



CDISC 360 Update: *Evolution of the CDISC Standards*

Peter Van Reusel,
CDISC Chief Standards Officer





Agenda

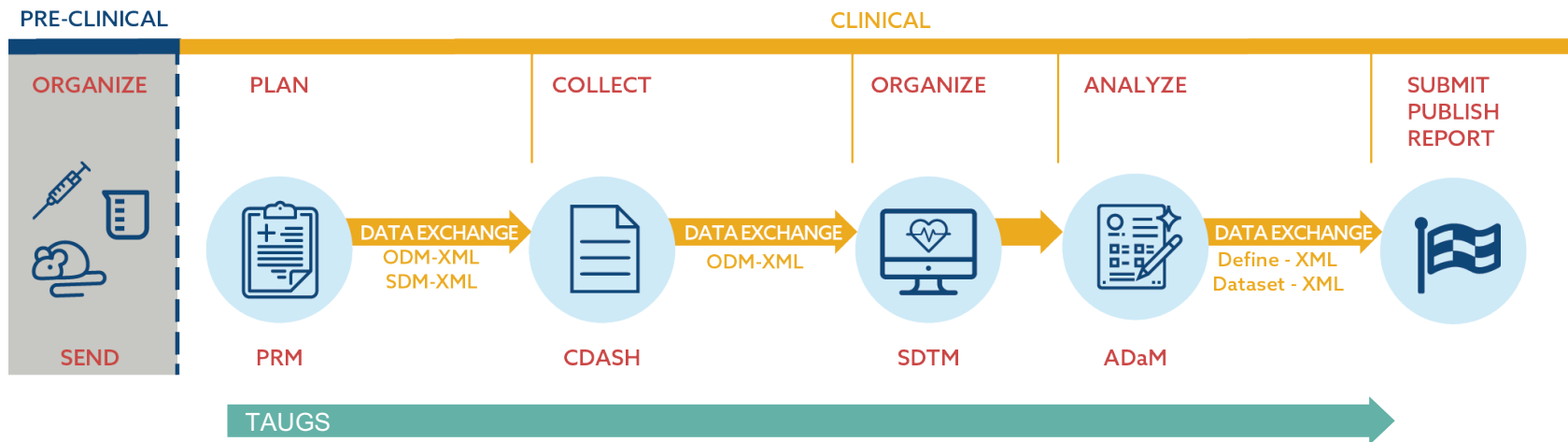
1. CDISC 360 Intro
2. Project Approach
3. Project Status
4. Achievements so far



1. CDISC 360 Intro

Today we are here

CDISC Standards in the Clinical Research Process



BRIDG, CONTROLLED TERMINOLOGY AND GLOSSARY



Defined structures

- CDISC Foundational models provide much needed structure

- Normative Content
- 2 dimensional (tables, columns)
- Standard to represent data

- The information itself is not defined

- We do not need new structures
- We need to define
 - Entities
 - Semantics (meaning)
 - Relationships between information
 - Rules in the data lifecycle

Question Text	Prompt	SDTM or CDASH Variable Name	BRIDG	Definition	CRF Completion Instructions	Information for Sponsors	Core
1 Were vital signs collected?	Vital signs collected?	VSPERF	Performed/Observation Result value	General prompt question regarding whether or not any VS were collected during the study. This provides verification that all other fields on the CRF were deliberately left blank. (NY) (See Section 2.2.)	Indicate if the vital signs were collected. If yes, include the appropriate details where indicated on the CRF.	The intent purpose of collecting this field is to help with data cleaning and monitoring. See Best Practice Section 3.4, FAQ #6. For the SDTM-based dataset, SDTIGIG variable VSSTAT is derived from a "No" value in VSPERF. This field does not map directly to an SDTM variable.	0
2 On what date were the measurements performed?	Date	VSDAT	Performed/Activity dateRange*	Date of measurements.	Record date of measurements using this format (DD-MON-YYYY).	The date of measurement can be derived from a collected date of visit and in such cases a separate measurement date field is not required. For the SDTM-based dataset, the SDTM IG variable VSSTAT is derived from a "No" value in VSPERF.	R/C

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

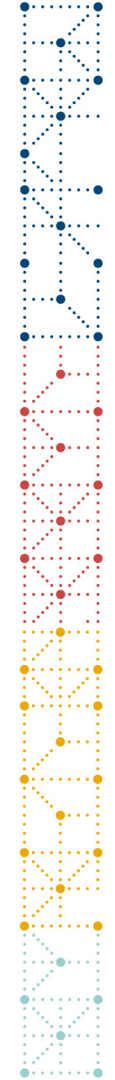
Variable Name	Variable Label	Type	Controlled Terms, Code list or Format	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		Identifier	Unique identifier for a study.	Req
DOMAIN	Domain Abbreviation	Char	VS	Identifier	Two-character abbreviation for the domain.	Req
USUBJID	Unique Subject Identifier	Char		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.	Req

Variable Name	Variable Label	Type	Code list/ Controlled Terms	Core	CDISC Notes
STUDYID	Study Identifier	Char		Req	DM.STUDYID
USUBJID	Unique Subject Identifier	Char		Req	DM.USUBJID
SUBJID	Subject Identifier for the Study	Char		Req	DM.SUBJID. SUBJID is required in ADSL, but permissible in other datasets.
SITEID	Study Site Identifier	Char		Req	DM.SITEID. SITEID is required in ADSL, but permissible in other datasets.
SITEGRY	Pooled Site Group y	Char		Perm	Character description of a grouping or pooling of clinical sites for analysis purposes. For example, SITEGR3 is the name of a variable containing site group (pooled site) names, where the grouping has been done according to the third site grouping algorithm, defined in variable metadata. SITEGR3 does not mean the third group of sites.
SITEGRYN	Pooled Site Group y (N)	Num		Perm	The numeric code for SITEGRY. One-to-one mapping to SITEGRY within a study.
REGIONY	Geographic Region y	Char		Perm	Character description of geographical region. For example, REGION1 might have values of 'Asia', 'Europe', 'North America', 'Rest of World'; REGION2 might have values of 'United States', 'Rest of World'.
REGIONYN	Geographic Region y (N)	Num		Perm	The numeric code for REGIONY. Orders REGIONY for analysis and reporting. One-to-one mapping to REGIONY within a study.

Why do we need to evolve?

- Data structures are known, but data meaning lacks full definition
- Standards are incomplete
 - protocol content, data collection instruments, analysis/endpoint definition
- Current clinical data standards are implemented inconsistently
 - Across studies and organizations
- Limited process automation in data processing
 - Study build, study conduct, and study reporting
 - Much manual programming needed in these processes
 - Some automation, but lack of fully-scaled automation
- Too much time needed for study specification
- High level of standards expertise needed





