CDISC 360 Update:
Evolution of the CDISC Standards

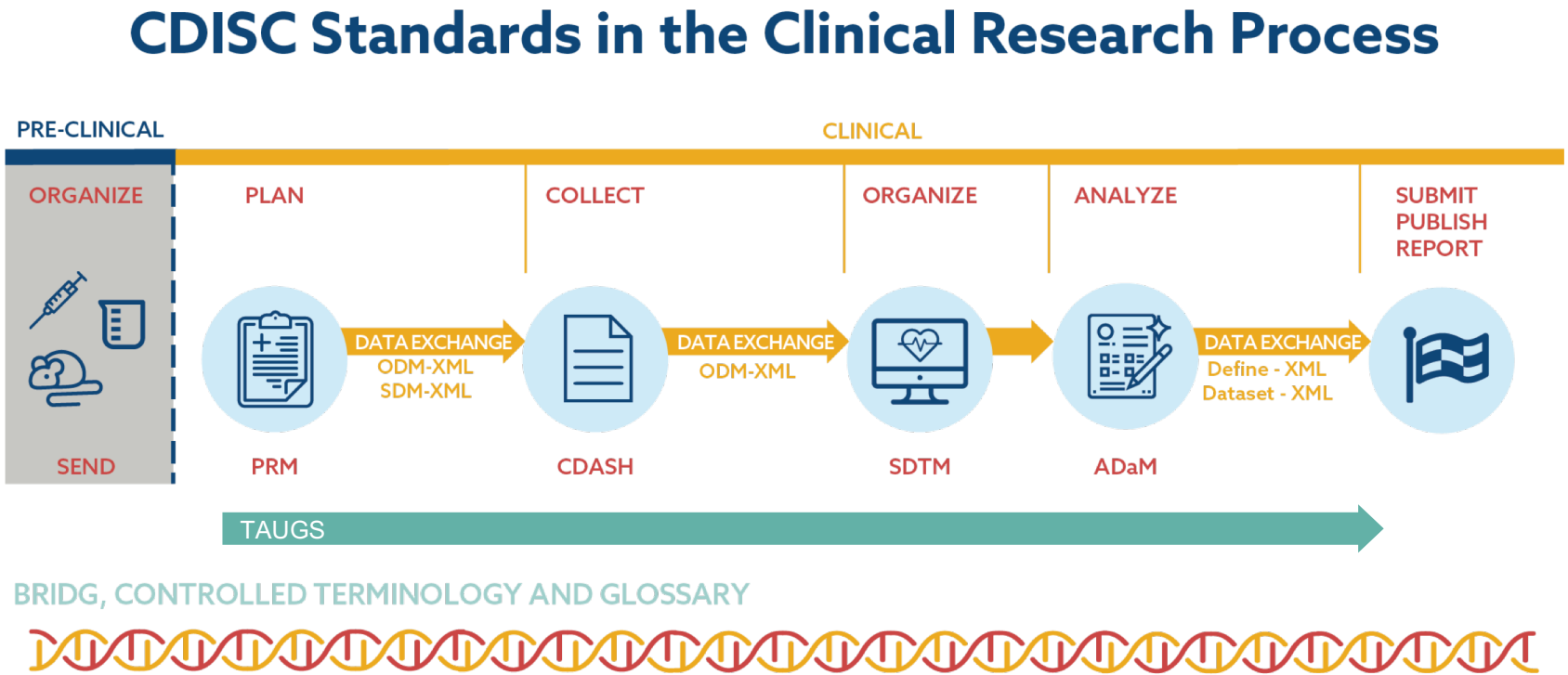
Peter Van Reusel,
CSO,
14-18 October 2019

Agenda

1. CDISC 360 Intro
2. Project Approach
3. Project Status
4. Concepts Development - status
5. Art of the Possible

1. CDISC 360 Intro

Today we are here



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	PerformedObservation 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**, SDTMIG variable VSTAT is derived from a "No" value in VSPERF. This field does not map directly to an SDTM variable.	O
2	On what date were the measurements performed?	Date	VSDAT	PerformedActivity .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	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, 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 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	Codelist/ 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***

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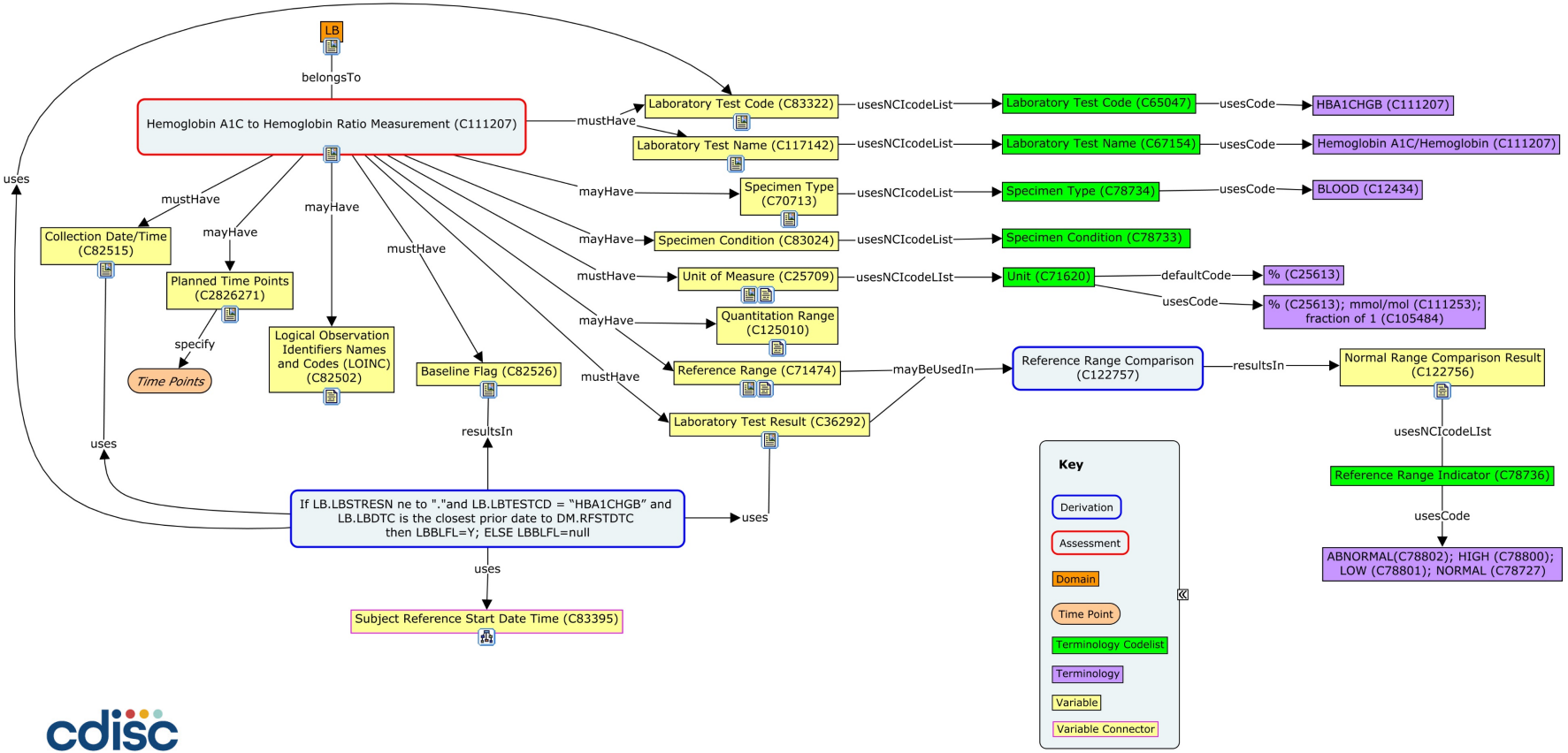
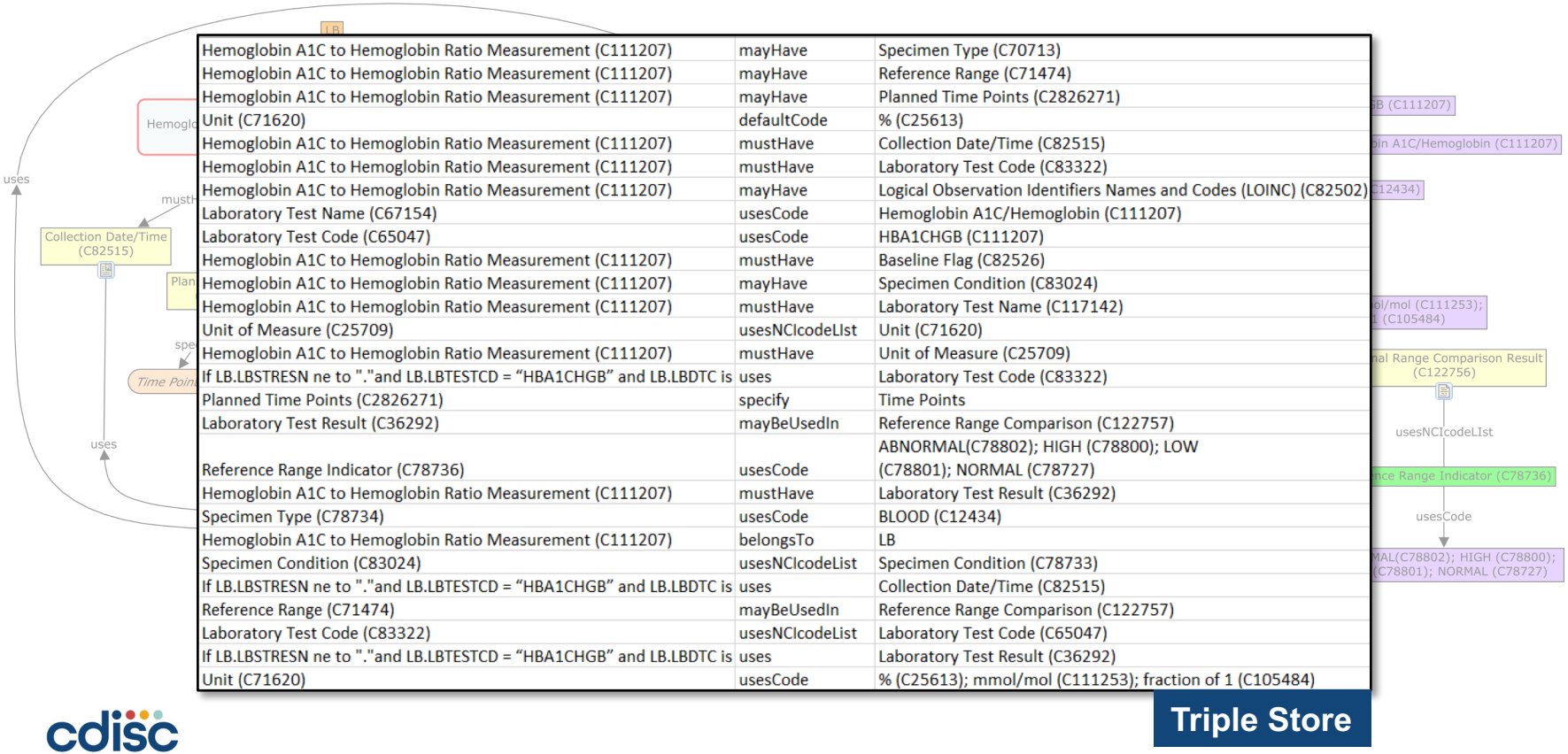
Biomedical Concept



