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2023
KOREA
INTERCHANGE
SEOUL | 11-14 DECEMBER

State of the CDISC Standards

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.

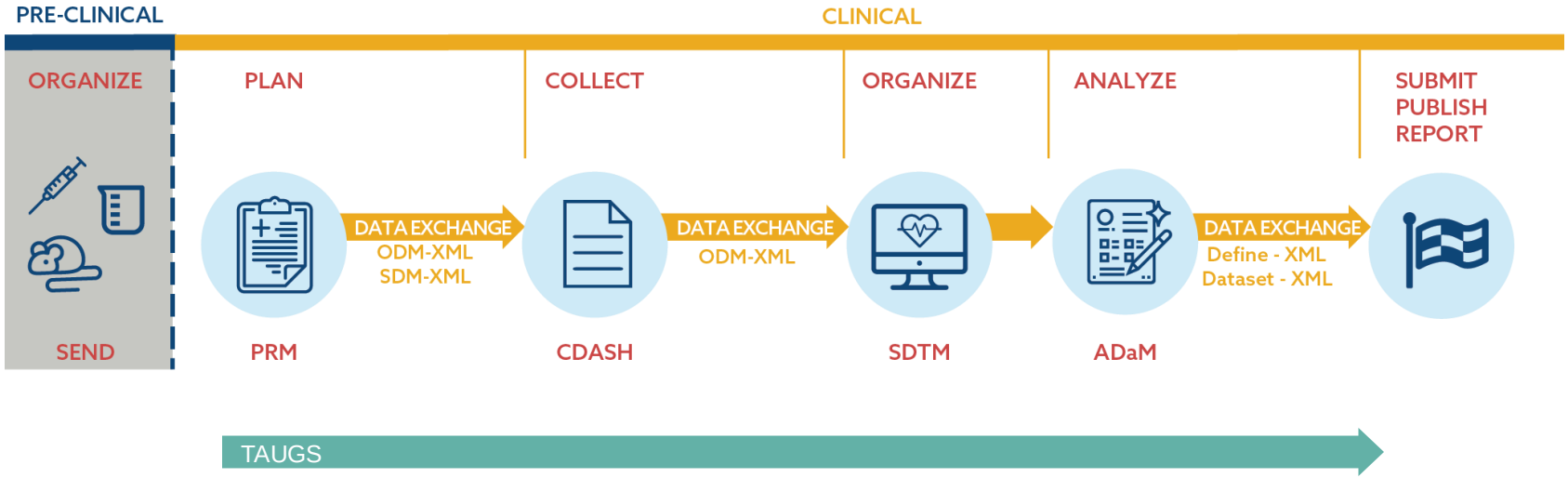
He previously served as CDISC's European Liaison, shepherding relationships with key European regulatory, academic, and biopharma stakeholders. Peter is also an active PHUSE collaborator.

