CDISC Library: Integrating and Surfacing 360 Content

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16 October 2019

Setting the Scene

High level overview that shows our initial efforts to integrate CDISC 360 content across the project work stream to generate outputs that can be surfaced for inspection

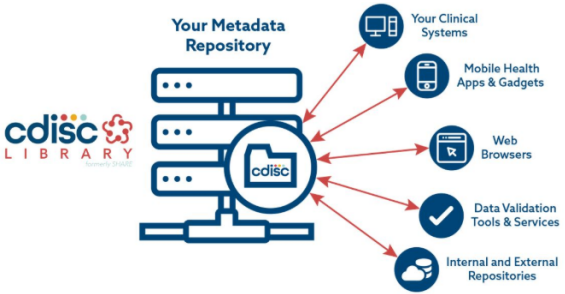
CDISC 360 and the CDISC Library

Goals:

- Increase study implementation automation
- Reduce study implementation variability

Building Tools using the CDISC Library

Create additional concept-based metadata published via the CDISC Library to support software tools that will provide additional study implementation automation while reducing the variability across CDISC standards implementations

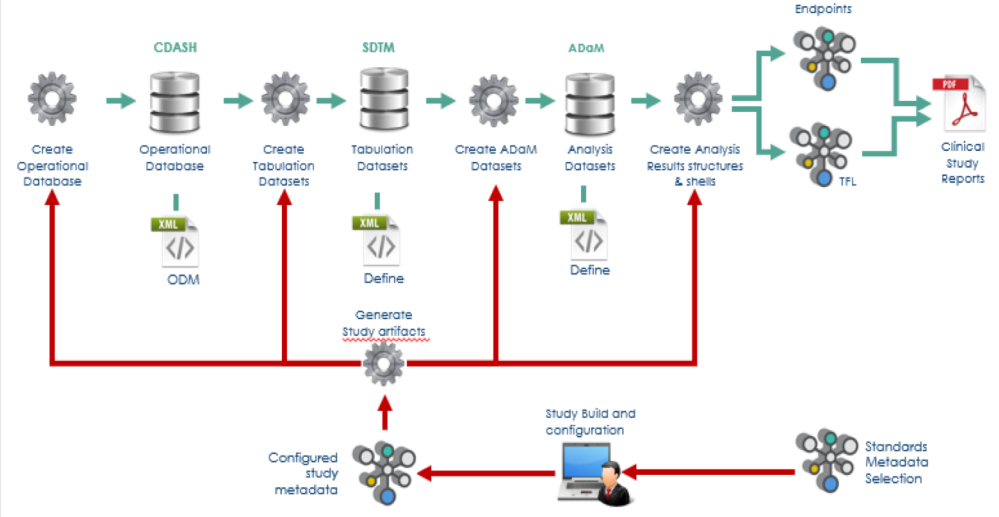


Integration: Data Flow Across the Workstreams

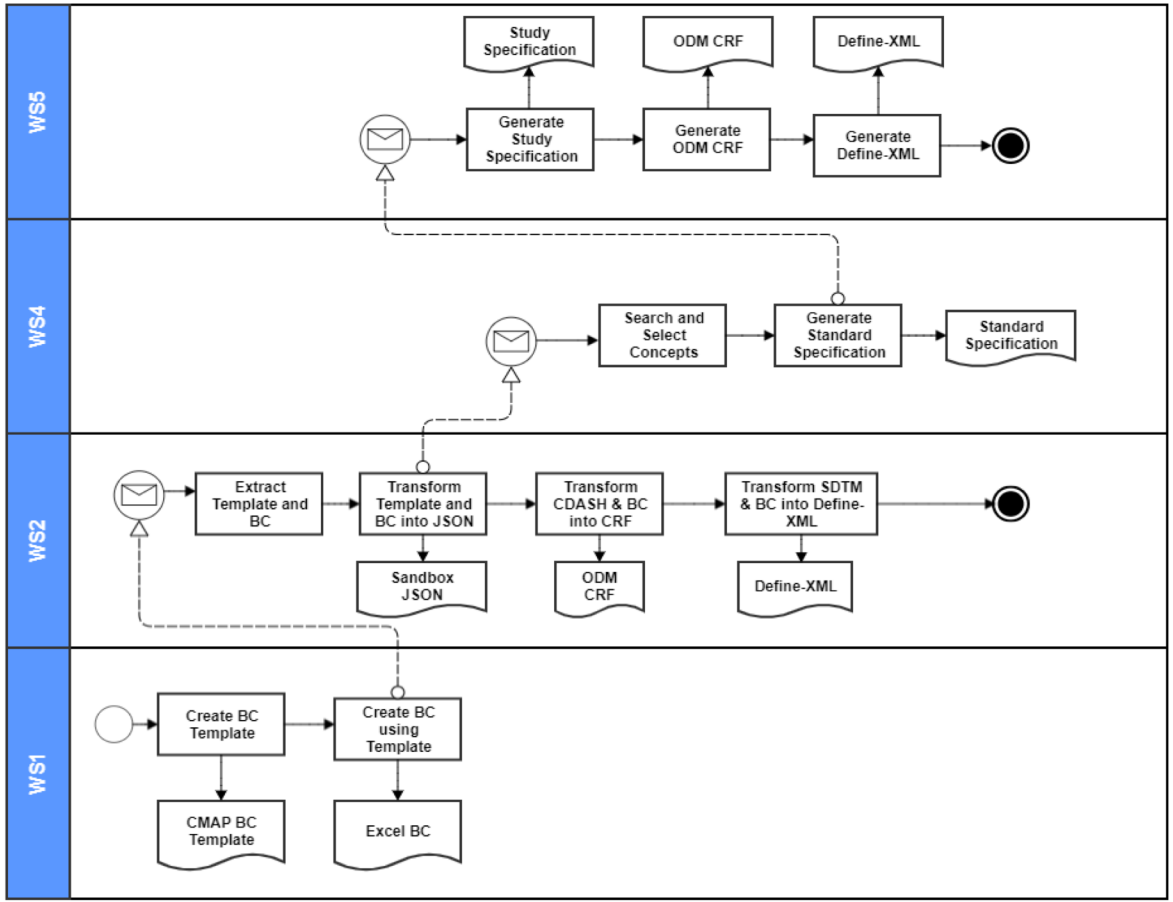
- Uses Biomedical Concepts to generate a CRF and Define-XML
- Uses BCs and CDISC Library to create a simple study specification
- Uses automation to test the metadata content
- Shows small subset of the work done in CDISC 360 to date

Demo Constraints:

- Focused on use cases 1 & 2
- Focused on work streams 1-5
- Focused on VS domain
- Not fully end-to-end



