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2023
US
INTERCHANGE
FALLS CHURCH, VA | 18-19 OCTOBER

State of the CDISC Standards

Christine Connolly, Head of Standards Projects, CDISC

Meet the Speaker

Christine Connolly

Title: Head of Standards Projects

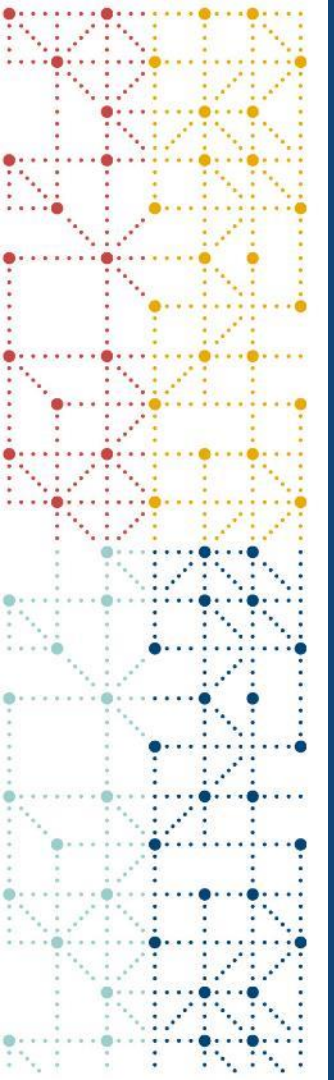
Organization: CDISC

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.