Agenda

1. CDISC 360: End to End Standards
2. Key Initiatives for 2023 and Beyond

CDISC 360: End to End Standards

Our Start



BRIDG, CONTROLLED TERMINOLOGY AND GLOSSARY

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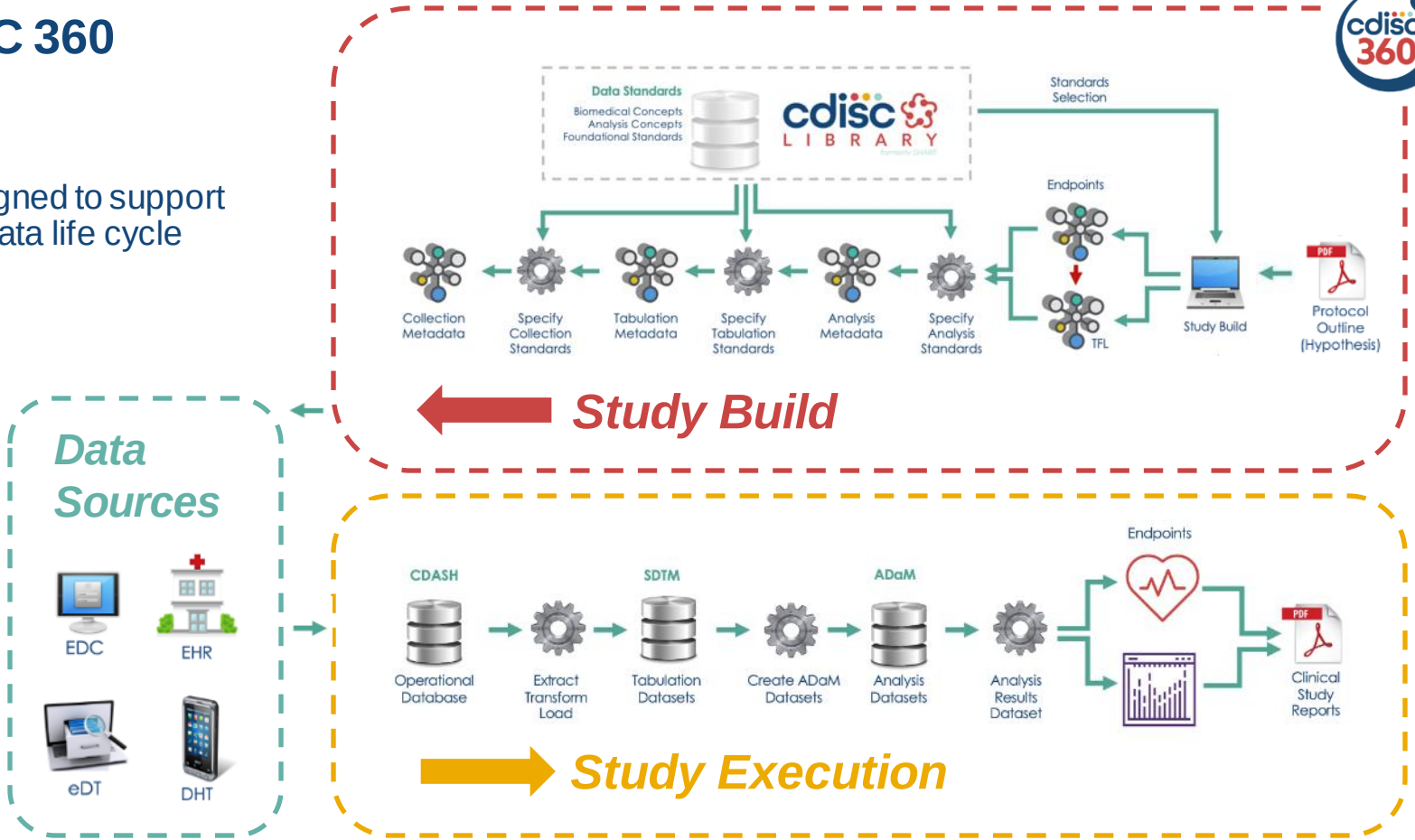
Continued Evolution of Standards

