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2023
JAPAN
INTERCHANGE
TOKYO | 10-11 JULY

Updates on CDISC Data Standards Projects

Peter Van Reusel
Chief Standards Officer
CDISC

Meet the Speaker

Peter Van Reusel

Title: Chief Standards Officer
Organization: CDISC

Peter Van Reusel provides executive leadership to the development and implementation of clinical standards in line with CDISC's strategy and operational plans, working closely with the President and CEO, as well as CDISC staff and stakeholders. He has over 20 years' experience in senior roles in pharma and at CROs, providing standards expertise and carrying out other standards work in various organizational settings. A long-time, CDISC-authorized instructor, Peter has helped significantly in developing CDISC training courses.

He previously served as CDISC's European Liaison, shepherding relationships with key European regulatory, academic, and biopharma stakeholders. Peter is also an active PHUSE collaborator.

Agenda

1. End to End Standards
2. Analysis Results Standard
3. Conformance Rules
4. Digital Data Flow – ICH M11 Electronic Protocol
5. Trial Master File

Foundational Standards Development 2023 Highlights

ADaM – Planning for a consolidated ADaMIG

SDS – Multiple Subject Participations – DM and DC domains

CDASH – Aligning with SDTMIG v3.4 including GF and CP domains

SEND – Implementing new domains including IS, CP, PI, OE, and SX

Medical Devices – Addressing how to represent multiple device components

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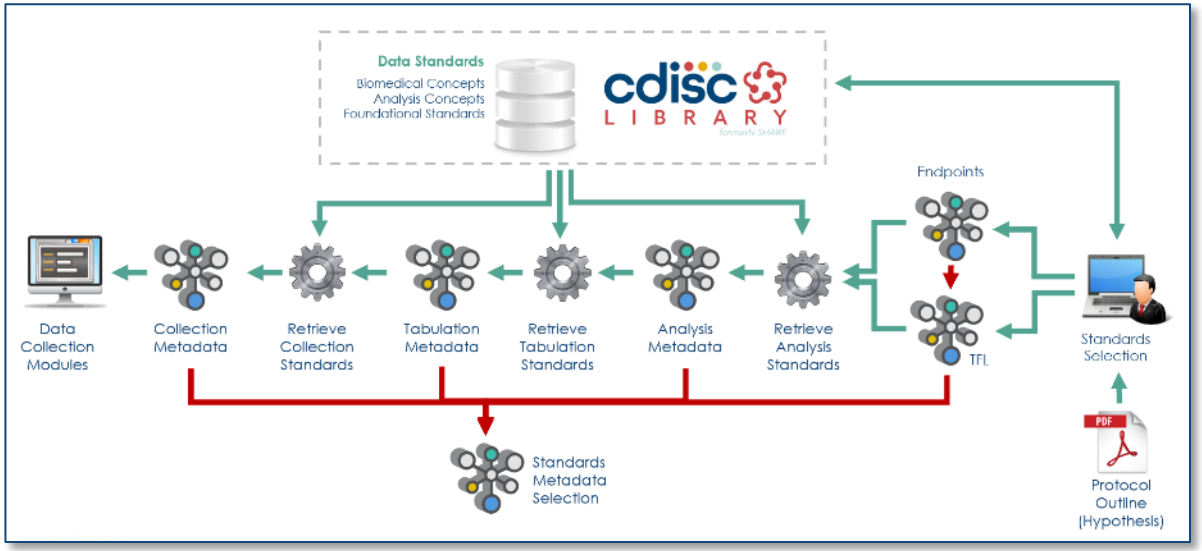
CDISC 360

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



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How Do CDISC Standards Continue to Evolve?

