WITH STANDARDS – UNLOCK THE POWER OF DATA

cdisc

2022
US
INTERCHANGE
26-27 OCTOBER | AUSTIN

# Biomedical Concepts: Vision and Value for the Community

Presented by Bess LeRoy & Jon Neville, CDISC

# Meet the Speakers

## Jon Neville

Title: Senior Standards Developer

Organization: CDISC

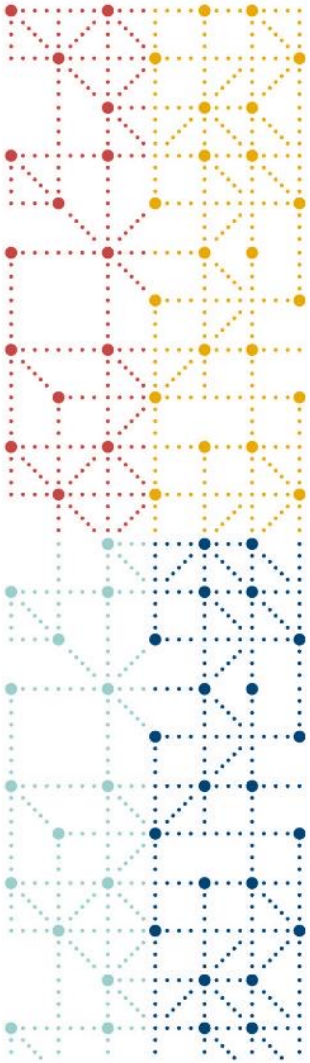
Jon got his start in CDISC standards working on a legacy data conversion project to create an integrated online SDTM data repository of 24 studies of Alzheimer's disease. He has since gained extensive experience with developing CDISC standards and has led, co-led or otherwise assisted in the development of more than 15 CDISC therapeutic area user guides. He is currently leading the development of a CDISC publication on considerations for using SDTM in observational studies.

## Bess LeRoy

Title: Head of Standards Innovation

Organization: CDISC

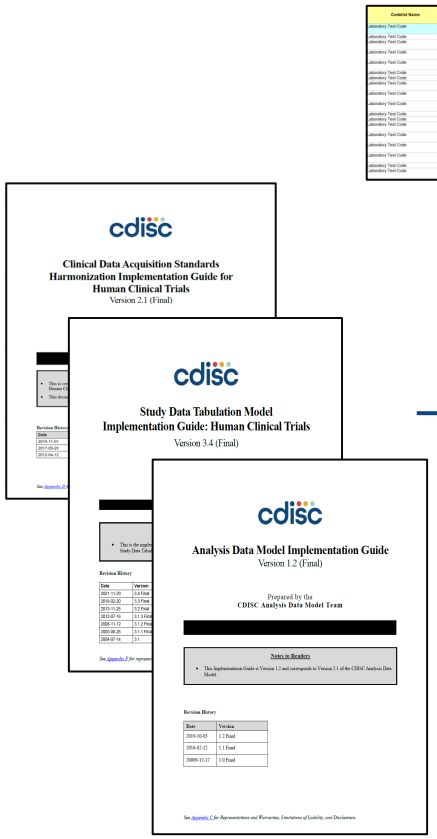
Bess has been a CDISC team member since 2011. She is a member of the CDISC Technical Leadership Team and leads the CDISC Global Governance Group. Bess has over 15 years' experience working in public health research and has held positions at the Framingham Heart Study, the Rotterdam Study, the Arizona Cancer Center, and the Critical Path Institute



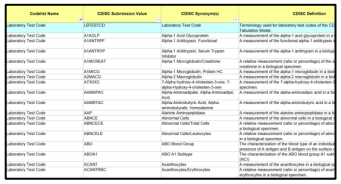
# Agenda

1. Background
2. CDISC COSMoS: Conceptual & Operational Standards Metadata Services
3. Looking Towards the Future

# How Standards Have Been Historically Implemented

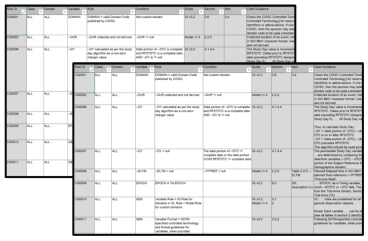



CDISC Implementation Guides

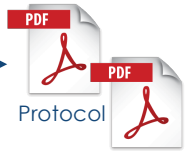


Controlled Terminology

Sponsor MDR

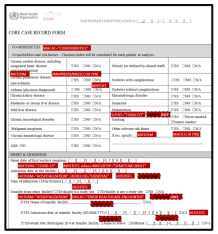


CDISC Conformance Rules



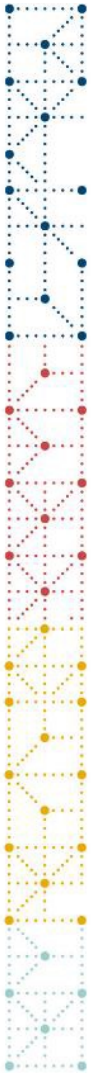

Protocol

SAP



CRFs

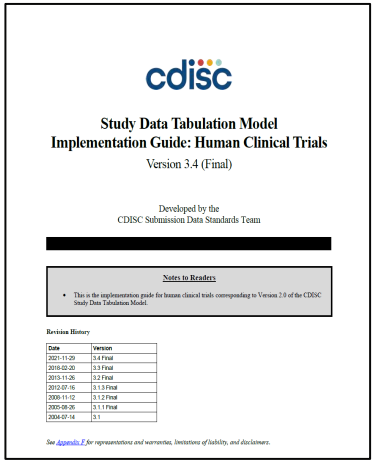
Conduct Study



## Simple Example…

Representing vital signs in SDTM using this approach

cdisc



cdisc

Study Data Tabulation Model
Implementation Guide: Human Clinical Trials
Version 3.4 (Final)

Developed by the
CDISC Submission Data Standards Team

Notes to Readers

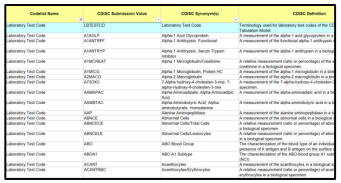
- This is the implementation guide for human clinical trials corresponding to Version 2.0 of the CDISC Study Data Tabulation Model.

Revision History

| Date | Version |
|---|---|
| 2021-11-29 | 3.4 Final |
| 2016-02-20 | 3.3 Final |
| 2013-11-26 | 3.2 Final |
| 2012-07-16 | 3.1.3 Final |
| 2009-11-12 | 3.1.2 Final |
| 2005-08-26 | 3.1.1 Final |
| 2004-07-14 | 3.1 |

*See Appendix E for representations and warranties, limitations of liability, and disclaimers.*

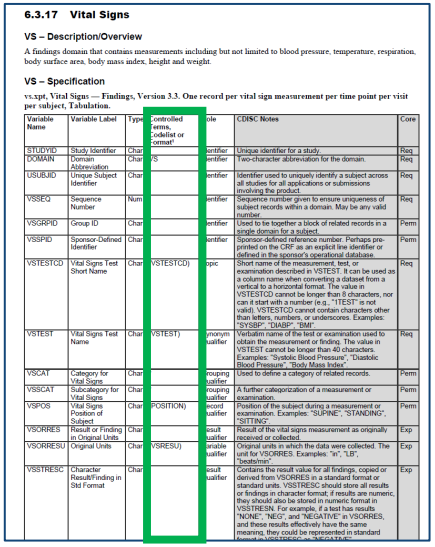
SDTMIG: 461 pages



Controlled Terminology

Controlled Terminology:
>35,000 terms in almost
1000 code lists

cdisc



6.3.17 Vital Signs

VS – Description/Overview

A findings domain that contains measurements including but not limited to blood pressure, temperature, respiration, body surface area, body mass index, height and weight.

