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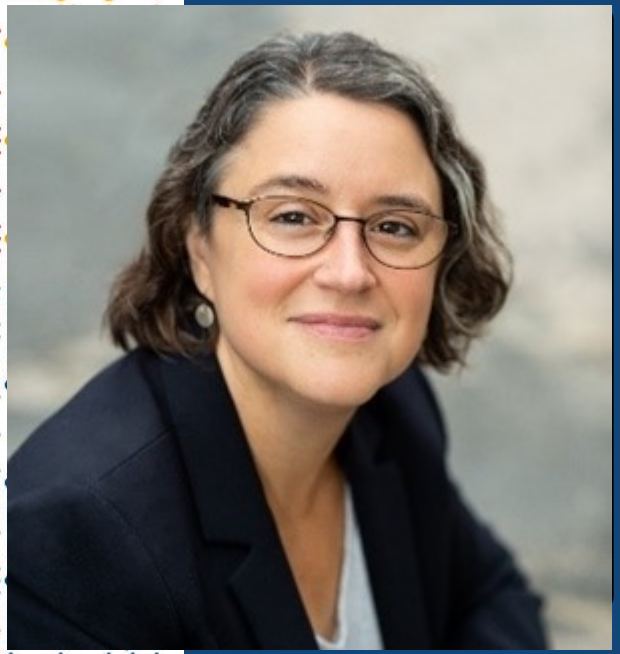
2023
CHINA
INTERCHANGE
BEIJING | 25-26 AUGUST

State of the CDISC Standards

Presented by Christine Connolly, Head of Standards Projects, CDISC



Meet the Speaker

Christine Connolly

Title: Head of Standards Projects

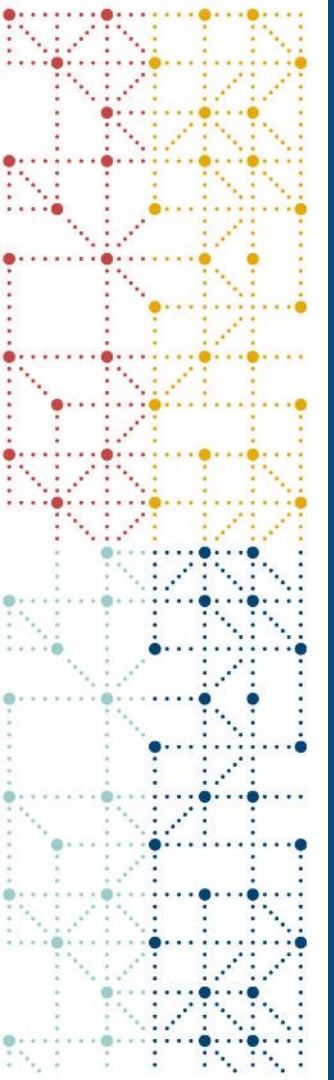
Organization: CDISC

Christine Connolly is the Head of Standards Projects at CDISC and an advocate for standardization given its potential to expedite development of preventive approaches, harm reduction strategies, and quality therapies to improve health outcomes.

Christine has a BS from Northeastern University and MPH from Boston University School of Public Health. She has led initiatives, developed, and implemented data standards for almost fifteen years and has twenty-five years of experience working in global clinical trials in both academic and pharmaceutical settings.