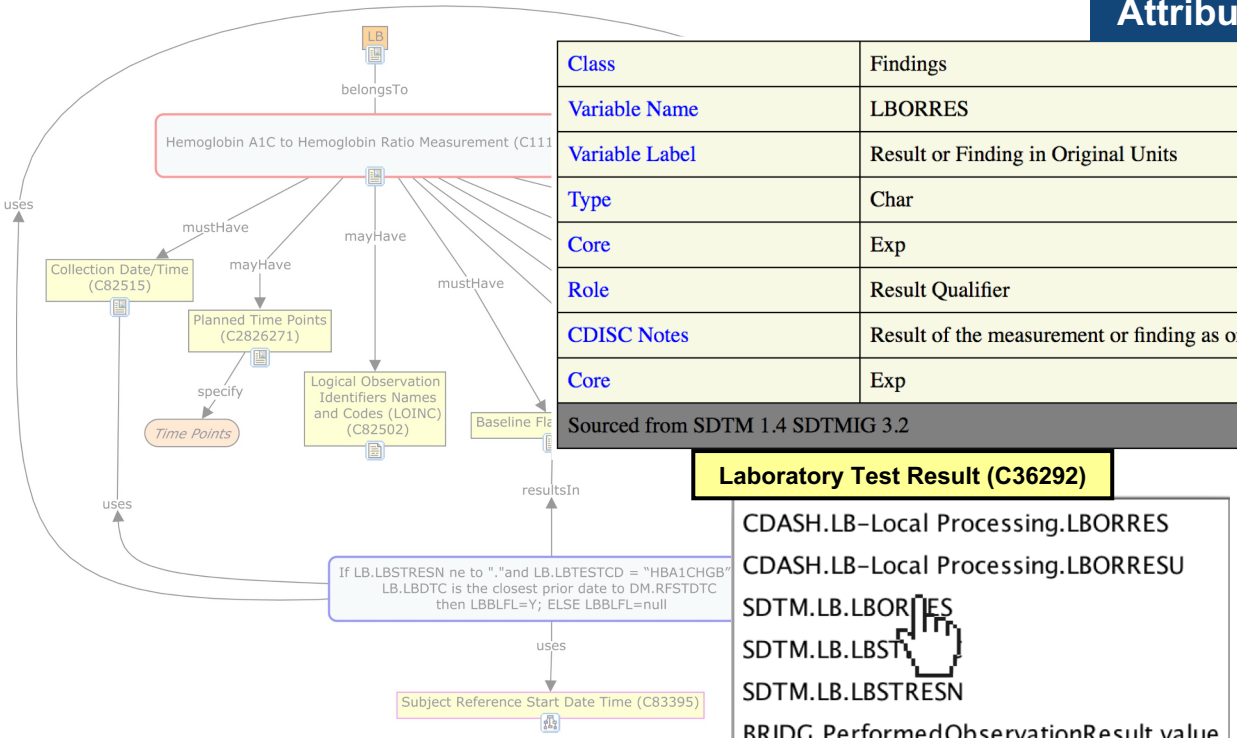
Biomedical Concept



Hemoglobin A1C to Hemoglobin Ratio Measurement (C111207)	mayHave	Specimen Type (C70713)
Hemoglobin A1C to Hemoglobin Ratio Measurement (C111207)	mayHave	Reference Range (C71474)
Hemoglobin A1C to Hemoglobin Ratio Measurement (C111207)	mayHave	Planned Time Points (C2826271)
Unit (C71620)	defaultCode	% (C25613)
Hemoglobin A1C to Hemoglobin Ratio Measurement (C111207)	mustHave	Collection Date/Time (C82515)
Hemoglobin A1C to Hemoglobin Ratio Measurement (C111207)	mustHave	Laboratory Test Code (C83322)
Hemoglobin A1C to Hemoglobin Ratio Measurement (C111207)	mayHave	Logical Observation Identifiers Names and Codes (LOINC) (C82502)
Laboratory Test Name (C67154)	usesCode	Hemoglobin A1C/Hemoglobin (C111207)
Laboratory Test Code (C65047)	usesCode	HBA1CHGB (C111207)
Hemoglobin A1C to Hemoglobin Ratio Measurement (C111207)	mustHave	Baseline Flag (C82526)
Hemoglobin A1C to Hemoglobin Ratio Measurement (C111207)	mayHave	Specimen Condition (C83024)
Hemoglobin A1C to Hemoglobin Ratio Measurement (C111207)	mustHave	Laboratory Test Name (C117142)
Unit of Measure (C25709)	usesNCIcodeLIst	Unit (C71620)
Hemoglobin A1C to Hemoglobin Ratio Measurement (C111207)	mustHave	Unit of Measure (C25709)
If LB.LBSTRESN ne to "."and LB.LBTESTCD = “HBA1CHGB” and LB.LBDTC is	uses	Laboratory Test Code (C83322)
Planned Time Points (C2826271)	specify	Time Points
Laboratory Test Result (C36292)	mayBeUsedIn	Reference Range Comparison (C122757)
Reference Range Indicator (C78736)	usesCode	ABNORMAL(C78802); HIGH (C78800); LOW (C78801); NORMAL (C78727)
Hemoglobin A1C to Hemoglobin Ratio Measurement (C111207)	mustHave	Laboratory Test Result (C36292)
Specimen Type (C78734)	usesCode	BLOOD (C12434)
Hemoglobin A1C to Hemoglobin Ratio Measurement (C111207)	belongsTo	LB
Specimen Condition (C83024)	usesNCIcodeList	Specimen Condition (C78733)
If LB.LBSTRESN ne to "."and LB.LBTESTCD = “HBA1CHGB” and LB.LBDTC is	uses	Collection Date/Time (C82515)
Reference Range (C71474)	mayBeUsedIn	Reference Range Comparison (C122757)
Laboratory Test Code (C83322)	usesNCIcodeList	Laboratory Test Code (C65047)
If LB.LBSTRESN ne to "."and LB.LBTESTCD = “HBA1CHGB” and LB.LBDTC is	uses	Laboratory Test Result (C36292)
Unit (C71620)	usesCode	% (C25613); mmol/mol (C111253); fraction of 1 (C105484)

