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INTERCHANGE

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The Development of CDISC Biomedical Concepts: Update and Next Steps

Presented by Jon Neville, Senior Director Standards Development,
CDISC Bess LeRoy, Head of Standards Innovation, CDISC

Meet the Speakers

Jon Neville

Title: Senior Director, Standards Development

Organization: CDISC

Jon Neville has 14 years' experience implementing and developing CDISC standards. He has led, co-led, or otherwise participated in many CDISC therapeutic-area data standards projects. Jon got his start in CDISC standards leading a legacy data conversion effort to create an integrated database of 24 Alzheimer's disease clinical trials. He has been participating on CDISC teams since 2010



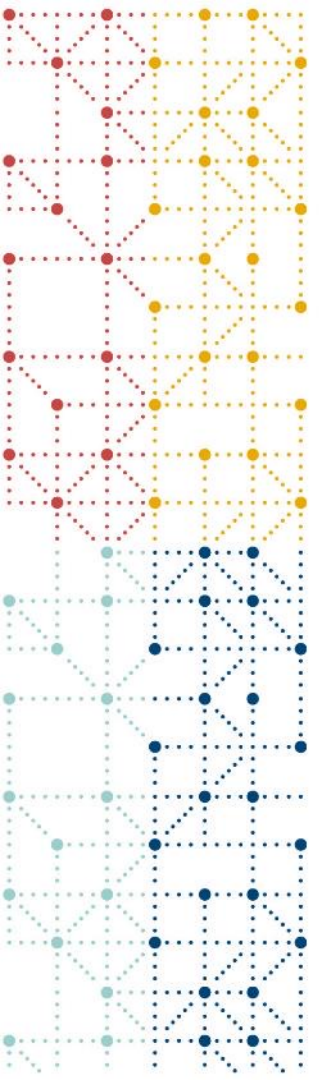
Bess LeRoy

Title: Head of Standards Innovation

Organization: CDISC

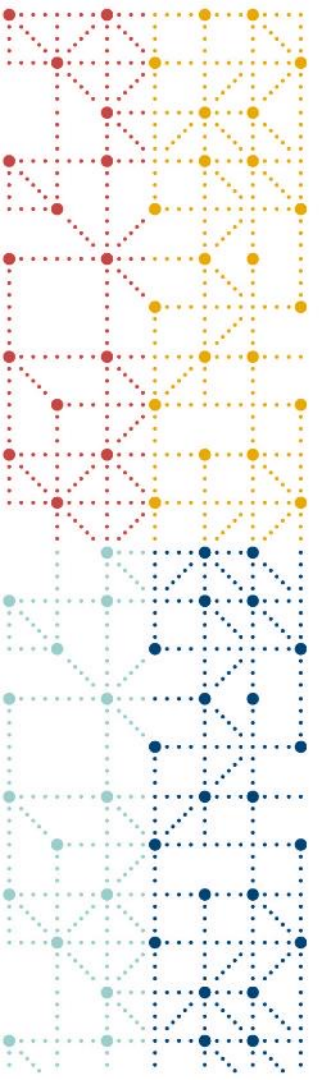
Bess LeRoy is the Head of Standards Development at CDISC. Bess has been a CDISC team member since 2011. She has over 15 years' experience working in public health research and has held positions at the Framingham Heart Study, the Rotterdam Study, the Arizona Cancer Center, and the Critical Path Institute.





Agenda

1. Background
2. CDISC Biomedical Concepts
3. Use Cases
4. Looking Towards The Future



Background

What are biomedical concepts?

Simple Example...