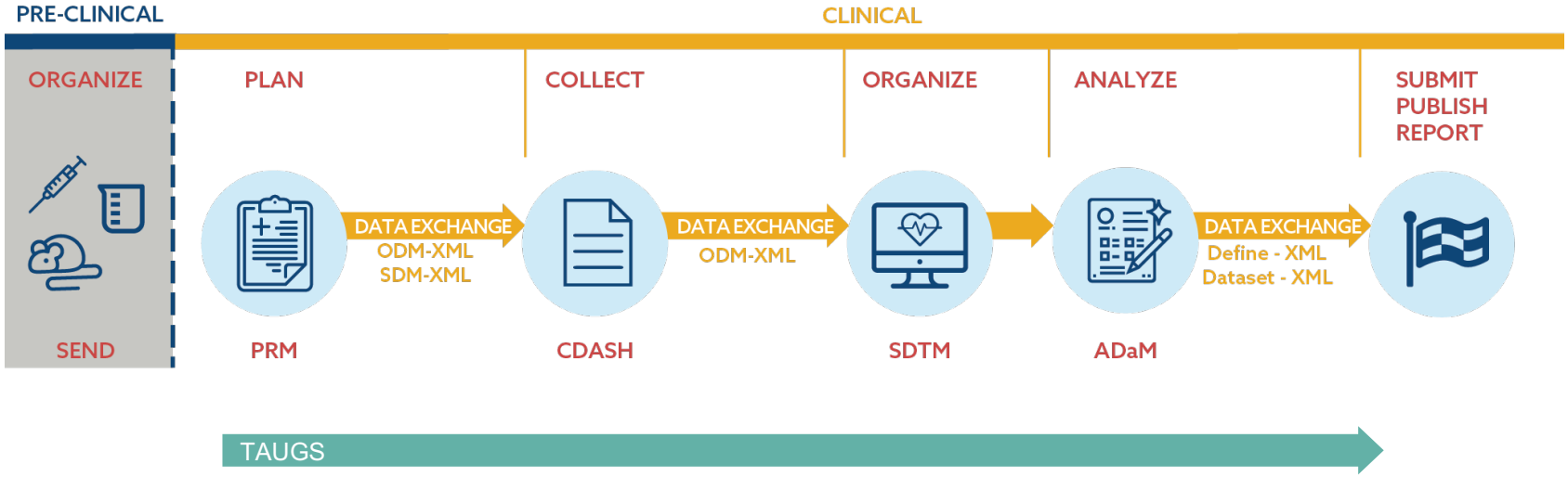
Agenda

1. CDISC End-to-End Standardization
2. Updates on Data Standards Projects



CDISC End-to-End Standardization

Together We Have Come a Long Way ….



BRIDG, CONTROLLED TERMINOLOGY AND GLOSSARY

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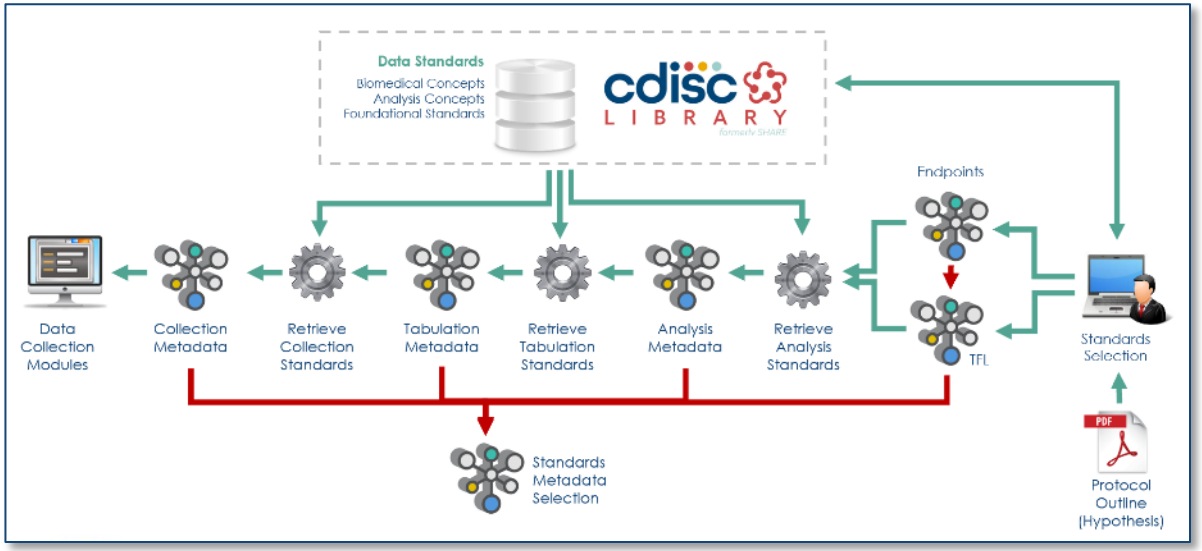
CDISC 360

Piloted development of linked biomedical concept metadata to enable end-to-end automation