- Standardize the meaning of the information
- Define the data processing (data flow)
- Provide machine-executable data flow definitions
- Standardize missing parts:
  - Protocol content
  - Collection instruments
  - Analysis / endpoint definitions and outputs
- Publish standards from one trusted source
- Make standards less complex for the end users

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Analysis Results Standards

Analysis Results Standards Key Results

Develop a technical specification to prospectively leverage Analysis Results Metadata to drive automation

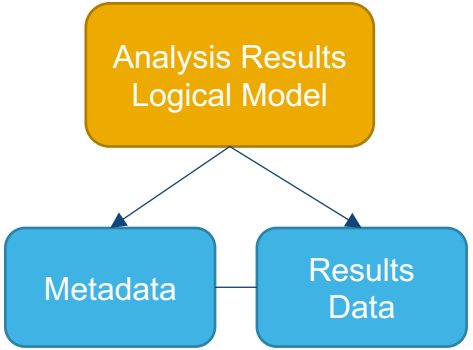
Develop a structure to represent Analysis Results as data

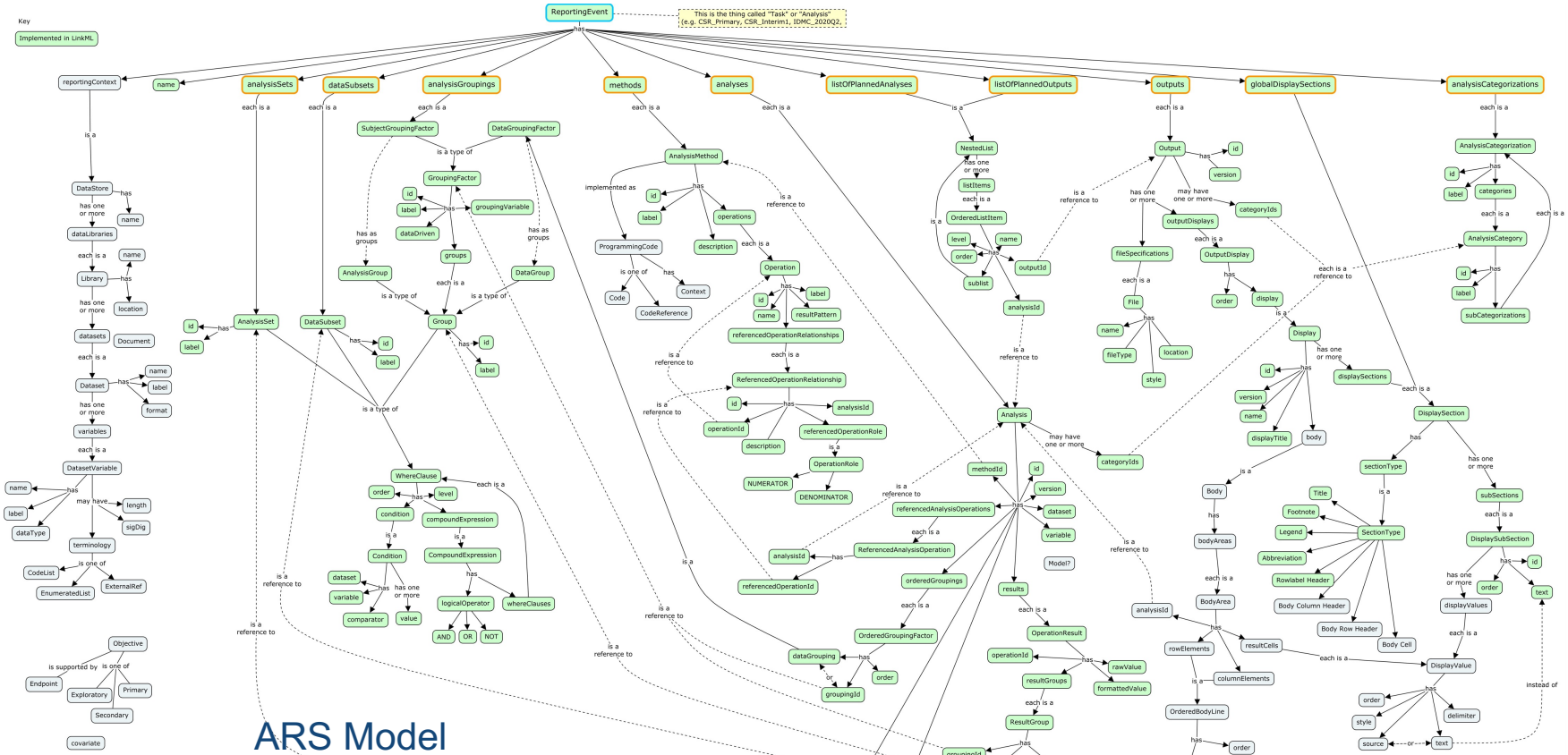
Develop a logical model to support a technical specification and an analysis results dataset

