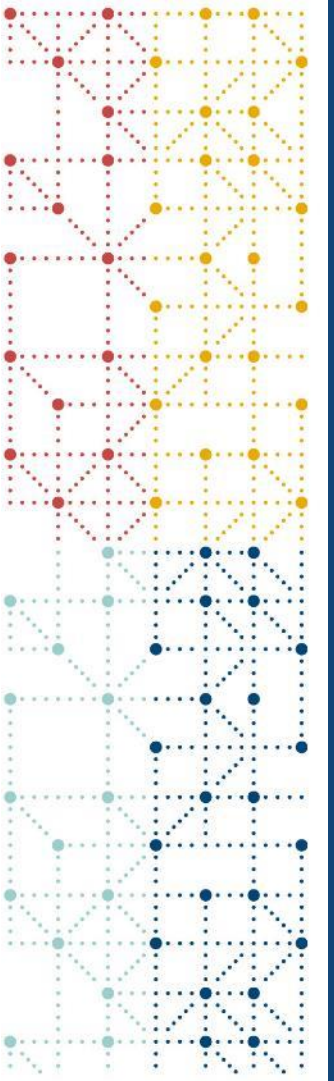
The TMF Reference Model Group and CDISC Affiliation: What's Next?

cdisc

June 27th, 2022

Agenda

1. CDISC Intro – Dave Evans
2. History of the TMF RM – Karen Roy
3. What is a Standard – Bess LeRoy
4. TMF RM Standard – Joanne Malia
5. Exchange Mechanism – Paul Fenton
6. Implementation –Kathie Clark, Mary Emanoil
7. Volunteering – Amy Palmer
8. The Future– Dave Evans



CDISC Background

Dave Evans - President & CEO, CDISC

***Mission**: To develop and support global, platform-independent data standards that enable information system interoperability to improve medical research and related areas of healthcare*

- Global Non-profit Consensus-based Standards Development Organization
- 20 Years of Regulatory Clinical Data Standards Development and Implementation
- Experienced Leadership Team and Dedicated Staff of 40+ Professionals and SMEs
- Volunteer Network of 1000+ Industry Experts
- 545+ Member Organizations
- Widely Adopted and Freely Available Clinical Research Data Standards
- Mature Standard Governance Processes
- Innovative Open-Source Technology for Standards Library and Metadata Management
- Involved in a wide range of emerging Industry Initiatives and Projects
- Collaborative Ecosystem of Relationships and Partnerships
  - Members, Regulators, Patient Foundations, Academia, SDOs and Industry
- Addition of TMF Reference Model to CDISC Family of Standards

CDISC – a look into this year

- Standards Initiatives from Regulatory Agencies
- Ongoing Therapeutic Area Projects
- Ongoing Activities and Projects on RWD/RWE & Data Sharing
- Standards Implementation for Registries and Academic Use
- New Industry Projects are on schedule for delivery
- Continue to build upon CDISC Library and Biomedical Concepts
- Continue to add content to eCRF Portal and QRS Library
- Collaboration with other SDOs on emerging Industry Initiatives
- Expansion into additional areas of Clinical Information Standards

Strategic Benefits for the Clinical Research Community

- Expansion of scope of clinical information standards to trial design, trial administration, clinical operations, regulatory documentation
- CDISC serves as the hub for cross-industry standards initiatives and the TMF RM will be part of that direction
- Strategically, there is a natural progression to the development and governance of standards, so why reinvent the wheel when so much work has already been done
- Evolution organizationally to embrace governance of clinical research information standards, not just the clinical data from where it originated.
- Broadening the harmonization of clinical research information standardization.

History of the TMF Reference Model

Karen Roy

Co-Founder and Chair of the TMF Reference Model Steering Committee

SVP of Clinical Marketing at Phlexglobal

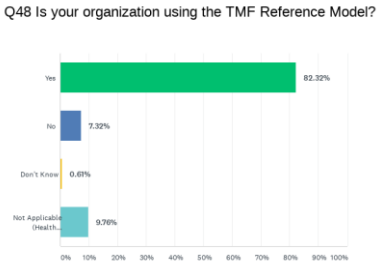
What *is* the Trial Master File?

The sponsor and the investigator shall keep a clinical **trial master file**. The clinical trial master file shall at all times contain the **essential documents** relating to that clinical trial which allow verification of the conduct of a clinical trial and the quality of the data generated […]. It shall be readily available, and directly accessible upon request, to the Member States.

[EU Regulation 536/2014]

What *is* the Trial Master File Reference Model?