Triple Store

Biomedical Concept

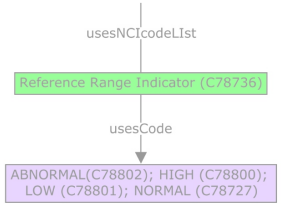


Attributes are linked to the element

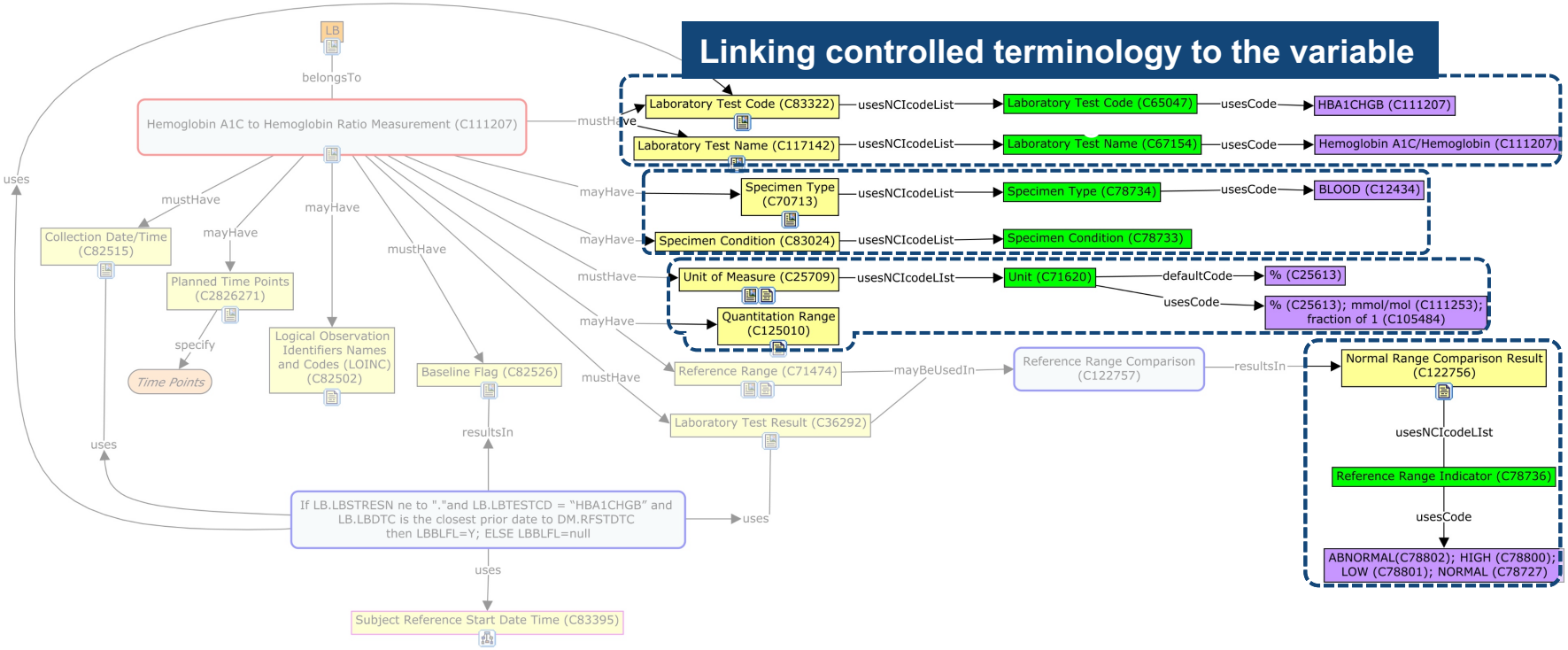
Class	Findings
Variable Name	LBORRES
Variable Label	Result or Finding in Original Units
Type	Char
Core	Exp
Role	Result Qualifier
CDISC Notes	Result of the measurement or finding as originally received or collected.
Core	Exp
Sourced from SDTM 1.4 SDTMIG 3.2	

Laboratory Test Result (C36292)

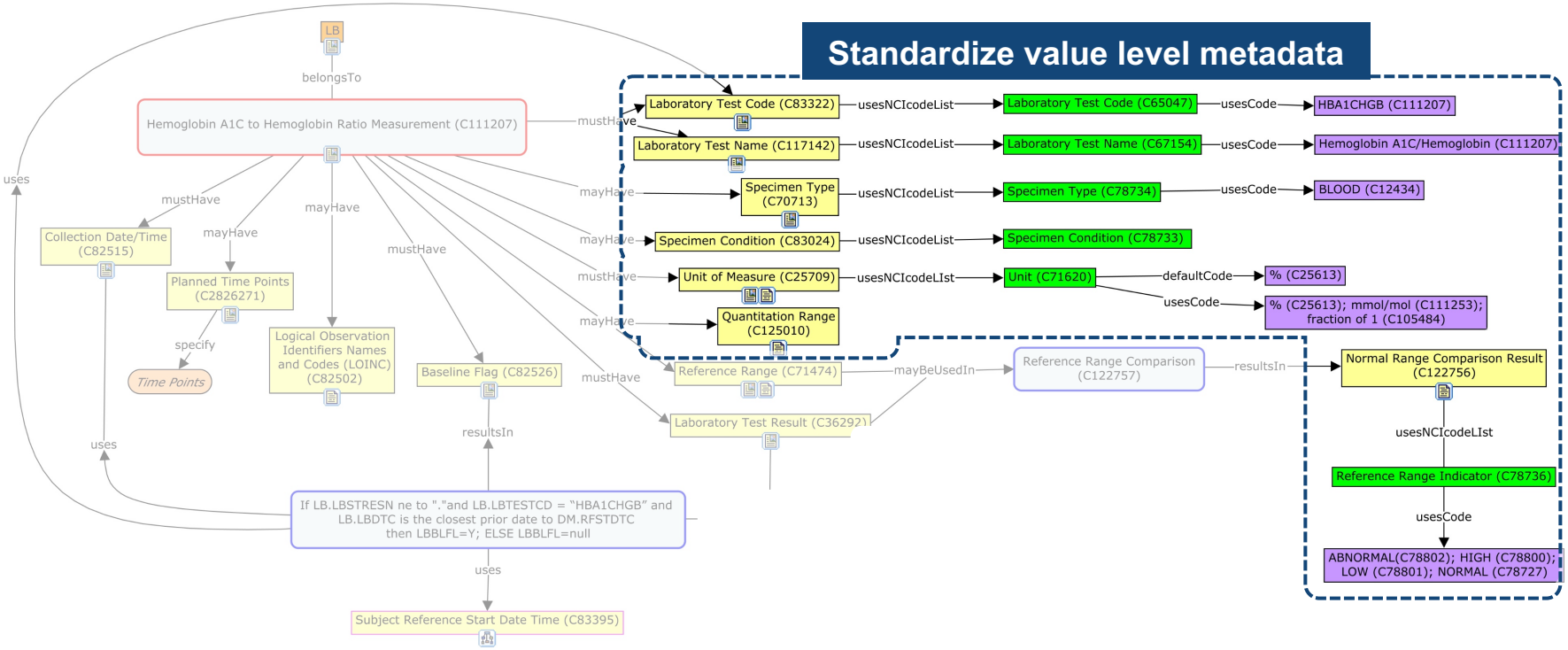
- CDASH.LB-Local Processing.LBORRES
- CDASH.LB-Local Processing.LBORRESU
- SDTM.LB.LBORRES
- SDTM.LB.LBST
- SDTM.LB.LBSTRESN
- BRIDG.PerformedObservationResult.value