- 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

CDISC 360

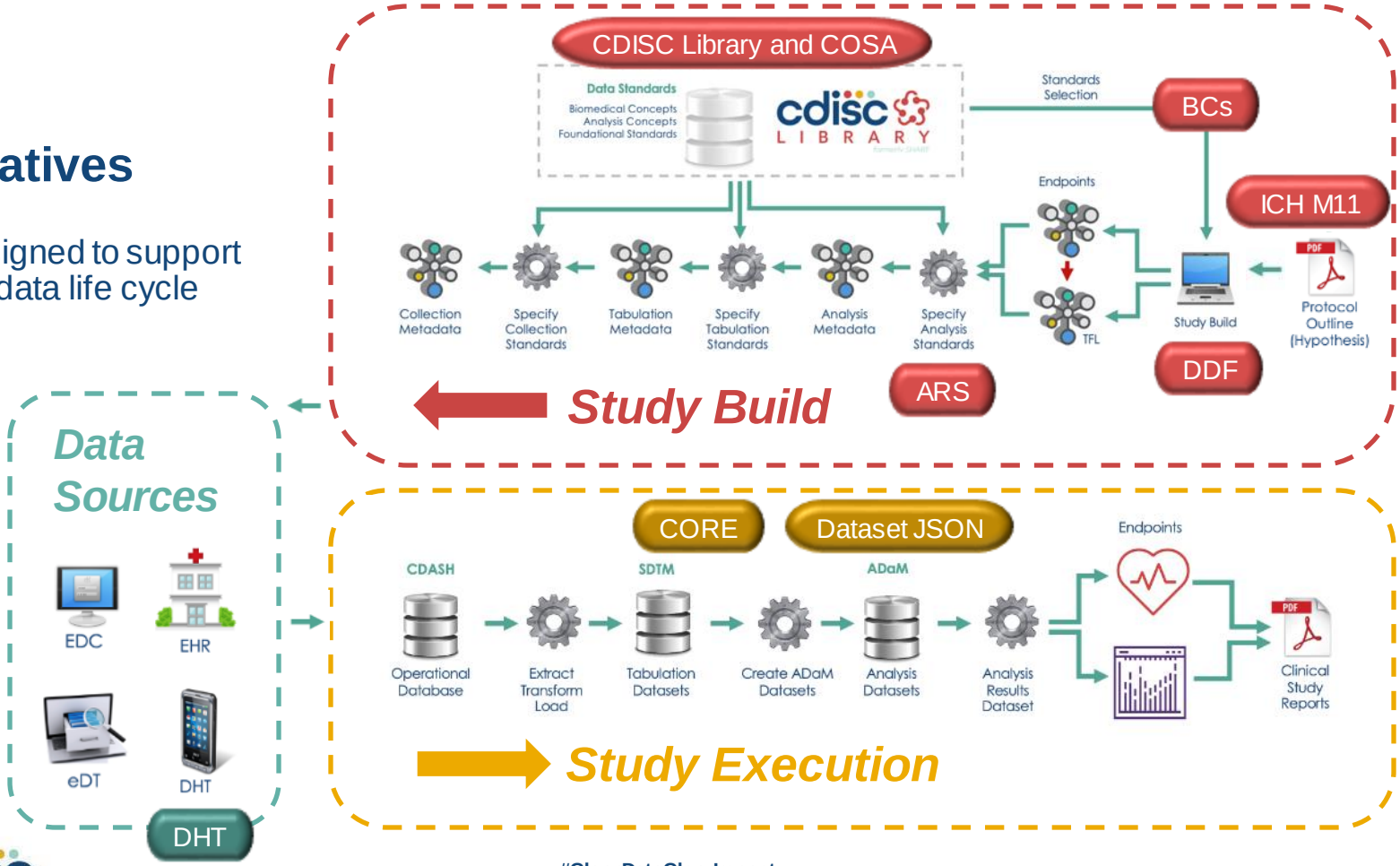
- Designed to support the data life cycle



Key Initiatives for 2023 and Beyond

Key Initiatives

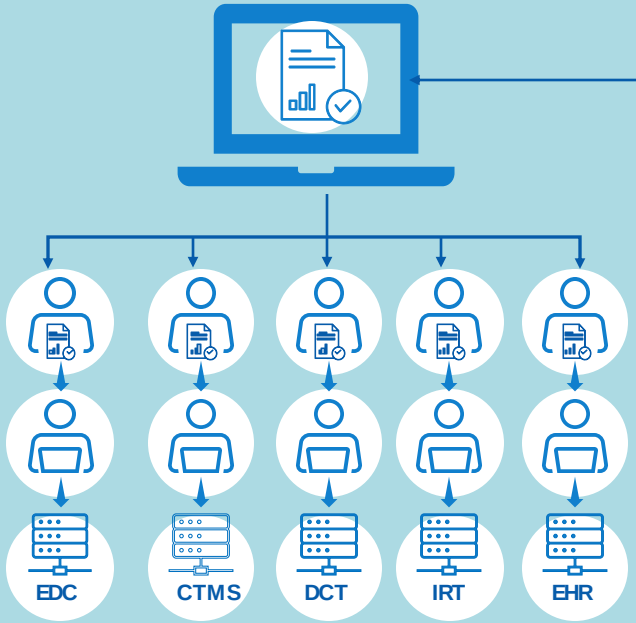
- Designed to support the data life cycle