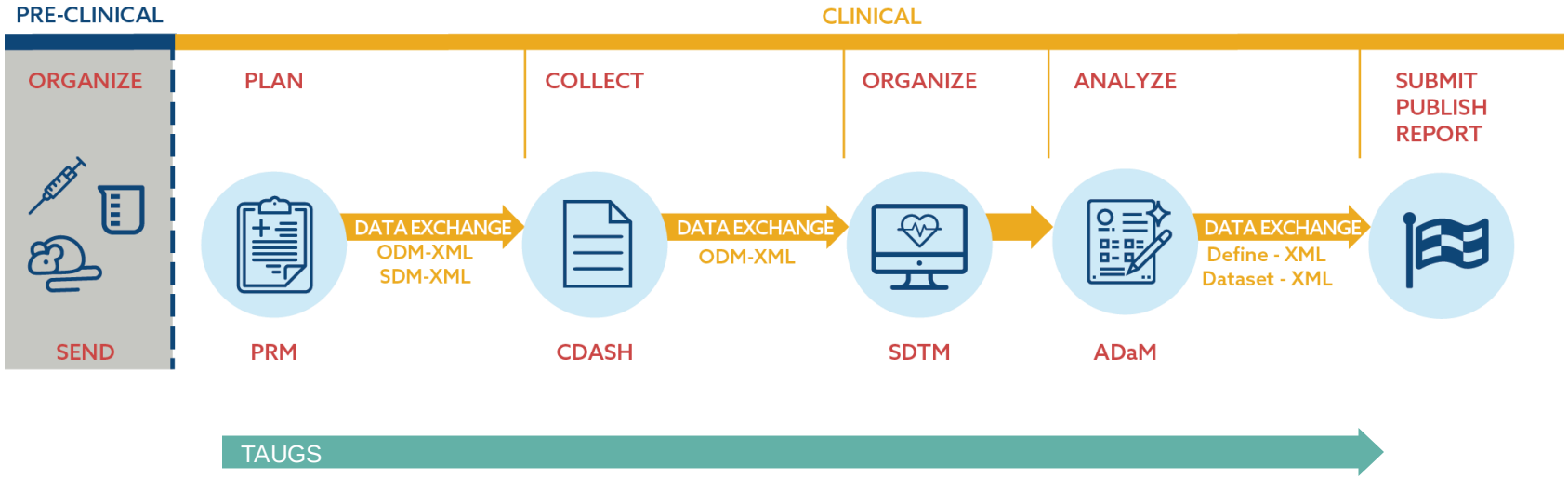
Agenda

1. Comprehensive Standardization
2. Key Initiatives for 2023 and Beyond



Comprehensive Standardization

Our Start



BRIDG, CONTROLLED TERMINOLOGY AND GLOSSARY

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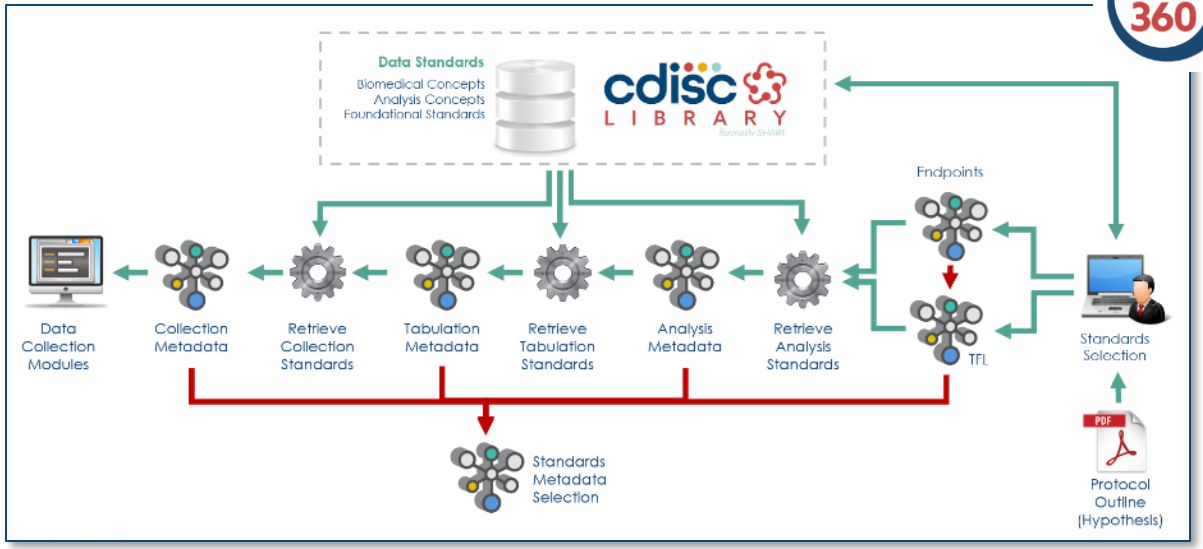
CDISC 360

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



Learnings

- **Complete** end-to-end standards when incomplete
- **Enrich** standards with the metadata for full meaning and relationships with a biomedical concept layer
- **Extend** the CDISC Library model with implementation level metadata
- **Collaborate** with industry for biomedical concepts

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

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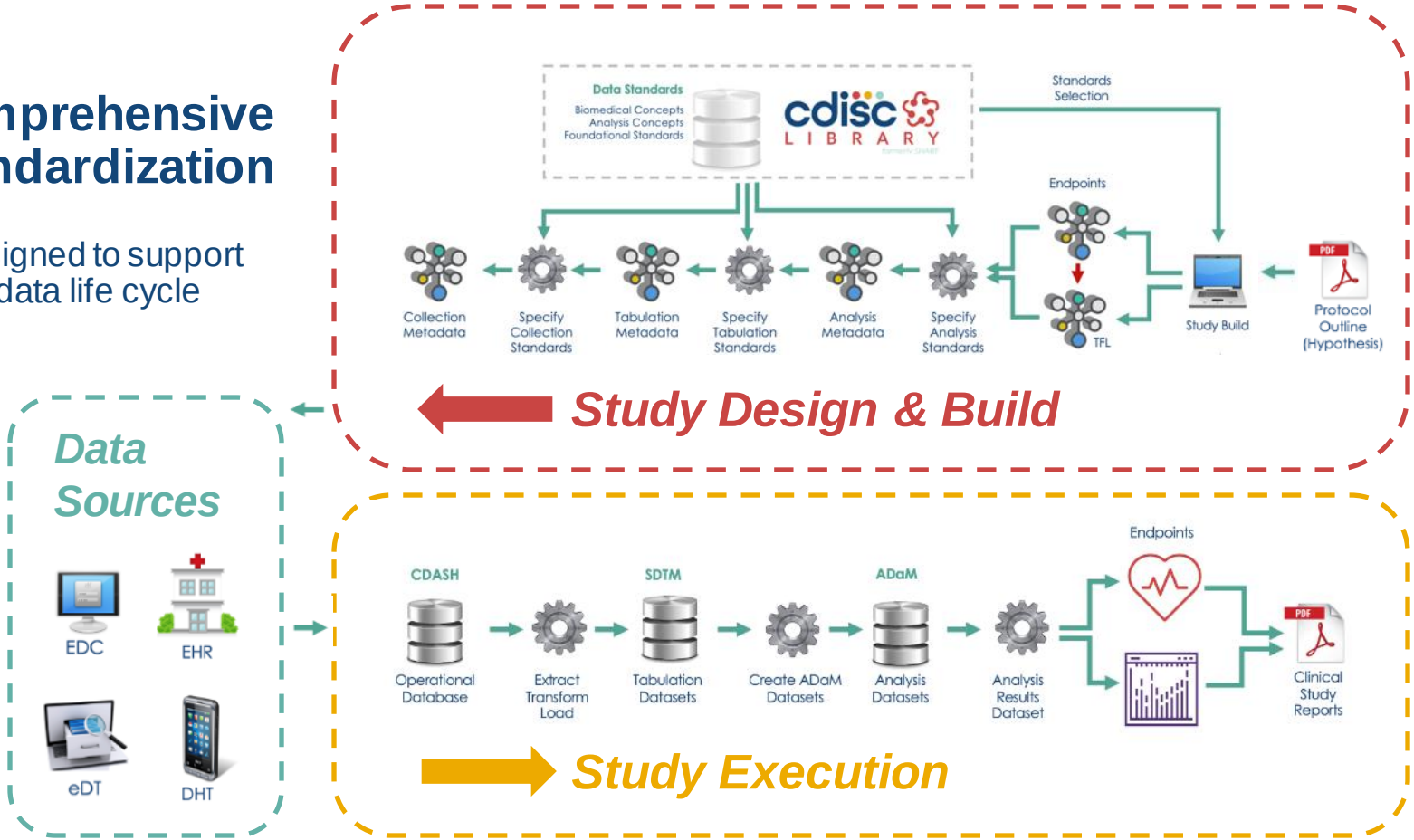
Comprehensive Standardization