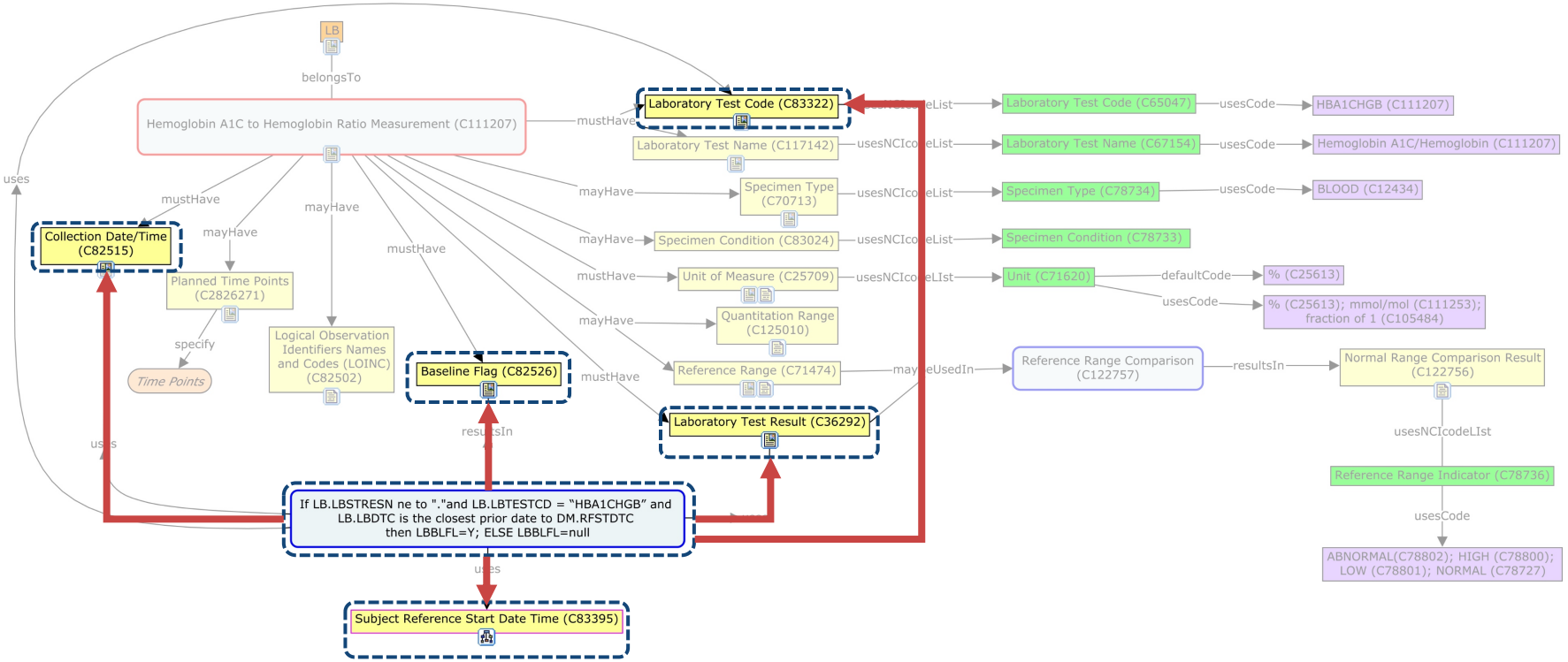
Biomedical Concept



Biomedical Concept

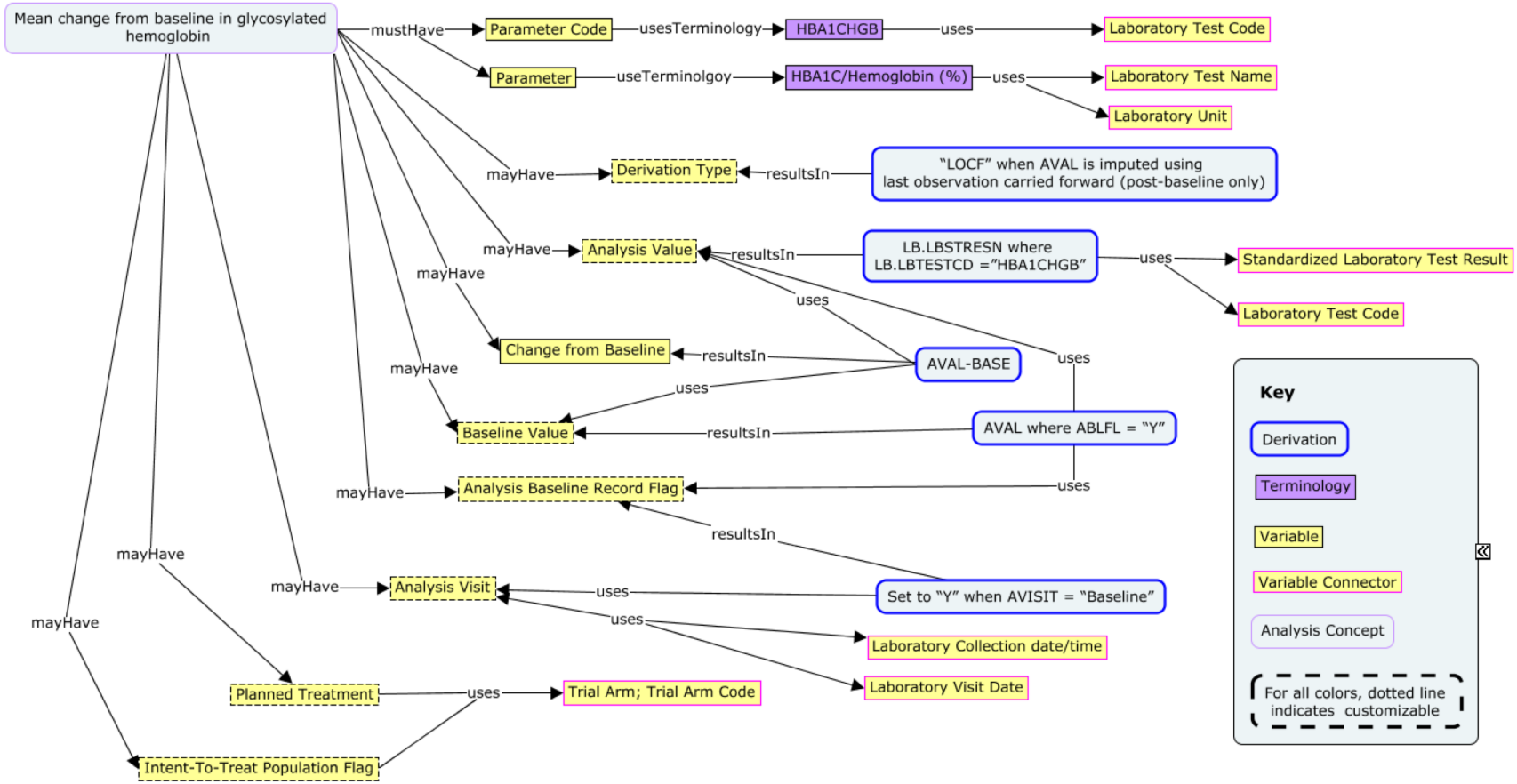


Biomedical Concept

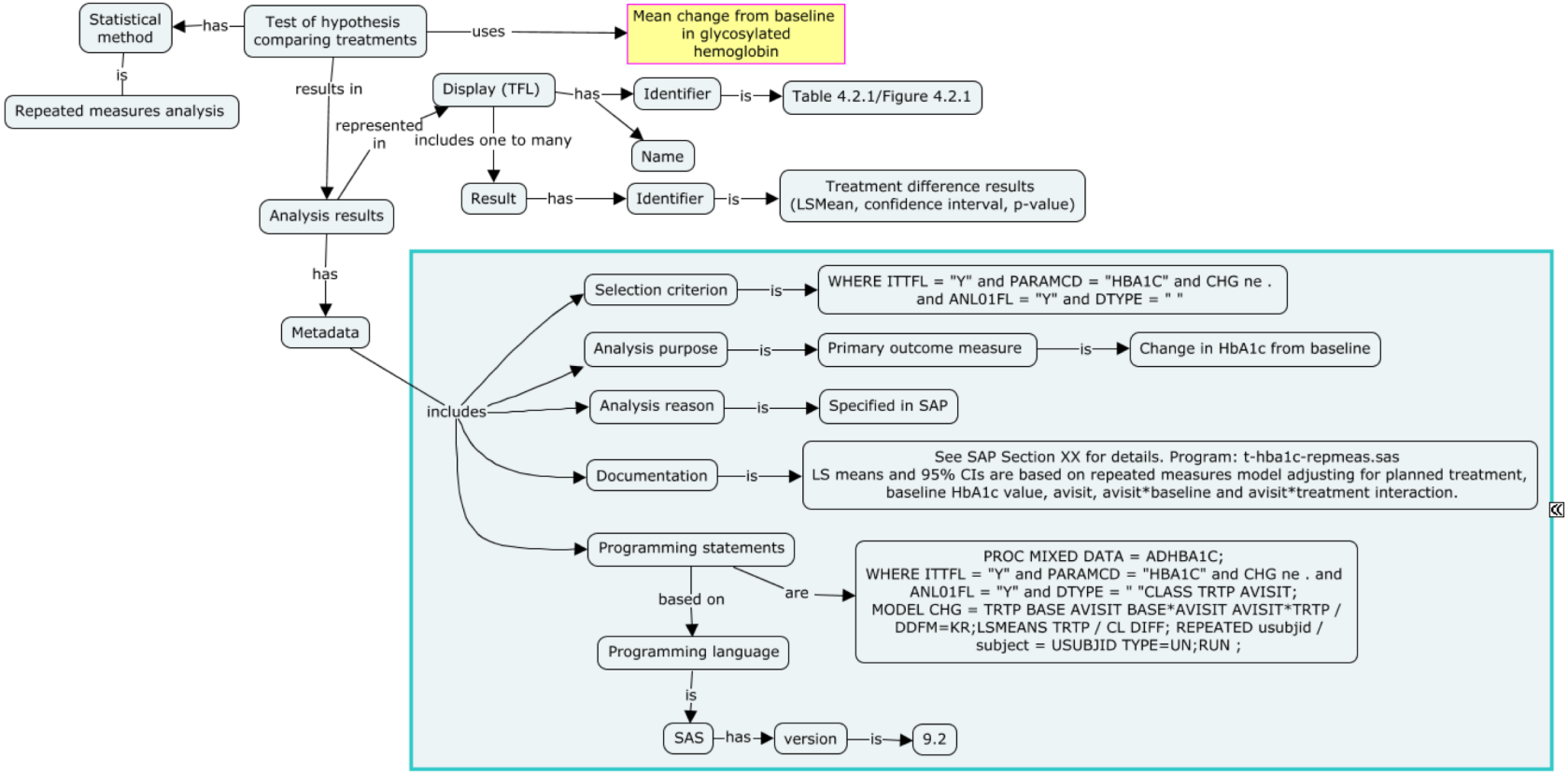


Machine Executable Algorithms

Analysis Concept

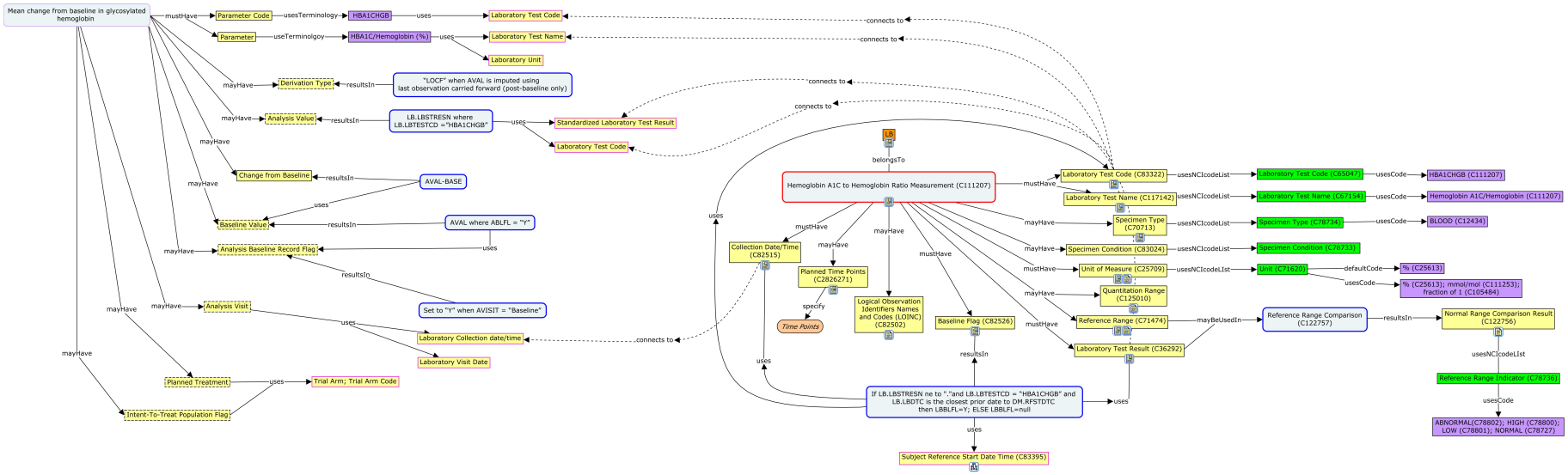


Analysis Result



One Model

Biomedical Concept Map