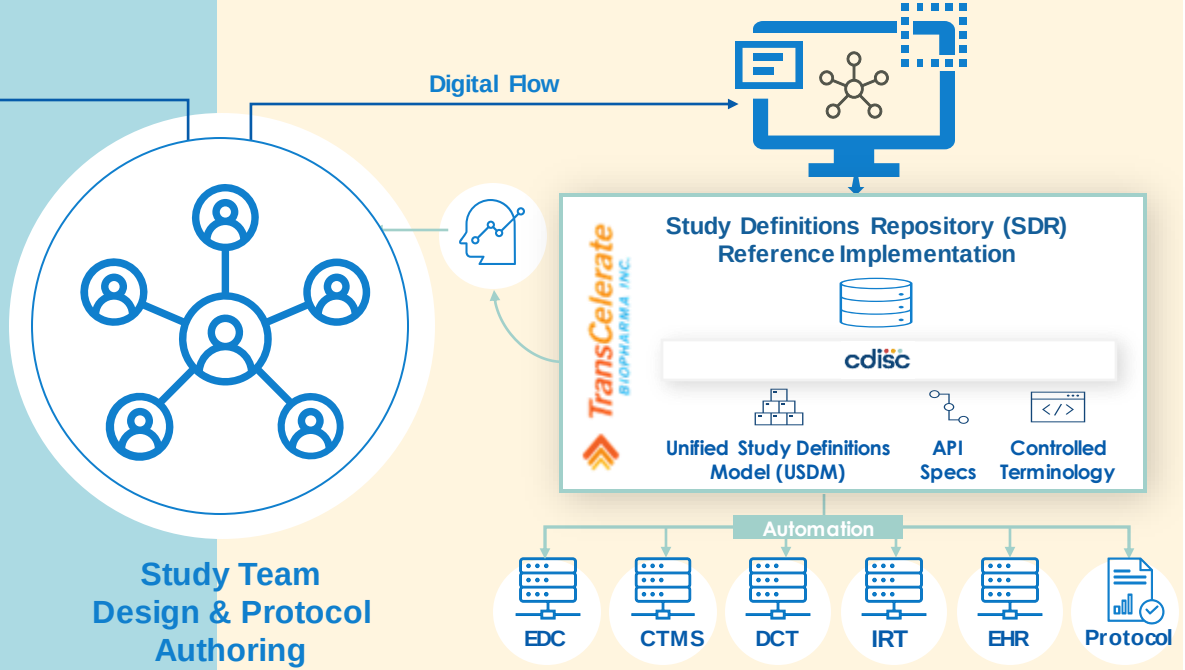
Digital Data Flow (DDF)