Illustrate and exercise with a set of common data displays

Moving Towards a Logical Model

- Logical model will incorporate the elements for both analysis results and associated metadata
- Model definition and documentation
- Illustrate and exercise with a common safety displays
  - Vital signs
  - Demographics
  - Adverse Events





ARS Model Representation using CMAP

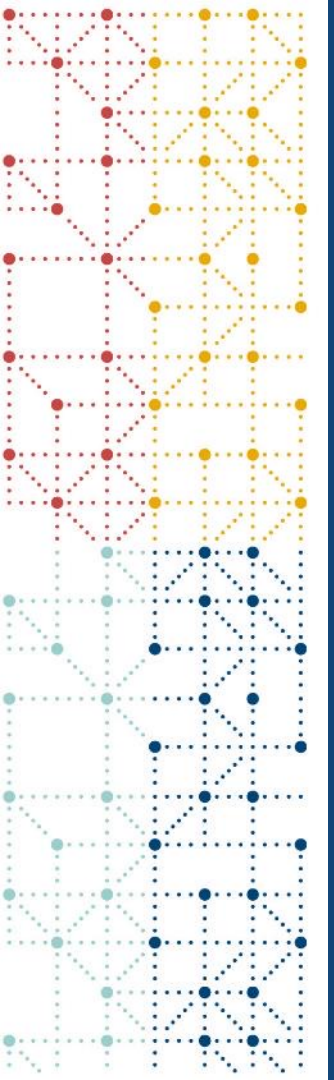
- https://github.com/cdisc-org/analysis-results-standard

Release Plan

Version 1.0

- Logical Model
- Common safety examples based on team developed tables
  - Demographics
  - Adverse Events
  - Vital signs

- CDISC ARS Hackathon: July 12th, 2023
- Anticipated CDISC Internal Review: July 21st, 2023
- Anticipated CDISC Public Review: October-November, 2023
- US Interchange Workshop: October 2023
- Anticipated Final Release: December 2023/January 2024



Conformance Rules - CORE

The Challenge

A single source of truth for all conformance rules

Consistency across conformance rule implementations

Central management and governance of rule specifications, regardless of source:

- CDISC – rules in the foundational standards
- FDA – FDA Validation Rules
- Community – proposed new/updated rules

Development, central management and governance of machine-executable rules from specifications