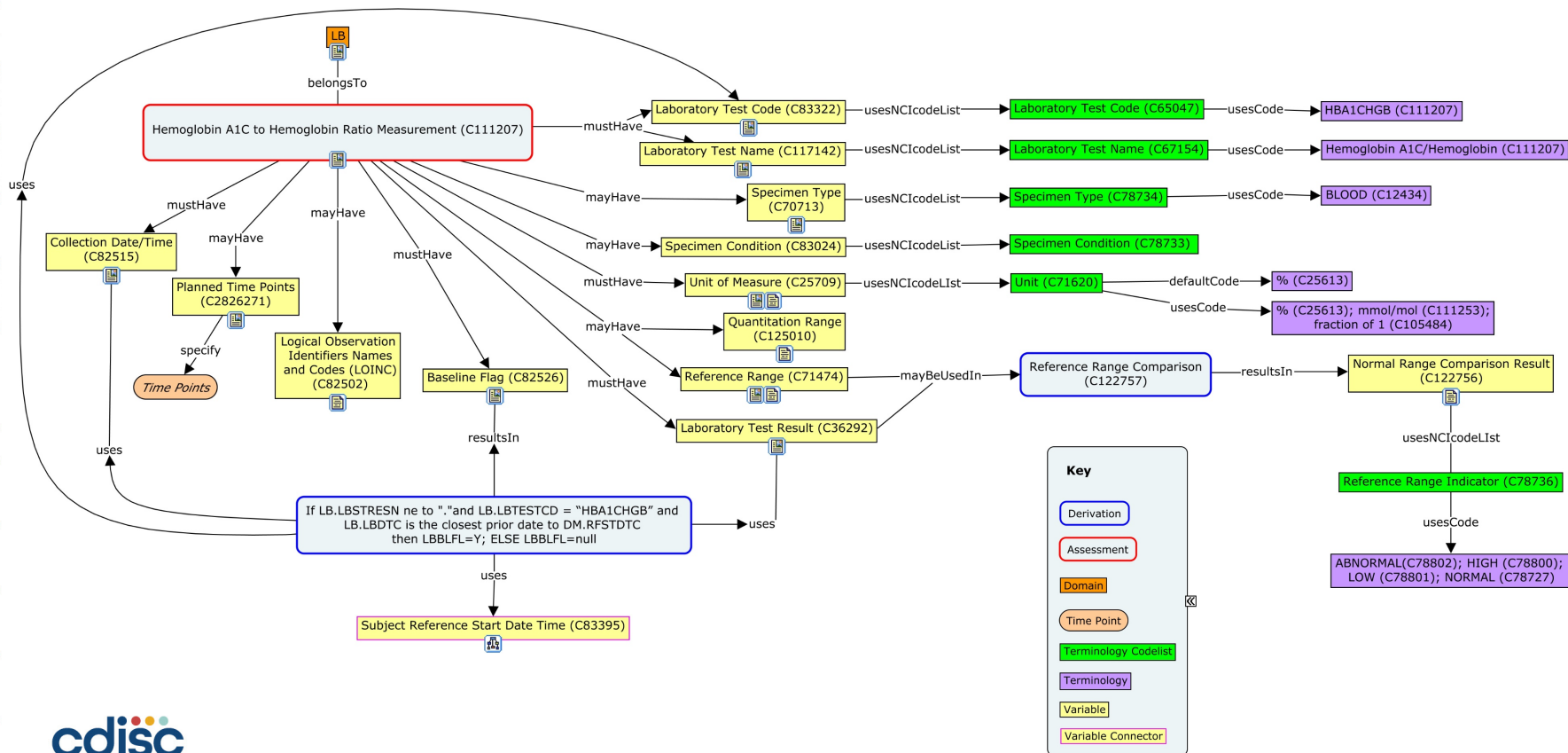
How do we evolve?

The CDISC 360 Project: Adding a conceptual layer to standards

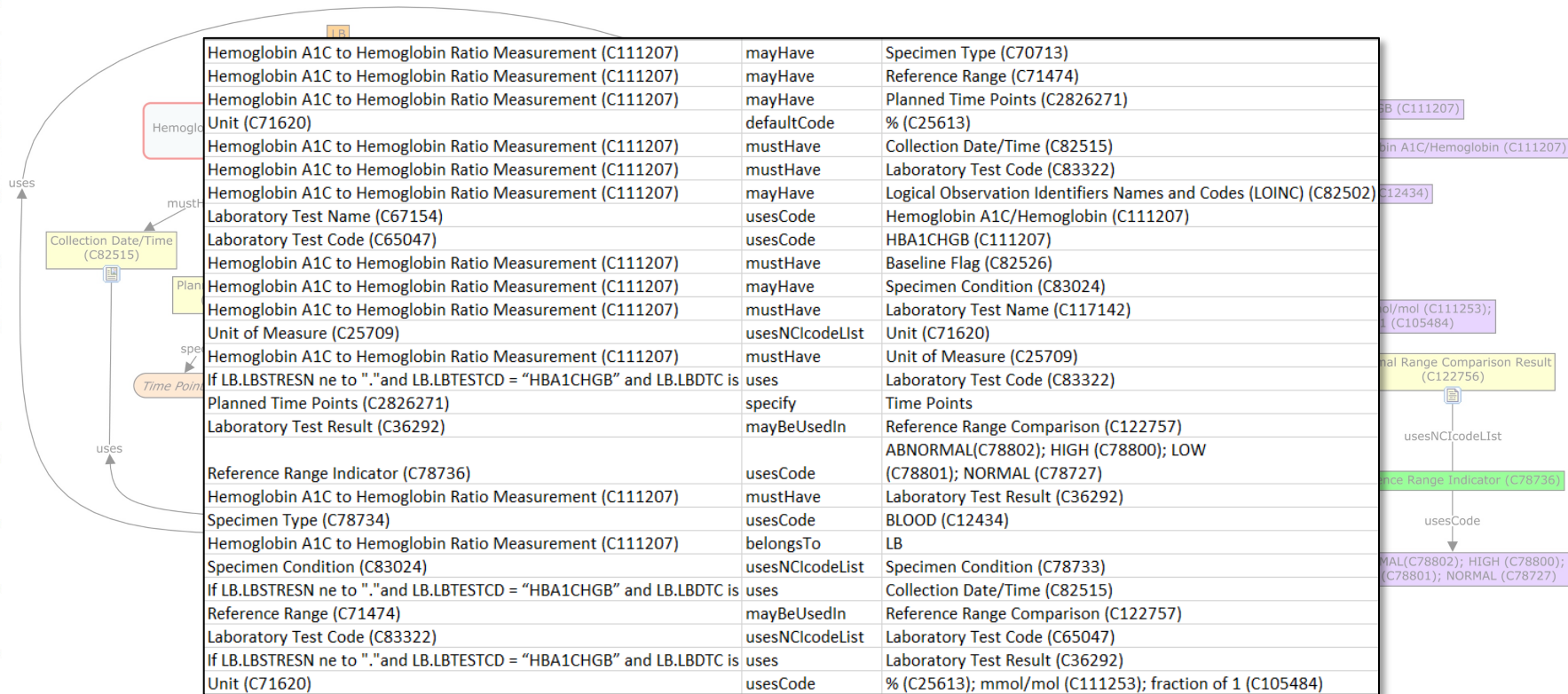
- Create and store standards as concepts which create meaning between data
- Electronically publish data standards as linked metadata
- Add computer executable process metadata which enables end to end automation
- CDISC 360 will develop concept-based standard definitions, and test and demonstrate end-to-end automation of study specification, data processing, and analysis

