirements and emerging technologies like wearables and eCOA/ePRO.”
Efficiency	“Provide more document examples and templates.”
Integration	“Connect the TMF Reference Model with eDMS, FHIR, and other relevant standards.”
Functionality	“Risk-based approach: Assign risk levels to artifacts to focus quality review efforts.”

Full Survey Results coming soon!

- October 23, Session 4E at the TMF US Interchange

- Late October – added to the CDISC TMF RM website, Resources page





The Road to Version 4

Full Presentation at TMF Interchange!

TMF Reference Model v4 Initiative

Overview

The last major version of the TMF RM (version 3.0) was released in 2015. Since then, there have been 3 minor versions of the model. More importantly there have been user and regulatory influences that make the refresh of the TMF RM necessary to remain current and usable by various stakeholders in the biopharmaceutical industry.

Goals

- ✓ Optimize for digital TMF
- ✓ Align with industry needs & relevancy for at least 5 years
- ✓ Align with ICH and country published regulatory requirements and guidance
- ✓ Use consistent terminology and definitions that are aligned with CDISC
- ✓ Meet the needs of the current generic TMF management process and eTMF system components including the expansion of sub-artifacts
- ✓ Has value added operational and indexing metadata by adding, removing, or updating columns and their entries which are associated with **sub-artifacts** of the TMF RM

Meet the TMF RM v4 Project Management Team!

Donna Dorozinsky
Founder and CEO of Just in Time GCP

Gillian Gittens
Director, eClinical Strategy & Solutions at TransPerfect

Lisa Mulcahy
Owner and Principal Consultant of Mulcahy Consulting

Paul Fenton
Founder and CEO of Montrium

Kathleen Mellet
Project Manager at Just in Time GCP

High Level 2024 Timeline

TMF General Meeting

September 2024

Project announcement to CDISC community

Jira Guidance Release

October 2024

The CCB and CDISC IT team will release training guidance to educate CDISC community on how to submit change requests

Change Submission Opens

October 2024

Following training, community can begin submitting requests

US CDISC Interchange

October 2024

TMF v4 team will provide status updates and energize the community to submit change requests

Evaluation of Change Submissions

October-December 2024

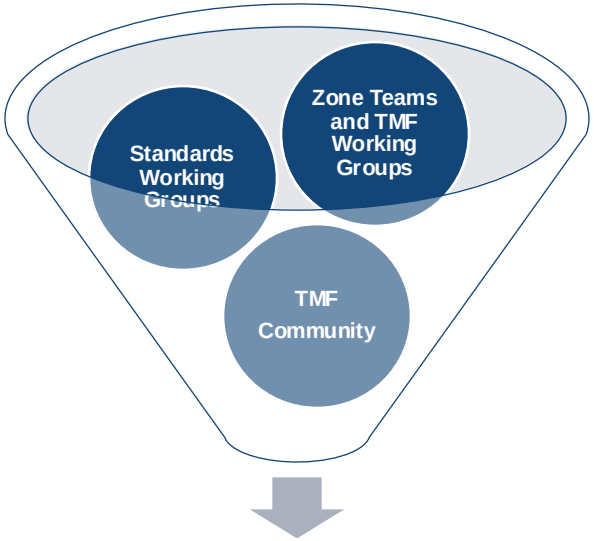
The Triage Committee will begin to evaluate change requests and triage to zone teams.

Zone Teams Begin Work

Q1 2025

Zone Teams will begin reviewing the change requests.

Change Request Submissions



Considerations for v4

Key Content Contributors

To ensure that v4 is aligned with industry needs and properly optimized for digital data flow, multiple groups will submit change requests for consideration.

CDISC Community: Submit change requests and provide feedback throughout the process. Complete a review of v4 draft once is it in a final state.

Zone Teams and TMF Working Groups: Provide feedback on zone changes and propose updates. Participate actively and attend meetings to meet project timelines and objectives.

Standards Working Groups: Support the development of metadata and digital optimization.

Key Content Reviewers

Due to the large number of change requests, we are introducing a new team to support with content reviews and change request triaging.