Efficient and transparent process for the community to

- Access specifications
- Access executable rules
- Propose new/updated rules

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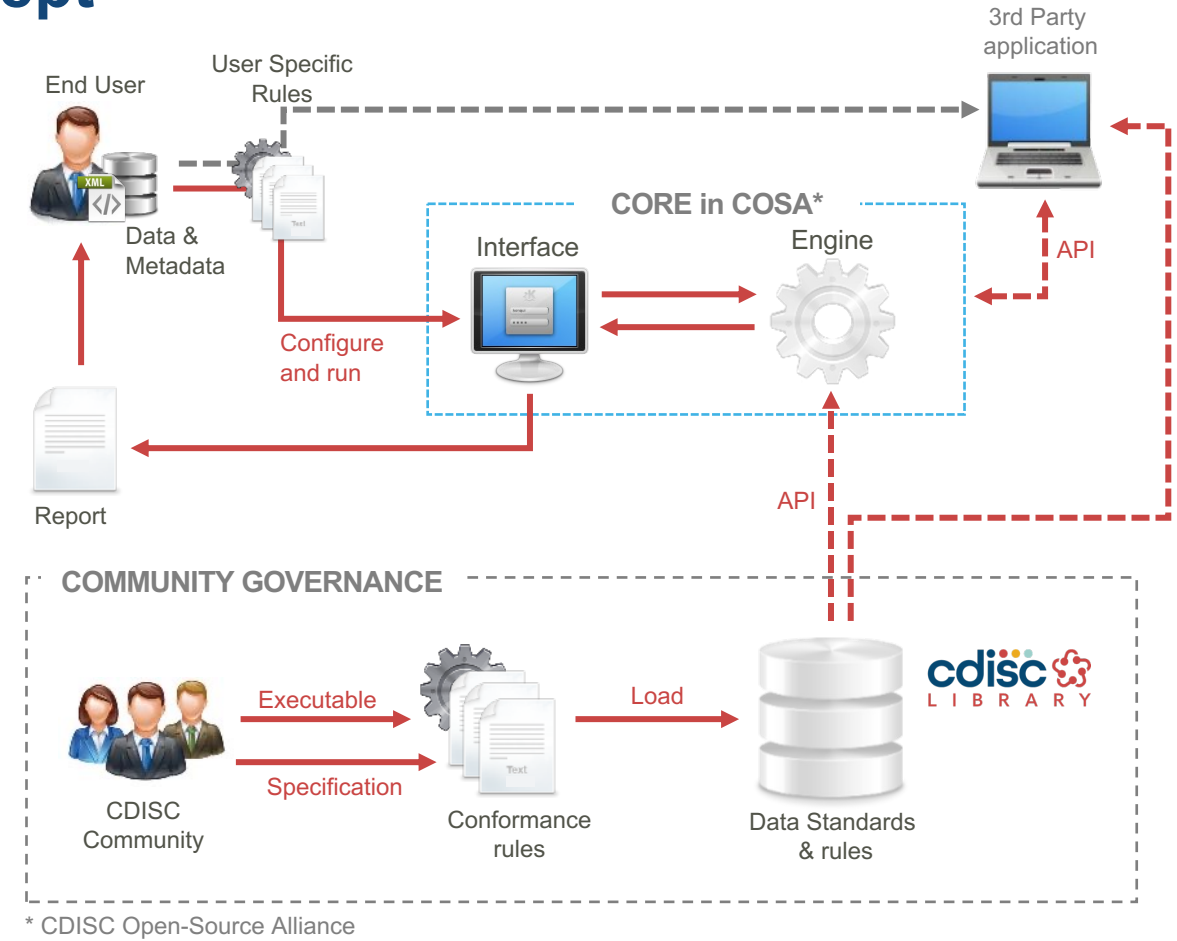
CORE Concept