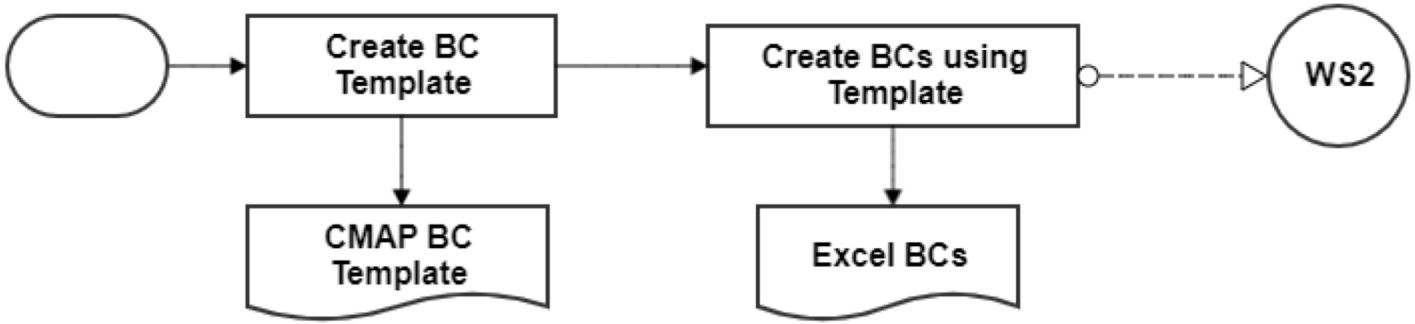
CDISC 360 US Interchange Demo



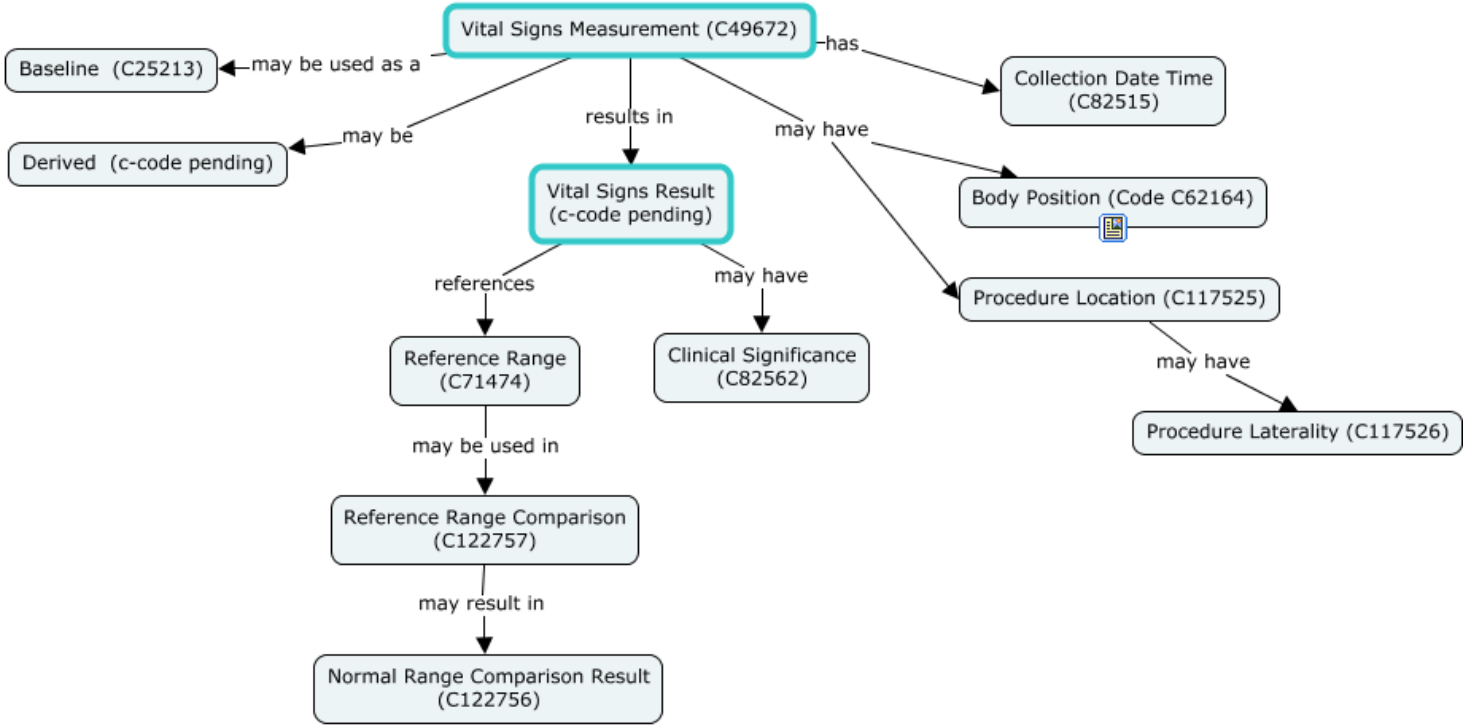
Enhance Standards: Workstream 1

Creating Templates and Biomedical Concepts to Enhance our Standards Metadata

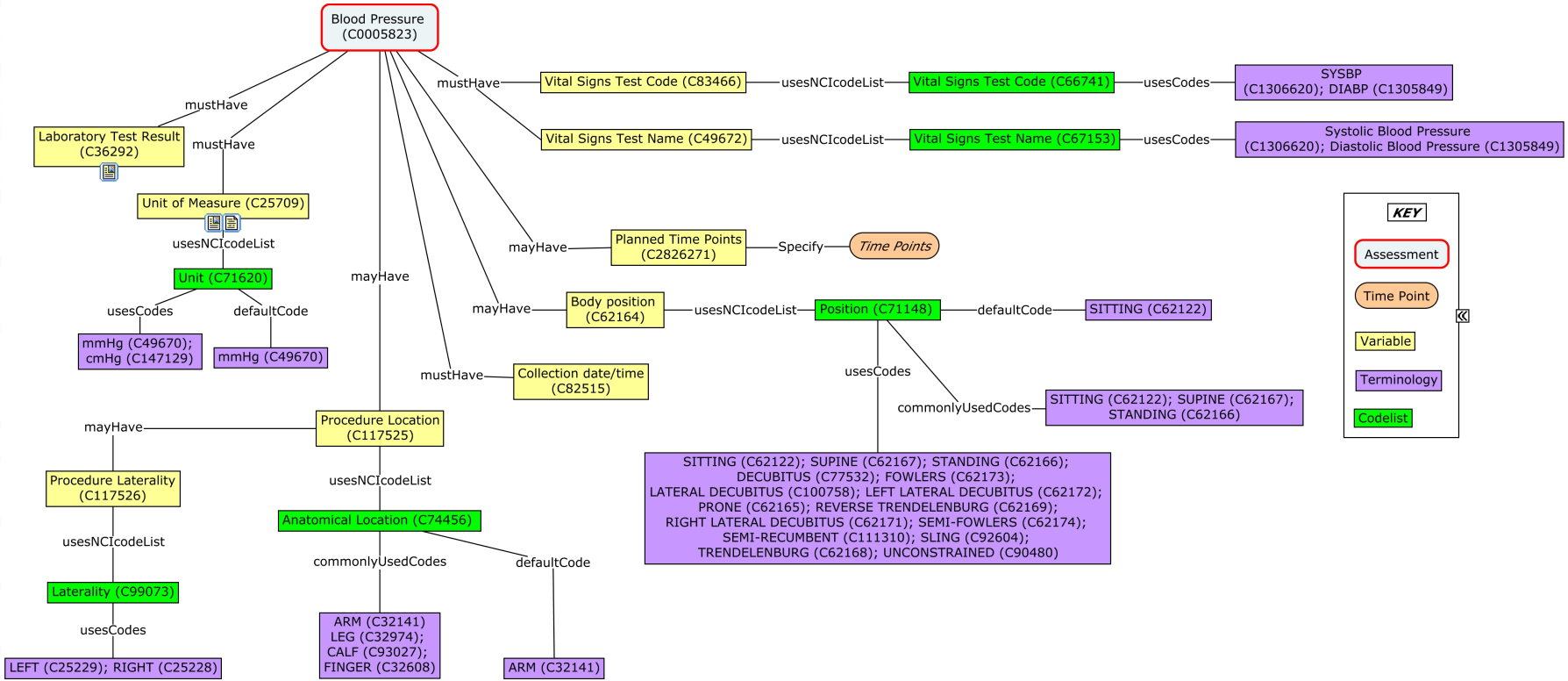
Enhance Standards (Workstream 1): Creating Biomedical Concepts (BCs)



Vital Signs Biomedical Concept Template



Blood Pressure Concept Map



Creating BCs in Excel

#	C-code	Biomedical Concept	Definition	Test Code	Test Name	Unit	Unit Type	Anatomic Location	Position	Result Type
1	Pending	Diastolic Blood Pressure	The blood pressure after the contraction of the heart while the chambers of the heart refill with blood. (NCI)	DIABP (C25299)	Diastolic Blood Pressure (C25299)	mmHg (C49670)	TBD	N/A	DECUBITUS (C77532); FOWLERS (C62173); LATERAL DECUBITUS (C100758); LEFT LATERAL DECUBITUS (C62172); PRONE (C62165); REVERSE TRENDELENBURG (C62169); RIGHT LATERAL DECUBITUS (C62171); SEMI-FOWLERS (C62174); SEMI-RECUMBENT (C111310); SITTING (C62122); SLING (C92604); STANDING (C62166); SUPINE (C62167); TRENDELENBURG (C62168); UNCONSTRAINED (C90480)	Numeric
2	Pending	Systolic Blood Pressure	The blood pressure during the contraction of the left ventricle of the heart. (NCI)	SYSBP (C25298)	Systolic Blood Pressure (C25298)	mmHg (C49670)	TBD	N/A	DECUBITUS (C77532); FOWLERS (C62173); LATERAL DECUBITUS (C100758); LEFT LATERAL DECUBITUS (C62172); PRONE (C62165); REVERSE TRENDELENBURG (C62169); RIGHT LATERAL DECUBITUS	Numeric

