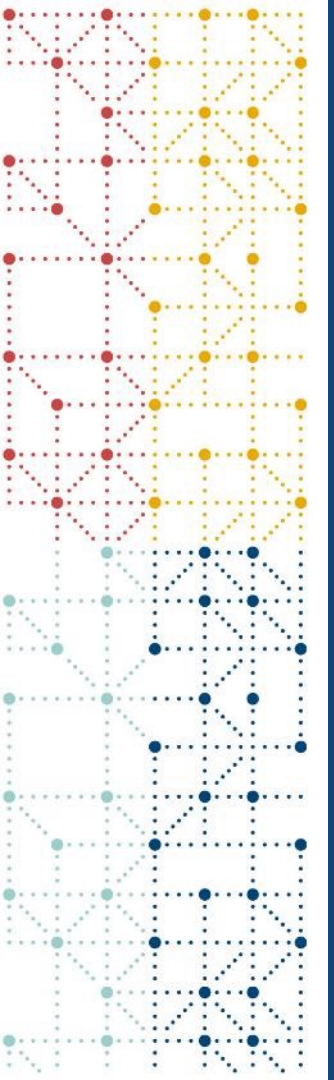
The TMF Reference Model General Meeting May 2023

Presenters:

- Karen Roy, Consultant, CDISC; Chair, TMF Reference Model Steering Committee
- Paul Fenton, CEO, Montrium; TMF Reference Model Steering Committee Member
- Leila Ponce, Sr Manager, Regional Clinical Trial Operations, Clinical Systems & Records Management, Seagen; Chair, Change Control Board
- Kate Santoro, Director, Operational Excellence Intellia Therapeutics; Vice-chair, Change Control Board
- Jamie Toth, Global Head, Trial Master File Management & Records ; TMF RM SC Member
- Kathie Clark, Product Director, CTMS and eTMF, Ennov; TMF RM SC Member
- Eldin Rammell, Head of Quality Assurance, Phlexglobal; TMF RM SC Member
- Todd Tullis, Director of Product Management , Veeva; TMF RM SC Member

Agenda

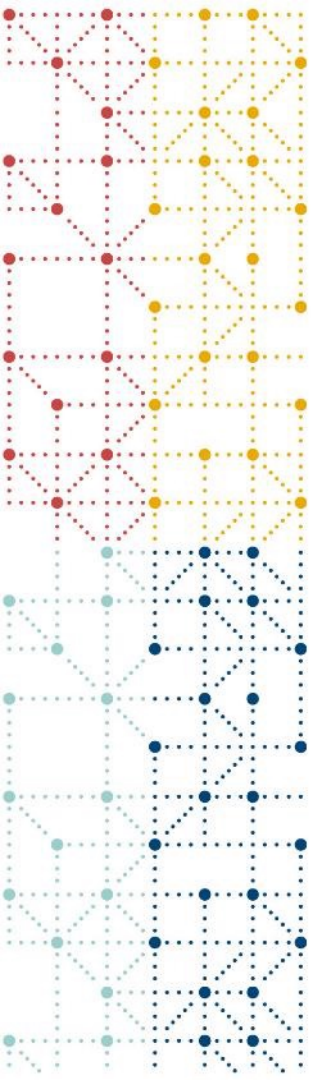
- 2023 Steering Committee
- CDISC Transition and New Initiatives
- TMF Reference Model Version 3.3
- Change Request Process
- Highlights from TMF Summit and EU CDISC Interchange
- ICH M11 and how it affects the future of TMF
- Regulatory Updates across the Globe
- Upcoming events and Q&A



2023 Steering Committee

Steering Committee Election Results

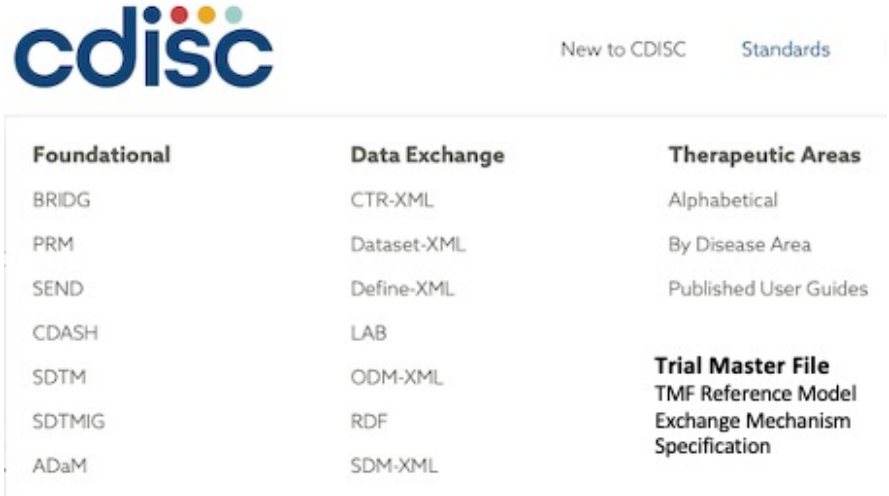
- 13 candidates nominated
- Re-elected:
  - Lisa Mulcahy, Mulcahy Consulting
  - Jamie Toth, BeiGene
  - Todd Tullis, Veeva
  - Donna Dorozinsky, Just in Time GCP
  - JP Miceli, Advanced Clinical
- Newly elected:
  - Eldin Rammell, Phlexglobal - Introduction



CDISC Transition and New Initiatives

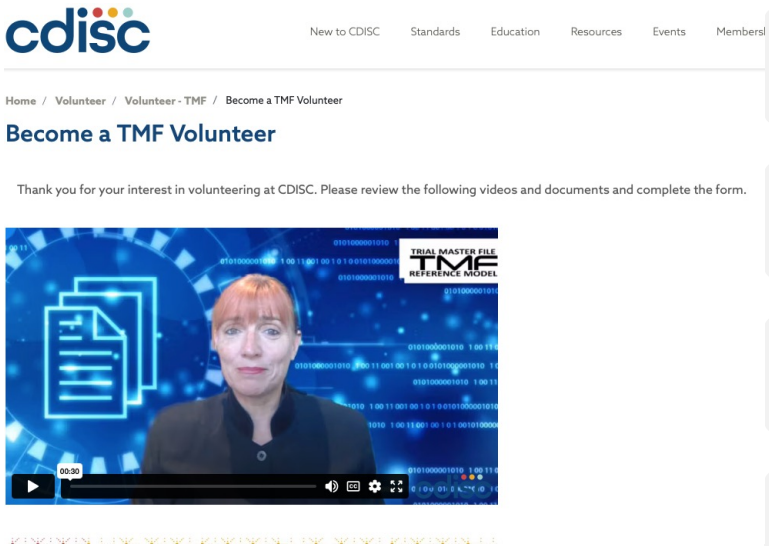
Website Transition – It is happening!!

