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2023
KOREA
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SEOUL | 11-14 DECEMBER

Updates on CDISC Data Science Projects

Sam Hume, DSc
VP, Data Science
CDISC

Meet the Speaker

Sam Hume

Title: VP, Data Science

Organization: CDISC

Sam Hume leads the CDISC Data Science team, which collaborates with CDISC staff and stakeholders to develop tools and standards that support clinical and translational data science. Sam directs delivery of the CDISC Library metadata repository that houses all CDISC standards, co-leads the CDISC Data Exchange Standards team, co-leads CORE, and leads the technical CDISC RWD efforts. He has 25 years' experience in clinical research informatics and has held a number of senior technology positions in the biopharmaceutical industry. He holds a doctorate in information systems.

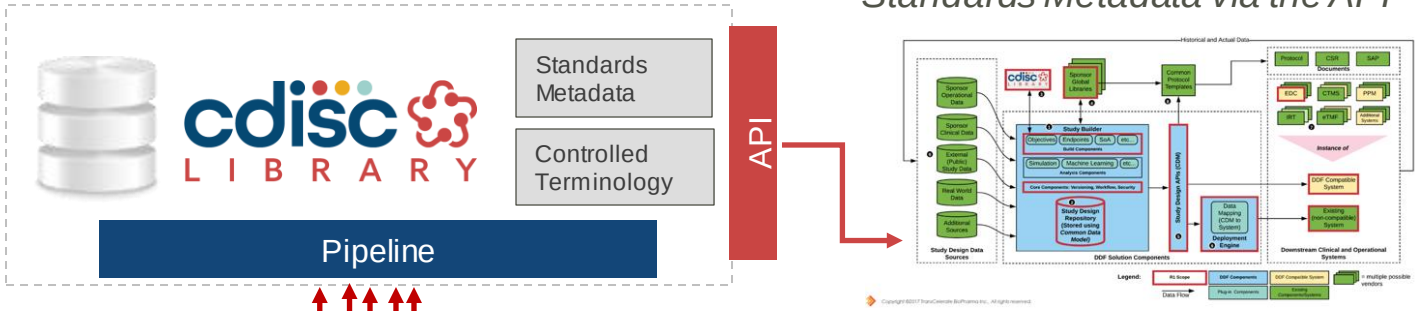
Agenda

1. CDISC Library
2. ODM v2.0
3. Dataset-JSON Pilot
4. COSA
5. OAK – SDTM Automation
6. CORE
7. Biomedical Concepts
8. Digital Data Flow / M11
9. CDISC Data Exchange Framework

