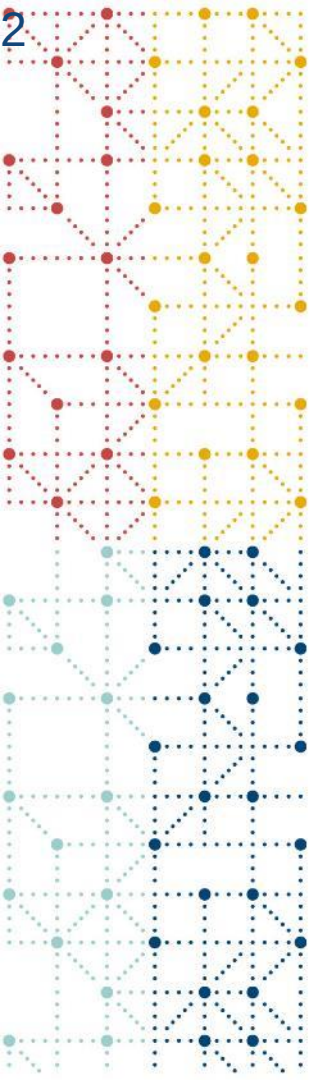
The TMF Reference Model
General Meeting March 2025

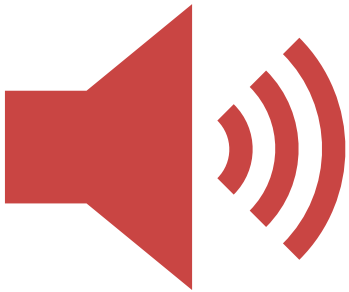
Presenters:

- Paul (Fenton) Carter, CEO, Montrium; Chair, TMF Reference Model Steering Committee
- Karen Roy, Consultant, CDISC; Outgoing Chair, TMF Reference Model Steering Committee
- Jamie Toth, Global Head, Trial Master File Management & Records, BeiGene; TMF RM SC Member
- Aryn Knight, Associate Vice President, Clinical innovation & Research Institute Memorial Hermann Health System
- Joanne Malia, Sr. Director, Development Records Mgmt, Regeneron, TMF RM SC Member
- Dawn Niccum, EVP, QA & Compliance, inSeption Group, TMF RM SC Member
- Miyuki Taguchi, Manager, TMF Operations, inSeption Group, CJUG TMF Sub-Team member
- Donna Dorozinsky, CEO, Just in Time, GCP, TMF Reference Model Steering Committee Member
- Lisa Mulcahy, Mulcahy Consulting, TMF Reference Model Steering Committee Member



Housekeeping

Housekeeping

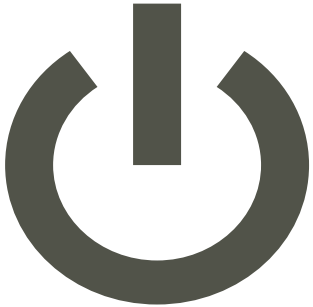


You will remain on **mute**

Housekeeping

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

Housekeeping



Audio Issues?

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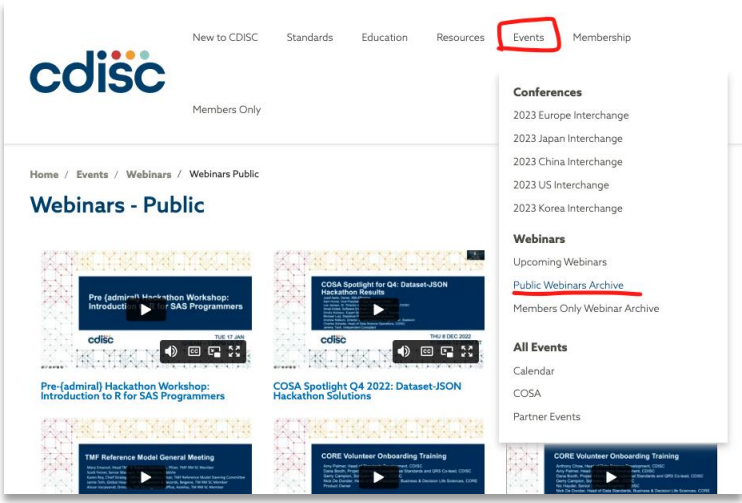
Second, check your local internet connection strength

