

CDISC 360

The Journey so Far and the Road Ahead

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28 April 2020





Agenda

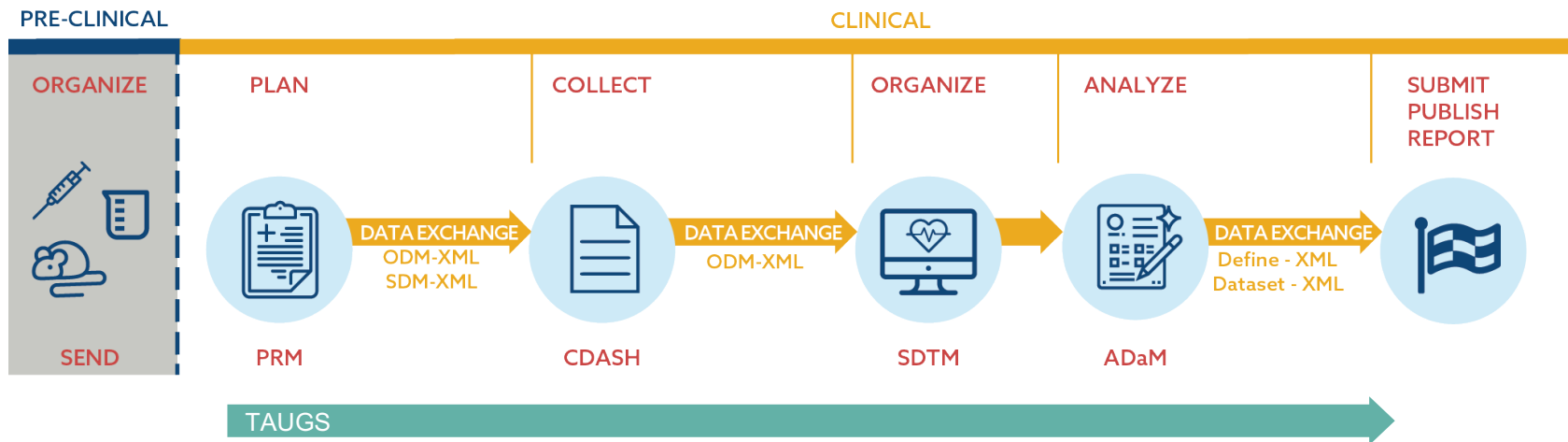
1. What is CDISC 360?
2. The Art of the Possible
3. Project Approach
4. The Journey So Far
5. What Follows 360?



What is CDISC 360?

Today we are here

CDISC Standards in the Clinical Research Process



BRIDG, CONTROLLED TERMINOLOGY AND GLOSSARY



Benefits Today

- CDISC Foundational models provide much needed structure

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

- Standards must now evolve to address further challenges to take standards benefits to next level

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, SDTIG 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 VTEST. 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.

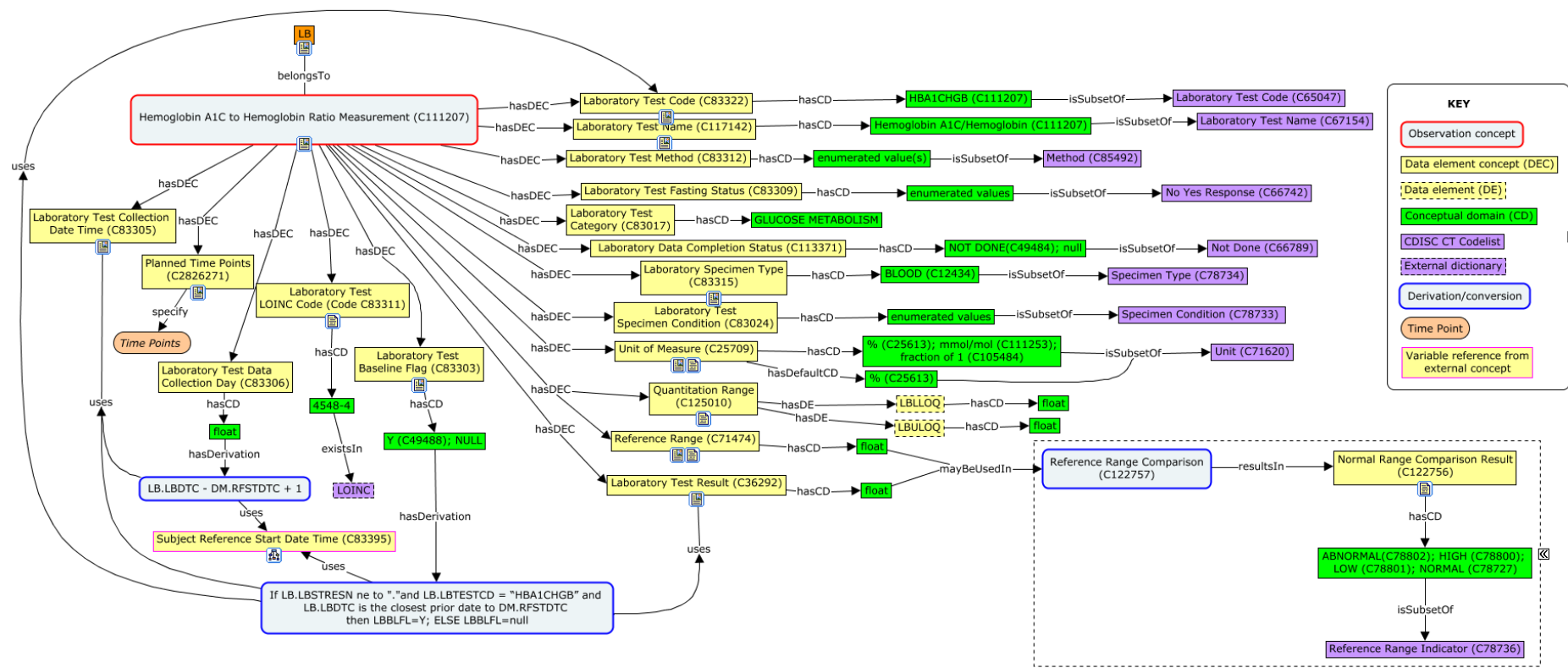
How do we evolve?

The CDISC 360 Project: Adding a conceptual layer to standards

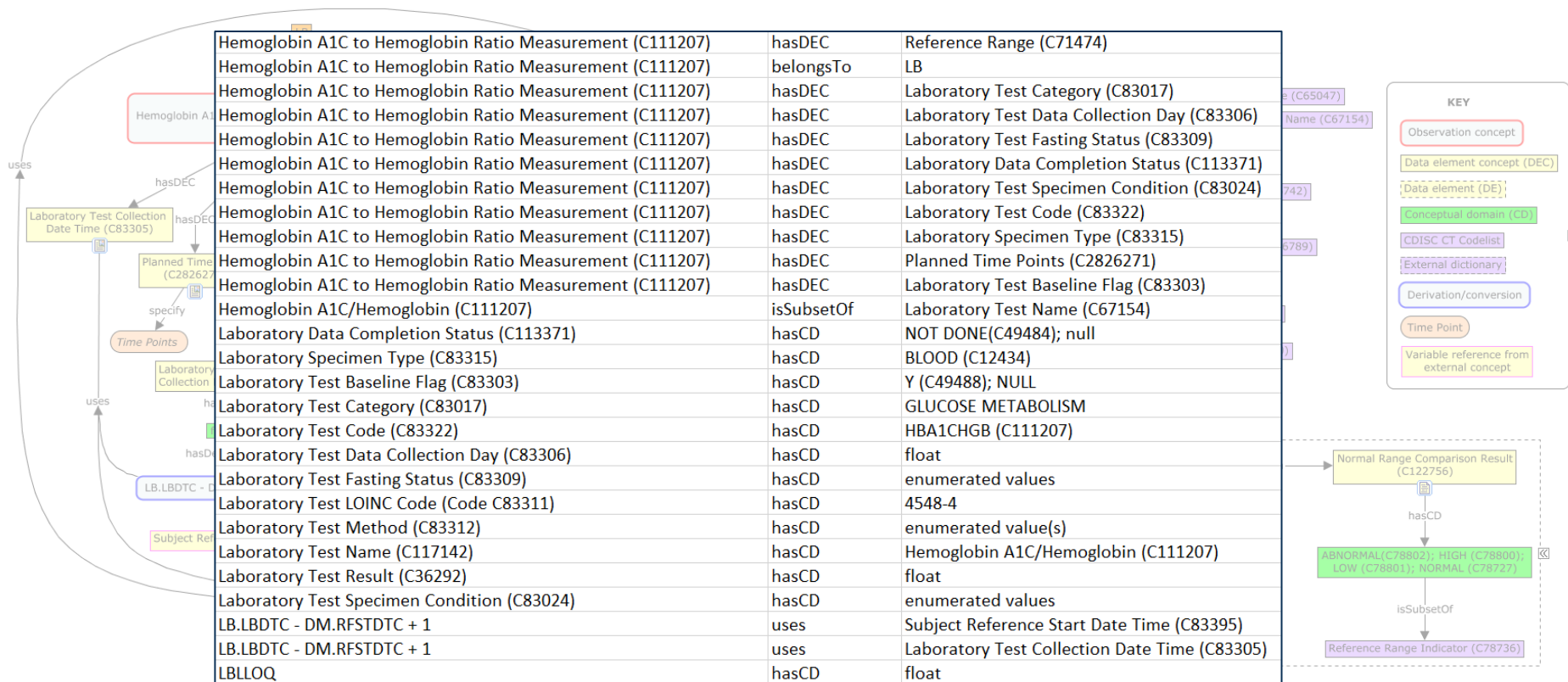
- Create and store standards as concepts which create meaning between data
- Electronically publish data standards as linked metadata
- Add computer executable process metadata which enables end to end automation
- CDISC 360 will develop concept-based standard definitions, and test and demonstrate end-to-end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