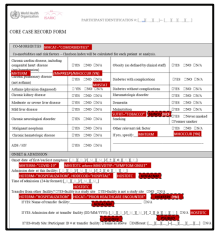
VS – Specification

vs.xpt, Vital Signs — Findings, Version 3.3. 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 link 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" is not valid). VSTESTCD cannot contain characters other than letters, numbers, or underscores. Examples: "SYSBP", "DIABP", "BMI". | Req |
| VSTEST | Vital Signs Test Name | Char | VSTEST) | Synonym Qualifier | Verbatim name of the test or examination used to obtain the measurement or finding. The value in VSTEST cannot be longer than 40 characters. Examples: "Systolic Blood Pressure", "Diastolic Blood Pressure", "Body Mass Index". | Req |
| VSCAT | Category for Vital Signs | Char | | Grouping Qualifier | Used to define a category of related records. | Perm |
| VSSCAT | Subcategory for Vital Signs | Char | | Grouping Qualifier | A further categorization of a measurement or examination. | Perm |
| VSPOS | Vital Signs Position of Subject | Char | POSITION) | Record Qualifier | Position of the subject during a measurement or examination. Examples: "SUPINE", "STANDING", "SITTING". | Perm |
| VSORRES | Result or Finding in Original Units | Char | | Result Qualifier | Result of the vital signs measurement as originally received or collected. | Exp |
| VSORRESU | Original Units | Char | VSRESU) | Variable Qualifier | Original units in which the data were collected. The unit for VSORRES. Examples: "in", "LB", "beats/min". | Exp |
| VSSTRESC | Character Result/Finding in Std Format | Char | | Result Qualifier | Contains the result value for all findings, copied or derived from VSORRES in a standard format or standard units. VSSTRESC should store all results or findings in character format; if results are numeric, they should also be stored in numeric format in VSSTRESN. For example, if a test has results "NONE", "NEG", and "NEGATIVE" in VSORRES, and these results effectively have the same meaning, they could be represented in standard format in VSSTRESC as "NEGATIVE". | Exp |

Vital Signs Domain:
Specification for how to
construct vital signs data

**Repeat 100s of times for all your study data concepts…**



CRFs

*vs.xpt*

| Row | STUDYID | DOMAIN | USUBJID | VSSEQ | VSTESTCD | VSTEST | VSPOS | VSORRES | VSORRESU | VSSTRESC | VSSTRESN | VSSTRESU | VSSTAT | VSREASND | VSLOC | VSLOBXFL | VISITNUM | VISIT | VISITDY | VSDTC | VSDY |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | ABC | VS | ABC-001-001 | 1 | SYSBP | Systolic Blood Pressure | SITTING | 154 | mmHg | 154 | 154 | mmHg | | | BRACHIAL ARTERY | Y | 1 | Baseline | 1 | 2022-06-19T08:45 | 1 |
| 2 | ABC | VS | ABC-001-001 | 2 | DIABP | Diastolic Blood Pressure | SITTING | 44 | mmHg | 44 | 44 | mmHg | | | BRACHIAL ARTERY | Y | 1 | Baseline | 1 | 2022-06-19T08:45 | 1 |
| 3 | ABC | VS | ABC-001-001 | 3 | HEIGHT | Height | | 157 | cm | 157 | 157 | cm | | | | Y | 1 | Baseline | 1 | 2022-06-19 | 1 |
| 4 | ABC | VS | ABC-001-001 | 4 | WEIGHT | Weight | | 90.5 | kg | 90.5 | 90.5 | kg | | | | Y | 1 | Baseline | 1 | 2022-06-19 | 1 |
| 5 | ABC | VS | ABC-001-001 | 5 | PULSE | Pulse Rate | | 72 | beats/min | 72 | 72 | beats/min | | | CAROTID ARTERY | Y | 1 | Baseline | 1 | 2022-06-19 | 1 |
| 6 | ABC | VS | ABC-001-001 | 6 | RESP | Respiratory Rate | | 34 | breaths/min | 34 | 34 | breaths/min | | | | Y | 1 | Baseline | 1 | 2022-06-19 | 1 |
| 7 | ABC | VS | ABC-001-001 | 7 | TEMP | Temperature | | 37.1 | C | 37.1 | 37.1 | C | | | EAR | Y | 1 | Baseline | 1 | 2022-06-19 | 1 |

Vital Signs Dataset

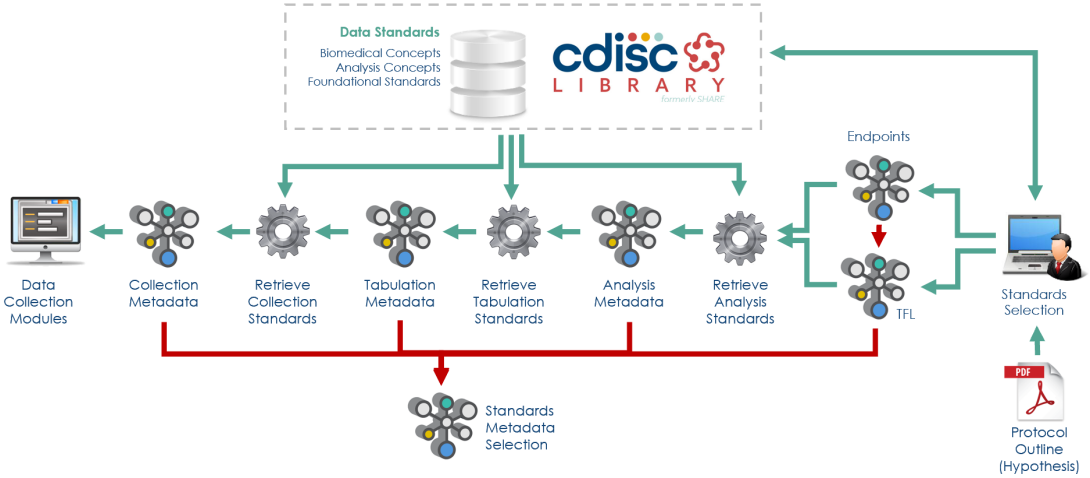
# The Problem with This Approach

- Labor-intensive; requires extensive knowledge of standards documents
- Subject to interpretation (and therefore, *mis*interpretation)
- Can result in inconsistent implementation

