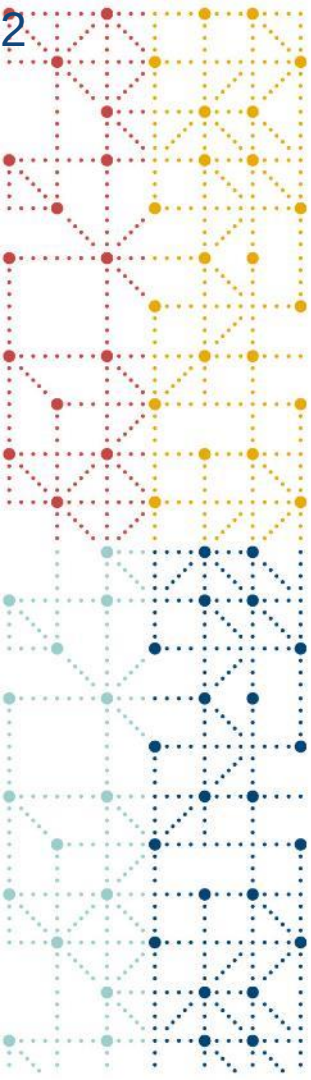
The TMF Reference Model
General Meeting December 2024

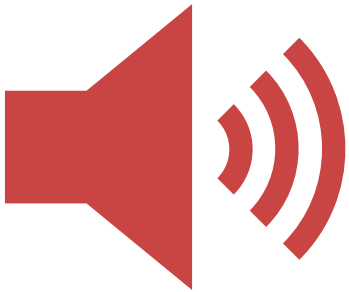
Presenters:

- Karen Roy, Consultant, CDISC; Chair, TMF Reference Model Steering Committee
- Todd Tullis, Director, Product Management, Veeva Vault; TMF Reference Model Steering Committee Member
- 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
- Donna Dorozinsky, CEO, Just in Time, GCP, TMF Reference Model Steering Committee Member
- Paul Fenton, CEO, Montrium; TMF Reference Model Steering Committee Member
- Lisa Mulcahy, Mulcahy Consulting, TMF Reference Model Steering Committee Member
- Gillian Gittens, Director, eClinical Strategy & Solutions; TransPerfect Lifesciences



Housekeeping

Housekeeping

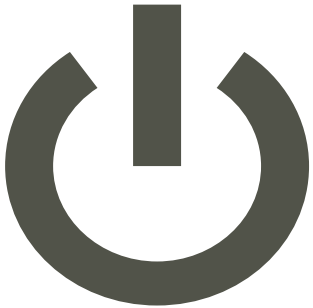


You will remain on **mute**

Housekeeping

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

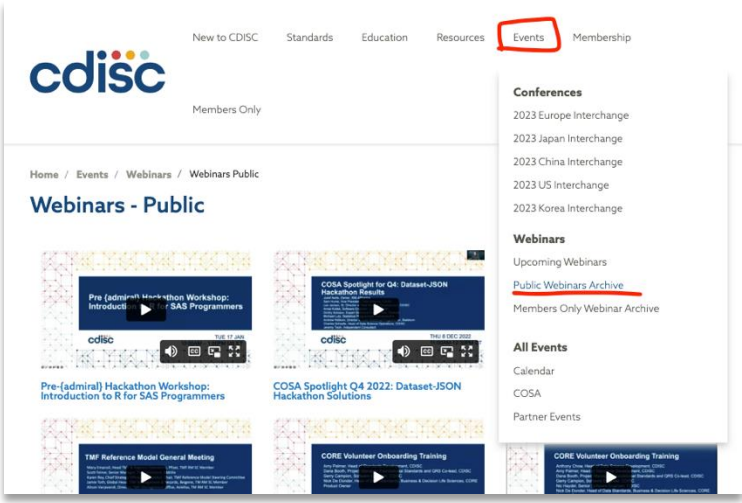
Housekeeping



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

- Moving into 2025
- US Interchange Recap
- Education Committee
- ISF Initiative
- Risk Initiative
- TMF Reference Model v4 Update
- Q&A

Moving into 2025

New Chair of SC: Paul Carter

New Chair Elect of SC: Jamie Toth

Overall Steering Committee Changes

- New Chair from 1st January 2025
- New position: Chair Elect from 1st January 2025
- New position: Past Chair from 1st January 2025
- New position: CDISC project manager – Kathleen Mellet

- Two new places open to election in February 2025
- Review charter to make sure you meet the criteria

  https://www.cdisc.org/sites/default/files/2023-05/TMF-RM-Steering-Committee-Charter-V4.0.pdf

Steering Committee

Thank you to Aaron Grant for all his work on the Steering Committee!

2024 US CDISC + TMF Interchange

Scottsdale, Arizona, USA
23-24 October

Plenary & Keynote

CDISC General Session

TMF General Session

Track A | Track B | Track C | Track D | Track E

350 total attendees
(~37% TMF)

- TMF Essentials
- Risk Based Approaches
- End of Study Challenges
- Audits and Inspections

- The Impact of Regulations
- TMF Management through Metrics
- Partnerships in TMF Management
- The TMF RM becoming a Standard

- Technology & Innovation in TMF Management
- Investigators and Inspectors

Summary/Highlights

Key themes

- CDISC: research convergence with clinical care
- TMF: Reference Model Version 4

- TMF plenary fun with Indiana Jones theme
- Challenges of integrating clinical trial management data with TMF
- Continued progress of Digital Data Flow initiative / ICH M11
- Applications of Artificial Intelligence in TMF
- Introduction of the ISF Reference Model initiative
- FDA perspective and re-organization “Office of Inspections and Investigations”
- *Fun & fright of Waymo self-driving taxis*

2025 CDISC + TMF Europe Interchange

Geneva, Switzerland
14-15 May 2025

https://www.cdisc.org/events/interchange/2025-europe-interchange

2025 CDISC + TMF US Interchange

Nashville, Tennessee
13 – 14 October 2025

Education Committee

TMF Education Highlights

- The Critical Role of Data Managers, Biostatisticians, and Programmers in TMF Excellence – Inaugural Course – 14 attendees – mix of core SMEs and TMF Professionals
  - "This session was a **great opportunity for eTMF managers** to bring their functional area leads to an eTMF session and have in depth discussions."
  - "I found the course **helpful in understanding the TMF reference guide** and getting to know the extent of the coverage. The instructors stressed the importance of continually updating the TMF versus saving it for the end, as well as testing the TMF content and links."
  - "The most helpful part of this training was the **interaction with Data Managers and Statisticians to discuss deliverables** in terms of records required in the eTMF."
  - "One of the most enlightening exercises was the group activity where we **mapped records and data to the TMF reference model** and identified the possible TMF repositories, etc."
- Next course virtual – 28 Jan 2025 0900-1300 EST (1500-1900 CET)