➔ *Test and demonstrate, but not building software*

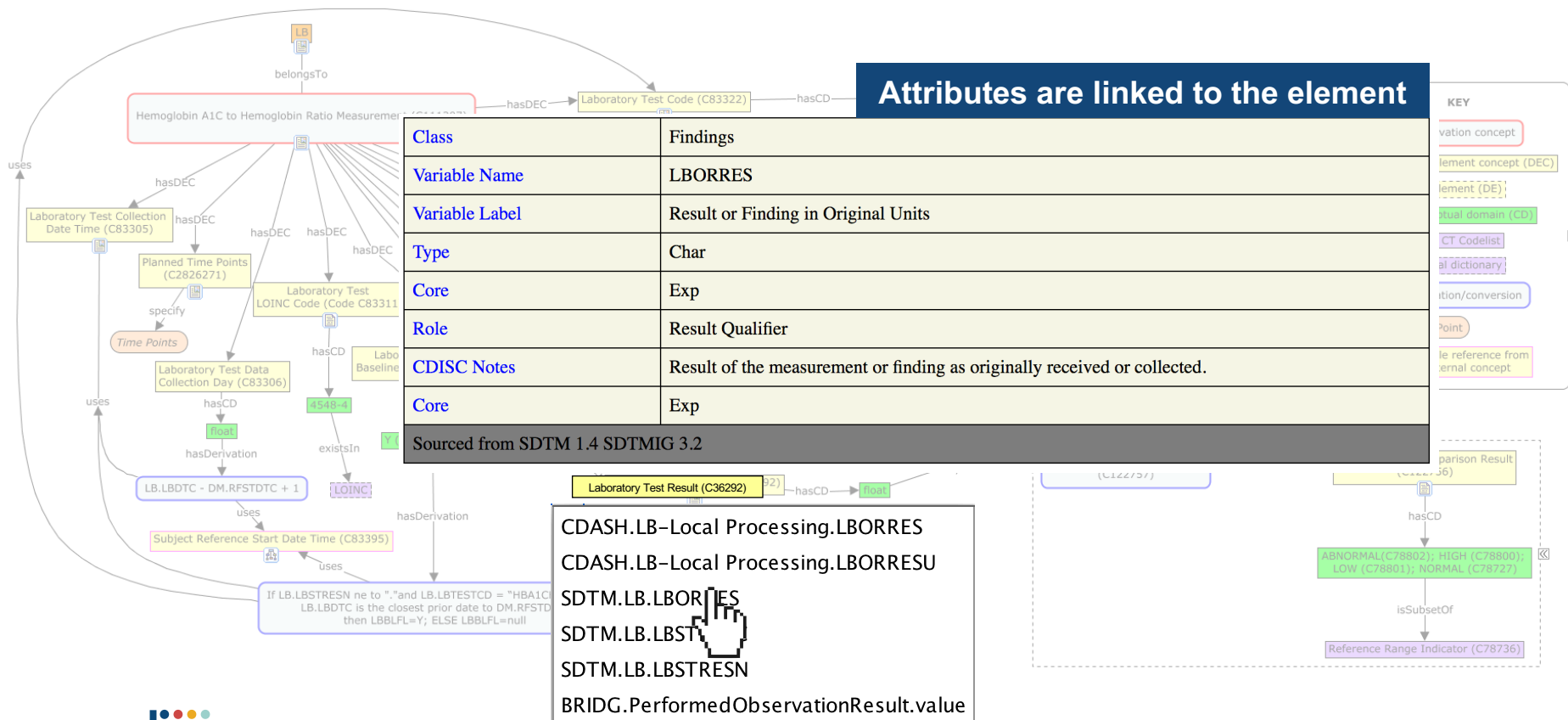
Biomedical Concept



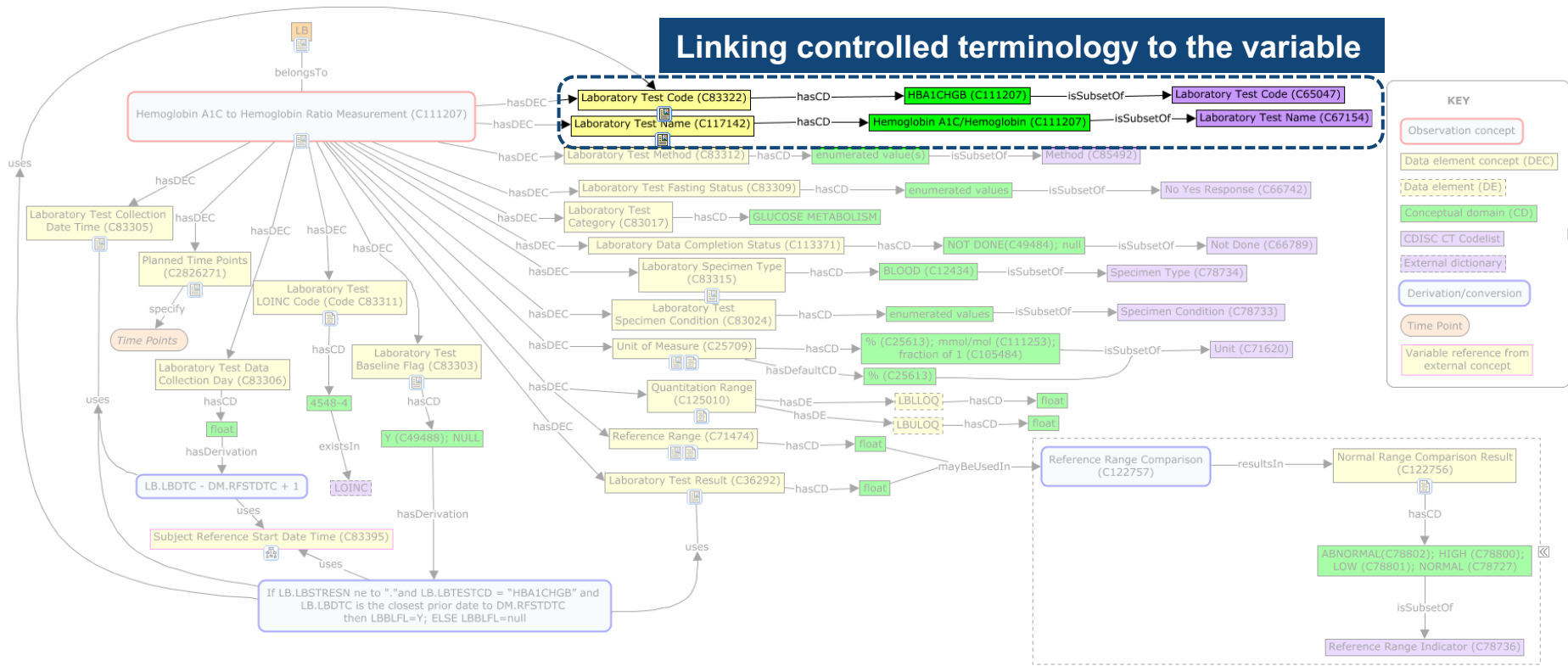
Biomedical Concept



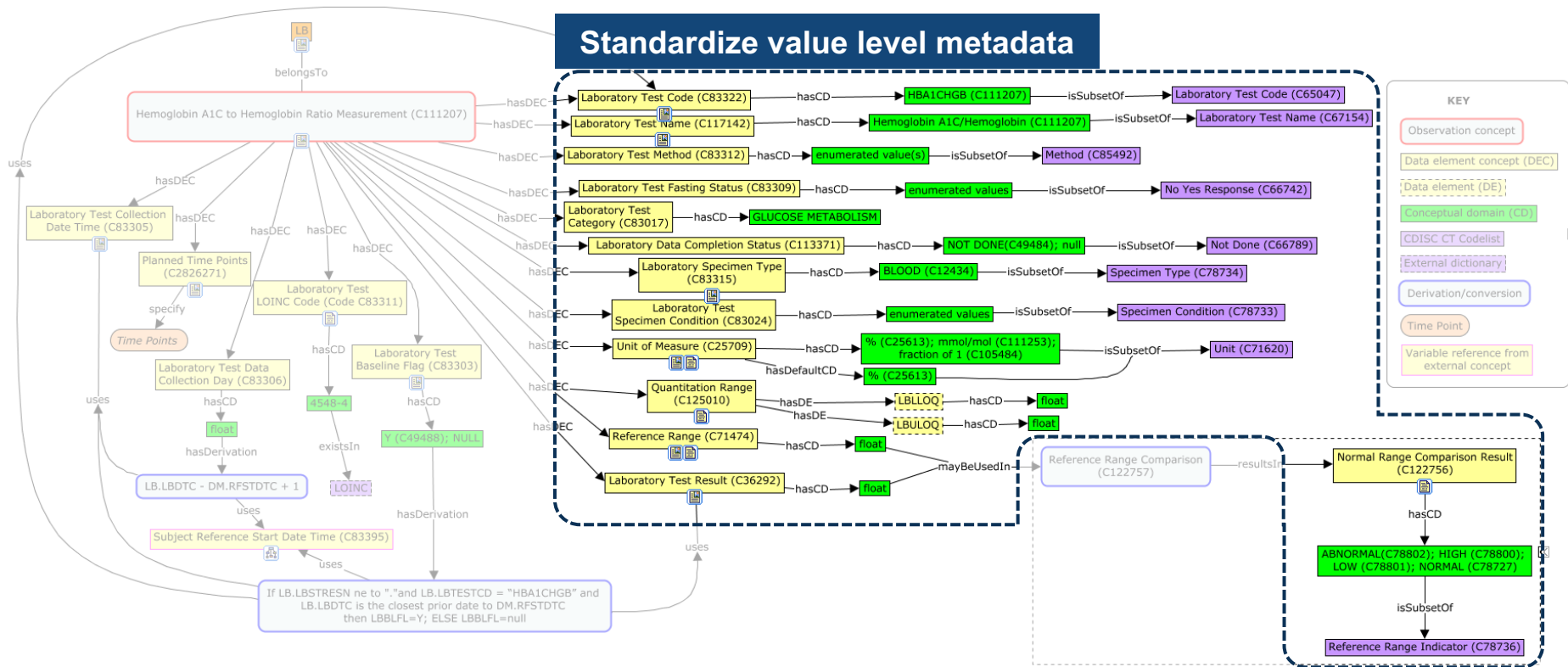
Biomedical Concept



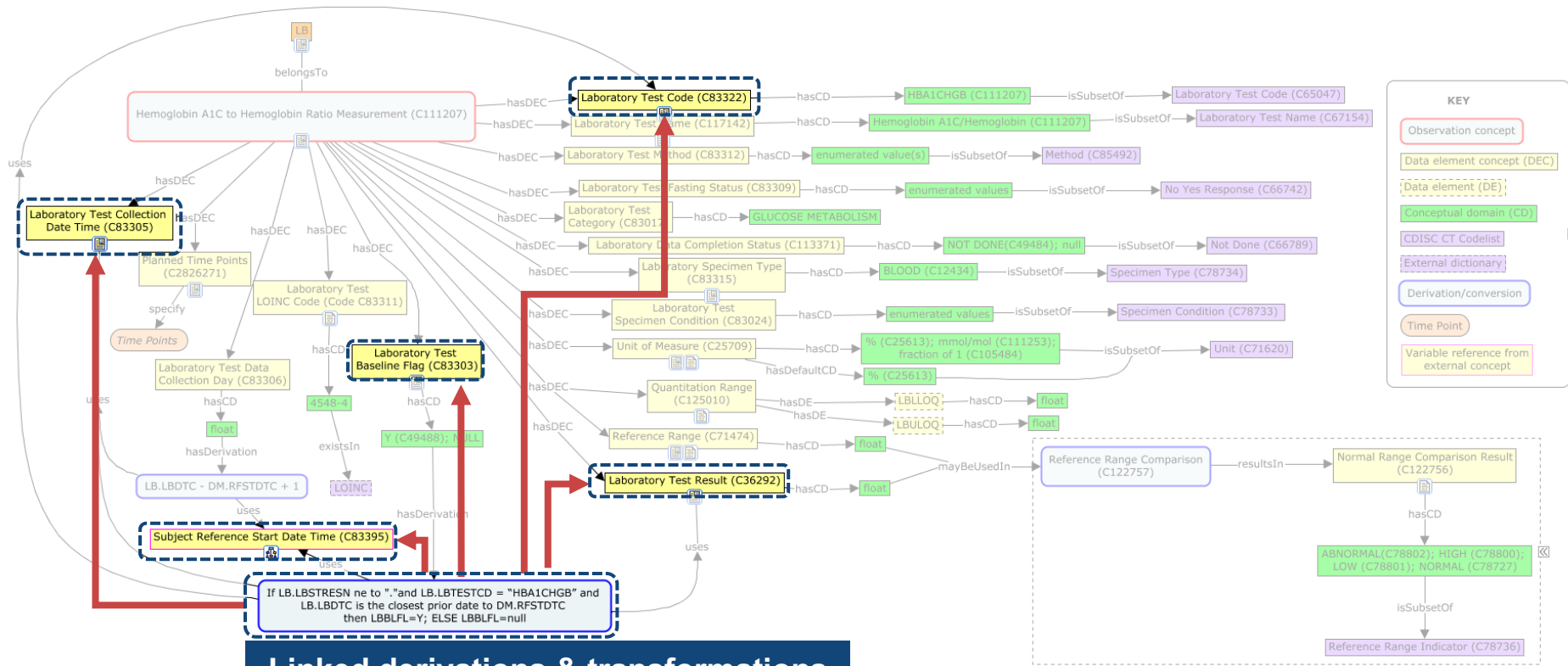
Biomedical Concept



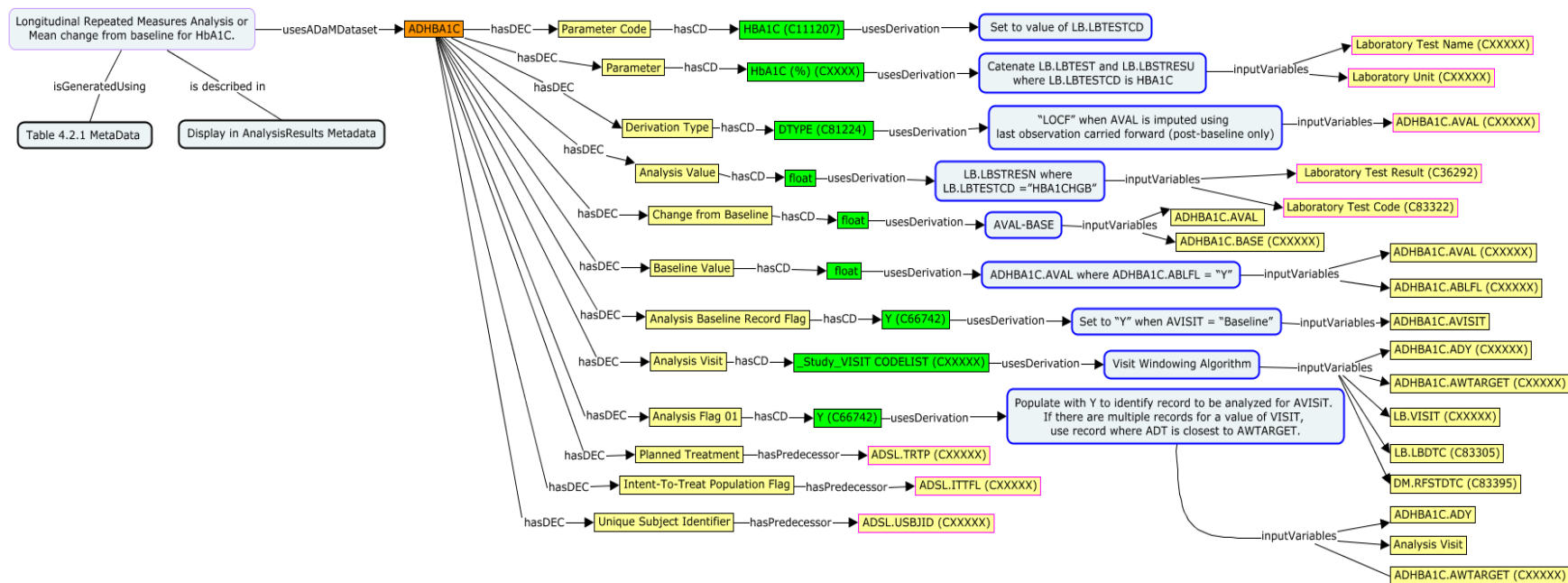
Biomedical Concept



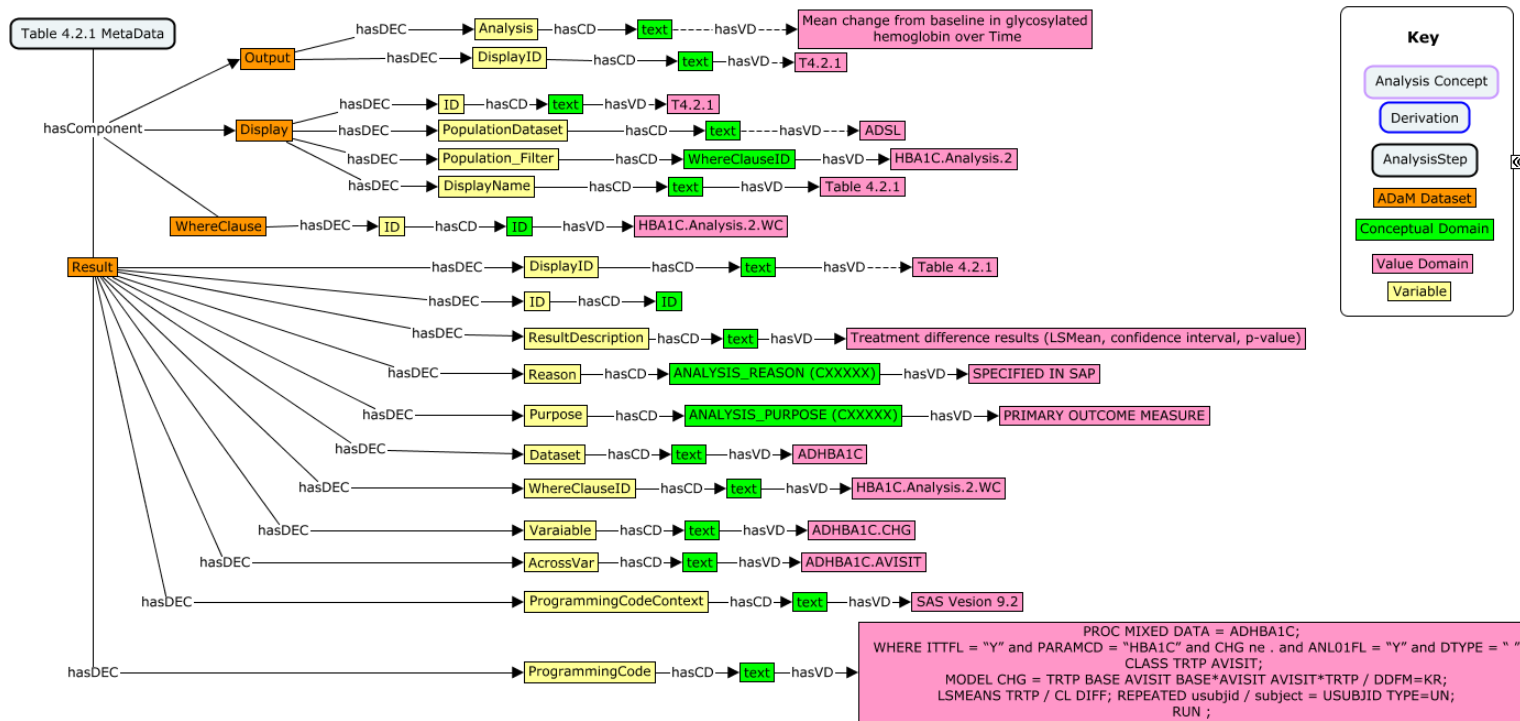