CDISC Library

CDISC Library: Standards as a Service

Software Applications Consume Standards Metadata via the API

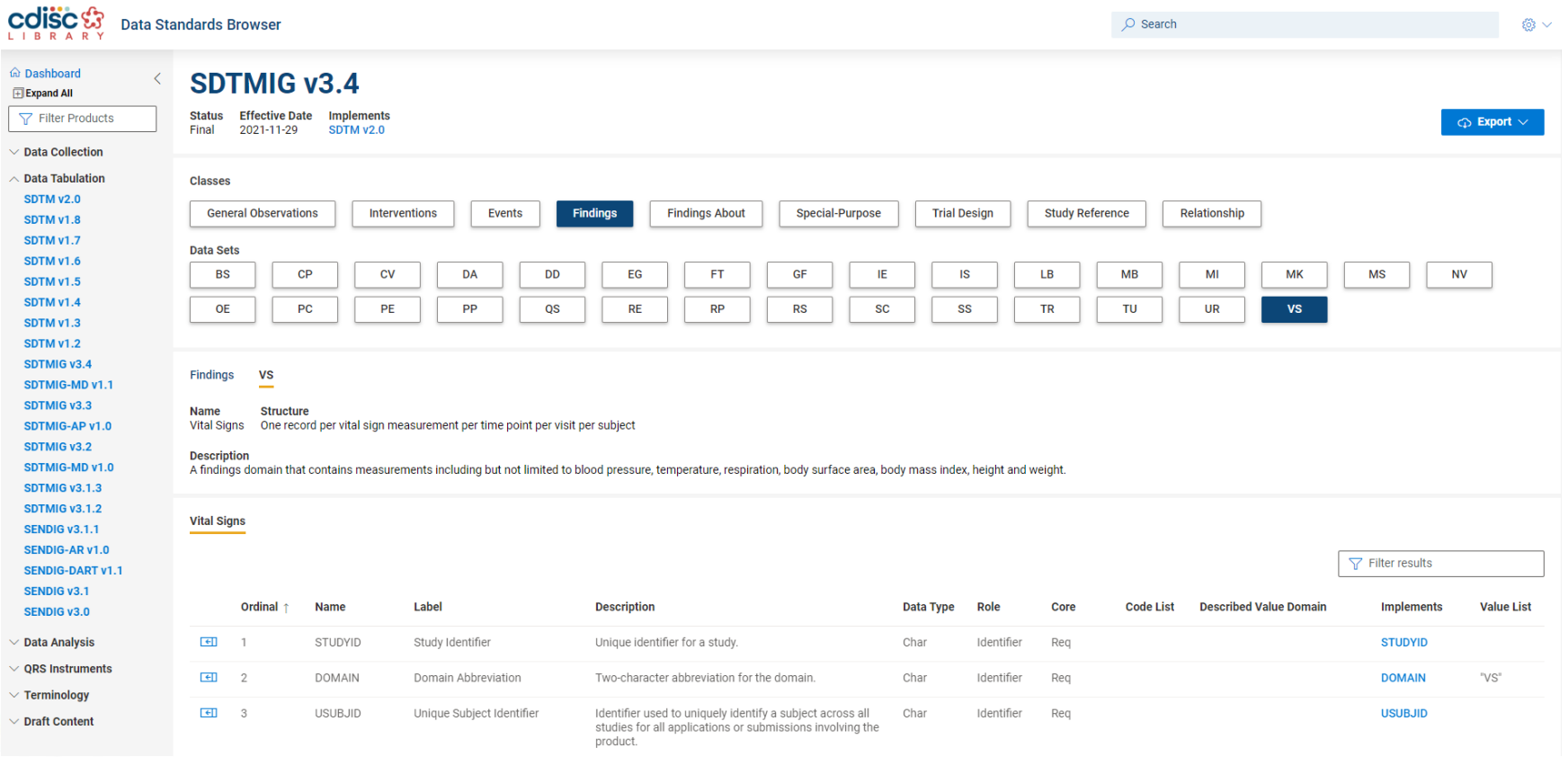


Executable Conformance Rules

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 Library Data Standards Browser



CDISC Library API

SDTM Implementation Guide (SDTMIG)

GET	**/mdr/sdtmig/{version}**	/mdr/sdtmig/{version}
GET	**/mdr/sdtmig/{version}/classes**	/mdr/sdtmig/{version}/classes
GET	**/mdr/sdtmig/{version}/classes/{class}**	/mdr/sdtmig/{version}/classes/{class}
GET	**/mdr/sdtmig/{version}/classes/{class}/datasets**	/mdr/sdtmig/{version}/classes/{class}/datasets
GET	**/mdr/sdtmig/{version}/datasets**	/mdr/sdtmig/{version}/datasets
GET	**/mdr/sdtmig/{version}/datasets/{dataset}**	/mdr/sdtmig/{version}/datasets/{dataset}
GET	**/mdr/sdtmig/{version}/datasets/{dataset}/variables**	/mdr/sdtmig/{version}/datasets/{dataset}/variables
GET	**/mdr/sdtmig/{version}/datasets/{dataset}/variables/{var}**	/mdr/sdtmig/{version}/datasets/{dataset}/variables/{var}
GET	**/mdr/root/sdtmig/datasets/{dataset}/variables/{var}**	/mdr/root/sdtmig/datasets/{dataset}/variables/{var}

ODM v2.0 and the Dataset-JSON Pilot

ODM v2.0 Data Exchange Standard

- Final publication August 2023
- Includes Dataset-JSON and a new version of Define-JSON is coming
- Major update to ODM v1.3.2 that breaks backwards compatibility

Study Setup	Integration	Data Exchange	End-to-end Standards
• Study Design Model	• Enhanced semantics	• Dataset-JSON	• Biomedical Concepts
• Flexible metadata beyond CRFs	• RWD / HL7 FHIR support	• JSON support	• Enhanced MethodDef
• Matrix forms	• Data Queries	• REST API*	• Traceability enhancements