➔ *Test and demonstrate, but not building software*

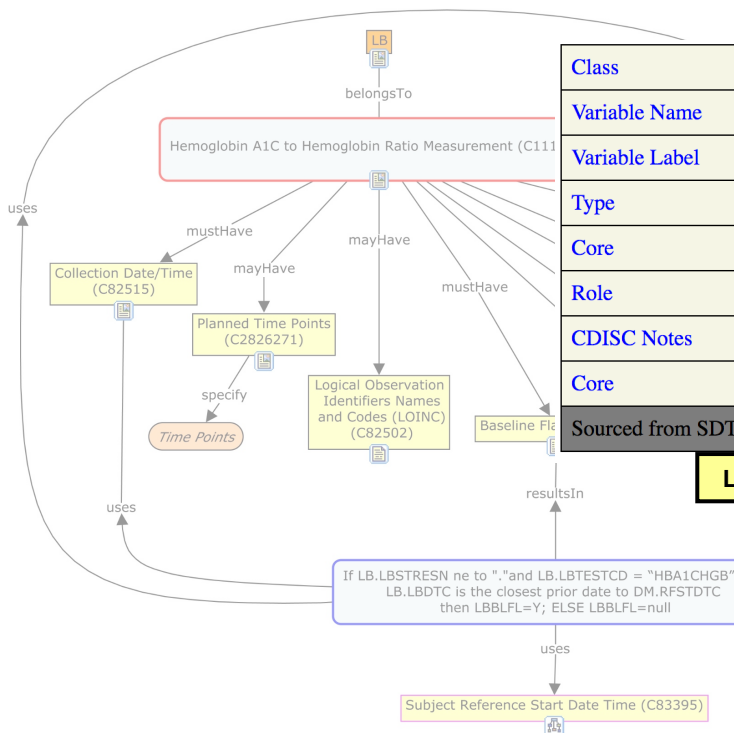
Biomedical Concept



Biomedical Concept



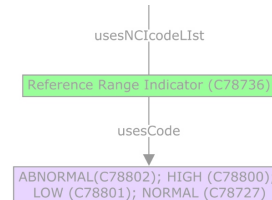
Attributes are linked to the element



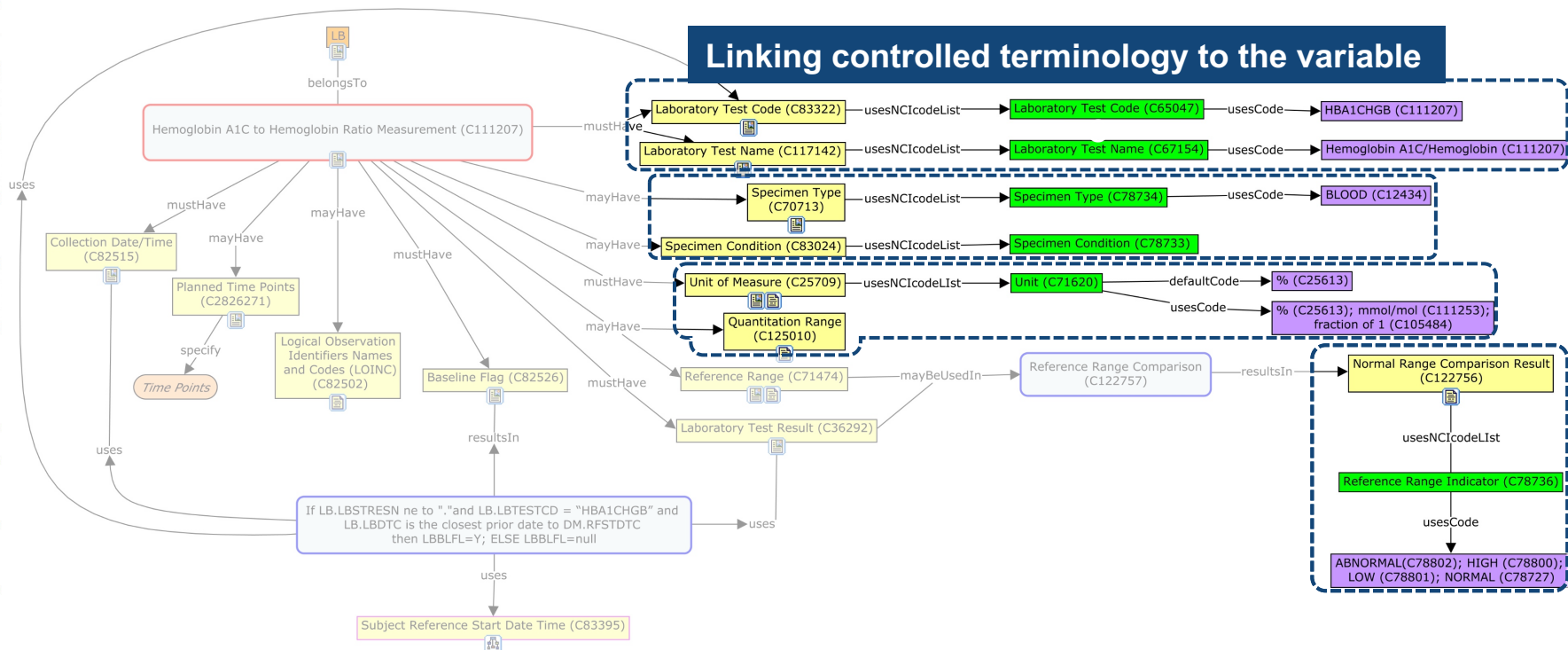
Class	Findings
Variable Name	LBORRES
Variable Label	Result or Finding in Original Units
Type	Char
Core	Exp
Role	Result Qualifier
CDISC Notes	Result of the measurement or finding as originally received or collected.
Core	Exp
Sourced from SDTM 1.4 SDTMIG 3.2	

Laboratory Test Result (C36292)

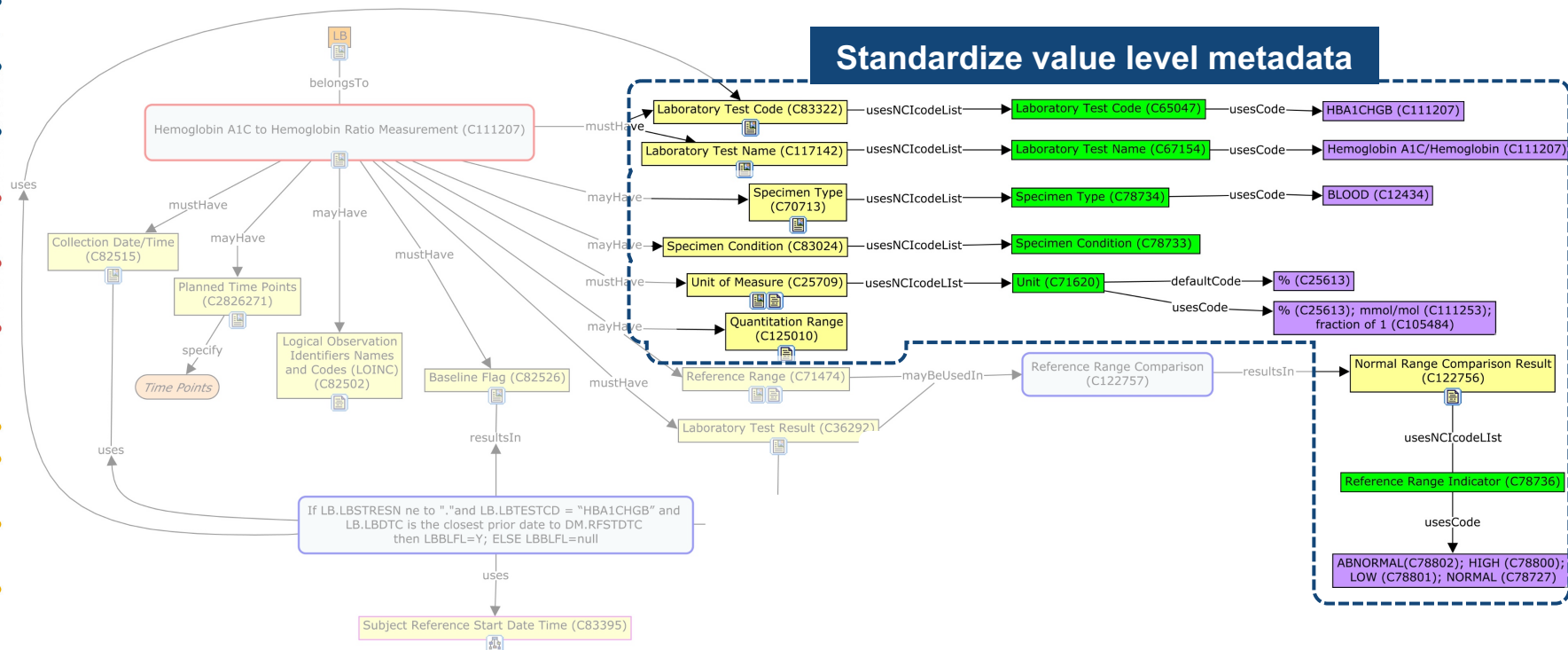
CDASH.LB-Local Processing.LBORRES
CDASH.LB-Local Processing.LBORRESU
SDTM.LB.LBORRES
SDTM.LB.LBST 
SDTM.LB.LBSTRESN
BRIDG.PerformedObservationResult.value