* CDISC Open-Source Alliance

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

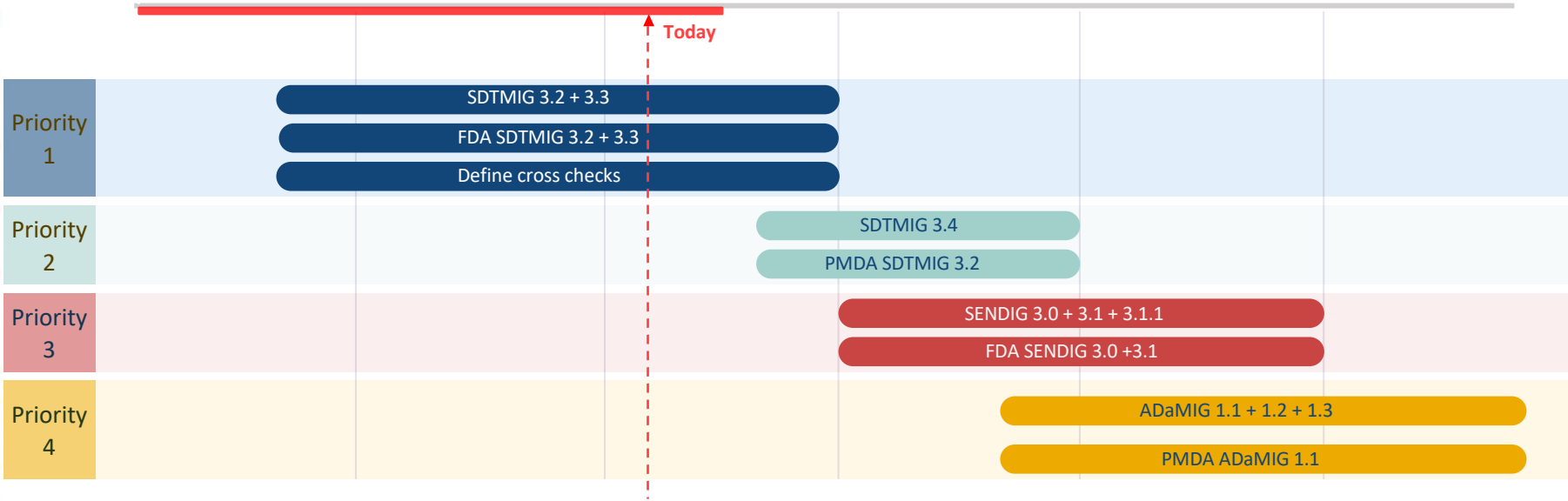
CDISC Library

API

3rd Party Applications

CORE Engine

Rules Development Priority



➡ *Timelines depend on community engagement*

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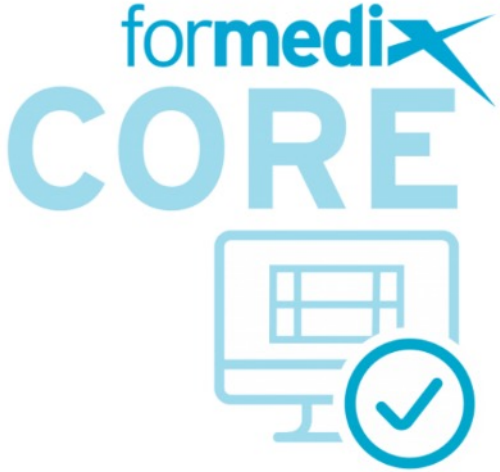
First vendor launch

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

- The complete ruleset for
  - SDTM 3.2 and SDTM 3.3
  - Define.xml crosscheck rules
  - FDA validator rules v1.6 (that apply to SDTM 3.2 and SDTM 3.3)
  - FDA rejection rules
- CORE Engine Stable Release
  - Engine can run all the rulesets above
  - Thorough testing and validation documentation
- Purpose
  - Test with real study data and roll out rules governance process

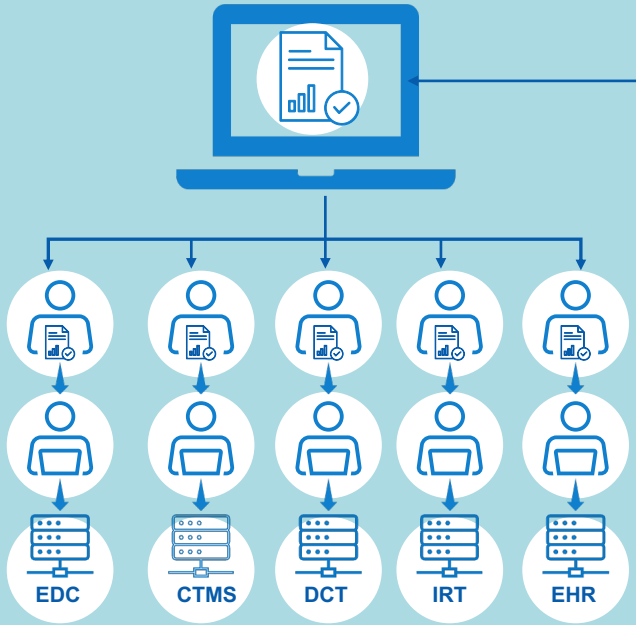
Implementers can integrate this stable version
Drive adoption and test with real study data