Housekeeping



Webinar Recording

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

Agenda

- A Vision for the Future
- Steering Committee & Interchange updates
- Community News
- ISF Initiative
- Risk Initiative
- ICH E6 R3
- TMF Reference Model v4 Update
- Q&A

A Vision for the Future

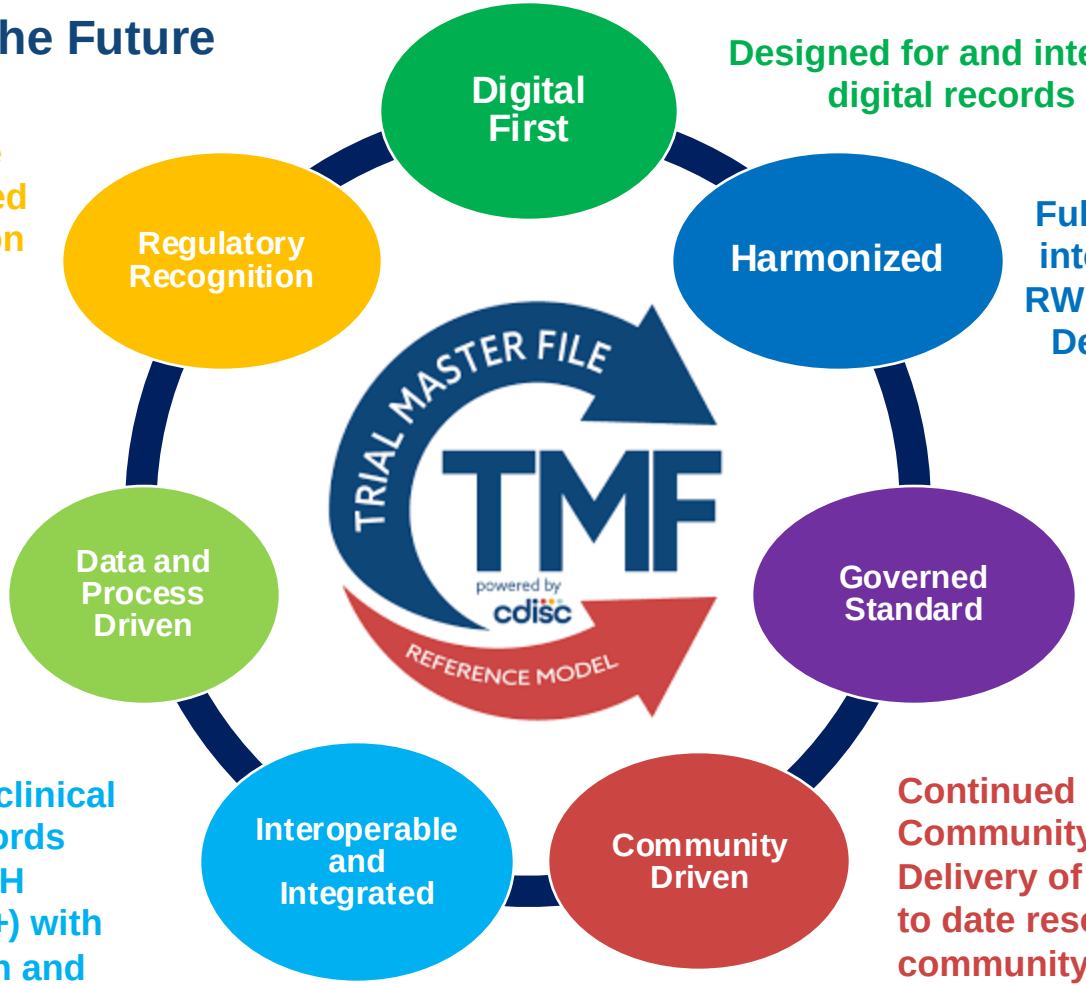
Paul (Fenton) Carter, CEO, Montrium; Chair, TMF Reference Model Steering Committee

A Vision for the Future

Mandated by the regulators as the standard to be used for the organization and provision of essential TMF records.

Comprehensive record and operational metadata standard, clinical process standards and standard milestones.

At the heart of the clinical system and records landscape (ICH M11/USDM/DDF ++) with strong integration and interoperability.



Designed for and interoperable with digital records and data.

Fully aligned and integrated CT(s), RWE, ISF and Med Device models.

