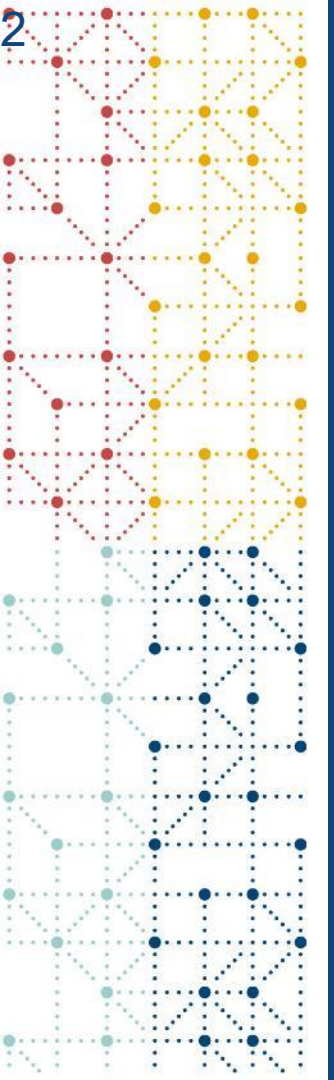
The TMF Reference Model General Meeting June 2025

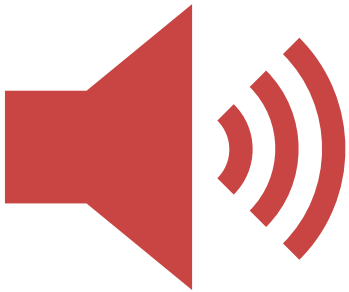
Presenters:

- Paul (Fenton) Carter, CEO, Montrium; Chair, TMF Reference Model Steering Committee
- Karen Roy, Consultant, CDISC; Outgoing Chair, TMF Reference Model Steering Committee
- Jamie Toth, Sr. Director, Global Trial Master File Management & Records, BeOne Medicines; Incoming Chair Elect, TMF Reference Model Steering Committee
- Joanne Malia, Sr. Director, Development Records Mgmt, Regeneron, TMF RM SC Member
- Dawn Niccum, EVP, QA & Compliance, inSeption Group, TMF RM SC Member
- Donna Dorozinsky, CEO, Just in Time, GCP, TMF Reference Model Steering Committee Member
- Lisa Mulcahy, Mulcahy Consulting LLC, TMF Reference Model Steering Committee Member
- Gillian Gittens, Director, eClinical Strategy & Solutions; TransPerfect Lifesciences, TMF RM SC Member



Housekeeping

Housekeeping

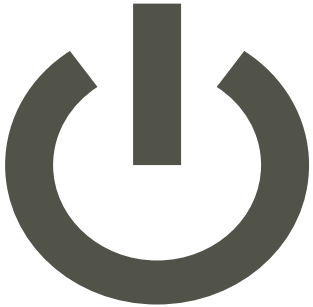


You will remain on **mute**

Housekeeping

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

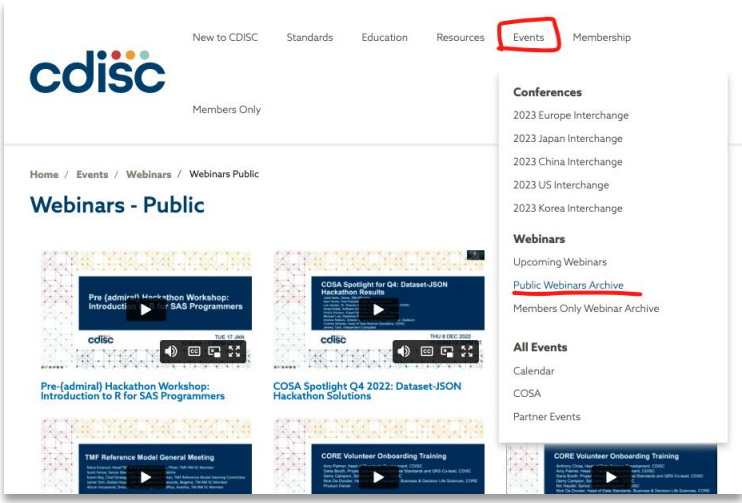
Housekeeping



Audio Issues?

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

Housekeeping

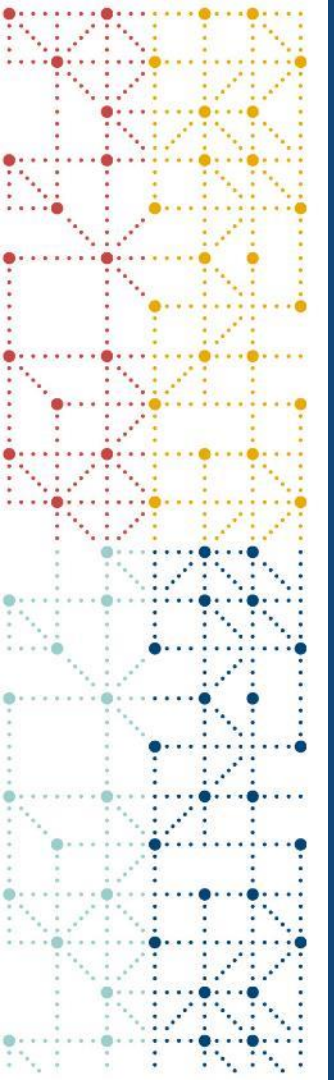


Webinar Recording

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

Agenda

- Announcements
- TMF v4 and Triage Committee Updates
- TMF Roadmap
- Events Update
- CDISC TMF Geneva Recap
- ISF Initiative
- Risk Initiative
- Training Update
- Q&A



Announcements

Paul (Fenton) Carter, CEO, Montrium; Chair, TMF Reference Model Steering Committee

New Steering Committee Members

Bryan Souder
Senior Director, TMF Head
Merck & Co., Inc.