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



ICH M11 Guideline

Structure and Content of a Clinical Protocol

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

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

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

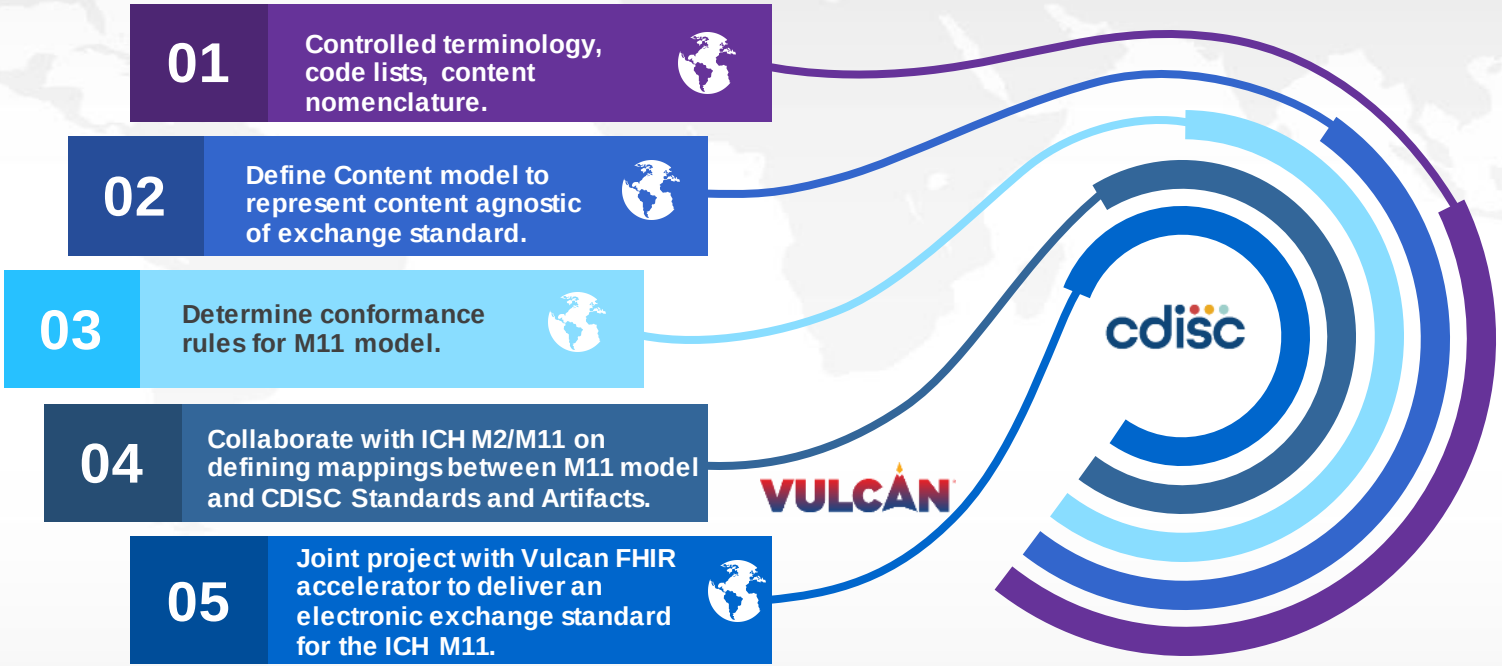
Trial Design

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

Biomedical Concepts

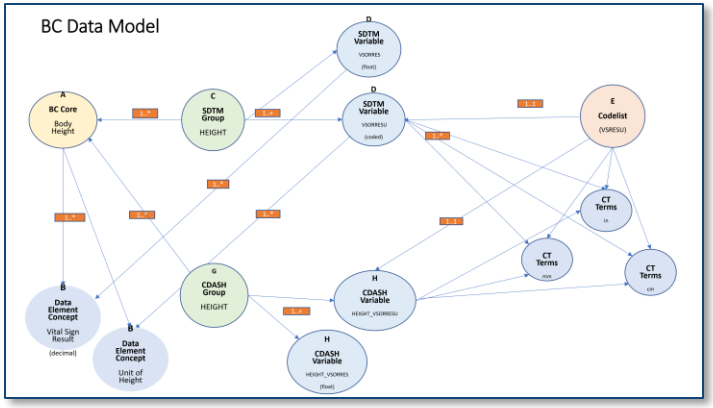
A pragmatic, iterative approach to creating biomedical concepts with a focus on providing tangible value for the CDISC community

Key Objectives:

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

Key Components:

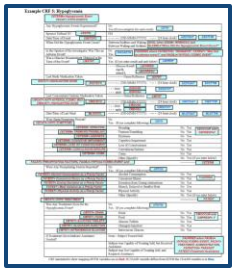
- Conceptual layer
- Implementation layer
- Logical data model



Biomedical Concepts: Semantics

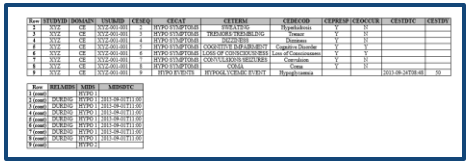
Representation of a BC in a specific standard with implementation details such as value level metadata, formats, terminology – alignment across standards

Analysis Results Standards (ARS)



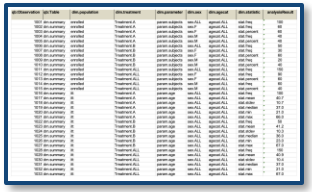
Data Collection

CDASH



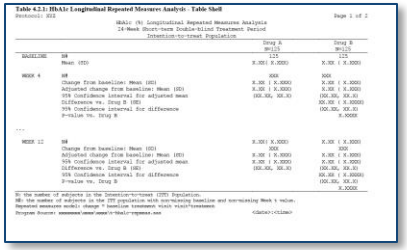
Data Aggregation

SDTM



Analysis

ADaM



Results

Opportunities for Standardization

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

ARS 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

ARS 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

Today

- Public Review in October 2023
- Final Release: Dec 2023/Jan 2024

Future

- Example implementation package with four TFL examples!
- Ideation of eTFL Portal

Digital Health Technologies (DHT)

Increased industry focus on digital health technologies

FDA | CDER | Small Business and Industry Assistance

INDUSTRY NEWS

FDA to Host Digital Health Technologies for Drugs Public Workshop

The U.S. Food and Drug Administration is hosting the virtual public workshop "Understanding Priorities for the Development of Digital Health Technologies to Support Clinical Trials for Drug Development and Review" on March 28th and 29th, 2023. The workshop will focus on understanding the priorities and challenges of developing Digital Health Technologies (DHTs) to support clinical drug trials.