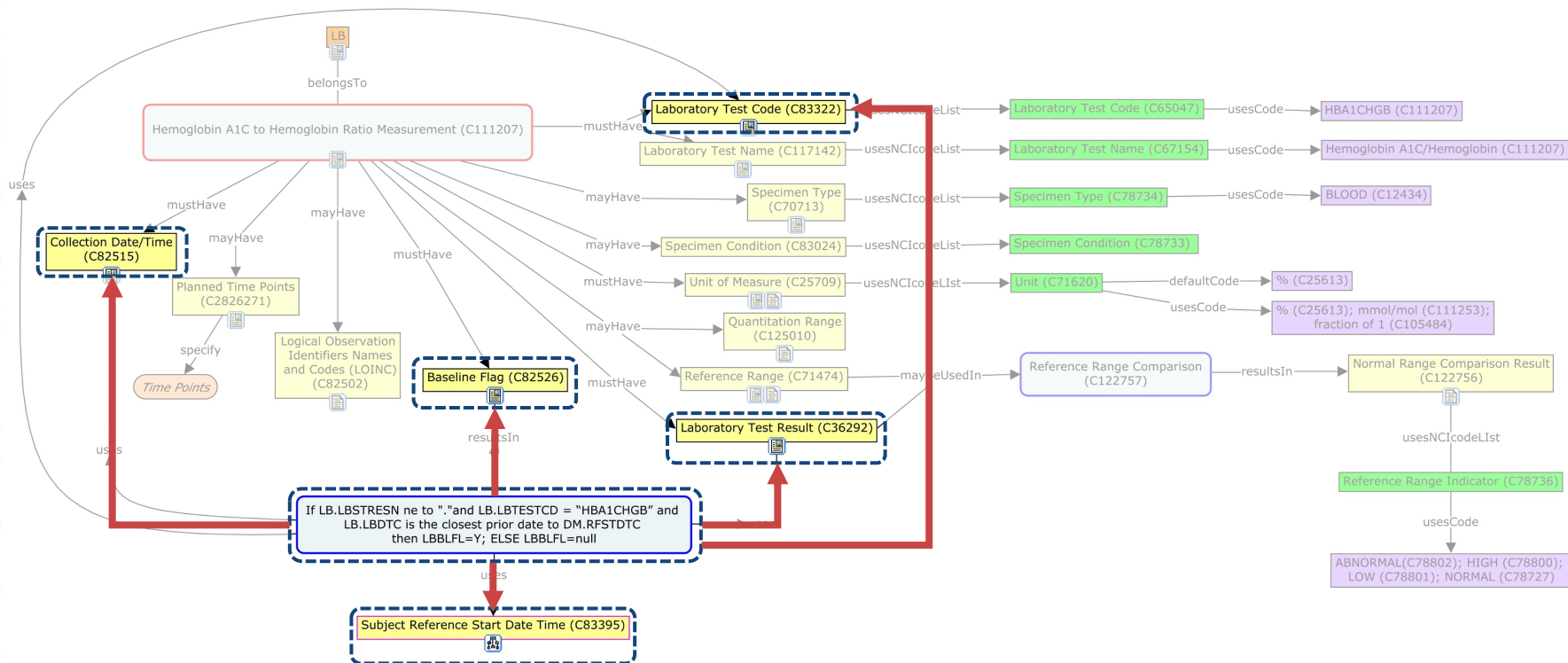
Biomedical Concept



Biomedical Concept

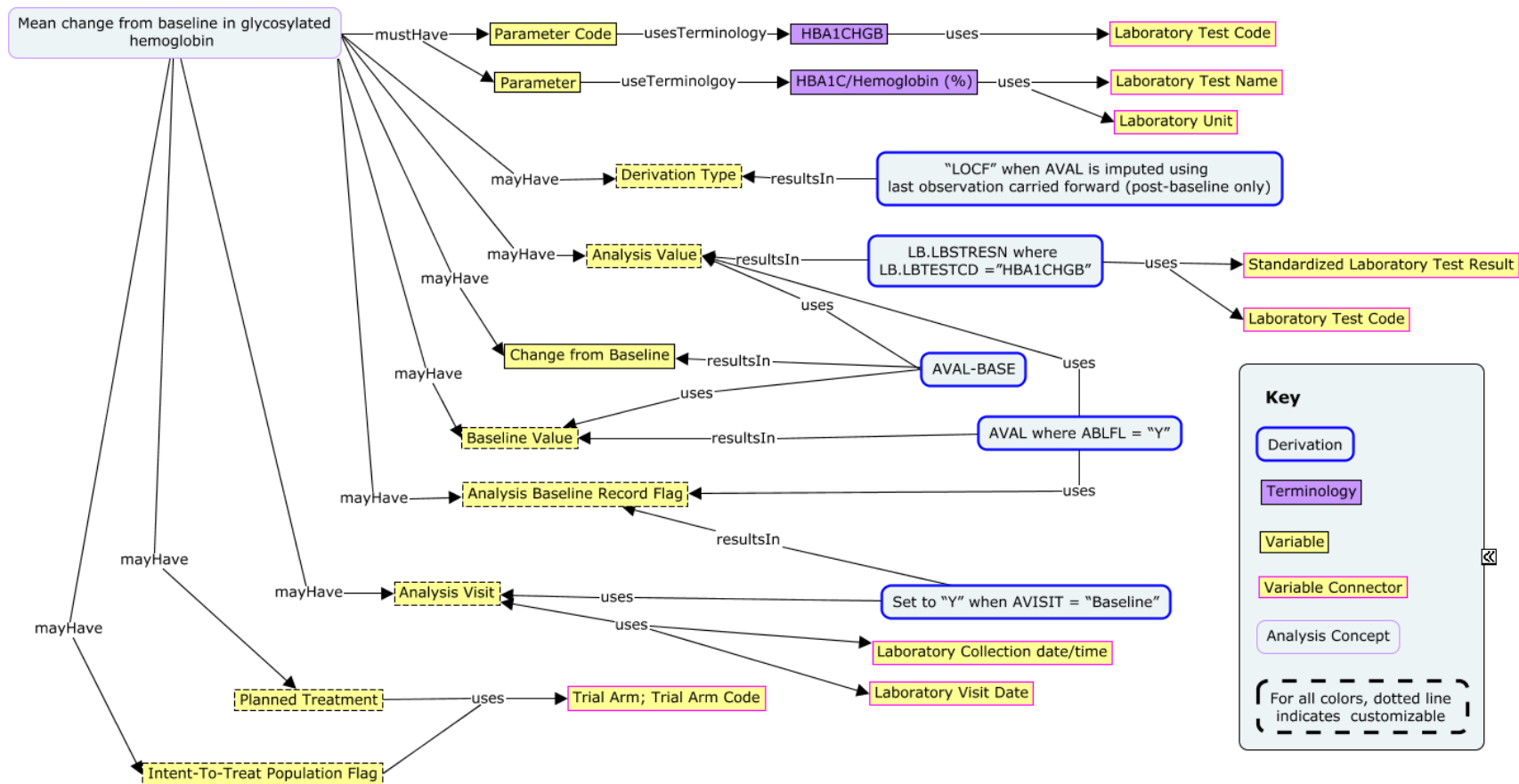


Biomedical Concept

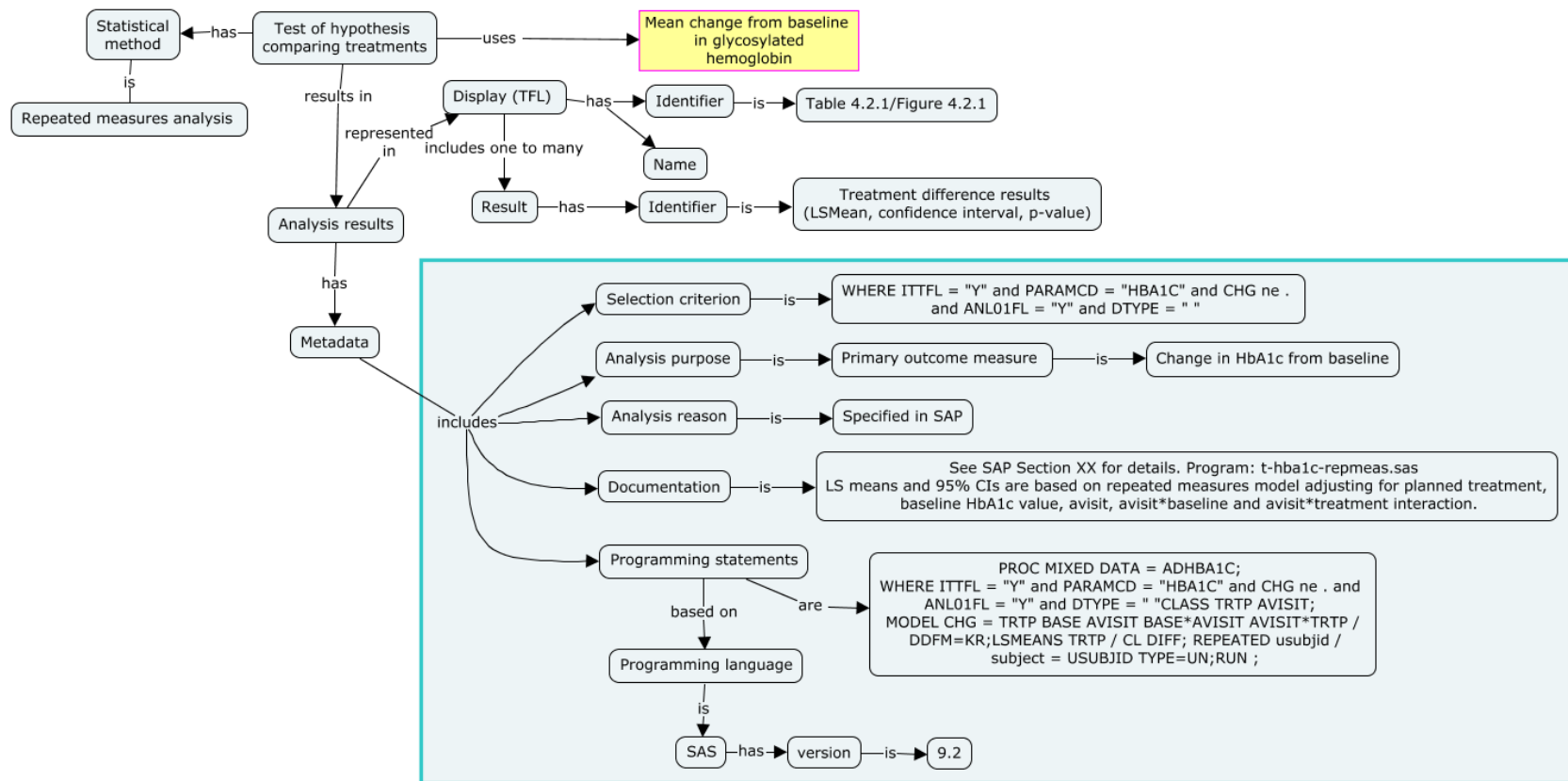


Machine Executable Algorithms

Analysis Concept

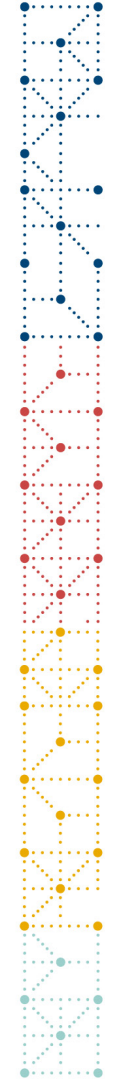


Analysis Result



Biomedical Concept Map





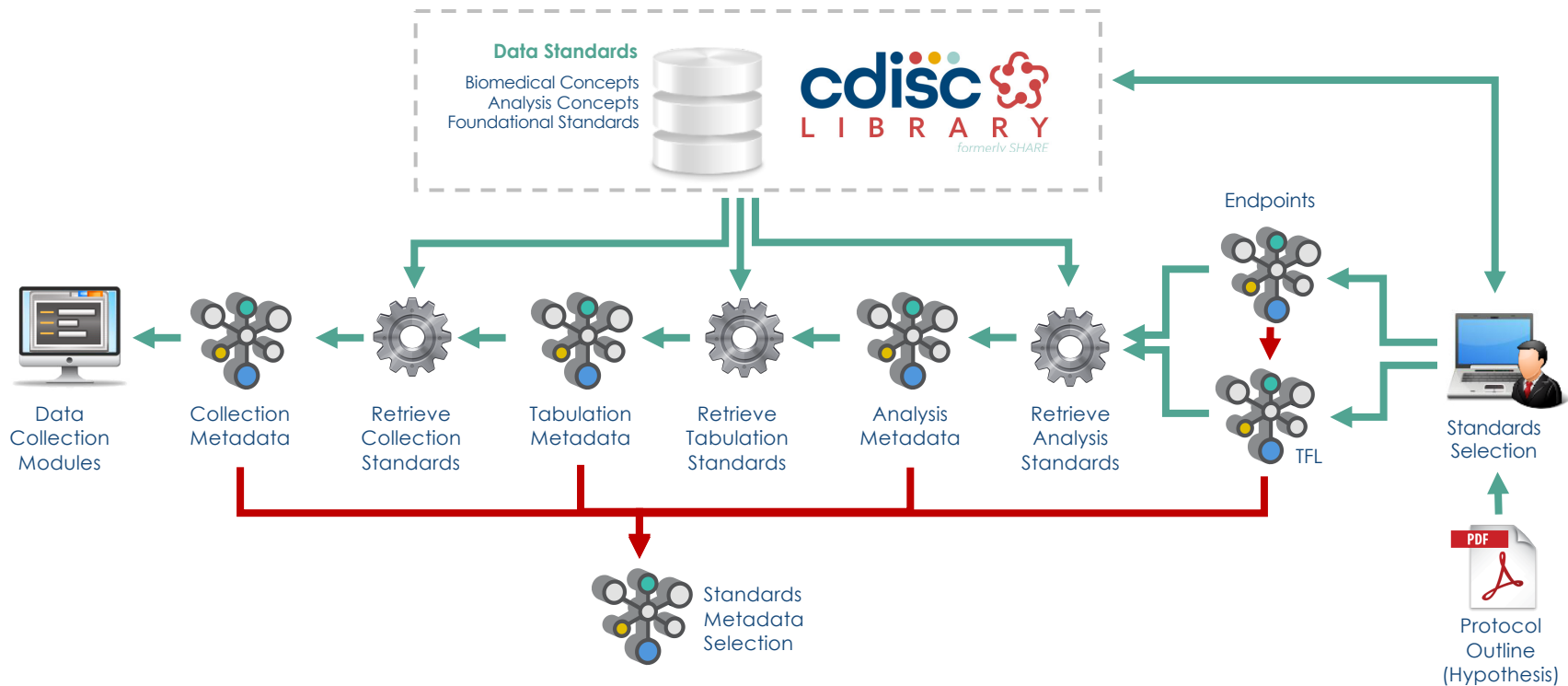
The Power of a Conceptual Model for Data Standards

- Linking controlled terminology to the variable – standardize value level metadata
- Machine readable definition of validation rules
- Linking derivations and algorithms to variable(s)
 - Include process metadata (ETL instructions)
- Possibility to standardize Analysis outputs and Collection instruments
 - Combining layout, variables, process information together
- Link Analysis Concepts to Biomedical Concepts
 - Choose an analysis and automatically obtain all related end-to-end metadata

→ **All of the above:** enables automation, increase confidence in results, true analysis traceability