Other Courses

- TMF Module 1: Introduction to the TMF Reference Model (FREE)
- 日本語 TMF Module 1: TMF Reference Model の紹介 (FREE)

- Fundamentals of the TMF Reference Model – Virtual Course on 21-23 Jan 2025 (0900-1200 EST; 1500-1800 CET)

- Upcoming: Introduction to Record Quality Check
  - In-depth, on-demand course
  - Projected to be available by the end of 1Q25

- In Discussion
  - Risk Based TMF Management
  - Advanced TMF Management
  - Investigator Site File Reference Model

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

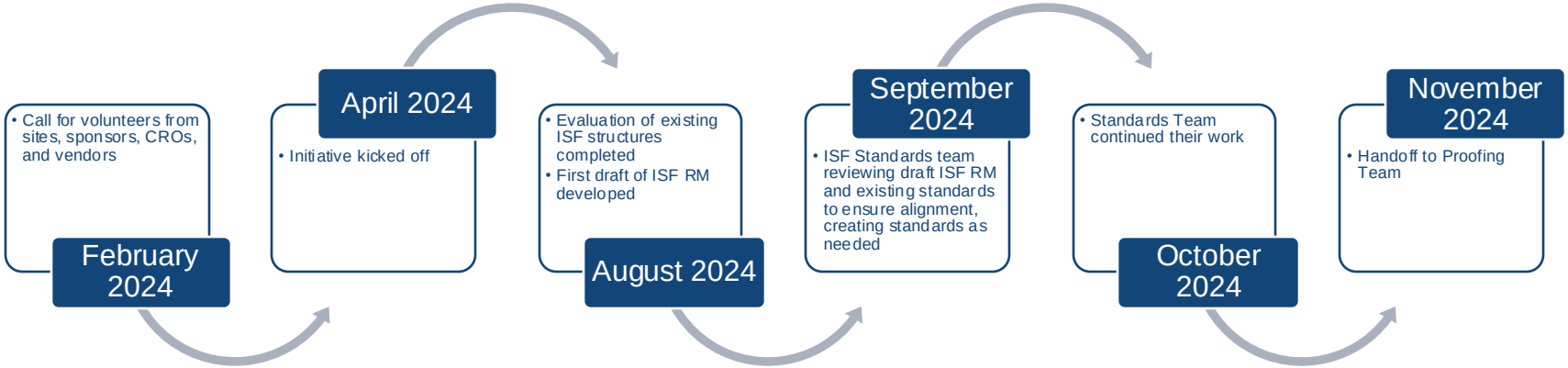
Goal:
To develop an Investigator Site File (ISF) reference model for sites to use that supplements the TMF Reference Model with the intention of standardizing ISF structure, file naming conventions, and how/where site-level essential records are filed.

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



Huge thanks to all on the ISF Working Group! We have accomplished much in a short amount of time!

Facts about an ISF

- 60% of ISF artifacts are sponsor sourced.
- An ISF, unlike a TMF needs to be available for operational purposes, so indexed **months before** the TMF.
- Sites only have one system, the ISF for all study functions operational and inspection readiness. Whereas a sponsor and CROs have +10 operational systems generating completed TMF content, which then subsequently are loaded to their TMF for inspection readiness.

Development of the ISF Structure

The ISF structure has been developed to meet the following objectives, defined based on the learnings during ISF vendor evaluation:

- Delineate ISF responsibilities between sponsor and site.
- Make ISF operation more efficient and of high quality.
- Support ISF inspection readiness, based on regulatory guidance.
- Support site operation throughput a study lifecycle, which means a site centric structure different to the TMF RM structure.
- Can be used by both novel and advanced sites, including local IRB/EC, testing facility or IP distribution center.
- Support both human and automated operation and exchanges.
- Align with existing TMF RM artifact definitions and indexing.
- Inclusive of existing vendor ISF offerings, so that vendors can adopt the ISF standard.

Snapshot of November Draft (not all sections visible/not final) to Show TMF Alignment

There are 9 packages which are time based/phases – **Selection, Activation, Completion, CloseOut**:

1. Planning
2. Study Library
3. IP and Trial Supplies
4. Regulatory, IRB/EC, and Other Review
5. Site Documentation
6. Contracting and Indemnity
7. Testing Facility
8. Monitoring
9. Data Management

Packages and **subpackages** are chronological functional structures, which generally reflects how and when a site will receive ISF content from a sponsor and help operational usage.

The good news: There is only about 3 additional artifacts that are ISF only!