The workshop will be convened by the Robert J. Margolis, MD, Center for Health Policy at Duke University under a cooperative agreement with FDA.

For more information on the Digital Health Technologies virtual public workshop and to register, please visit FDA's Meeting's, Conferences & Workshops (Drugs).

Standards Through Partnership

DIGITAL MEDICINE SOCIETY

To advance the ethical, effective, equitable, and safe use of digital medicine to redefine healthcare and improve lives

DATACC

Digital Health Measurement Collaborative Community

by DiME

A collaborative community hosted by DiMe with the FDA's Center for Devices and Radiological Health

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To advance data standards and transform incompatible formats, inconsistent methodologies, and diverse perspectives to amplify data's impact for research and global health.

Volunteers

CDISC Digital Health Technologies (DHT)

Partner

- Expert organizations
- Expert volunteers

Standardize

Concepts, device attributes, endpoints, and best practices

Resources

Robust & aligned

Scope

June - October

Develop

Start in November

Deliver

2024 staged releases

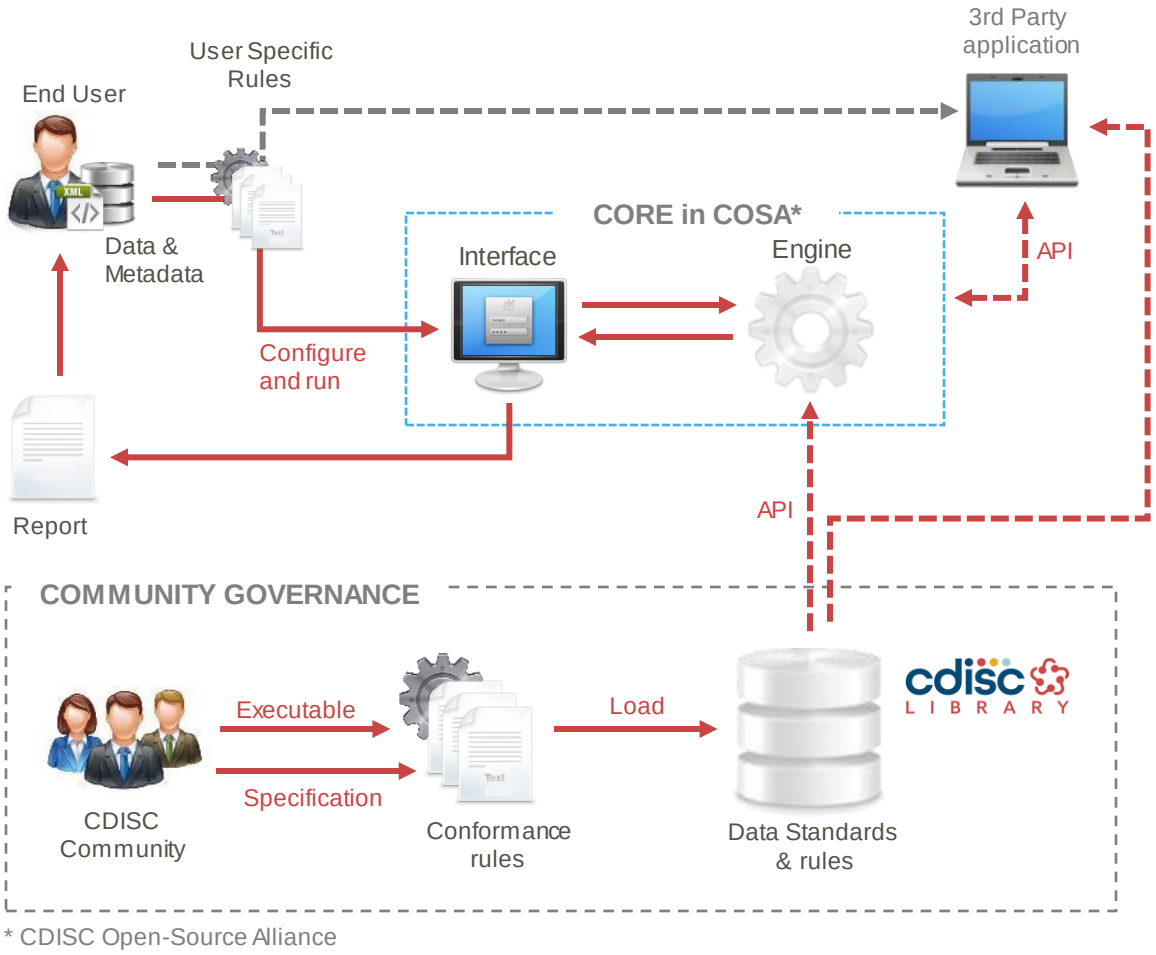
CDISC Open Rules Engine (CORE)