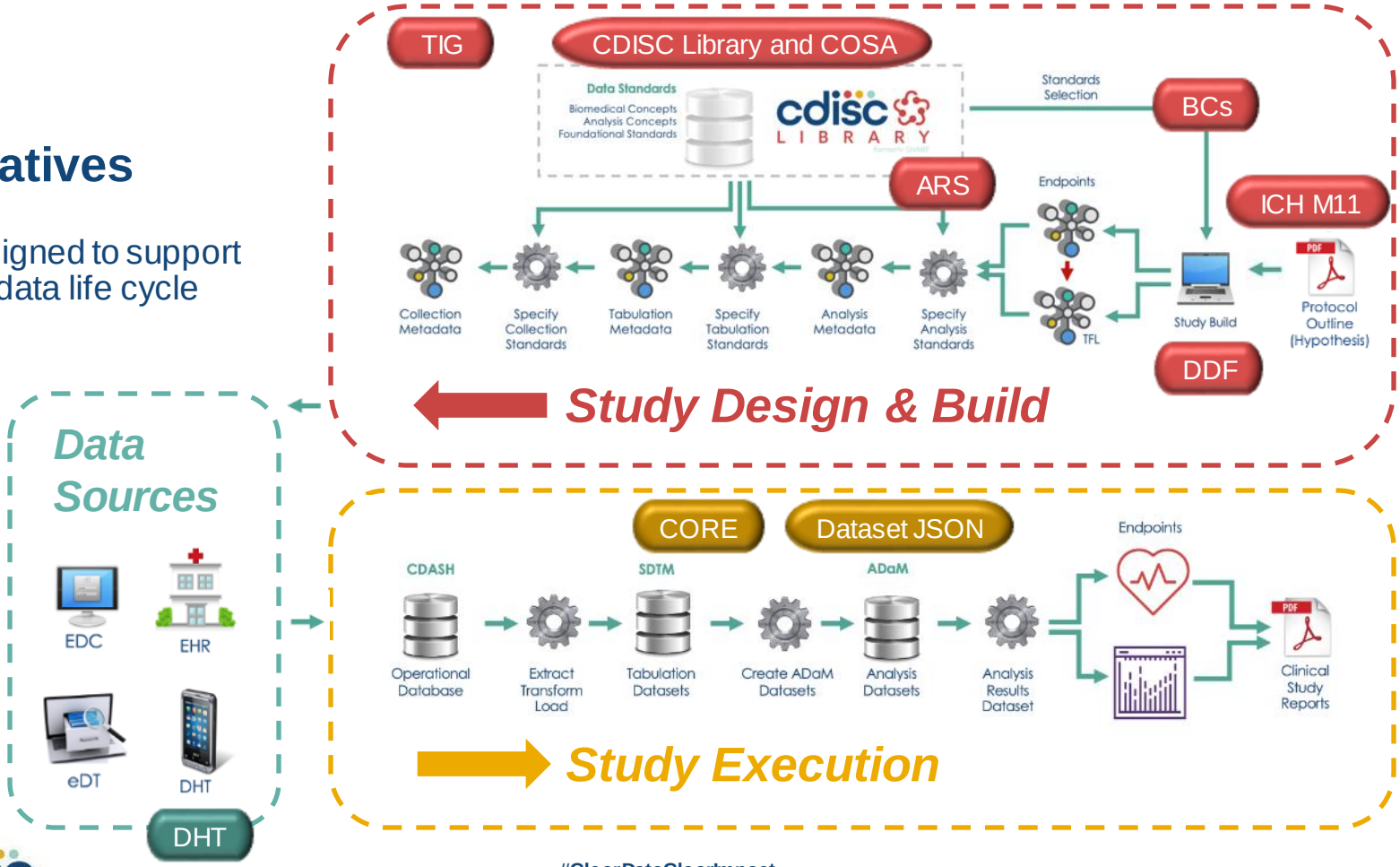
- Designed to support the data life cycle