- TMF Reference Model and Exchange Mechanism Specification will be on the Standards page



- There will be a separate TMF page with all the Resources

Reminder how to 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

https://www.cdisc.org/volunteer/tmf/form

The NEW Initiatives

- The Standards Team – Paul Fenton leading

- The Education Team – Dawn Niccum leading

- The CDISC TMF Interchange – We need you!

NEW ANNUAL CONFERENCE

2023 CDISC TMF INTERCHANGE

28-29 SEPTEMBER
BALTIMORE

The CDISC TMF Interchange

Program Development

- Program committee
- Call for abstracts deadline 31-May!!
- Submission review based on merit

Abstract Acceptance Criteria

- Potential to educate audience
- Anticipated audience interest
- Timeliness of topic
- Uniqueness of the topic and approach
- Vendor neutrality

Exhibiting and Sponsoring

- Exhibitor pricing reduces with tier of membership
- Sponsor pricing reduces if you BECOME a member:

10%

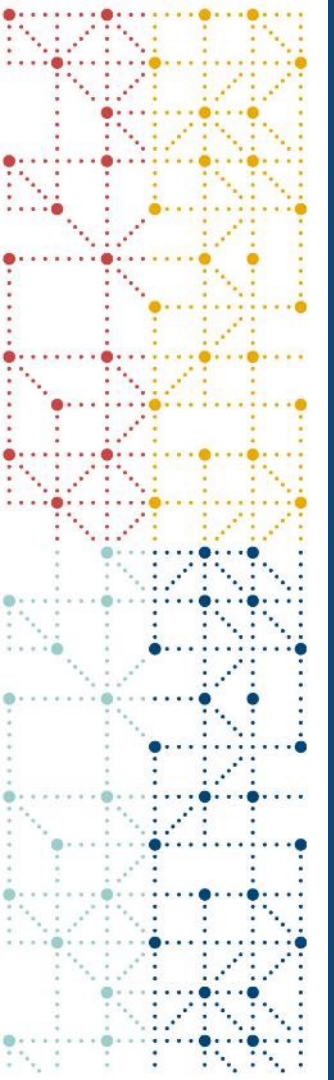
15%

Education Team

- Purpose
  - Oversee the development of training courses through CDISC to increase and support the knowledge of the TMF RM.
- Trainings
  - Format: in-person, webinars, and eLearning
  - CEUs will be available
  - Supported by CDISC's education team
- First Deliverable:
  - In-Person Workshop at the CDISC TMF Interchange – 27 Sep

Standards Team

- Purpose
  - To oversee the move of the TMF Reference Model from a de-facto standard to a formal standard
- Four Initiatives
  1. Migration of TMF RM to CDISC Library
  2. Evolution of EMS/Interoperability
  3. TMF RM Standard Alignment and Management
  4. Controlled terminology and M11 protocol mapping
- Next Steps
  - All volunteers who selected Standards or EMS were surveyed (79)
  - 54 replied – 38 volunteered
  - Groups formed …



TMF Reference Model Version 3.3

TMF Reference Model, version 3.3

- Final approval – 31 March 2023
- Minor update
  - Changes to the Overview Tab
    - Correct references to CDISC
  - Changes to artifact definitions
  - Changes to document filing levels
  - Additional new sub-artifacts
  - Device Study Changes:
    - Additional ISO 14155 reference column (Column K)

Changes to Artifact Definitions

- 01.01.03 - Quality Plan
- 02.01.05 - Financial Disclosure Summary
- 04.03.01 - Notification to IRB or IEC of Safety Information
- 05.02.10 - Financial Disclosure Form
- 05.03.02 - Site Training Material
- 05.04.01 - Subject Log
- 05.04.05 - Additional Monitoring Activity

Changes to Document Level

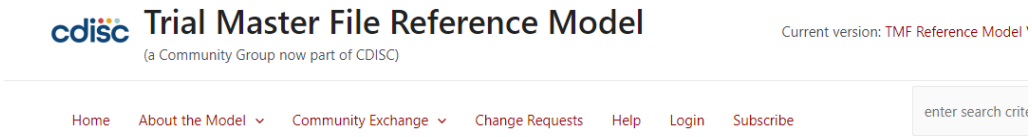
- 05.01.01 - Site Contact Details
- 05.02.13 - Indemnity
- 10.05.02 - Tracking Information

New Sub-artifacts

- 02.01.03 - Protocol Synopsis
- 02.03.01 - Clinical Study Report
- 04.03.01 - Notification to IRB/IEC of Safety Information
- 05.03.02 - Site Training Material
- 05.04.02 - Source Data Verification
- 05.04.03 - Monitoring Visit Report
- 05.04.05 - Additional Monitoring Activity
- 06.01.09 - IP Quality Compliant Form
- 06.02.03 - IP Verification Statements
- 06.02.04 - Certificate of Analysis

TMF Reference Model, v3.3

- Tab 1 – v3.3 - Clean
- Tab 2 – v3.3 - Markup
  - Shows in red text all changes made
- Release Notes
  - Available as separate document
  - Details all changes made to the RM
- Where to Find?
  - Tmfrefmodel.com - top right corner: Current version: TMF Reference Model V3.3