Representing vital signs in SDTM using this approach



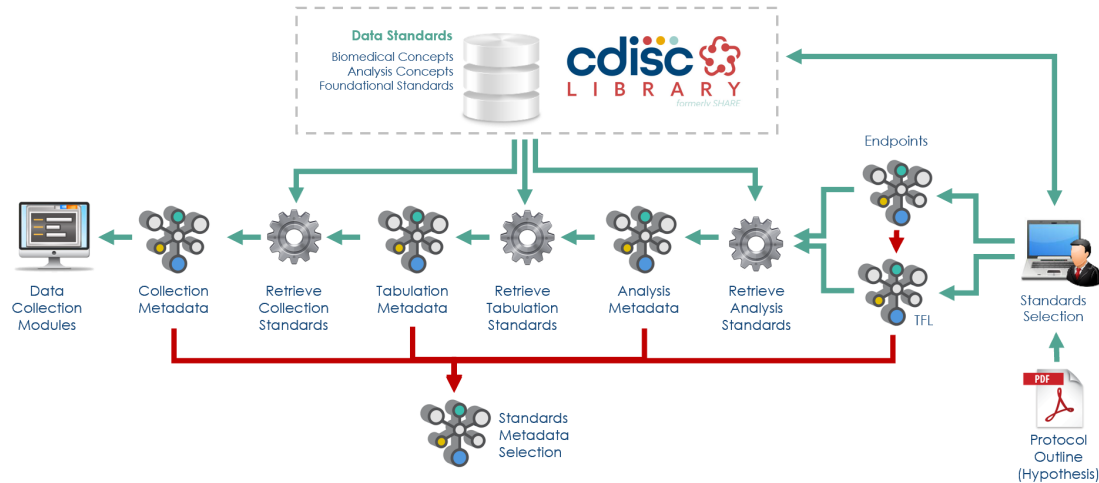
The problem with this approach

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

The intense effort required is a barrier to standards adoption

How we evolve: CDISC Library

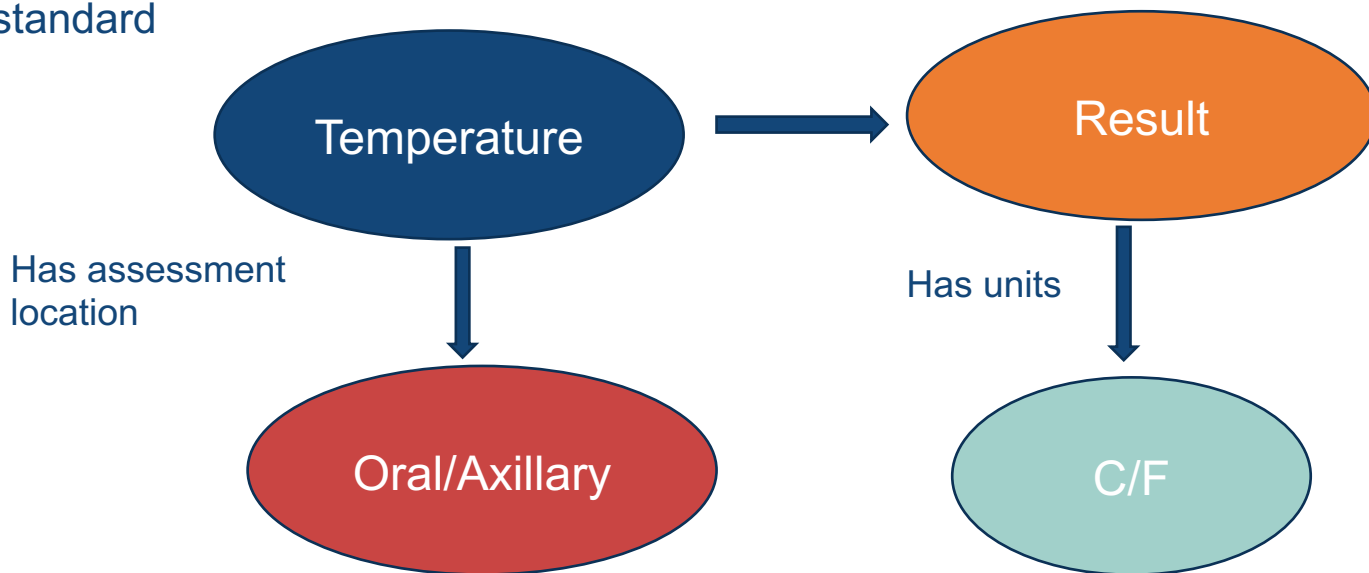
- Electronically publish data standards as groups of linked metadata
- Define relationships between variables, associated terminology codelists, and linkages across standards
- ***CDISC 360 Piloted development of linked biomedical concept metadata to enable end to end automation***