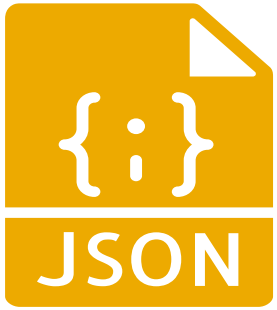
What is Dataset-JSON and Advantages

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
- Similar file sizes relative to current required format
- Remove variable naming, width, or format limitations
- Simple transformation to/from SAS data



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What are the goals of the pilot?

Milestone 1: Short Term

- Pilot 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
- Allow FDA to evaluate how internal tools can support JSON format

➔ **Success Criteria: Demonstrate that Dataset-JSON can transport information with no disruption to business**

Milestone 2: Development of future strategy

- Evaluate how current and future industry standards can benefit without XPT limitations
  e.g., Variable names > 8, labels > 40, data > 200
- Evaluate combining metadata with data
  e.g., Define-XML / Define-JSON based
- Enhanced conformance rules
- FDA to utilize findings to evaluate tool redevelopment plan to natively consume files in JSON format

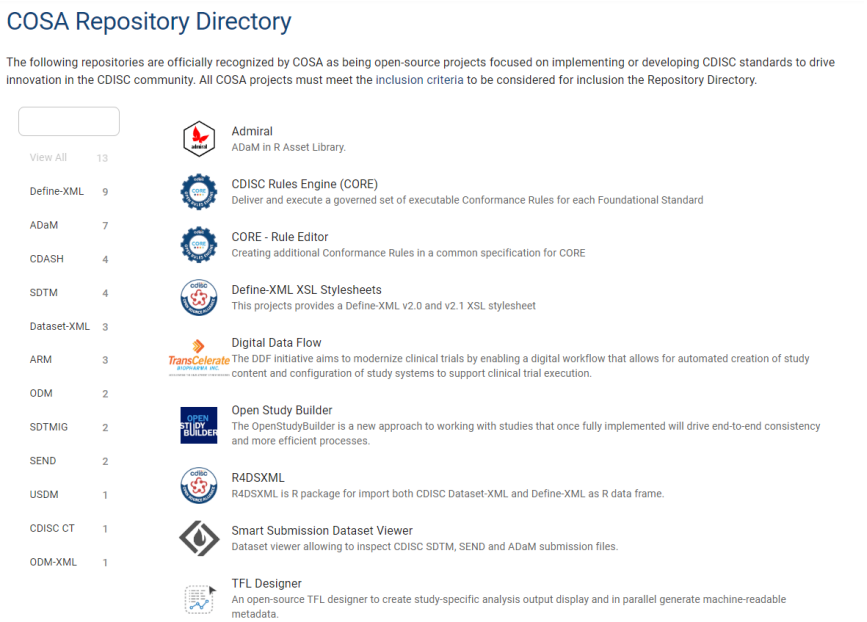
➔ **Success Criteria: Demonstrate the viability of Dataset-JSON as the primary transport option**

CDISC Open-Source Alliance (COSA)

CDISC Open-Source Alliance (COSA)

COSA Mission: The CDISC Open-Source Alliance (COSA) supports, promotes, and sometimes sponsors open-source and free software development projects that create tools for implementing or developing CDISC standards to drive innovation in the CDISC community.

- > 25 open-source projects
- 11 Quarterly webinars
- 4 Hackathons
- 4 workshops
- Collaborate with PHUSE and Pharmaverse
- COSA booth at Interchanges
- Open-source is trending…



https://cosa.cdisc.org/

OAK: Automating SDTM Generation

Transformation Algorithms

- Targets the automated generation of SDTM from CDASH
  - Roche has achieved 80% automated SDTM transformations
- Language neutral algorithms that function as transformation rules
- Combine algorithms to perform all SDTM transformations
- Also transforms non-CDASH data
- Algorithms will be loaded into the CDISC Library
  - Accessible via the Library API

Open-Source R Package

- Creating an R package to automate the transformations
- Software executes the transformation algorithms