Key Initiatives for 2023 and Beyond

Key Initiatives

- Designed to support the data life cycle



Study Design & Build

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

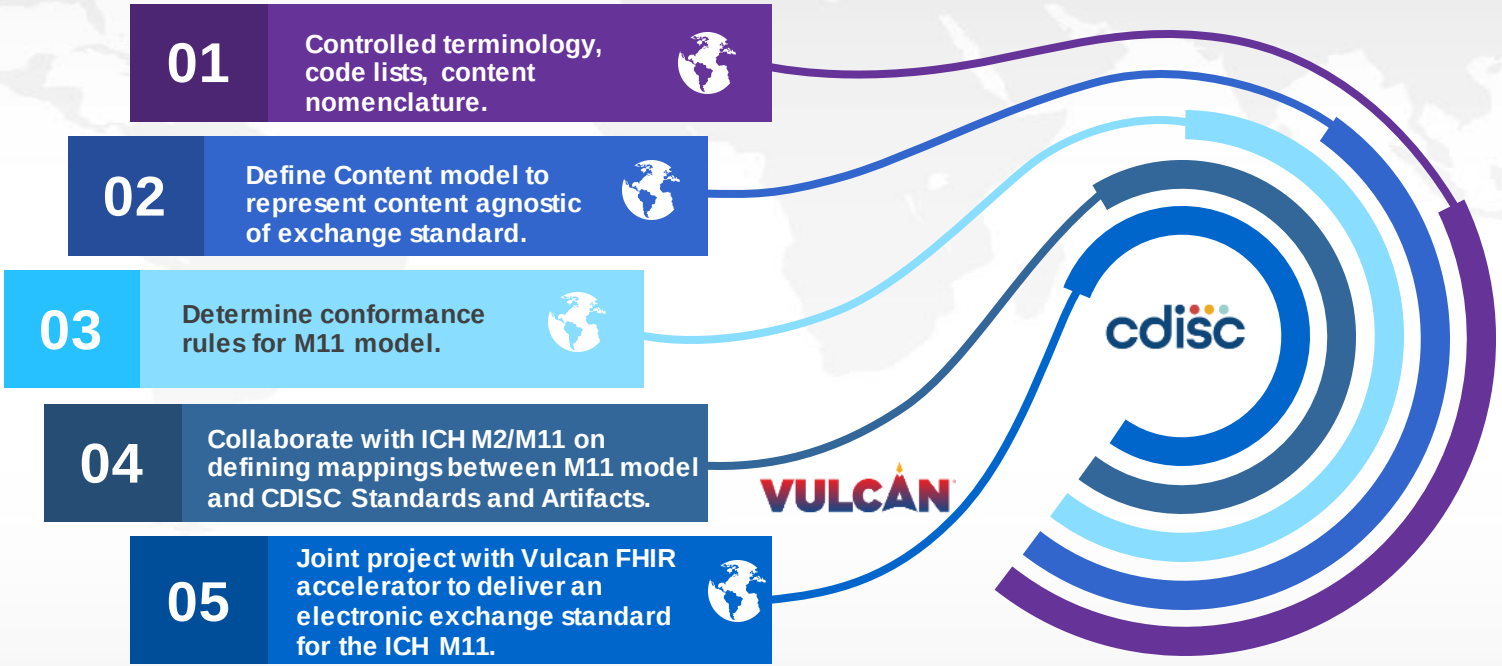
Trial Design

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

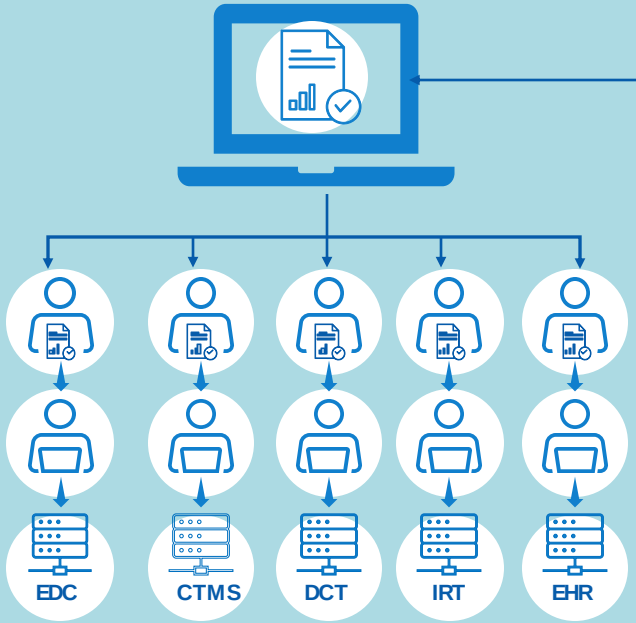


* M11 Clinical Electronic Structure Harmonized Protocol presentation - Panagiotis Telonos, EMA - CDISC Europe Interchange 2023