Transcelerate Digital Data Flow
ICH M11: electronic protocol

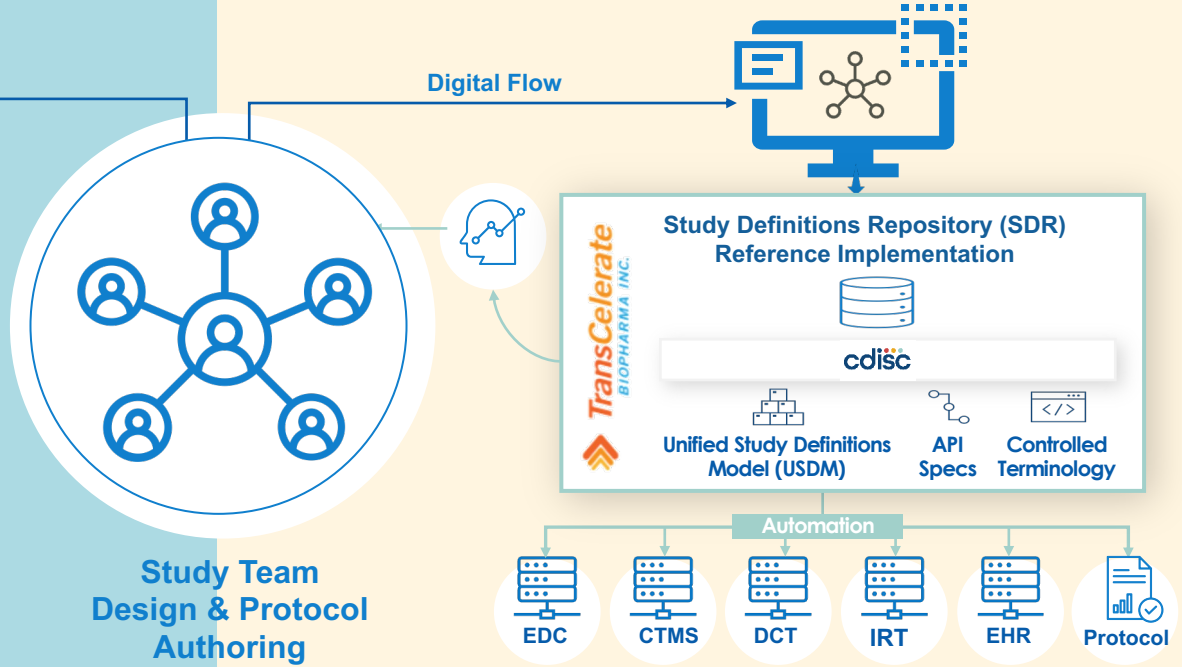
Digital Data Flow (DDF) Initiative

Write Once, Read Many

TODAY: Document-based paradigm for protocol creation, interpretation, and transcription into consuming systems