zone_name	section_name	artifact_name	artifact_no	isf_sponsor_sourced	isf_site_sourced	organization_role	person_rol	time_phase	role	package	sub_package
01-Trial Management	01.01-Trial Oversig	01.01.01-Trial Master File Plan	01.01.01	TRUE	FALSE	Sponsor	NULL	2-Activation	1-Sponsor	1-Planning	1.04-TMF and Source Data Plan
02-Central Trial Documents	02.01-Product and	02.01.20-Protocol Clarification	02.01.20	TRUE	FALSE	Sponsor	NULL	3-Completion	1-Sponsor	2-Study Library	2.04-Study Material
02-Central Trial Documents	02.01-Product and	02.01.21-Protocol Summary of Ch	02.01.21	TRUE	FALSE	Sponsor	NULL	3-Completion	1-Sponsor	2-Study Library	2.04-Study Material
02-Central Trial Documents	02.02-Subject Doc	02.02.01-Subject Diary	02.02.01	TRUE	FALSE	Sponsor	NULL	2-Activation	1-Sponsor	2-Study Library	2.05-Subject Material
02-Central Trial Documents	02.04-General	02.04.01-Relevant Communicatio	02.04.01	TRUE	FALSE	Sponsor	NULL	5-Functional	1-Sponsor	2-Study Library	2.09-Relevant Communication
02-Central Trial Documents	02.04-General	02.04.02-Tracking Information	02.04.02	TRUE	FALSE	Sponsor	NULL	5-Functional	1-Sponsor	2-Study Library	2.10-Tracking Documentation
03-Regulatory	03.04-General	03.04.02-Tracking Information	03.04.02	TRUE	FALSE	Sponsor	NULL	5-Functional	1-Sponsor	4-Regulatory, IRB/EC or Other Review	4.09-Tracking Documentation
03-Regulatory	03.04-General	03.04.03-Meeting Material	03.04.03	TRUE	FALSE	Sponsor	NULL	5-Functional	1-Sponsor	4-Regulatory, IRB/EC or Other Review	4.10-Meeting Material
03-Regulatory	03.04-General	03.04.04-Filenote	03.04.04	TRUE	FALSE	Sponsor	NULL	5-Functional	1-Sponsor	4-Regulatory, IRB/EC or Other Review	4.11-Filenote
04-IRB or IEC and other Appro	04.01-IRB or IEC T	04.01.01-IRB or IEC Submission	04.01.01	FALSE	TRUE	Site	NULL	2-Activation	2-Site	4-Regulatory, IRB/EC or Other Review	4.02-Submissions
04-IRB or IEC and other Appro	04.01-IRB or IEC T	04.01.04-IRB or IEC Documentatio	04.01.04	FALSE	TRUE	irb	NULL	2-Activation	2-Site	4-Regulatory, IRB/EC or Other Review	4.01-Qualifications
05-Site Management	05.02-Site Set-up	05.02.06-Other Curriculum Vitae	05.02.06	FALSE	TRUE	Site	site_staff	2-Activation	2-Site	5-Site Documentation	5.05-Qualifications

ISF Initiative: Ongoing and Future Activities

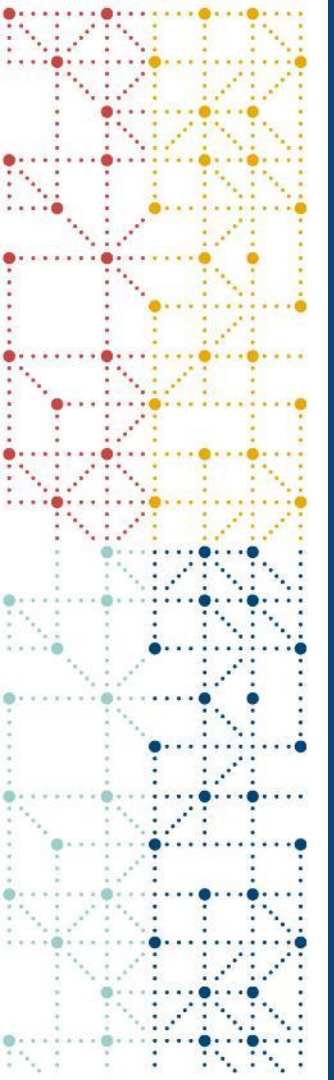
- First draft version of the ISF reference model expected to be completed **by December 2024 or early January 2025**.
  - Formal CDISC internal review will be followed prior to public comment.
  - Alignment with TMF RM v4.0 activities will take place.
- Outreach is ongoing and will continue throughout the initiative.
- Training will be provided upon publication of the final ISF reference model.

Risk Initiative

Risk Initiative

1. Workstream 1: White paper (ready for release in early Q1 2025)
    - Nine + volunteers
    - Reviewed by:
        - Steering Committee
        - Two regulators with passion for TMF
2. Workstream 2: Toolkit (to be released with white paper)
    - Consistency checks
    - UAT by group of volunteers
3. Workstream 3: Training modules (in development)
    - Webinar planned in conjunction with release
    - Modules for considerations across the lifecycle

COMING SOON!



TMF Reference Model v4 Update

Meet the Speakers

Donna Dorozinsky
TMF RM V4 Lead

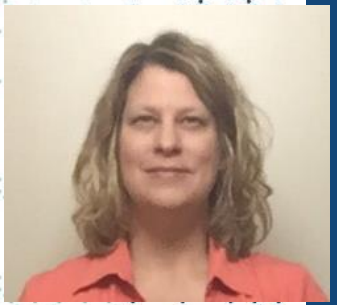
Title: Founder & CEO

Organization: Just in Time GCP

Paul Fenton
Incoming SC Chair

Title: Founder & CEO

Organization: Montrium



Lisa Dotterweich Mulcahy
Triage Committee Lead

Title: Owner & Principal Consultant

Organization: Mulcahy Consulting

Gillian Gittens
Triage Committee Lead

Title: Director, eClinical Strategy & Solutions

Organization: TransPerfect Lifesciences

Kathleen Mellet

Title: CDISC TMF Project Manager

Organization: Just in Time GCP

History of the TMF Reference Model

2009 to 2010

Initial meeting: 2009
V1.0 released: 2010

Called the DIA TMF RM

2011 to 2013

Multiple releases (1.1, 1.2, and 2.0)

- Regulator and industry feedback
- Investigator Site Files
- Devices
- Process-based metadata
- Investigator Initiated Studies

2014 to 2021

- Separated from DIA, so "DIA" no longer in name
- Formalization with a Steering Committee and a Change Control Board
- TMF RM website
- Release of the Exchange Mechanism Specification
- Releases of V3.0, 3.1, 3.2