Liz Farrell
Director, Compliance and TMF Oversight
Agios Pharmaceuticals

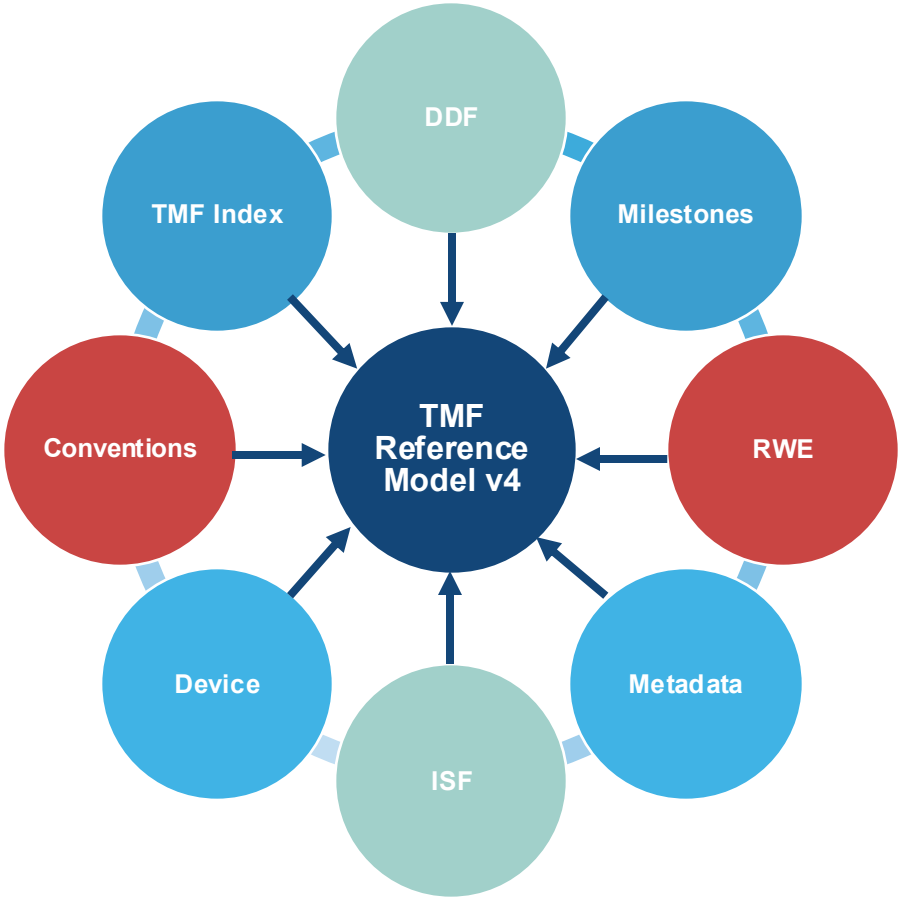
Richard Shore
Managing Consultant Eraneos UK Ltd

TMF v4 & Triage Committee Updates

Donna Dorozinsky, CEO, Just in Time, GCP, TMF Reference Model Steering Committee Member
Lisa Mulcahy, Mulcahy Consulting, TMF Reference Model Steering Committee Member

A vision for the Future:

TMF Reference Model v4



Goals of the TMF Reference Model v4 Initiative

- ✓ 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
- ✓ Broaden engagement across industry and provide a platform for knowledge transfer to prepare the next generation to continue the standard

Not just about refreshing the Reference Model, but about Refreshing the Community!

Where Are We Today?