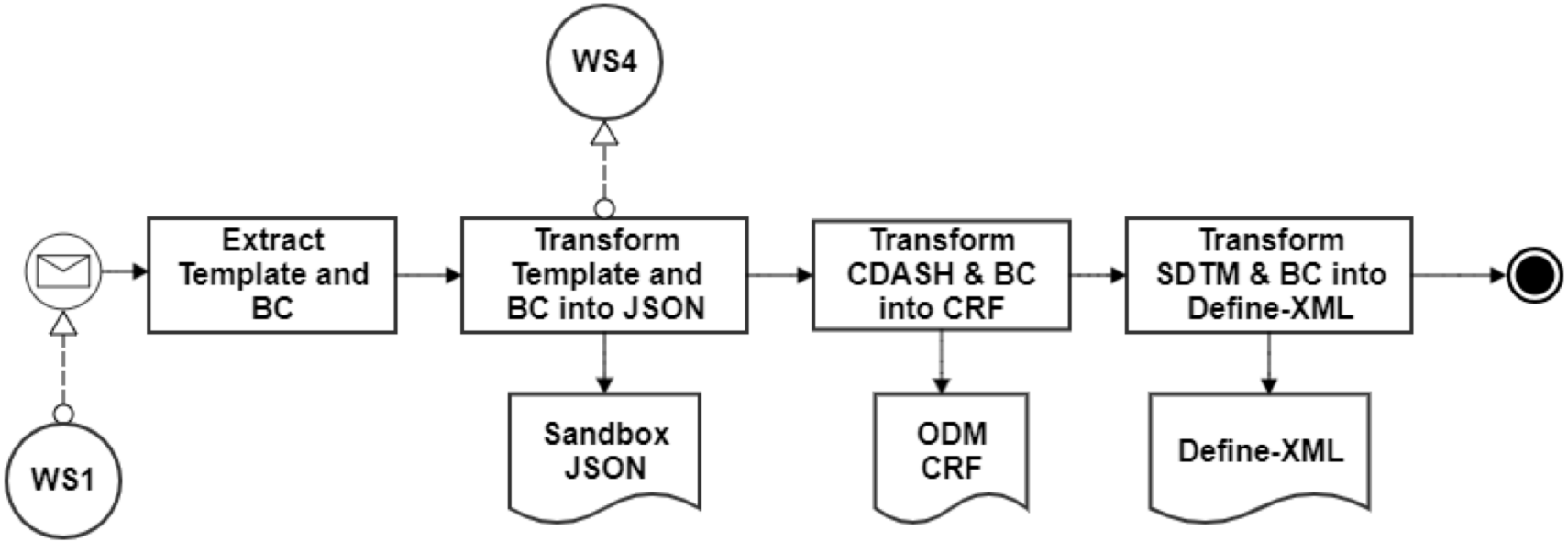
What do Biomedical Concepts Do?

- A biomedical concept is a unit of knowledge created by a unique combination of characteristics (ISO 11179)
  - Independent of a standards implementation
- Include an identifier, name, label, and definition
- Specify valid units
- Specify the needed qualifiers
- Specify valid controlled terminology subsets

Publish Standards: Workstream 2

Transforming Biomedical Concepts into Machine-readable Metadata and Publishing them via the CDISC Library

Publish Standards (Workstream 2): Transforming BCs into Machine-readable Metadata



Generating the CRF and Define-XML are for testing purposes

What does the CDISC Library Do?

- Provides access to CDISC standards metadata
- Machine-readable metadata as linked data
- Provides access to the CDISC controlled terminology
- Ultimately will provide access to the foundational standards as well as the CDISC 360 content via the API

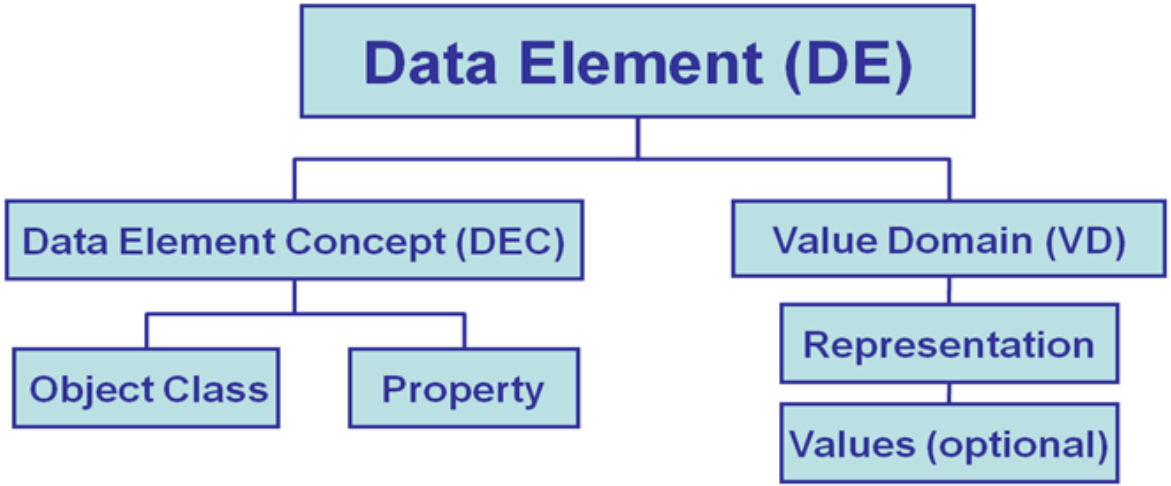

```
{
    "ordinal": "16",
    "name": "VSORRES",
    "label": "Vital Signs Result",
    "definition": "Result of the vital signs measurement as originally received or collected.",
    "questionText": "What was the result of the measurement?",
    "prompt": "Result",
    "completionInstructions": "Record the vital sign result.",
    "implementationNotes": "N/A",
    "simpleDatatype": "Char",
    "mappingInstructions": "Maps directly to the SDTMIG variable listed in the column with the
    "core": "HR",
    "_links": {
        "self": {
            "href": "/mdr/cdashig/2-0/domains/VS/fields/VSORRES",
            "title": "Vital Signs Result",
            "type": "Data Collection Field"
        },
        "parentProduct": {
            "href": "/mdr/cdashig/2-0",
            "title": "Clinical Data Acquisition Standards Harmonization Implementation Guide fo
            "type": "Implementation Guide"
        },
        "parentDomain": {
            "href": "/mdr/cdashig/2-0/domains/VS",
            "title": "Vital Signs",
            "type": "CDASH Domain"
        },
        "rootItem": {
            "href": "/mdr/root/cdashig/domains/VS/fields/VSORRES",
            "title": "Version-agnostic anchor element for field VS.VSORRES",
            "type": "Root Data Element"
```

Generating the Vitals Signs CRF: What's Missing?

- What vital signs tests are included
- What units apply per tests
- What qualifiers are required for a specific test
- Valid controlled terminology subsets
- Common vs repeating content
- Specific (ODM) datatypes
- Length and SignificantDigits

Question: Where is the Height Variable?