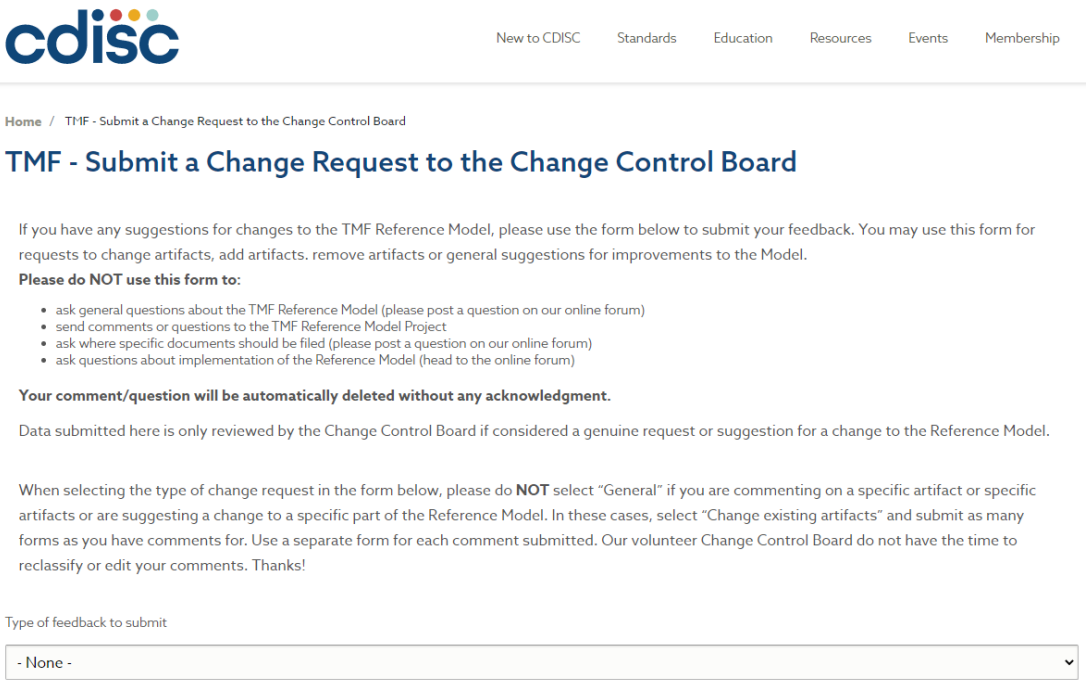
  - Future – The RM will be moved to the CDISC website
    - TMF Reference Model Home

Special Thank You!

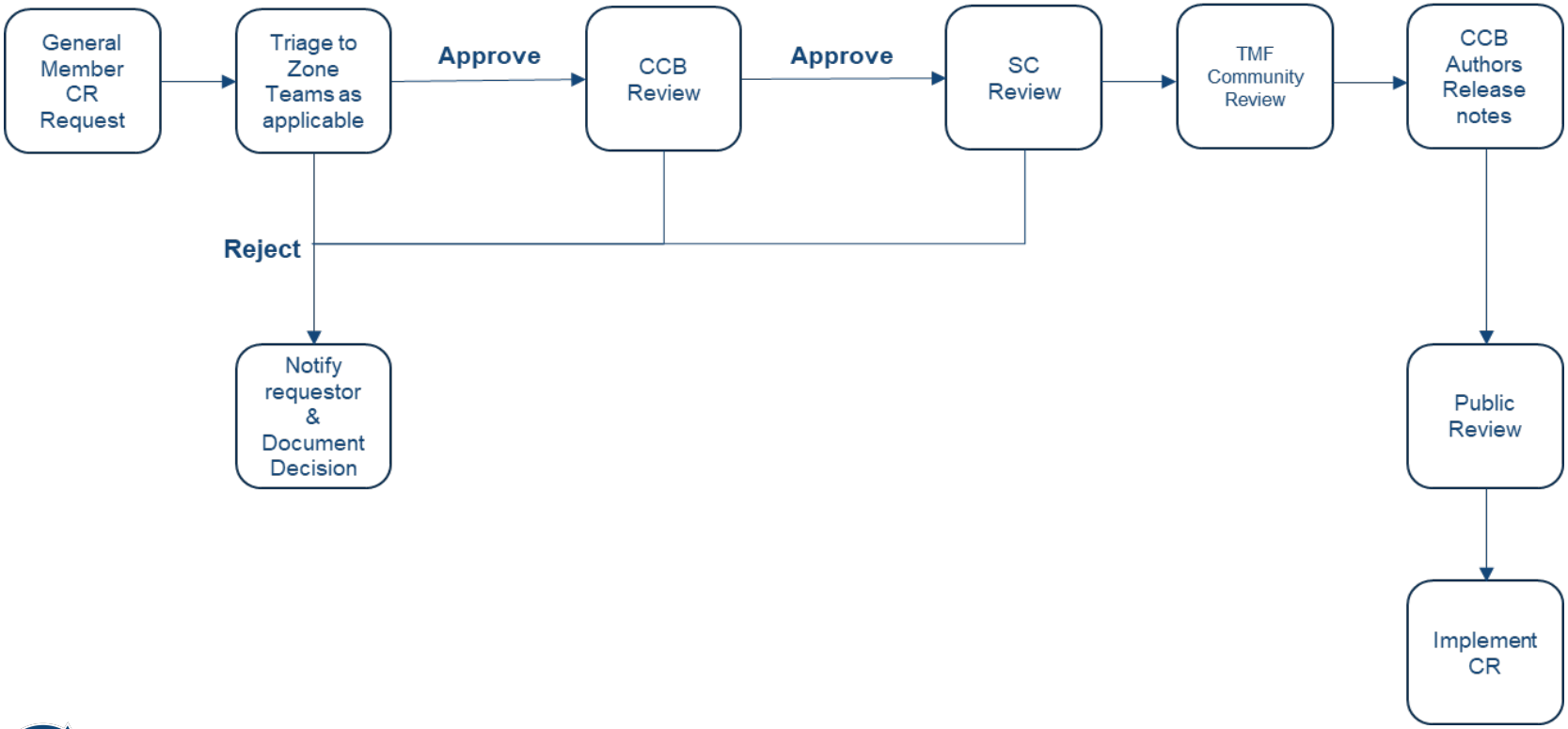
- Device Team:
  - Joanne Bilmazes
  - Jane Marie Johnson
  - Jeanine Hembt
  - Melissa Piscioneri
  - Harsha Kadri
  - Christy Nini
  - Sabrina Anand
  - Rochelle Longest

How to Make a Change Request

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



Process Flow for Change Request



Highlights from US TMF Summit & CDISC EU Interchange

US TMF Summit

March 21-23, 2023 – West Palm Beach, Florida
200 attendees
CDISC Involvement: Workshop held on TMF Plan Template
Presentations on CDISC future plans

My Top 3!

1. **FDA keynote -**
   - Inspectors are now called 'Investigators'!
   - Direct or guided access to sponsor's computer system. They cannot sign off on system training forms but are allowed to complete them.
   - What they are looking for when conducting inspections... follow the BIMO! - Team information, Investigator selection and monitoring, Contracted services (CRO, Vendors), Monitor selection, SAE reporting, Data/safety monitoring board and DM committee.
   - Relevant correspondence is an important part of the TMF. When reviewing correspondence investigators look for communication with clinical investigators/ CROs, outlining key study information and decisions. There should always be an SOP outlining the Communication Plan.
   - Investigators expect to see Sponsor oversight on a study; it becomes a problem when you don't do it!
   - Considerations for your systems: FDA (investigators) should be unblinded to all records.
   - A reminder that - "If it's not documented, it didn't happen!"