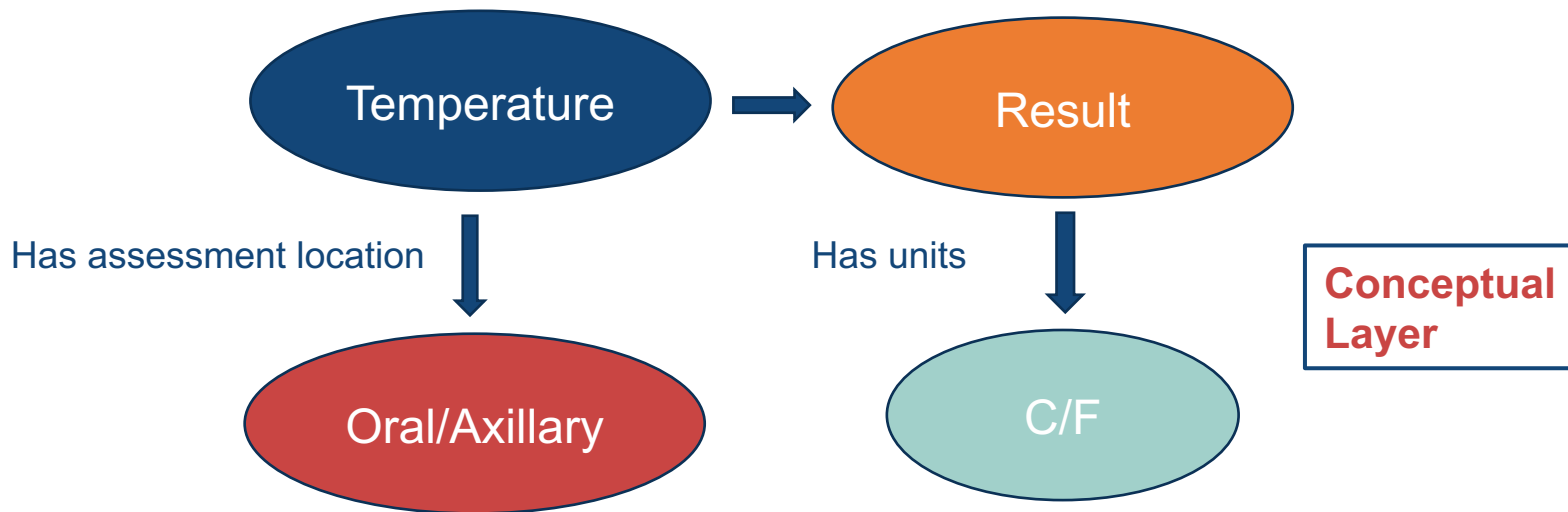
What is a Biomedical Concept (BC)?

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

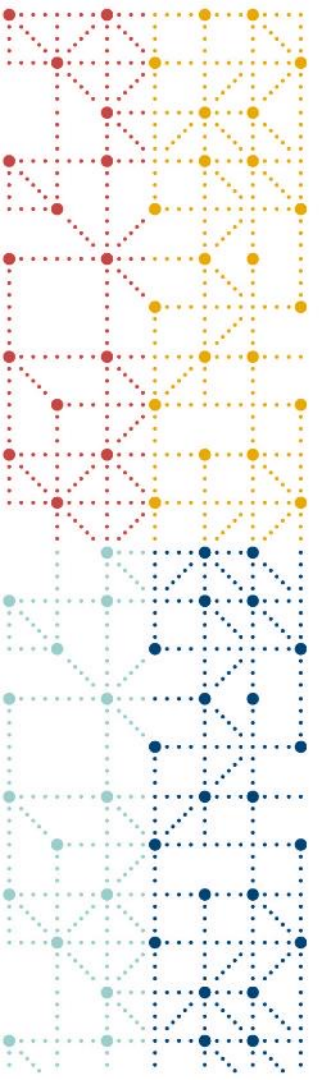


What Is a Biomedical Concept (BC)?



VSTEST	VSTESTCD	VSORRES	VSUNIT	VSLOC
Temperature	TEMP	101.3	F	ORAL

Implementation Layer



Biomedical Concepts at CDISC



CDISC Biomedical Concepts: Objectives

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

Key Components of CDISC BCs



Conceptual Layer

Implementation Layer

Logical Data Model

Conceptual Layer

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

NCIthesaurus
22.04d (Release date:2022-04-25)

NCI Thesaurus Hierarchy [Send to Printer](#)

- Activity
- Administrative Activity
- Clinical or Research Activity
- Intervention or Procedure
 - Behavioral, Psychological or Informational Intervention
 - Biomarker Analysis
 - Cancer Diagnostic or Therapeutic Procedure
 - Diagnostic Procedure
 - Observation
- Observation
 - Vital Signs Measurement
 - Blood Pressure
 - Systolic Blood Pressure