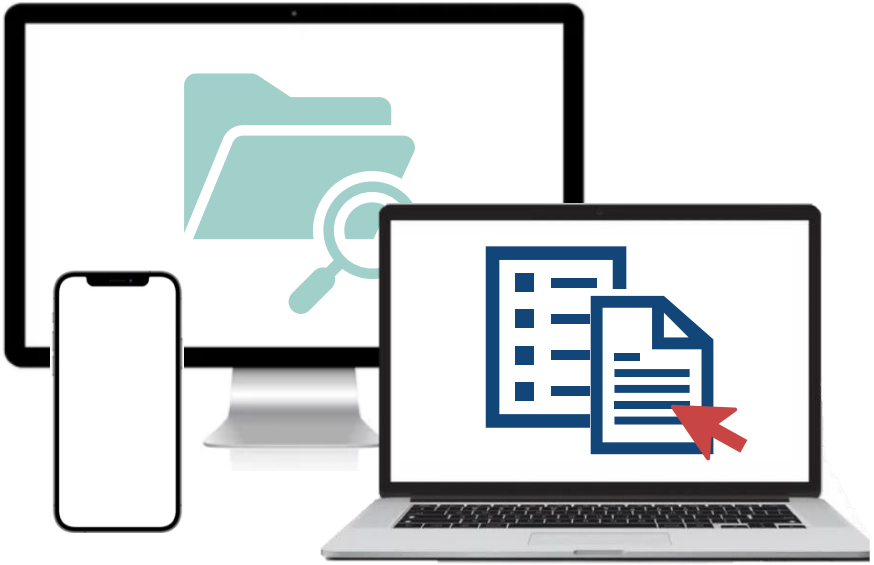
2022 to 3Q2024

- TMF RM become part of CDISC organization.
- TMF RM supported by CDISC processes and systems to advance the model and future strategies
- Release of V3.3

4Q2024 forward

- Continued support by CDISC for the TMF RM to achieve its goals
- **Comprehensive Review by Industry to Version 4.0 and move towards digital TMF**

How we manage TMFs today has changed



Regulatory Evolution

GDPR

ICH

M11, E8 (R1), & E6 (R3)

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

9 March 2023
EMA/INO/GCP/112288/2023
Good Clinical Practice Inspectors Working Group (GCP IWG)

Guideline on computerised systems and electronic data in clinical trials

Conducting Clinical Trials With Decentralized Elements

Guidance for Industry, Investigators, and Other Interested Parties

Medicines & Healthcare products Regulatory Agency

MHRA

Medicines & Healthcare products Regulatory Agency (MHRA)

'GXP' Data Integrity Guidance and Definitions

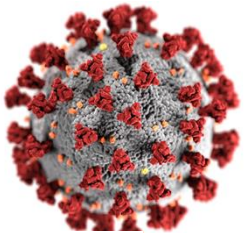
European Commission

Clinical Trials Regulation EU No 536/2014

Electronic Systems, Electronic Records, and Electronic Signatures in Clinical Investigations

Questions and Answers

Guidance for Industry



Guidance

Risk-Adapted Approach to clinical trials and Risk Assessments

Published 28 January 2022

A Risk-Based Approach to Monitoring of Clinical Investigations

Questions and Answers

Guidance for Industry

Submitting Documents Using Real-World Data and Real-World Evidence to FDA for Drug and Biological Products

Guidance for Industry

Informed Consent

Guidance for IRBs, Clinical Investigators, and Sponsors

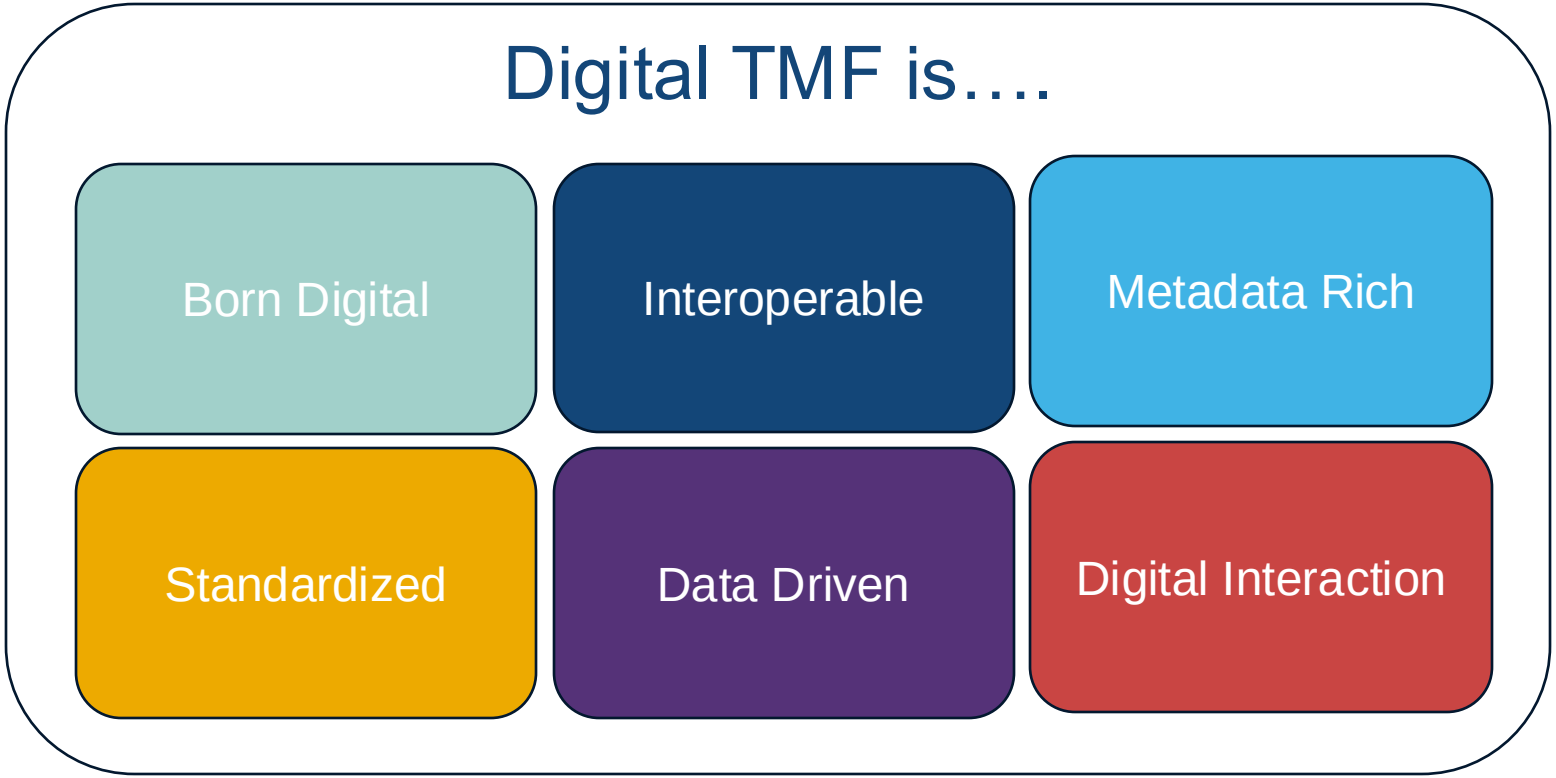
TransCelerate BIOPHARMA INC.