Formally managed and recognized standard which is fully supported by the CDISC organization.

Continued strong Community engagement. Delivery of training and up to date resources for the community.

Steering Committee Updates

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

TMF Steering Committee Updates

2025 CDISC TMF Steering Committee nominations have been closed!

- Call for nominations was released on February 3rd and was closed on February 28th.
- Thank you to everyone who took the time to submit nominations!!

Next Steps

- A voting link will be shared with the TMF Community for review and voting later this week
- The new Steering Committee members will be announced in early April

TMF Steering Committee Updates

Welcome Rob Jones and Jim Horstmann!!

TMF Practice Area Product Manager
Phlexglobal (Cencora PharmaLex)

Senior Product Manager, Vault eTMF
Veeva Systems

2025 CDISC + TMF Europe Interchange

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

The ONLY TMF Conference in Europe in 2025!

2025 CDISC + TMF Europe Interchange

Geneva, Switzerland
14-15 May 2025

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

The agenda is live, and registration is open. Early bird rate finishes 14th March.

If you are interested in attending, visit the CDISC website or scan the QR Code below to learn more:

Upcoming Events in 2025!

2025 CDISC + TMF US Interchange

The Call for Abstracts is Open – Deadline 25th April

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

Community News

Miyuki Taguchi, Manager, TMF Operations, inSeption Group, CJUG TMF Sub-Team member

Japan User Community – Presenter Miyuki Taguchi

The Establishment of TMF Sub-Team Under The CDISC Japan User Group (CJUG) SDTM

There was no TMF user community in Japan for the purpose of continuously sharing information and exchanging opinions about TMF as a formal organization.

CJUG (CDISC Japan User Group) is CDISC's user network in Japan, where members, such as regulators, pharmaceutical companies, CROs, academia, and IT vendors participate in working groups of each CDISC standard. CJUG is working to promote the CDISC standard in Japan.

For Japan TMFers to freely exchange information and knowledge, learn about TMF, CJUG TMF Sub-Team was established in Jan 2025.

26 members have signed-up from Pharma, CRO, Service provider, consultant and academia.

'This new initiative aims to enhance collaboration and provide greater support for the growing needs of Trial Master File (TMF) implementation and standardization in Japan.

Our team is committed to driving progress and sharing best practices to address challenges in the clinical trial ecosystem. Whether you're already engaged in TMF projects or exploring ways to optimize your processes, we welcome your interest and input.'

By Akira Soma – The head of J3C (Japan CDISC Coordinating Committee)

ISF Initiative

Jamie Toth, TMF RM SC Member

Aryn Knight, Associate Vice President, Clinical innovation & Research Institute Memorial Hermann Health System

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 TIMELINE

We are here!

STAGE 1

Launch - February 2024

Call for volunteers from sites, sponsors, CROs & vendors

Kickoff – April 2024

Initiative kicked off with ~45 volunteers; subteams (5) formed

STAGE 2

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 3

Proofing – November–December 2024

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

STAGE 4

CDISC Review – January-March 2025

ISF RM provided feedback to TMF RM V4

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

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

Meet with CCB and allow review.

STAGE 5

Public launch – Target: May 2025

Training to begin after public launch/comments

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

ISF VERSION 1.0

Count of artifact_no	Column Labels												
	1-Selection		1-Selection Total	2-Activation		2-Activation Total	3-Conduct		3-Conduct Total	4-Closeout		4-Closeout Total	Grand Total
Row Labels	1-Sponsor	2-Site		1-Sponsor	2-Site		1-Sponsor	2-Site		1-Sponsor	2-Site		
1-Planning	3	2	5	2	2	4							9
2-Study Library				12	2	14	7	5	12	1		1	27
3-IP and Trial Supplies				10		10	13	3	16	1	1	2	28
4-Regulatory, IRB/EC or Other Review				4	7	11		2	2		2	2	15
5-Site Documentation	1	1	2	5	12	17	1		1				20
6-Contracting and Indemnity		1	1	3	2	5							6
7-Testing Facility				2	6	8	2	2	4				12
8-Monitoring	1		1	2		2	2	1	3	1		1	7
9-Data Management				4	1	5	2	5	7	2		2	14
Grand Total	5	4	9	44	32	76	27	18	45	5	3	8	138

These Zones/Sections are aligned into time based/phases based on how an Inv. Site handles their Operations

ISF Version 2.0 ISF will be part of Version 4.0 TMF RM

ISF INITIATIVE: ONGOING & FUTURE ACTIVITES

- After formal CDISC internal review, public comment will commence – likely in May.
- ISF Version 1.0 to launch in 2025.
- Alignment with TMF RM v4.0 activities will take place; feedback already given. These will go into ISF Version 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 version 1.0 ISF reference model.

