CDISC Key Initiatives for 2023 and beyond

Peter Van Reusel
Chief Standards Officer, CDISC

CDISC Italian UN, Milan, 12 May 2023

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

- CDISC Key Initiatives
- CORE : CDISC Conformance Rules

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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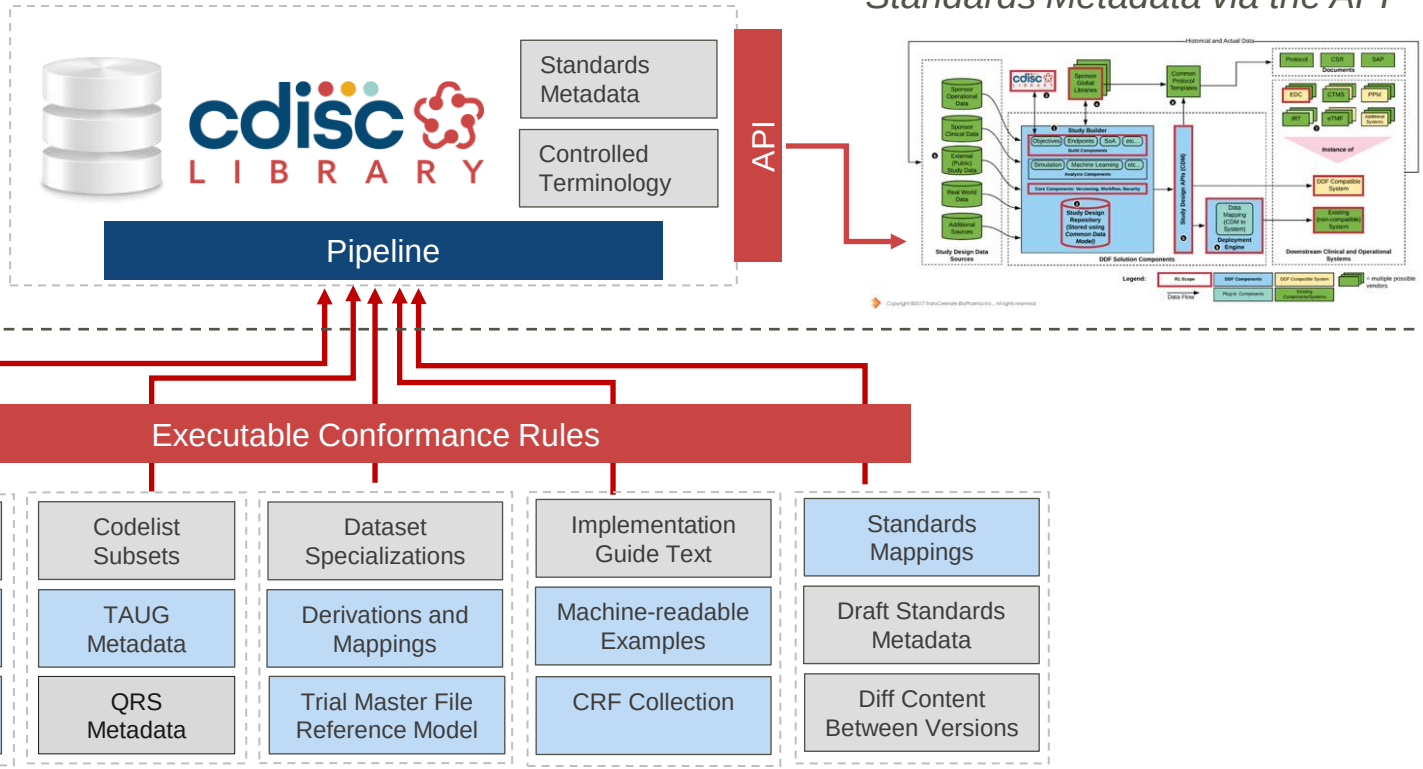
CDISC Library: Standards as a Service

Software Applications Consume Standards Metadata via the API



REST architecture principles at work

CDISC Open-Source Alliance (COSA)

Community Driven Development

Supports and promotes open-source software projects that create tools for implementing or developing CDISC standards to drive innovation in the CDISC community

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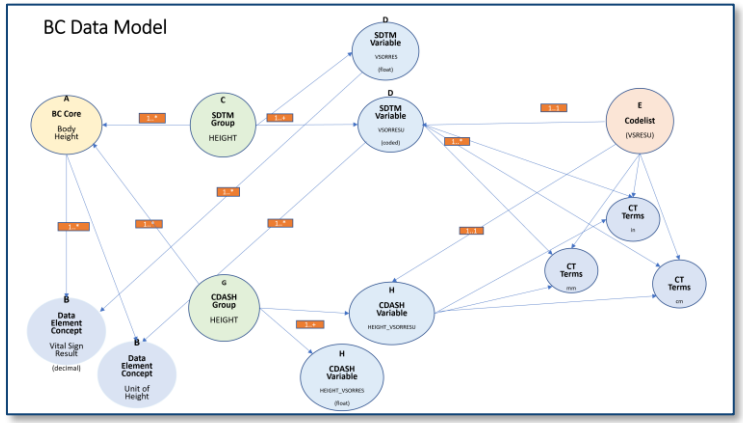
https://cosa.cdisc.org