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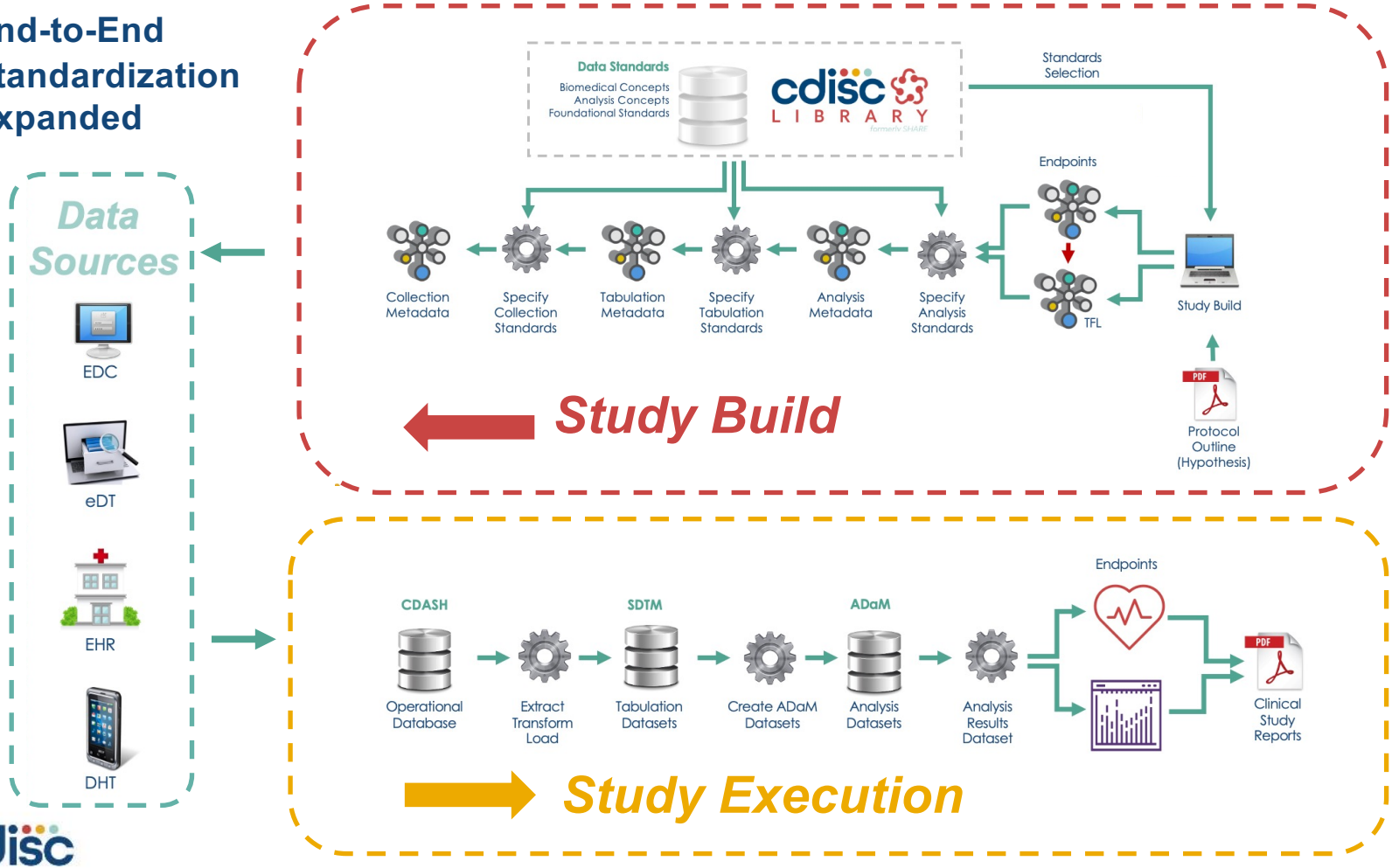
End-to-End Standardization Expanded



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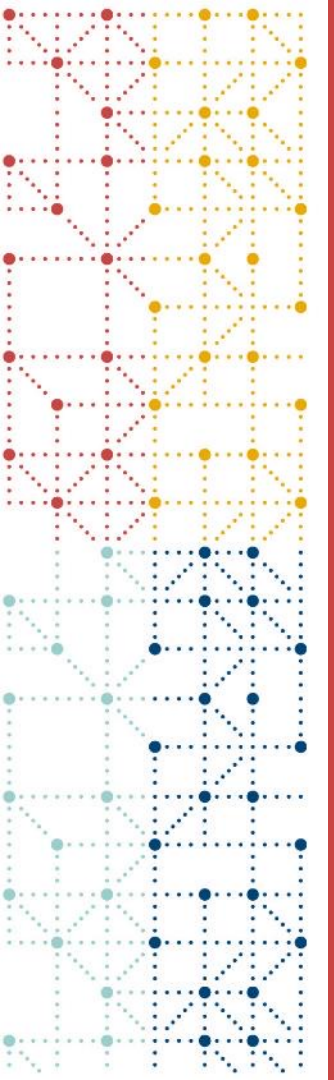
CDISC Standards Continue to Evolve

- Standardizing the meaning of the information
- Defining the data processing (data flow)
- Providing machine-executable data flow definitions
- Standardizing missing parts:
  - Protocol content
  - Collection instruments
  - Analysis / endpoint definitions and outputs
- Publishing standards from one trusted source
- Making standards less complex for the end users

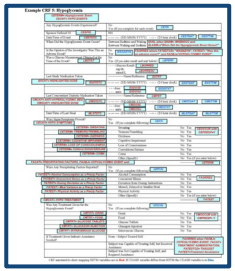
Updates on Data Standards Projects

- Analysis Results Standards
- Conformance Rules
- Tobacco Implementation Guide
- Digital Data Flow – ICH M11 Electronic Protocol
- Trial Master File



