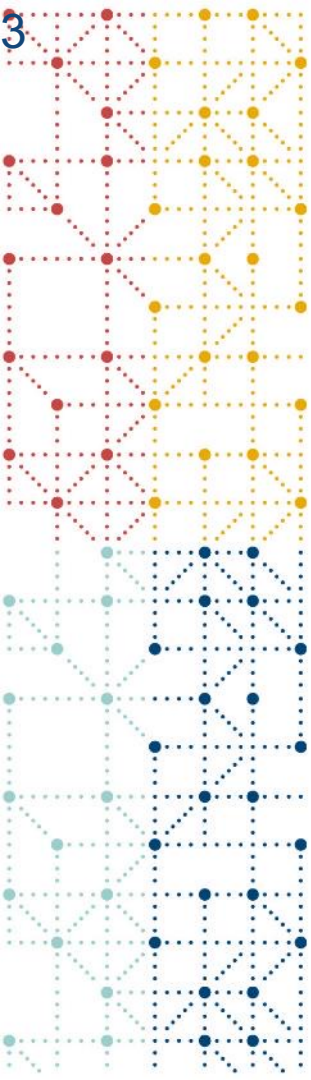
TMF Reference Model General Meeting Q3

THU 7 SEP
11:00AM – 12:30PM US ET

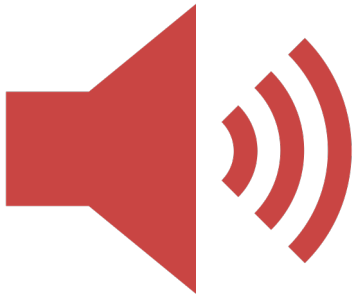
Today’s Agenda

1. Housekeeping
2. Feature Presentation
3. Q&A
4. Upcoming Learning Opportunities & Events



Housekeeping

Housekeeping



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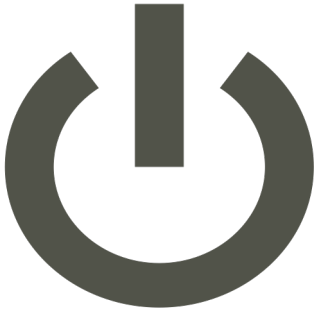
Housekeeping

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

Housekeeping



Audio Issues?

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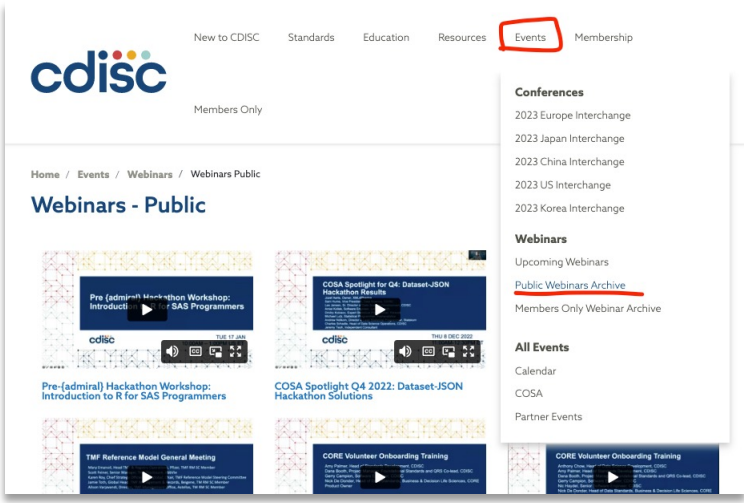
Second, check your local internet connection strength

Housekeeping



Webinar Recording

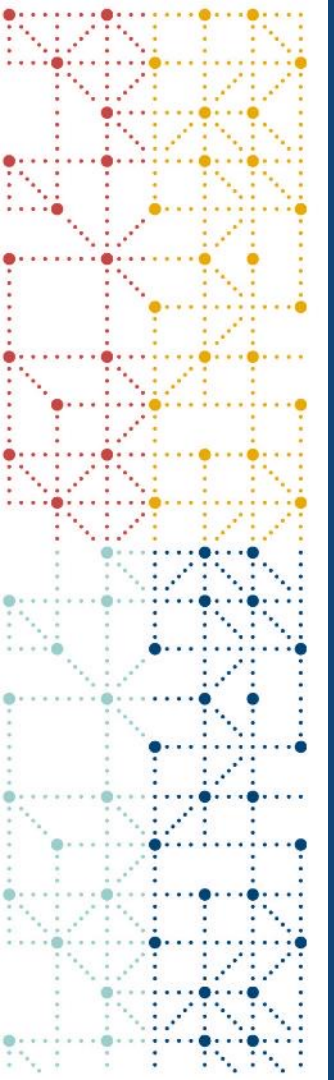
A recording of this webinar will be available in the Public Webinar Archive on the CDISC website.

The TMF Reference Model
General Meeting Presenters

- Karen Roy, Consultant, CDISC; Chair, TMF Reference Model Steering Committee
- Kate Santoro, Director, Operational Excellence Intellia Therapeutics; Vice-chair, Change Control Board
- Eldin Rammell, Head of Quality Assurance, Phlexglobal; TMF RM SC Member
- Joanne Malia, Director, Clinical Documentation Management, Regeneron; TMF RM SC Member
- Dawn Niccum, Executive Vice President, QA & Compliance, inSeption; TMF RM SC Member
- Jamie Toth, Global Head, Trial Master File Management & Records, BeiGene ; TMF RM SC Member

Agenda

- TMF Reference Model Version 3.3.1
- TMF Reference Model Website
- CDISC TMF Interchange
- ‘Fundamentals of TMF’ training course
- Risk Initiative
- MHRA Stakeholder Meeting on ICH E6 R3
- Upcoming events and Q&A