CDISC Biomedical Concepts

A pragmatic, iterative approach to creating biomedical concepts with a focus on providing tangible value for the CDISC community



Key Objectives:

- Reduce variability in standards implementations
- Increase metadata-driven automation
- Reduce barriers to operational implementation

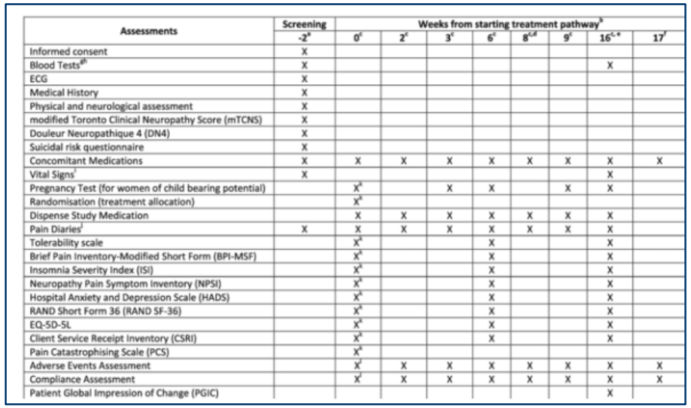
Key Components:

- Conceptual layer
- Implementation layer
- Logical data model

CDISC Biomedical Concepts: Semantics

Representation of a BC in a specific standard with implementation details such as value level metadata, formats, terminology – alignment across standards

Biomedical Concepts Initial Use Cases



Assessments	Screening	Weeks from starting treatment pathway[3]							
	-2[a]	0[f]	2[g]	3[f]	6[f]	8[f,d]	9[f]	16[f,e]	17[f]
Informed consent	X								
Blood Tests[gh]	X							X	
ECG	X								
Medical History	X								
Physical and neurological assessment	X								
modified Toronto Clinical Neuropathy Score (mTCNS)	X								
Douleur Neuropathique 4 (DN4)	X								
Suicidal risk questionnaire	X								
Concomitant Medications	X	X	X	X	X	X	X	X	X
Vital Signs[i]	X							X	
Pregnancy Test (for women of child bearing potential)		X[a]		X	X		X	X	
Randomisation (treatment allocation)		X[b]							
Dispense Study Medication		X	X	X	X	X	X	X	
Pain Diaries[j]	X	X	X	X	X	X	X	X	
Tolerability scale		X[a]			X			X	
Brief Pain Inventory-Modified Short Form (BPI-MSF)		X[a]			X			X	
Insomnia Severity Index (ISI)		X[a]			X			X	
Neuropathy Pain Symptom Inventory (NPSI)		X[a]			X			X	
Hospital Anxiety and Depression Scale (HADS)		X[a]			X			X	
RAND Short Form 36 (RAND SF-36)		X[a]			X			X	
EQ-5D-5L		X[a]			X			X	
Client Service Receipt Inventory (CSRI)		X[a]			X			X	
Pain Catastrophising Scale (PCS)		X[a]							
Adverse Events Assessment		X[f]	X	X	X	X	X	X	X
Compliance Assessment		X[f]	X	X	X	X	X	X	X
Patient Global Impression of Change (PGIC)								X	

Retrieve a list of assessments for a study

VS (Vital Signs) - [SDTMIG 3.1.2]

Related Supplemental Qualifiers Dataset: SUPPVS (Supplemental Qualifiers for VS)

Variable	Where Condition	Label / Description	Type	Length or Display Format	Controlled Terms or ISO Format
VSORRES VLM		Result or Finding in Original Units	text	30	
	VSTESTCD = "DIABP" (Diastolic Blood Pressure)	Diastolic Blood Pressure in Orig U	integer	2	
	VSTESTCD = "FRMSIZE" (Body Frame Size)	Body Frame Size - Orig	text	6	Size • "SMALL" • "MEDIUM" • "LARGE"
	VSTESTCD = "HEIGHT" (Height)	Height in Orig U	float	5.1	