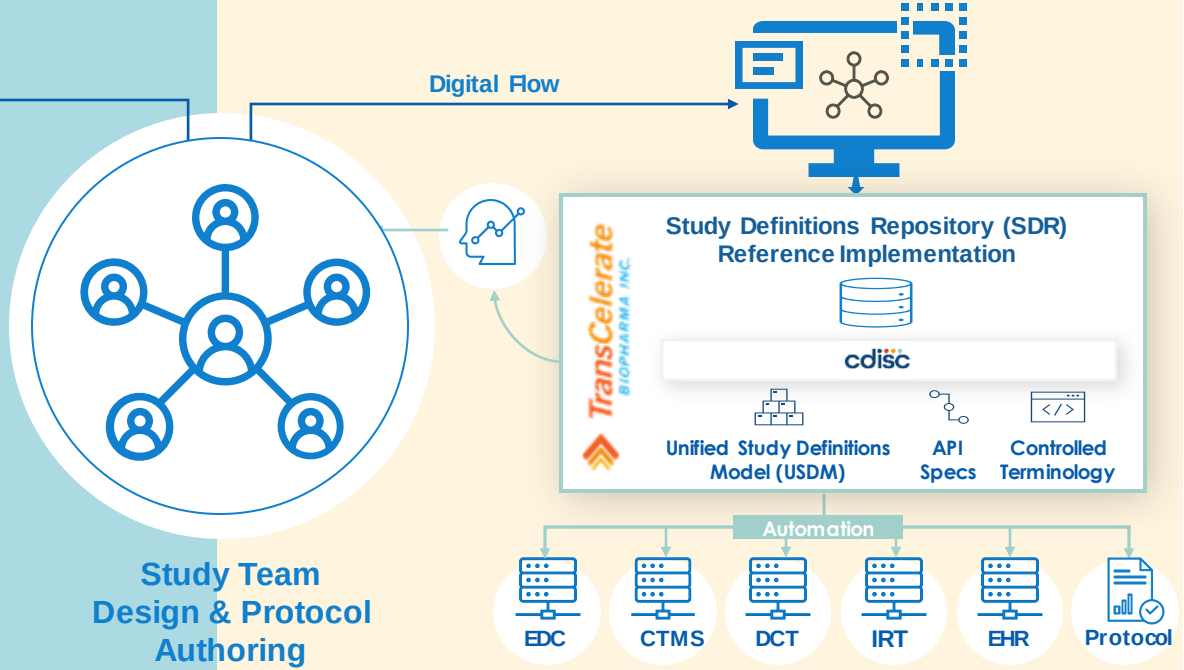
Digital Data Flow (DDF)

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



Biomedical Concepts

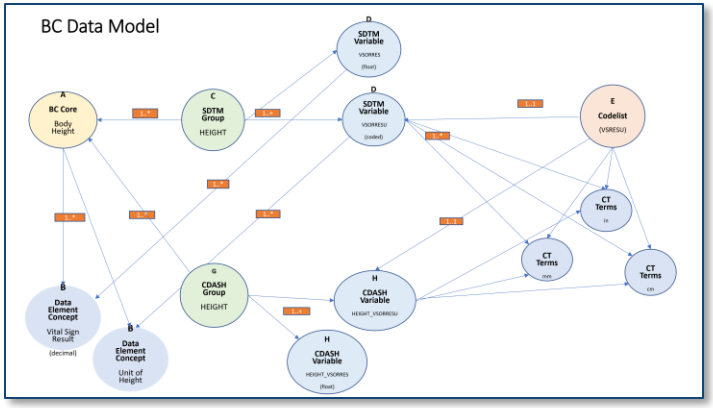
A pragmatic, iterative approach to creating biomedical concepts with a focus on providing tangible value for the CDISC community