A Standardised structure, contents and naming of these Essential documents

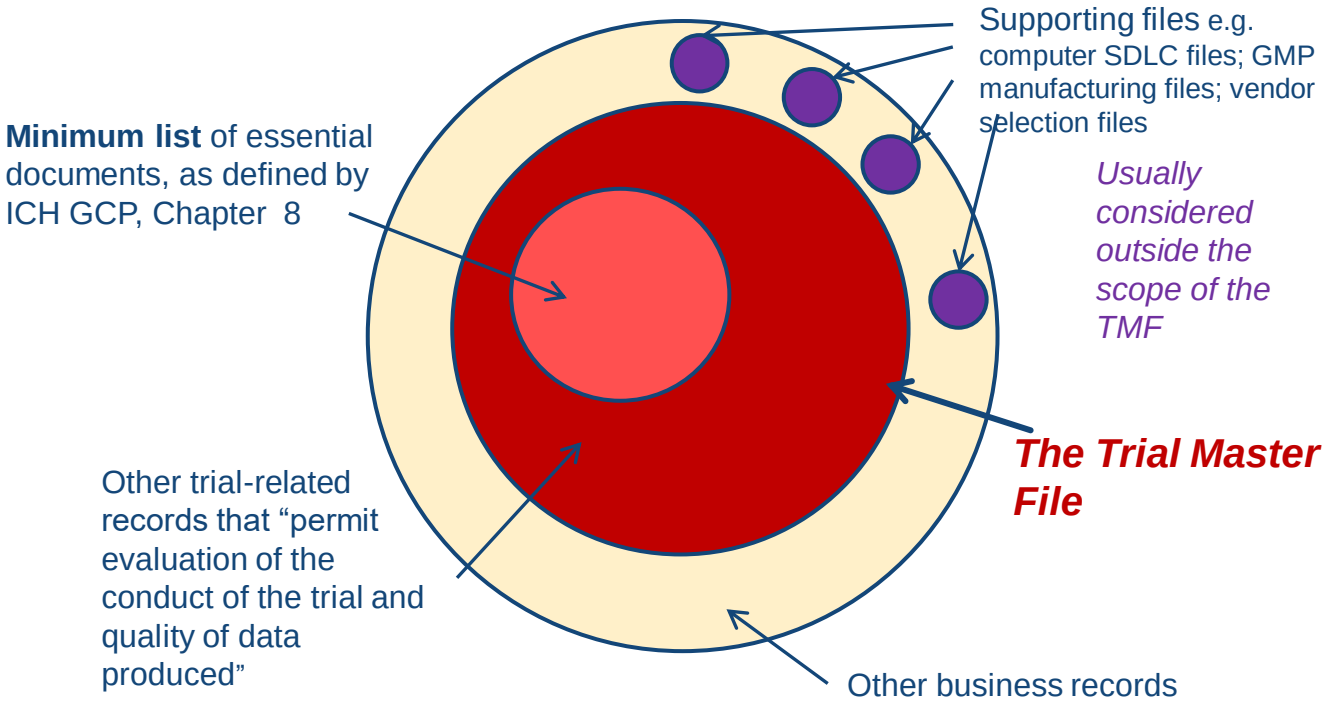


Source: Annual TMF Ref Model Survey 2019
From 247 Respondents

Why a TMF Reference Model?

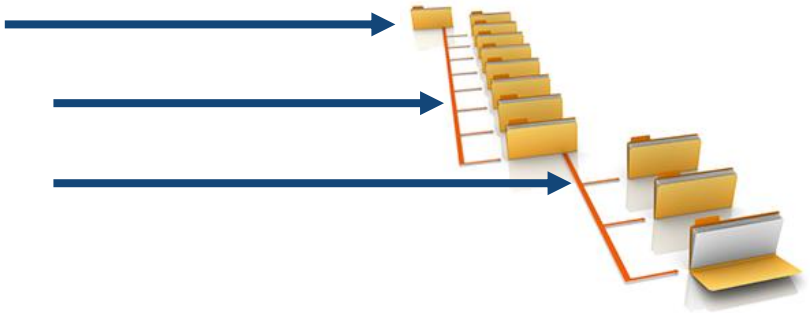
- ICH GCP Section 8.2 – 8.4
- “The **minimum** list of essential documents that has been developed.....”
- ICH GCP did **NOT** provide a comprehensive contents list for the TMF
  - Examples of missing documentation:
    - Electronic systems
    - Data management and statistical methodology
    - Safety monitoring
- Everyone had their own customised structure – Sponsors, CROs and third parties