V4 Kick-off
Sept 2024

Community Feedback Sept through March

Working Groups (Vendor, CSV, ICH E6 R3, Metadata, ISF, Device, RWE,
Oct 2024

Triage Committee
Nov 2024

Zone Team Review
June 2025

Key Operational Decisions Endorsed by the SC

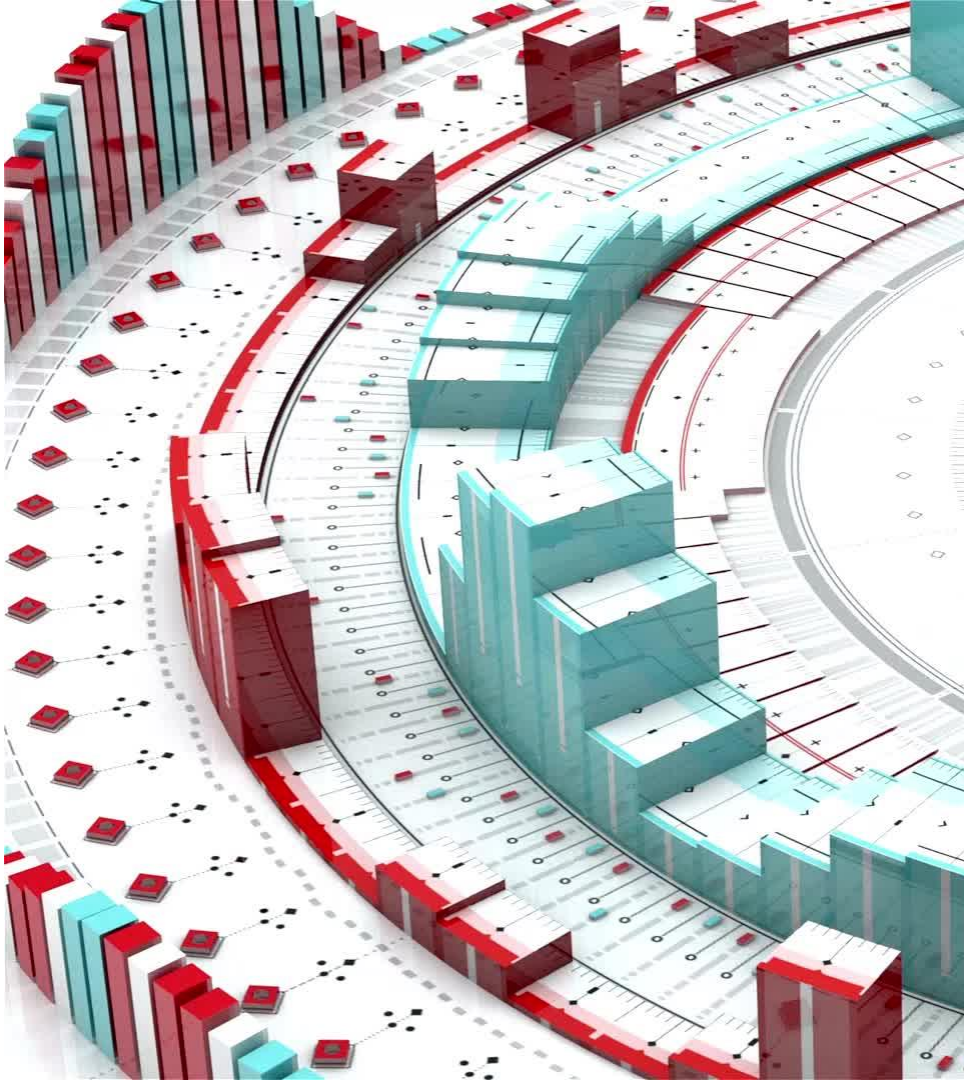
Endorsements to Date

Building on What's Strong

Will continue to present in MSExcel Format

Sub-artifacts will become part of the standard, but we are giving them a new name

- Artifact becomes **Record Group**
- Sub-artifact becomes **Record Type**



UID

- Each **Record Type** will have a unique ID that defines its type and location
- If a **Record Type** repeats across zones, each **Record Type** will have a UID for that zone (i.e. Communications)
- As **Record Types** are added the next available number is assigned
- If a **record type** is removed, that number is not reused
- If a location of a **Record Type** is moved, the UID stays the same and moves with the **Record Type** to the new location
- With V4, the UID will change from 3 digits to 5 digits and will be assigned to **Record Types** level, not Record Groups.
    - Leverage existing UIDs to create a 5 digit code with the **Record Type**, with the provision that if you move a **Record Type** to another record group, the number stays with it. The intent is to make mapping a bit easier from V3.3 to V4.
    - If an organization wishes to add a custom **Record Type** that does not exist in V4, they will use 9 as the first number. This will denote that it is a **Record Type** that is unique to that organization. Custom Artifacts will be 90000-99999

Example

- Currently in V3.3
  - The artifact TMF Plan is UID #260 with the following sub-artifacts associated with it
    - Trial Master File Plan
    - Evidence of Quality Review
    - Request to Lock TMF
    - Trial Master File Index
    - Trial Master File Report
  - UID Numbering for artifacts in V3.3 goes as high as 259
- V4
  - **Record Groups** will no longer have UID numbers; UIDs will be at the **Record Type** level.
    - Trial Master File Plan - #00001 (Keeps the original UID from V3.3 making it 5 digits)
    - Evidence of Quality Review #00260
    - Request to Lock TMF #00261
    - Trial Master File Index #00262
    - Trial Master File Report #00263
- Rules for assigning UID will be established to guide industry and published in the Implementation Guide
- This has been fully vetted and agreed to by the Vendor Working Group.

System – 01.01.01

Retain current numbering for record group, but do not create numbers for the record types. Adding a new level of numbering creates challenges for change management downstream. While we do not intend to get rid of numbering, as we move more towards a digital standard, system numbering becomes less critical. In some ways the numbering system is duplicative of the UID

We recognize that we will need a master tracking document that maps where we have changed a system number with the release of V4.

Product Level Records

V4 will be comprised of **Trial, Country, & Site records**

Program level records will be managed by each vendor individually but will not be part of V4.