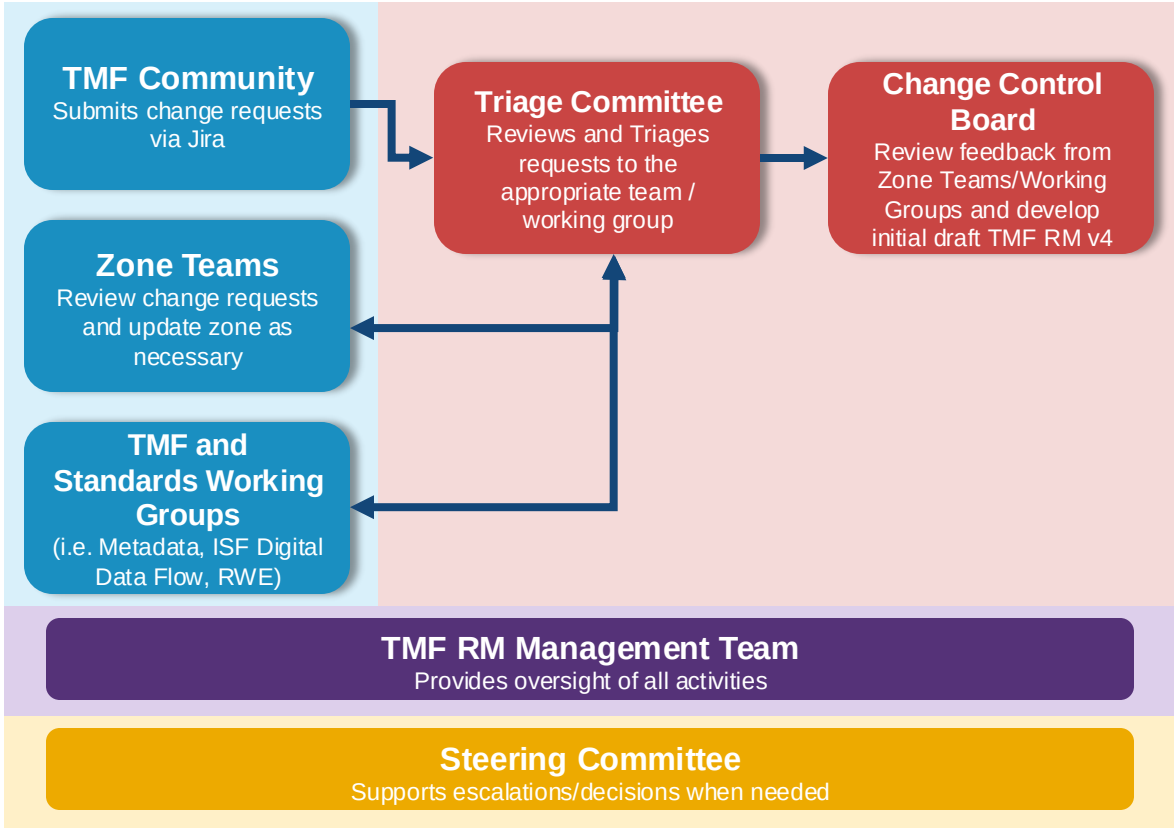
Triage Committee (New Team): Combination of TMF and Standards SMEs that will review all public requests, determine appropriateness of request, and ensure consistency across zones.

Change Control Board: Following Triage committee reviews and zone team feedback, the CCB will conduct a review of the proposed changes and will develop draft v1.

Submission and Review of Change Requests

The process flow provides a high-level overview for the following project groups:

- Key Content Contributors
- Key Content Reviewers
- Management & Oversight
- Escalations



How to get involved

We are actively seeking Zone Lead and Zone Team volunteers to support the refresh!

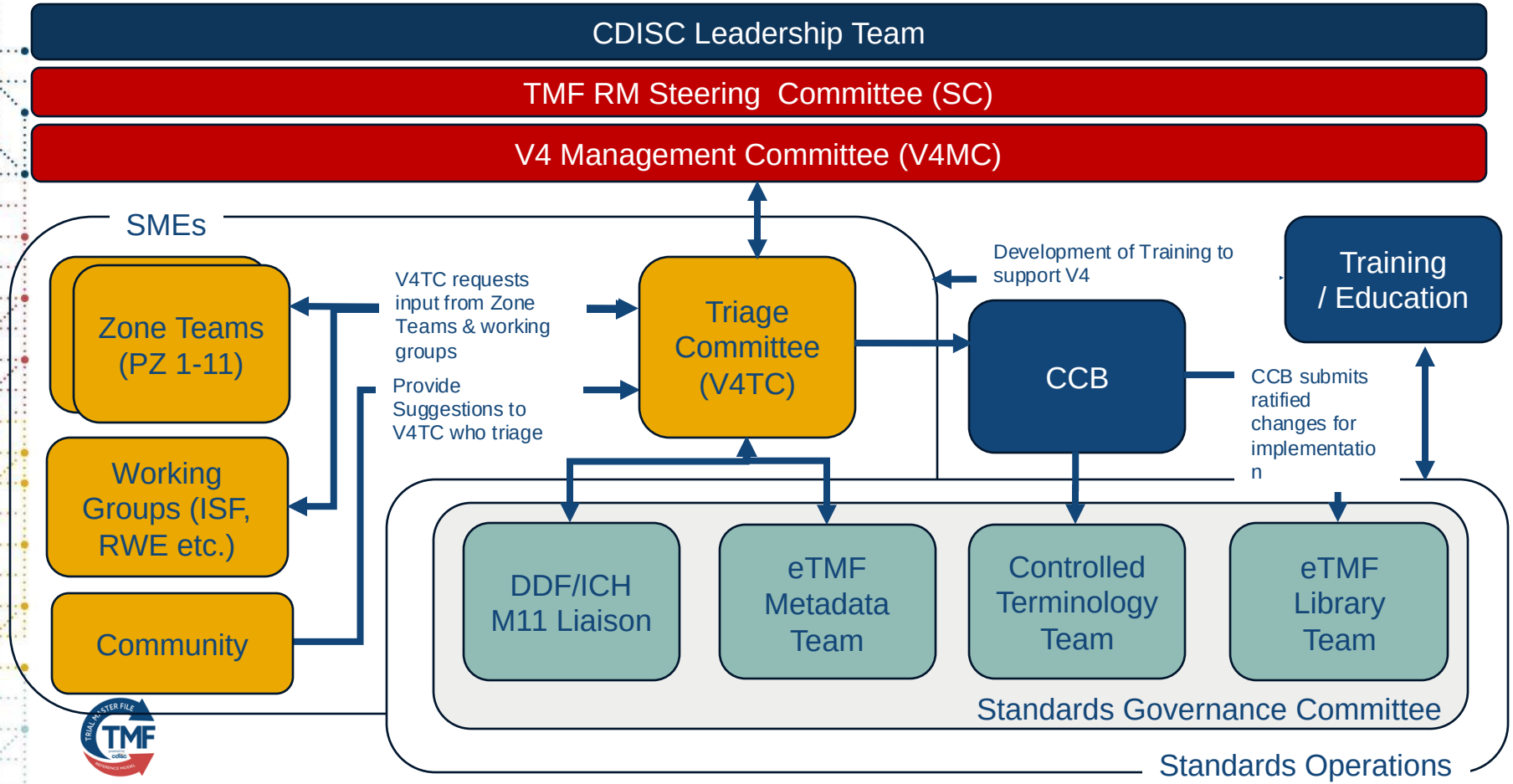
Click the link below or scan the QR code to see which zones still need members and get involved!