TRIAL MASTER FILE TMF cdisc REFERENCE MODEL

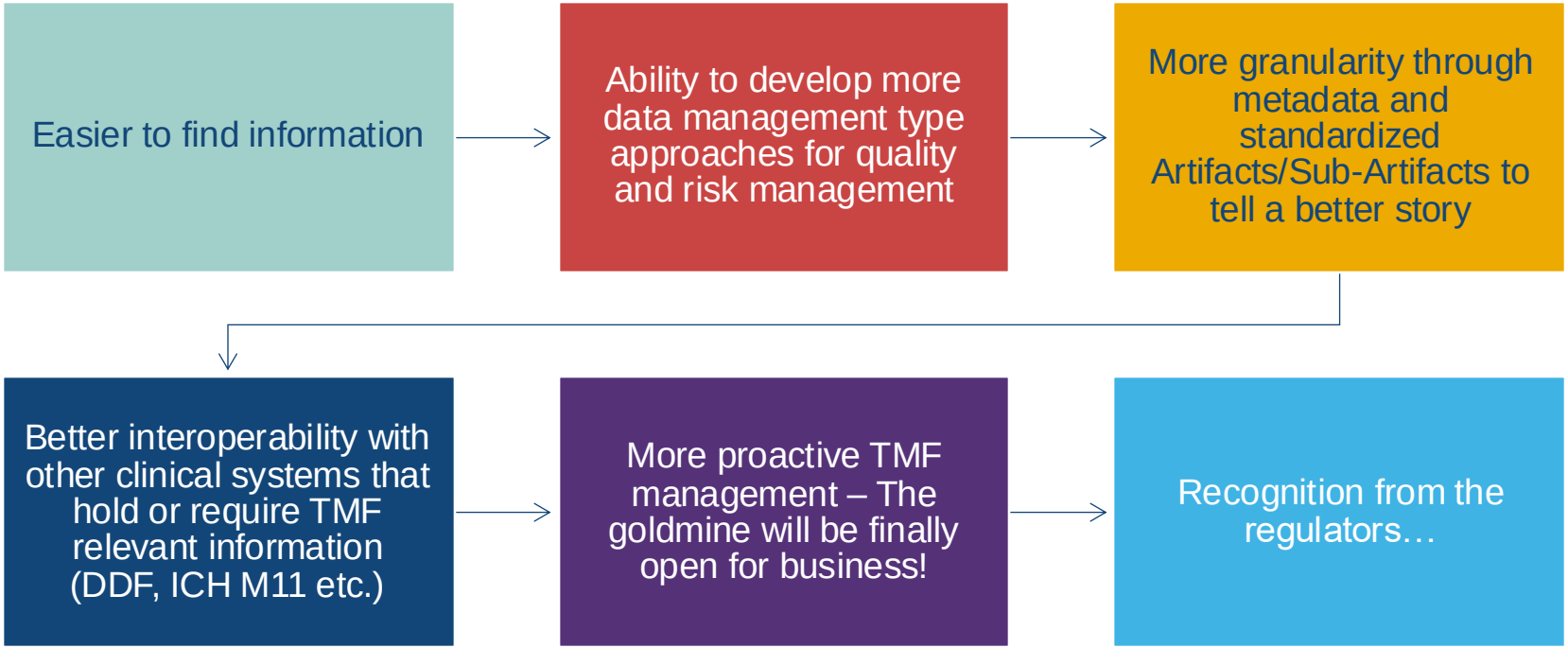
U.S. Department of Health and Human Services
Food and Drug Administration
Office of Clinical Policy
Center for Drug Evaluation and Research
Center for Biologics Evaluation and Research
Center for Devices and Radiological Health

August 2023

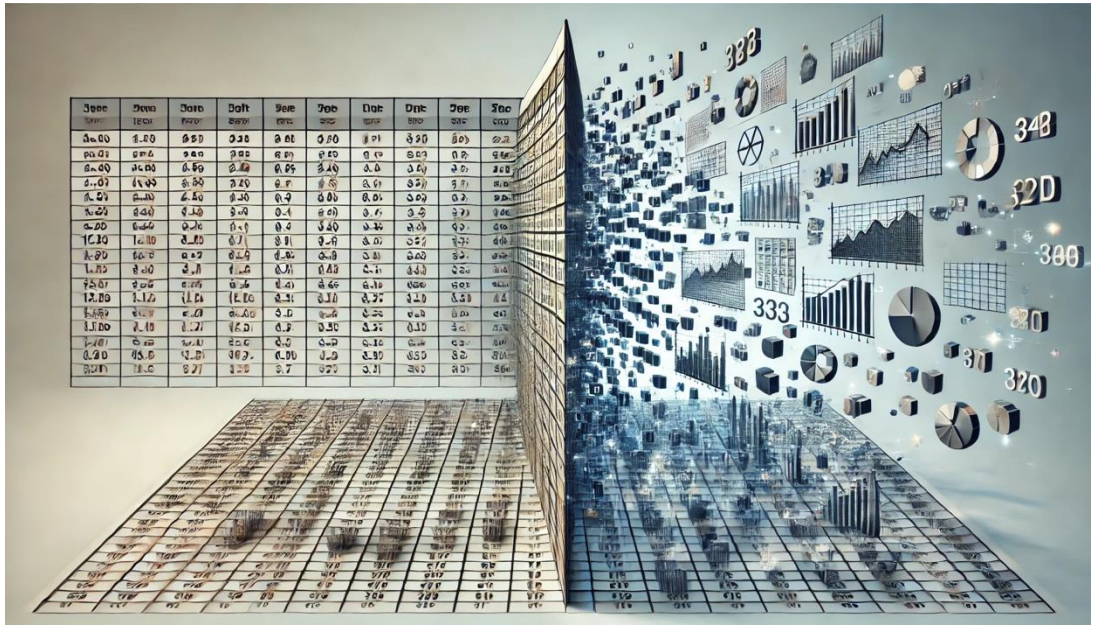
What is Digital TMF?



Why do we need to become a Digital TMF Standard?