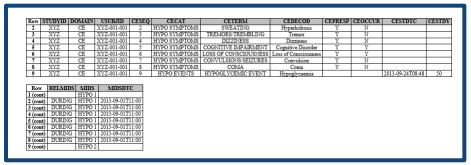
Analysis Results Standards (ARS)

Analysis Results Standards (ARS)



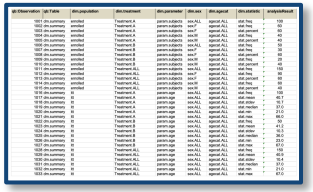
Data Collection

CDASH



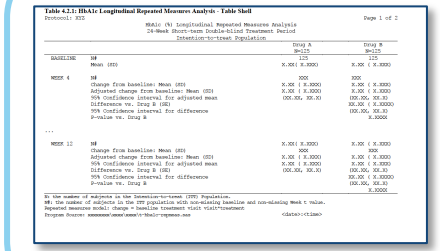
Data Aggregation

SDTM



Analysis

ADaM



Results

Opportunities for Standardization

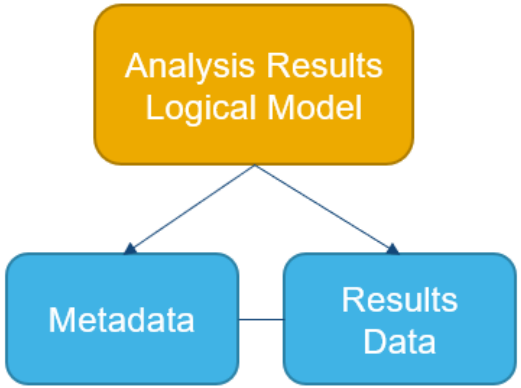
- Dataset structure and metadata for results to support traceability, use, and automation

ARS Objectives

Storage of results in a data structure to support:

- Traceability to Protocol/SAP and to input ADaM data
- Reproducibility and reuse of analyses and results

Facilitate automation with analysis results metadata



Learn more: https://www.cdisc.org/standards/foundational/analysis-results-standards

Analysis Results Standards Key Results

Logical model that describes analysis results and associated metadata

User Guide to illustrate how analysis results metadata can be used to create a structure to represent analysis results as data

User Guide to illustrate how analysis results metadata can be used prospectively to drive automation

Release Plan

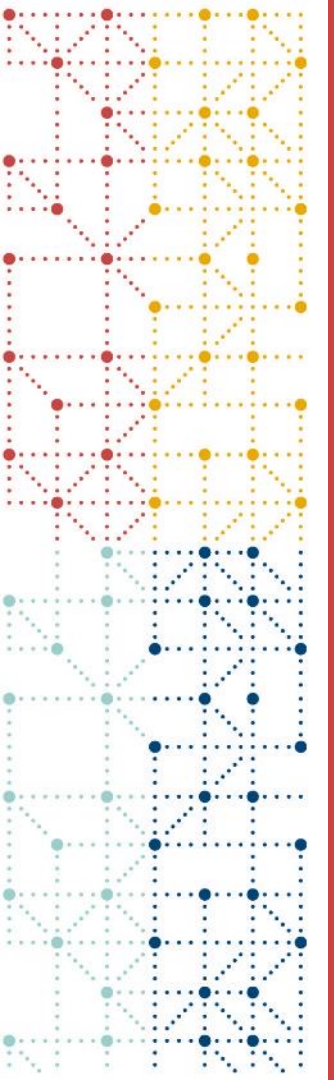
Analysis Results Standard Model v1.0

- The logical model to support a technical specification and an analysis results dataset

Analysis Results User Guide Version 1.0

- How analysis results metadata can be used to create a structure to represent analysis results as data
- How analysis results metadata can be used prospectively to drive automation
- Includes common safety examples

- CDISC Public Review: October 2023
- US Interchange Workshop: October 2023
- Anticipated Final Release: December 2023/January 2024



Conformance Rules

CDISC Open Rules Engine (CORE)