Risk Initiative

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

RISK Initiative - Where are we today?

Objective:

Consider opportunities for taking a risk-based approach across the whole TMF management lifecycle, from planning and establishing TMF management processes and systems through to long-term archiving of TMF content

- White paper completed and any impact from newly released ICH E6 R3 assessed / addressed.
- Risk Toolkit is finishing its UAT and received feedback will be incorporated
- Training slide deck has been developed and is being QC'ed.

Expectation: Release prior to or at the CDISC Interchange in Geneva!

ICH E6 R3

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

GCP Guideline

ICH : International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use

- 23 Members ; 38 Observers

- E6: Guideline for Good Clinical Practice

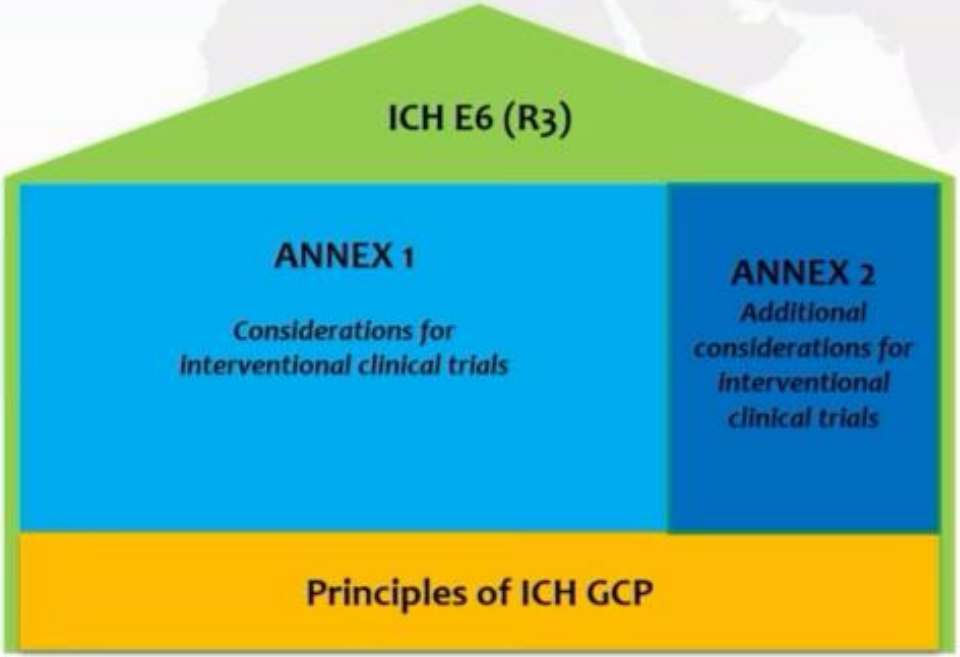
Version	Date
E6 (initial)	1-May-96
R1	10-Jun-96
R2	9-Nov-16
R3	6-Jan-25

- **Scope:**

Applies to interventional clinical trials of investigation products that are intended to be submitted to regulatory authorities. The Principles of GCP ….may also be applicable to other interventional clinical trials of investigational products that are not intended to support marketing authorisation applications in accordance with local requirements

ICH
harmonisation for better health

OVERVIEW OF ICH E6(R3)



New structure

Principles are in the core part of the guideline – **focus should be on their fulfilment**

E6(R3) Guideline

E6(R3) Principles and Annex 1 replacing E6(R2)

I. INTRODUCTION

II. PRINCIPLES OF ICH GCP

III.ANNEX 1

1. Institutional Review Board/Independent Ethics Committee (IRB/IEC)
2. Investigator
3. Sponsor
4. Data Governance – Investigator and Sponsor **(new)**

APPENDICES

Appendix A. Investigator's Brochure
Appendix B. Clinical Trial Protocol and Protocol Amendment(s)
Appendix C. Essential Records for the Conduct of a Clinical Trial

GLOSSARY

ANNEX 2 – *under public consultation from November 2024 to March 2025*

Annexes provide the basis for the appropriate interpretation and application of the principles….various approaches may be considered provided they are justified and achieve the intended purpose of the principles.