Analysis Concept Map

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

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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*

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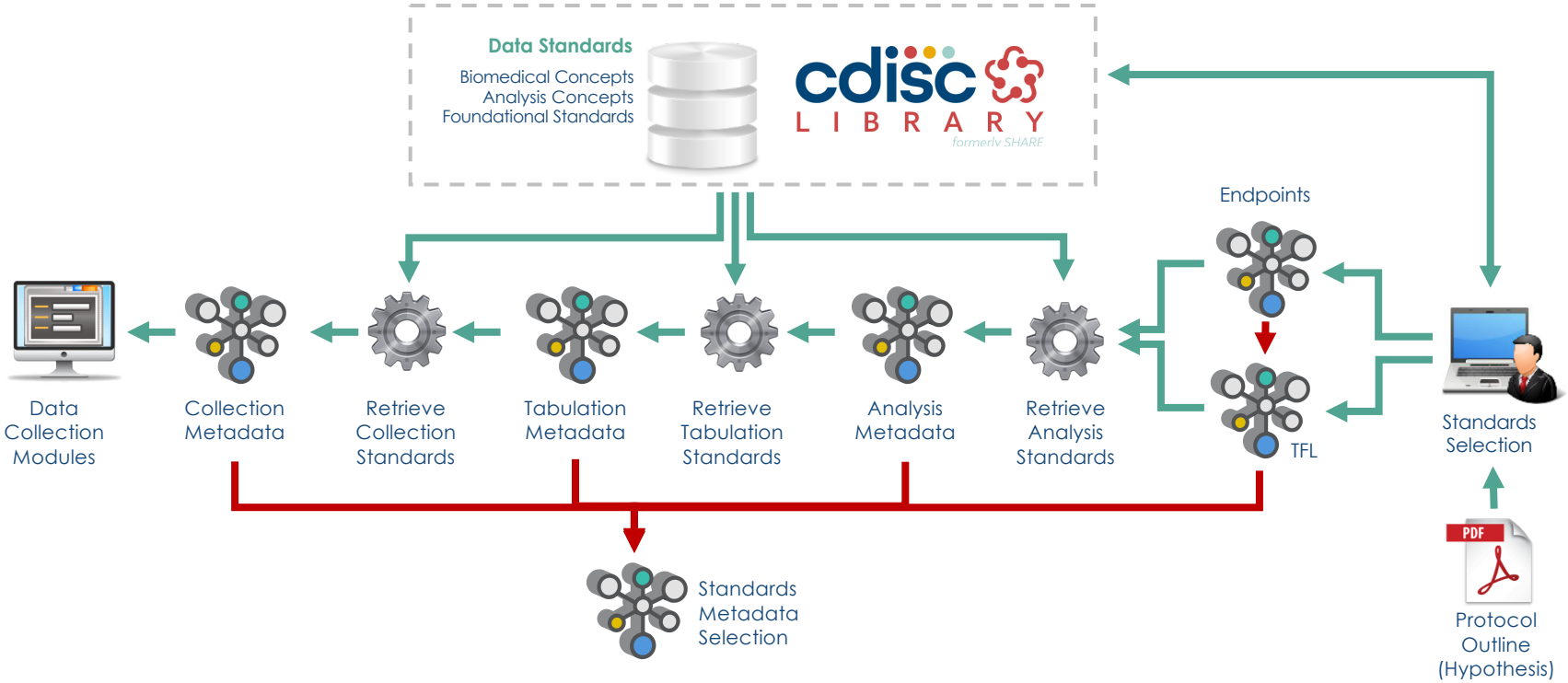
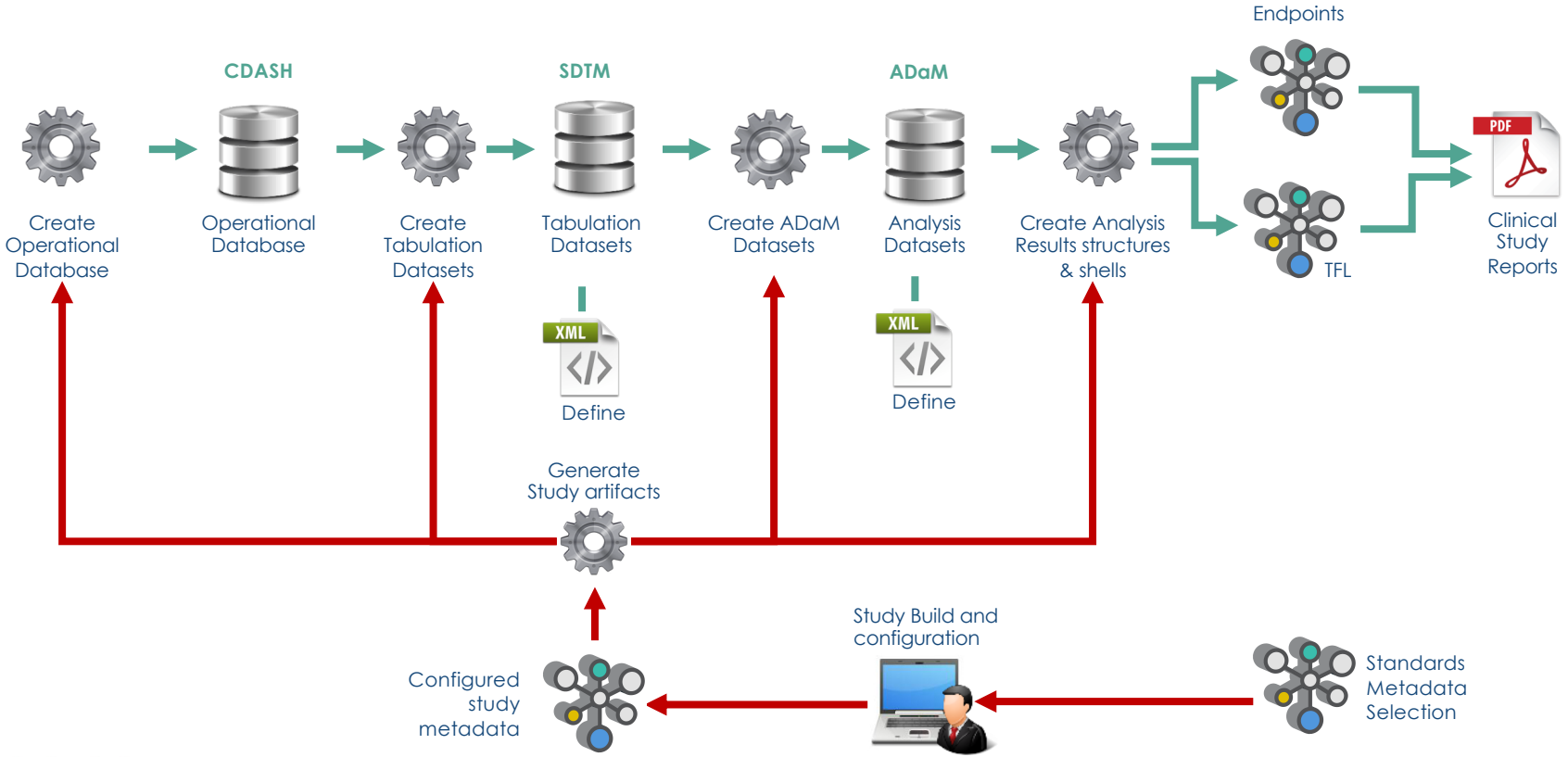
Use Case 1 : Define