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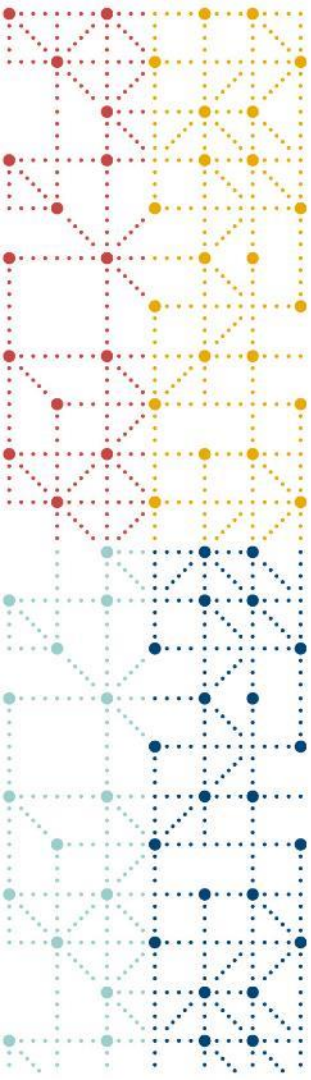


CORE

CORE Software: Engine and Rule Editor

- Each project
  - Has a public GitHub repository on the cdisc-org account and is listed on the COSA Directory
  - Has been released under the MIT open-source license
  - Development is led by CDISC
  - Still under development, but are being actively used
  - Can be extended (supports the development of software extensions)

- CORE Engine
  - Written in Python
  - Makes use of the Venmo Business Rule Engine

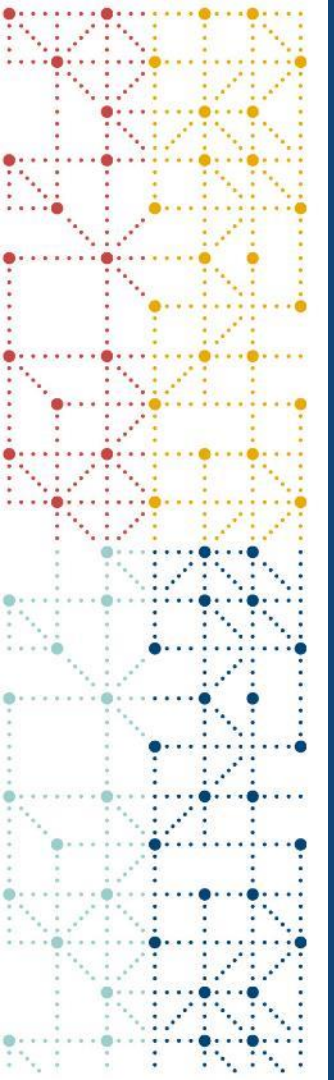
- CORE Rule Editor
  - Written in TypeScript
  - Makes use of the VSCode editor

Running the CORE Engine

- Source Code
  - Available on GitHub using the MIT open-source license
- CLI executable available in GitHub
  - Cached rules
  - Windows, Mac, and Linux install packages
  - Unzip and run
  - Will need datasets to validate
- Engine available on PyPI
  - Engine is a component that can be used in your own code
- Desktop versions
  - Vendor released versions of CORE
  - Includes a user-friendly UI
  - Easier for non-technical users to evaluate
- View a short CORE demonstration
  - https://www.cdisc.org/core
  - See **CORE on GitHub** tab

CORE Engine extensibility

- Operations
  - Define an operation on a dataset, e.g., variable_permissibility, mean
- Dataset Builder
  - Used to define a dataset to match a rule type
- Dataset Reader
  - Used to define dataset formats for reading, e.g., SAS v5 XPORT, Dataset-JSON, CSV
- Data Service
  - Define the service from which the dataset will be read, e.g., local, Azure, AWS
- Checks
  - Used in rule tests, e.g., equal_to, non_empty, matches_regex
- Cache
  - Used to interface with a cache for rules and metadata, e.g., in memory, Redis
- Reporting
  - Defines a type of reporting, e.g., Excel, JSON
- Logging
  - Specifies what and to what level of detail logs are generated



Biomedical Concepts

CDISC Biomedical Concepts and SDTM Dataset Specializations

Pragmatic Implementation of Biomedical Concepts

3 Key pieces

- Conceptual Layer – abstract BC's
  - Provides semantics - aligned with NCI terminology
  - Supports **study design**, Schedule of Activities (SOA)

- Extend foundational standards
  - Add explicit relationships between variables
  - Additional operational metadata, e.g., data type, etc.