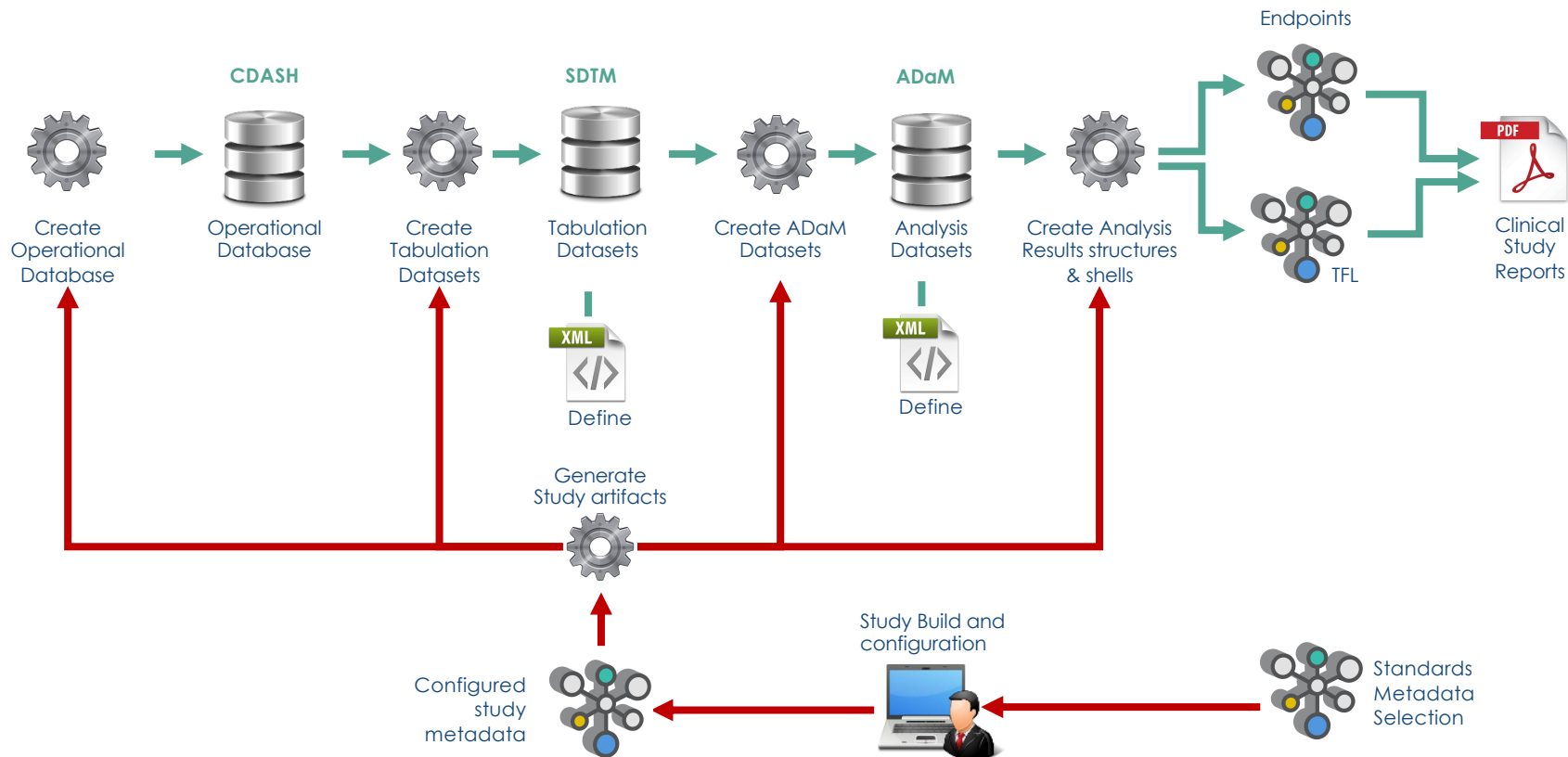
Use Case 1 : Define

Selecting standards concepts and linked metadata needed for a study



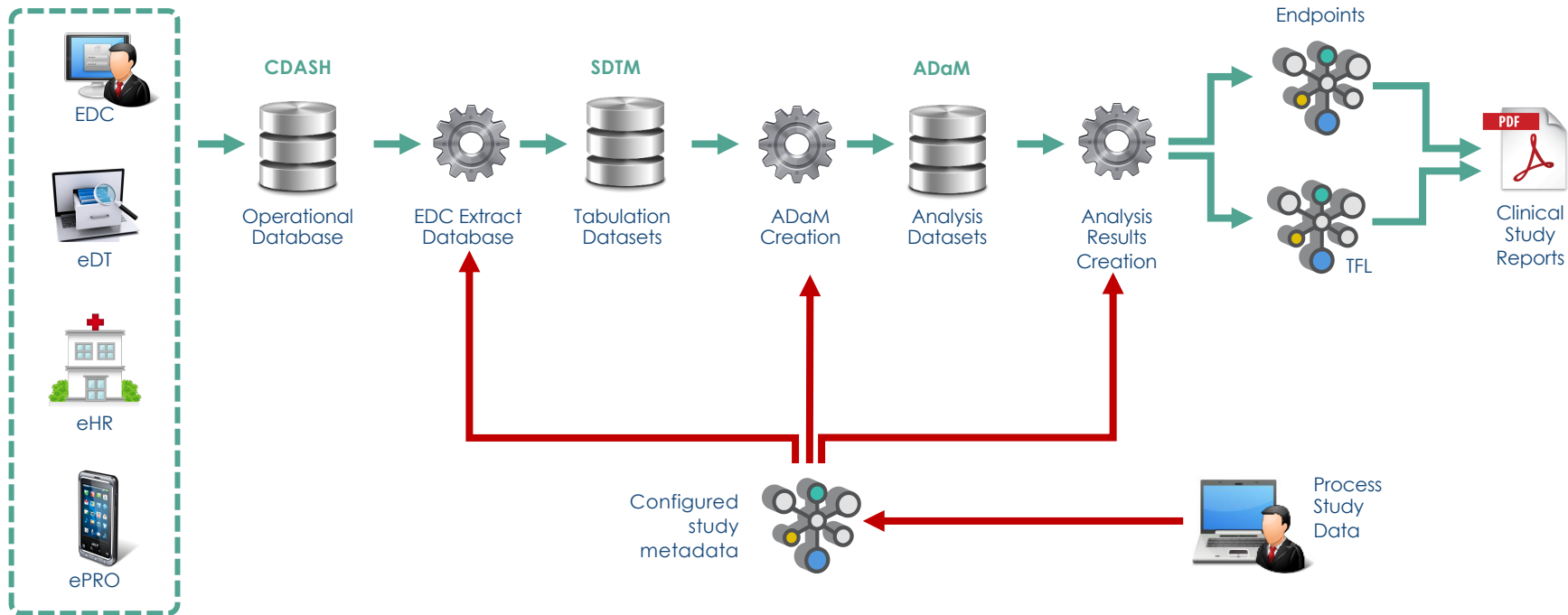
Use Case 2 : Build

Adding study design, concept configuration & generate artifacts



Use Case 3 : Execute

Automatic population of data into artifacts



Expected Outcome

- Learn
 - What works and what doesn't
- Assessment
 - Technology Gap Analysis
 - Standards Gap Analysis
- Building a base for the future
 - Inform and involve stakeholders
 - Effort calculation and Cost / Benefit Analysis
 - Scale up to deliver the standards metadata needed
 - Partnerships with vendors to ensure tools are made available





2. Project Approach

CDISC 360 Advisory Committee

CDISC 360 Leadership Team

- **David Bobbitt**
CDISC Chief Executive Officer
- **Peter Van Reusel**
CDISC Chief Standards Officer
- **Sam Hume**
CDISC Vice President Data Sciences
- **Barry Cohen**
CDISC 360 Project Manager

CDISC 360 Board Representation

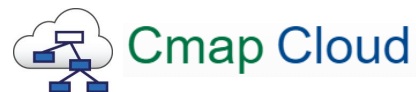
- **Chris Decker** - dWise
- **Dave Evans** - Accenture
- **Dave Hardison** - Deloitte
- **Pandu Kulkarni** - Lilly
- **Steve Rosenberg** - Oracle
- **Ulo Palm** - * Transcelerate

CDISC 360 Committee Members

- **Praveen Garg** - Astra Zeneca
- **Patrick Genyn** - Johnson & Johnson
- **Brooke Hinkson** - Merck
- **Ulo Palm** - Allergan
- **Mike Hamidi** - CDISC

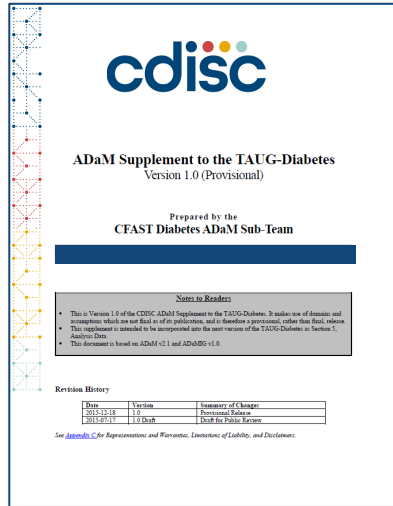
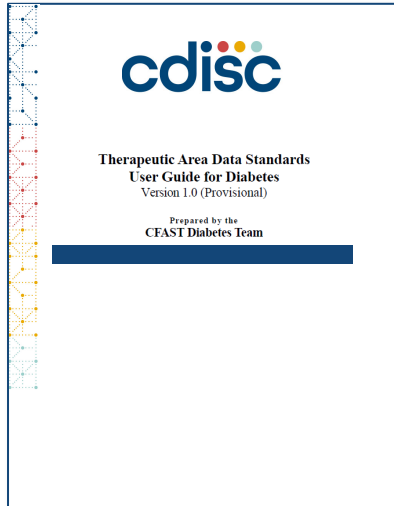
Collaboration Tools

- **CDISC 360 Wiki**
 - Collaborative content
- **Jira**
 - Issues management
- **CMap Cloud**
 - Concept map development
- **Slack**
 - Instant messaging
- **Cloud Collaboration Platform**
 - Use case demo environment



Project Standards Scope

Diabetes TAUG



- 1 or 2 statistical endpoints
- 3 to 4 ADaM datasets
- 7 to 8 SDTM datasets
- 15 Data Collection Modules

→ **Reason for this scope:** the Diabetes TAUG provides standardized artifacts from analysis outputs to data collection. This allows the project team to focus on innovation and not on establishing a new data standard.