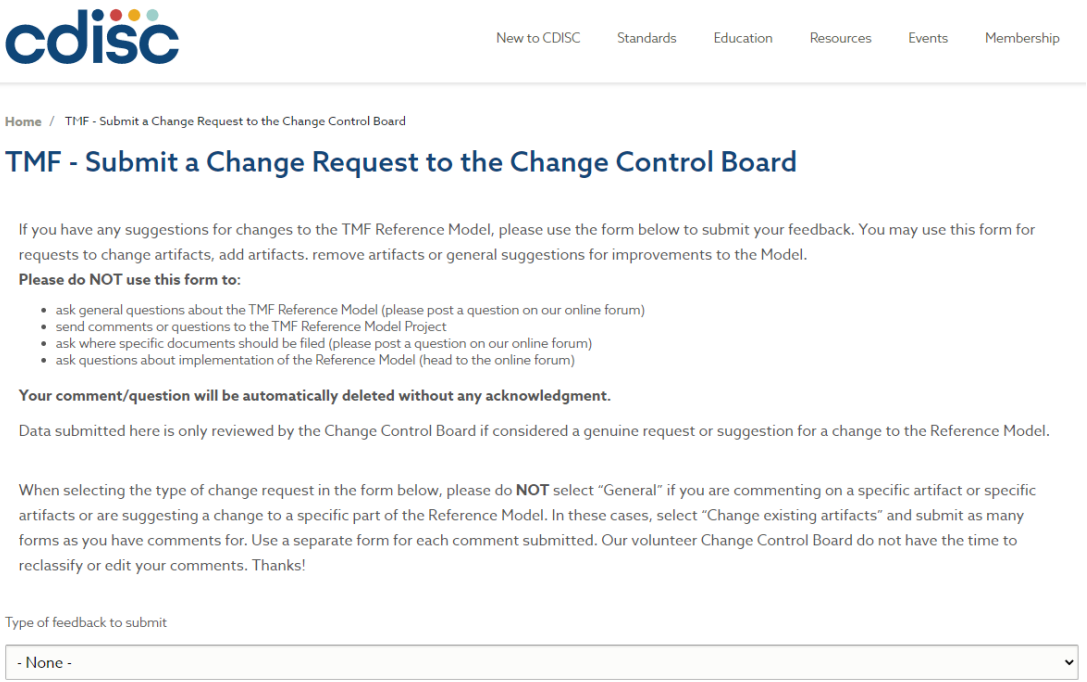
TMF Reference Model Version 3.3.1

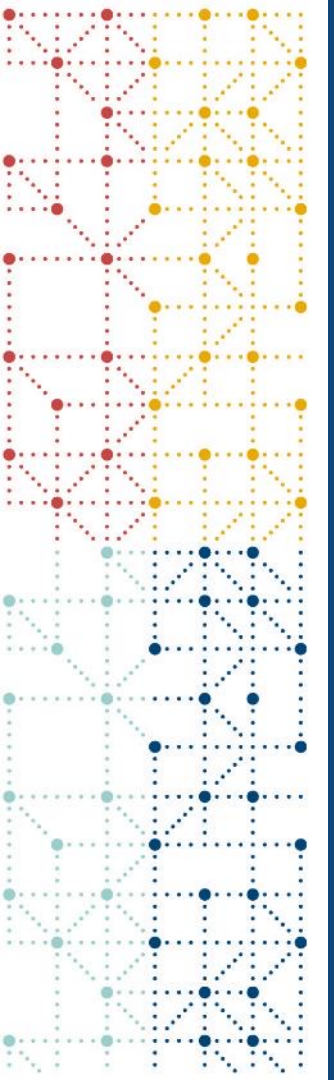
TMF Reference Model, v3.3.1

- Minor Release
  - Corrected typographical errors
    - Artifact definitions
      - 01.01.08 - Monitoring Plan
      - 01.04.04 - Trial Team Evidence of Training
    - Sub-artifact correction
      - 05.03.02 - Site Training Material
    - Glossary
  - Clarification
    - Co-monitoring visit reports
      - 05.04.05 - Additional Monitoring Activity
- Updated Version & Release Notes
  - Now available
  - TMFRefModel.com