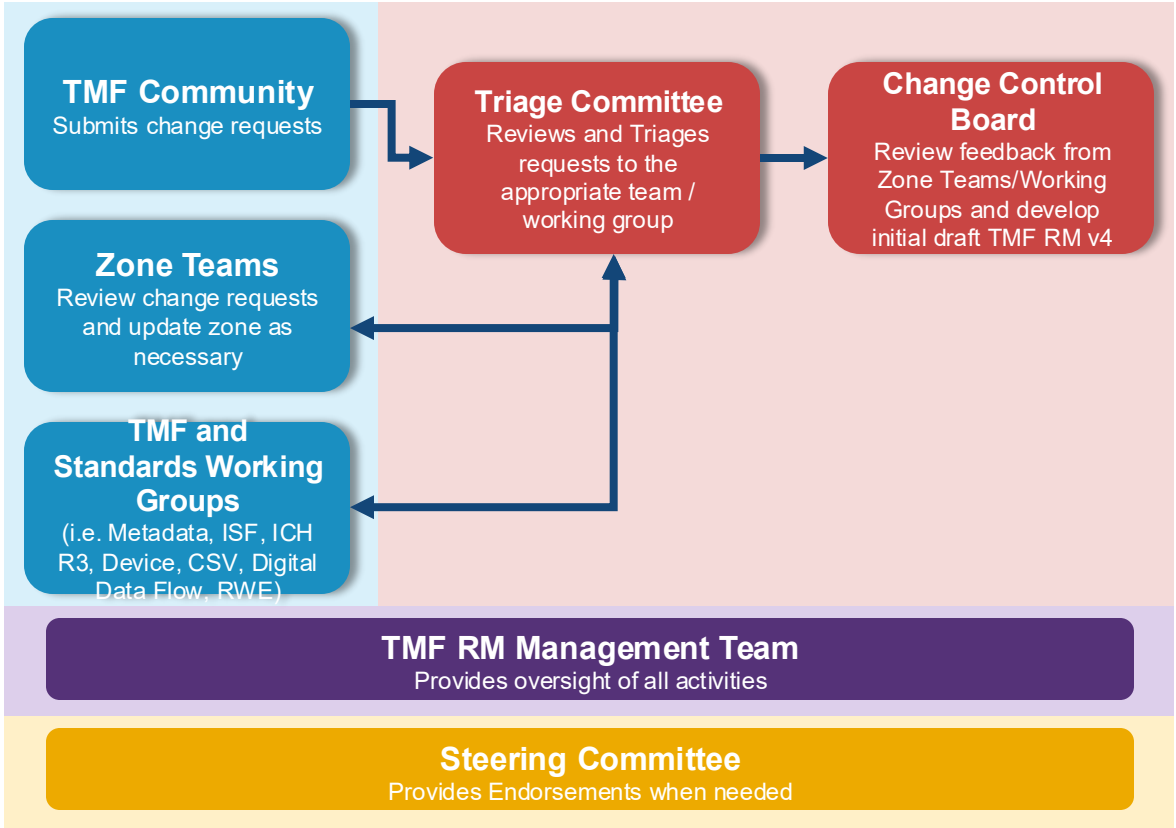
Next Steps

- Expanding our Working Groups (Computer Systems, ICH E6 R3, EU CTR, Devices)
- Beginning to send changes to the Zone Teams for consideration
- Vendors are fully informed of decisions to date
- V4 Management Committee is building additional conventions that will drive further updates based on impact of incorporating Record Types into the Standard
- Beginning conversations with regulators.

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



Zone Triage Committee Member & Zone Team Lead - A Partnership During Reviews for TMF RM V4

TMF RM SC

TMF RM V4 MT

Triage Committee

Zone Triage Committee Members

Zone Team Leads

Partnership

*Input Waves:
Community, Workgroups: EUCTR, ICH GCP R3, CSV, Metadata, Device, ISFv2, and RWEv2 … then Community & Public Reviews

Zone Team Lead Receives Triaged Input* to Consider from Zone Triage Committee Member

Zone Team Lead Coordinates and Leads Zone Team Reviews

Zone Team Lead Captures Feedback on Worksheet

Zone Team Lead Prepares Draft of Zone Record Groups and Record Types for CCB

Zone Triage Committee Member
1) Support Project Updates to Zone Teams 2) Filters Up Questions to Triage Committee and TMF RM V4 MT. 3) Facilitates Cross Zone Consistency and Alignment

Current Status and Next Steps

Current Status:

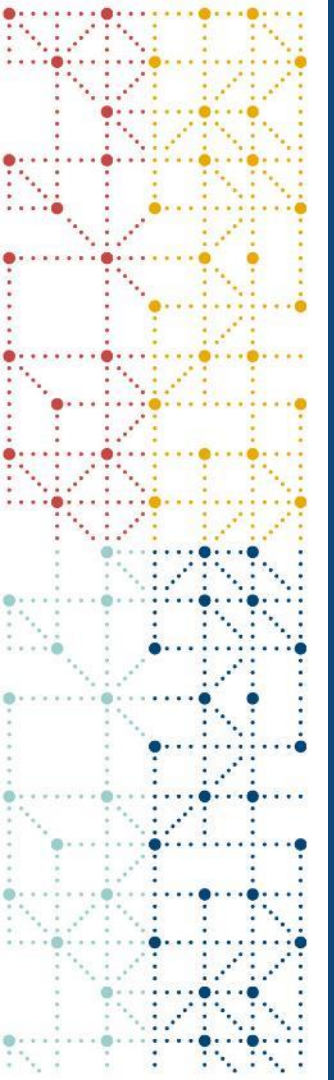
•Community Feedback review by Triage Committee is underway

•Preparation of worksheets for Zone Team Review will follow TC review

Next Steps:

- Access for Zone Team Leads (ZTL) to SharePoint where the worksheets stored will soon start – confirmation of access will be requested
- Conventions for Changes and Managing Feedback
  - Additional on-boarding regarding these conventions will be given.
  - Instructions on how to capture the decisions on feedback and other changes on the Zone-specific worksheet will be created to ensure as much consistency as possible.
- Meeting with TC and ZTLs to kick-off review stage

  Planning of meeting date(s) to commence



TMF Roadmap

Paul (Fenton) Carter, CEO, Montrium; Chair, TMF Reference Model Steering Committee

A Vision for the Future

- Digital-First
- Harmonized
- Governed Standard
- Community-Driven
- Interoperable and Integrated
- Data and Process-Driven
- Regulatory Recognition

CDISC TMF RM Roadmap 2025-2028

	2025		2026		2027		2028	
	H1	*H2*	*H1*	*H2*	*H1*	*H2*	*H1*	*H2*
Planned Versions of CDISC TMF RM Standard					*v4*			*v4.1*
Core Standard Development								
Review and formalize Sub-artifacts into Record Types								
Review and consolidate Artifacts into Record Groups								
Align with ICH E6 R3 Appendix C Essential Records								
Create / Update Controlled Terminology for all record types								
Digital TMF Metadata Standard / Interoperability								
Enhance and expand digital TMF metadata standard				R1				R2
Align metadata standard with USDM				R1				
Create and Update Controlled Terminology for all metadata/value lists								
Development of / or Alignment to existing Audit Trail Standard								
Auxiliary Standards / Mappings								
Map TMF RM Record Types to ICH M11								
Investigator Site File RM	R1			R2				
Real World Evidence RM			R2					
Medical Device RM				R1				
Cross Referencing of CSV Records								
TMF RM Standard Management Tools								
Develop requirements for database type tool to manage standard								
Implementation of tool to manage TMF RM & migrate V4								
Development of APIs to allow querying of TMF RM Standard								
Update TMF Reference Model Implementation Guide (TMFIG)								
Training and Community Engagement								
Training Activities								
Community Engagement Activities								
Other tools and frameworks								
Maintenance of Risk Based Approach Framework / Tools								
Update and maintenance of standard conventions including date conventions, metrics conventions etc.								
Update TMF Plan Template								
Engagement with the regulators								
Regular touchpoint meetings with regulators to inform them of progress and new releases								