- Implementation Layer - Dataset Specializations with VLM definitions
  - Supports programmers
  - Pre-configured building blocks for **Define-XML**
  - Link to BCs with unambiguous semantics & definitions
  - Dataset specializations as an extended dataset structure

Common Semantics in the Data Pipeline

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

Simplified Model Separates BCs and Dataset Specializations

Base VS Dataset Definition

vs.xpt, Vital Signs — Findings, Version 3.2. One record per vital sign measurement per time point per visit per subject, Tabulation

Variable Name	Variable Label	Type	Controlled Terms, Codelist or Format	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		Identifier	Unique identifier for a study.	Req
DOMAIN	Domain Abbreviation	Char	VS	Identifier	Two-character abbreviation for the domain.	Req
USUBJID	Unique Subject Identifier	Char		Identifier	Identifier used to uniquely identify a subject across all studies for all applications or submissions involving the product.	Req
VSSEQ	Sequence Number	Num		Identifier	Sequence Number given to ensure uniqueness of subject records within a domain. May be any valid number.	Req
VSGRPID	Group ID	Char		Identifier	Used to tie together a block of related records in a single domain for a subject.	Perm
VSSPID	Sponsor-Defined Identifier	Char		Identifier	Sponsor-defined reference number. Perhaps pre-printed on the CRF as an explicit line identifier or defined in the sponsor's operational database.	Perm
VSTESTCD	Vital Signs Test Short Name	Char	(VSTESTCD)	Topic	Short name of the measurement, test, or examination described in VSTEST. It can be used as a column name when converting a dataset from a vertical to a horizontal format. The value in VSTESTCD cannot be longer than 8 characters, nor can it start with a number (e.g."1TEST"). VSTESTCD cannot contain characters other than letters, numbers, or underscores. Examples: SYSBP, DIABP, BMI.	Req

Add explicit relationships between variables

Add operational metadata such as data type, length, significant digits, value

Add relationships to concept-based dataset definition specializations

VS.HEIGHT specialization

vs.xpt, Vital Signs — Findings, Version 3.2. One record per vital sign measurement per time point per visit per subject, Tabulation

Variable Name	Variable Label	Type	Controlled Terms, Codelist or Format	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		Identifier	Unique identifier for a study.	Req
DOMAIN	Domain Abbreviation	Char	VS	Identifier	Two-character abbreviation for the domain.	Req
USUBJID	Unique Subject Identifier	Char		Identifier	Identifier used to uniquely identify a subject across all studies for all applications or submissions involving the product.	Req
VSSEQ	Sequence Number	Num		Identifier	Sequence Number given to ensure uniqueness of subject records within a domain. May be any valid number.	Req
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VS.SYSBP specialization

vs.xpt, Vital Signs — Findings, Version 3.2. One record per vital sign measurement per time point per visit per subject, Tabulation

Variable Name	Variable Label	Type	Controlled Terms, Codelist or Format	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		Identifier	Unique identifier for a study.	Req
DOMAIN	Domain Abbreviation	Char	VS	Identifier	Two-character abbreviation for the domain.	Req
USUBJID	Unique Subject Identifier	Char		Identifier	Identifier used to uniquely identify a subject across all studies for all applications or submissions involving the product.	Req
VSSEQ	Sequence Number	Num		Identifier	Sequence Number given to ensure uniqueness of subject records within a domain. May be any valid number.	Req
VSGRPID	Group ID	Char		Identifier	Used to tie together a block of related records in a single domain for a subject.	Perm
VSSPID	Sponsor-Defined Identifier	Char		Identifier	Sponsor-defined reference number. Perhaps pre-printed on the CRF as an explicit line identifier or defined in the sponsor's operational database.	Perm
VSTESTCD	Vital Signs Test Short Name	Char	(VSTESTCD)	Topic	Short name of the measurement, test, or examination described in VSTEST. It can be used as a column name when converting a dataset from a vertical to a horizontal format. The value in VSTESTCD cannot be longer than 8 characters, nor can it start with a number (e.g."1TEST"). VSTESTCD cannot contain characters other than letters, numbers, or underscores. Examples: SYSBP, DIABP, BMI.	Req