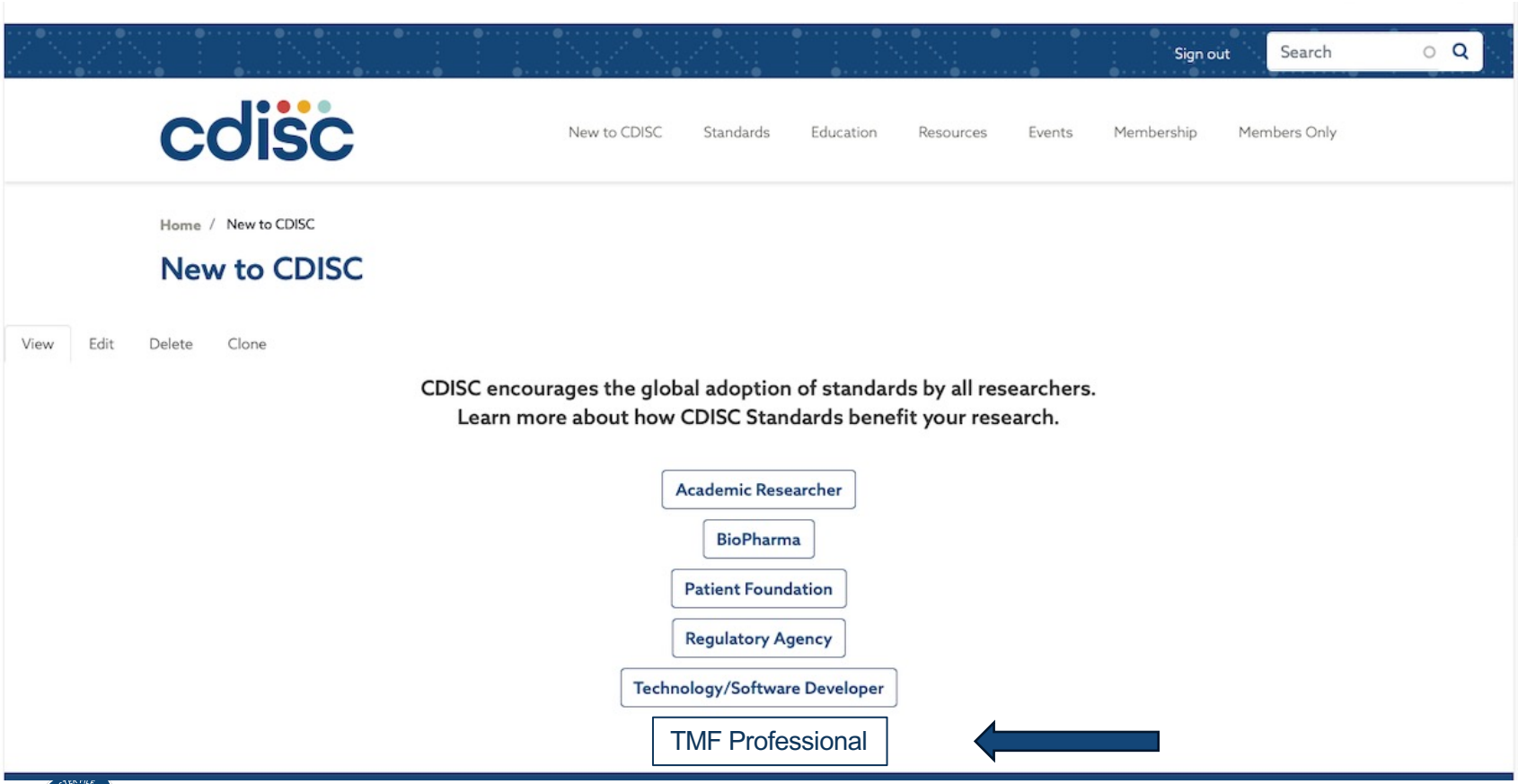
How to Make a Change Request

https://www.cdisc.org/tmf/change-request-form





TMF Reference Model Website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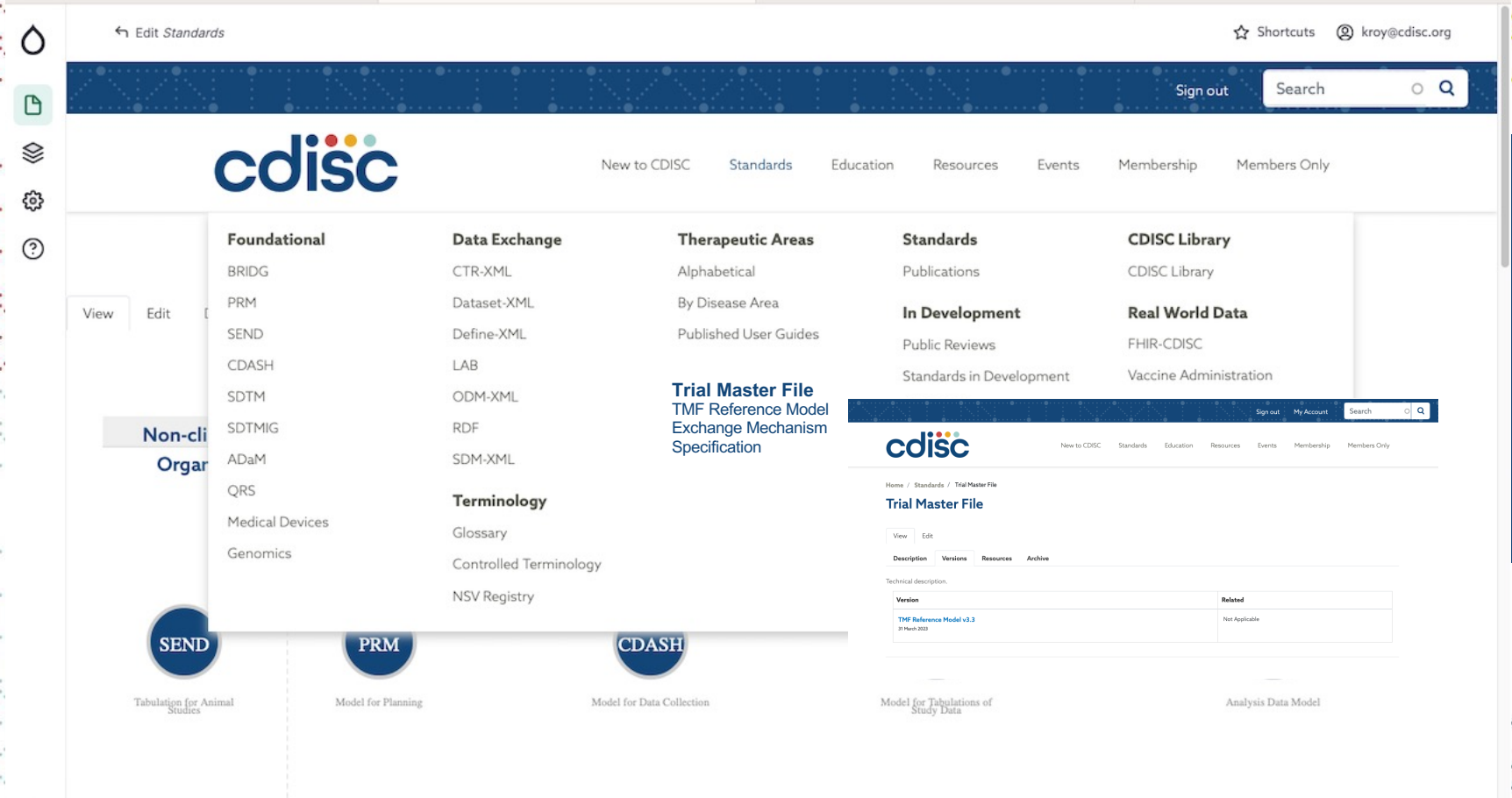
Patient Foundation
Regulatory Agency
Technology/Software Developer
TMF Professional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Alphabetical
By Disease Area
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Trial Master File
TMF Reference Model Exchange Mechanism Specification
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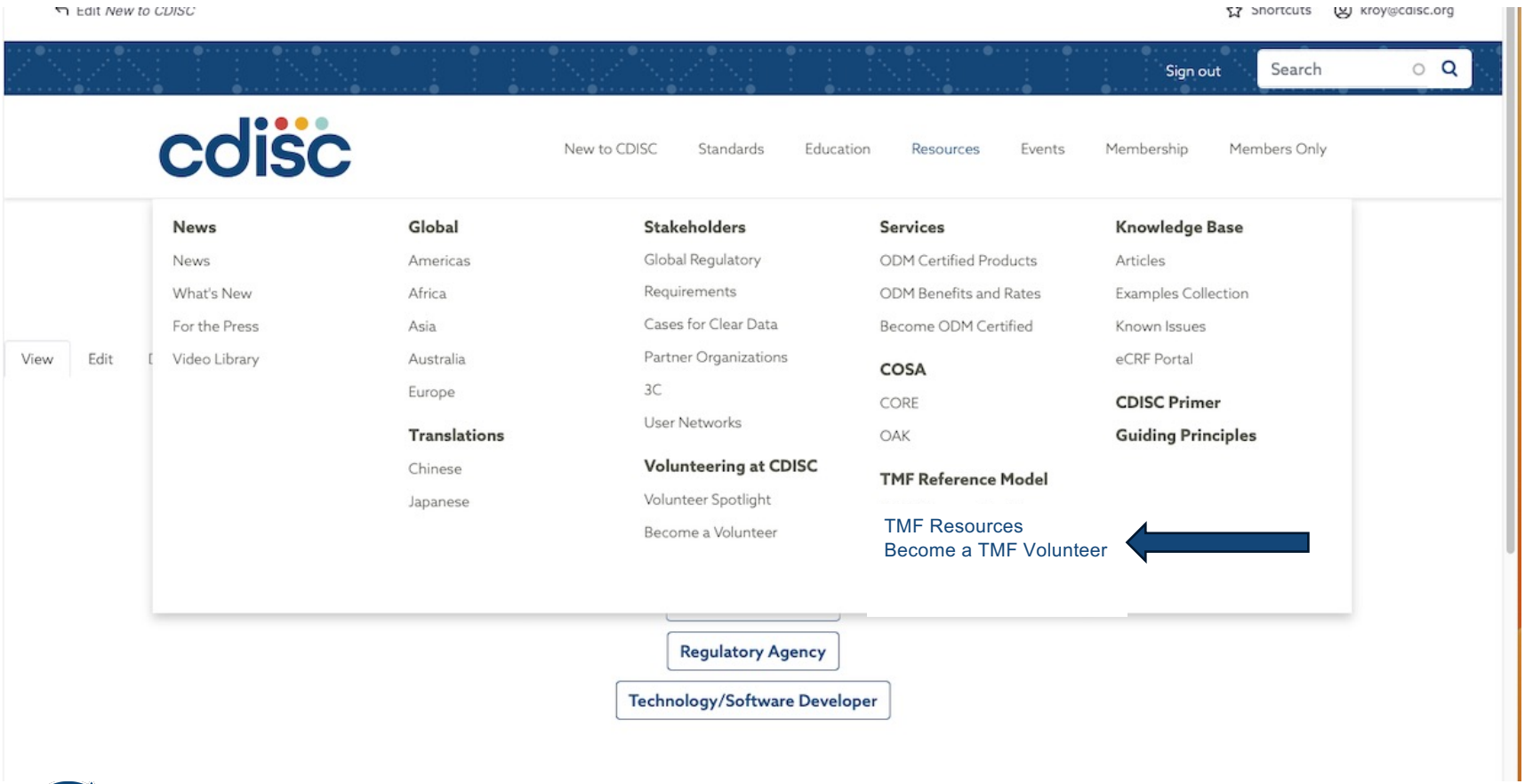
Resources
Archive
Technical description.
Version
Related
TMF Reference Model v3.3
31 March 2023
Not Applicable
SEND
Tabulation for Animal Studies
PRM
Model for Planning
CDASH
Model for Data Collection
Model for Tabulations of Study Data
Analysis Data Model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Volunteer Spotlight
Become a Volunteer
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ODM Certified Products