**The intense effort required is a barrier to standards adoption**

# How We Evolve: CDISC Library

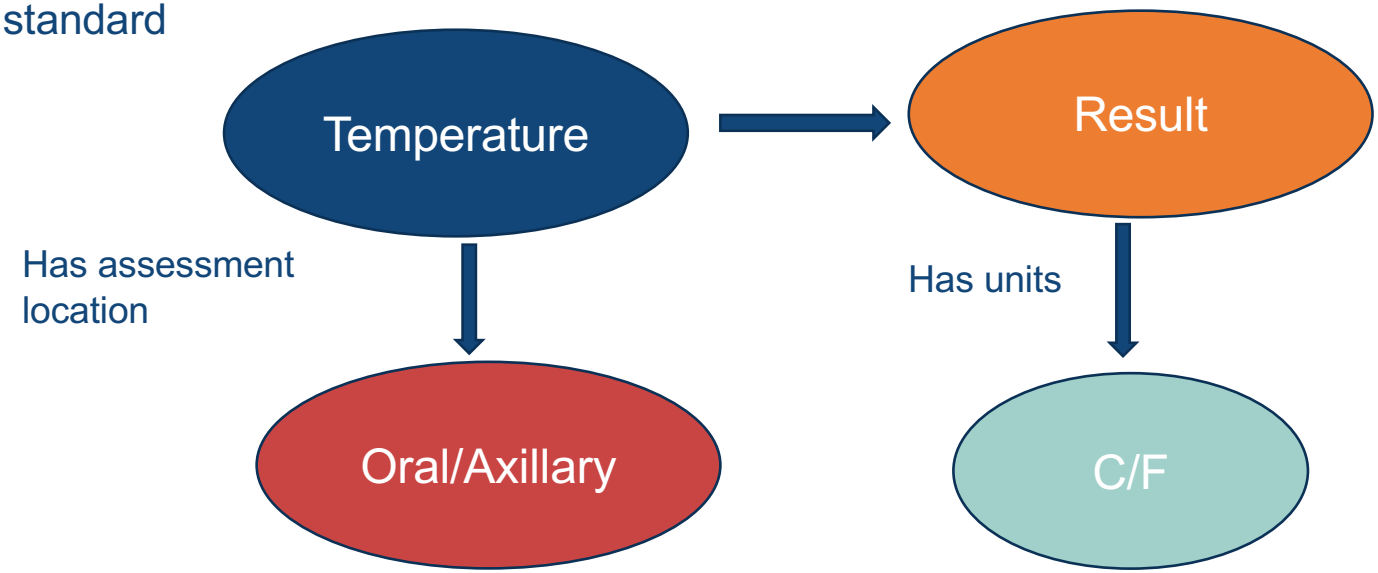
- Electronically publish data standards as groups of linked metadata
- Define relationships between variables, associated terminology codelists, and linkages across standards
- ***CDISC 360 Piloted development of linked biomedical concept metadata to enable end to end automation***



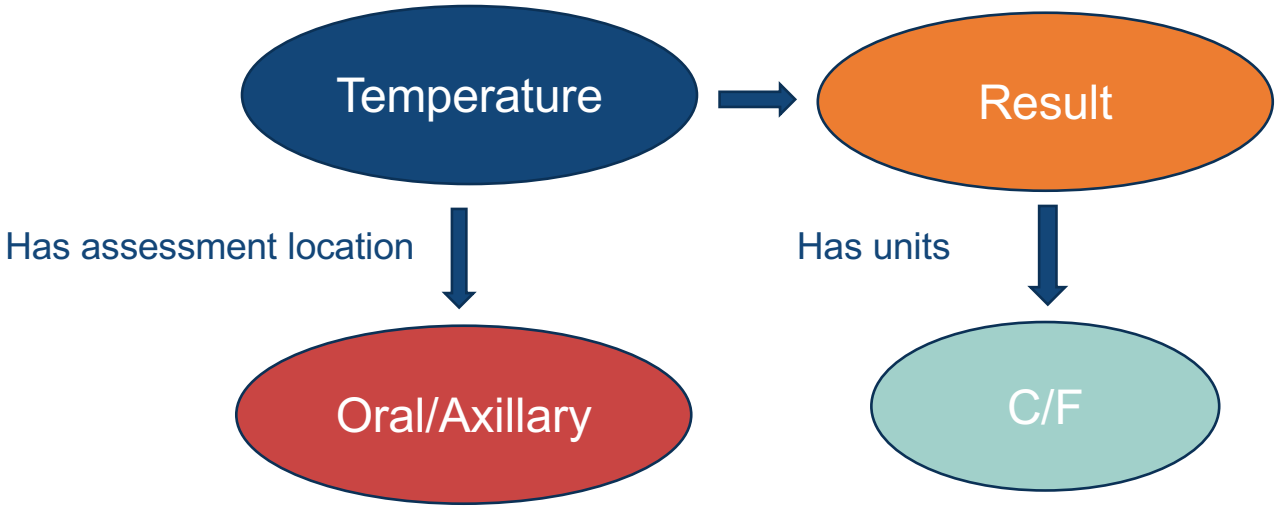
# What Is a Biomedical Concept (BC)?

ISO 11179 Definition: *A unit of knowledge created by a unique combination of characteristics*

- Independent of study
- Independent of a representation in any standard, but can be tethered to a standard



# What Is a Biomedical Concept (BC)?




**Conceptual Layer**

| VSTEST | VSTESTCD | VSORRES | VSUNIT | VSLOC |
|---|---|---|---|---|
| Temperature | TEMP | 101.3 | F | ORAL |

**Implementation Layer**

cdisc

# Why Develop BCs?

- Representation of CDISC standards as metadata (CDISC Library) helps promote automation of CDISC standards
- Developing BCs allows accurate and **more consistent implementation** of the ***conceptual content*** being implemented

# Focus On Your Data. Let the Standards Come To YOU

Your data
"shopping list"

CDISC
Library

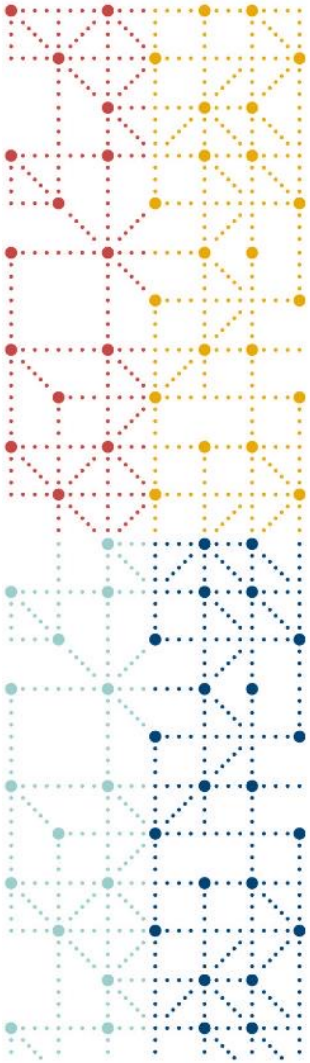
Retrieve your BCs as
machine-readable files

vs.xpt

| Row | STUDYID | DOMAIN | USUBJID | VSSEQ | VSTESTCD | VSTEST | VSPOS | VSORRES | VSORRESU | VSSTRESC | VSSTRESN | VSSTRESU | VSSTAT | VSREASND | VSLOC | VSLOBXFL | VISITNUM | VISIT | VISITDY | VSDTC | VSDY |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | ABC | VS | ABC-001-001 | 1 | SYSBP | Systolic Blood Pressure | SITTING | 154 | mmHg | 154 | 154 | mmHg | | | BRACHIAL ARTERY | Y | 1 | Baseline | 1 | 2022-06-19T08:45 | 1 |
| 2 | ABC | VS | ABC-001-001 | 2 | DIABP | Diastolic Blood Pressure | SITTING | 44 | mmHg | 44 | 44 | mmHg | | | BRACHIAL ARTERY | Y | 1 | Baseline | 1 | 2022-06-19T08:45 | 1 |
| 3 | ABC | VS | ABC-001-001 | 3 | HEIGHT | Height | | 157 | cm | 157 | 157 | cm | | | | Y | 1 | Baseline | 1 | 2022-06-19 | 1 |
| 4 | ABC | VS | ABC-001-001 | 4 | WEIGHT | Weight | | 90.5 | kg | 90.5 | 90.5 | kg | | | | Y | 1 | Baseline | 1 | 2022-06-19 | 1 |
| 5 | ABC | VS | ABC-001-001 | 5 | PULSE | Pulse | | 72 | beats/min | 72 | 72 | beats/min | | | CAROTID ARTERY | Y | 1 | Baseline | 1 | 2022-06-19 | 1 |
| 6 | ABC | VS | ABC-001-001 | 6 | RESP | Respiratory Rate | | 34 | breaths/min | 34 | 34 | breaths/min | | | | Y | 1 | Baseline | 1 | 2022-06-19 | 1 |
| 7 | ABC | VS | ABC-001-001 | 7 | TEMP | Temperature | | 37.1 | C | 37.1 | 37.1 | C | | | EAR | Y | 1 | Baseline | 1 | 2022-06-19 | 1 |