Project Standards Scope

FDA Use Case



- 2 safety endpoints:
 - MACE: Major Adverse Cardiac Event
 - AKI: Acute Kidney Injury
- Turn specifications into standard concepts
- Verify analysis outputs and endpoint data vs. specifications
- Explore traceability: analysis outputs to specifications

→ **Reason for this scope:** Document FDA standard safety analysis requirements that may be expressed in the analysis concept maps; ensure the enhanced standards meet reviewers' needs

CDISC 360 Workstreams



*Enhance
Standards*



*Publish
Standards*

Study
Library



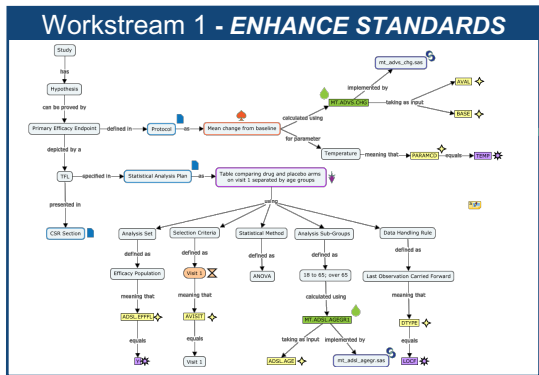
Define

Build

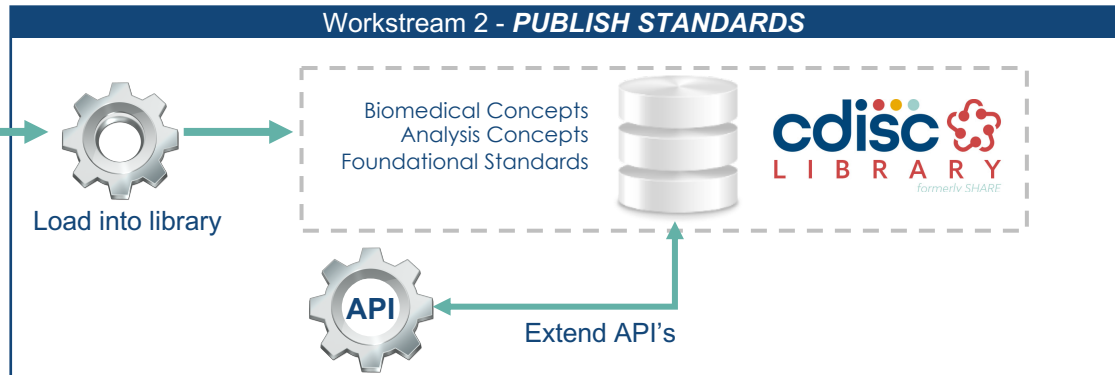
Execute



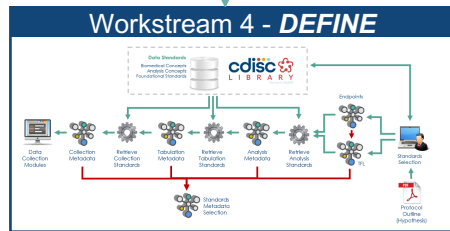
CDISC 360 Workstreams



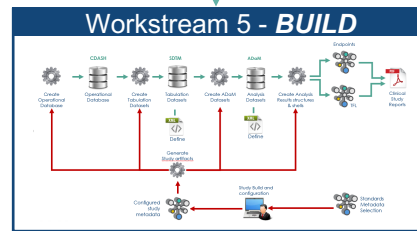
Create concepts in knowledge graphs



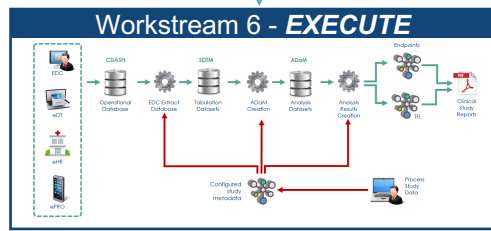
Transform concepts in machine readable form



Identify and select standards specification (Use Case 1)



Configure study specification and create artifacts (Use Case 2)



Automatically process and transform data (Use Case 3)



3. Project Status

Project Timeline

#	Stage	Start	End
1	Initiation, scoping, and internal staffing	Oct 2018	Nov 2019
2	Planning, recruiting CDISC member participants	Dec 2019	Feb 2019
3	Align with Transcelerate Digital Data Flow Initiative	Oct 2018	Jan 2019
3	Onboarding CDISC member participants	Mar 2019	Apr 2019
5	Kickoff, workstreams briefing	Apr 2019	Apr 2019
6	Execution of agile sprints	Apr 2019	Oct 2019
7	Project evaluation – Stage 1 (CDISC US Interchange)	Oct 2019	Oct 2019
8	Execution of agile sprints	Nov 2019	Mar 2020
9	Project evaluation – Stage 2 (CDISC EU Interchange)	Mar 2020	Mar 2020
10	Execution of agile sprints	Apr 2020	Nov 2020
11	Project evaluation – Stage 3 (CDISC US Interchange)	Nov 2020	Nov 2020

← We are here

Participation Summary

29 Organizations

67 Resources specified

Organization Types:

- Pharma-Biotech Sponsor: 18
- CRO: 4
- Technology Provider: 6
- Regulatory: 1



abbvie



AMGEN®



B:OMARIN®

C+R
RESEARCH



GILEAD

Johnson & Johnson

Lilly



MERCK



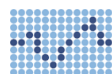
Microsoft

novo nordisk



ORACLE®

Otsuka



PharmaStat®

PINNACLE²¹



SANOFI



S-CUBED



VITA DATA SCIENCES
a division of SOFTWARE WORLD



xclinical

cdisc

Workstream Teams

WS 1

Lead: Bess LeRoy

Manuel Anido
Joyce George
Swarupa Sudini
Jon Neville
Sally Cassells
Mikkel Traun
Chithra Subramaniam
Pei-Ling Chu
Sterling Hardy
Abnilash Chimbirithy
Venkata Maguluri
Yogesh Gupta
Carol Baker
Lauren Shinaberry

WS 2

Lead: Sam Hume

Francis Dsa
Stephen Pearce
Edward Altman
Haiping Yu
Jeanne Wagner
Erika Liu
Dave Iberson-Hurst
Nicolas de Saint Jorre
Roger Gagali Angoh

WS 4

Lead: Mikkel Traun

Trevor Mankus
Stephen Pearce
Rajesh Modi
Bharat Palakurthi
Lex Jansen
Sujit Khune
Roger Gagali Angoh