Publish BC content as Define-XML document including value level metadata

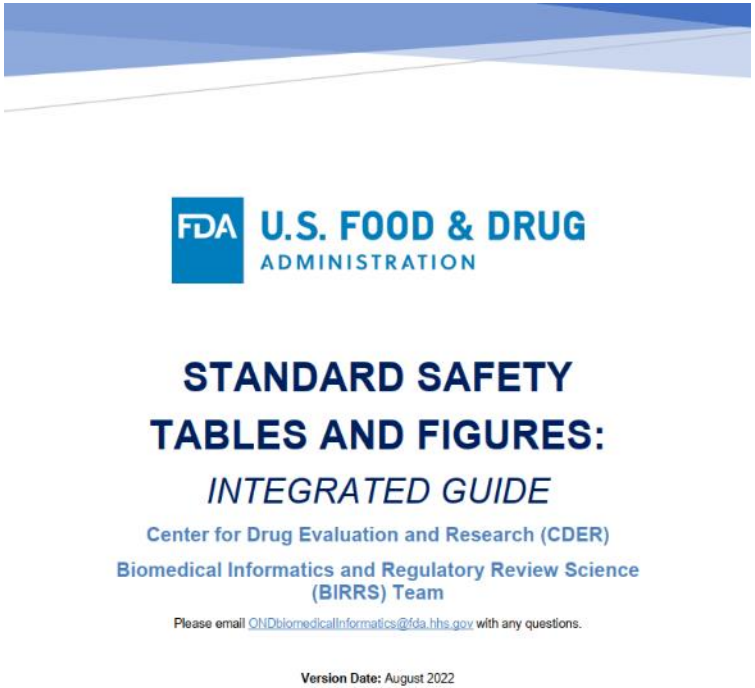
Analysis Results Standard Objectives

- Use analysis results metadata to drive the automation of results
- Support storage, access, processing and reproducibility of results
- Improved navigation and reusability of analyses and results
- Traceability to Protocol/SAP and to input ADaM data

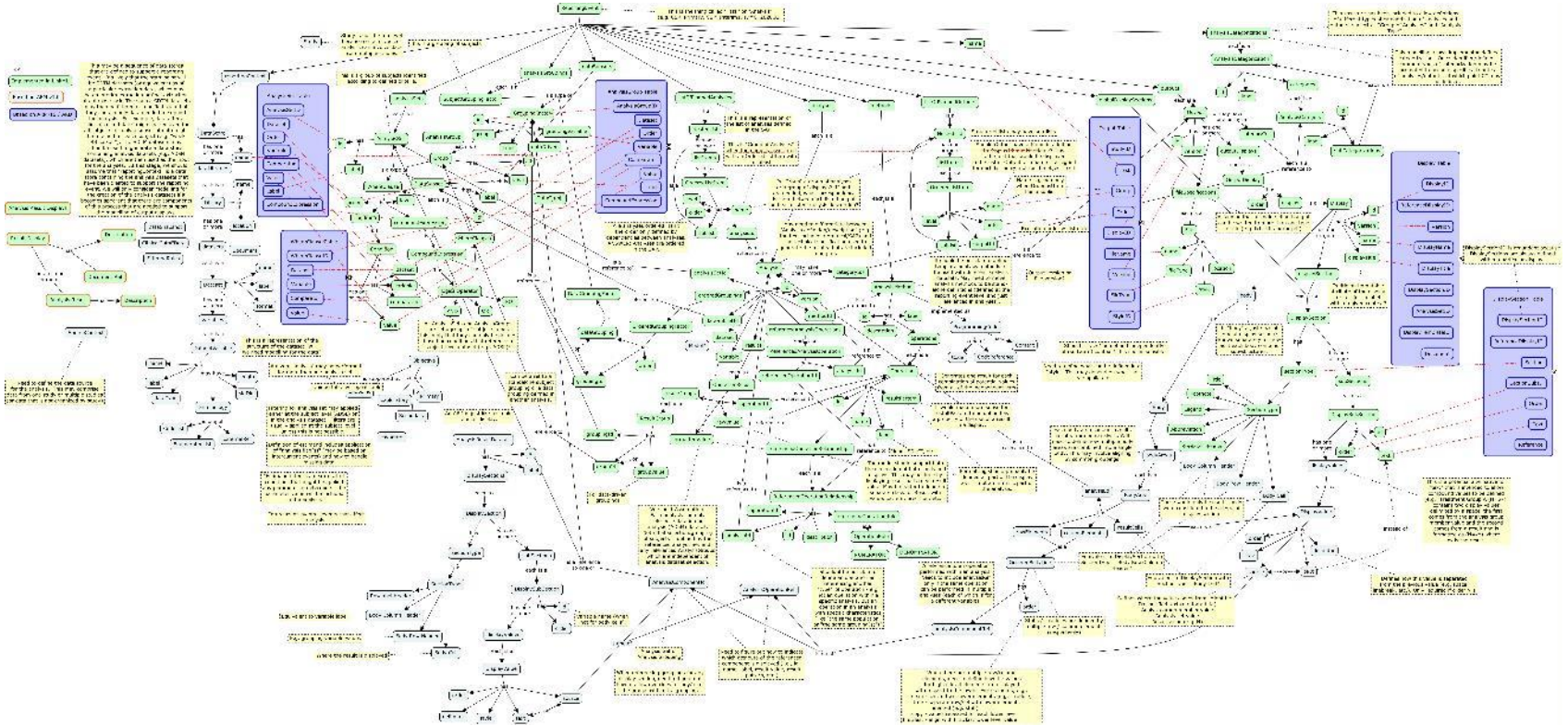
Analysis Results Standard

- Working on the API specification
- Planning a COSA Hackathon in June
- ARS model / schema is drafted (next slide)

- Planning to implement 4 FDA TFLs in ARS
- Release as example implementation package
- Ideating eTFL Portal