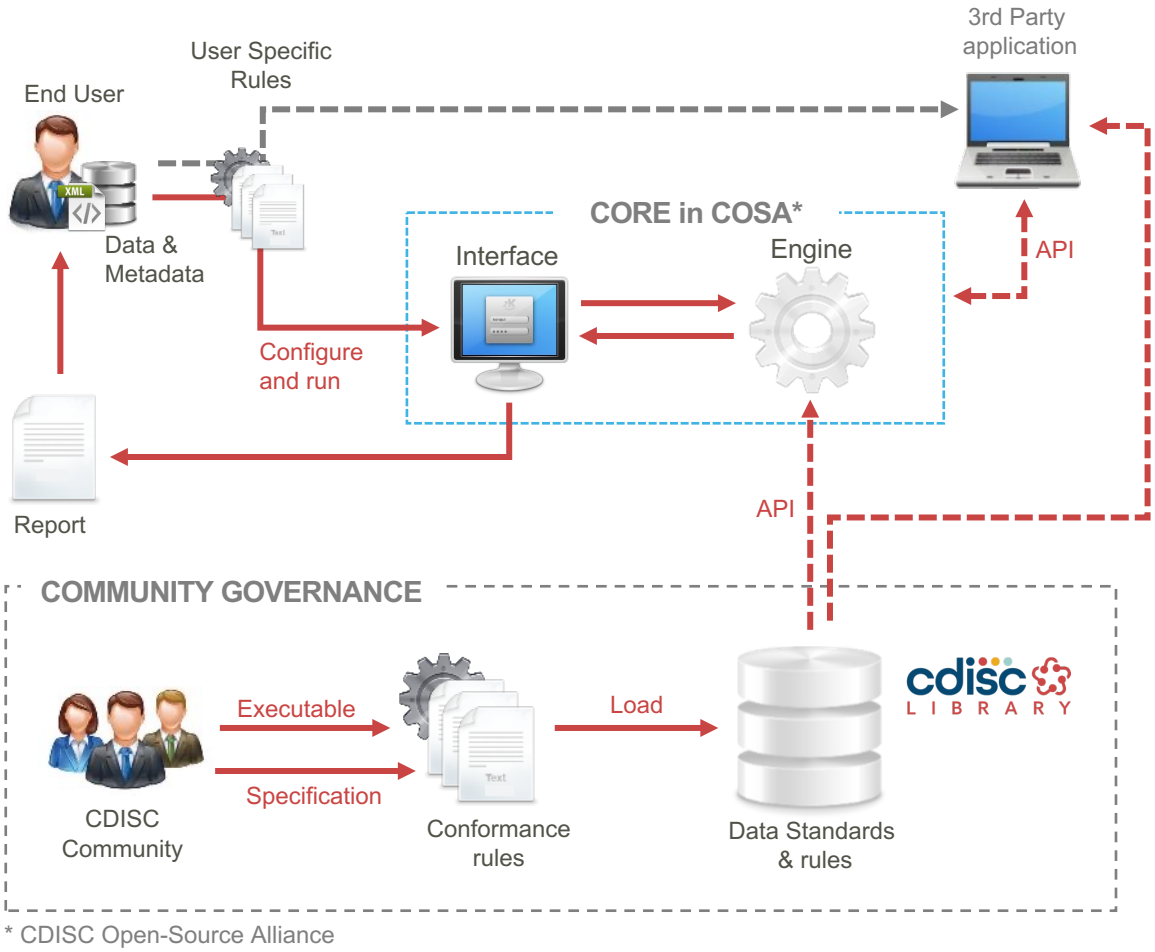
CDISC Open Rules Engine (CORE)

Learn more: https://www.cdisc.org/core

Ensure	• Each standard has a set of unambiguous, executable Conformance Rules • Consistency across Conformance Rule implementations
Expedite	• Availability of executable Conformance Rules for new Foundational Standards
Create	• Executable Conformance Rules vetted by the CDISC development teams
Develop	• An open-source engine that serves as a Reference Implementation
Publish	• Rules in the CDISC Library and the engine under the CDISC Open Source Alliance (COSA)

CORE Concept

CORE Initiative = Rules + Engine



CORE Rules Governance

Rules Governance Team

(CDISC; Regulatory Agencies; Community)

Rule Specifications

cdisc Standards

Provide rule specs

Regulatory

Provide validation rules

Community

Propose new / updated rule specs

Rules Gov Team Activities

- Receive specifications
- Load to central catalog

Rules Gov Team Activities

- Govern specs content
- Curate content
- Mark rules for dev.
- Prioritize rules for dev.

Central Specifications Catalog

Freely Available

CORE Rules (executable)

Rules Gov Team Activities

- Govern CORE Rules dev. process
- Assign Rules for development
- Review/approve Rules for release