Biomedical Concept



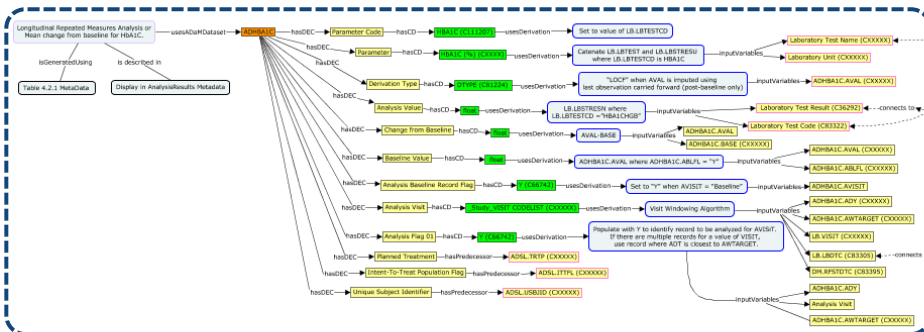
Analysis Concept



Analysis Result Concept



Analysis Concept Map



→ The Biomedical Concept and Analysis Concept are **ONE MODEL**



The Art of the Possible

CDISC 360 – Art of the Possible

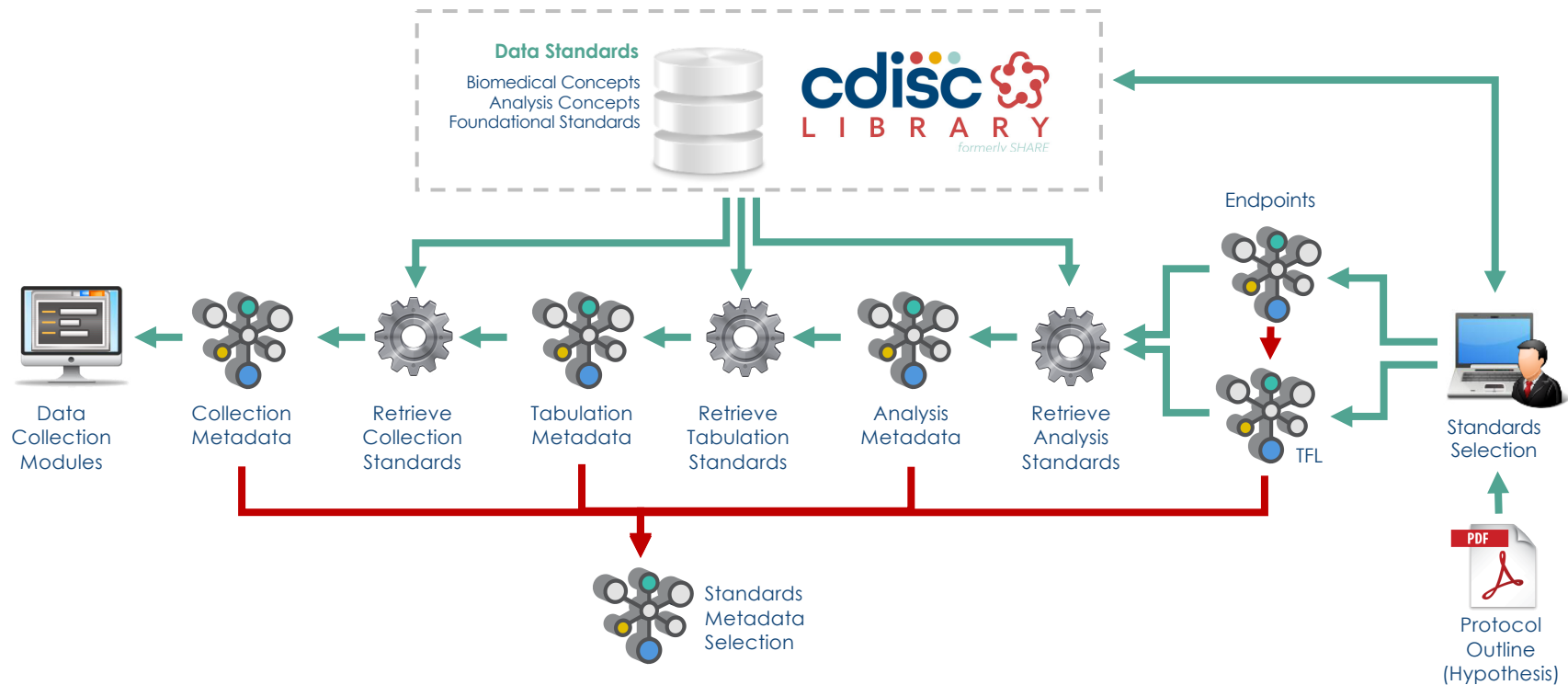
- What will follow is a User Experience presentation
- Purpose:
 - Illustrate how the CDISC 360 concept model will enable automation