BC Curation Template (Conceptual Layer)

package_date	bc_categories	bc_id	ncit_code	parent_bc_id	short_name	synonyms	result_scale	definition	system	system_name	code	dec_id	ncit_dec_code	dec_label	data_type	example_set
2022-10-26	Vital Signs; Body Measurements	C164634	C164634		Body Height	Height	Quantitative	The vertical measurement or distance from the base to the top of a subject or participant.	http://loinc.org/	LOINC	8302-2					
2022-10-26	Vital Signs; Body Measurements	C164634	C164634		Body Height							C173522	C173522	Vital Signs Result	decimal	
2022-10-26	Vital Signs; Body Measurements	C164634	C164634		Body Height							C168688	C168688	Unit of Height	string	Centimeter; Inch; Millimeter; Meter
2022-10-26	Vital Signs; Body Measurements	C81328	C81328		Body Weight	Weight	Quantitative	The weight of a subject.	http://loinc.org/	LOINC	29463-7					
2022-10-26	Vital Signs; Body Measurements	C81328	C81328		Body Weight							C173522	C173522	Vital Signs Result	decimal	
2022-10-26	Vital Signs; Body Measurements	C81328	C81328		Body Weight							C48208	C48208	Unit of Weight	string	Kilogram; Gram; Pound

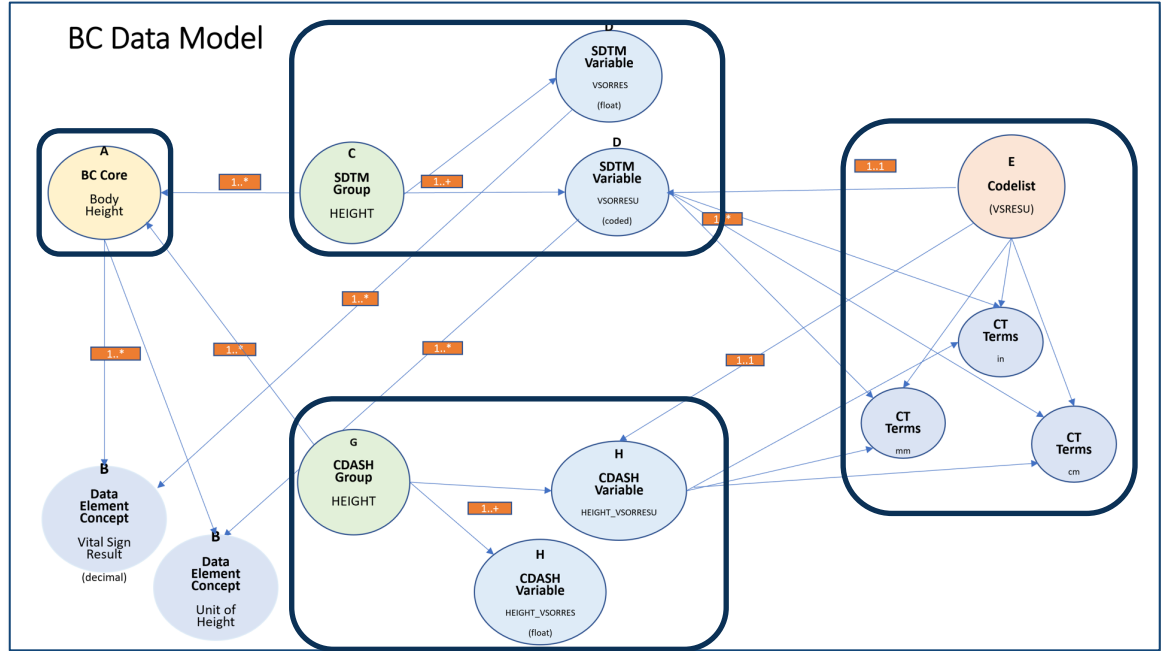
SDTM BC Curation Template (Implementation Layer)

(a subset of model attributes shown)