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



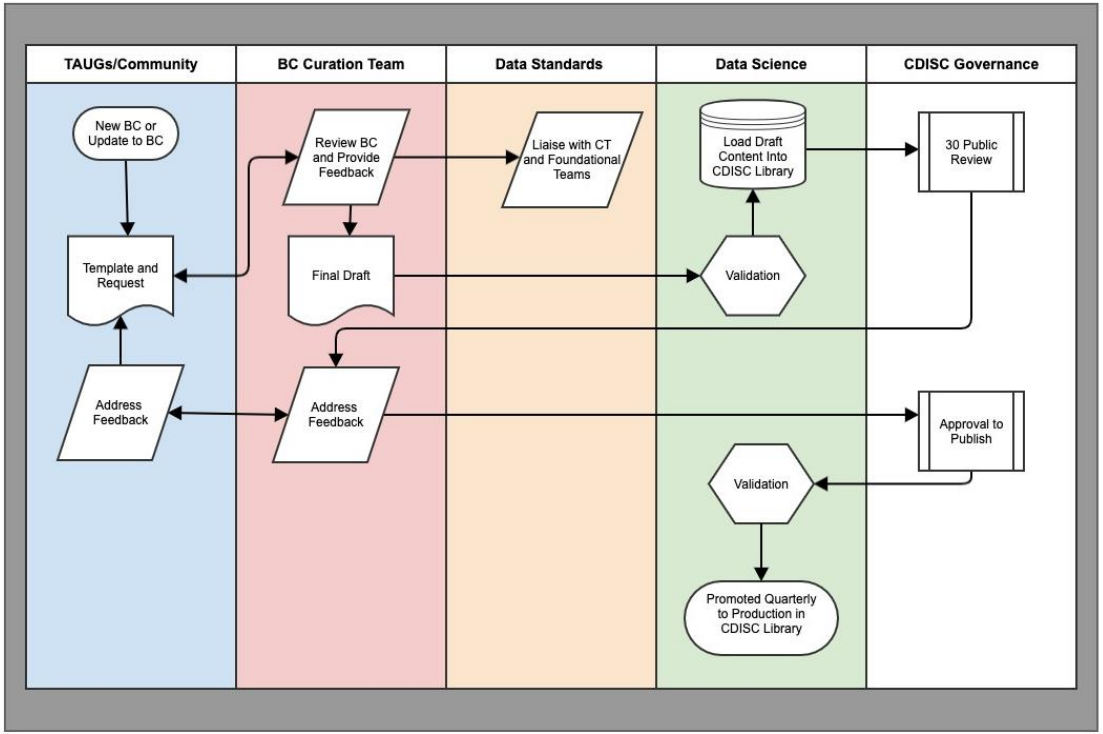
Biomedical Concepts: Semantics

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

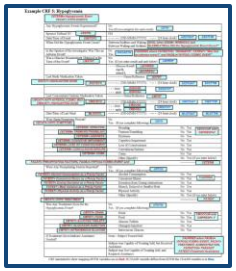
Biomedical Concepts: Governance

- Light-weight CDISC curation and process
- 30-day Public Review
- Published quarterly
- Mechanism for community change requests

Draft Governance Process

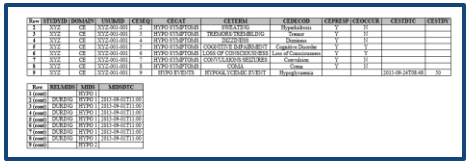


Analysis Results Standard (ARS)



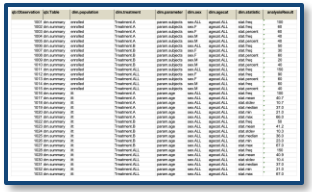
Data Collection

CDASH



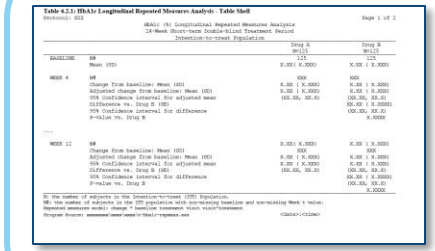
Data Aggregation

SDTM



Analysis

ADaM



Results

Opportunities for Standardization

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

Analysis Results Standard Key Objectives

Leverage analysis results metadata to drive the automation of results

Support storage, access, processing, traceability and reproducibility of results

Develop a logical model that describes analysis results and associated metadata

User Guide to illustrate and exercise model with common safety displays

Analysis Results Standard

✓ **ARS COSA Hackathon**
- Readout at CDISC US Interchange and COSA spotlight December

Public Review in October

✓ Analysis Results Standard Model v1.0

✓ Analysis Results User Guide Version 1.0

Planning
- Implement four example TFLs in ARS
- Release as an example implementation package
- Ideation for an eTFL Portal

Tobacco Implementation Guide (TIG) v1.0

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*)

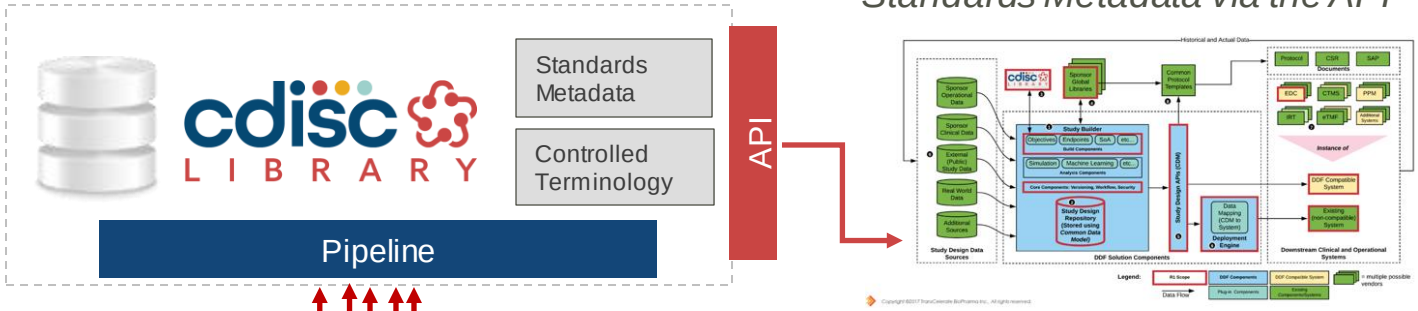
Measures of Adherence (*Conformance Rules*)

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

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

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

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https://cosa.cdisc.org

Learn More!