 - For illustration only: CDISC 360 will not deliver software to the industry
- UX presentation link:
 - <https://xd.adobe.com/view/93e3e8f6-5b33-405f-4e76-e17af5f29990-e5d2/>



Project Approach

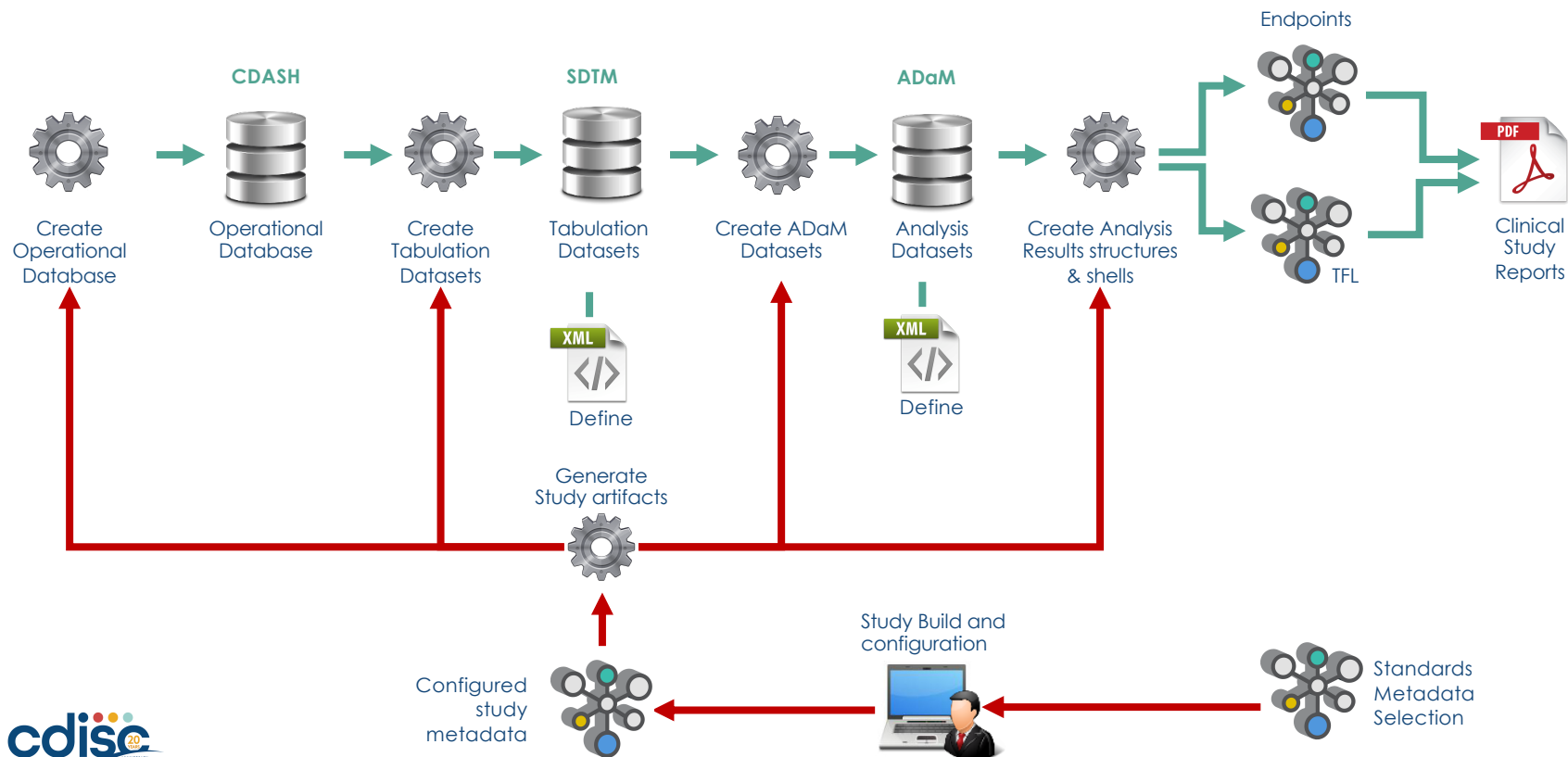
Use Case 1 : Define

Selecting standards concepts and linked metadata needed for a study

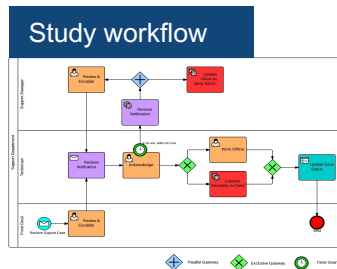
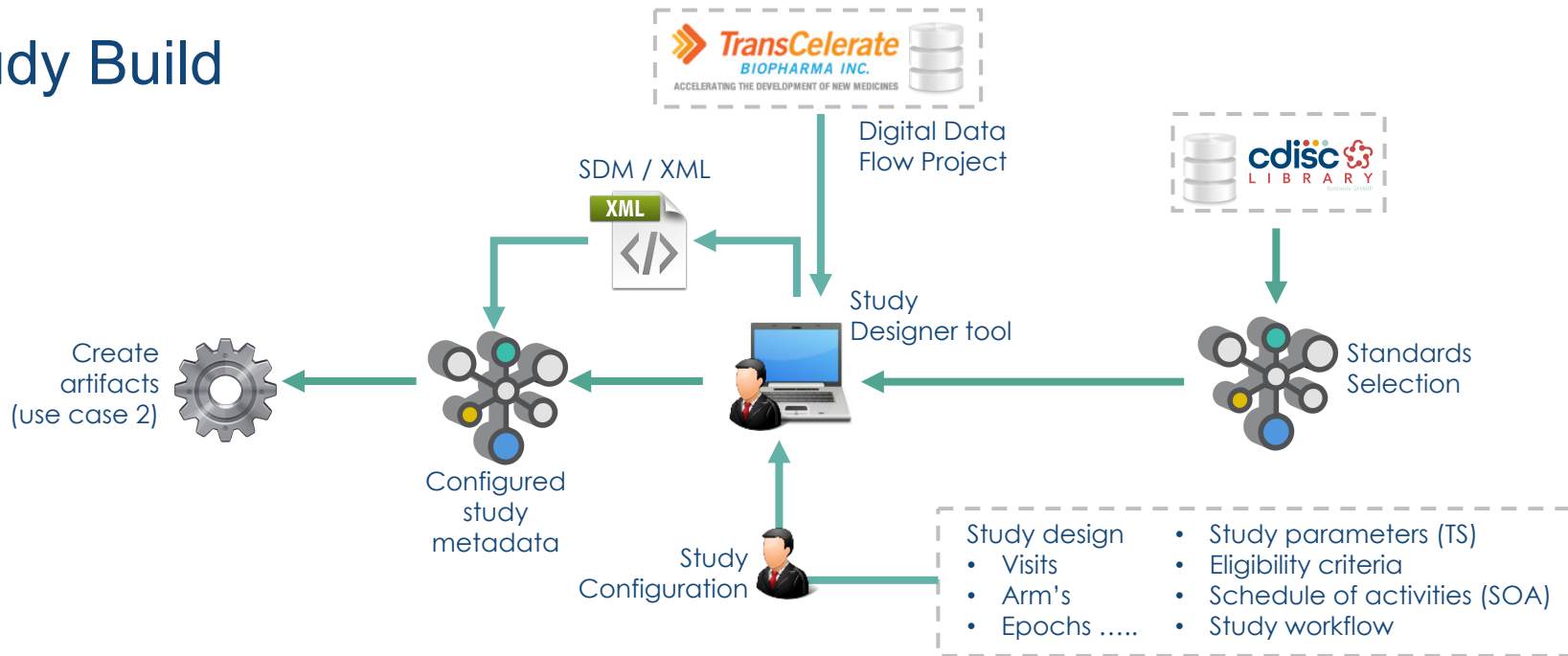