Defining the TMF Reference Model



Structure and Content of the Model

- Data held in a simple Excel spreadsheet
  - Easy for non-technical people to use!
- Hierarchical structure
  - 11 Zones
  - 48 Sections
  - 249 Artifacts



607 Sub-Artifacts

Development of the TMF Reference Model

DIA DEVELOP INNOVATE ADVANCE

Document & Records Management Community

2009 to 2010

Initial meeting in 2009 with first version being released in 2010

2011 to 2013

Multiple releases including Regulator feedback, Investigator Site Files, Devices, Process based metadata. Workgroups established

Separated from DIA

2014 to 2021

Formalization with a Steering Committee. **Release of the Exchange Mechanism Specification** and Version 3

2022 onwards

Forward to Compliance

Strategy Pillars for the Future

What is a Standard

Bess LeRoy

Head of Standards Development

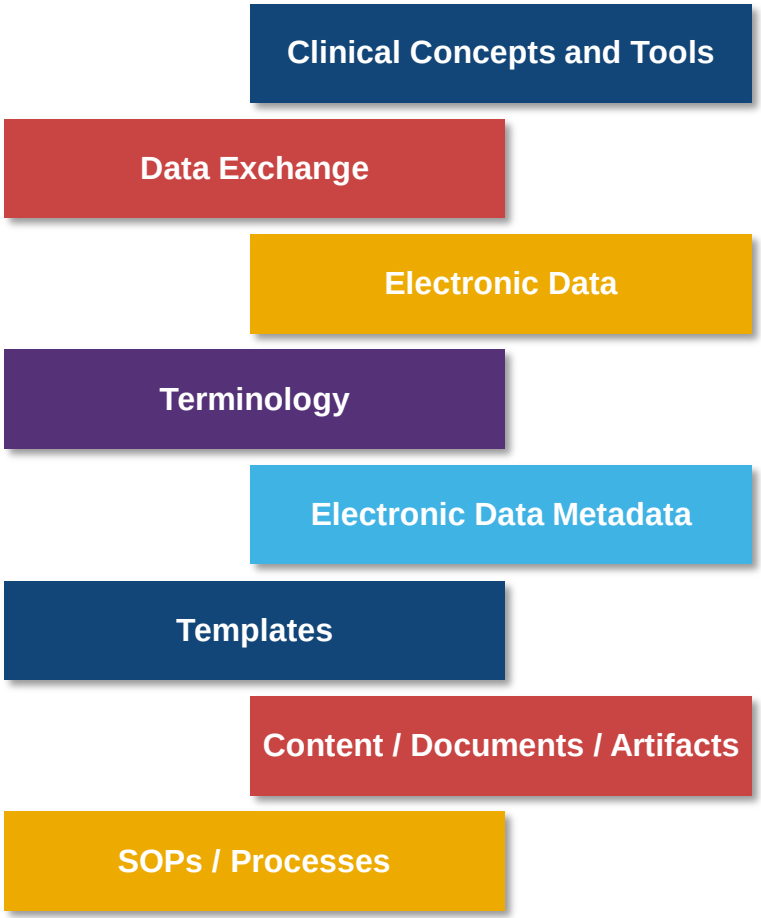
CDISC

What is a Standard?

Webster's Dictionary

- "**something established by authority,** custom, or general consent as a model or example"
- "the type, model, or example commonly or **generally accepted** or adhered to; criterion set for usages or practices: moral *standards"*
- "**a level of excellence**, attainment, etc. regarded as a measure of adequacy", e.g., the *standard* of care

Flavors of Standards in Clinical Research



Consensus Based Standards

Consensus

- Consensus is defined as general agreement but not necessarily unanimity

Openness

- Processes are open and transparent
- Interested parties are provided meaningful opportunities to participate in standards development

Source: OMB Circular A-119: Federal Participation in the Development and Use of Voluntary Consensus Standards and in Conformity Assessment Activities, January 2016

Consensus Based Standards

Balance

- There should be meaningful involvement from a broad range of parties, with no single interest dominating the decision-making

Due Process

- Due process shall include documented and publicly available policies and procedures