You're most of the way there towards implementing CDISC for your data!

cdisc



# CDISC COSMoS

Conceptual & Operational Standards Metadata Services

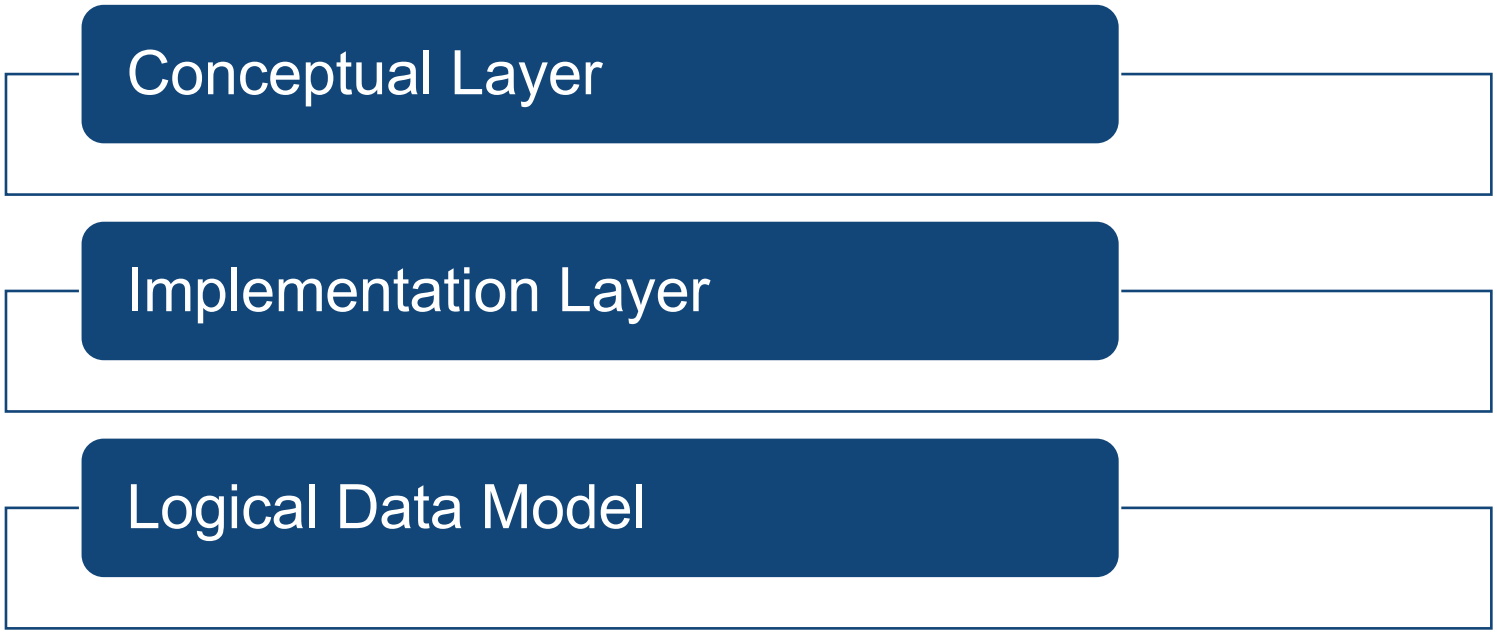
# What Is COSMoS?

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

**Key Objectives:**

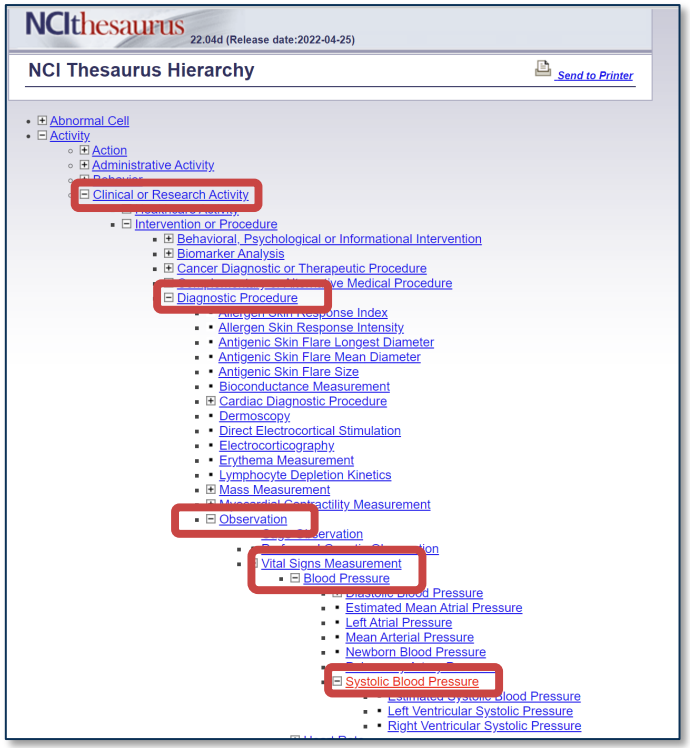
- Reduce variability in standards implementations
- Increase metadata-driven automation
- Reduce barriers to operational implementation

# Key Components of COSMoS



# Conceptual Layer

- Consistent reference definitions provide consistent meaning across studies, all phases of development
- Data standard agnostic
- Rooted in NCI Hierarchy
- All indexed by C-Codes
- Provides for consistency in standards implementation