- Height is a VS TEST, but not a variable
- You might think of Height as a virtual variable
- It needs to be defined as a Data Element for use as a field in CDASH, or a variable in SDTM
- Biomedical Concepts help us to create a Height data element



Transforming Biomedical Concepts into JSON

"designation": "Height",
"conceptId": "X25347",
"label": "Height Biomedical Concept",
"definition": "The vertical measurement or distance from the base…",
"testCode": "HEIGHT",
"testConceptId": "C25347",
"testName": "Height",
"loincCode": "8302-2",
"resultType": "Numeric",
"unitList": ["cm (C49668)", "in (C48500)", "mm (C28251)"],
"standardUnit": "cm (C49668)",

Standards and Biomedical Concepts Work Together

VS Domain from CDISC Library


```
{
    "ordinal": "16",
    "name": "VSORRES",
    "label": "Vital Signs Result",
    "definition": "Result of the vital signs measurement as originally received or collected.",
    "questionText": "What was the result of the measurement?",
    "prompt": "Result",
    "completionInstructions": "Record the vital sign result.",
    "implementationNotes": "N/A",
    "simpleDatatype": "Char",
    "mappingInstructions": "Maps directly to the SDTMIG variable listed in the column with the
    "core": "HR",
    "_links": {
        "self": {
            "href": "/mdr/cdashig/2-0/domains/VS/fields/VSORRES",
            "title": "Vital Signs Result",
            "type": "Data Collection Field"
        },
        "parentProduct": {
            "href": "/mdr/cdashig/2-0",
            "title": "Clinical Data Acquisition Standards Harmonization Implementation Guide fo
            "type": "Implementation Guide"
        },
        "parentDomain": {
            "href": "/mdr/cdashig/2-0/domains/VS",
            "title": "Vital Signs",
            "type": "CDASH Domain"
        },
        "rootItem": {
            "href": "/mdr/root/cdashig/domains/VS/fields/VSORRES",
            "title": "Version-agnostic anchor element for field VS.VSORRES",
            "type": "Root Data Element"
```


Height BC from CDISC 360


```
{
    "designation": "Height",
    "conceptId": "X25347",
    "label": "Height Biomedical Concept",
    "definition": "The vertical measurement or distance from the base to the top of an object;
    "testCode": "HEIGHT",
    "testConceptId": "C25347",
    "testName": "Height",
    "loincCode": "8302-2",
    "resultType": "Numeric",
    "unitList": [
        "cm (C49668)", "in (C48500)", "mm (C28251)"
    ],
    "standardUnit": "cm (C49668)",
    "_links": {
        "self": {
            "href": "/mdr/bc/1-0/VS/X25347",
            "title": "Height Biomedical Concept",
            "type": "Biomedical Concept"
        },
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            "title": "Vital Signs Biomedical Concepts",
            "type": "VS Biomedical Concept"
        },
        "rootItem": {
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            "title": "Version-agnostic anchor resource for Biomedical Concept Height",
            "type": "Root Data Element"
        },
```
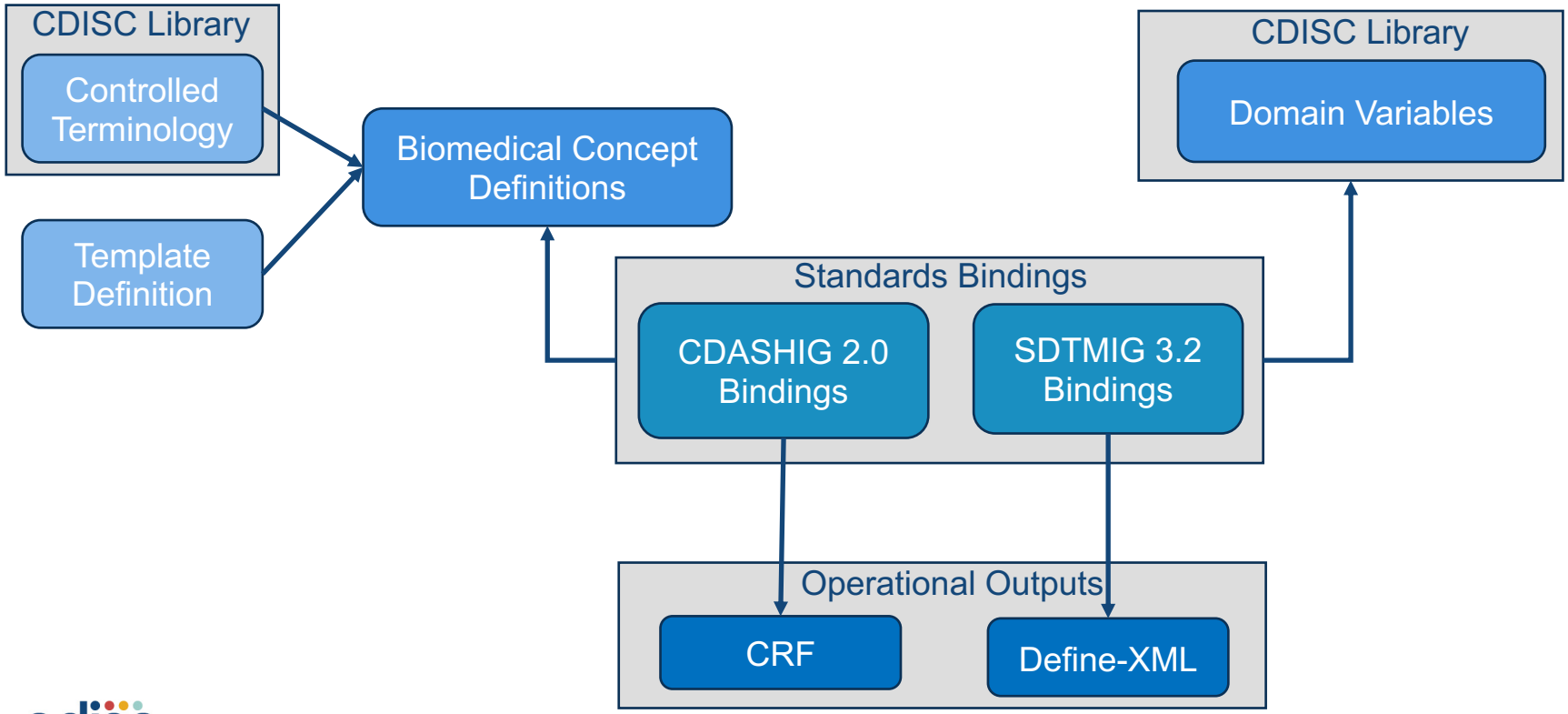
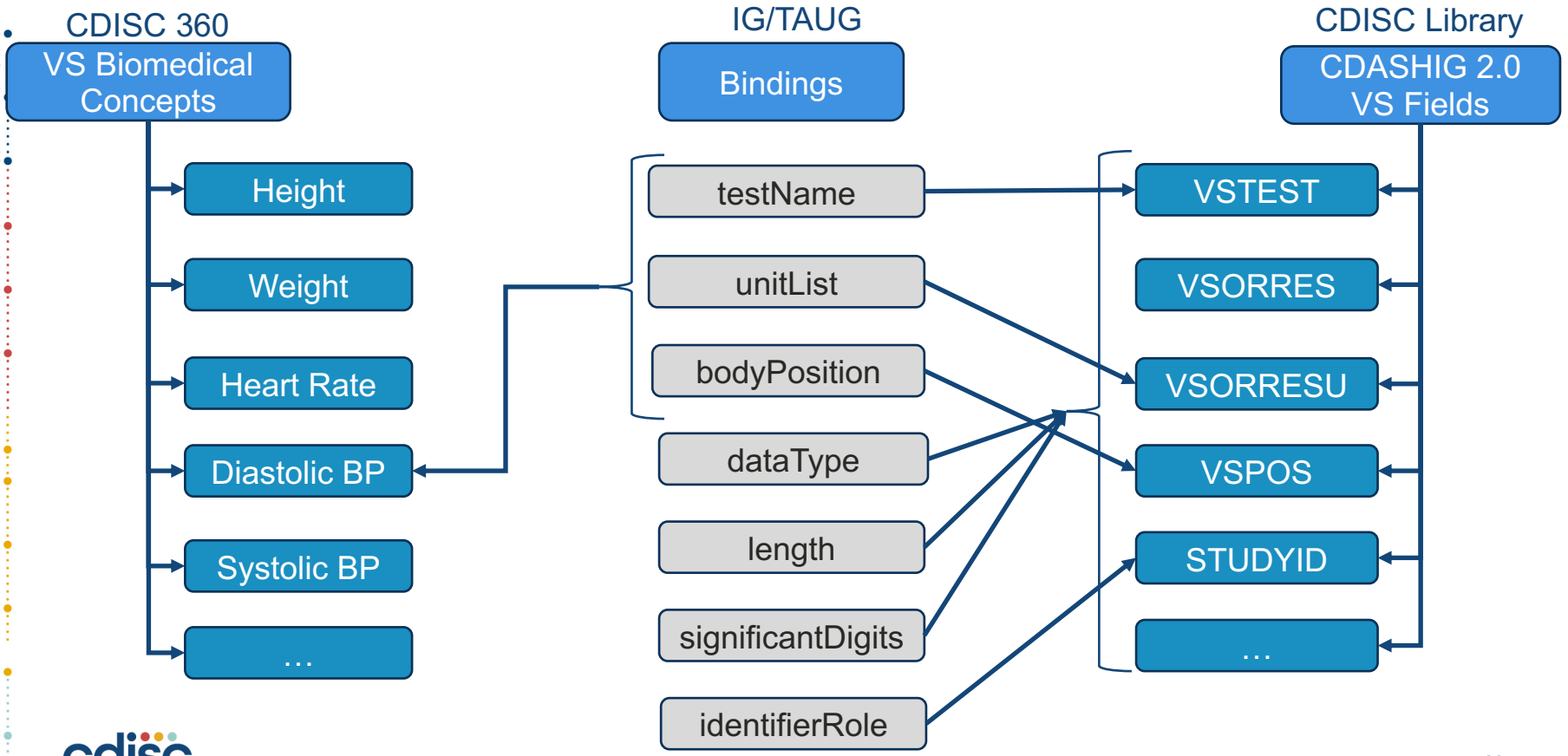
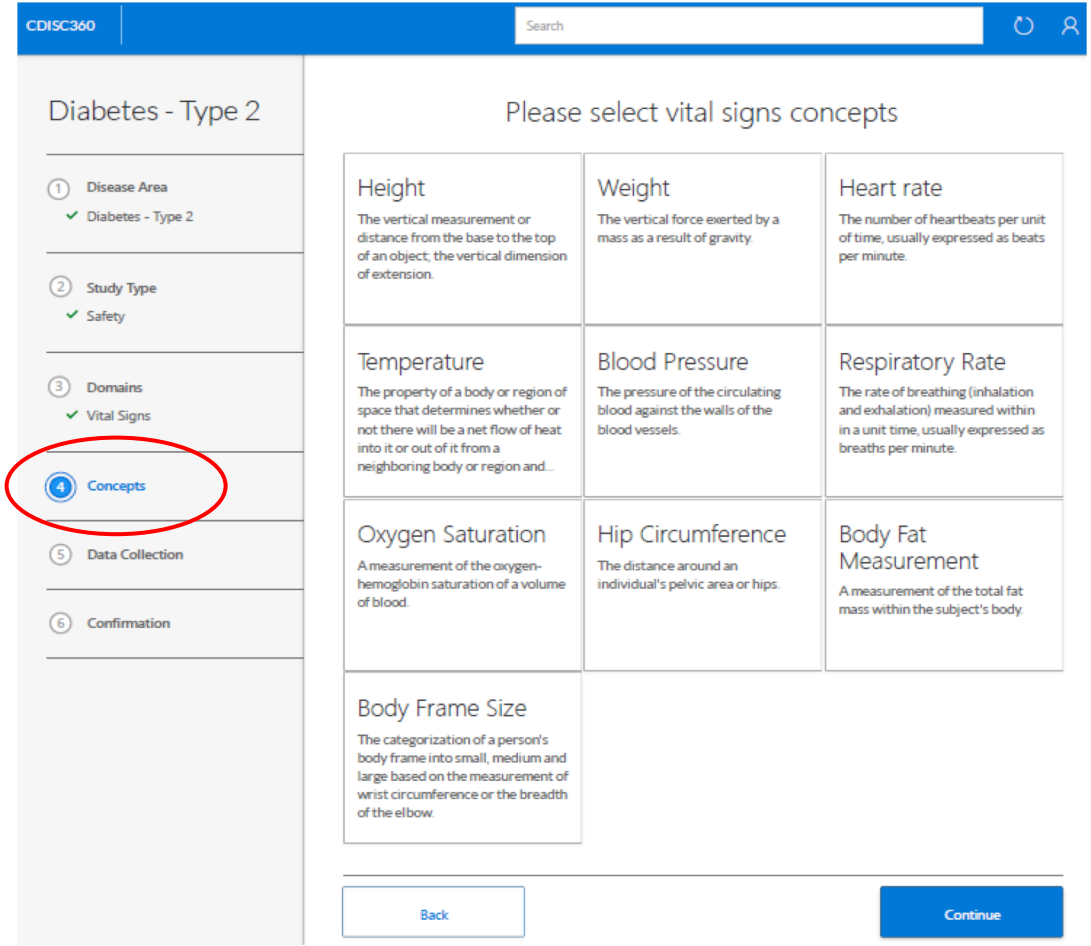