2. **Audit trails -**
   - Ensuring there is a process in place for both audit trail review and user access, and both should be conducted regularly.
   - Reviewing users access to systems and ability to reconstruct the course of events with audit trials.
   - Understanding how your audit trial works and have the process, evidence and outcome documented.

3. **Interactive 2 day mock inspection activity with 9 teams!**
   - ~190 (10 vendor judges) people were put into 'color teams' and got a chance to meet people they otherwise may not have...just like when an inspection may begin!
   - The teams worked on solving key problems for an upcoming mock inspection!

Also heard about: M11, EU CTR, structured data vs. unstructured data, engaging with functions and CROs, reporting, dashboards, CTQs, inspection readiness, and a variety of panels...and more!

CDISC EU Interchange

April 25-27, 2023 – Copenhagen, Denmark
~375 attendees
CDISC Involvement: Workshop held on What is the TMF RM
Presentations on CDISC TMF future plans aboard TMF-Air !

My Top 3!

The format of the conference – merit driven abstracts with true educational value.

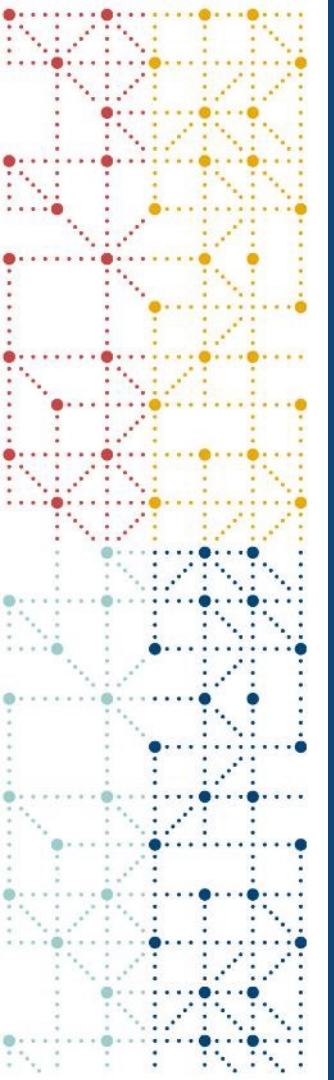
1. Big data was a theme!

Tracks included – CDISC Foundational, Biomed Concepts, Governance, Real World Data, Optimization Use Cases, Secondary Use of CDISC, Analysis Results Standard, Core, Regualtory, Submissions, Digital Data Flow (DDF).

2. ICH M11 and CDISC collaboration. CDISC is truly looking to become the Clinical Research Standard, not just data. It folds so neatly into the TMF as well.

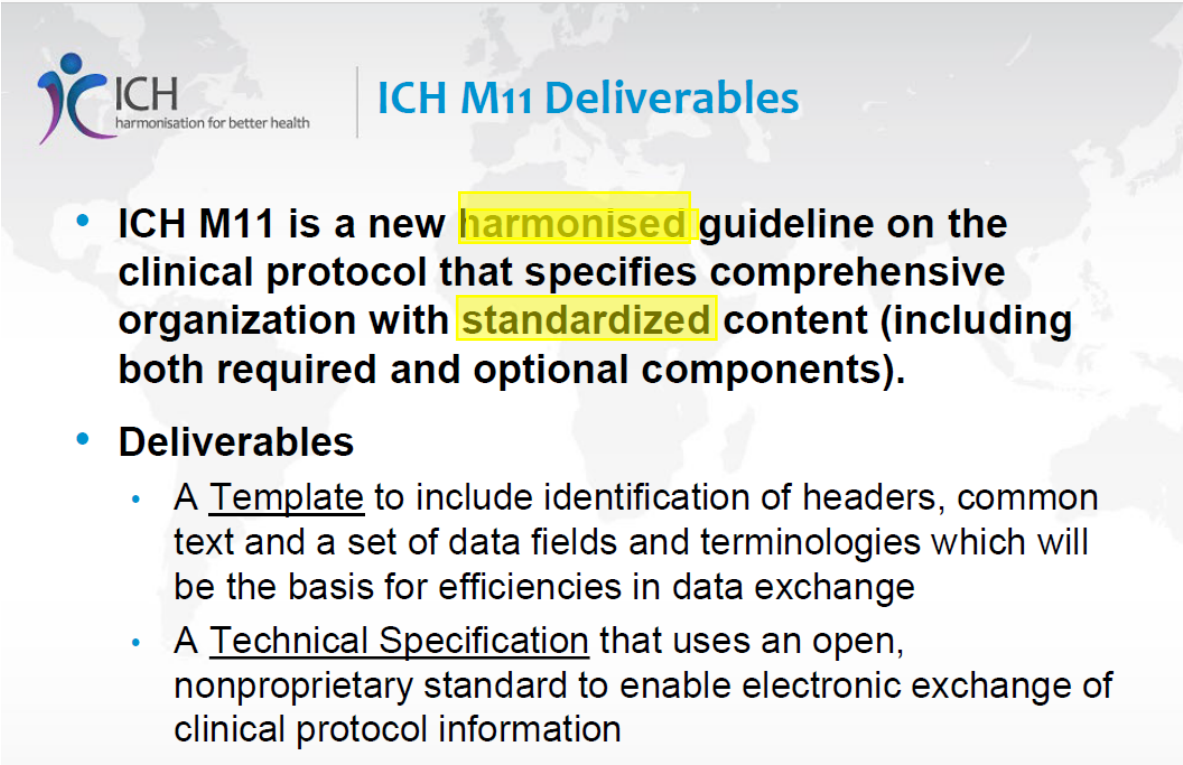
3. The number of Statisticians and Programmers who interact with the TMF, and their keenness to go back to their organisations and spread the word!

Norwegian Medicines Agency (NoMA), PMDA, EMA, FDA all attended and presented!



ICH M11, DDF and the Future of the TMF

What is M11?



CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL (CESHARP)

M11 Status

- In Step 2b **Draft Guideline adoption by Regulators**
- Comment period just concluded
  - Published in the Federal Register on Dec 22 2022
  - Put out for comment by Health Canada Nov 18, 2022 and EMA on Oct 26, 2022
  - Other Health Authorities include ANVISA (Brazil), Swissmedic
- CDISC/TransCelerate Digital Data Flow (DDF) was “consulted” as part of preparing the draft guidance (along with other prior initiatives)
- Laegemiddelstyrelsen, the Danish Medical Agency, recently published "Protocol template in accordance with CTR Annex I“
  - "It may be helpful to consult the International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) M11 template for more detailed guidance for the set-up of the trial protocol. Please be aware that the **ICH M11 template is not considering all requirements by the CTR and hence, is not a standalone template for clinical trials in EU**."
-

Protocol Template

"The Template and Technical Specification are applicable to interventional clinical trials of medicinal products across all phases and therapeutic areas of clinical research."