Principles

- Additional clarification and streamlining of principles – **11 principles in R3**
- New dedicated principles for **risk proportionality** and **roles and responsibilities**

ICH E6 (R3) PRINCIPLE	TOPIC	ICH E6 (R2) PRINCIPLE
1	Ethical Principles	2.1, 2.2, 2.3, 2.7, 2.11
2	Informed Consent	2.9
3	IRB/IEC Review	2.6
4	Science	2.4, 2.5
5	Qualified Individuals	2.8
6	Quality	2.13
7	**Risk Proportionality**	**N/A**
8	Protocol	2.5
9	Reliable Results	2.10
10	**Roles and Responsibilities**	**N/A**
11	Investigational Products	2.12

What's different?

- **Terminology**

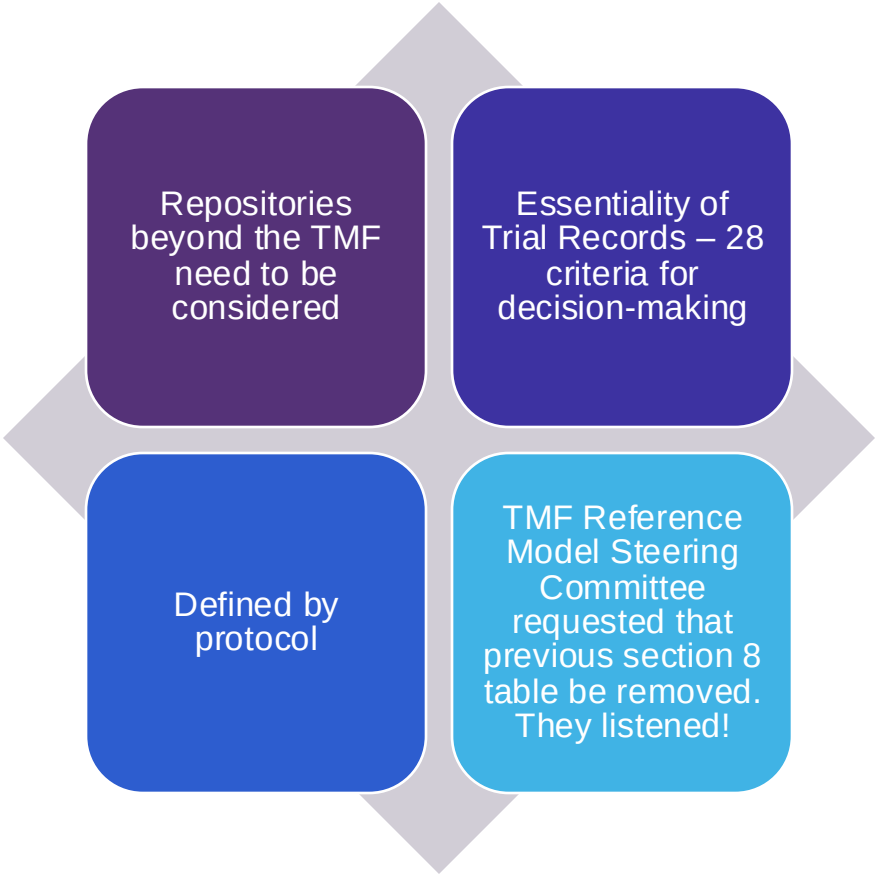
Current	Now Know As
Documents	Records
CROs/Vendors	Service Providers
Subjects	Participants

- Read the glossary – some "definitions" have been enhanced
  - *For example:* Audit Trail: Metadata records that allow the appropriate evaluation of the course of events by capturing details on actions (manual or automated) performed relating to information and data collection and, where applicable, to activities in computerised systems. The audit trail should show activities, initial entry and changes to data fields or records, by whom, when and, where applicable, why. In computerised systems, the audit trial should be secure, computer-generated and time stamped.
- Future-proof: enhanced clarity with less room for interpretation
- Expectations for records are throughout the document in the various sections in Annex 1 and the Appendix 3
- Inspectors being trained on Risk Proportionality approaches