Applying Biomedical Concepts



Applying Biomedical Concepts: Binding to Standards



We want to select a set of vital signs concepts



ODM CRF Generated using BCs, Bindings, & Standards

ODM-based VS CRF

```
<MetaDataVersion Description="CDASH BC CRF Example" Name="CDASH CRF Example" OID="MDV.CDISC360.DEMO1">
    <FormDef Name="VS Form" OID="F.VS" Repeating="Yes">
        <ItemGroupRef ItemGroupOID="IG.BC.VS.COMMON" Mandatory="No"/>
        <ItemGroupRef ItemGroupOID="IG.BC.VS.TEMPERATURE" Mandatory="No"/>
        <ItemGroupRef ItemGroupOID="IG.BC.VS.HEIGHT" Mandatory="No"/>
        <ItemGroupRef ItemGroupOID="IG.BC.VS.DIASTOLICBP" Mandatory="No"/>
        <ItemGroupRef ItemGroupOID="IG.BC.VS.SYSTOLICBP" Mandatory="No"/>
        <ItemGroupRef ItemGroupOID="IG.BC.VS.WEIGHT" Mandatory="No"/>
        <ItemGroupRef ItemGroupOID="IG.BC.VS.HEARTRATE" Mandatory="No"/>
    </FormDef>
    <ItemGroupDef Name="VS Common" OID="IG.BC.VS.COMMON" Repeating="No">
        <ItemRef ItemOID="IT.BC.VS.STUDYID" Mandatory="Yes" OrderNumber="1"/>
        <ItemRef ItemOID="IT.BC.VS.SITEID" Mandatory="Yes" OrderNumber="2"/>
        <ItemRef ItemOID="IT.BC.VS.SUBJID" Mandatory="Yes" OrderNumber="3"/>
        <ItemRef ItemOID="IT.BC.VS.VISIT" Mandatory="No" OrderNumber="4"/>
        <ItemRef ItemOID="IT.BC.VS.VSPERF" Mandatory="No" OrderNumber="6"/>
        <ItemRef ItemOID="IT.BC.VS.VSDAT" Mandatory="No" OrderNumber="7"/>
        <ItemRef ItemOID="IT.BC.VS.VSTIM" Mandatory="No" OrderNumber="8"/>
    </ItemGroupDef>
    <ItemGroupDef Name="VS Temperature" OID="IG.BC.VS.TEMPERATURE" Repeating="No">
        <ItemRef ItemOID="IT.BC.VS.TEMPERATURE.VSTEST" Mandatory="Yes" OrderNumber="1"/>
        <ItemRef ItemOID="IT.BC.VS.TEMPERATURE.VSORRES" Mandatory="Yes" OrderNumber="2"/>
        <ItemRef ItemOID="IT.BC.VS.TEMPERATURE.VSORRESU" Mandatory="No" OrderNumber="3"/>
    </ItemGroupDef>
```

Stylesheet rendering of ODM VS CRF

Group: VS Temperature

OID=IG.BC.VS.TEMPERATURE, Repeating=No

What is the vital sign test name?	○ Temperature
What was the result of the measurement?	_____ . _____
What was the unit of the measurement?	○ C ○ F

Group: VS Height

OID=IG.BC.VS.HEIGHT, Repeating=No

What is the vital sign test name?	○ Height
What was the result of the measurement?	_____ . _____
What was the unit of the measurement?	○ cm ○ in ○ mm

Group: VS DiastolicBP

OID=IG.BC.VS.DIASTOLICBP, Repeating=No

What is the vital sign test name?	○ Diastolic Blood Pressure
What was the result of the measurement?	_____
What was the unit of the measurement?	○ mmHg ○ cmHg
What was the position of the subject during the measurement?	○ SITTING ○ STANDING ○ SUPINE

Generating a Vital Signs Define-XML: What's Missing?