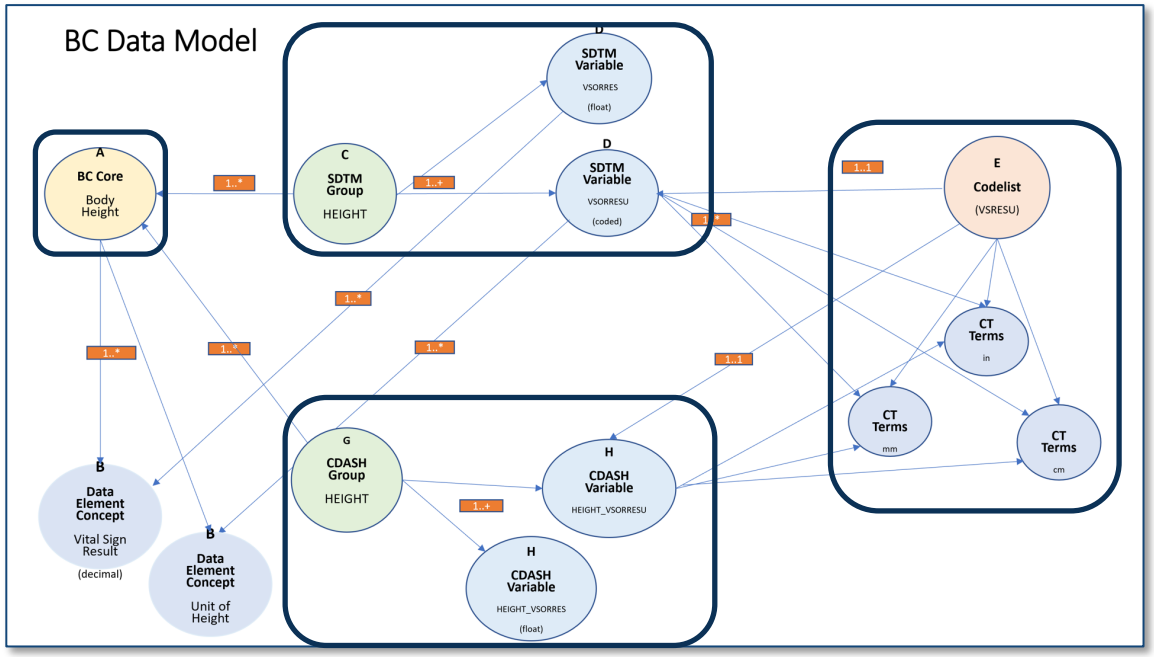
# Implementation Layer

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


cdisc

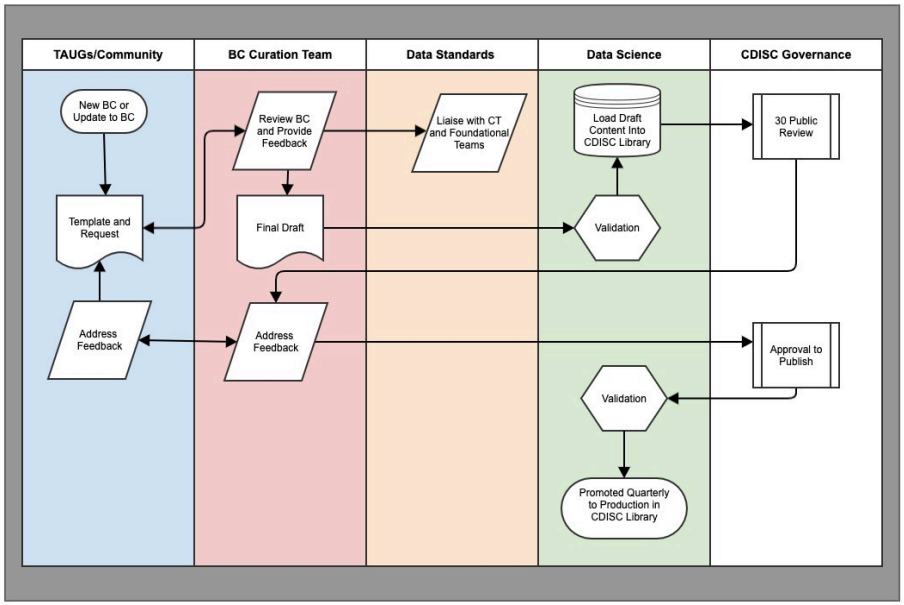
# Logical Data Model

- Concept specific value level metadata
- Add explicit relationships between variables
- Additional operational metadata, e.g., data type, format, etc.
- Creation of structured machine-readable YAML files validated with conformance rules
- Searchable and retrievable via CDISC Library APIs



# BC Governance

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




**Draft governance process**

# *Initial COSMoS Use Cases*

*Retrieve a list of assessments for a study*

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

# Use Case 1: Support Study Design – Schedule of Assessments

## BC Conceptual Layer

- Accurate and consistent implementation of conceptual content
- Retrievable standards agnostic assessments for a study SOA
- Includes pointers to pre-configured SDTM and CDASH dataset specializations

| Assessments | Screening | Weeks from starting treatment pathway[b] | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | -2[a] | 0[c] | 2[c] | 3[c] | 6[c] | 8[c,d] | 9[c] | 16[c,e] | 17[f] |
| Informed consent | X | | | | | | | | |
| Blood Tests[g,h] | 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[k] | | X | X | | X | X | |
| Randomisation (treatment allocation) | | X[k] | | | | | | | |
| Dispense Study Medication | | X | X | X | X | X | X | X | |
| Pain Diaries[j] | X | X | X | X | X | X | X | X | |
| Tolerability scale | | X[k] | | | X | | | X | |
| Brief Pain Inventory-Modified Short Form (BPI-MSF) | | X[k] | | | X | | | X | |
| Insomnia Severity Index (ISI) | | X[k] | | | X | | | X | |
| Neuropathy Pain Symptom Inventory (NPSI) | | X[k] | | | X | | | X | |
| Hospital Anxiety and Depression Scale (HADS) | | X[k] | | | X | | | X | |
| RAND Short Form 36 (RAND SF-36) | | X[k] | | | X | | | X | |
| EQ-5D-5L | | X[k] | | | X | | | X | |
| Client Service Receipt Inventory (CSRI) | | X[k] | | | X | | | X | |
| Pain Catastrophising Scale (PCS) | | X[k] | | | | | | | |
| Adverse Events Assessment | | X[l] | X | X | X | X | X | X | X |
| Compliance Assessment | | X[l] | X | X | X | X | X | X | X |
| Patient Global Impression of Change (PGIC) | | | | | | | | X | |

# Use Case 2: Define-XML – Value Level Metadata

## Pre-configured Define-XML Building Blocks

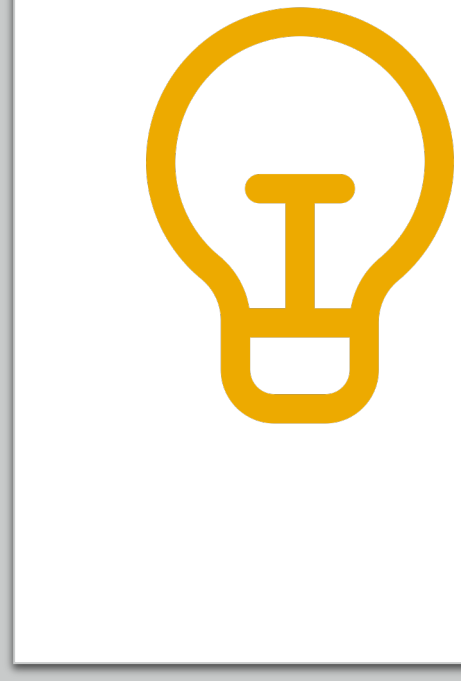
- Practical implementation of BCs at the SDTM implementation layer
- Pre-configured and ready to go value level metadata
- Templates to support consistent curation
- Fully opinionated and out of the box – allows for tweaks as needed
- Immediate benefit to data management and programming producing SDTM

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<br>• "SMALL"<br>• "MEDIUM"<br>• "LARGE" |
| | VSTESTCD = "HEIGHT" (Height) | Height in Orig U | float | 5.1 | |


```
{
    "name": "VSTESTCD",
    "isNonStandard": false,
    "codelist": {…
    },
    "assignedTerm": {
        "conceptId": "C25347",
        "value": "HEIGHT"
    },
    "role": "Topic",
    "relationship": {
        "subject": "VSTESTCD",
        "linkingPhrase": "is decoded by the value in",
        "predicateTerm": "IS_DECODED_BY",
        "object": "VSTEST"
    },
    "comparator": "EQ",
```