ODM Benefits and Rates
Become ODM Certified
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CORE
OAK
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Examples Collection
Known Issues
eCRF Portal
CDISC Primer
Guiding Principles
TMF Resources
Become a TMF Volunteer
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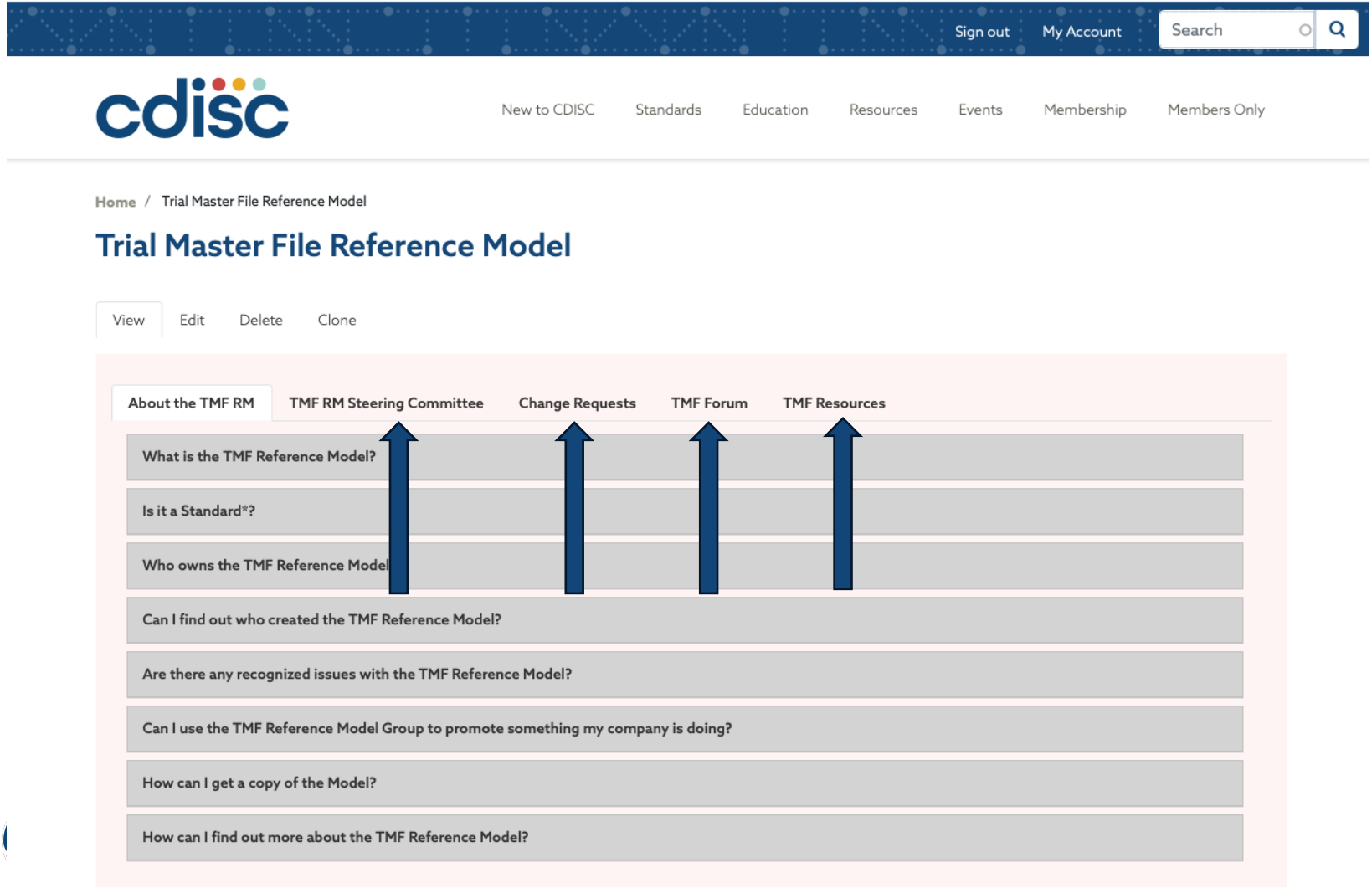
Technology/Software Developer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Trial Master File Reference Model
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About the TMF RM
TMF RM Steering Committee
Change Requests
TMF Forum
TMF Resources
What is the TMF Reference Model?
Is it a Standard*?
Who owns the TMF Reference Model
Can I find out who created the TMF Reference Model?
Are there any recognized issues with the TMF Reference Model?
Can I use the TMF Reference Model Group to promote something my company is doing?
How can I get a copy of the Model?
How can I find out more about the TMF Reference Model?