Appeals Process

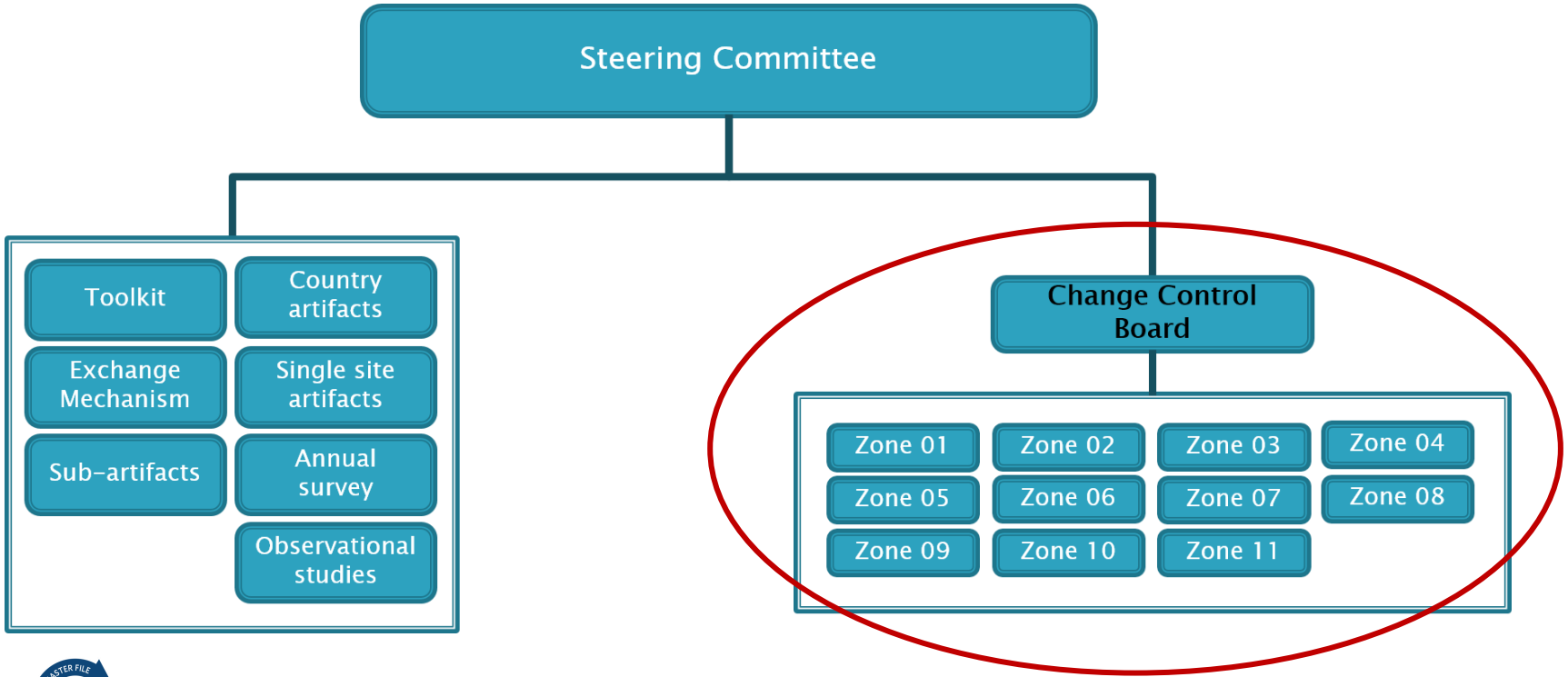
- An appeals process shall be available for the impartial handling of procedural appeals

Source: OMB Circular A-119: Federal Participation in the Development and Use of Voluntary Consensus Standards and in Conformity Assessment Activities, January 2016

Managing the TMF Reference Model

Joanne Malia - Director, Clinical Documentation Management, Regeneron Pharmaceuticals, Inc.; Member, TMF Reference Model Steering Committee