# Learn More at Session 6B!

**Session 6, Track B - Business Optimization & Technical Topics**

11:00 – 13:00

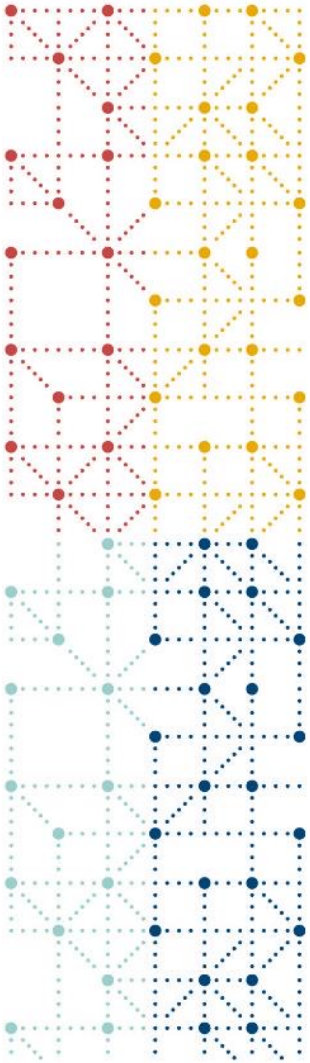
Chair: Anthony Chow, CDISC

Ballroom B

11:00 - 11:30

**COSMoS Technical Implementation, API Layer and Use Cases**

Lex Jansen & Linda Lander, CDISC



## Looking Towards the Future

- Adding CDISC Library functionality
- Adding to conceptual and implementation layers

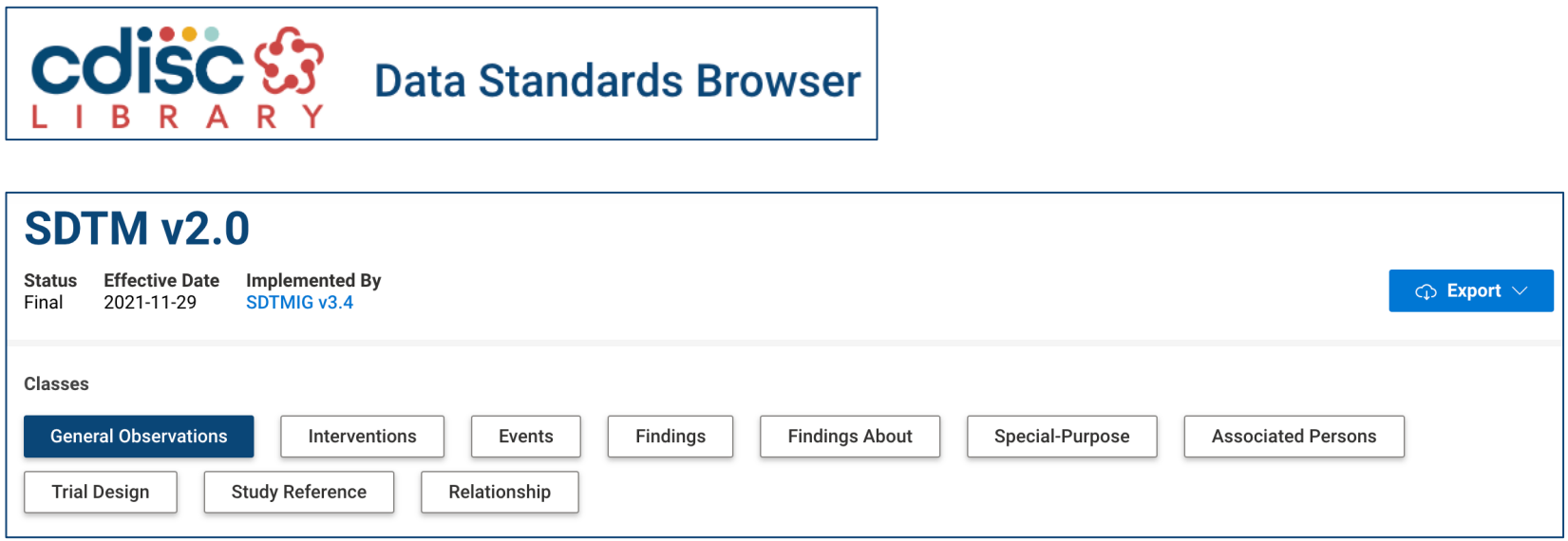
# Adding Functionality to CDISC Library

BCs and Implementations Accessible Through the Data Standards Browser

BC Authoring Tool

# Searchable and Retrievable BCs via CDISC Library APIs and Data Standards Browser

cdisc LIBRARY Data Standards Browser

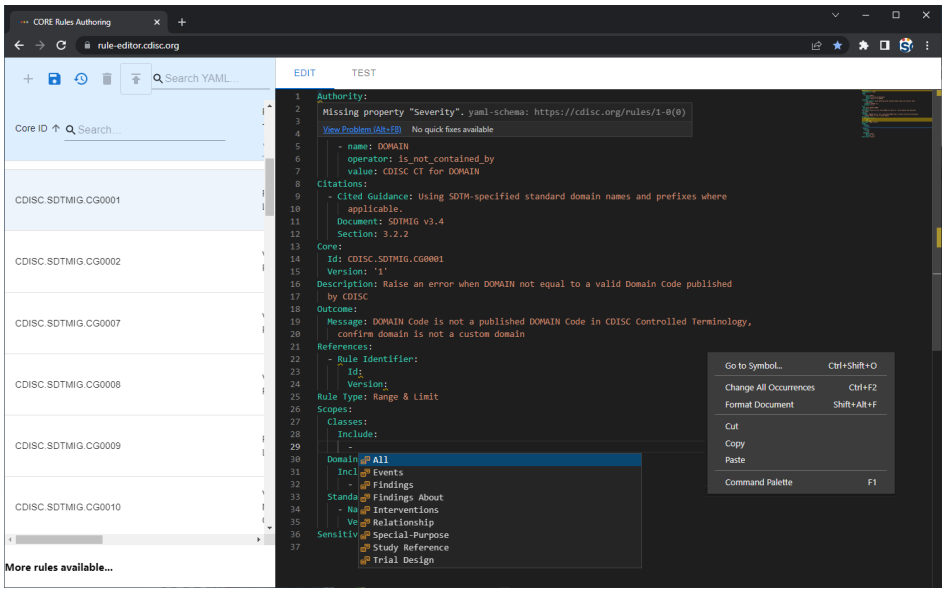



cdisc

# BC Authoring Tool

Web-based editor

- YAML specification
- Conversion to JSON machine-executable code+
- Similar to CORE Rules Editor