package_date	bc_id	dec_id	sdtmig_start_version	sdtmig_end_version	domain	vlm_source	vlm_group_id	short_name	sdtm_variable	codelist	codelist_submission_value	value_list	assigned_term	assigned_value
2022-10-26	C164634		3-2		VS	VS.VSTESTCD	HEIGHT	Height	VSTESTCD	C66741	VSTESTCD		C25347	HEIGHT
2022-10-26	C164634		3-2		VS	VS.VSTESTCD	HEIGHT	Height	VSTEST	C67153	VSTEST		C25347	Height
2022-10-26	C164634	C173522	3-2		VS	VS.VSTESTCD	HEIGHT	Height	VSORRES					
2022-10-26	C164634	C168688	3-2		VS	VS.VSTESTCD	HEIGHT	Height	VSORRESU	C66770	VSRESU	in; cm; m		
2022-10-26	C164634	C173522	3-2		VS	VS.VSTESTCD	HEIGHT	Height	VSSTRESC					
2022-10-26	C164634	C173522	3-2		VS	VS.VSTESTCD	HEIGHT	Height	VSSTRESN					
2022-10-26	C164634	C168688	3-2		VS	VS.VSTESTCD	HEIGHT	Height	VSSTRESU	C66770	VSRESU			
2022-10-26	C81328		3-2		VS	VS.VSTESTCD	WEIGHT	Weight	VSTESTCD	C66741	VSTESTCD		C25208	WEIGHT
2022-10-26	C81328		3-2		VS	VS.VSTESTCD	WEIGHT	Weight	VSTEST	C67153	VSTEST		C25208	Weight
2022-10-26	C81328	C173522	3-2		VS	VS.VSTESTCD	WEIGHT	Weight	VSORRES					
2022-10-26	C81328	C48208	3-2		VS	VS.VSTESTCD	WEIGHT	Weight	VSORRESU	C66770	VSRESU	kg; LB; g		
2022-10-26	C81328	C173522	3-2		VS	VS.VSTESTCD	WEIGHT	Weight	VSSTRESC					
2022-10-26	C81328	C173522	3-2		VS	VS.VSTESTCD	WEIGHT	Weight	VSSTRESN					
2022-10-26	C81328	C48208	3-2		VS	VS.VSTESTCD	WEIGHT	Weight	VSSTRESU	C66770	VSRESU			

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



Focus on your data. Let the standards come to YOU



Your data
"shopping list"



CDISC
Library



Retrieve your BCs as
machine-readable files



Row	STUDYID	DOMAIN	USUBJID	VSSEQ	VSTESTCD	VSTEST	VSPPOS	VSORRES	VSORRESU	VSTSTRES	VSTSTRESN	VSTSTRESU	VSSTAT	VSREASND	VSLOC	VSLBFL	VISITNUM	VISIT	VISITDY	VSDTC	VSDY
1	ABC	VS	ABC-001-001	1	SVSBP	Systolic Blood Pressure	SITTING	154	mmHg	154				BRACHIAL ARTERY	Y	1	Baseline	1	2022-06-19T08:45	1	1
2	ABC	VS	ABC-001-001	2	DIABP	Diastolic Blood Pressure	SITTING	44	mmHg	44				BRACHIAL ARTERY	Y	1	Baseline	1	2022-06-19T08:45	1	1
3	ABC	VS	ABC-001-001	3	HEIGHT	Height		159	cm						Y	1	Baseline	1	2022-06-19	1	1
4	ABC	VS	ABC-001-001	4	WEIGHT	Weight		90.5	kg	90.5					Y	1	Baseline	1	2022-06-19	1	1
5	ABC	VS	ABC-001-001	5	PULSE	Pulse		72	beats/min	72	72			CAROTID ARTERY	Y	1	Baseline	1	2022-06-19	1	1
6	ABC	VS	ABC-001-001	6	RESPIRATORY RATE	Respiratory Rate		34	breaths/min	34	34				Y	1	Baseline	1	2022-06-19	1	1
7	ABC	VS	ABC-001-001	7	TEMP	Temperature		37.1	C	37.1	37.1			EAR	Y	1	Baseline	1	2022-06-19	1	1

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





Use Cases



Initial Biomedical Concept Use Cases

*Retrieve a List of
Assessments for a Study*

*Publish BC content as
Define-XML document
including Value Level
Metadata*

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



- 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: SEVERE COVID-19 PNEUMONIA (Roche)