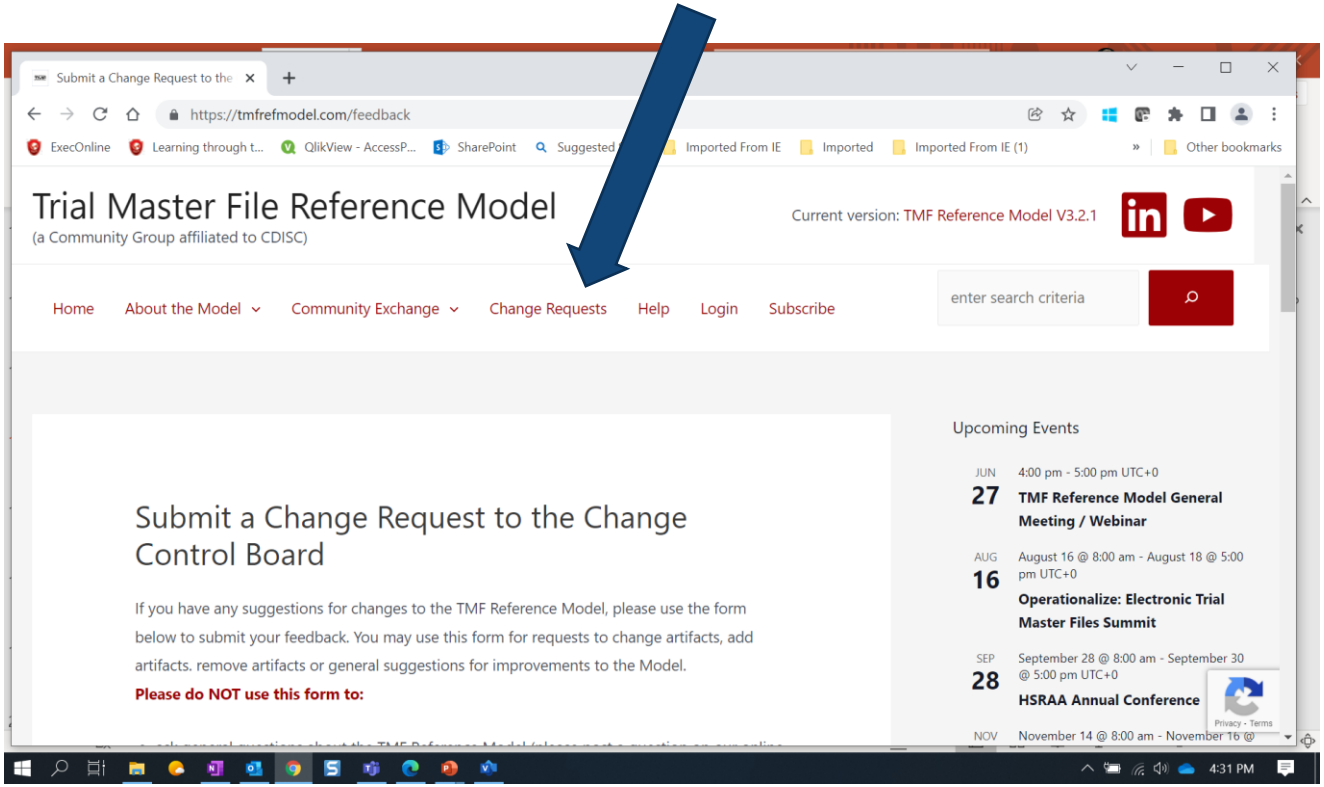
TMF Reference Model Change Overview/Framework



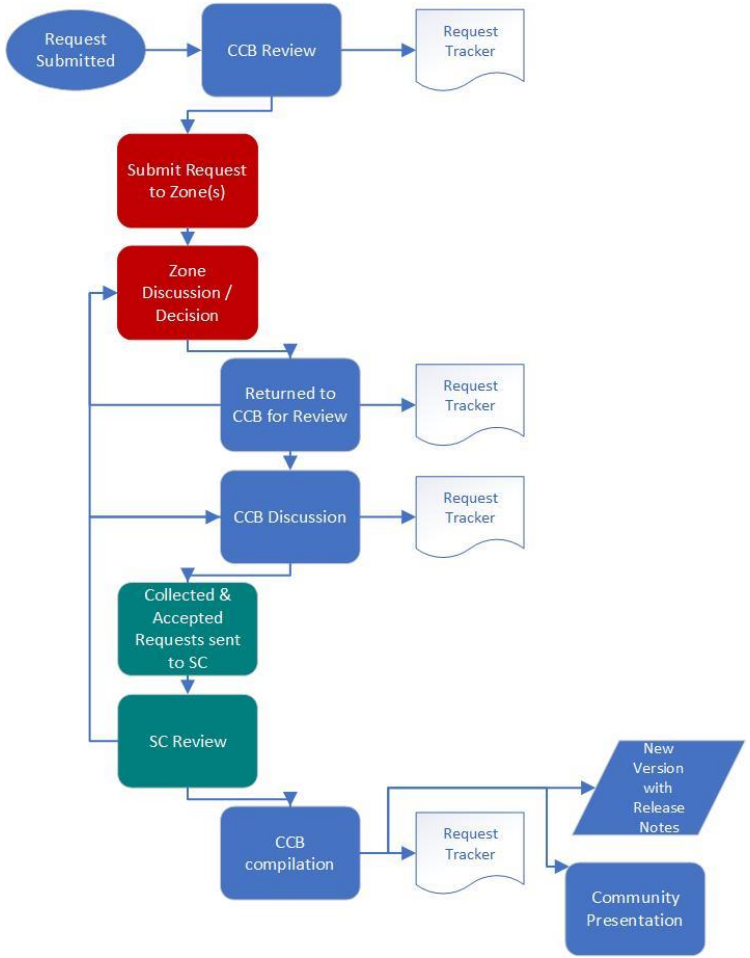
Who Controls the Versions?