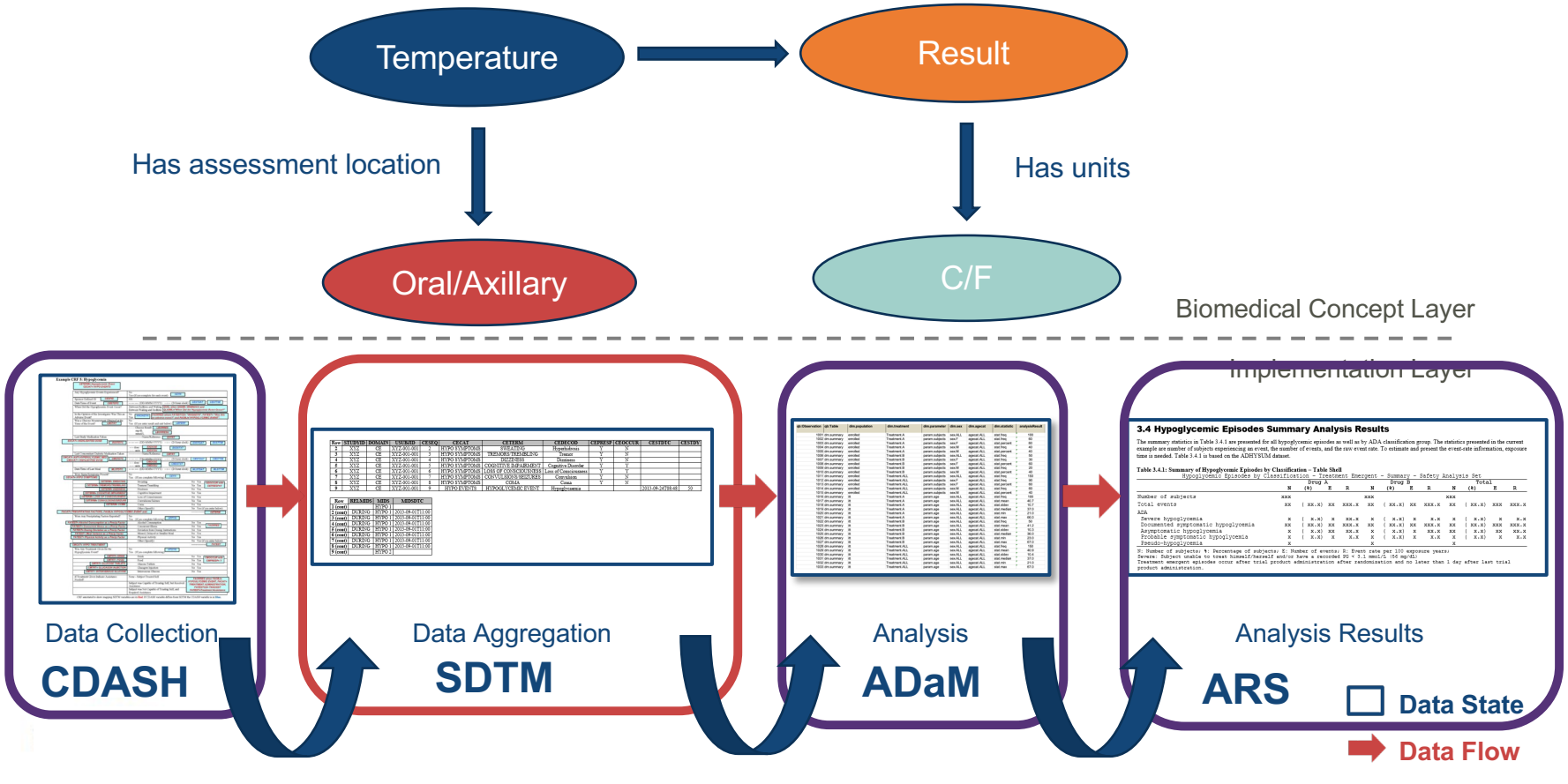



Example: CORE Rule Editor

# Adding to Conceptual and Implementation Layers

- End to end standardization
  - Addition of Collection and Analysis Concepts
  - Derivations and transformations
- Use Digital Data Flow initiative to generate schedule of assessments
- Development of BCs for all new standards
- Connecting to real-world data
- Community collaboration through the donation and curation of BCs

# End to End Standardization: Expanding the Implementation Layer



# Use of BCs in TransCelerate Digital Data Flow Initiative (DDF)

TransCelerate BIOPHARMA INC.

- The DDF initiative aims to modernize clinical trials by enabling a digital workflow to allow for the automated creation of study assets and configuration of study systems to support clinical trial execution.

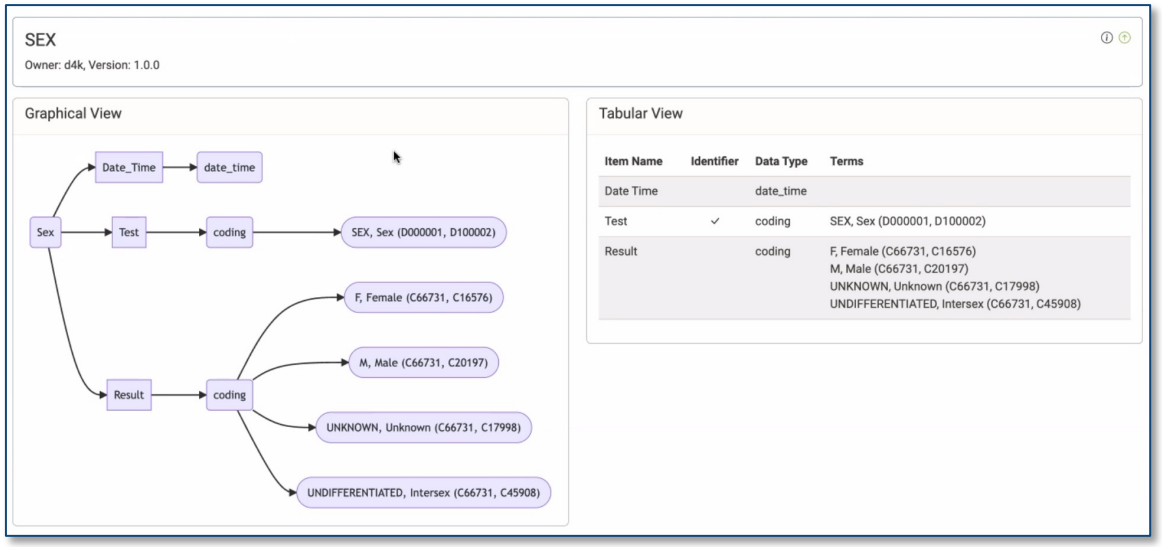
- Use of BCs to support schedule of assessments

| Assessments | Screening | Weeks from starting treatment pathway[b] | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | -2[a] | 0[c] | 2[c] | 3[c] | 6[c] | 8[c,d] | 9[c] | 16[c,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[k] | | X | X | | X | X | |
| Randomisation (treatment allocation) | | X[k] | | | | | | | |
| Dispense Study Medication | | X | X | X | X | X | X | X | |
| Pain Diaries[j] | X | X | X | X | X | X | X | X | |
| Tolerability scale | | X[k] | | | X | | | X | |
| Brief Pain Inventory-Modified Short Form (BPI-MSF) | | X[k] | | | X | | | X | |
| Insomnia Severity Index (ISI) | | X[k] | | | X | | | X | |
| Neuropathy Pain Symptom Inventory (NPSI) | | X[k] | | | X | | | X | |
| Hospital Anxiety and Depression Scale (HADS) | | X[k] | | | X | | | X | |
| RAND Short Form 36 (RAND SF-36) | | X[k] | | | X | | | X | |
| EQ-5D-5L | | X[k] | | | X | | | X | |
| Client Service Receipt Inventory (CSRI) | | X[k] | | | X | | | X | |
| Pain Catastrophising Scale (PCS) | | X[k] | | | | | | | |
| Adverse Events Assessment | | X[l] | X | X | X | X | X | X | X |
| Compliance Assessment | | X[l] | X | X | X | X | X | X | X |
| Patient Global Impression of Change (PGIC) | | | | | | | | X | |

# Using BCs to Build Schedule of Assessments

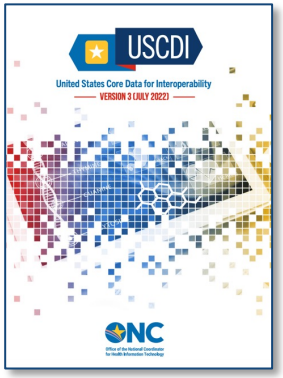
- Schedule of assessments consists of groupings of biomedical concepts