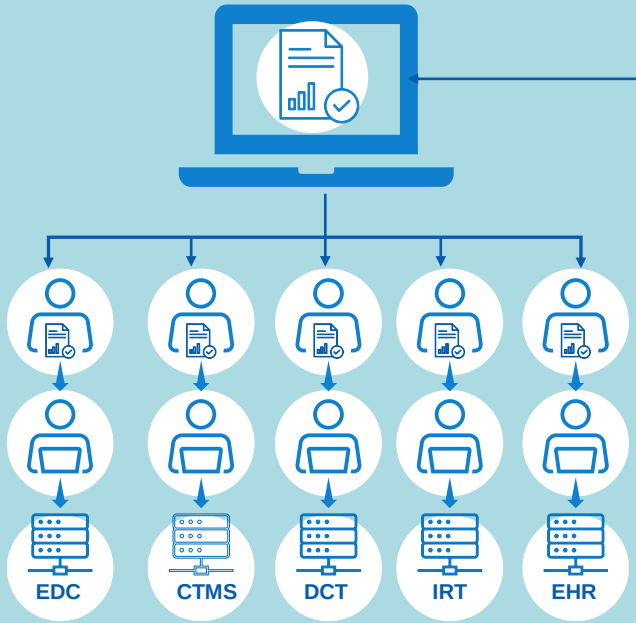
ARS Schema



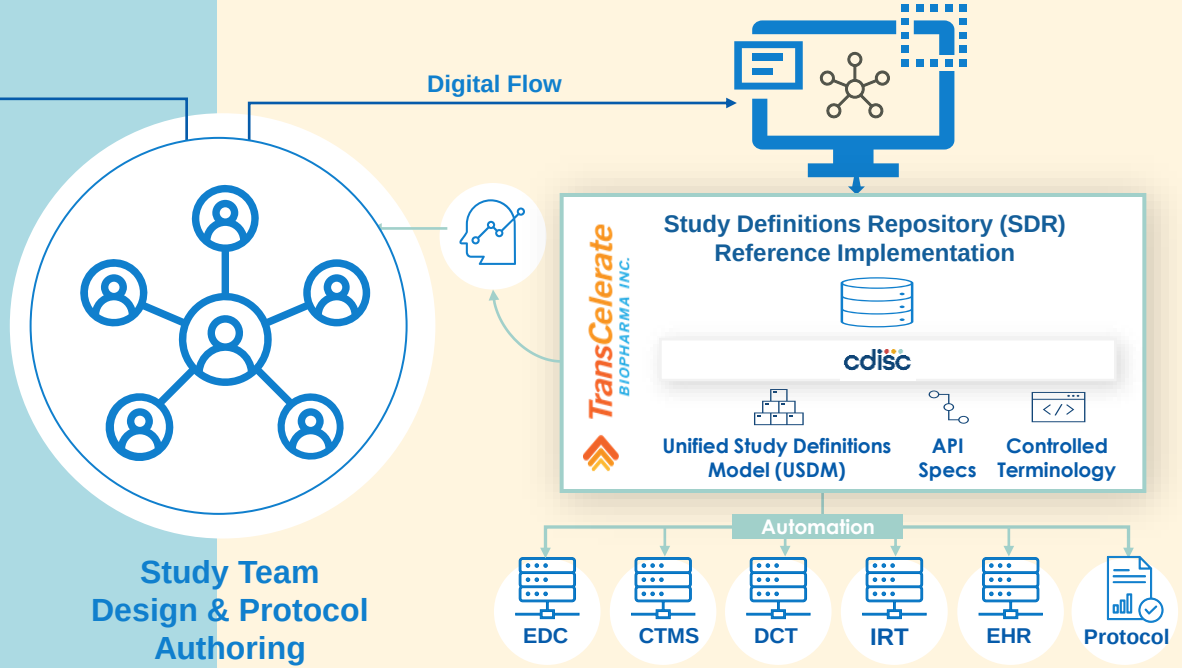
Digital Data Flow (DDF) Initiative

Write Once, Read Many

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



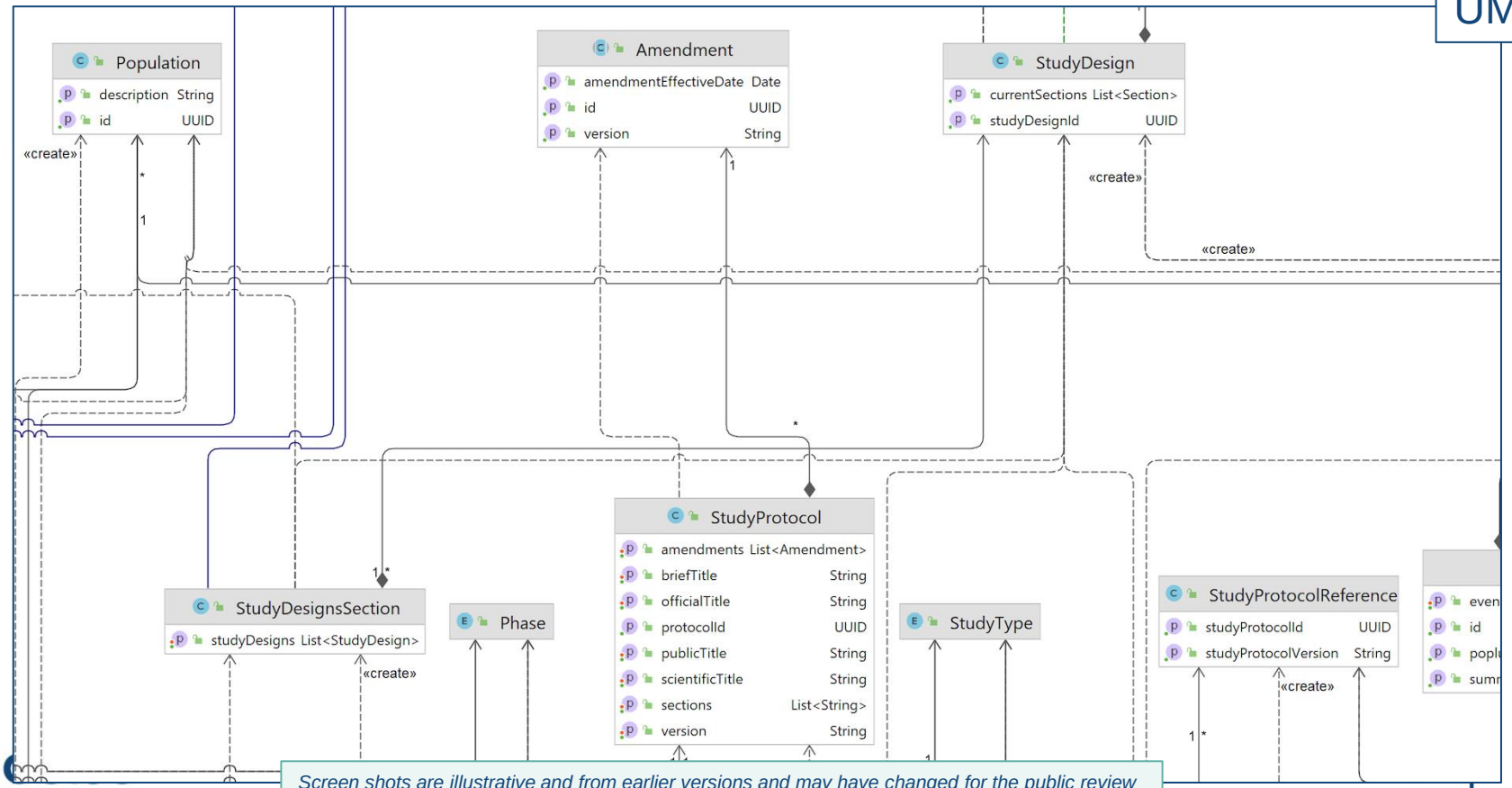
TOMORROW: Digital paradigm for protocol creation, with fully automated data flow and interoperability between systems



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

SAS v5 XPT format is the current standard for exchanging tabular datasets

- Currently Mandated by regulatory agencies
- Limitations of XPT v5
  - Numeric limitations, antiquated format
  - Stores data in its own numeric way
  - Character limitations, no UTF-8 encoding
    - No support for characters from other languages
  - String & Column limitations (variable names > 8, labels > 40, data > 200)
  - No metadata extensibility
- Considered outdated and antiquated
- Technology ‘stigma’

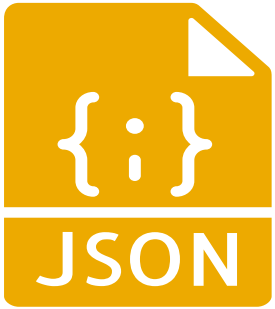
What is Dataset-JSON and Advantages

What is JSON?
An open standard file format and data interchange format that uses human-readable text to store and transmit data objects consisting of attribute–value pairs and arrays

What is Dataset-JSON?
A dataset exchange standard for exchanging tabular data leveraging JSON designed to meet the regulatory submission needs and eliminating limitations of legacy formats

Dataset-JSON advantages…

- Based on the JSON standard used worldwide
- Open-source and truly human readable
- Same or smaller file sizes relative to current required format
- Remove variable naming, width, or format limitations
- Simple transformation to/from SAS data



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Proposed Dataset-JSON Pilot

Milestone 1: Short Term

- Pilot submissions using JSON format with existing XPT ingress/egress to carry the same data
- Same content, different suitcase, no disruption to business process on either side
- In parallel, evaluate how FDA toolset can support JSON format and identify tool upgrade roadmap

➔ **Success Criteria: Accept Dataset-JSON as a transport format option (in addition to existing XPT format)**

Milestone 2: Long Term

- Enhance the CDISC SDTM and ADaM standards beyond XPT limitations (e.g. Variable names > 8, labels > 40, data > 200
- New Define-XML / Define-JSON based on ODM v2.0
- Enhanced conformance rules
- Collaborate with FDA to develop plan to retool their environment to natively consume JSON