- **Change Control Board Structure**
  - Kelley Robinson, Sention Therapeutics: Chair
  - Leila Ponce, Seagen Pharmaceuticals: Deputy Chair and Zone Team Liaison
- **Deliverables**
  - Meeting monthly
  - Change Control Procedure, RACI and CR Tracker
  - Reviewing and categorising all current change requests
  - Triaging all change requests to Zone Teams
  - Delivery of new versions in concert with Steering Committee

To Request a Change



Change Request Process



Version Definition

- Maintenance release e.g. v3.0.1
  - e.g. minor typographic changes, clarification, sub-artifacts
- Minor release e.g. v3.1
  - Substantial change in content but no compatibility issues e.g. additional optional column (milestones)
- Major release e.g. v4.0
  - Change likely to have compatibility issues with prior version e.g. addition/removal of artifacts

Current version is 3.2.1

Exchange Mechanism

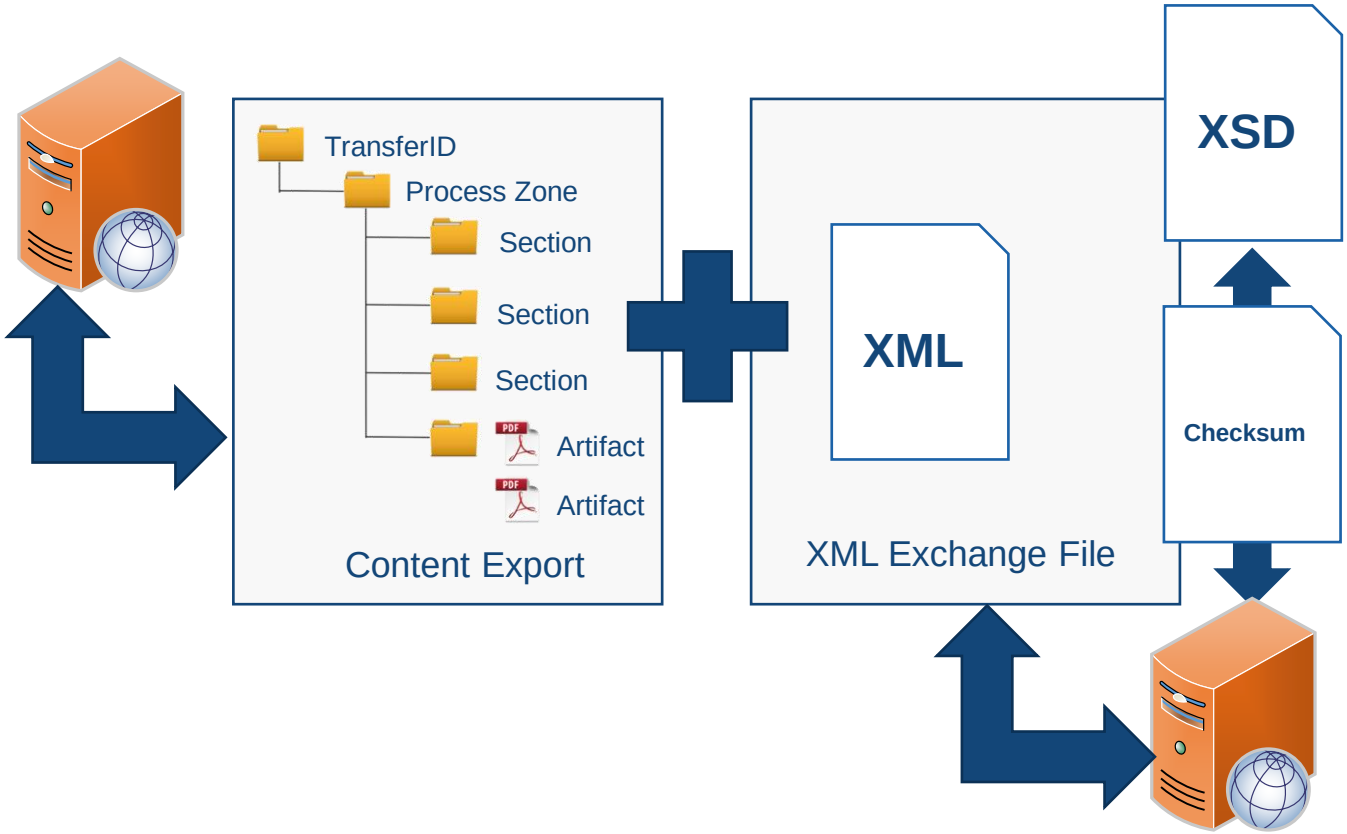
Paul Fenton – President and CEO, Montrium; Member, TMF Reference Model Steering Committee