- Value Level Metadata
- List of applicable tests
- Valid set of units for each test
- ODM Datatypes for Define-XML
- Length and SignificantDigit values
- Standard units
- Valid controlled terminology subsets (e.g. body position)

Define-XML Generated using BCs, Bindings, & Standards

Define-XML v2.1 VLM

```
<MetaDataVersion Description="SDTMIG BC Define-XML Example" Name="SDTM Define Example"
    OID="MDV.CDISC360.DEMO1">
    <def:Standards>
        <def:Standard Name="SDTMIG" OID="STD.1" Status="Final" Type="IG" Version="3.2"/>
        <def:Standard Name="CDISC/NCI" OID="STD.2" PublishingSet="SDTM" Status="Final"
            Type="CT" Version="2018-06-29"/>
    </def:Standards>
    <def:ValueListDef OID="VL.VS.VSORRES">
        <ItemRef ItemOID="IT.VS.VSORRES.Temperature" Mandatory="No">
            <def:WhereClauseRef WhereClauseOID="WC.VS.VSTESTCD.TEMP"/>
        </ItemRef>
        <ItemRef ItemOID="IT.VS.VSORRES.Height" Mandatory="No">
            <def:WhereClauseRef WhereClauseOID="WC.VS.VSTESTCD.HEIGHT"/>
        </ItemRef>
        <ItemRef ItemOID="IT.VS.VSORRES.DiastolicBP" Mandatory="No">
            <def:WhereClauseRef WhereClauseOID="WC.VS.VSTESTCD.DIABP"/>
        </ItemRef>
        <ItemRef ItemOID="IT.VS.VSORRES.SystolicBP" Mandatory="No">
            <def:WhereClauseRef WhereClauseOID="WC.VS.VSTESTCD.SYSBP"/>
        </ItemRef>
        <ItemRef ItemOID="IT.VS.VSORRES.Weight" Mandatory="No">
            <def:WhereClauseRef WhereClauseOID="WC.VS.VSTESTCD.WEIGHT"/>
        </ItemRef>
        <ItemRef ItemOID="IT.VS.VSORRES.HeartRate" Mandatory="No">
            <def:WhereClauseRef WhereClauseOID="WC.VS.VSTESTCD.HR"/>
        </ItemRef>
    </def:ValueListDef>
```

Stylesheet rendering of Define-XML VS

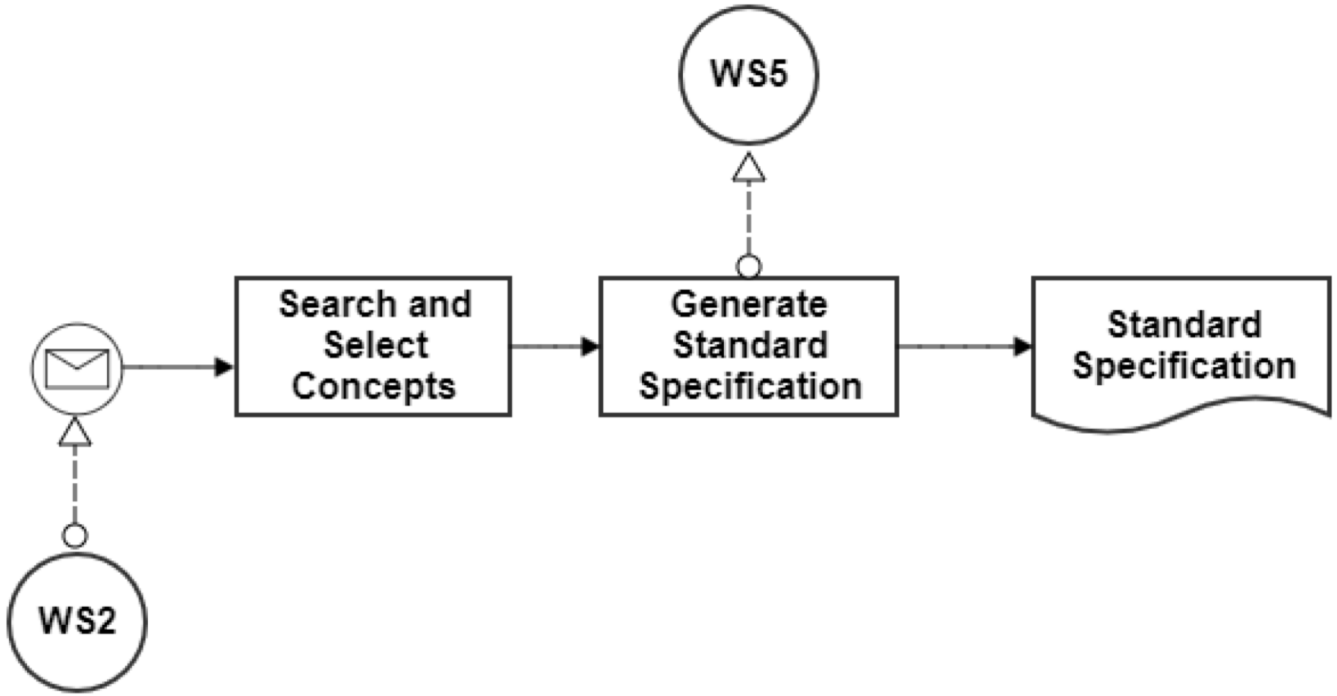
VS (Vital Signs) - [SDTMIG 3.2]

Variable	Where Condition	Label / Description	Type	Length or Display Format	Controlled Terms or ISO Format	Origin / Source / Method / Comment
STUDYID		Unique identifier for a study.	text	40		
DOMAIN		Two-character abbreviation for the domain.	text	2		
USUBJID		Identifier used to uniquely identify a subject across all studies for all applications or submissions involving the product.	text	40		
VSSEQ		Sequence Number given to ensure uniqueness of subject records within a domain. May be any valid number.	integer	4		
VSTESTCD		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.	text	8	Vital Signs Test Code [6 Terms]	
VSTEST		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.	text	40	Vital Signs Test Name [6 Terms]	
VSORRES VLM		Result of the vital signs measurement as originally received or collected.	text	30		
	VSTESTCD = "TEMP"	VSORRES for Temperature	float	4		
	VSTESTCD = "HEIGHT"	VSORRES for Height	float	5		
	VSTESTCD = "DIABP"	VSORRES for Diastolic Blood Pressure	integer	3		
	VSTESTCD = "SYSBP"	VSORRES for Systolic Blood Pressure	integer	3		
	VSTESTCD = "WEIGHT"	VSORRES for Weight	float	6		
	VSTESTCD = "HR"	VSORRES for Heart Rate	integer	3		
VSORRESU VLM		Original units in which the data were collected. The unit for VSORRES. Examples: IN, LB, BEATS/MIN.	text	20		
	VSTESTCD = "TEMP"	VSORRESU for Temperature	text		Units for Vital Signs Results Temperature • "C" • "F"	