Trial Master File Reference Model

View | Edit | Delete | Layout | Revisions | Clone | Translate

About the TMF RM | TMF RM Steering Committee | Change Requests | TMF Forum | TMF Resources

Surveys | TMF Plan | eMail Management | Quality and Inspections | Metrics | eTMF Selection | Other TMF Tools | Real World Studies

EU CTR

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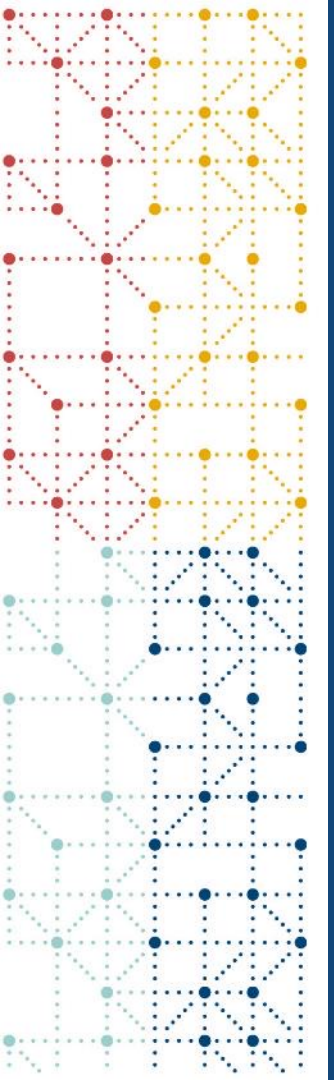

CDISC TMF Interchange

NEW ANNUAL CONFERENCE

2023 CDISC TMF INTERCHANGE

28-29 SEPTEMBER
BALTIMORE

Sponsors

Sponsors

Ruby

Just in Time GCP

Ruby

inSeption GROUP

Sapphire

PHLEXGLOBAL

A PHARMALEX Company

Sapphire

Daelight SOLUTIONS

Sapphire

TRANSPERFECT LIFE SCIENCES

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Exhibitors


Exhibitors
Just in Time GCP
PHLEXGLOBAL
A PHARMALEX Company
Daelight
SOLUTIONS
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arkivum
montrium
rednucleus
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Veeva

Sponsoring and Exhibiting (3 remaining)

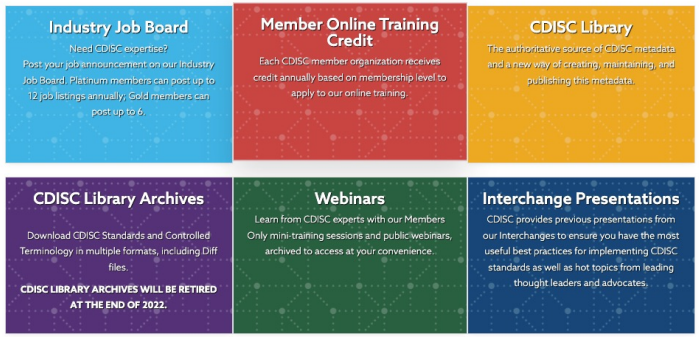
- Exhibitor pricing reduces with tier of company membership
- Sponsor pricing reduces if your company BECOMES a member:

10%

15%

Why Become a Member?