What is the eTMF-EMS

Electronic Trial Master File – Exchange Mechanism Standard

- An extension of the TMF RM which focuses on the transfer of content, metadata, audit trail and eSig information
- A TMF metadata standard
- A mechanism for exchanging TMF content between systems
- A method for describing TMF artifacts which is comprehensible by both humans and machines

How it works


TransferID
Process Zone
Section
Section
Section
Artifact
Artifact
Content Export
XML
XML Exchange File
XSD
Checksum

How could it be used?

- **Final eTMF transfer** to sponsor from CRO for archiving
- **Interim transfer of eTMF content** to central eTMF or other trial management system
- **Migration of eTMF** content following **merger and acquisition**
- **Migration of eTMF** content following **upgrade** or change of eTMF system
- **Long term archiving** of eTMF content and associated metadata

Where are we with EMS?

- Version 1 of the specification and schema was launched
- Some vendors have started to implement
- Uptake has not been as strong as we had hoped
- We need to re-engage with the sponsor, CRO and vendor community to drive adoption
- We need guidance on how to evolve the EMS moving forward - this is where CDISC can help!

Implementation

Kathie Clark - Product Director, CTMS and eTMF, Ennov; Member, TMF Reference Model Steering Committee

Mary Emanoil – Head TMF & Registry Operations, Pfizer; Member, TMF Reference Model Steering Committee

Implementation/Transition Approach

Overview

- Core team defined for transition
  - Members from both CDISC and TMF Reference Model Steering Committee
  - Weekly meetings to define, prioritize and report on activities
- Implementation Plan created
  - Goals & Objectives - Short Term and Long Term
  - Governance
  - TMF Reference Model Maintenance & Rollover
  - Sub-teams
  - Communications

Short Term Goals

- Maintain forward momentum of TMF activities without disruption
- Develop standards governance and formalization plan for TMF under CDISC
- Develop TMF Marketing and Communication Plan
- Develop membership framework for TMF in CDISC
- Load all TMF Models into CDISC Library

CDISC Implementation Areas

- Membership – Karen Roy, Sheila Leaman, Amy Palmer
- Communications – Kathie Clark, Rhonda Facile
- Events – Mary Emanoil, Sheila Leaman
- Standards – Joanne Malia, Peter Van Reusel, Bess LeRoy
- Technology – Paul Fenton, Sam Hume

CDISC Implementation Progress

Completed

- Memorandum of Understanding signed on 6-Apr-2022
- Presentation at CDISC Board Meeting on 8-Apr-2022
- CDISC Press Release 27-Apr-2022
- TMF Summit Keynote 03-May-2022

Upcoming

- Volunteer transition
- Charter updates
- Final implementation plans for
  - Model governance
  - Technology
  - Website content
  - Events

Coming Soon—CDISC Tools for TMF RM

- Wiki
  - Team Collaboration And Development Space
  - Repository Of Draft Standards / Mechanism For Public Review
  - Project Status Updates
- Jira
  - Issue tracking tool
  - Supports comment resolution
  - Integrates with the Wiki
- Knowledge Base and FAQs
  - Curated articles and FAQS