ICH M11 and Digital Data Flow (DDF)

- Session 2: Second Opening Plenary
- Session 6A: Digital Data Flow

Biomedical Concepts (BCs)

- Session 5A: CDISC Strategic Updates Biomedical Concepts & CORE

Analysis Results Standards (ARS)

- Session 3C: ARS Hands-On Workshop

Tobacco Implementation Guide (TIG) v1.0

- Session 5B: Updates Towards Regulatory

CDISC Open-Source Alliance (COSA)

- Session 4C: COSA Session - 360 & End-to-End

Data Sources

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

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Learn More!

Digital Health Technologies (DHTs)

- Session 4A: Real World Data + Implementation

Study Execution

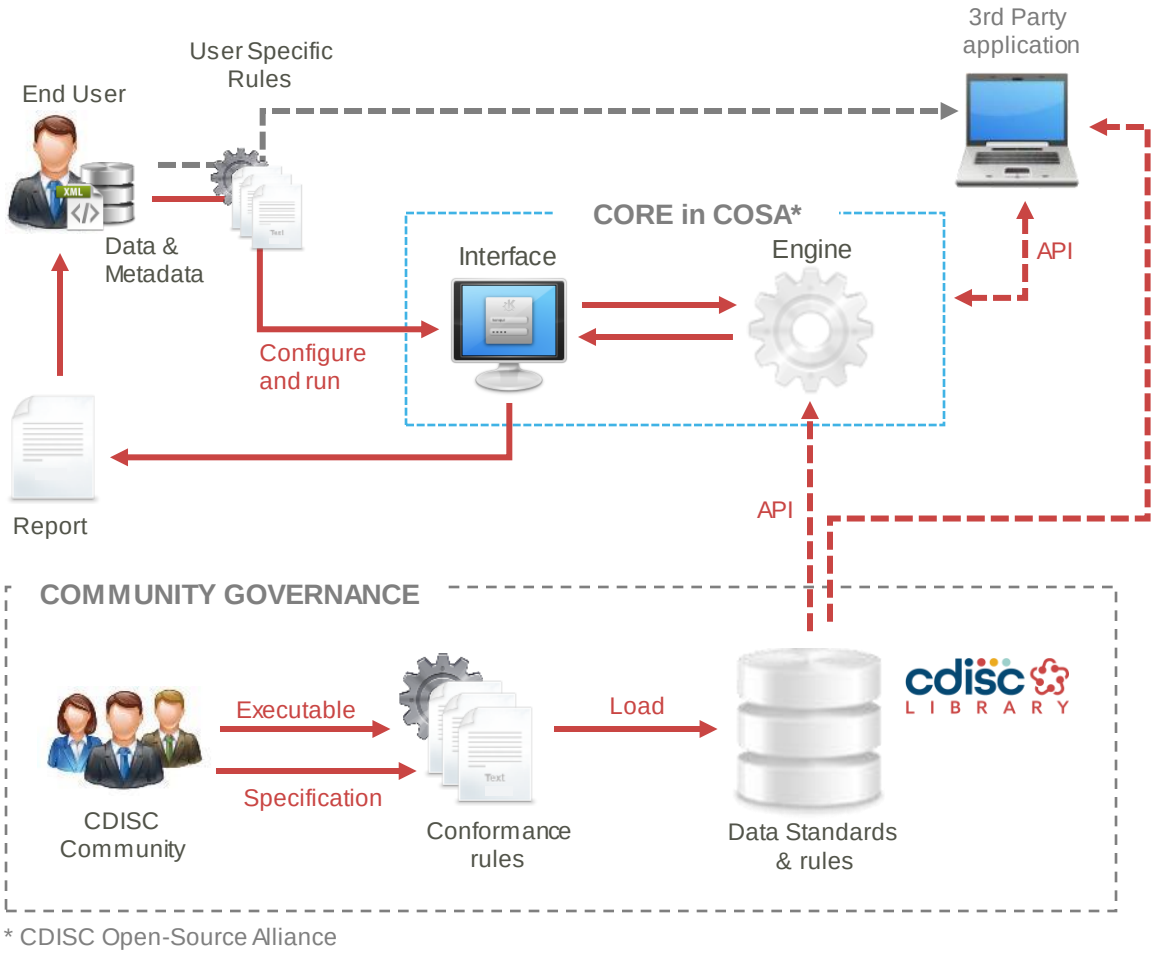
CDISC Open Rules Engine (CORE)

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)

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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