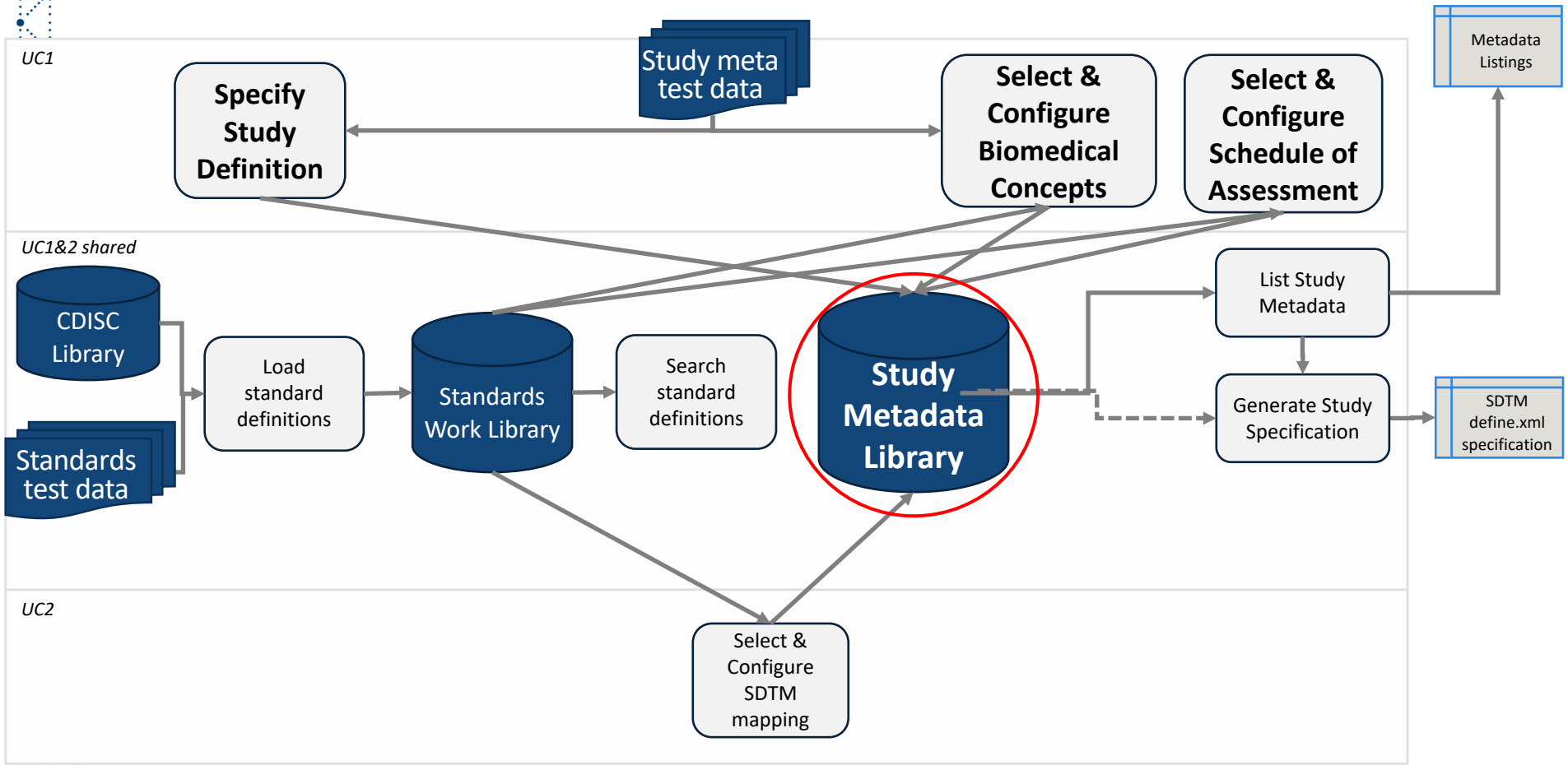
Define: Workstream 4

Define a Standards-based Study Specification for Developing Study Specific Standards Metadata

Define (Workstream 4): Create Standard Specification



Using a Study Metadata Library to Configure the Study Specification



Selecting & Configure Study Specification Content

Vital Signs in the Working Library

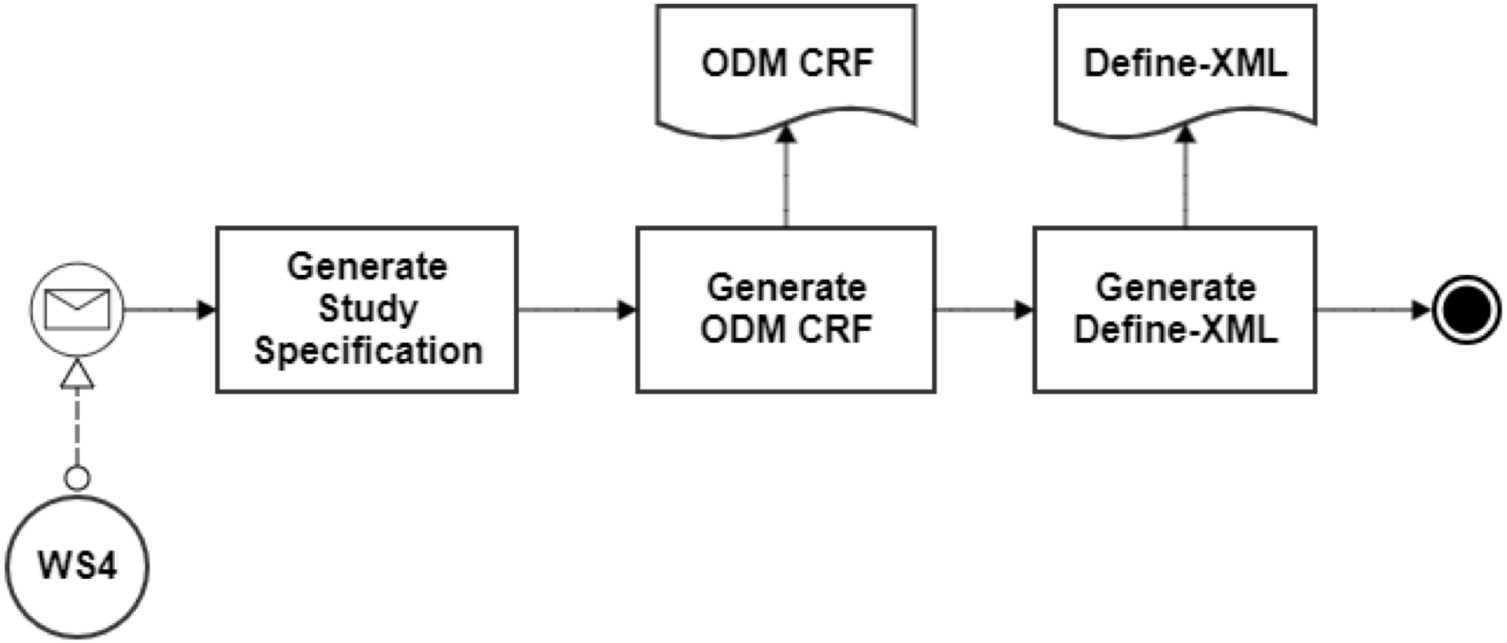
VSORRES in the Working Library


```
{
  "core": "HR",
  "question": "What was the result of
the measurement?",
  "name": "VSORRES",
  "data_type": "Char",
  "definition": "Result of the vital
signs measurement as originally
received or collected.",
  "label": "Vital Signs Result",
  "prompt": "Result",
  "ordinal": 16
}
```