Other Factors?



We are living in a digital 3D world, and we are working with a 2D spreadsheet

It's just not meeting our needs

The Reference Model is not just about categorizing data – it's about how we manage that data

TMF is data! – everything we talk about at this meeting and in our daily jobs is data driven

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 a transformation of the TMF RM critical.

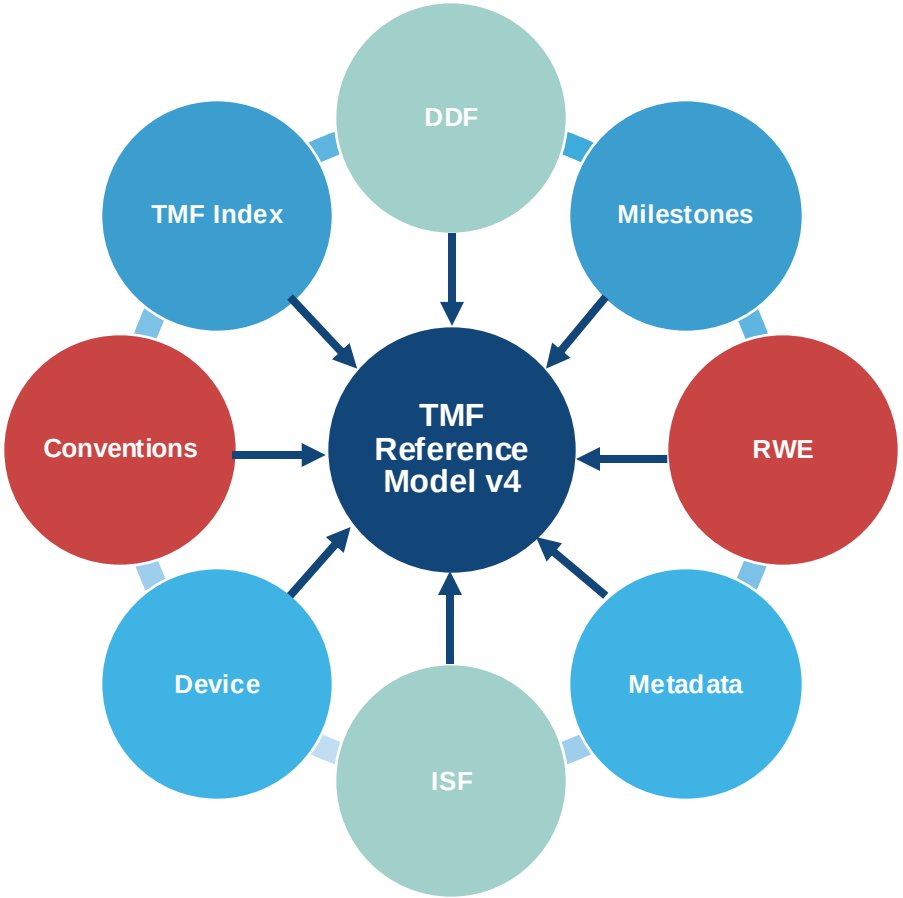
Goals

- ✓ 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
- ✓ Formalize Sub-artifacts
- ✓ Addition of standardized metadata
- ✓ Support the transformation of how we manage TMF today and tomorrow.

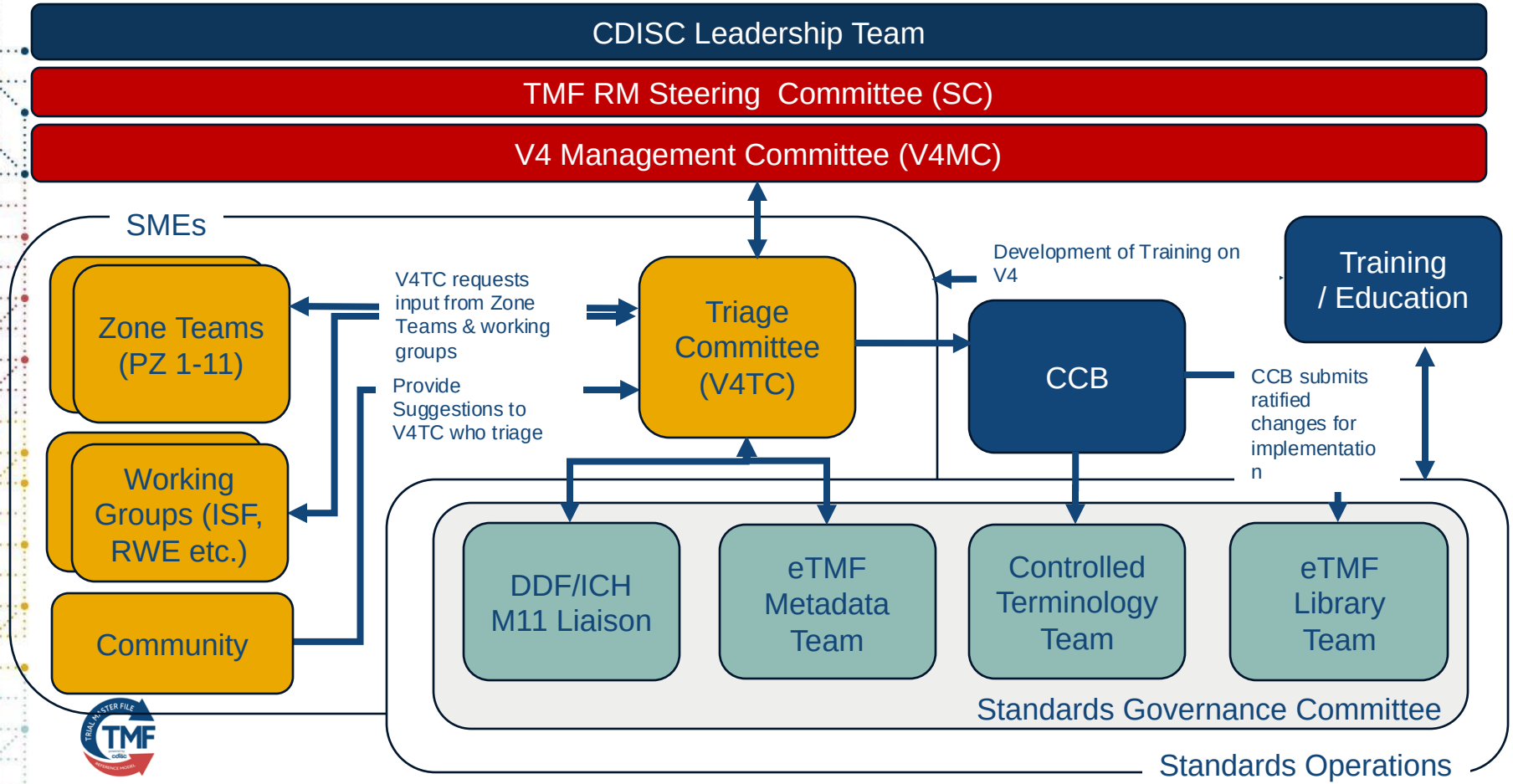
Not just about refreshing the Reference Model, but about Refreshing the Community!