Appendix 1
Schedule of Activities: Days 1 and 2

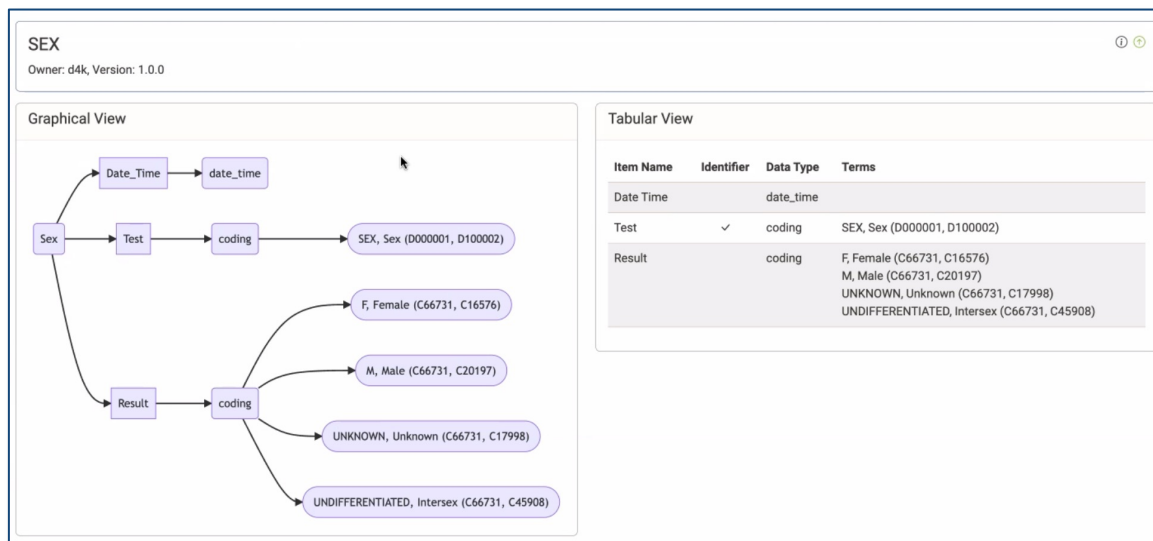
Study Day	Screening ^{a, b}	Baseline			
	-2 to 0	1	2	3	4
Time Post Initial Treatment (Assessment Window)		0 Pre-dose (-4 hrs)	15 min After end of infusion (+1 hr)	24 hrs (±4 hrs)	36 hrs (±4 hrs)
Informed consent	x				
Inclusion/exclusion criteria	x	x			
Demographic data	x				
Randomization		x			
Medical history		x			
Complete physical examination ^c	x				
Weight		x			
COVID-19 diagnosis ^d	x				
Chest X-ray/CT scan ^e	x				
ECG	x				
Pregnancy test ^f	x				
PaO ₂ /FIO ₂ ^g	x		← Optional →		
SpO ₂ ^h	x	x	x	x	x
Vital signs ^h	x	x	x	x	x
Ordinal scoring ⁱ		x		x	
Adverse events ^j		x		x	
Concomitant medications ^k		x		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