Core Standard Development

RECORD TYPES

Review and formalize sub-artifacts into Record Types

ARTIFACTS

Review and Consolidate Artifacts into Record Groups

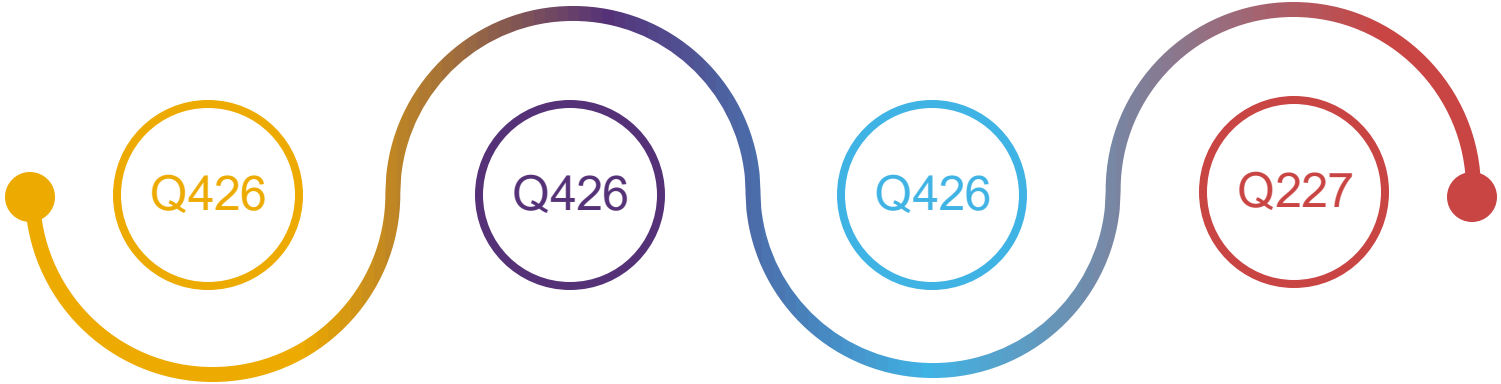
ICH E6 R3

Align with ICH E6 R3 Appendix C Essential Records

CONTROLLED TERMINOLOGY

Create / Update Controlled Terminology for all record types

Digital TMF Metadata Standard / Interoperability



METADATA R1

Enhance and expand digital TMF metadata standard

USDM

Align metadata standard with USDM

CONTROLLED TERMINOLOGY

Create and Update Controlled Terminology for all metadata/value lists

AUDIT TRAIL

Development of / or Alignment to existing Audit Trail Standard

Ancillary Standards and Mappings

ICH M11

Map TMF RM Record Types to ICH M11

ISF RM R2

Investigator Site File RM second revision which aligns with v4

RWE RM R2

Real World Evidence RM second revision which aligns with v4

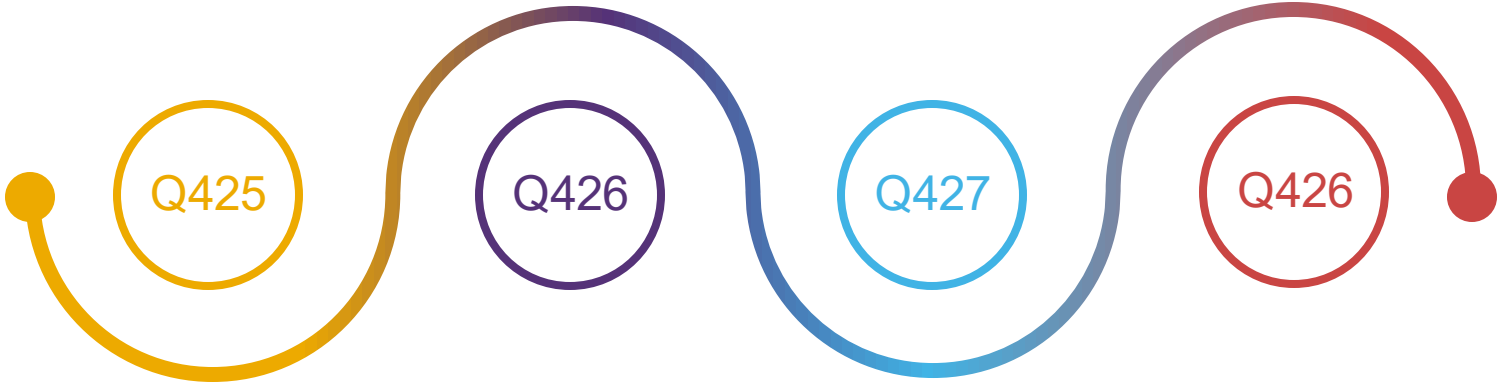
MEDICAL DEVICE RM R1

Creation of a specific RM for Medical Device

CSV

Cross referencing of CSV records for trial relevant systems both trial specific and enterprise aspects

TMF RM Standard Management Tools



REQUIREMENTS

Develop requirements for database type tool to manage standard

TOOL DEV

Implementation of tool to manage TMF RM & migrate V4

API

Development of APIs to allow querying of TMF RM Standard

TMFIG

Update TMF Reference Model Implementation Guide (TMFIG)

Training, guidance and frameworks

TRAINING PROGRAM

Continued development of TMF training courses at all levels

RISK FRAMEWORK

Maintenance and Evolution of Risk Based Approach Framework / Tools

STANDARD CONVENTIONS

Update and maintenance of standard conventions including date conventions, metrics conventions etc.