Selecting standards concepts and linked metadata needed for a study

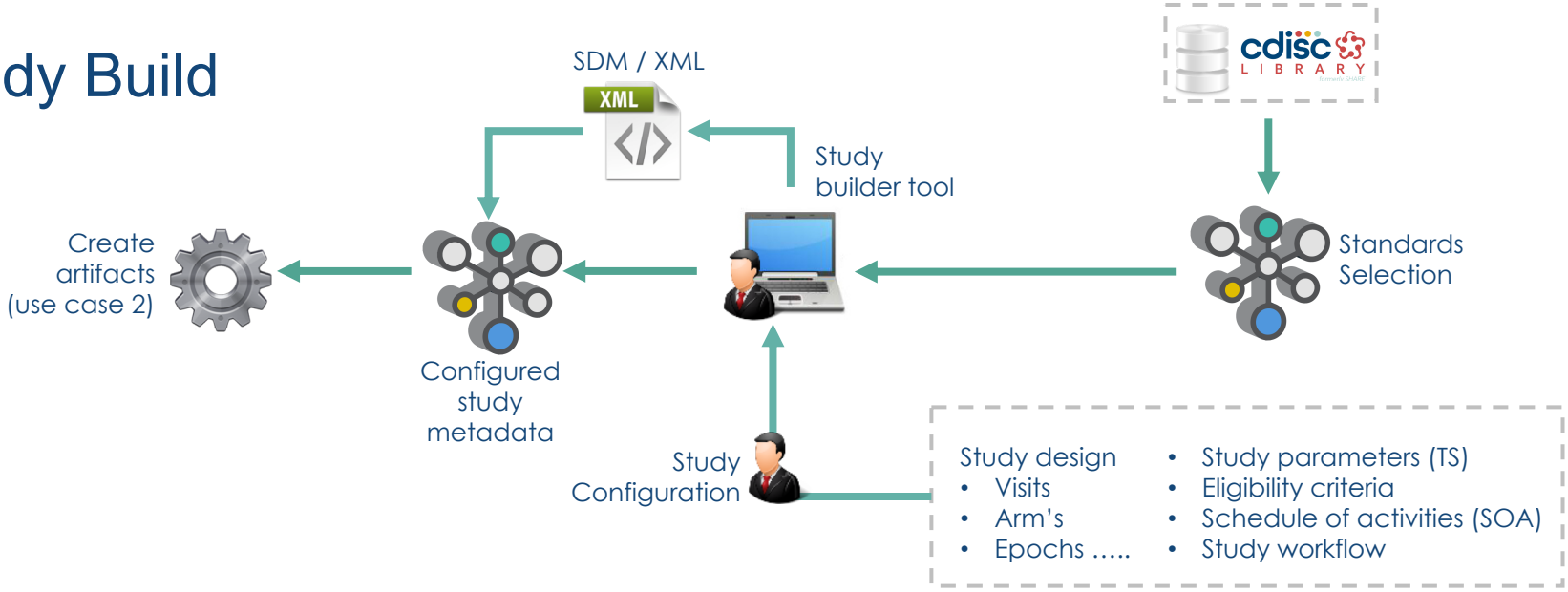


Use Case 2 : Build

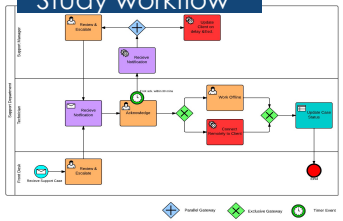
Adding study design, concept configuration & generate artifacts



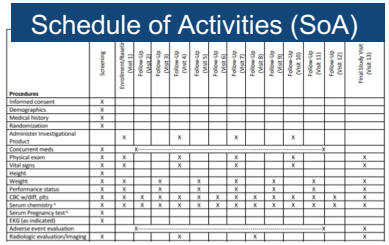
Study Build



Study workflow

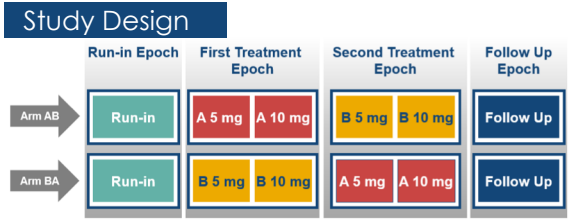


Schedule of Activities (SoA)



Procedures	Screening	Enrollment/Baseline (Visit 1)	Follow-Up (Week 2)	Follow-Up (Week 4)	Follow-Up (Week 6)	Follow-Up (Week 8)	Follow-Up (Week 10)	Follow-Up (Week 12)	Follow-Up (Week 14)	Follow-Up (Week 16)	Follow-Up (Week 18)	Follow-Up (Week 20)	Follow-Up (Week 22)	Follow-Up (Week 24)	Final Study Visit (Week 26)
Informed consent	X														
Demographics	X														
Medical history	X														
Randomization	X														
Administer Investigational Product		X				X				X				X	
Concurrent meds	X		X												X
Physical exam	X	X				X				X				X	
Vital signs	X	X				X				X				X	
Height	X														X
Weight	X	X				X				X				X	
Performance status	X	X				X				X				X	
CBC w/diff, plts	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Serum chemistry*	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Serum Pregnancy test*	X														
EKG (as indicated)	X														
Adverse event evaluation		X													X
Radiologic evaluation/Imaging	X					X				X					X