Rules Development

Community

Publish

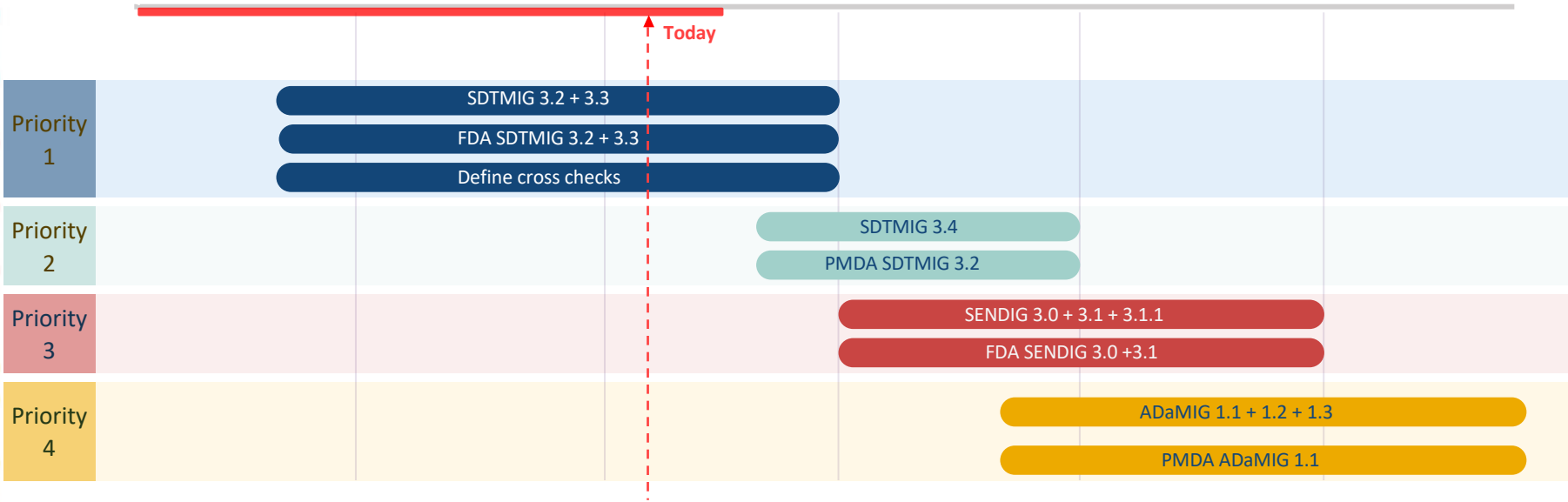
CDISC Library

API

3rd Party Applications

CORE Engine

Rules Development Priority



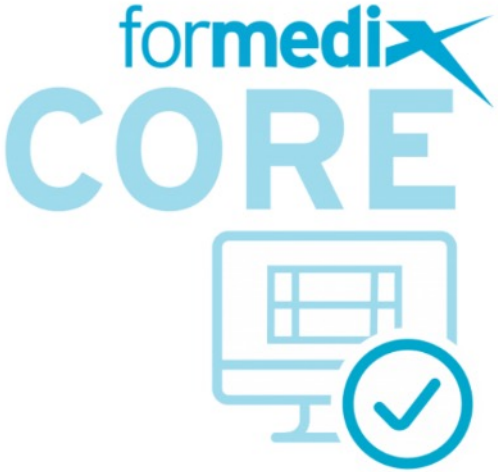
➡ *Timelines depend on community engagement*

First Vendor Launch

Introducing Formedix CORE: a free-to-use desktop app incorporating the CDISC Open Rules Engine

Formedix CORE is a free, downloadable Windows desktop application that allows you to validate datasets using the CDISC Open Rules Engine (CORE). The application provides an easy way to run validations on local data and identify standards conformance issues.

DOWNLOAD CORE



Next Milestone

Complete Ruleset for:

- SDTMIG 3.2 and SDTMIG 3.3
- Define.xml crosscheck rules
- FDA validator rules v1.6 (that apply to SDTMIG 3.2 and SDTMIG 3.3)
- FDA technical rejection criteria

CORE Engine Stable Release

- Engine can run all the rulesets above
- Thorough testing and validation documentation

Implementers can integrate this stable version
Drive adoption and test with real study data

Purpose

- Test with real study data and establish the rules governance process

Tobacco Implementation Guide (TIG)

Tobacco Implementation Guide (TIG) v1.0

- Proactively designed to reflect use cases unique to tobacco product data
- A single, comprehensive **hybrid implementation guide** for tobacco product data submissions

An overview of standards and general implementation

With guidance by topics and use cases; e.g.

- Product Description
- Nonclinical
- Individual Health
- Population Health

Key scientific concepts and maps

Data Collection (*CDASH eCRFs*, *ODM-XML*)

Data Tabulation (*SEND*, *SDTM Human Clinical*, *Define-XML*)

Analysis (*ADaM*, *Define-XML*)

Common Language (*Controlled Terminology*)

Measures of Adherence (*Conformance Rules*)

Accessible in platforms which optimize use (including *CDISC website*, *CDISC Library*)

Education and Outreach (including *webinars*, *formal training*)

TIG v1.0

Learn more: https://www.cdisc.org/tig

The TIG v1.0 is CDISC's **first *hybrid* implementation guide**.