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



* CDISC Open-Source Alliance

CORE Rules Governance

Rules Governance Team

(CDISC; Regulatory Agencies; Community)

Rule Specifications

CORE Rules (executable)

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

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

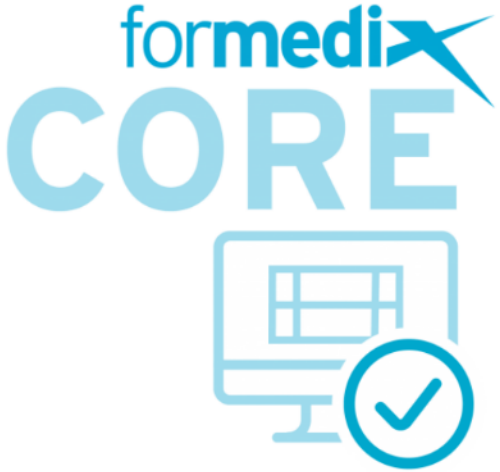
CORE Engine

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

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’

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

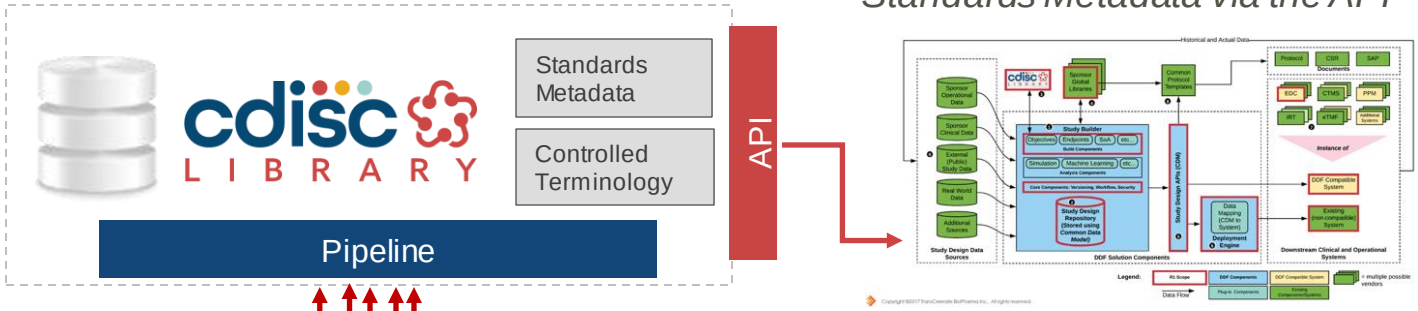
- Enhance the CDISC SDTM and ADaM standards beyond XPT limitations (e.g. Variable names > 8, labels > 40, data > 200
- New Define-XML / Define-JSON based on ODM v2.0
- Enhanced conformance rules
- Collaborate with FDA to develop plan to retool their environment to natively consume JSON

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

Dataset-JSON Pilot

CDISC Library: Standards as a Service

Software Applications Consume Standards Metadata via the API



Executable Conformance Rules

Biomedical Concepts	Codelist Subsets	Dataset Specializations	Implementation Guide Text	Standards Mappings
Analysis Results Standard	TAUG Metadata	Derivations and Mappings	Machine-readable Examples	Draft Standards Metadata
Tables, Listings, and Figures	QRS Metadata	Trial Master File Reference Model	CRF Collection	Diff Content Between Versions

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

https://cosa.cdisc.org

Relentless Collaboration

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Thank you!