- To ensure the CDISC standards remain open and free
- To support CDISC in the development and maintenance of global standards
- To work with the CDISC community and be a voice in the development of clinical research standards
- To impact the development of regulatory requirements for submissions
- To access members only resources and benefits
- To gain visibility in the marketplace



NEW MEMBERSHIP RATES (US$) - Effective 1 January 2022

Total Number of Employees in Organization	GOLD Member Annual Fee	PLATINUM Member Annual Fee	First Year PLATINUM Member One-Time Contribution
1-19	$1,690	$4,500	Annual fee + $4,500
20-99	$4,500	$7,315	Annual fee + $7,315
100-999	$9,570	$11,820	Annual fee + $11,820
1,000-9,999	$24,200	$27,015	Annual fee + $27,015
10,000-24,999	$32,640	$36,580	Annual fee + $36,580
25,000-49,999	$39,395	$47,270	Annual fee + $47,270
50,000 +	$55,445	$65,280	Annual fee + $65,280

Academic Institutions, Government Agencies, Non-Profit Organizations, please contact: **membership@cdisc.org** for rates

Agenda

Dave Evans, Karen Roy, CDISC
Calvert Ballroom / Salon C

9:00 - 9:20
CDISC TMF Welcome
Karen Roy, CDISC

9:20 - 10:10
Keynote Presentation: How TransCelerate Initiatives Impact the TMF
Dr. Rob DiCicco, TransCelerate BioPharma Inc.

10:10 - 11:00
FDA: Where Does the TMF Fit In?
FDA Speaker Invited

Agenda

11:30 - 13:00

Session 2: Regulations and Inspections

Laura Naranjo, Daiichi Sankyo

Calvert Ballroom / Salon C

11:30 - 12:15

Panel: ICH E6 (R3) - Analyzing the Impact on the TMF

Moderator: Donna Dorozinsky, Just in Time GCP

12:15 - 13:00

Panel: Inspections from the View of All Stakeholders

Moderator: Vittoria Sparacio, Novartis

Agenda

14:00 - 15:30
Session 3A: TMF Reference Model as a Tool

14:00 - 15:30
Session 3B: TMF Reference Model Becoming a Standard

15:30 - 16:00
Afternoon Break

16:00 - 17:30
Session 4A: TMF Health

16:00 - 17:30
Session 4B: TMF Interoperability

17:40 - 18:45
Session 5: Interactive Session

Evening Event

Agenda

08:30 - 09:20

Session 6: Opening Innovation Panel

Karen Roy, CDISC

Calvert Ballroom / Salon C

8:30 - 9:20

Panel: Practical Ways to Leverage Automation and AI to Reduce Effort While Increasing Compliance in TMF Management

Moderator: James O'Keefe, Astrix

Agenda

09:30 - 10:30
Session 7A: Technology in TMF Management

09:30 - 10:30
Session 7B: TMF Culture and Engagement

10:30 - 11:00
Morning Break

11:00 - 12:30
Session 8A: Sponsor-CRO Co-Operation

11:00 - 12:00
Session 8B: End of Study

12:05 - 13:45
Session 9: Engagement Across Sponsor, CROs, and Vendors

12:45 - 13:45
Session 10: Interactive Session

13:45
Final Lunch

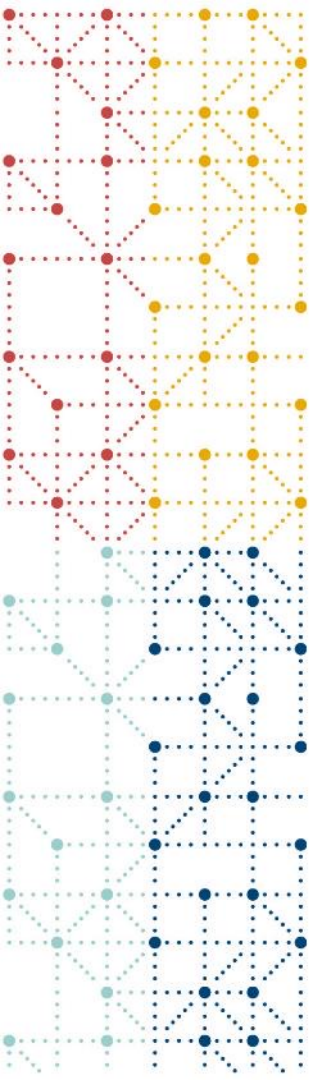
CDISC TMF Interchange

- First CDISC TMF Interchange
- 125 registrants thus far – target 150!
- Chairs:
  - Karen Roy
  - Jamie Toth
  - Paul Fenton
- First of many more to come! EU CDISC Interchange in Berlin in April 2024

2023 CDISC TMF Interchange

Baltimore, Maryland
28-29 September 2023

https://www.cdisc.org/events/interchange/2023-cdisc-tmf-interchange



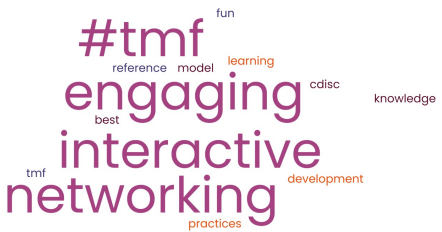
‘Fundamentals of TMF’ training course

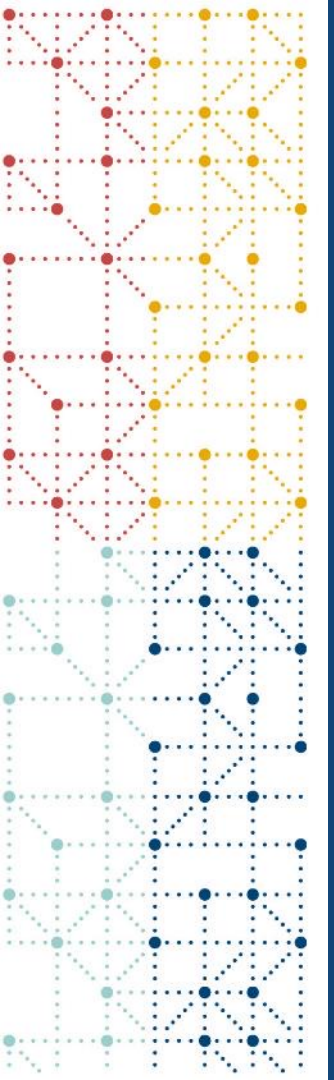
Fundamentals of the TMF Reference Model

- First in-person course – a full day of too much fun!
- 12 registrants thus far – maximum 25
- Instructors:
  - Lisa Mulcahy
  - Jackie Morrill
  - Jenn Stamper
  - Dawn Niccum
- CEUs will be offered
- First of many more to come!