Includes "pharmaceuticals, biologics, vaccines, cell or gene therapy products (when applicable), as well as drug-device combination products when registered as a drug."

Table of Contents

Technical Spec (Structured Data)

- Fields in the template are defined in terms of type (text, number, date, pick list…)
- As a result, the entire protocol is build from tagged data blocks (although many are free text)

Term (Variable)	Trial Phase
Data Type	Pick list
Topic, Value or Header	D
Definition	
User Guidance	For trials combining investigational drugs or vaccines with devices, classify according to the phase of drug development.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Title Page
Relationship (reference to high level conceptual model)	
Value	Early Phase 1 Phase 1 Phase 1/Phase 2 Phase 2 Phase 2/Phase 3 Phase 3 Phase 4 Other
Business rules	**Value Allowed:** yes **Relationship:** n/a **Concept:** Protocol short title
Duplicate field in other sections	

ICH Member

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

26 October 2022
EMA/CHMP/ICH/778800/2022
Committee for Human Medicinal Products

ICH M11 technical specification
Step 2b

Transmission to CHMP	3 October 2002
Adoption by CHMP	13 October 2022
Release for public consultation	26 October 2022
Deadline for comments	26 February 2023

Comments should be provided using this template. The completed comments form should be sent to ich@ema.europa.eu

Structured?

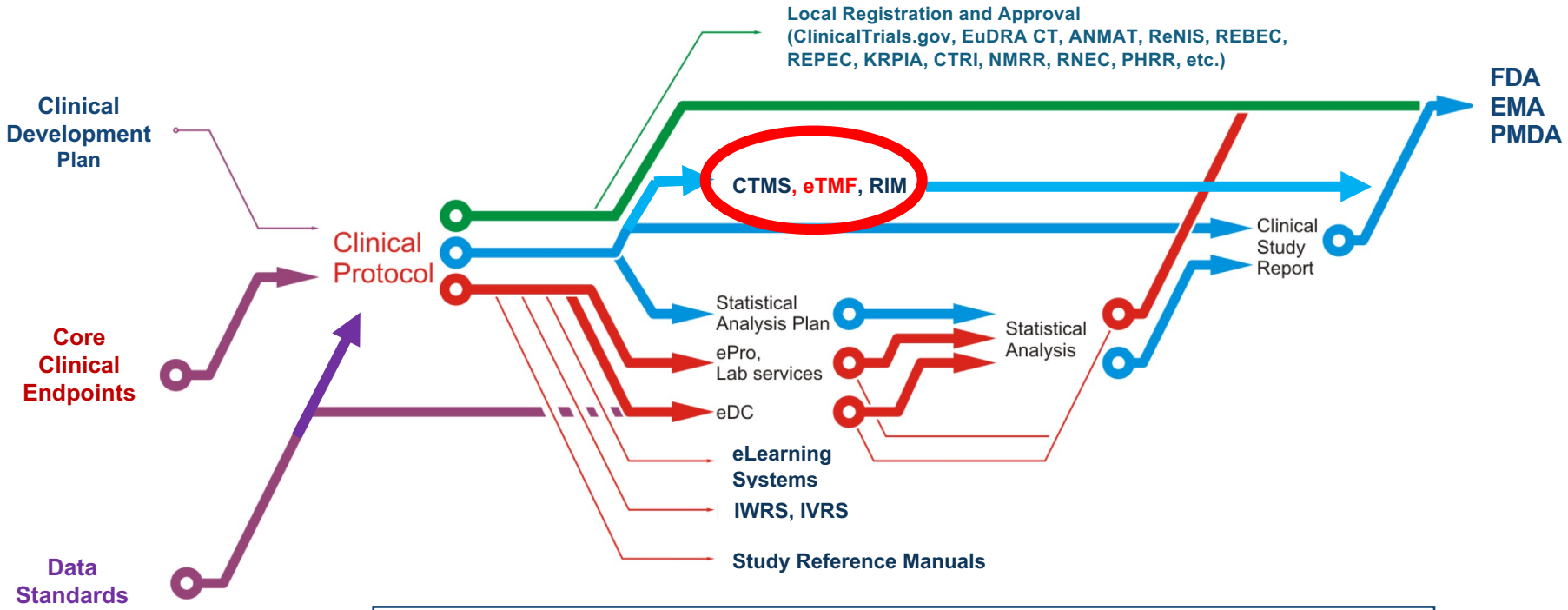
Term (Variable)	Inclusion Criteria
Data Type	Text
Topic, Value or Header	
Definition	Inclusion criteria are characteristics that define the population under trial, for example, those criteria that every potential participant must satisfy, to qualify for trial entry.
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Population
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Structured?

Trial Inclusion/Exclusion—One Record per Trial Inclusion or Exclusion Criterion

#	Variable Name	Variable Label	Type	Format	Role	Variable(s) Qualified	Usage Restrictions	Variable C-code	Definition	Notes	Examples
1	STUDYID	Study Identifier	Char		Identifier			C83082	A sequence of characters used by the sponsor to uniquely identify the study.		
2	DOMAIN	Domain Abbreviation	Char		Identifier			C49558	An abbreviation for a collection of observations, with a topic-specific commonality.	2-character abbreviation, which must be "TI".	
3	IETESTCD	Inclusion/Exclusion Criterion Short Name	Char		Topic					Short name IETEST. It can be used as a column name when converting a dataset from a vertical to a horizontal format. The value in IETESTCD cannot be longer than 8 characters, nor can it start with a number (e.g., "1TEST"). IETESTCD cannot contain characters other than letters, numbers, or underscores. The prefix "IE" is used to ensure consistency with the IE domain.	
4	IETEST	Inclusion/Exclusion Criterion	Char		Synonym Qualifier	IETESTCD				Full text of the inclusion or exclusion criterion. The prefix "IE" (rather than TI) is used to ensure consistency with the IE domain.	
5	IECAT	Inclusion/Exclusion Category	Char		Grouping Qualifier					Used for categorization of the inclusion or exclusion criterion. The prefix "IE" (rather than TI) is used to ensure consistency with the IE domain.	"INCLUSION", "EXCLUSION"
6	IESCAT	Inclusion/Exclusion Subcategory	Char		Grouping Qualifier					A further categorization of the exception criterion. Can be used to distinguish criteria for a substudy or to categorize major or minor exceptions. The prefix "IE"	"MAJOR", "MINOR"
										(rather than TI) is used to ensure consistency with the	
7	TIRL	Inclusion/Exclusion Criterion Rule	Char		Rule					Rule that expresses the criterion in computer-executable form.	
8	TIVERS	Protocol Criteria Versions	Char		Record Qualifier					The number of this version of the inclusion/exclusion criteria. May be omitted if there is only 1 version.	