Use Case 2 : Build

Adding study design, concept configuration & generate artifacts

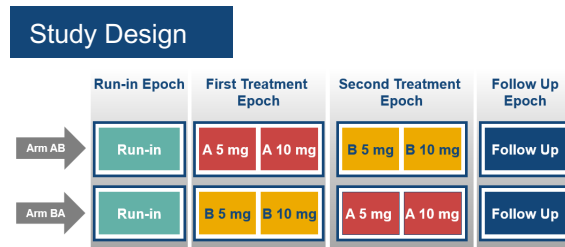


Study Build



Schedule of Activities (SoA)

Procedures	Screening	Run-in	First Treatment Epoch	Second Treatment Epoch	Follow-up
Randomization	X				
Baseline assessment	X				
Run-in		X			
First treatment epoch			X		
Second treatment epoch				X	
Follow-up					X
Dropout					X
Adverse event evaluation					X

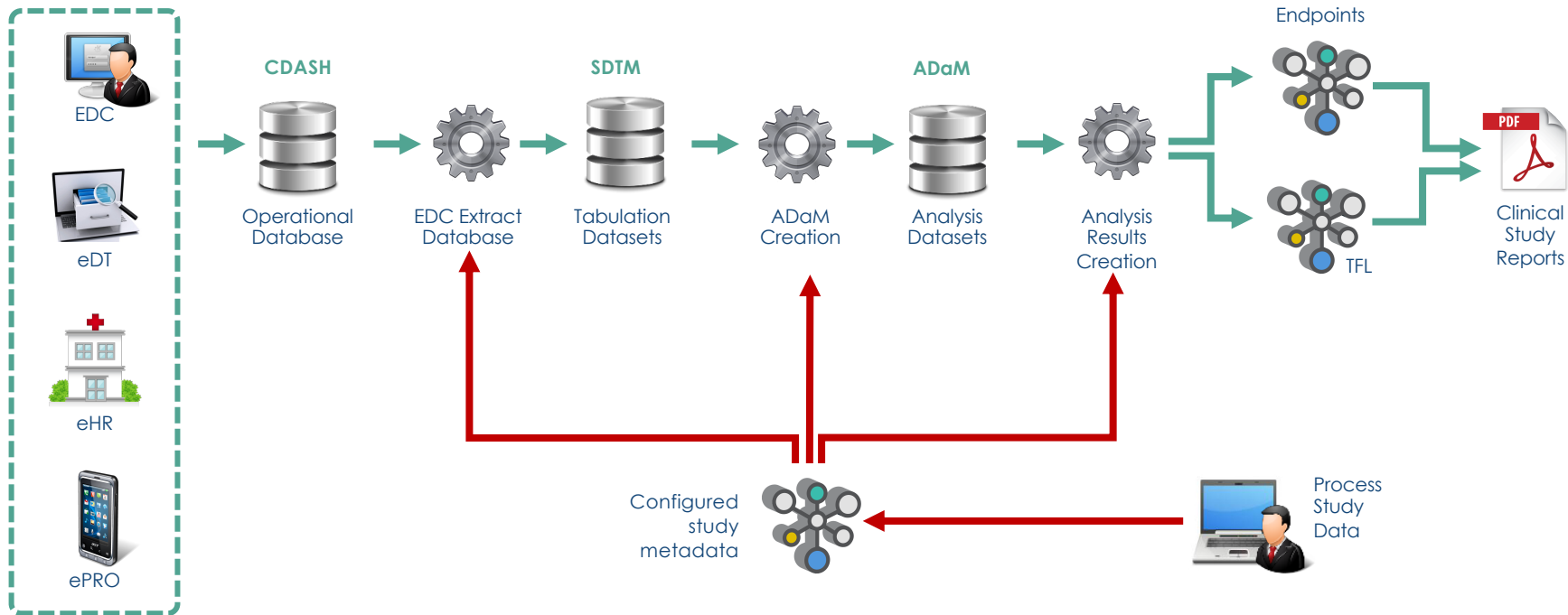


Study Parameters (TS)

STUDY	DOMAIN	TSID	TSID	TSID	TSID	TSID	TSID	TSID	TSID
XYZ	TS	1	ADON	Added as to Existing Treatment	Y		C0488	C0488	2011-06-10
XYZ	TS	1	AGESEX	Maximum Age of Subjects	P01Y			ISO 8881	
XYZ	TS	1	AGESEX	Minimum Age of Subjects	P01M			ISO 8881	
XYZ	TS	1	LENGTH	Planned Study Length	P01M			ISO 8881	
XYZ	TS	1	PLANIB	Planned Number of Subjects	300				
XYZ	TS	1	RANDOM	Randomized	Y		C0488	C0488	2011-06-10
XYZ	TS	1	STOPOP	Stop of Participants	NOTH		C0488	C0488	2011-06-10
XYZ	TS	1	STOPRLE	Study Stop Rules	STOPRLE				
XYZ	TS	1	TRIND	Trial Randomization	DOUBLE BLIND		C1328	C0488	2011-06-10
XYZ	TS	1	TRIND	Trial Randomization	PLACERO		C0488	C0488	2011-06-10
XYZ	TS	1	TRIND	Trial Randomization	Randomized		1913001	KNOWED	
XYZ	TS	1	TRIND	Trial Randomization	TREATMENT		C0488	C0488	2011-06-10

Use Case 3 : Execute

Automatic population of data into artifacts



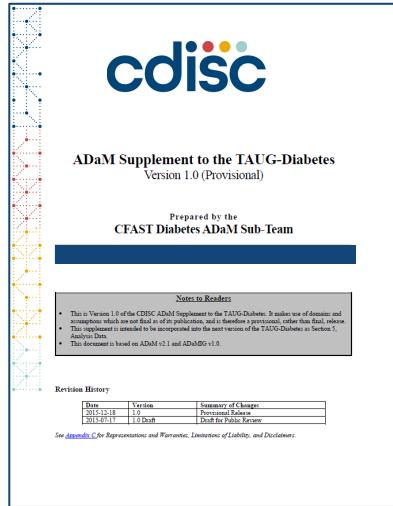
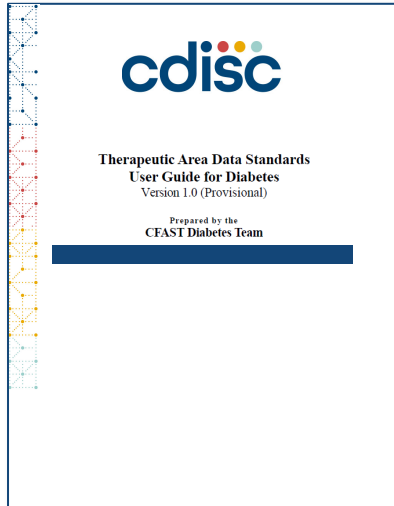
Expected Outcome

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



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*



Bess LeRoy,
CDISC Metadata Engineer

*Publish
Standards*



Sam Hume,
CDISC VP Data Science

Study
Metadata
Library



Define



Mikkel Traun,
Novo Nordisk

Build



Tianna Umann,
Microsoft

Execute

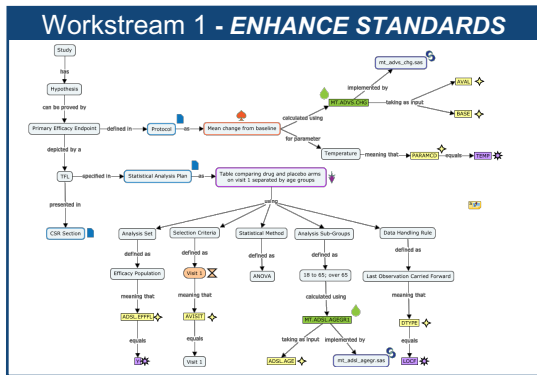


Bhavin Busa,
Vita Data Sciences

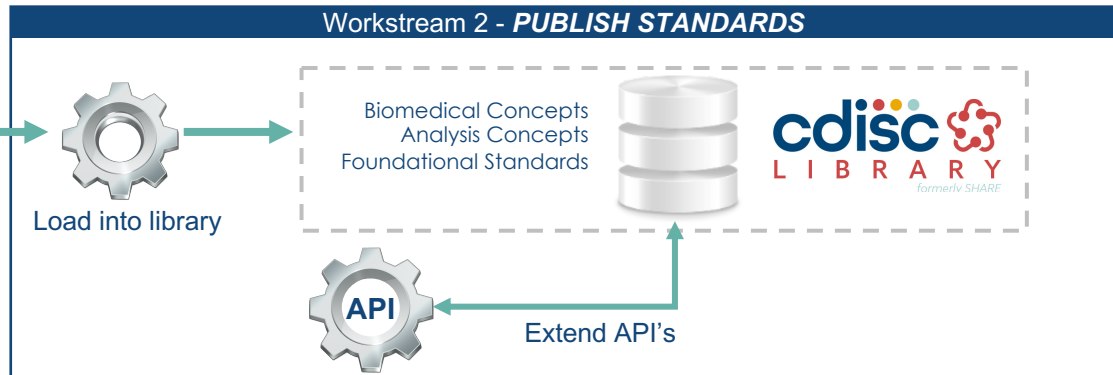
Industry



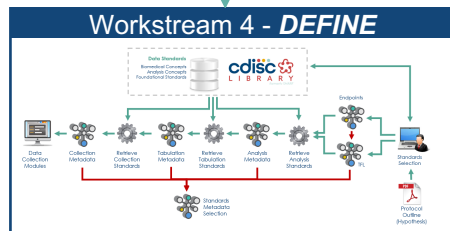
CDISC 360 Workstreams



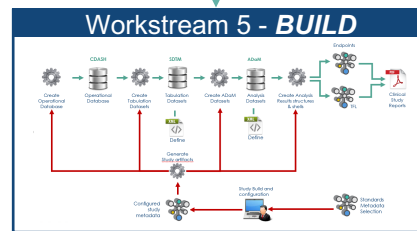
Create concepts in knowledge graphs



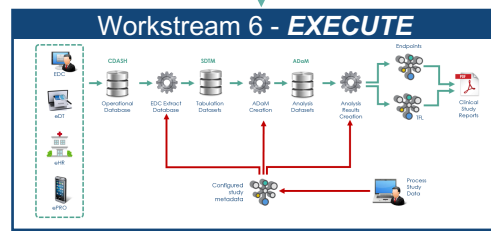
Transform concepts in machine readable form