Course Agenda

- History & Basics of the Model
- What Is a TMF?
- Managing the TMF
- People, Process, & Technology
- Regulations & Developing
- TMF Repositories, Index & Plan
- TMF Health
- Timeliness, Completeness, Quality
- Preparing, Transferring, Long-term Management
- Archiving
- TMF Oversight
- Outsourcing & Ensuring an Inspection Ready TMF





Risk Initiative

New initiative !

- **Co-leads:** Joanne Malia (Regeneron) & Eldin Rammell (Phlexglobal)
- Project objective:
  - Recent regulatory guidance encourages adoption of a **risk-based approach** to the design, conduct and management of clinical trials
  - Meaning of "risk-based approach" is
    - Not well understood as a concept
    - Interpreted differently across industry
    - Not well understood in the context of TMF management
  - Project aims to:
    - Encourage improved understanding
    - Encourage a more consistent approach

How?

- Project team will:
  - Identify where a risk-based approach could be taken across the TMF life-cycle
  - Identify potential methodologies for risk management e.g.
    - Risk scoring
    - Documenting risk
    - Adapting TMF-related activities based on risk
    - Tools and techniques
  - Differentiate between
    - A suggestion/option for consideration;
    - A recommended approach, based on the team's experience and expertise; and
    - A requirement that is specifically identified in a published regulation or guideline

Next steps

- Look out for a "call for volunteers"

- Respond if you
  - Have an interest in the topic **and**
  - Have some experience, skill or knowledge to contribute **and**
  - Have the time to attend meetings and follow through on actions

- The project will likely have sub-teams..... so sub-team leaders needed too!

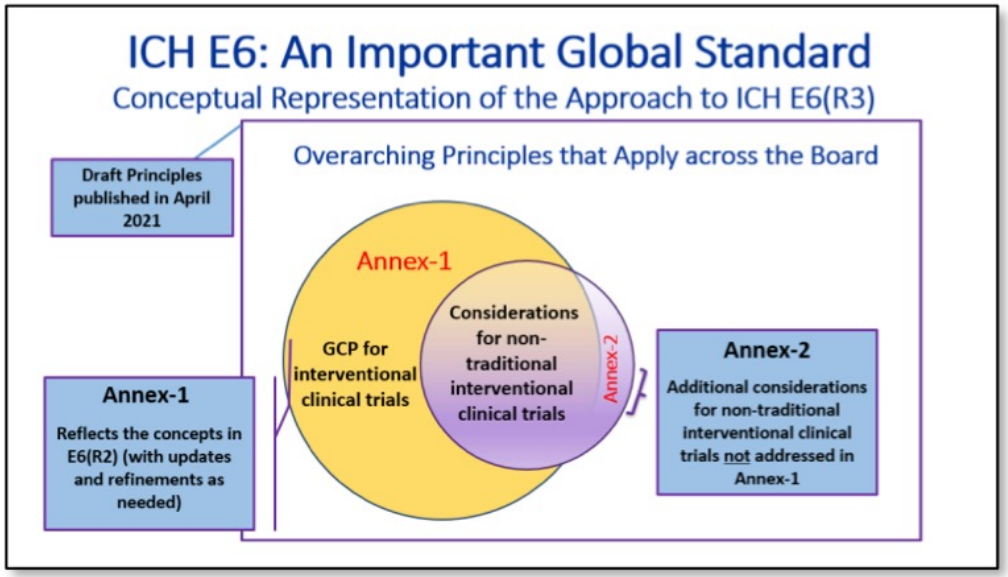
MHRA Stakeholders Meeting on ICH E6 R3

Karen Roy and Jamie Toth

ICH E6 R3 – 'Risk Proportionate GCP'

Quality by Design

Risk-based approach and proportionality



Guidance throughout the trial – concept, design, conduct, analyze, (archive)

Flexible framework

Applicable to all human trials

Support advances in CT designs

Remain relevant as technology evolves

Succinct – Details in the training

Why ICH E6 R3???

- Lack of flexibility complaints by Research organizations in 22 countries
- Unable to use guidance for trials outside traditional scope
- No coverage of clinical systems
- Data governance missing
- Too much detail in areas

MHRA Stakeholder Feedback – 18th July 2023

- MHRA now a full regulatory member of ICH (previously observer through PICS) – since May 2022
- Significant Clinical Trial focus following independent report – Corporate plan for 2023 to 2026 in place
- UK Medicines for Human Use Regulation 2004 will be updated – principles will become a legal requirement
- Full compliance expected if trial is supporting Marketing Authorisation
- Compliance with principles for all trials involving an IMP

Karen Roy, represented CDISC TMF Reference Model

Jamie Toth, represented Health Sciences Records & Archives Association (HSRAA)

ICH E6 (R3)

- Draft endorsed under Step 2 (19-May-2023)
- Public consultation was open until 05-Sep for most Health Authorities
- Current guideline replaced with:
  - Principles (drafted March 2021)
  - Annex 1 (GCP for Interventional trials, similar content to current guideline)
  - Glossary
  - Appendix A: Investigator Brochure
  - Appendix B: Protocol and Amendments
  - **Appendix C: Essential records**