The Clinical Trial Information Flow (TransCelerate/CDISC)



TransCelerate's Digital Data Flow Initiative seeks to enable the flow of digital study protocol data in order to improve study design and accelerate start-up through automation of processes and setup of study execution systems.

ICH M11 and TransCelerate Digital Data Flow

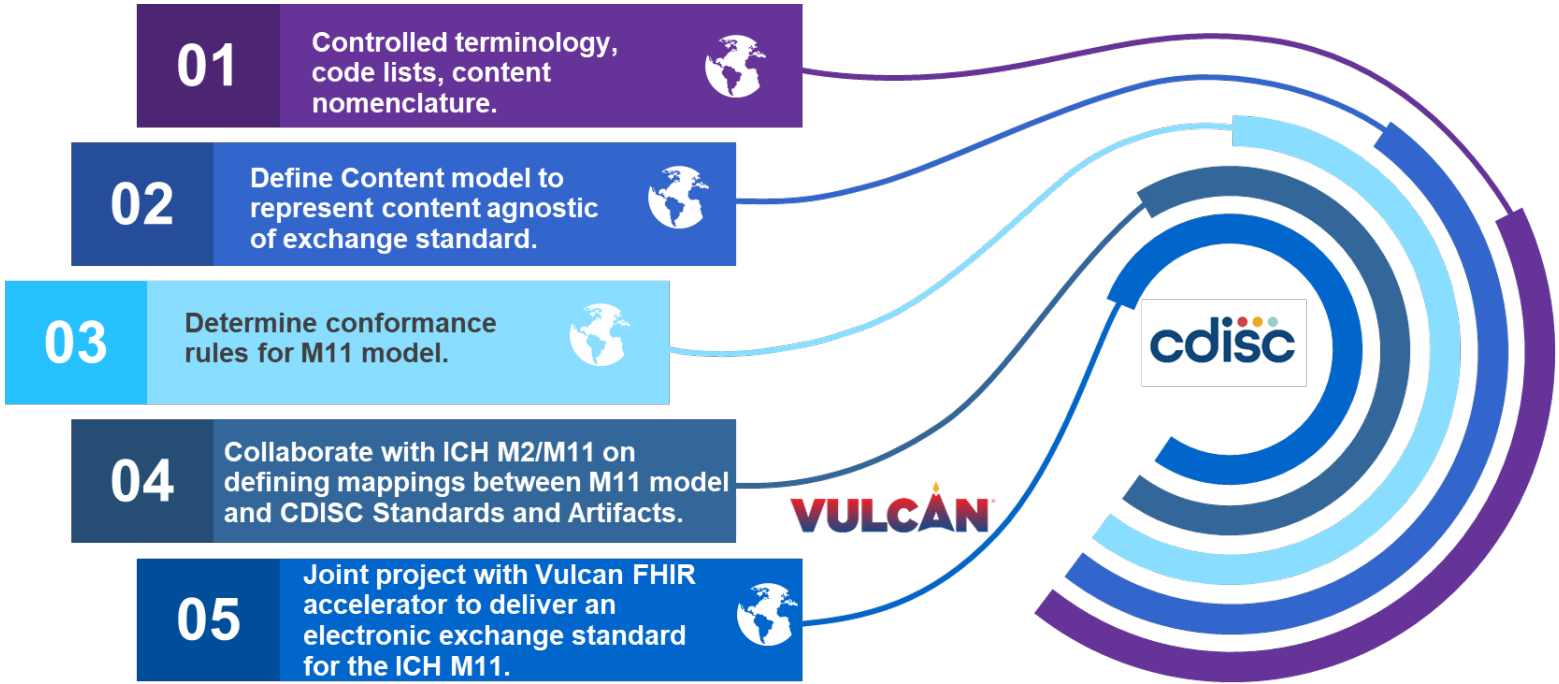
ICH M11

- Purpose: to introduce the clinical protocol template and the technical specification to ensure that protocols are **prepared in a consistent fashion** and **provided in a harmonised data exchange format acceptable to the regulatory authorities**.

TransCelerate/CDISC DDF

- Purpose: **automate and expedite the study start-up process by revolutionizing how data flows** across clinical trial systems, beginning with upstream (e.g., study builder) and downstream (e.g., electronic data capturing/EDC, clinical trial management system/CTMS) clinical systems

CDISC M2/M11 potential engagement



Source: "M11 Clinical Electronic Structured Harmonised Protocol", 2023 CDISC European Interchange, Copenhagen, 26-27 April, Panagiotis Telonis (EMA) and Jimita Parekh (Medible, Inc.)

Impact on TMF: What Does ChatGPT Say?

- ICH M11 provides guidance on the electronic submission of clinical trial data to regulatory agencies, but it **does not directly address the trial master file (TMF) itself**. However, the implementation of ICH M11 **may indirectly impact the TMF by promoting the use of electronic systems and improving data quality and consistency**.
- Here are some ways that the implementation of ICH M11 could impact the TMF:
  - Electronic TMFs: The implementation of ICH M11 could promote the use of electronic TMFs, ... This could lead to more efficient management of TMFs, as well as easier access to TMF …
  - Standardization: ICH M11 is intended to promote the standardization of clinical trial data across different regions and regulatory agencies. This may also lead to greater standardization of the TMF across different trials and sponsors, which could facilitate the sharing of TMF data between different parties.

Structured Protocol Data → TMF

1. Storyboard and central hub for both Health Authorities and Study/TMF managers
2. Study Design (unblinding, randomization, interim analysis, edit checks…) drives TMF planning / completeness
3. Protocol Amendments drive process to plan and obtain required documents
4. Standardization streamlines the exchange of documents and data between organizations (TMF Ref Model Exchange Standard)
5. Deviations, Relevant Correspondence – tied to section so that it can be seen in one click

TMF Planning Activities

- Based on the characteristics of the protocol, specific documents are planned:
  - Control (for example, placebo, active comparator...)
  - Trial intervention assignment method (for example, randomisation, stratification…)
  - Blinding
  - Committees (common examples include Data Monitoring Committee, Dose Escalation Committee, or Endpoint Adjudication Committee…)
  - And in the future maybe predict what documents are needed by comparing protocols or discerning other rules
- Data in protocol populates is entered once and used many times
  - Study name and code
  - Trial design details
  - Etc.
- Values populate both document metadata and document content, as applicable

Protocol Amendment (1 of 3)

Imagine you are in your editing tool, and you start the process for a protocol amendment…

You use your protocol preparation/authoring tool to add the amendment with a user-friendly UI.