Enhanced Key Concepts

- Quality by Design (QbD) (builds on E8)
- Pushes Critical Thinking / Decision Making
- **Risk Proportionality** (the new Risk Based approach)
  - *Not about taking risks but identifying and managing potential risks*
- All studies are not equal – importance of the protocol
- Sponsor should not place unnecessary burden on sites and participants
- Data Governance section added to support Data Integrity

Essential Records



Key Record Changes / Clarification

- Has defined roles and responsibilities for records, including for computerized systems.
- Investigators should keep sponsors informed of the name of the person responsible for maintaining the essential records during the retention period.
- Sponsor should implement measures to safeguard the blind.
- Data governance section is extensive – requires a careful read.
- Sponsor should inform investigators and service providers in writing of record retention requirements for essential records and should notify them when the trial-related records are no longer needed.
- Sponsor should notify the appropriate authorities of the transfer of ownership of the essential records and should include the investigator if the sponsorship of the trial changes.
- Sponsor and investigator should maintain a record of where essential records are located including source records.
- Sponsor and investigator should ensure essential records are collected and filed in a timely manner.
- Need to consider the essential records that are not specific to a study but are to the investigational product, facilities or processes and systems including computerized systems.

Potential New Records

Documentation of selection, assessment* and oversight of service providers conducting important trial-related activities
Trial-specific training records*
Documentation of delegation of trial-related activities by the investigator*
Documentation of collection, processing and shipment of body fluids/tissue samples
Documentation of body fluids/tissue samples storage conditions
Documentation of investigational product storage conditions, including during shipment
Records of relabelling of investigational product at the investigator site
Instructions for use of important trial-specific systems (e.g., interactive response technologies (IRTs) user manual, electronic CRF (eCRF) manual)*
Records demonstrating fitness for purpose (e.g., maintenance and calibration) for equipment used for important trial activities*
Records and reports of noncompliance including protocol deviations and corrective and preventative actions
Documentation relating to data finalisation for analysis (e.g., query resolutions, SAE reconciliation, quality control reports, coding completion, output data sets)
Documentation of trial-specific computerised system validation (e.g., specifications, testing, validation report, change control)*
Documentation of the assessment of fitness for purpose for non-trial-specific computerised systems used in the trial (e.g., clinical practice computerised systems)*
Documentation relating to the statistical considerations and analysis (e.g., sample size calculations,* analysis sets decisions, analysis data sets, analysis programs, quality control records and outputs)
Trial-specific plans (e.g., risk management,* monitoring,* safety,* data management,* data validation* and statistical analysis) and procedures
Procedures,* meeting minutes and submissions to the IDMC/adjudication committee(s)

Take home message

Risk Proportionality

Lots of good info within R3 – requires a careful read!

TMF Reference Model v4 Update

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

Lisa Mulcahy, Mulcahy Consulting, TMF Reference Model Steering Committee Member

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

Aaron Grant, Head of Innovation, Just in Time GCP; Triage Committee Member

Progress to Date

The v4 team and Workstreams have been conducting workshops and holding meetings with the extensive network of industry SMEs and vendor groups to coordinate and align changes.