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)

360 Participation Summary

Project Kickoff:

36 Resources specified

20 Organizations

Today:

107 Resources specified

38 Organizations

- Pharma-Biotech Sponsor: 20
- CRO: 6
- Technology Provider: 11
- Regulatory: 1

➔ *Still onboarding new participants*

➔ *Contributions vary due to project complexity and time available*



abbvie



AMGEN®



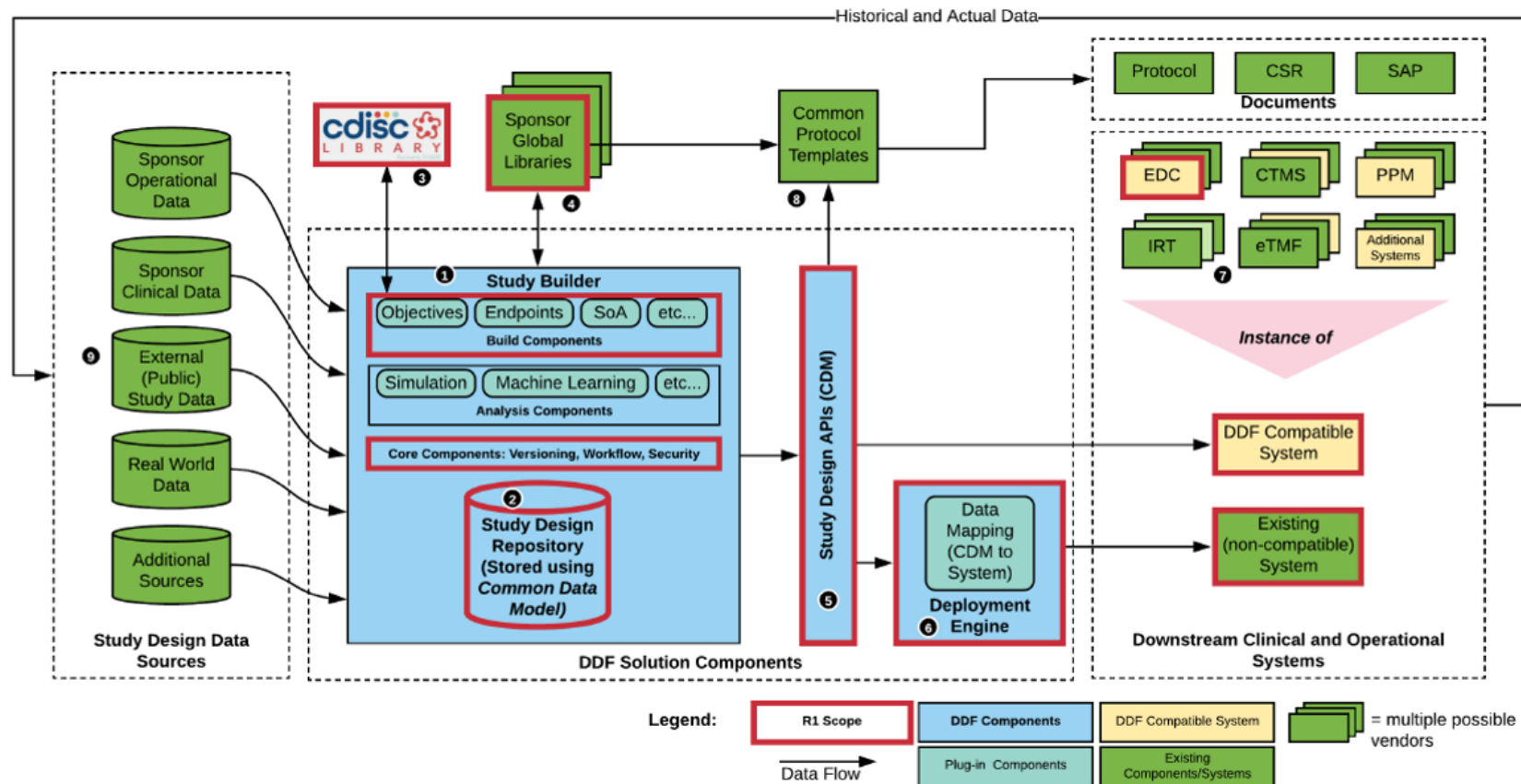
BIOMARIN®



Deloitte.



TransCelerate DDF Study Builder - Conceptual System Architecture





The Journey So Far

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)	Oct 2020	Oct 2020

← We are here

CDISC 360 To Date – March 2020

- 15 sprints across 12 months
- Increasing our concept-based standards knowledge in iterative fashion

2020 - MAR

EU Interchange

- Create study designs using standards and study metadata library
- Automated, metadata-driven creation of SDTM and ADaM datasets, and TFLs

2020 - JAN

Building Momentum

- ISO11179 concept based templates, metamodels, bindings
- Include data & TFL transformation engines
- Expand cloud infrastructure

2019 – April 8th

Kick-off

- Kick-off meeting
- Workstreams Briefing
- Over 45 participants

2019 - JUL

Gaining Traction

- More volunteers, tools, access, training
- User story development
- Initial concept-based standards
- Test study definitions and data

2019 - OCT

US Interchange

- Convert concepts to machine-readable form
- Study Metadata Library prototype
- “360 Test Study” components and metadata
- Identify two safety endpoint analyses with FDA



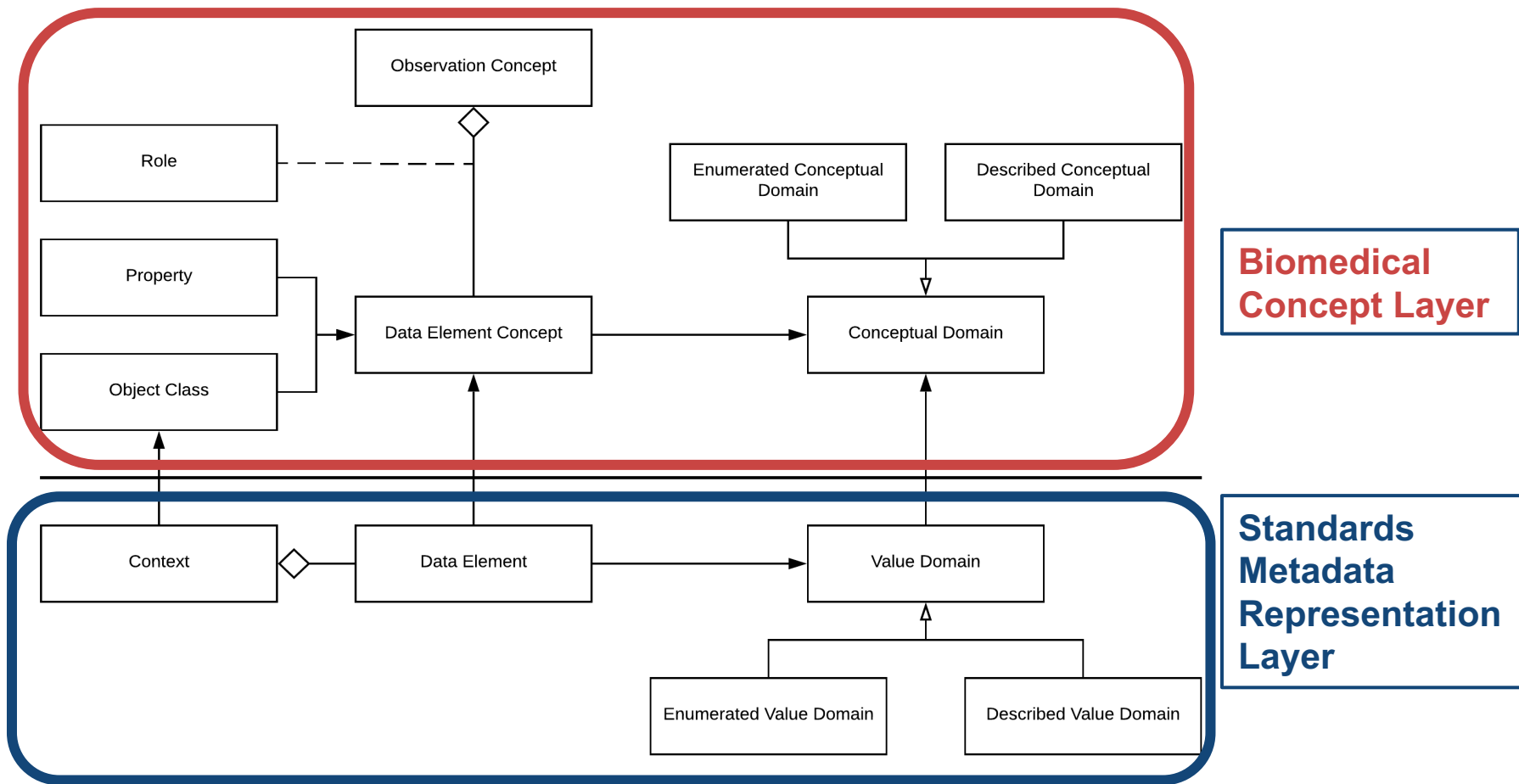


Workstream Highlights

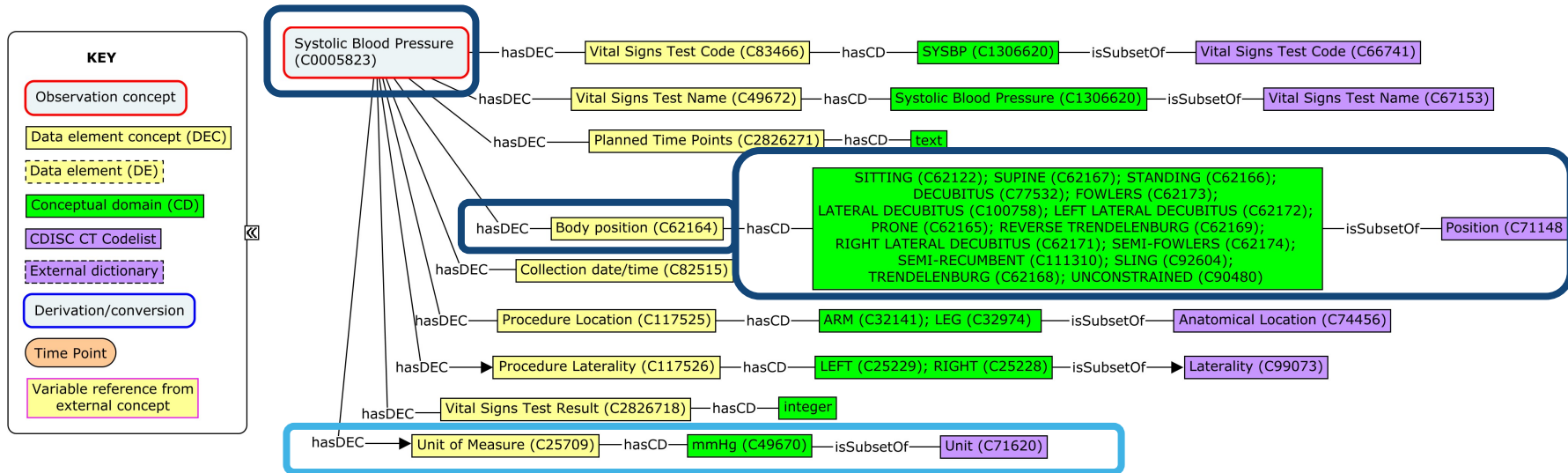
Concept Development Highlights

- Adapting biomedical concepts to ISO11179
 - ISO 11179 is an international standard for representation of metadata
- Linking biomedical concept templates to binding files
- Defined approach to add transformations and derivations to concept maps