M11

History of Amendments

{#/A total of #} prior {global} amendments have occurred, as shown in the table below:

Document	Sponsor Approval Date (dd/mmm/yyyy)	Approximate {(#/%)} Enrolled
[Amendment x]	[Amendment x Date]	{(#/%)} {globally/locally}}
[Amendment x]	[Amendment x Date]	{(#/%)} {globally/locally}
[Amendment x]	[Amendment x Date]	{(#/%)} {globally/locally}
Original Protocol	[Original Protocol Date]	0

Protocol Amendment (2 of 3)

You answer a series of questions about the amendment (non exhaustive example)

Amendment Number:	[Amendment Number] Enter the amendment number. the protocol, indicate Not Appl
Amendment Scope:	[Amendment Scope] [Count Acceptable entries for amendm "Country-specific/Regional" Use the ISO-3166 region or cou or EU). For global trials delete field.
Compound Number(s):	[Compound Number]

Reason(s) for Amendment:	Primary: [Primary Reason for Amendment] * Select from the following (multiple selections allowed): • Regulatory agency request to amend • New regulatory guidance • IRB/IEC feedback • New safety information available • Manufacturing change • Adaptive clinical trial IMP addition • Change in strategy • Change in standard of care • New data available (other than safety data) • Investigator/site feedback • Recruitment difficulty • Inconsistency and/or error in the protocol • Protocol design error • Other: [Describe]	Other: [Other Reason for Amendment] * Select from the following (multiple selections allowed): • Regulatory agency request to amend • New regulatory guidance • IRB/IEC feedback • New safety information available • Manufacturing change • Adaptive clinical trial IMP addition • Change in strategy • Change in standard of care • New data available (other than safety data) • Investigator/site feedback • Recruitment difficulty • Inconsistency and/or error in the protocol • Protocol design error • Other: [Describe] • Not applicable
Summary of the Amendment:	[Summary of Amendment] Specify on the primary reason for the amendment with details specific to the trial. If more than one key change prompted the amendment, discuss briefly. Incidental changes which are included in the amendment but unrelated to the key changes do not need to be described here.	
Is this amendment likely to have a substantial impact on • safety or rights of the participants, or	[Yes/No] Indicate whether the current amendment is likely to have a significant impact on either of the criteria listed.	

Protocol Amendment (3 of 3): Impact on eTMF

- eTMF creates placeholders (or whatever planning mechanism is used)
  - Signature pages (or data equivalents) for each site in an impacted country
  - Ethics submissions and approvals
  - Regulatory submissions and approvals
  - Other impacted documents (informed consent, sample CRF, etc.)
- eTMF tracks completion of the package
- HA inspector or Study Manager can click through the information to reconstruct the process
- Over time, you can easily analyze reasons for and impact of amendments in reports and dashboards
- And maybe estimate the cost of an amendment?

Traceability and Mapping Example:
Protocol Amendment

CLICK HERE

From the Protocol title page:

Protocol Number:	ENN-PK-101
Amendment Number:	4
Amendment Scope:	Country-specific/Regional CA, US

List of documents associated with the protocol:

Document	Country	Status	Finalization Date
Regulatory Submission	United States	Planned	
Regulatory Submission	Canada	Final	23-Jan-2023
Regulatory Approval	Canada	Planned	
(many more…)			

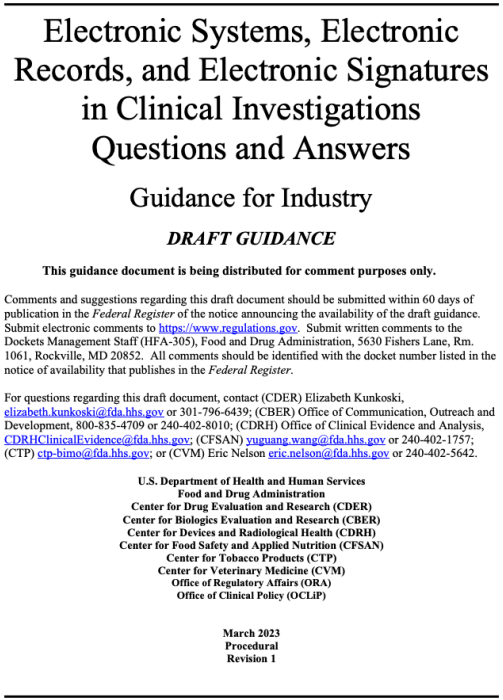
Regulatory Updates

FDA Draft Guidance:
Electronic Systems, Electronic Records, and Electronic Signatures in Clinical Investigations: Questions and Answers

- Issued 15 March 2023 (link)
- CLOSED for comments 15 May 2023

- When final, will supersede the guidance *Computerized Systems Used in Clinical Investigations (May 2007)*

- *eTMF is specifically identified as an example of an electronic system that may produce required records for a clinical investigation*



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

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Elizabeth Kunkoski, elizabeth.kunkoski@fda.hhs.gov or 301-796-6439; (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010; (CDRH) Office of Clinical Evidence and Analysis, CDRHClinicalEvidence@fda.hhs.gov; (CFSAN) yuguang.wang@fda.hhs.gov or 240-402-1757; (CTP) ctp-bimo@fda.hhs.gov; or (CVM) Eric Nelson eric.nelson@fda.hhs.gov or 240-402-5642.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Center for Food Safety and Applied Nutrition (CFSAN)
Center for Tobacco Products (CTP)
Center for Veterinary Medicine (CVM)
Office of Regulatory Affairs (ORA)
Office of Clinical Policy (OCLiP)

March 2023
Procedural
Revision 1

FDA Draft Guidance:
Electronic Systems, Electronic Records, and Electronic Signatures in Clinical Investigations: Questions and Answers