- Developed in partnership with the FDA-CTP
- A new stand-alone **foundational standard**
- A **single guide** for collection, tabulation, and analysis
  - With references for data exchange

- CDISC Public Review: October 2023
- Anticipated Final Release: April 2024

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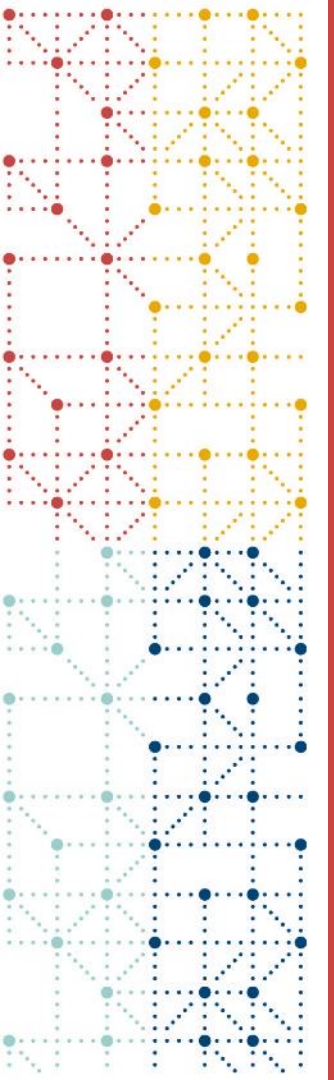
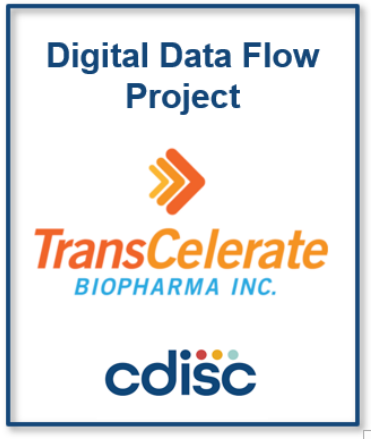


Digital Data Flow (DDF)

ICH M11 Electronic Protocol

Digital Data Flow (DDF)

Learn more: https://www.cdisc.org/ddf



Development:

- Unified Study Definitions Model (USDM)
- Reference Architecture
- Study Definitions Repository (SDR)

Collaboration:

- TransCelerate Biopharma, Stakeholders, Vendors and CDISC

Phase 1 ☑	Phase 2 ☑	Phase 3 2024 March
Base study design model	Model extension POC for protocol population	Include ICH M11 in model Demonstrate population: • Clinical trial registries • Trial Design domains

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ICH Harmonised Guideline
Structure and Content of a Clinical Protocol
M11

The **Template** presents the format and structure of the protocol, including the table of contents, common headers, and contents


ICH
harmonisation for better health

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL

(CESHARP)

M11 TEMPLATE

The **Technical Specification** presents the conformance, cardinality, and other technical attributes that enable the interoperable electronic exchange of protocol content


ICH
harmonisation for better health

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL

(CESHARP)

M11 TECHNICAL SPECIFICATION

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ICH M11 Clinical Protocol Template

4.1 Description of Trial Design

Describe the trial intervention model (for example, single group, parallel group, cross-over, factorial, sequential), the expected number of participants, and the control method (for example, placebo, active comparator, low dose, historical, standard of care, sham procedure, or none [uncontrolled]).

If applicable, indicate the type of trial (for example, superiority, non-inferiority, dose escalation, or equivalence).