A vision for the Future:

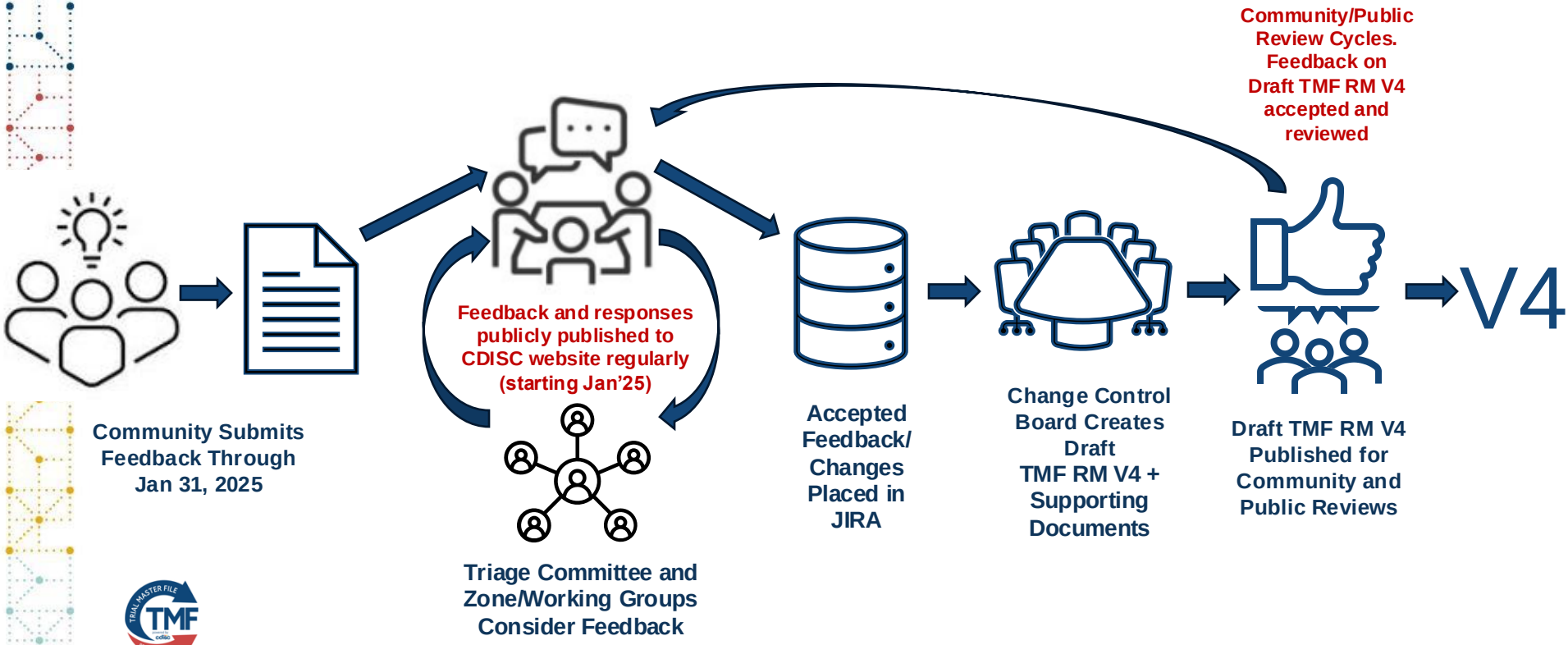
TMF Reference Model v4



V4 (TMF RM) org chart



TMF RM V4 Feedback Process



Meet the Triage Committee Team!

Zone	Assignment
1	Jessica Vicari
2	Sarah Hitching
3	Kathie Clark
4	Marion Mays
5	Liz Farrell
6	Vittoria Sparacio
7	Jackie Morrill
8	Curran Murphy
9	Steph Viscomi
10,11	David Ives

Working Group	Assignment
DDF, ICH	Nick Hargaden
RWE	Stuart McCully
Device	*TBD*
ISF	Brittany Walker
Metadata	Aaron Grant
EU CTR	Martina Duevel
Cross-Zone	Eldin Rammell

Triage Committee Status

- ✓ Members selected - broad spectrum of global SMEs from industry
- ✓ Roles & responsibilities defined e.g. zones assigned, review feedback
- ✓ Time commitment and meeting cadence agreed - weekly, 1 hour meetings
- ✓ Communication method set up - CDISC Wiki space for meeting content
- ✓ Processes being finalized - from feedback submission to change control

Call for Feedback

We need support from the TMF Community!