- Demographics
  - Sex
  - Date of Birth
  - Age
  - Race
  - Ethnicity



# Connecting to Real-World Data

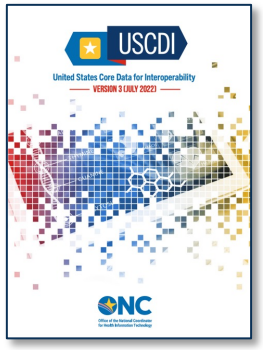
- FDA assessing the use of RWD to support regulatory decisions
- Office of the National Coordinator for Health IT (ONC) promotes the use of standards in health care
- The United States Core Data for Interoperability (USCDI) is a standardized set of data elements for nationwide, interoperable health information exchange
- Electronic health care record (EHR) systems will be required support the USCDI




**Vital Signs**

- Systolic Blood Pressure
- Diastolic Blood Pressure
- Heart Rate
- Respiratory Rate
- Body Temperature
- Body Height
- Body Weight
- Pulse Oximetry
- Inhaled Oxygen Concentration
- BMI Percentile (2 - 20 years)
- Weight-for-length Percentile (Birth - 24 Months)
- Head Occipital-frontal Circumference Percentile (Birth- 36 Months)

# Linking Across Implementation Layers




HL7 FHIR

**US Core Implementation Guide**
5.0.1 - STU5 Release US

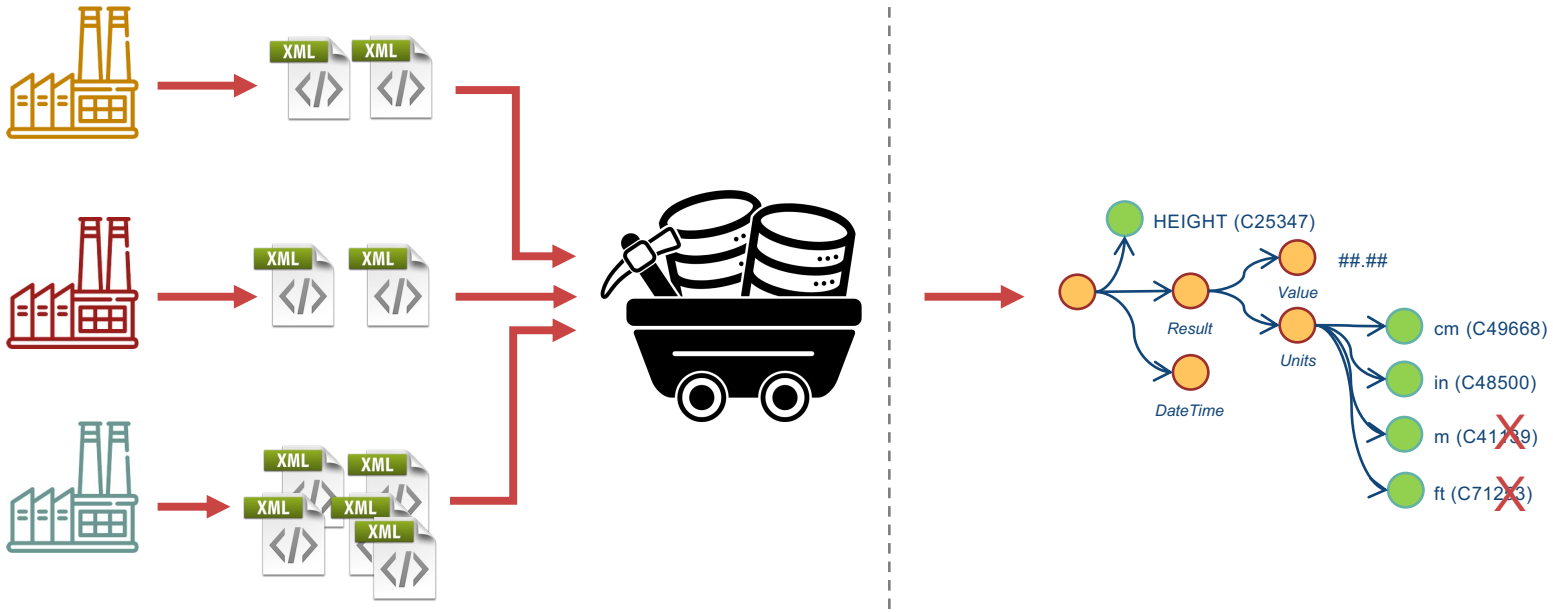
cdisc

# Representation of USCDI in HL7 FHIR and CDISC SDTM

| USCDI Data Element: Ethnicity | | | |
|---|---|---|---|
| **US Core v5.0.1 based on HL7 FHIR 4.0.1 Value Set: OMB Ethnicity Categories** | | **CDISC STDMIG v3.2 Value Set: Ethnic Group** | |
| **Display** | **Code** | **Submission Value** | **Code** |
| Hispanic or Latino | 2135-2 | HISPANIC OR LATINO | C17459 |
| Not Hispanic or Latino | 2186-5 | NO HISPANIC OR LATINO | C41222 |
| Asked but Unknown | ASKU | NOT REPORTED | C43234 |
| Unknown | UNK | UNKNOWN | C17998 |

# Community Collaboration

# Mining and Curation Collaboration



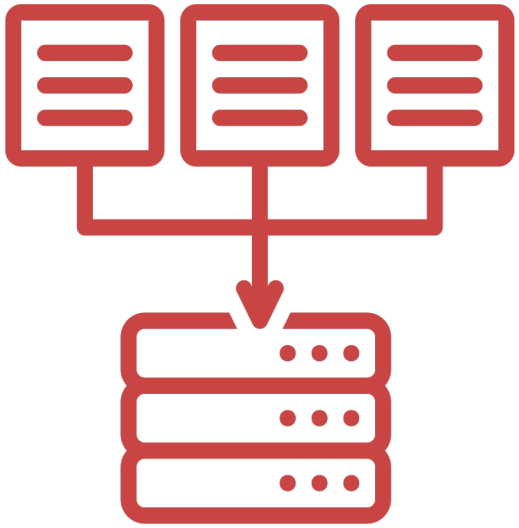

Mining concepts

Curating concepts

cdisc

# Additional Sources of BCs

- Mining datasets
- Donation of company created BCs
- Code Table mapping files
- LOINC to LB mapping
- NCI Thesaurus

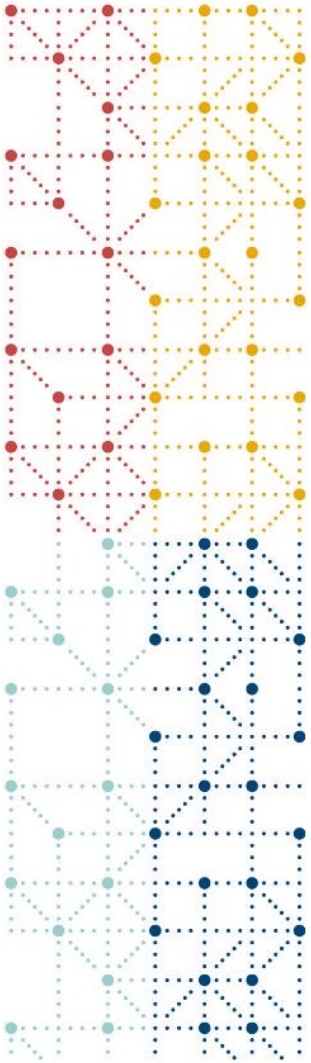


cdisc

# Summary/Conclusions

- BCs provide consistent meaning around collected concepts
  - Everyone is speaking the same language
  - Conceptual layer details provide for easily browsable catalog to drill down into the data you need to collect
- BCs have the power to significantly lower barriers to implementation of standards
  - Start with the concepts, the standards implementation details come along with them
  - Sponsors no longer need to spend as much effort poring over documentation to match their data with implementation details
- BCs provide consistent implementation of standards

cdisc



# Thank You!

cdisc