Volunteering

Amy Palmer

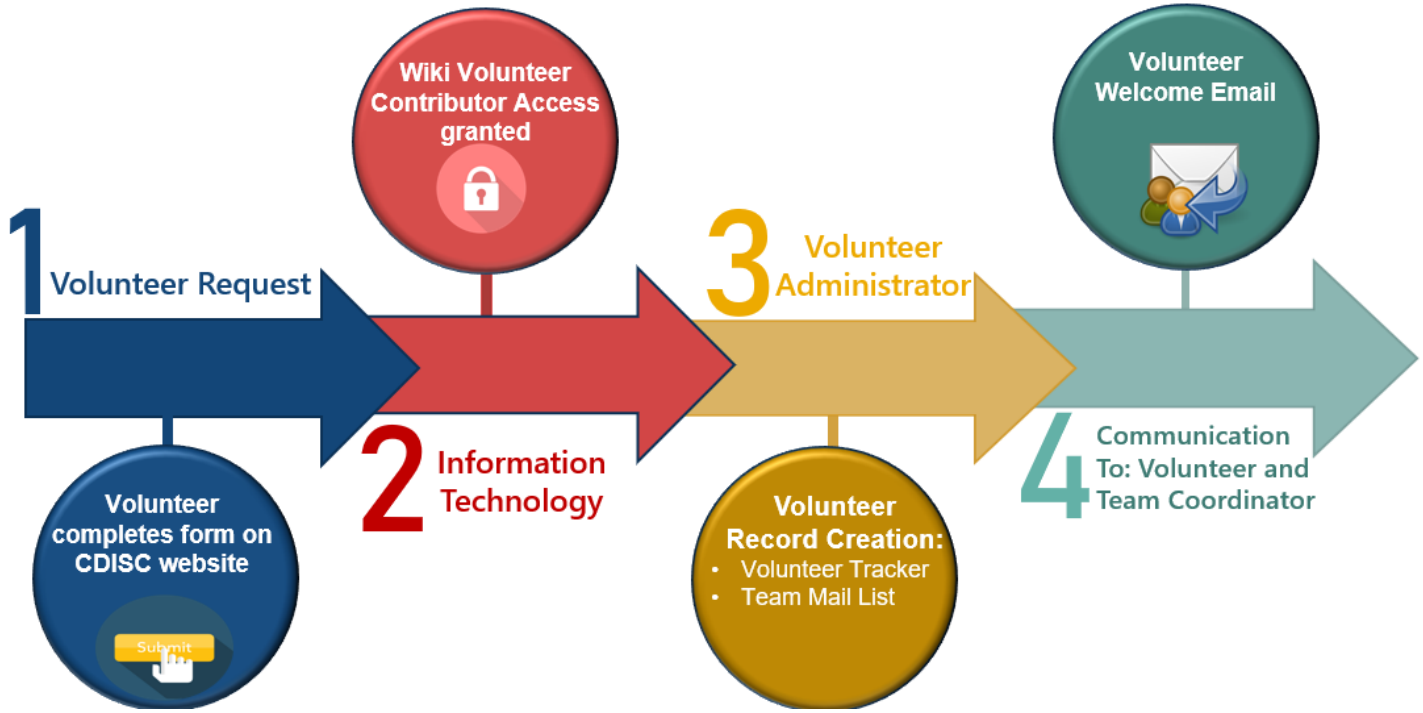
Head of Standards Development

CDISC

Registering as a Volunteer

- Navigate to https://www.cdisc.org/volunteer/tmf/form
- Review videos, CDISC policies, procedures, and CDISC and TMF charters
- Provide contact information
- Choose one or more TMF Volunteer Groups
- Submit form
- CDISC Volunteer Coordinator will begin onboarding process

Volunteer Onboarding



CDISC MEMBERSHIP

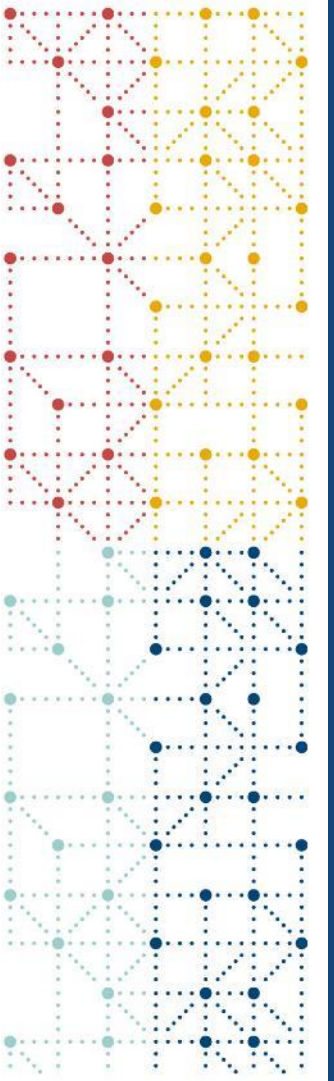
Become a Member!

Join nearly 500 member organizations that contribute to bringing clarity to data.

Already a Member?

Thank you! It is our members' support which enables us to develop standards, keeping it free and accessible to all.

Email: membership@cdisc.org



The Future

Dave Evans - President & CEO, CDISC

Thank You!