Volunteer for a Zone Team or Zone Lead Role

TMF Reference Model Zone Teams - Call for Volunteers

As a reminder Zone Team support will begin in **Q1 2025**

V4 (TMF RM) org chart



TMF Standards Operations Group

- Four teams to support the development and management of the TMF RM standard
- Will collaborate closely with the triage committee and CCB to integrate changes over time
- Composed of four teams:
  - Digital Data Flow / ICH M11 Team
  - Controlled Terminology Team
  - TMF Metadata Standard Team
  - Library Team

Digital Data Flow (DDF) / ICH M11 team

- Will collaborate with the DDF team to ensure alignment with the TMF RM
- Initially will focus on making sure metadata nomenclature is aligned with the USDM model
- A member of this team will sit on the Triage Committee
- This team will collaborate very closely with the Metadata Team
- As M11 evolves, they will also start to map the TMF RM to M11 to allow navigation of the TMF by digital protocol and also to identify protocol parameters which could help us better predict what to expect in the TMF
- The primary deliverable from this team will be a mapping of the TMF RM to ICH M11

Controlled Terminology Team

- Has already encoded all artifacts to standard CDISC terms
- Will continue to help codify all additional components such as sub-artifacts, metadata etc. as V4 evolves

TMF Metadata Standard Team

- Will generate a baseline set of indexing and operational metadata for the Triage Committee
- This set will be generated from existing adhoc standards including from vendors
- We will also align to USDM where possible
- A matrix will be produced which associates metadata to sub-artifacts, artifacts, sections and process zones (to allow for inheritance)
- A member of this team will sit on the Triage Committee
- Deliverables will include a formal standard specification, the matrix and a logical model

Library team

- Initial responsibility is to establish clear requirements on how we want to store and access the TMF RM
- Once we have the requirements CDISC will be able to identify what is the best solution for the ongoing housing and management of the TMF RM
- We need to store V4 in more of a database like system
- This team will also be responsible for the continuous updating and publishing of changes to the model
- They will collaborate primarily with the CCB

Using M11 and DDF to facilitate completeness and long-term retention

TMF RM Standard Structure, terms and metadata

CDISC Library

Many of these systems contain data and artifacts that are TMF relevant or that could drive TMF completeness

Key parameters about the clinical trial drives which artifacts we should expect i.e. Interim Analysis, randomization etc.

APIs

Clinical Systems

DDF
USDM
SDR

M11 Digital Protocol

Parameters

Artifacts

eTMF

Digital Dataflow leverages the Digital protocol to distribute protocol information to all downstream systems using Digital Data Flow and the Unified Study Definition Model (USDM) standard

By mapping the TMF RM artifacts to M11 we can navigate the TMF by digital protocol

+ Completeness
+ Timeliness
+ Quality

CDISC CT

TMF Specific
Metadata
Artifacts
Events / Milestones

EMS

Controlled Terminology across all standards facilitates understanding of terms and identification of artifacts

Questions?

Thank You!!!

https://www.cdisc.org/events/webinar/tmf-reference-model-general-meeting-q3