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	<ul style="list-style-type: none">• "SMALL"• "MEDIUM"• "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",
```

BCs now available via CDISC Library API as JSON output

Biomedical Concepts (BC)

GET /mdr/bc/packages

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

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

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

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

Study Data Tabulation Model Dataset Specializations (SDTM)

GET /mdr/specializations/sdtm/packages

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

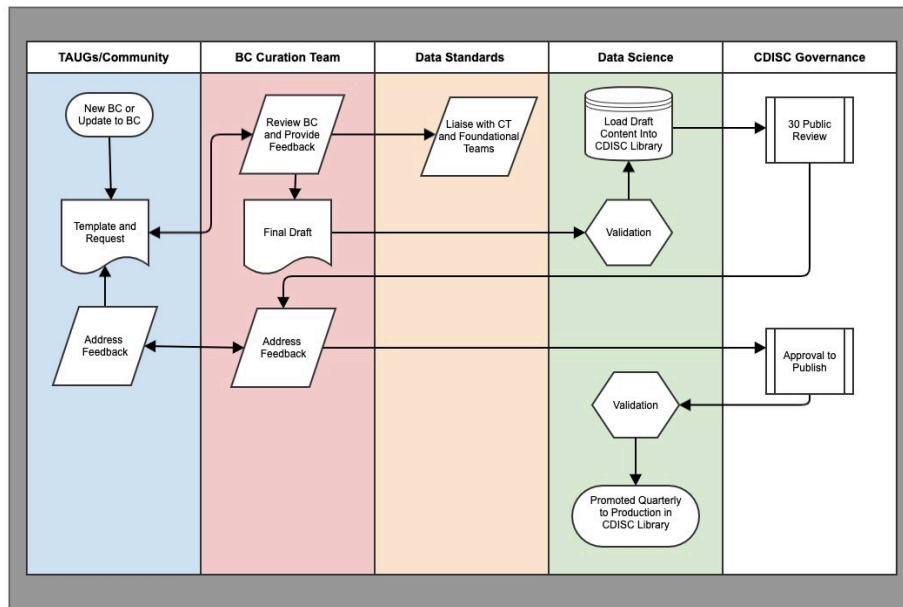
GET /mdr/specializations/sdtm/packages/{package}/datasetspecializations/{datasetspecialization}

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

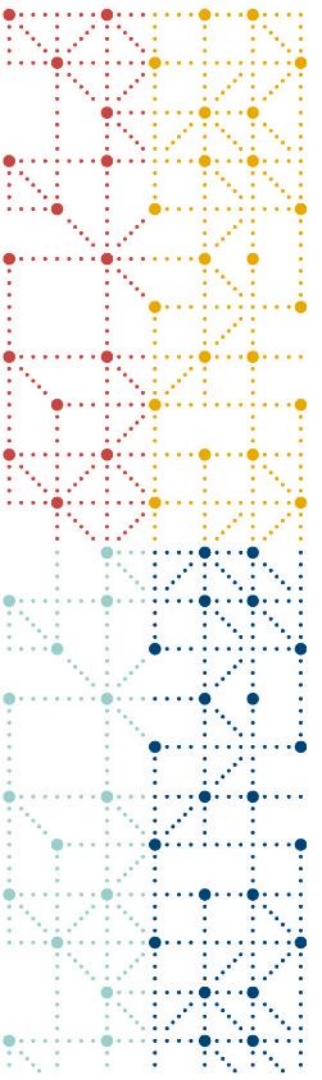
GET /mdr/specializations/sdtm/packages/{package}/datasetspecializations/{datasetspecialization}/variables/{variable}

BC Governance

- Light-weight CDISC curation and governance process
- 30-day Public Review
- Publish semi-annual
- Mechanism for community change requests



Draft governance process