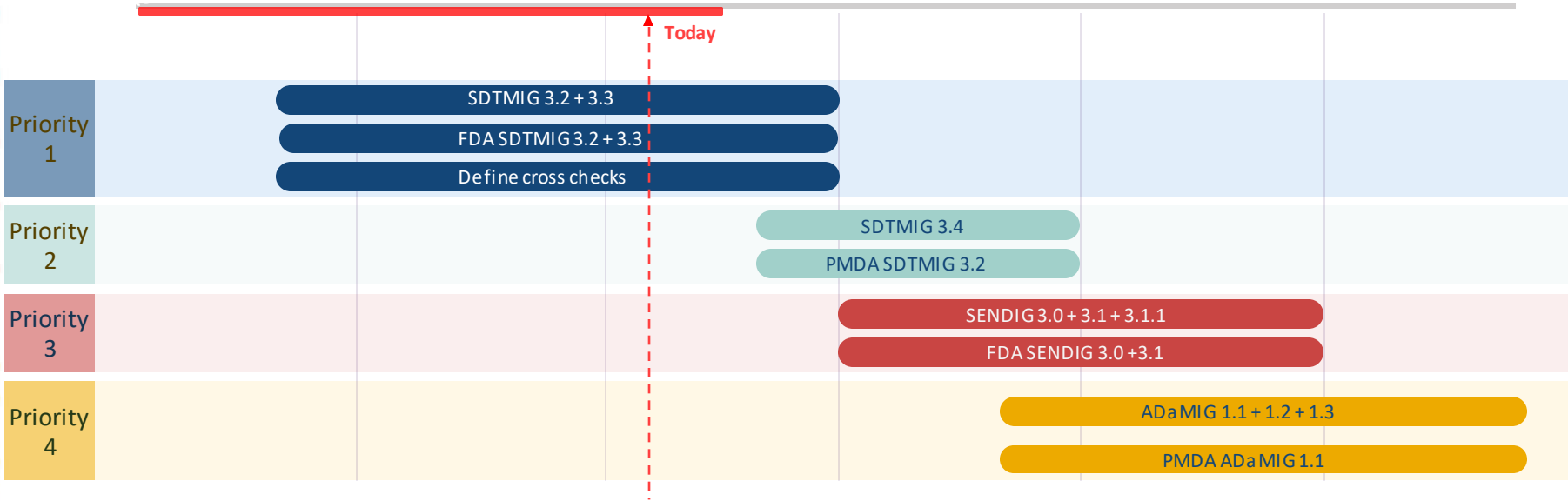
CDISC Library

API

3rd Party Applications

CORE Engine

Rules Development Priority



➡ *Timelines depend on community engagement*

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

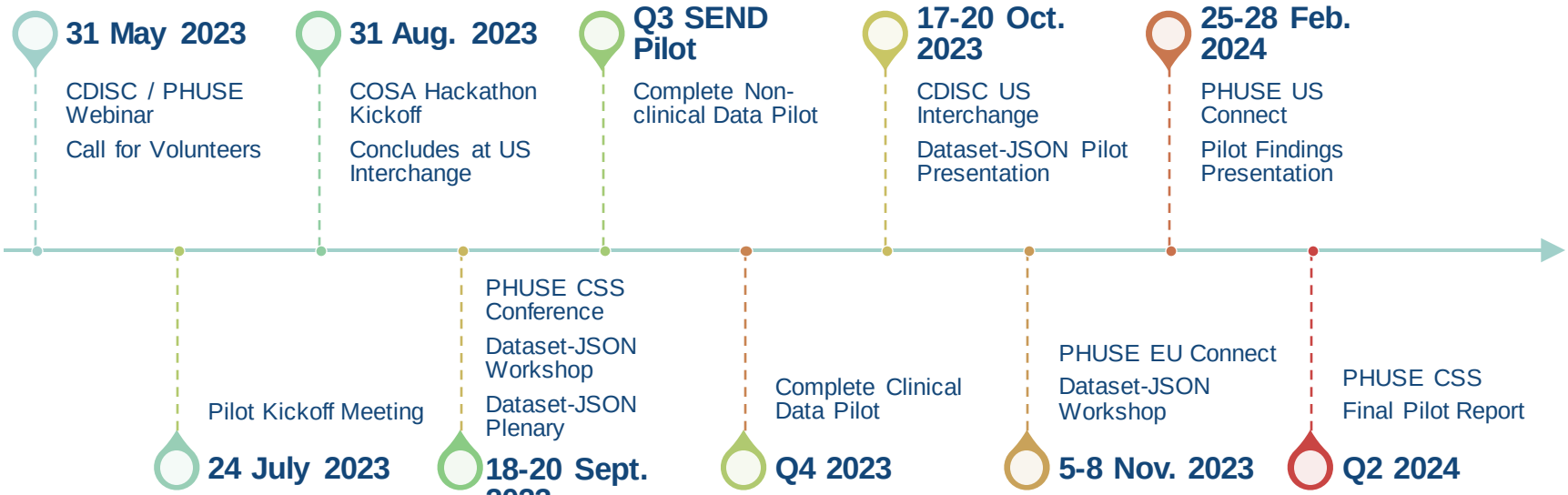
➔ **Success Criteria: Accept Dataset-JSON as a transport format option (in addition to existing XPT format)**

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



Learn More!

CDISC Open Rules Engine (CORE)

- Session 5A: CDISC Strategic Updates Biomedical Concepts & CORE
- Session 6C: CORE Workshop

Dataset-JSON

- Session 2: Second Opening Plenary

Relentless Collaboration

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Thank you!