TMF PLAN

Update TMF Plan Template to better align with digital TMF concepts and ICH E6 R3

REGULATOR ENGAGEMENT

Regular touchpoint meetings with regulators to inform them of progress and new releases

Events Update

Karen Roy, Consultant, CDISC; Outgoing Chair, TMF Reference Model Steering Committee

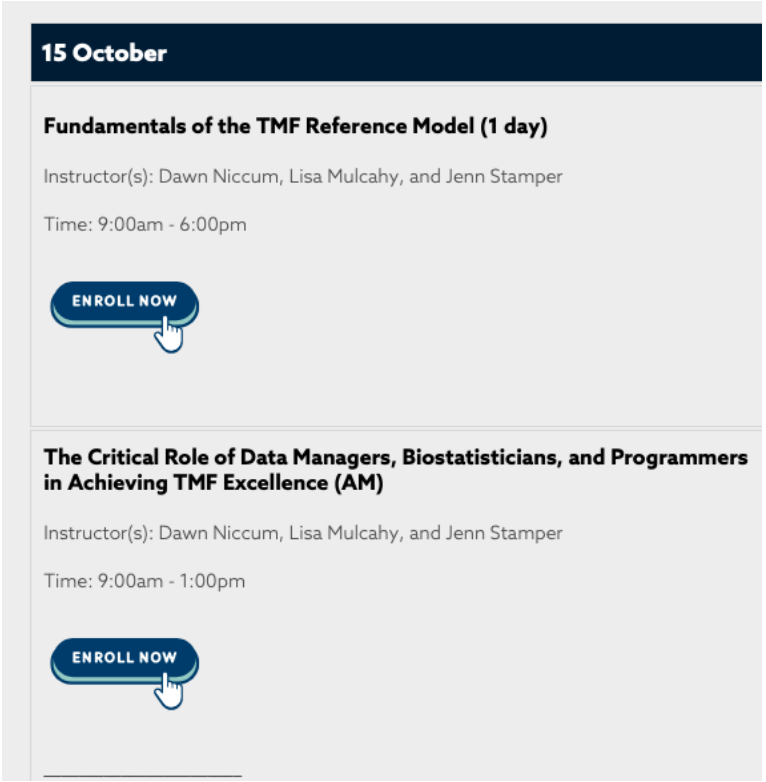
Upcoming Events in 2025!

2025 CDISC + TMF US Interchange

- 48 Abstracts received
- TMF program in development

Registration is now open! Scan the QR code to register or visit the CDISC Website

Attend TMF Training in Nashville



Sponsor or Exhibit in Nashville

Sponsors

Ruby

Just in Time GCP

Tote Bag Sponsor

Sycamore Informatics

SPA PROTOCOL | MDR METADATA | CDR DATA | SCE ANALYSIS

Exhibitors

Just in Time GCP

CONNECT LIFE SCIENCES

INTEGO CLINICAL

Arkivum

ZAVIATO

TATA CONSULTANCY SERVICES

EPISTA LIFE SCIENCE

CLYMB CLINICAL

SGS

CERTARA

Upcoming CDISC Days

KOREA CDISC DAY
All the Insights, All the Impact, All in One Day!

Korea CDISC Day | 24 June 2025
June 2025

Sponsorships

INDIA CDISC DAY
All the Insights, All the Impact, All in One Day!

India CDISC Day | 19 July 2025
July 2025

Program | Sponsorships

CHINA CDISC DAY
All the Insights, All the Impact, All in One Day!

China CDISC Day | 29 August 2025
August 2025

Sponsorships

Other Events

What	When	Where
Montrium TMF Week	09-Jun to 13-Jun-2025	Virtual
Arkivum ArkFest	15-Jul to 17-Jul-2025	Virtual
Fierce Biotech Week	07-Oct to 09-2025	Boston, MA, USA
RQA Conference	05-Nov to 07-Nov-2025	Belfast, Ireland
HSRAA Bi-Annual Conference	March 2026 TBD	Amsterdam, Netherlands
AGxPE Bi-Annual Conference	April 2026 TBD	TBD, USA

CDISC TMF Geneva Recap

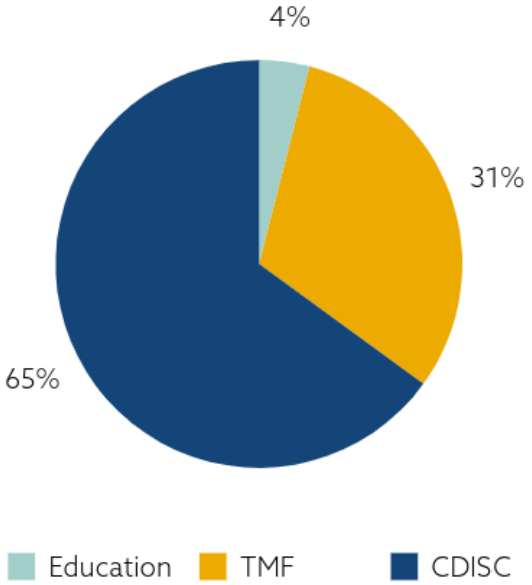
Gillian Gittens, Director, eClinical Strategy & Solutions; TransPerfect Lifesciences, TMF SC Member

TMF Tracks and Themes:

- ICH E6 R3
- Technology and AI
- Culture and Engagement
- Risk Based Approaches
- Fundamentals
- Interoperability
- Management
- Partnerships
- The Future

Attendees:

- Over 400 registrants for whole Interchange
- 31% for TMF Tracks



Your TMF RM Steering Committee (Most of them!)