Looking Towards the Future

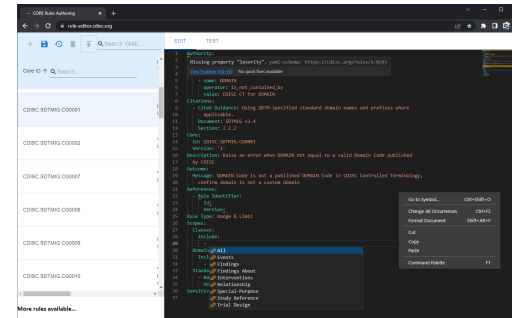
- Adding CDISC Library functionality
- Adding to conceptual and implementation layers

Adding Functionality to CDISC Library

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



- Web-based editor for BC authoring

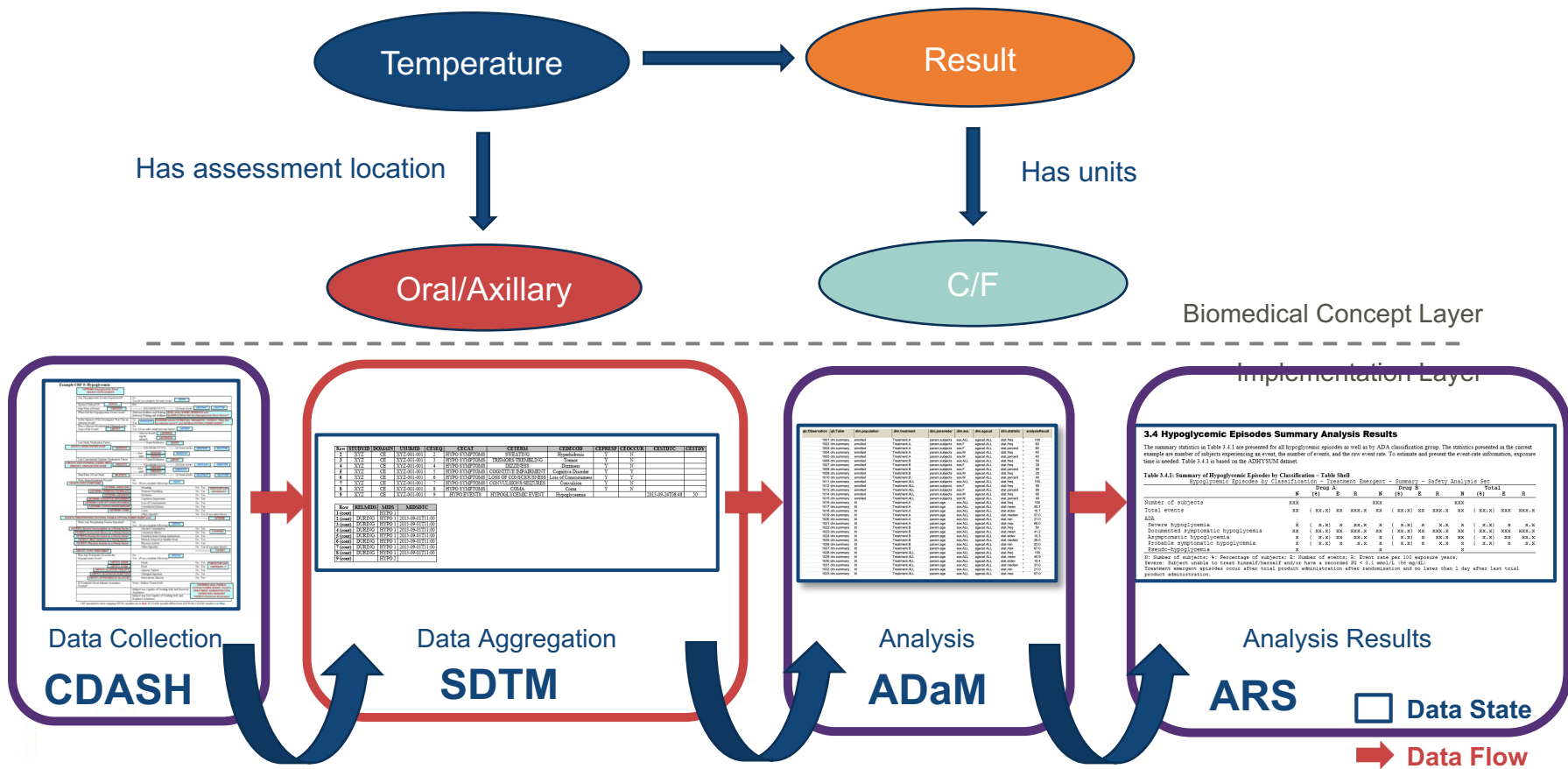




Adding to Conceptual and Implementation Layers

- End to end standardization
 - Addition of Collection and Analysis Concepts
 - Derivations and transformations
- Development of BCs for all new standards
- Community collaboration through the donation and curation of BCs

End to End Standardization: Expanding the Implementation Layer



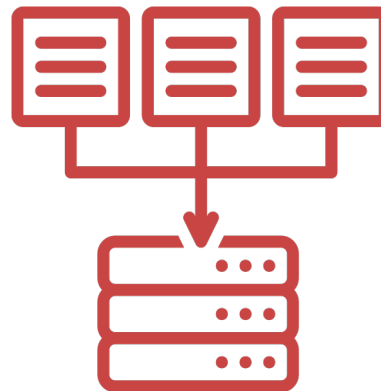
Development of BCs for Therapeutic Areas

- Oncology Team authoring BCs using CDISC framework for Disease Response Criterion standards
- Tobacco Implementation Guide (TIG)



Additional Sources of BCs

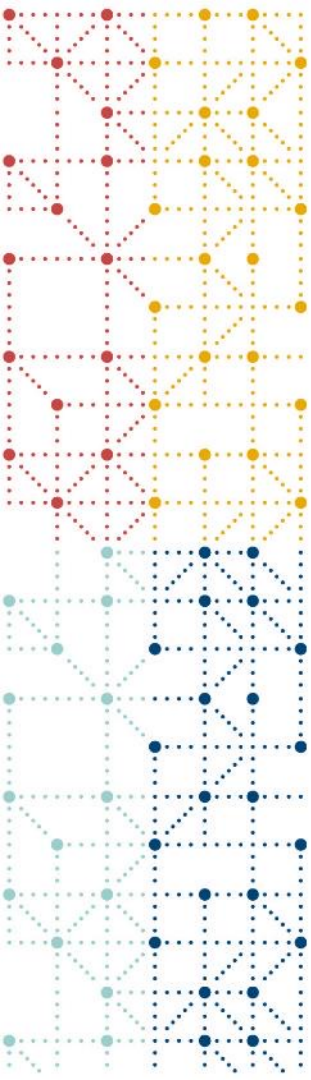
- Donation of company created BCs
- Mining datasets
- Code Table mapping files
- LOINC to LB mapping
- NCI Thesaurus





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



Thank You!

A special thank you to Lex Jansen and Linda Lander