VS.HR specialization

vs.xpt, Vital Signs — Findings, Version 3.2. One record per vital sign measurement per time point per visit per subject, Tabulation

Variable Name	Variable Label	Type	Controlled Terms, Codelist or Format	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		Identifier	Unique identifier for a study.	Req
DOMAIN	Domain Abbreviation	Char	VS	Identifier	Two-character abbreviation for the domain.	Req
USUBJID	Unique Subject Identifier	Char		Identifier	Identifier used to uniquely identify a subject across all studies for all applications or submissions involving the product.	Req
VSSEQ	Sequence Number	Num		Identifier	Sequence Number given to ensure uniqueness of subject records within a domain. May be any valid number.	Req
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For each dataset specialization update the variable definitions to match what is needed to represent the concept. A concept code and name is added to each dataset definition. A Where Clause for the specialization maybe added.

Concept codes/name added to dataset metadata and used to provide the semantics for each specialization

Concept-specific codelist subsets created for use in the specializations. Maintained as part of the CT dictionary. A column value or default will be specified.

Biomedical Concept System

API Endpoints in CDISC Library

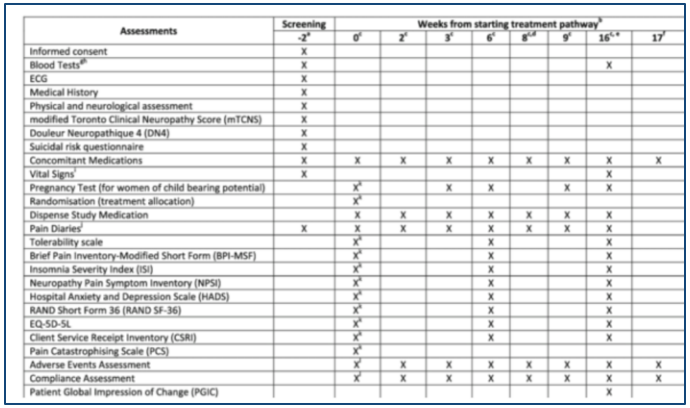
Biomedical Concepts (BC)

GET	/mdr/bc/packages
GET	/mdr/bc/packages/{package}/biomedicalconcepts
GET	/mdr/bc/packages/{package}/biomedicalconcepts /{biomedicalconcept}

Study Data Tabulation Model Dataset Specializations (SDTM)

GET	/mdr/specializations/sdtm/packages
GET	/mdr/specializations/sdtm/packages/{package}/datasetspecializations
GET	/mdr/specializations/sdtm/packages/{package}/datasetspecializations /{datasetspecialization}

Initial Use Cases



Assessments	Screening	Weeks from starting treatment pathway[3]							
	-2[4]	0[5]	2[6]	3[7]	6[8]	8[5,9]	9[10]	16[5,11]	17[7]
Informed consent	X								
Blood Tests[4b]	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[1]	X							X	
Pregnancy Test (for women of child bearing potential)		X[4]		X	X		X	X	
Randomisation (treatment allocation)		X[5]							
Dispense Study Medication		X	X	X	X	X	X	X	
Pain Diaries[1]	X	X	X	X	X	X	X	X	
Tolerability scale		X[3]			X			X	
Brief Pain Inventory-Modified Short Form (BPI-MSF)		X[3]			X			X	
Insomnia Severity Index (ISI)		X[3]			X			X	
Neuropathy Pain Symptom Inventory (NPSI)		X[3]			X			X	
Hospital Anxiety and Depression Scale (HADS)		X[3]			X			X	
RAND Short Form 36 (RAND SF-36)		X[3]			X			X	
EQ-5D-5L		X[3]			X			X	
Client Service Receipt Inventory (CSRI)		X[3]			X			X	
Pain Catastrophising Scale (PCS)		X[3]							
Adverse Events Assessment		X[5]	X	X	X	X	X	X	X
Compliance Assessment		X[5]	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