"The Trial Master File is the Oracle – it holds the answers, but only if you know how to read them"

ISF Initiative

Jamie Toth, Sr. Director, Global Trial Master File Management & Records, BeOne Medicines; TMF RM SC Member and Incoming Chair Elect

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.

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:

- **Evaluation**: Review of existing ISF structures
- **Standards**: Setting standards
- **Proofing**: Review of deliverables
- **Outreach**: Presentations, publications, and white papers
- **Training**: Training the industry on ISF RM

Feedback Received in Geneva – May 2025

- *The site is responsible for their documentation, but they typically follow the sponsor's guidelines.* ***It's important to ensure that the investigator is on board with following a new/changed ISF model.***

- *Standards will facilitate the work of inspectors and auditors, but* ***it's crucial to remember that these standards should also assist monitors who are at the site regularly*** *and often lack the support that inspectors receive during their visits.*

Timeline

Launch - February 2024

Call for volunteers from sites, sponsors, CROs & vendors

Kickoff – April 2024

Initiative kicked off with ~46 volunteers; subteams (5) formed

STAGE 1

Subteam activity – April–August 2024

Evaluation of existing ISF structures completed; first draft of ISF RM developed

September – November 2024

Standards team reviewed draft and existing standards to ensure alignment; second draft of ISF RM

STAGE 2

Proofing – November–December 2024

Proofing team reviewed second draft of ISF RM; finalized draft is ready for review

STAGE 3

CDISC Review – January-June 2025

ISF RM provided feedback to TMF RM V4

ISF RM is ready for 1st stage of CDISC review with TMF RM SC

Review ~97 comments from CDISC TMF RM SC/ Follow ups related to comments.

Targeted Review with Site Stakeholders

Resubmit for 2nd stage of CDISC review with TMF RM SC

Meet with CCB and allow review.

STAGE 4

Public launch – Target: July 2025

Training to begin after public launch/comments

STAGE 5

We are here!

Outreach is ongoing with presentations & updates at various conferences, webinars, etc.

ISF RM Release 1.0

A	D	G	J	K	L
ISF Zone Combined #/Name	ISF Section Combined #/Name	ISF Artifact Combined #/Name	ISF SubArtifact Name	TMF Artifact Group	ISF Inclusion
ISF_02_Study Library	ISF_02.02_Trial Team Details	ISF_02.02.01_Trial Team Details	Sponsor/CRO Contact Details Trial Team Details	01.02.01 Trial Team Details	Core
ISF_02_Study Library	ISF_02.03_Product or Device Materials	ISF_02.03.01_Investigator's Brochure	Investigator's Brochure Investigator's Brochure Addendum Investigator's Brochure Extension Investigator's Brochure Summary of Changes Report of Prior Investigations	02.01.01 Investigator's Brochure	Core
ISF_02_Study Library	ISF_02.03_Product or Device Materials	ISF_02.03.02_Marketed Product Material	Marketed Product Material Package Insert Summary of Product Characteristics	02.01.11 Marketed Product Material	Core
ISF_02_Study Library	ISF_02.04_Protocol and Amendments	ISF_02.04.01_Protocol	Protocol	02.01.02 Protocol	Core
ISF_02_Study Library	ISF_02.04_Protocol and Amendments	ISF_02.04.02_Protocol Amendment	Protocol Amendment Protocol Summary of Changes	02.01.04 Protocol Amendment	Core
ISF_02_Study Library	ISF_02.04_Protocol and Amendments	ISF_02.04.03_Protocol Clarification	Protocol Clarification	02.01.04 Protocol Amendment	Recommended
ISF_02_Study Library	ISF_02.04_Protocol and Amendments	ISF_02.04.04_Protocol Synopsis	Protocol Synopsis	02.01.03 Protocol Synopsis	Core
ISF_02_Study Library	ISF_02.05_Investigators Meeting Material	ISF_02.05.01_Investigators Meeting Material	Investigators Meeting Material SIV or KOM Materials Training Materials Training Agenda Training Attendance Sheet Training Minutes Administrative Coordination Report	01.04.03 Investigators Meeting Material	Core

Row Labels	Count of ISF Artifact Combined #/Name
ISF_01_Planning and Procedures	20
ISF_02_Study Library	10
ISF_03_Participant Materials	8
ISF_04_Regulatory Submissions	2
ISF_05_IRB or IEC	6
ISF_06_Other Committees	2
ISF_07_Site Documentation	20
ISF_08_IP or Device Documentation	16
ISF_09_Trial Supply Documentation	3
ISF_10_Testing Facility Documentation	8
ISF_11_Monitoring Logs and Reports	6
ISF_12_Safety Events, Logs, and Reports	4
ISF_13_Study and/or Participant Data and Logs	6
ISF_14_Correspondence and Notes to File	2
Grand Total	**113**

These Zones/Sections are aligned to TMF Ref Model 3.3.1

ISF Release 2.0 will be part of Version 4.0 TMF RM

Ongoing & Future Activities

- After formal CDISC internal review, **public comment** will commence – likely in June/July.
- ***ISF Release 1.0 to launch in 2025***.
  - This version will be in alignment with TMF RM 3.3.1.
- ***Alignment with TMF RM v4.0*** activities will take place; feedback already given.
  - These will go into ISF Release 2.0 and be part of V4.
- **Outreach** is ongoing and will continue throughout the initiative.
- **Training** will be provided upon publication of the final Release1.0 ISF reference model.