WS 5

Lead: Tianna Umann

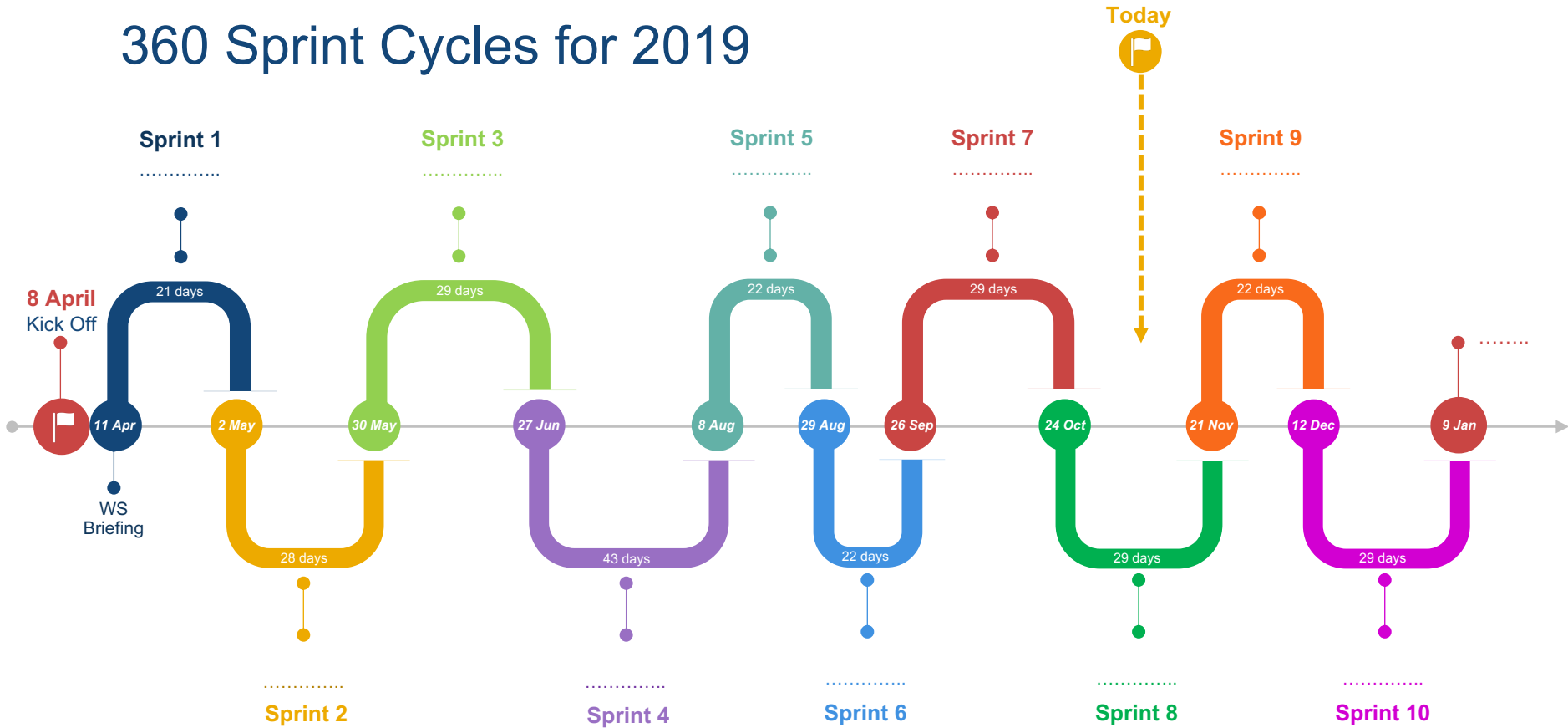
Asavari Mehta
Ram Govindaraju
Devi Gohimukkula
Francis Dsa
Tobias Krøgholt
Smitha Karra
David Parkinson
Lauren Shinaberry
Jeanne Wagner

WS 6

Lead: Bhavin Busa

Binoy Varghese
Rick Rozinskas
Gina Selby
Naveen Kommuru
Jimmy Zhao
Anoop Ambika
Spandana Chelmillla
Lex Jansen
Prasanna Murugesan
Vinay S
Siva Tedla

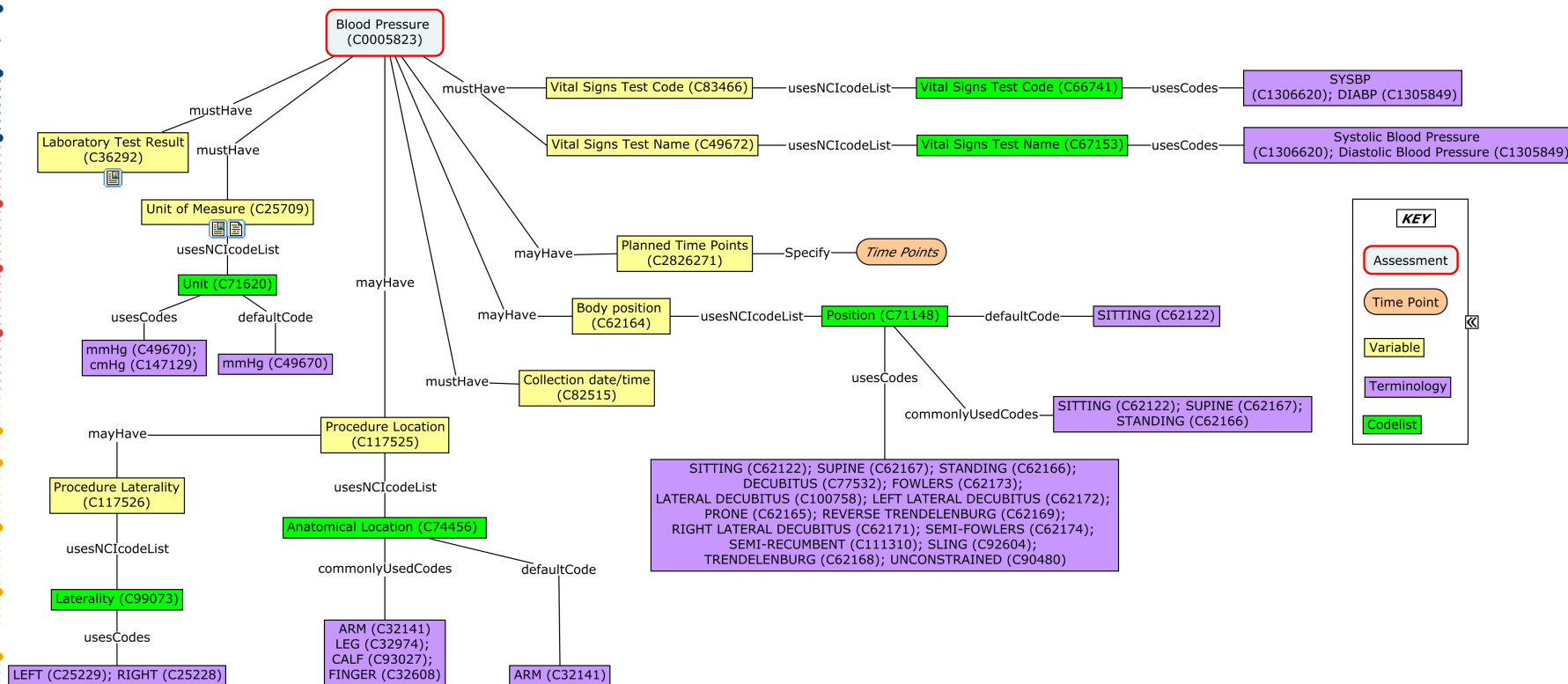
360 Sprint Cycles for 2019





4. Achievements so far

First Stable Concept Maps



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)",
```

User Experience to demonstrate use cases

Powered by  Microsoft

Search



1 Disease Category
✓ Endocrine

2 Disease Area
✓ Diabetes - Type 2

3 Study Focus
✓ Safety

4 Domains
✓ Vital Signs

5 Concepts

6 Data Collection

7 Confirmation

Please select vital signs concepts

Height ✓ The vertical measurement or distance from the base to the top of an object, the vertical dimension of extension.	Weight ✓ The vertical force exerted by a mass as a result of gravity.	Heart rate ✓ The number of heartbeats per unit of time, usually expressed as beats per minute.
Temperature ✓ The property of a body or region of space that determines whether or not there will be a net flow of heat into it or out of it from a neighboring body or region and...	Blood Pressure ✓ The pressure of the circulating blood against the walls of the blood vessels.	Respiratory Rate The rate of breathing (inhalation and exhalation) measured within in a unit time, usually expressed as breaths per minute.
Oxygen Saturation A measurement of the oxygen-hemoglobin saturation of a volume of blood.	Hip Circumference The distance around an individual's pelvic area or hips.	Body Fat Measurement A measurement of the total fat mass within the subject's body.
Body Frame Size The categorization of a person's body frame into small, medium and large based on the measurement of wrist circumference or the breadth of the elbow.		

Back

Continue

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 I",
  "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"
    },
    "parentProduct": {
      "href": "/mdr/bc/1-0/VS",
      "title": "Vital Signs Biomedical Concepts",
      "type": "VS Biomedical Concept"
    },
    "rootItem": {
      "href": "/mdr/root/bc/domains/VS/concepts/Height",
      "title": "Version-agnostic anchor resource for Biomedical Concept Height",
      "type": "Root Data Element"
    }
  }
}
```

Generate a Vital Signs CRF based on ODM

Common fields
appear once

Test fields repeat

 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	

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"	



Thank You!

Peter Van Reusel





KEEP
CALM
AND
VOLUNTEER
NOW!