Opportunities for Standardization

- Integration of structured content into narrative content

ICH M11 Technical Specification

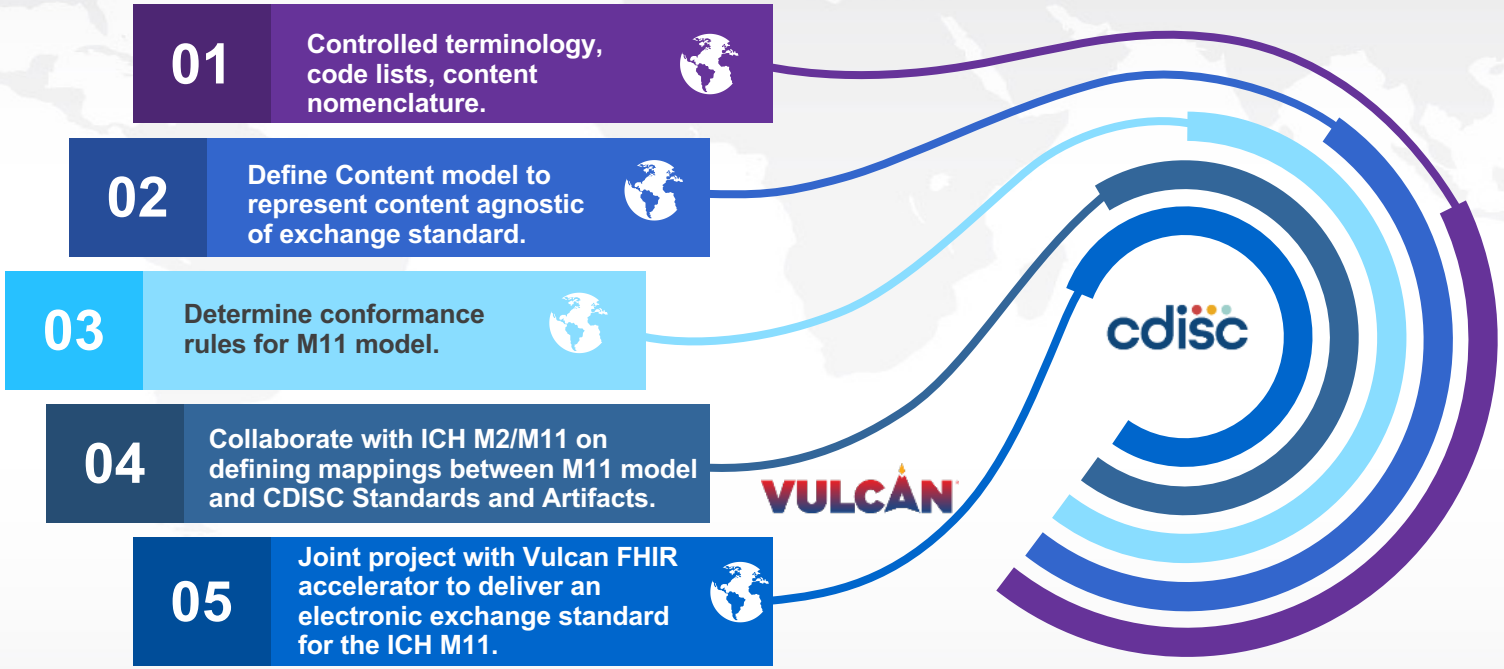
Trial Design

Term (Variable)	Type of Trial
Data Type	List
Topic, Value or Header	D
Definition	
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Design
Relationship (reference to high level conceptual model)	
Value	Superiority, non-inferiority, dose escalation, or equivalence
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

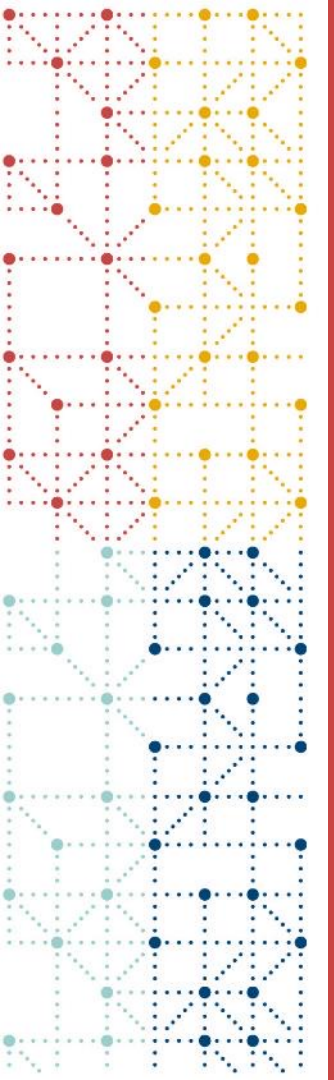
Opportunities for Standardization

- Variables
- Concept/terminology
- Codelist
- Conformance

CDISC and Vulcan engagement



* M11 Clinical Electronic Structure Harmonized Protocol presentation - Panagiotis Telonos, EMA - CDISC Europe Interchange 2023



Trial Master File (TMF)

Trial Master File (TMF)

What is the TMF?

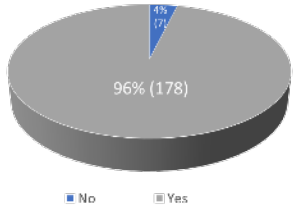
The sponsor and the investigator shall keep a clinical **trial master file**. The clinical trial master file shall at all times contain the **essential documents** relating to that clinical trial which allow verification of the conduct of a clinical trial and the quality of the data generated […]. It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

[EU Regulation 536/2014]

What is the TMF Reference Model?

- Standardised structure, contents and naming of these Essential documents
  - Used widely by industry

2022 Survey:
Organizations using TMF Reference Model



TMF Path Forward

Teams are established:

- **Education** team for training development
- **Standards** team to incorporate TMF into the CDISC suite of standards

The **2023 CDISC TMF Interchange** will be held in September!

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

Thank You!

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