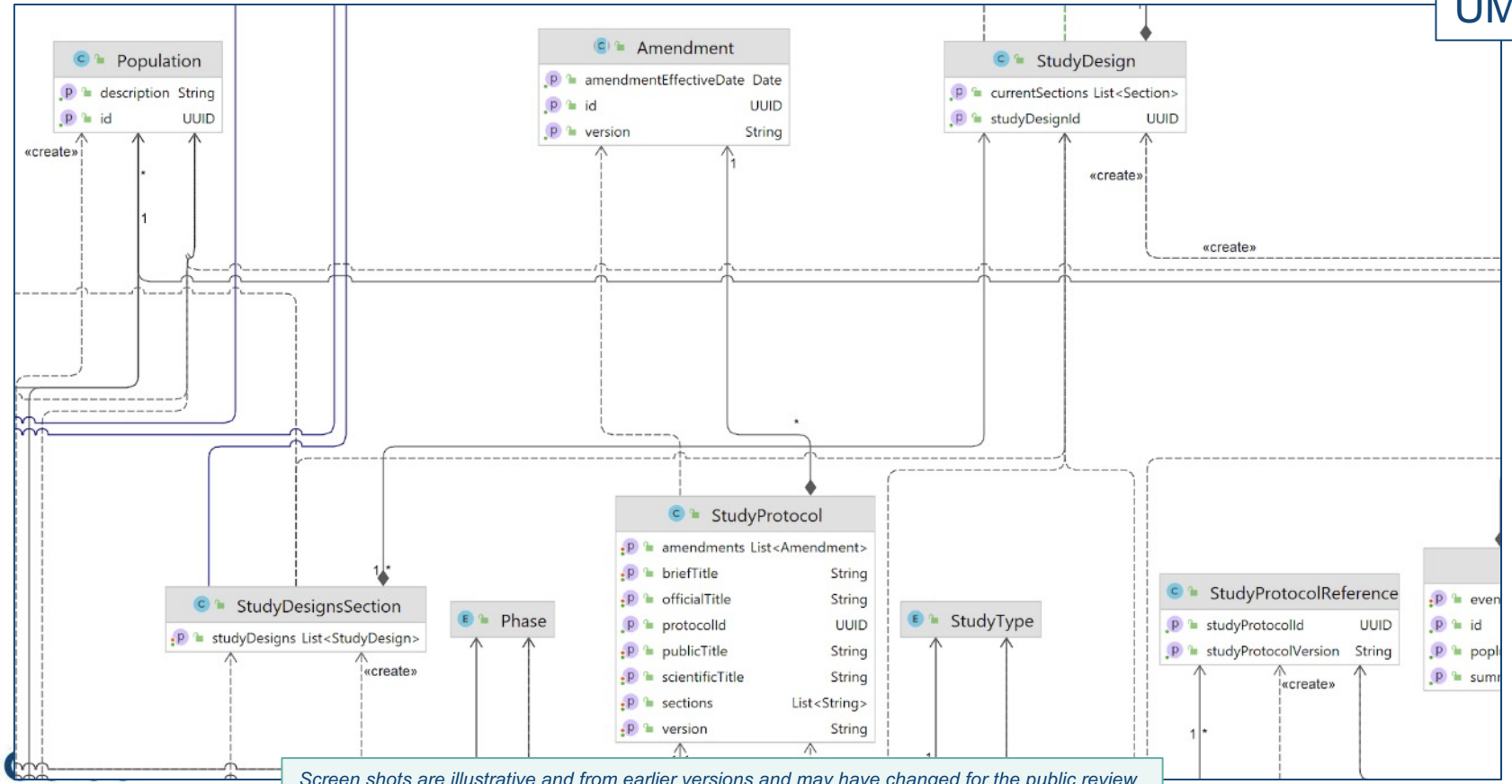
TOMORROW: Digital paradigm for protocol creation, with fully automated data flow and interoperability between systems



Unified Study Definitions Model (USDM) Class Diagram

The UML class diagram (normative) as well as SQL Data Dictionary, Entity Relationship Diagram and example JSON output (informative)

UML



Screen shots are illustrative and from earlier versions and may have changed for the public review

ICH M11:Clinical Electronic Structured Harmonised Protocol Components

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

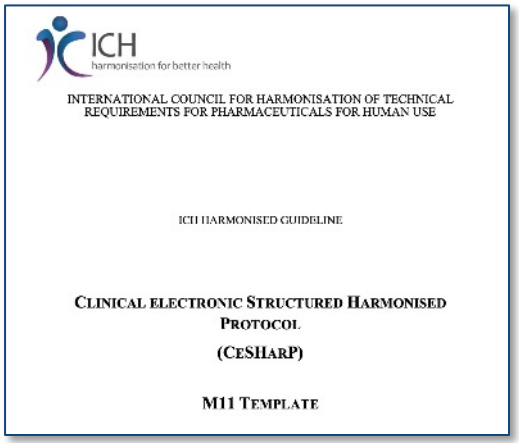
ICH HARMONISED GUIDELINE

CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL

(CESHARP)

M11 TECHNICAL SPECIFICATION

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

M11 TEMPLATE

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Template for Description of Trial Design

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).