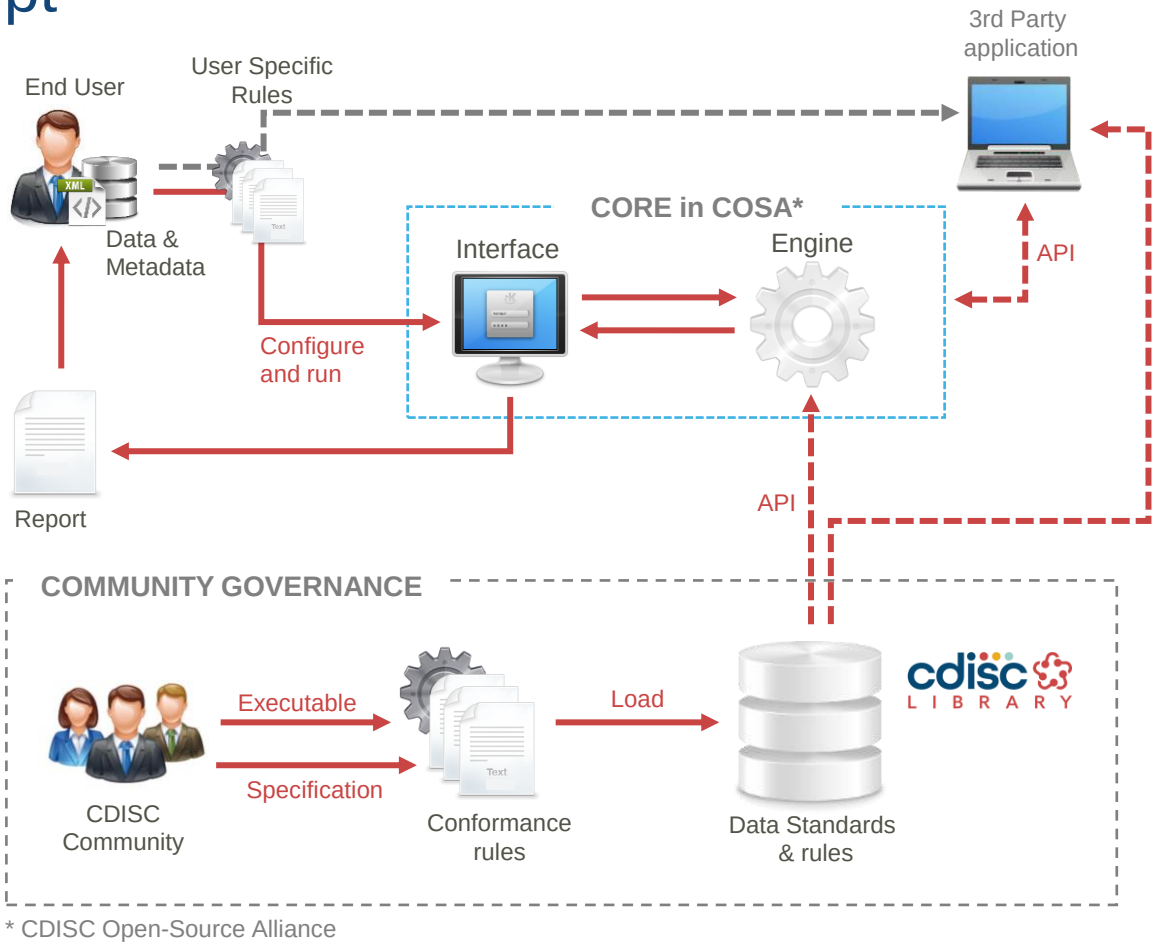
➔ **Success Criteria: accept advanced Dataset-JSON as the only transport format option and deprecate XPT**

Conformance Rules - CORE

The Challenge

- A single source of truth for all conformance rules
- Consistency across conformance rule implementations

CORE Concept



* CDISC Open-Source Alliance

CORE Rules Governance

Rules Governance Team

(CDISC; FDA; Community)

Rule Specifications

cdisc Standards — Provide rule specs

FDA — 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

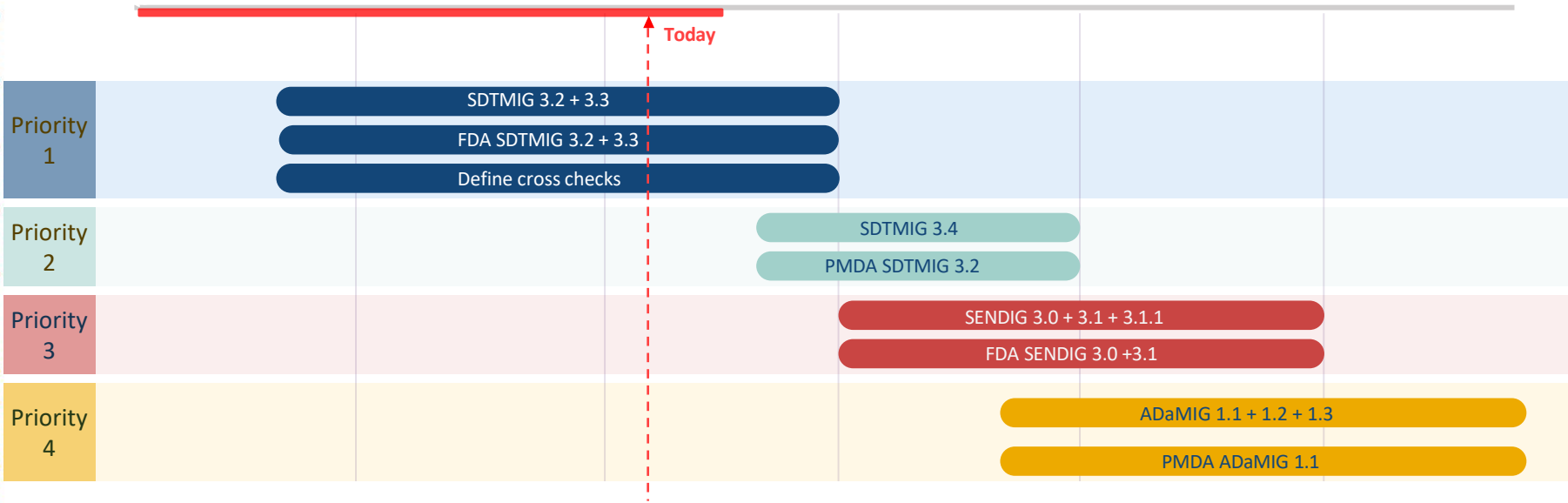
CORE Engine (cdisc CORE OPEN RULES ENGINE)