CDISC 360 ISO 11179 Model



Concept Development based on ISO 11179: Systolic Blood Pressure



Binding Files

vs_bindings_v0.1

Search Sheet

Home Insert Page Layout Formulas Data Review View

Paste

Calibri (Body) 11

Conditional Formatting

Format as Table

Cell Styles

Alignment

Number

Cells

Editing

A2

VSTEST

	A	B	C	D
1	Operational Variable Name	Library Variable Name	Library Variable Href	EnumeratedValues.Title
2	VSTEST	VSTEST	/mdr/sdtmig/3-2/datasets/VS/variables/VSTEST	Codelist
3	VSTESTCD	VSTESTCD	/mdr/sdtmig/3-2/datasets/VS/variables/VSTESTCD	Codelist
4	VSORRES	VSORRES	/mdr/sdtmig/3-2/datasets/VS/variables/VSORRES	
5	VSORRESU	VSORRESU	/mdr/sdtmig/3-2/datasets/VS/variables/VSORRESU	Codelist
6	VSTRESN	VSTRESN	/mdr/sdtmig/3-2/datasets/VS/variables/VSTRESN	
7	VSTRESU	VSTRESU	/mdr/sdtmig/3-2/datasets/VS/variables/VSTRESU	Codelist
8	STUDYID	STUDYID	/mdr/sdtmig/3-2/datasets/VS/variables/STUDYID	
9	DOMAIN	DOMAIN	/mdr/sdtmig/3-2/datasets/VS/variables/DOMAIN	Codelist Term
10	USUBJID	USUBJID	/mdr/sdtmig/3-2/datasets/VS/variables/USUBJID	
11	VSSEQ	VSSEQ	/mdr/sdtmig/3-2/datasets/VS/variables/VSEQ	
12	VISITNUM	VISITNUM	/mdr/sdtmig/3-2/datasets/VS/variables/VISITNUM	
13	VSDTC	VSDTC	/mdr/sdtmig/3-2/datasets/VS/variables/VSDTC	
14	VSBLFL	VSBLFL	/mdr/sdtmig/3-2/datasets/VS/variables/VSBLFL	Codelist
15				
16				
17				

Context Dataset TEMP HEIGHT WEIGHT +

Ready

100%

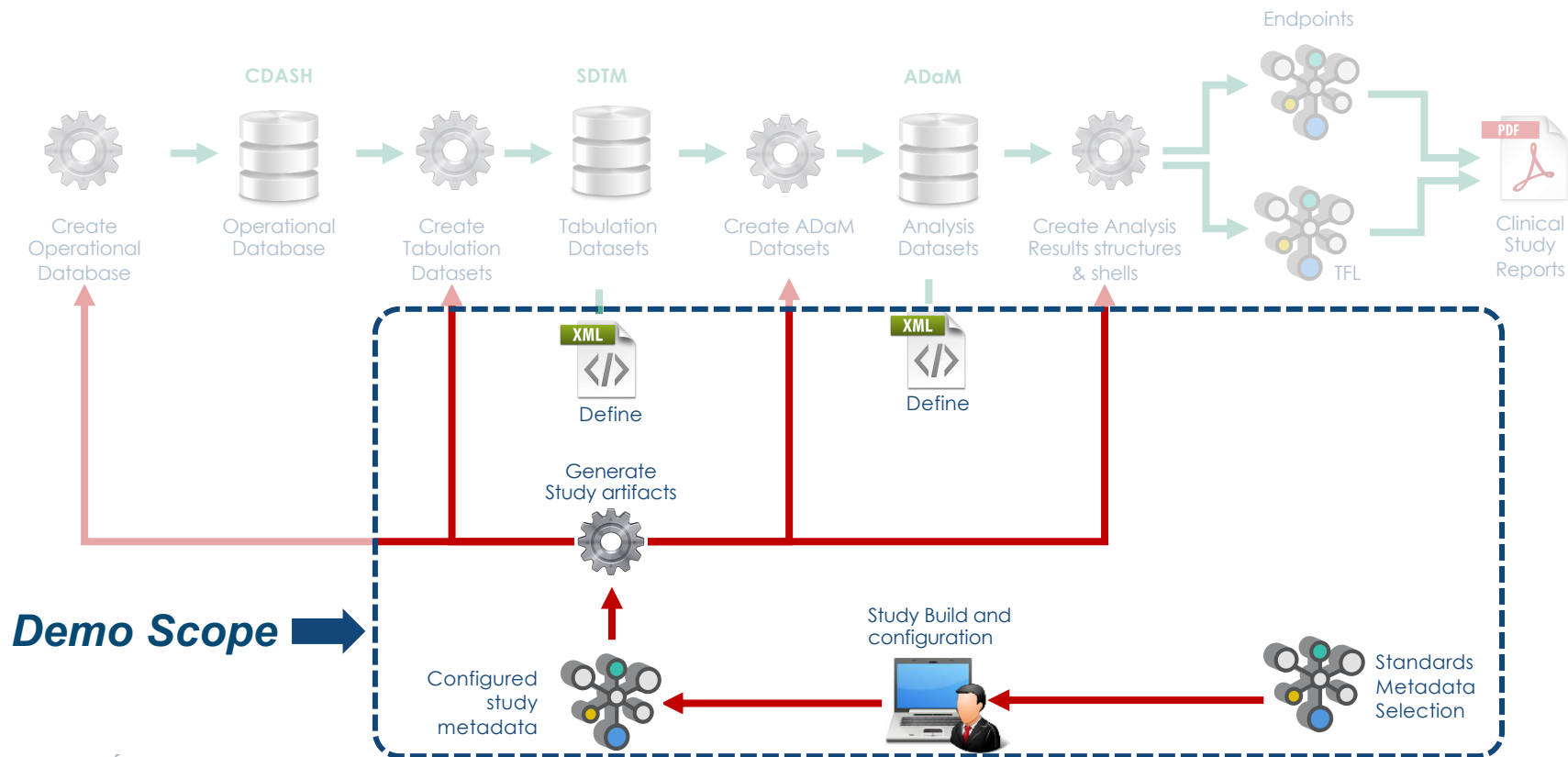


Concept Development: Next Steps

- **Biomedical and Analysis concepts model and templates:**
 - Test BCs (Lab, Exposure, Demographics, Trial Design, Vital Signs)
 - Test ACs (ADSL)
 - CRFs
- **Data flow metadata:**
 - System-agnostic transformations and derivations
 - Link data flow metadata to concepts
 - Test use of data flow metadata
- **End-to-End from CDASH to ADSL:**
 - For metadata (data state and data flow) and data