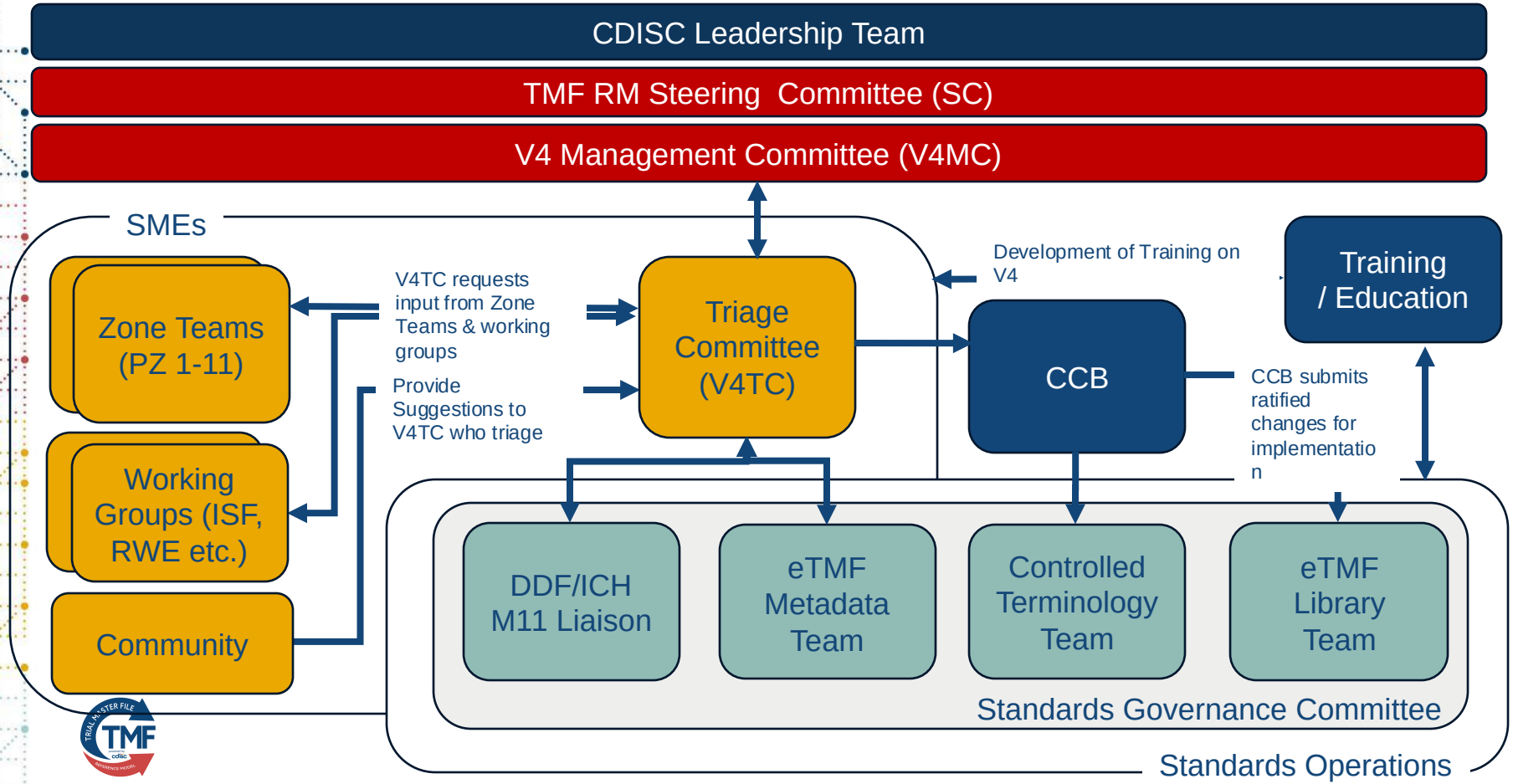
1. **Finalized decision to Rename Artifacts and Sub-artifacts to Record Group and Record Type.**
2. Beginning the exercise of combining all feedback from different groups and individuals.
3. Triage Committee will be initiating reviews of changes submitted to date and then taking these changes to the Zone Teams
4. We remain on schedule for an anticipated release in early 2027.

Fully Adopted & Confirmed Changes

- Change in term of Artifact to Record Group
- Change in term of Subartifact to Record Type & these are no longer recommended, but part of the Reference Model

	A	B	C	D	E	F	G	H
1	TMF Reference Model							Version 4 Draft
2								
3	Zon	Zone Nam	Section	Section Name	Artifact	Artifact name (Record Group)	Definition / Purpose	Recommended Subartifacts (Record Type)

V4 (TMF RM) org chart



Vendor Workgroup for V4

- Goals are to discuss V4 changes and how they affect vendor community. Gain feedback to V4 leadership
  - Looking at technical changes to the architecture of the reference model
  - Looking at metadata standards
- Representatives are Product Managers from each company representing roadmap and current state capabilities
- Current Vendors:

Veeva, montrium, Trial Interactive, IQVIA, EGNYTE, cencora PharmaLex, KIVO, florence, PHARMASEAL

Any other vendors wishing to participate, please reach out to Kathleen Mellet at kmellet@cdisc.org

Call for Action

The v4 team is looking for volunteers for the ICH E6 R3 working group to ensure that the RM is positioned to meet the needs of the community in terms of content to be added in support of R3 requirements.

If you are interested in joining, please reach out to Kathleen Mellet.

Contact information: kmellet@cdisc.org

Questions?

Thank You!!!