Technical Specification for Description of 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	

- Variables
- Concept/Terminology
- Code lists
- Conformance

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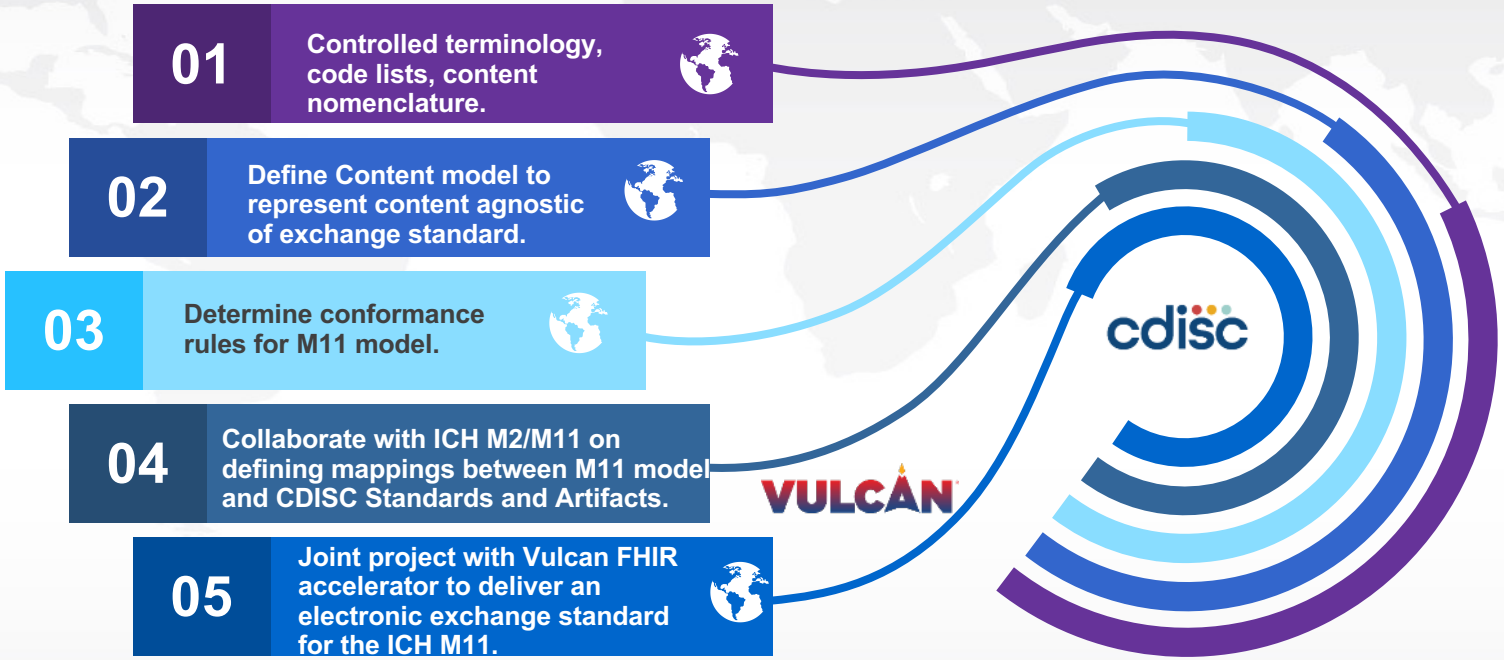
CDISC and Vulcan engagement



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

Trial Master File (TMF)

What is the Trial Master File?

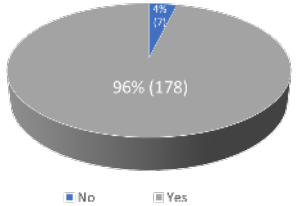
The sponsor and the investigator shall keep a clinical **trial master file**. The clinical trial master file shall at all times contain the **essential documents** relating to that clinical trial which allow verification of the conduct of a clinical trial and the quality of the data generated […]. It 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

2022 Survey:
Organizations using TMF Reference Model



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TMF Initiatives

- The Education Team
- The Standards Team
- The CDISC TMF Interchange!

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Thank You!

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