Rules Development Progress

Components	Status										
	OPEN	DONE	BLOCKED	UNIT TESTING	QC IN PROGRESS	READY TO PUBLISH	PUBLISHED	AWAITING QC	AUTHOR IN PROGRESS	BACK TO AUTHOR	T:
ADaMIG v1.0	312	0	0	0	0	0	7	2	0	0	**321**
ADaMIG v1.1	417	0	0	0	0	0	7	2	0	0	**426**
ADaMIG v1.2	589	0	0	0	0	0	7	2	0	0	**598**
ADaMIG v1.3	549	0	5	4	0	0	8	11	17	2	**596**
FDA SDTMIG v3.2	493	0	0	0	0	0	0	0	0	0	**493**
FDA SDTMIG v3.3	501	0	0	0	0	0	0	0	0	0	**501**
FDA SENDIG DART v1.1	350	0	0	0	0	0	0	0	0	0	**350**
FDA SENDIG v3.0	316	0	0	0	0	0	0	0	0	0	**316**
FDA SENDIG v3.1	330	0	0	0	0	0	0	0	0	0	**330**
FDA SENDIG v3.1.1	335	0	0	0	0	0	0	0	0	0	**335**
FDA SENDIG-AR v1.0	466	0	0	0	0	0	0	0	0	0	**466**
SDTMIG v3.2	169	35	11	0	1	0	192	0	7	2	**417**
SDTMIG v3.3	150	45	11	1	1	0	232	0	7	2	**449**
SDTMIG v3.4	6	59	45	10	3	0	277	2	40	1	**443**
SENDIG v3.0	259	0	0	0	2	0	3	0	0	0	**264**
SENDIG v3.1	174	2	2	3	2	5	7	96	11	1	**303**
SENDIG v3.1.1	307	0	0	0	2	0	3	0	0	0	**312**
SENDIG-DART v1.1	353	0	0	0	2	0	3	0	0	0	**358**
Total Unique Issues:	**6076**	**141**	**74**	**18**	**13**	**5**	**746**	**115**	**81**	**8**	**7277**

Statistieken **18** van **18**.
Bekijk in Jira

Rules Development Priority



➡ *Timelines depend on community engagement*

CORE Engine is Open-Source

- Open-source framework
  - Listed in the COSA (CDISC Open-Source Alliance) directory
  - Permissive MIT open-source license
  - Provided via GitHub
- Free to all in CDISC community
- Very flexible implementation options

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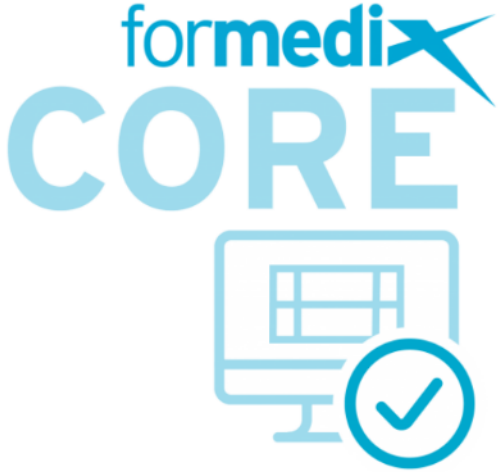
First vendor launch