Overall Changes

- Significant re-organization to be much more logical
  - Extended principles of GCP
    - New e.g. Periodic review of safety information, Transparency
    - Updated e.g. Informed consent and legal representative
  - Four key sections: IRB/IEC, Investigator, Sponsor and Data Governance (new! applicable to Investigator and Sponsor)
  - IB, Protocol, Essential Records as Appendices
- Subject replaced by Participant
- Document replaced by Record (to include data!)
- CRO replaced by Service Provider
- Risk is a theme throughout
- Read Andy Fisher's excellent article:
  https://mhrainspectorate.blog.gov.uk/2023/05/26/ich-e6-r3-good-clinical-practice/

Investigator Impact for TMF

- The investigator/institution should maintain the trial records as specified in Appendix C (2.12.11) – but it doesn't say what in Appendix C
  - Will Investigators be expected to keep everything?
- The investigator/institution should have control of all essential records generated by the investigator/institution before, during and after the trial – but what about Sponsor provided eISFs? Investigator can only be responsible for what they can influence
  - The Investigator should take measures to prevent accidental or premature destruction of these records.
  - The Investigator is responsible for data integrity
- No longer required for CV to be supplied – just proof the Investigator is qualified
- Trial specific training and delegation log completion can be risk-based i.e. not needed if activities = routine care
- New technologies for Informed Consent, and reducing re-consent requirements

Sponsor Impact for TMF

- Sponsor appointed service providers for Investigator activities – Investigator retails decision and responsibility. To be reflected in agreements
- Service provider replaces CRO to broaden, and more stringent guidance on selection and oversight of them. Agreements to be signed before any activities
- Significant focus on Oversight – more documentation?
- Risk is a key focus – identification, control, communication, review and reporting
- Remote site visits or centralized monitoring included
- Periodic safety reporting impacting IB updates and proportionality

Data Governance Impact on TMF

- Data life cycle is defined (although archiving is missing!)
- Review of data and metadata – NOT making sure the audit trail is accurate (4.2.3)
  - Procedures for review of trial-specific data, audit trails and other relevant metadata should be in place. It should be a planned activity, and the extent and nature should be adapted to the individual trial and adjusted based on experience during the trial.
- Requirement for validation of data transfers to ensure no data has been lost due to the lack of adequate transfer processes
- Detailed validation expectations, including technical support
- Requirements impacts all systems used during clinical trials

Essential Records: ICH E6 R2 vs ICH E6 R3

R2

- Section 8 covers TMF Records
- Refers to TMF as a single repository
- No specific list of criteria to decide if a document is TMF
- Table of minimum essential documents split before, during and after clinical phase
- Clear indication of what is required in Investigator TMF

R3

- Appendix C covers TMF Records
- Refers to TMF being one of multiple repositories holding TMF records
- Detailed criteria for deciding if a record is essential
- Table of records: Table 1: Essential Records for all Trials and Table 2: Potential Essential Records
- No indication as to what is required in Investigator TMF (ISF)
- Third Party documents are are not even mentioned

What else does R3 include for TMF?

- Proportional approach
- Updated approach to management of TMF
- Incorporates electronic systems and signatures
- Clarifies original version (or certified copy) should be retained by responsible party; addresses version control
- Access of records during the trial across Sponsor and Investigator systems acceptable
- TMF retention timelines in accordance with local regulations

So what do HSRAA and TMF RM Committees think??

LOSE THE TABLES IN APPENDIX C!

WHY??

- New tables may mean users replace CDISC TMF RM with new record types and new numbering.
  - TMF RM IS THE DEFACTO STANDARD
- Essential and Potential Essential Records may mean everyone includes everything
- The Essentiality Criteria are excellent for decision making (although a few missing like oversight and risk) and should be the basis to define a TMF
- The CDISC TMF RM should be part of the training

K J

So what do HSRAA and TMF RM Committees think??

- It states that the Investigator / institution should maintain trial records as specified in Appendix C, but Appendix C does not give any indication as to what is key for the Investigators. This will lead to the Investigators being expected to keep everything
- Risk is mentioned throughout, but no acceptance criteria for risk assessments
- R3 implies any computerised systems used in clinical trials, which is very broad. Need clarification that limited to systems used directly in the conduct of a clinical trial to produce data or records
- R3 states that clinical trial-related records should be retained - that is too broad from an archiving perspective. Need clarification to cover TMF and specific data / records

Upcoming Events

Upcoming Events

- 27th to 29th September, Baltimore: CDISC TMF Interchange
- 3rd to 5th October, Dublin: HSRAA Conference
- 14th to 16th November, London: EU TMF Summit
- 24th to 25th April, Berlin: ***CDISC EU TMF Interchange!***

- General Meetings:
  - 5th December

CDISC Events in 2023

Our Categories

Beijing

Baltimore

Falls Church

Sulzbach

Seoul

Balatonfüred

Marlborough

Dublin

Paris

Brussels

CDISC Newcomers

CT

SEND

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CDISC Education Training Courses

- Information available at: www.cdisc.org
- Register at: https://learnstore.cdisc.org/
- Contact us at: training@cdisc.org

UPCOMING TRAININGS

SCAN ME

VIRTUAL

Dates throughout September and October

IN-PERSON

Baltimore, MD | 27 September

Falls Church, VA | 15-17 October

Sulzbach, Germany | 13-16 November

Seoul, South Korea | 11-12 December

*CEUs available for trainings, not including CDISC for Newcomers.

CDISC for Newcomers
5 September
9:00AM-12:00PM US ET

Define-XML
25-29 September
9:00AM-12:00PM US ET

CDASH Fundamentals
6-8 September
9:00-12:00 US ET

CDASH Advanced Topics
18-20 September
9:00-12:00 US ET

SDTM Theory & Application
11-15 September
9:00AM-12:30PM US ET

SDTM Advanced Topics
25-29 September
9:00AM-12:00PM US ET

ADaM Core Theory & Application
18-20 September
9:00-12:30 US ET

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2-5 October
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Opening for Questions (and hopefully Answers!)

Thank you

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