Risk Initiative

Joanne Malia, Sr. Director, Development Records Mgmt, Regeneron, TMF RM SC Member

Risk Initiative – White Paper and Tool Released!

- White Paper and Tool released at CDISC Interchange in Geneva
- Minor editing of paper complete (v. 1.1)
- Social media releases will be coming in June
- Training module is going through review – Executive summary coming soon

White Paper

Tool

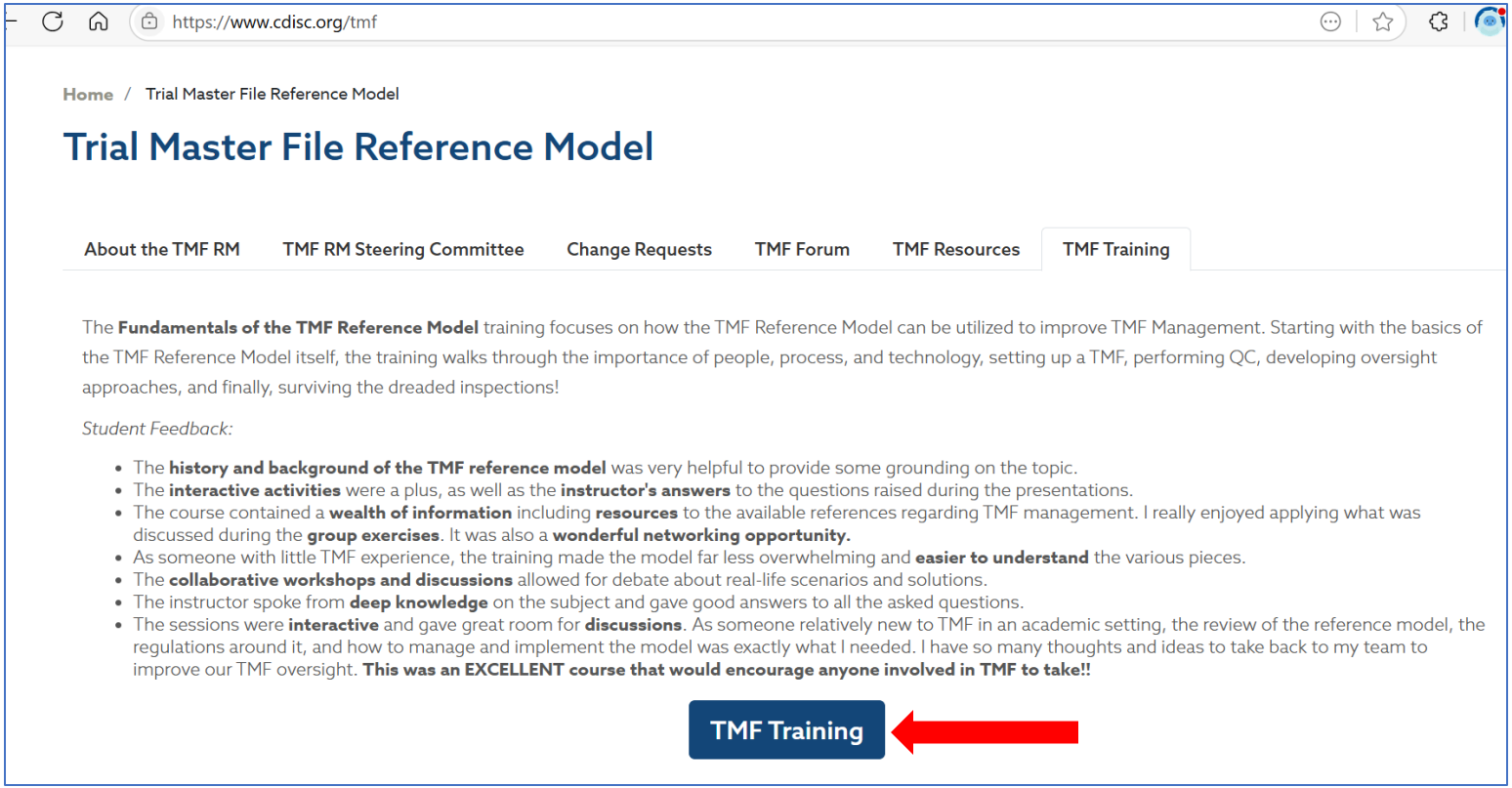
Thank you to the entire team!

Training Update

Lisa Mulcahy, Mulcahy Consulting LLC, TMF Reference Model Steering Committee Member
Dawn Niccum, EVP, QA & Compliance, inSeption Group, TMF RM SC Member

Available TMF-Related Trainings Available Through CDSIC

www.cdisc.org/tmf



Upcoming CDISC TMF-Related Trainings

Fundamentals of the TMF Reference Model

Methods of Delivery: Virtual or Face-to-Face

Virtual: 3 hours per day for 3 days; Face-to-Face: 8 hours

View Course

- Virtual: June 17, 18, and 19, 2025
- Face-to-Face: US CDISC + TMF Interchange October 15, 2025

The Critical Role of Data Managers, Biostatisticians, and Programmers in Achieving TMF Excellence

Methods of Delivery: Virtual or Face-to-Face

Virtual: 4 hours; Face-to-Face: 4 hours

- Virtual: June 24, 2025
- Face-to-Face: US CDISC + TMF Interchange October 15, 2025

TMF Module 1: Introduction to the TMF Reference Model (FREE TRAINING)

Online (self-paced)

On-Demand, Self-Paced Online

- Virtual: on demand

日本語 TMF Module 1: TMF Reference Model の紹介 (FREE)

Online (self-paced)

On-Demand, Self-Paced Online

- Virtual: on demand

Questions?

Thank You!!!