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Digital Data Flow / ICH M11

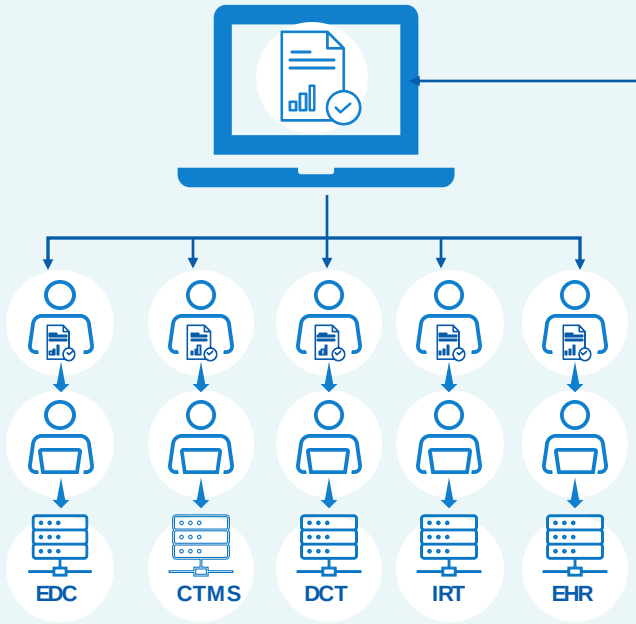
A TransCelerate Project with CDISC Developing the Reference Architecture as a Standard

https://www.transceleratebiopharmainc.com/assets/digital-data-flow-solutions/

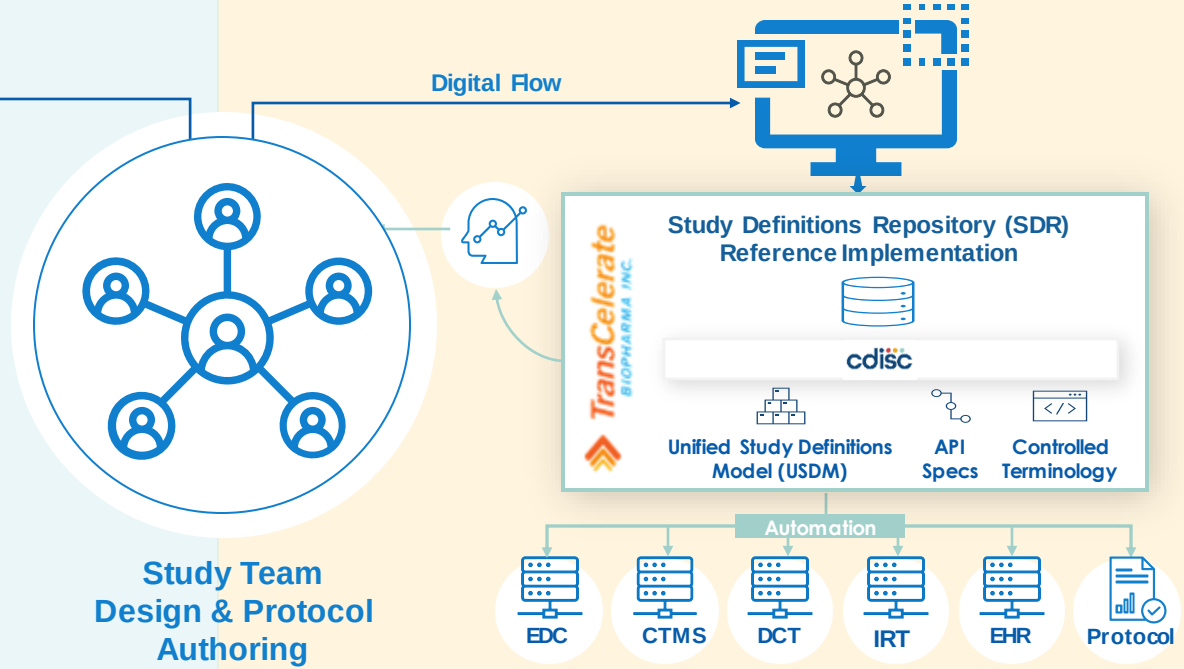
TransCelerate Digital Data Flow (DDF) Ambition

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



CDISC DDF Phase Two

Oct 2022 – June 2023

Digital Data Flow Reference Architecture

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)

Application Programming Interface (API) Specification
The API definition (normative) in JSON and HTML forms

CDISC Controlled Terminology
The controlled terminology (normative) developed for the project. Provided in an Excel format so as to be easily searched and filtered.