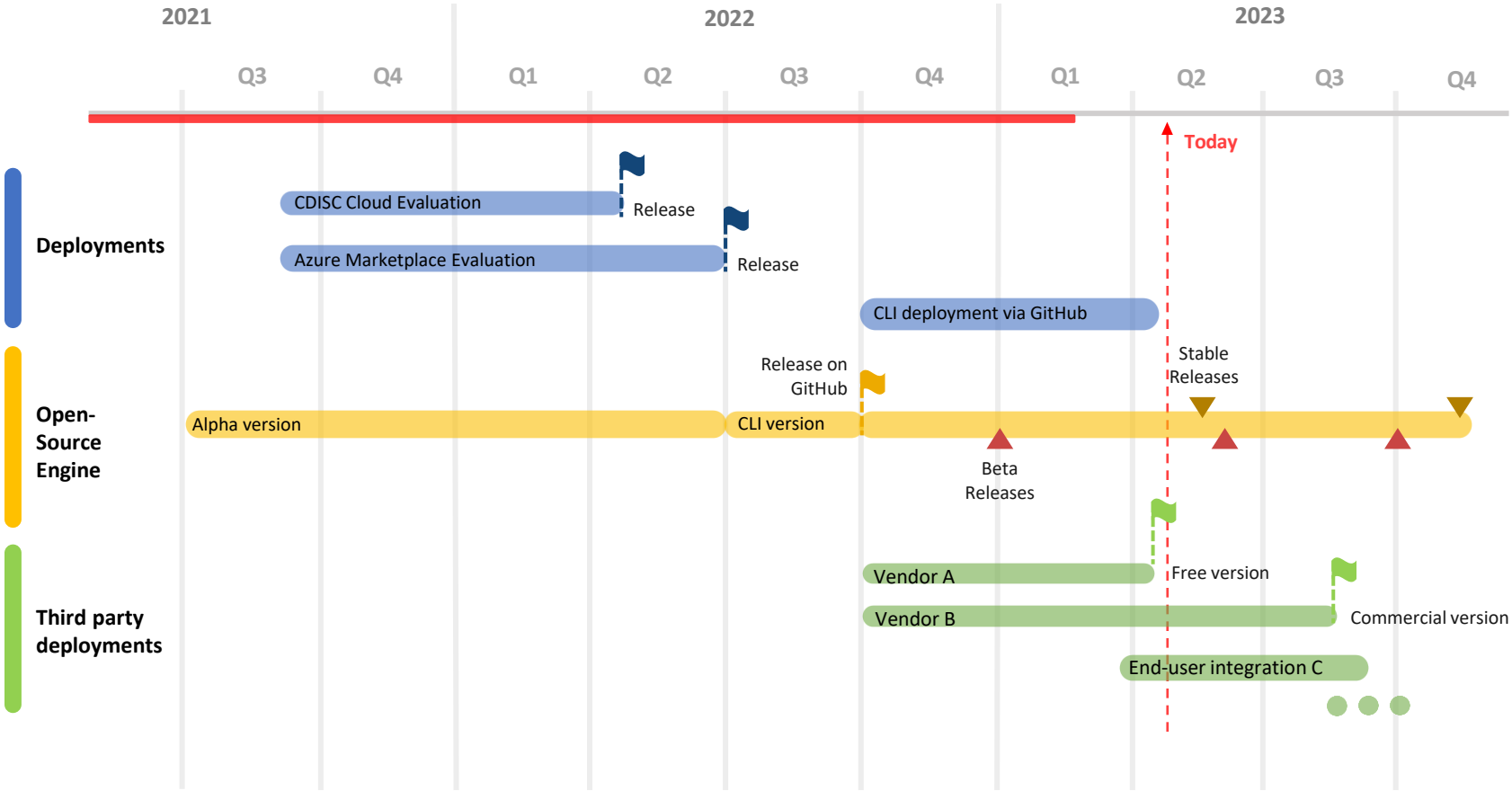
Introducing Formedix CORE: a free-to-use desktop app incorporating the CDISC Open Rules Engine

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



Engine and Deployments Overview



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

CORE Future State

- Rules
  - Full set of executable rules for submission standards (SDTM, SEND, ADaM)
  - Including Regulatory-specific rules
  - Including Define.xml cross-check rules

  ➔*Continuing volunteer engagement is critical!*

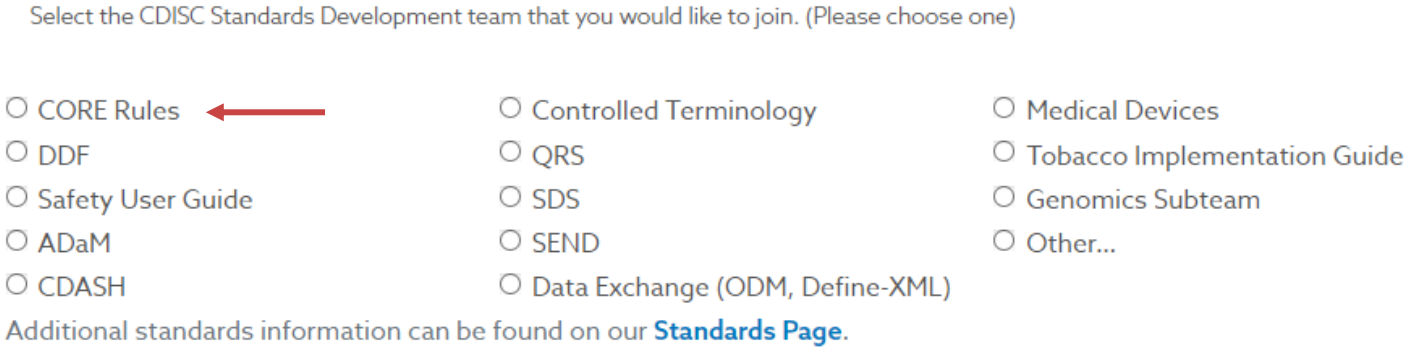
- CORE is the Reference Engine
  - Engine with all basic functionality for full set of machine-executable rules
  - Includes a validation package

- CDISC will establish a CORE certification program
  - To verify output of different applications versus the CORE Reference Engine
  - CDISC conformance rules are the single version of the truth

Rules are part of the Standards!
Expect Regulatory Agencies to mandate use of CDISC Conformance Rules

How to sign up as a volunteer

- https://www.cdisc.org/volunteer/form
  - Select CORE Rules Team



Relentless Collaboration

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Thank you!