Potential TMF Implications *(not comprehensive)*

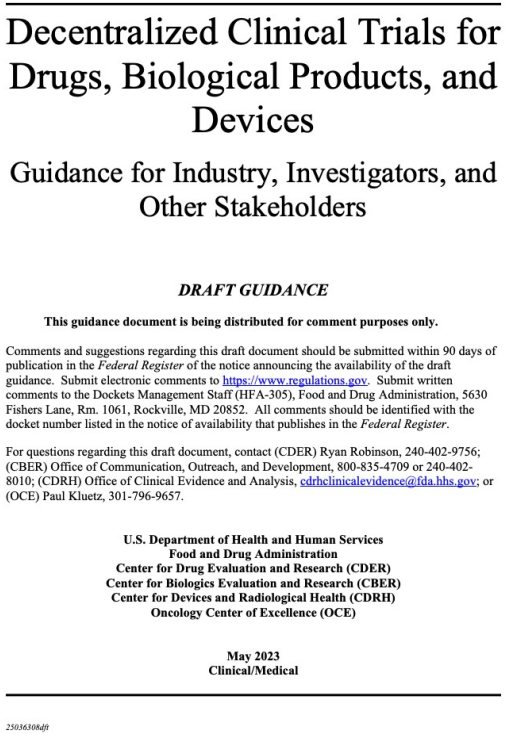
- **Q5:** eTMF data backup locations expected to be specified in an SOP
- **Q7:** eTMF systems are expected to have completed a risk-based validation
- **Q8:** What to expect during FDA inspection regarding eTMF system documentation
- **Q11:** Implies requirements for a cumulative record of eTMF system access
- **Q12:** Requirements & expectations for eTMF audit trails
- **Section C:** Expectations for oversight of eTMF Service Providers, and information expected to be provided by Sponsor for FDA inspection

FDA Draft Guidance: Decentralized Clinical Trials for Drugs, Biological Products, and Devices

- Issued 01 May 2023 (link)
- Submit comments by 01 Aug 2023

- Decentralized Clinical Trial refers to a clinical trial where some or all of the trial-related activities occur at locations other than traditional clinical trial sites.

- Related draft guidance: *Digital Health Technologies for Remote Data Acquisition in Clinical Investigations (December 2021)*.



Decentralized Clinical Trials for Drugs, Biological Products, and Devices

Guidance for Industry, Investigators, and Other Stakeholders

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Ryan Robinson, 240-402-9756; (CBER) Office of Communication, Outreach, and Development, 800-835-4709 or 240-402-8010; (CDRH) Office of Clinical Evidence and Analysis, cdrhclinicalevidence@fda.hhs.gov; or (OCE) Paul Kluetz, 301-796-9657.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Oncology Center of Excellence (OCE)

May 2023
Clinical/Medical

2503630dft

FDA Draft Guidance:
Decentralized Clinical Trials for Drugs, Biological Products, and Devices

Implications for content of specific TMF artifacts *(not comprehensive)*

- **Line 199:** Data Management Plan
- **Line 224:** Case Report Forms
- **Line 230:** Monitoring Plan
- **Line 267-335:** 1572/Investigational Device Exemption
- **Line 359:** Informed Consent Form
- **Line 444-470:** Safety Monitoring Plan

- **Lines 147, 210, 419, 434:** Protocol

FDA Draft Guidance:
Decentralized Clinical Trials for Drugs, Biological Products, and Devices

Implications for TMF inventory & related processes *(not comprehensive)*

- **Line 300:** suggest investigators keep a "task log" for local HCPs
- **Line 509:** expectations for transfer of source data from local HCPs to (principal) investigator
- **Line 526:** telehealth interactions are not considered electronic records – but documentation of such interactions captured in electronic form are

ICH E6 (R3)

- Draft endorsed under Step 2 (19-May-2023)
- Public consultation open
- 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**
- EMA public workshop July 13/14
- Consultation also via MHRA (tba)

ICH E6 (R3)

Main features re: TMF

- Document table currently in chapter 8 has gone
- Documents "maintained in or referred to from repositories, including, for example, the trial master file or investigator site file"
  - i.e. the TMF is just 1 example of where essential documents might be stored
- Location sponsor versus site not defined
- Criteria for "**essentiality**" defined
- List of "essential records for all trials" - Table 1
- List of "potential essential records" - Table 2

IMPORTANT: Make time to read AND provide feedback

EMA: Guideline on computerized systems and electronic data in clinical trials

- Adopted 07-Mar-23
  - *Effective 07-Sep-23, Last draft 17-Dec-21*
- Extensive document (52 pages) providing much-needed guidance
- Broad scope:
  - eTMF one of numerous systems identified
  - Whilst documents and derived data are within scope, main focus is on data (aka raw data, subject data) and associated systems e.g. eCOA, ePRO, eCRFs, imaging, IRT, eTMFs, site portals
  - Metadata, risk management, eSigs, data protection, validation, access control, system training, data migration, certified copies, cloud solutions, archiving, decommissioning

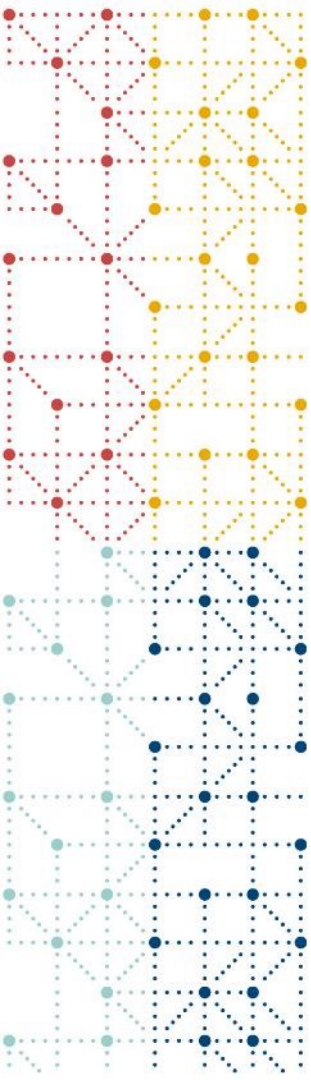
EMA: Guideline on computerized systems and electronic data in clinical trials

Key points:

- Underlying principles, including ALCOA++, criticality & risk, validation
- CSV appendix
  - Risk based; leveraging vendor validation; responsibility of sponsor; periodic review; change control
- User management appendix
  - Review of user access; least privilege rule
- Security appendix
  - Physical security; vulnerability management e.g. penetration testing; security incident management; system security

EMA Accelerating Clinical Trials in the EU (ACT EU)

- Public consultation open on revision of transparency rules of the Clinical Trials Information System (CTIS)
- Interim guidance document published
- Open until 28-Jun-2023
- https://ec.europa.eu/eusurvey/runner/TransparencyRulesPublicConsultationCTIS
- Impact?
  - Conduct an appropriate data protection impact assessment (DPIA) for personal data that might be accessible via CTIS
  - Maintain records of evidence of the DPIA



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

- General Meetings:
  - 7th September
  - 5th December

Opening for Questions (and hopefully Answers!)

Thank you

https://www.cdisc.org/events/webinar/tmf-reference-model-general-meeting-q2