Test Files
Examples of USDM JSON files

Implementation Guide
Improved explanation of the model and its use, examples etc

DDF Phase 3 adds Conformance Rule POC

V2.0.0

https://github.com/cdisc-org/DDF-RA

CDISC Data Exchange Framework

CDISC's Data Exchange Framework

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

Application Programming Interface (API) Specification
The API definition (normative) in JSON and HTML forms

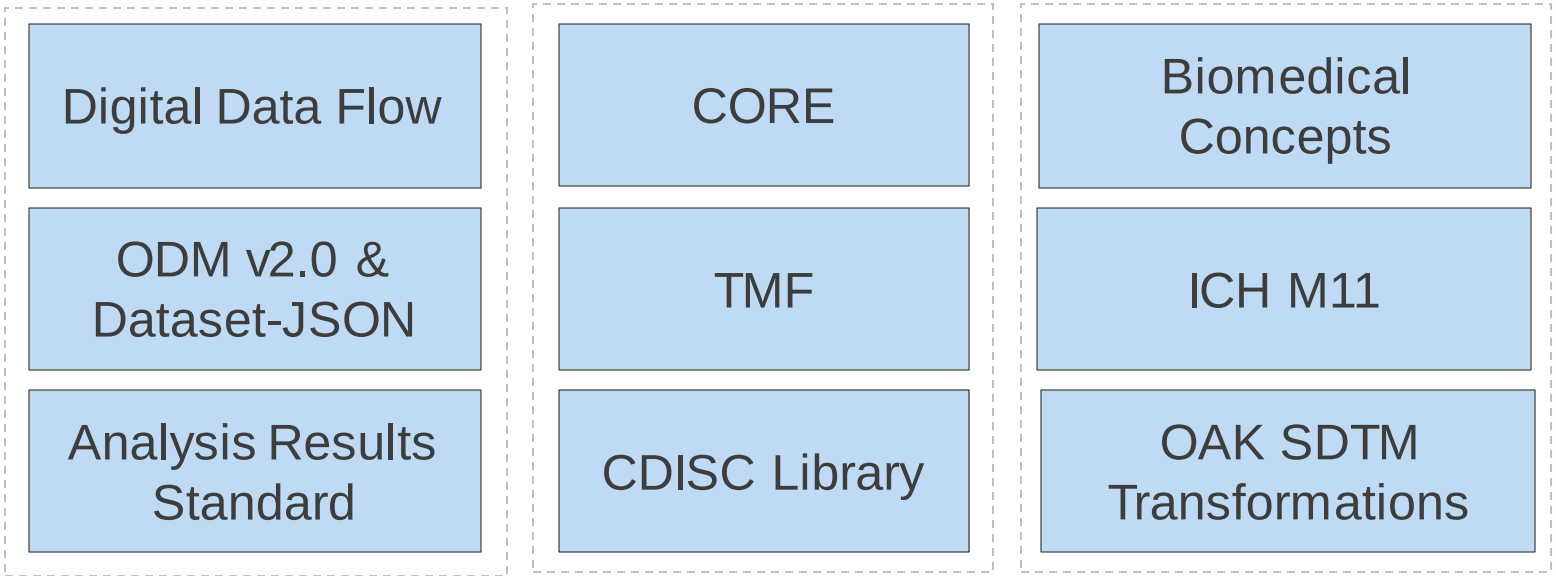
CDISC Controlled Terminology
The controlled terminology (normative) developed for the project and published quarterly in the CDISC Library.

JSON
The API returns an JSON payload by default. Examples provided as JSON files. The API may also support XML and other media types.

Biomedical Concepts
Semantics that work across standards, including RWD, coupled with dataset specializations that provide pre-configured standards.

Framework: Model + API + CT + JSON + BC

CDISC's Data Exchange Framework Today



Thank You!

Sam Hume, DSc

shume@cdisc.org

https://www.linkedin.com/in/sam-hume-dsc