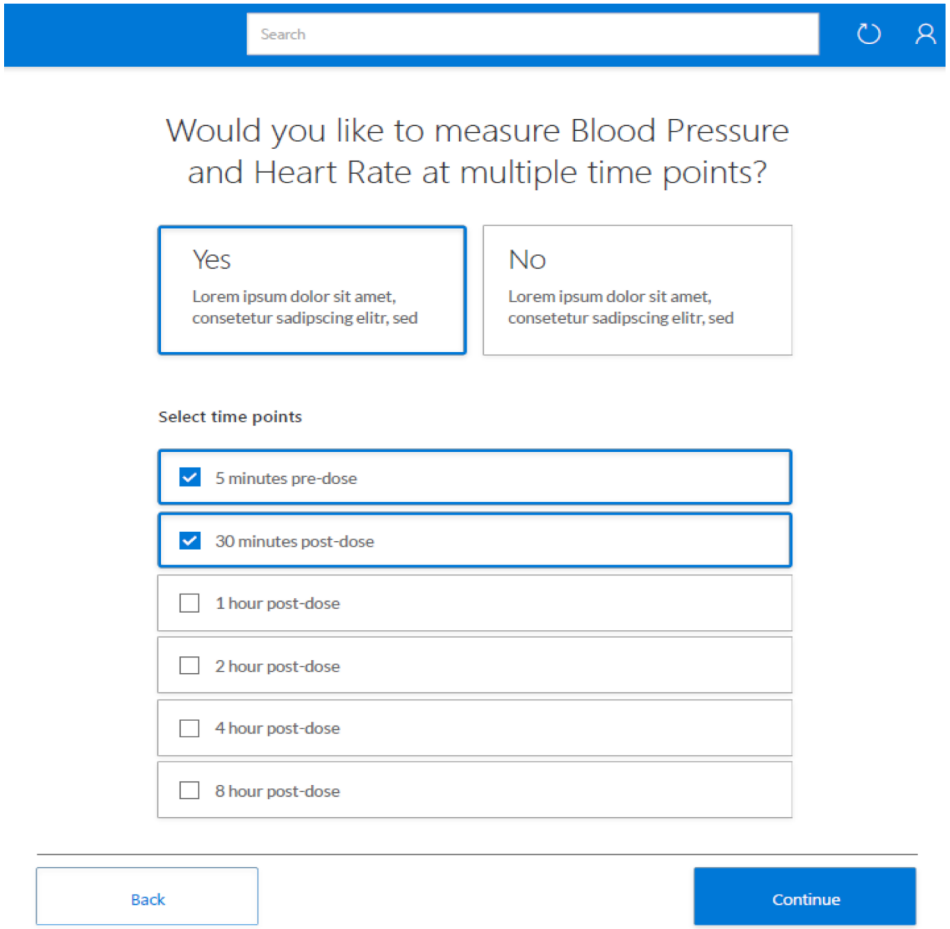
Build: Workstream 5

Build Study Metadata Artifacts

Build (Workstream 5): Generate Study Metadata Artifacts



We want to generate a CRF from CDISC Library



Select the versions of the standards to use

Which CDASH version is needed?

- ○ Option 1.1
- ◉ Option 2.0

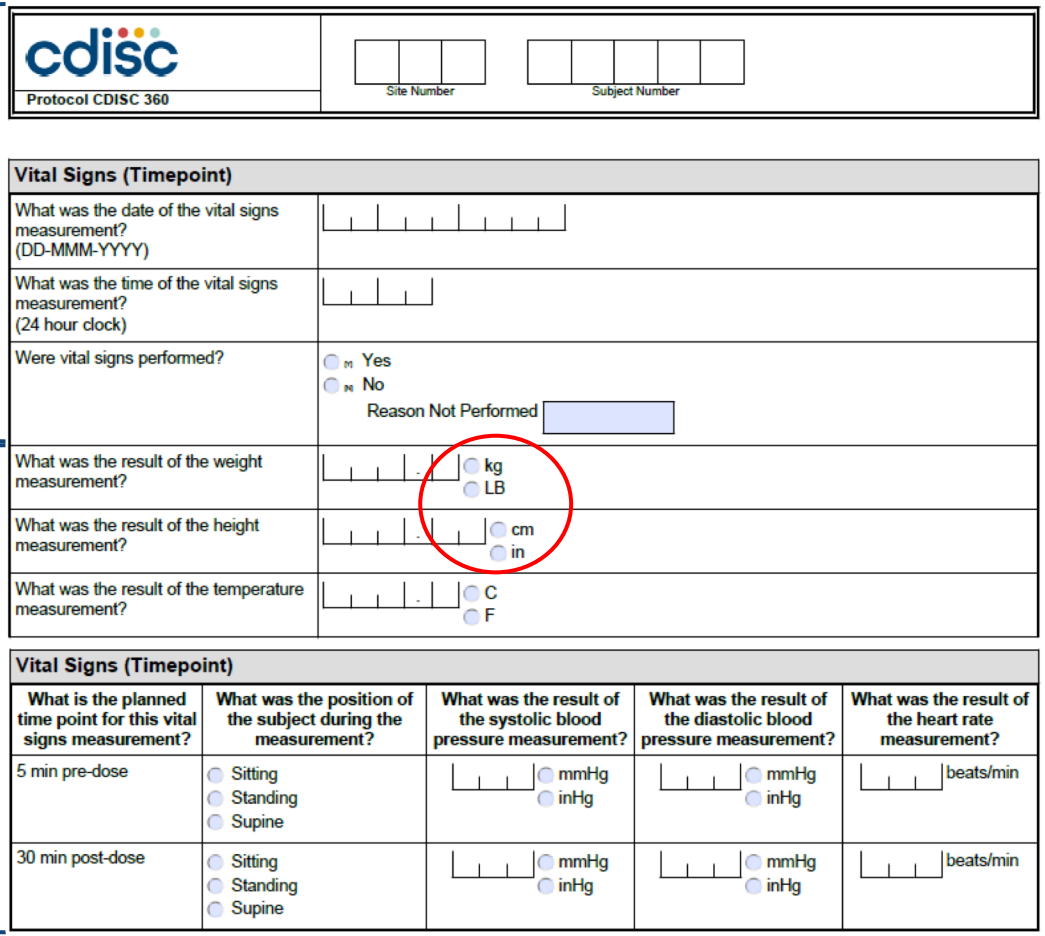
Which Terminology version is needed?

- ○ 2019-09-03
- ◉ 2019-06-06
- ○ 2019-03-01
- ○ 2018-11-20

Generate a Vital Signs CRF based on ODM

Common fields appear once

Test fields repeat



cdisc

Protocol CDISC 360

Site Number

Subject Number

Vital Signs (Timepoint)

What was the date of the vital signs measurement? (DD-MMM-YYYY)	
What was the time of the vital signs measurement? (24 hour clock)	
Were vital signs performed?	Yes No Reason Not Performed
What was the result of the weight measurement?	kg LB
What was the result of the height measurement?	cm in
What was the result of the temperature measurement?	C F

Vital Signs (Timepoint)

What is the planned time point for this vital signs measurement?	What was the position of the subject during the measurement?	What was the result of the systolic blood pressure measurement?	What was the result of the diastolic blood pressure measurement?	What was the result of the heart rate measurement?
5 min pre-dose	Sitting Standing Supine	mmHg inHg	mmHg inHg	beats/min
30 min post-dose	Sitting Standing Supine	mmHg inHg	mmHg inHg	beats/min

cdisc

Generate a Vital Signs define.xml based on Define-XML

VS (Vital Signs) - [SDTMIG 3.2]

Variable	Where Condition	Label / Description	Type	Length or Display Format	Controlled Terms or ISO Format	Origin / Source / Method / Comment
STUDYID		Unique identifier for a study.	text	40		
DOMAIN		Two-character abbreviation for the domain.	text	2		
USUBJID		Identifier used to uniquely identify a subject across all studies for all applications or submissions involving the product.	text	40		
VSSEQ		Sequence Number given to ensure uniqueness of subject records within a domain. May be any valid number.	integer	4		
VSTESTCD		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.	text	8	Vital Signs Test Code [6 Terms]	
VSTEST		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.	text	40	Vital Signs Test Name [6 Terms]	
VSORRES VLM		Result of the vital signs measurement as originally received or collected.	text	30		
	VSTESTCD = "TEMP"	VSORRES for Temperature	float	4		
	VSTESTCD = "HEIGHT"	VSORRES for Height	float	5		
	VSTESTCD = "DIABP"	VSORRES for Diastolic Blood Pressure	integer	3		
	VSTESTCD = "SYSBP"	VSORRES for Systolic Blood Pressure	integer	3		
	VSTESTCD = "WEIGHT"	VSORRES for Weight	float	6		
	VSTESTCD = "HR"	VSORRES for Heart Rate	integer	3		
VSORRESU VLM		Original units in which the data were collected. The unit for VSORRES. Examples: IN, LB, BEATS/MIN.	text	20		
	VSTESTCD = "TEMP"	VSORRESU for Temperature	text		Units for Vital Signs Results Temperature • "C" • "F"	

Conclusion

What does the demonstration tell us?

Key Points

- The new CDISC 360 metadata enables implementers to more completely generate metadata artifacts
- The metadata can be used by different technology implementations
- Future sprints will incrementally change the metadata used in the demo
- Future sprints will expand on the scope of the current demonstration
- Ultimately, the new metadata will be available in the CDISC Library

Session 3, Track B: CDISC 360 Use Cases - Industry Perspectives

- Use Case 1: DEFINE - End to Start Standards Specification
- Use Case 2: BUILD - Study Configuration & Artifact Creation
- Use Case 3: EXECUTE - Automated Data Processing
- Pacific Ballroom 14-15
  - 14:00 – 15:30

Thank You!