Use Case 2 : Build

Adding study design, concept configuration & generate artifacts



360 Use Case 1-2 Demo – Study Designer

cdisc360 Study Designer

LibraryStudiesDefineDesignSelectBuildListHelp

CDISC360-2mt

Summary

Objectives / Endpoints

Derived Assessments ⚠

Collected Assessments ⚠

Schedule of Activities

Data Collection ⚠

Tables, Figures and Listings ⚠

Objectives and Endpoints

ObjectivesEndpoints

Add objective(s) from Library

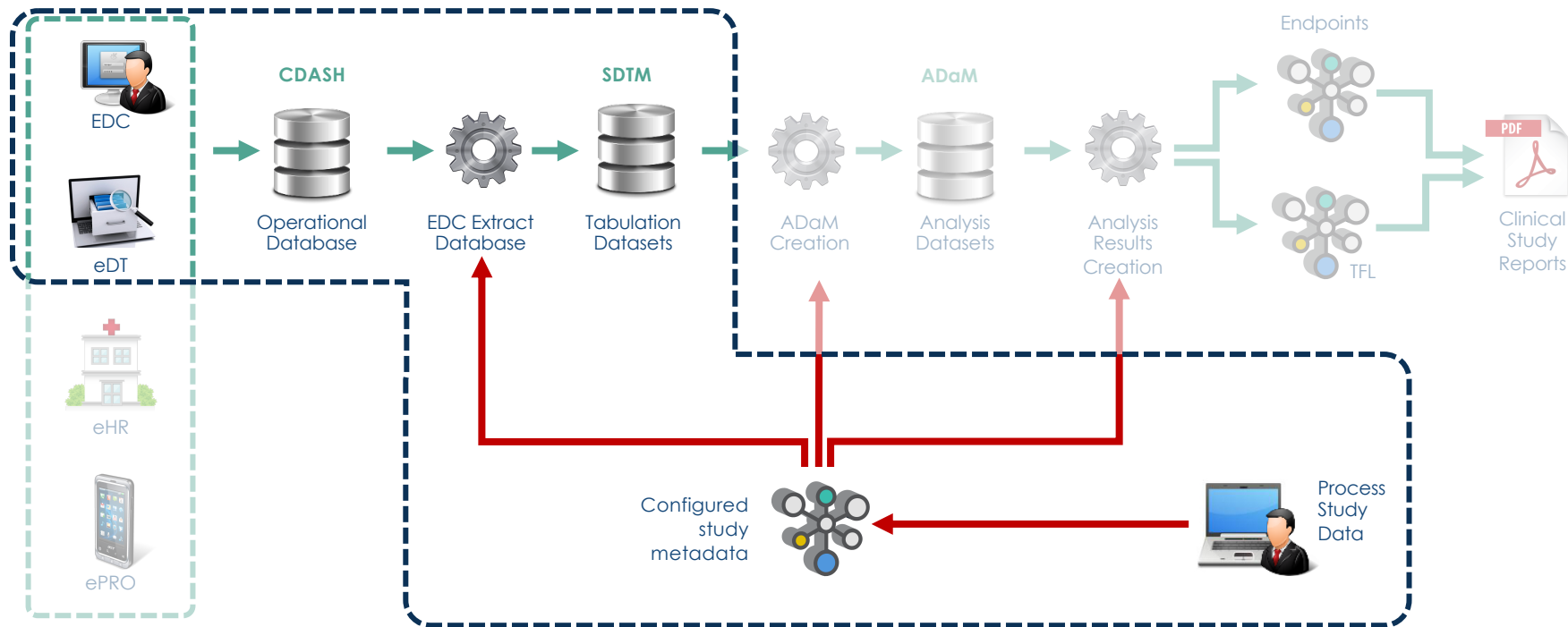
Objectives for the study

Search

Study	Order	Level	Objective	DateFrom	DateTo	Status	Mdv	Retired
CDISC360-2	1	Trial Primary Objective	To demonstrate superiority in the efficacy of human insulin to Metformin in glycated hemoglobin (HbA1c) change from Baseline to Week 26	2020-04-23 10:51:16	2286-11-20 17:46:39	Final	1.0	<input type="checkbox"/>
CDISC360-2	1	Trial Primary Objective	To demonstrate superiority in the efficacy of human insulin to Metformin in Hemoglobin A1C/Hemoglobin change from Baseline to Week 26	2020-04-23 10:51:16	2286-11-20 17:46:39	Final	1.0	<input type="checkbox"/>
CDISC360-2	1	Trial Primary Objective	To demonstrate superiority in the efficacy of human insulin to Metformin in Hemoglobin A1C/Hemoglobin change from Baseline to Week 14	2020-04-23 10:51:16	2286-11-20 17:46:39	Final	1.0	<input type="checkbox"/>

Use Case 3 : Execute

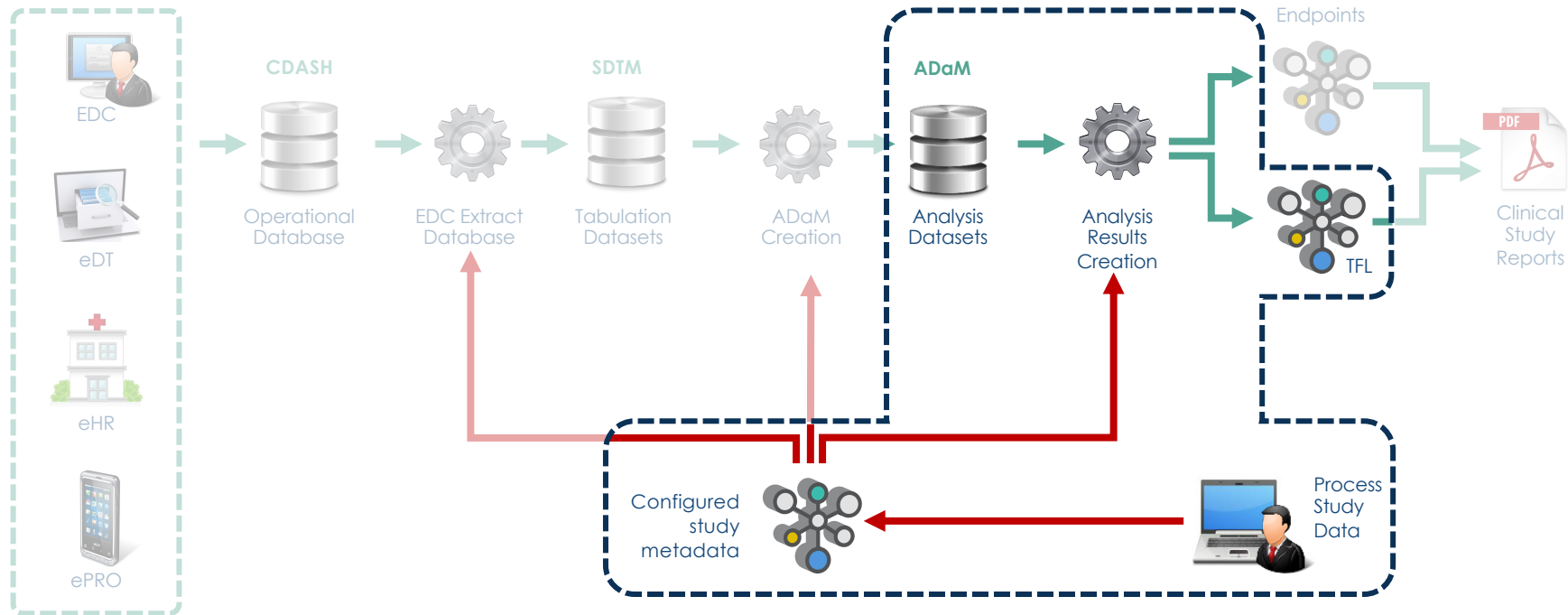
Automatic population of data into artifacts



Data Collection Scope

Use Case 3 : Execute

Automatic population of data into artifacts



CDISC360 – WS6 TFL Automation

Customize Template

Generate SAS Program and XML

TFL Automation

1 Choose Folder

2 Table 14.1.1.1
You've selected: DEMOG

3 Download SAS Code

Study - CDISC
Table 14.1.1.1
Demographic characteristics (Safety Population)

2

Population Dataset
adsl

Population Variable
SAFFL

Population Comparator
eq

Population Value
Y

Across Variable
TRTA

Across Label Header 1
METFORMIN

Across Label Header 2
HUMAN INSULIN

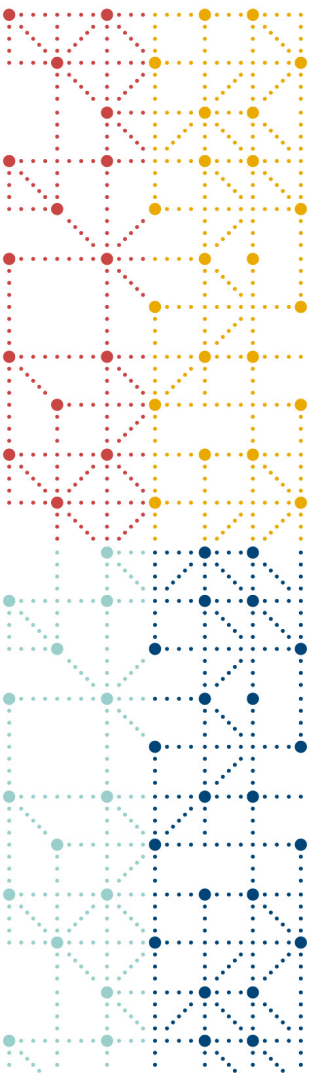
Row Label Header
Characteristics

"Age (years)"

Analysis Dataset
adsl

Analysis Variable
AGE

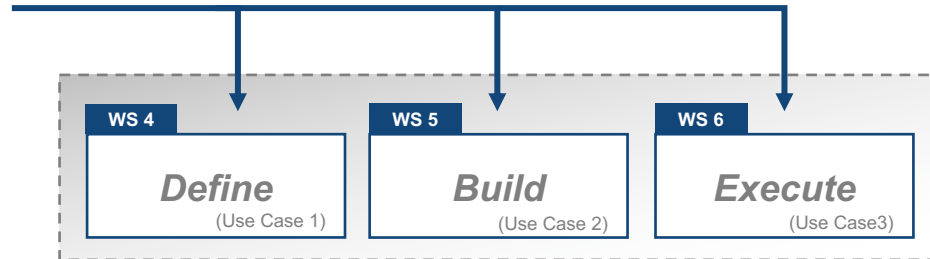
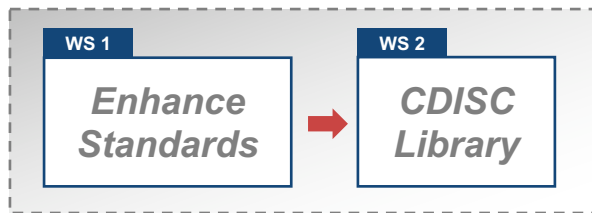
n	xxx
Mean	xx.x
SD	xx.xx
Min	xx
Q25	xx.x
Median	xx.x
Q75	xx.x



What Follows 360?



Proof Of
Concept



Implement



Industry
Implementation

Regulatory



Provide requirements

Submission data following regulatory requirements

What Follows 360 - Inventory of Work (1)

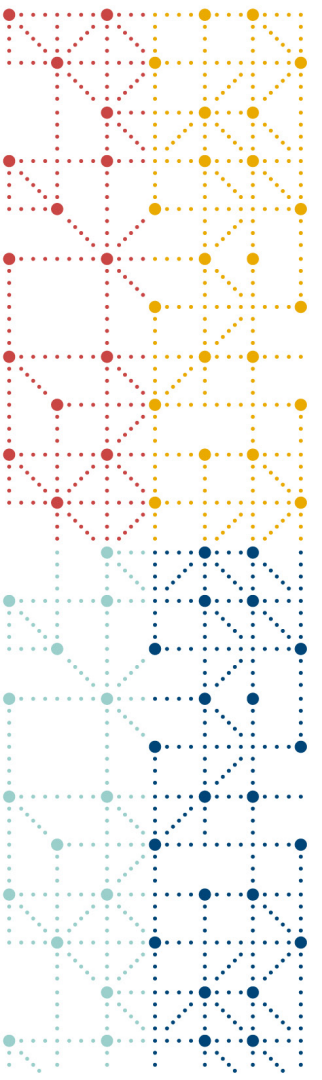
- **Missing** standards
 - Data Collection instruments
 - Analysis Results
 - Endpoint definitions
 - Safety User Guide
 - Collection → Tabulation → Analysis
- **Enrich** existing standards
 - What
 - Clinical assessments
 - Interventions
 - Events
 - Therapeutic Areas
 - How
 - Stabilize Biomedical and Analysis concept templates
 - Add transformations and derivations content



What Follows 360 - Inventory of Work (2)

- Evolve **library** technology and schema
 - Refine and test the CDISC 360 models
 - Refine and deploy CDISC 360 software tools
 - Integrate the CDISC 360 models into the CDISC Library model
 - Update the API to add new CDISC 360 model endpoints
 - Update the CDISC Library Data Standards Browser to include CDISC 360 content
 - Update the CDISC Library standards load software
- Evolve toward collaborative **curation**
 - Develop and rollout governance process
 - Create CDISC Library standards development and curation tools
 - Develop standards curation training
 - Enhance CDISC Library to load community standards implementations





Thank you