Study Design

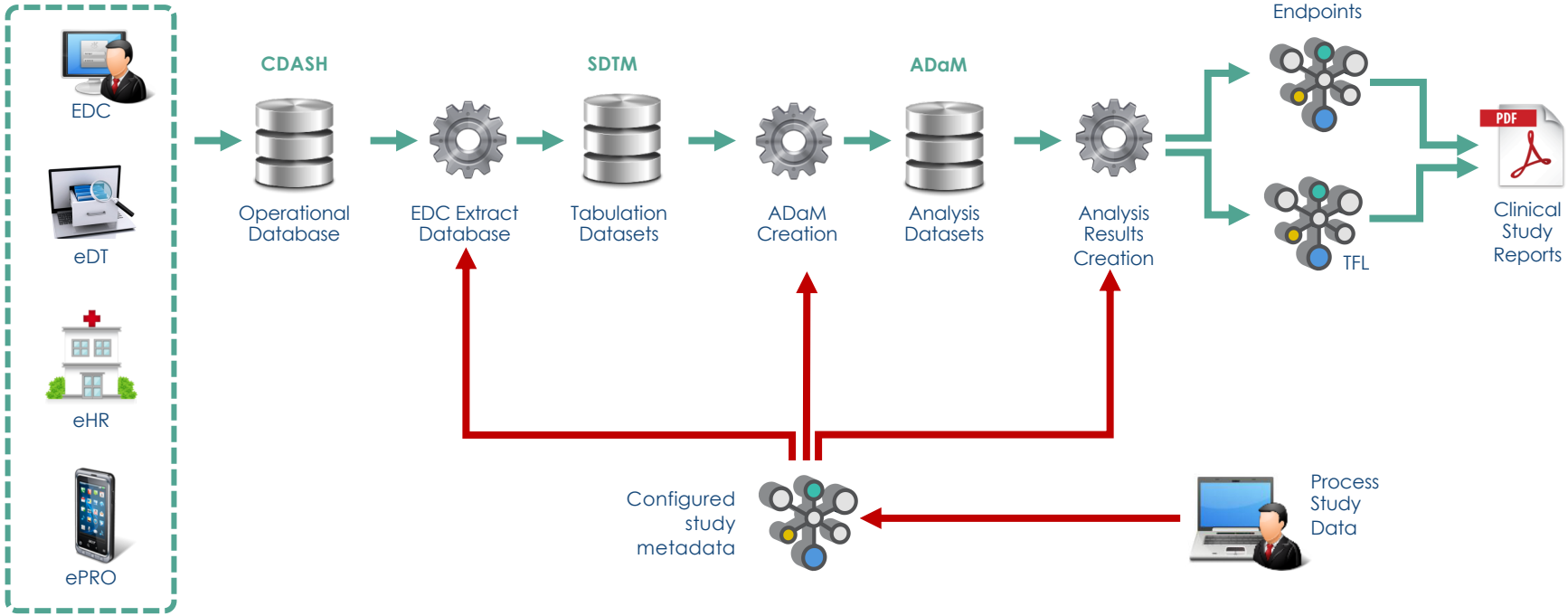


Study Parameters (TS)

XYZ	TS	1		ALSOIN	Existing Treatments	Y		C49488	CDISC	2011-06-10
XYZ	TS	1		AGEMAX	Planned Maximum Age of Subjects	P70Y			ISO 8601	
XYZ	TS	1		AGEMIN	Planned Minimum Age of Subjects	P18M			ISO 8601	
XYZ	TS	1		LENGTH	Planned Trial Length	P3M			ISO 8601	
XYZ	TS	1		PLANSUB	Planned Number of Subjects	300				
XYZ	TS	1		RANDOM	Trial is Randomized	Y		C49488	CDISC	2011-06-10
XYZ	TS	1		SEXPOP	Sex of Participants	BOTH		C49636	CDISC	2011-06-10
XYZ	TS	1		STOPRULE	Study Stop Rules	INTERIM ANALYSES FOR FUTILITY				
XYZ	TS	1		TBLIND	Trial Blinding Schema	DOUBLE BLIND		C15228	CDISC	2011-06-10
XYZ	TS	1		TCNTRL	Control Type	PLACEBO		C49648	CDISC	2011-06-10
XYZ	TS	1		TDIGRP	Diagnosis Group	Neurofibromatosis Syndrome (Disorder)		19133005	SNOMED	
XYZ	TS	1		TINDTP	Trial Indication Type	TREATMENT		C49656	CDISC	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
  - Effort calculation and Cost / Benefit Analysis
  - Scale up to deliver the standards metadata needed
  - Partnerships with vendors to ensure tools are made available

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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

Confluence

JIRA


Cmap Cloud

slack

Azure

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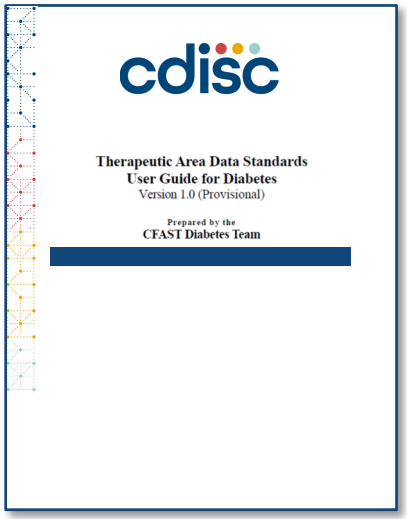
Project Standards Scope
Diabetes TAUG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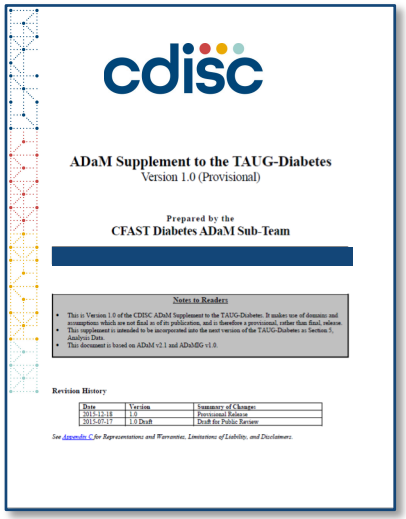
Therapeutic Area Data Standards
User Guide for Diabetes
Version 1.0 (Provisional)

Prepared by the
CFAST Diabetes Team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ADaM Supplement to the TAUG-Diabetes
Version 1.0 (Provisional)

Prepared by the
CFAST Diabetes ADaM Sub-Team

Notes to Readers

- This is Version 1.0 of the CDISC ADaM Supplement to the TAUG-Diabetes. It makes use of domains and assumptions which are not final as of its publications, and is therefore a provisional, rather than final, release.
- This supplement is intended to be incorporated into the next version of the TAUG-Diabetes as Section 5, Analysis Data.
- This document is based on ADaM v2.1 and ADaMIG v1.0.

Revision History

Date	Version	Summary of Changes
2015-12-18	1.0	Provisional Release
2015-07-17	1.0 Draft	Draft for Public Review

See Appendix C for Representations and Warranties, Limitations of Liability, and Disclaimers.