- We have developed a Microsoft Form (similar to the intake form on the CDISC website) to collect all feedback from the community.
- A communication was released this morning via email which includes more information as well as a link to the form

Please submit all feedback for TMF Reference Model version 4 by the end of January 2025

Submit Feedback for TMF Reference Model v4

High Level TMF v4 Timeline

Quarter:	3Q24	4Q24	1Q25	2Q25	3Q25	4Q25	1Q26	2Q26	3Q26	4Q26	1Q27
Teams	**Project Management**: Planning		**Project Management**: plan and timelines management, communications, project meetings, status updates, meeting presentation preparations								
CCB	**Change Control Board** Configure Jira (August)				**Change Control Board** Review of proposed changes & creation of draft V4 (Jul-Aug)		**Change Control Board** Review the Proposed changes & draft the Summary of Changes (Mar-Apr)			**Change Control Board** Creation of final V4 and final Summary of Changes (Nov-Dec)	
Triage	**Triage Committee** Call for volunteers and assemble team (Sep)	**Triage Committee** Review feedback and Triage (Oct-Apr)		**Triage Committee** QC of changes (May-Jun)	**Triage Committee** Support creation of draft v4 (Jul-Aug)	**Triage Committee** Review of Community feedback & Triage to Zone Teams (Oct-Nov)	**Triage Committee** QC of changes (Feb)		**Triage Committee** Review of Public feedback & Triage to Zone Team (Jul-Aug)	**Triage Committee** Address any changes from Zones and Standards (Oct)	
Public								**Public** Review of proposed V4 (Jun)			
Community		**Community** Begin submitting change requests (Dec-Jan)			**Community** Review of proposed V4 (September)						**Community** Release to community (Mar 2027)
Zone Teams & TMF Working Groups	**Zone Teams / Working Groups** Call for and assemble Leads and Members (Sep-Nov)		**Zone Team/ Working Groups Meetings** (Delivery of all proposed changes to CCB by Apr 2025)			**Zone / Working Groups** Address Community feedback (Dec-Jan)			**Zone / Working Groups** Address Public feedback (Sep)		
SteerCo								**Steering Committee** Review of draft v4 (May)			**Steering Committee** Final review and approval (Feb)
Copy Editing											**CDISC Copy Editing Team** Review of draft V4 (Jan)
Standrds Working Groups	**Standards** Engage Standards Committee	**Standards** Assemble working groups	**Standards** (Delivery of all proposed changes to CCB by Apr 2025)			**Standards** Address Community feedback (Dec-Jan)			**Standards** Address Public feedback (Sep)		
Education								**Education Committee** Engage and plan (Apr)	**Education Committee** Development of Training		
Tools									**TMF RM Tools Team** Engage		

How to get involved?

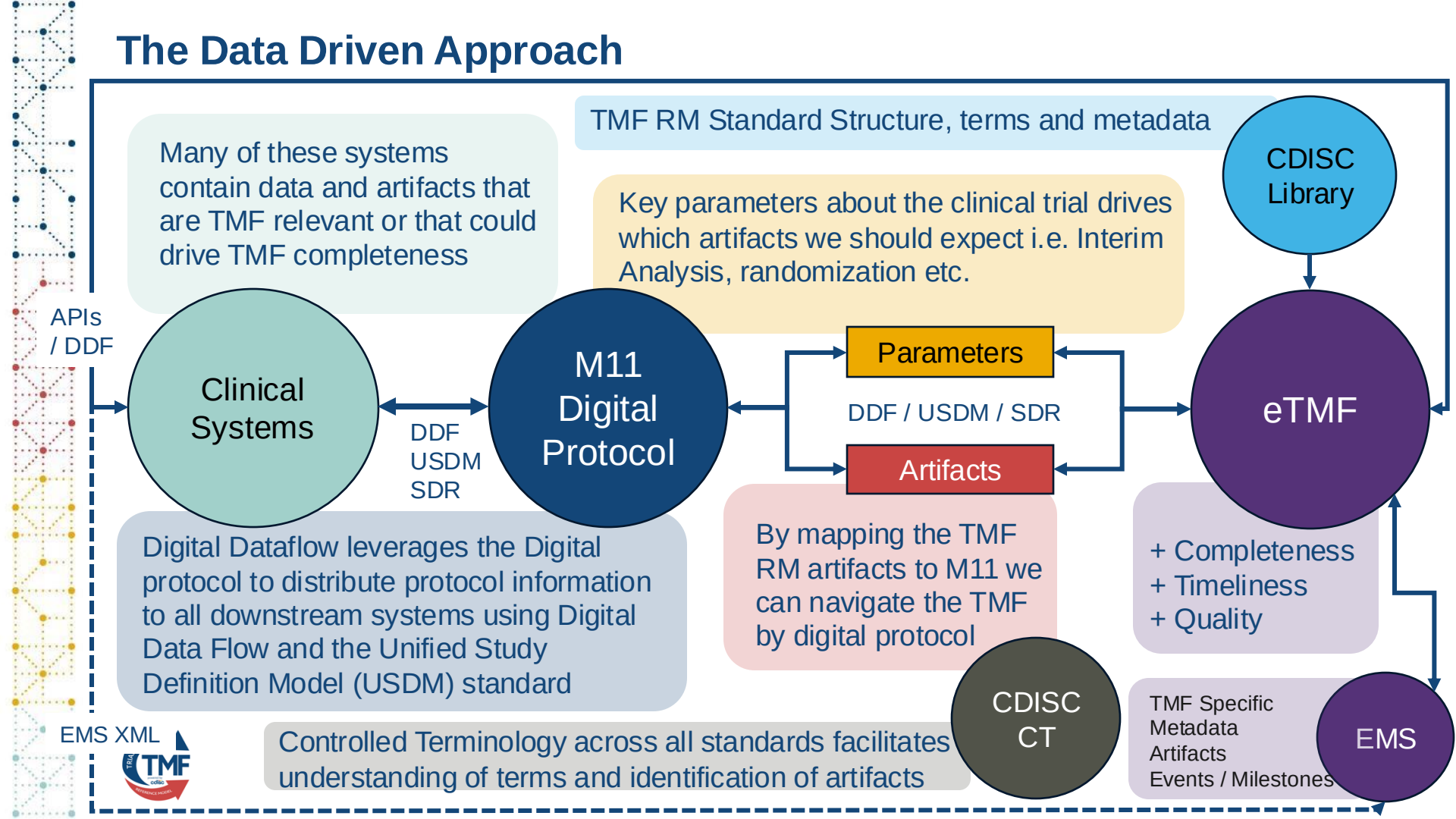
We are actively seeking volunteers to support the refresh!

Step 1: Sign up to become a CDISC TMF Volunteer

Step 2: Once you have completed sign up, notify the team:

- If you would like to join **Zone Teams 7, 8, or 11** please contact the Kate (kate.santoro@intelliatx.com) and Leila (Leila.Canlas@Pfizer.com)
- A call for membership in **Working Groups** (i.e Metadata or RWE) will come out in January.

The Data Driven Approach



Questions?

Thank You!!!

https://www.cdisc.org/events/webinar/tmf-reference-model-general-meeting-q4