- 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.*

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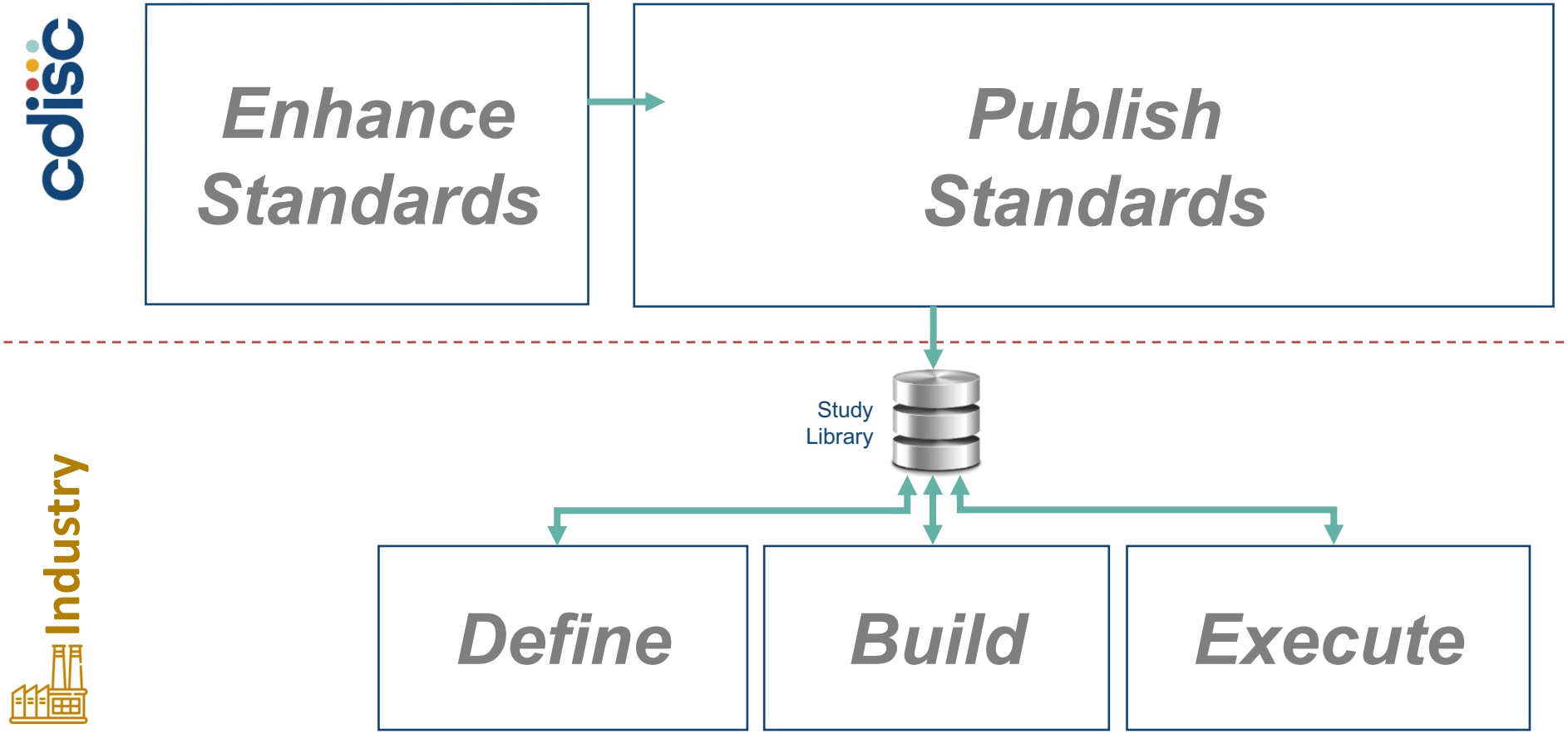
Project Standards Scope
FDA Use Case

- 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

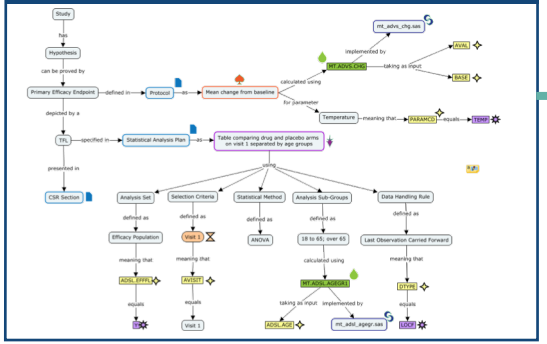
→ ***Reason for this scope:*** *Document FDA standard safety analysis requirements that may be expressed in the analysis concept maps; ensure the enhanced standards meet reviewers' needs*

CDISC 360 Workstreams



CDISC 360 Workstreams

Workstream 1 - *ENHANCE STANDARDS*



Create concepts in knowledge graphs

Workstream 2 - *PUBLISH STANDARDS*

Load into library

Biomedical Concepts
Analysis Concepts
Foundational Standards

cdisc LIBRARY
formerly SHARE

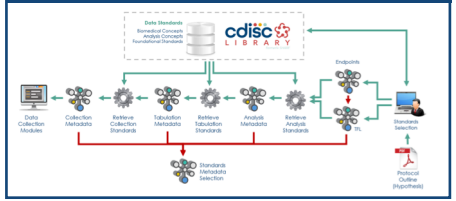
API

Extend API's

Transform concepts in machine readable form

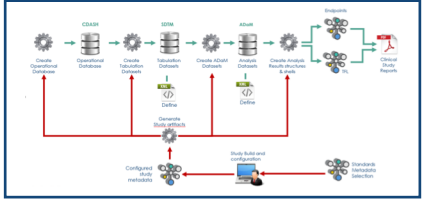
Study Library

Workstream 4 - *DEFINE*



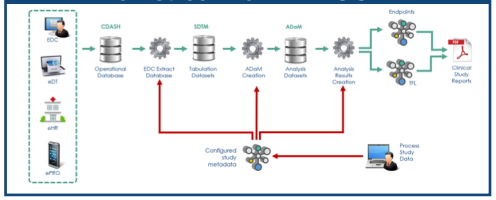
Identify and select standards specification (Use Case 1)

Workstream 5 - *BUILD*



Configure study specification and create artifacts (Use Case 2)

Workstream 6 - *EXECUTE*



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

Participation Summary

29 Organizations

67 Resources specified

Organization Types:

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


abbvie
Allergan
AMGEN
AstraZeneca
BIOMARIN
C+R RESEARCH
Celgene
dMed 缔脉
FDA
formedix
GILEAD
Johnson & Johnson
Lilly
MERCK
Microsoft
novo nordisk
ORACLE
Otsuka
Pfizer
PharmaStat
PINNACLE 21
SANOFI
S-CUBED
sas
TALENTMINE
VITA DATA SCIENCES
a division of SOFTWORLD
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

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

WS 4

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

WS 5

Lead: Tianna Umann

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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 Chelmilla
Lex Jansen
Prasanna Murugesan

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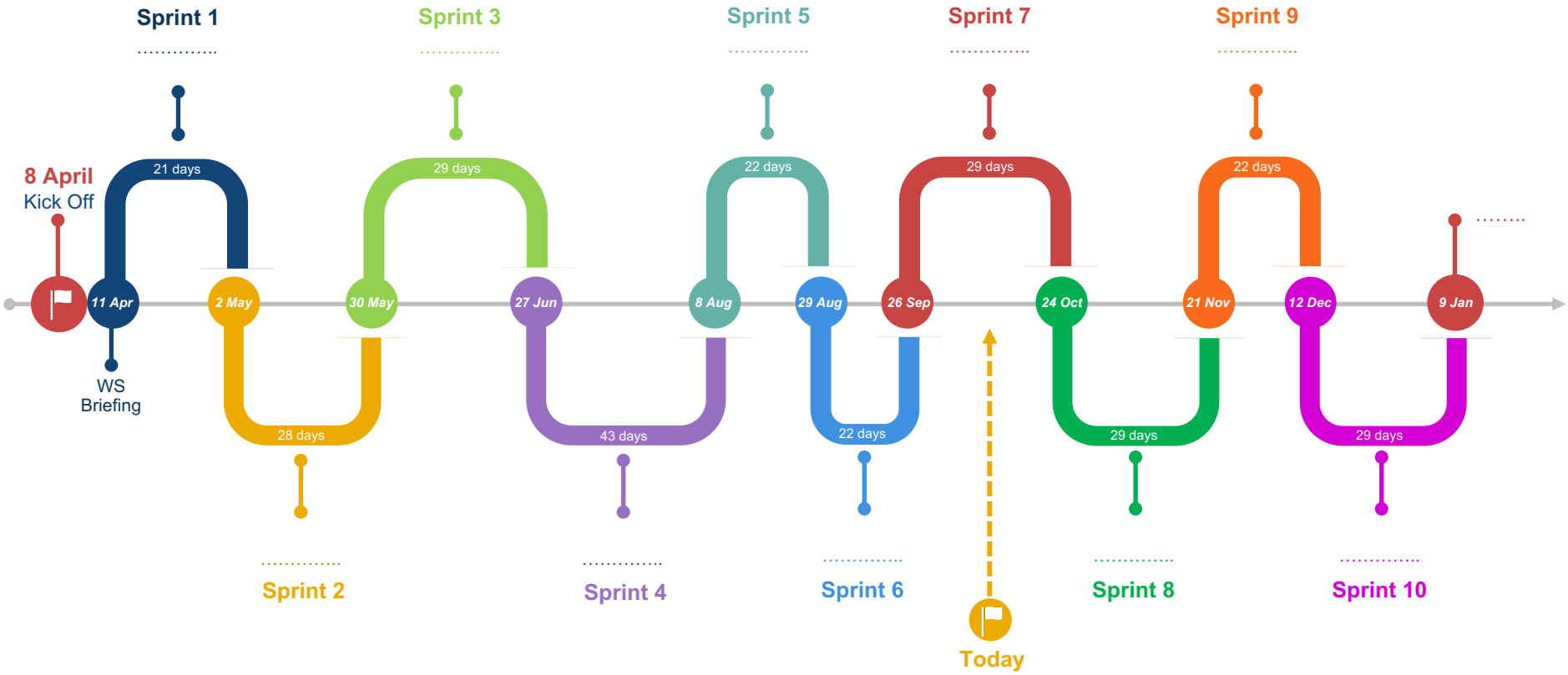
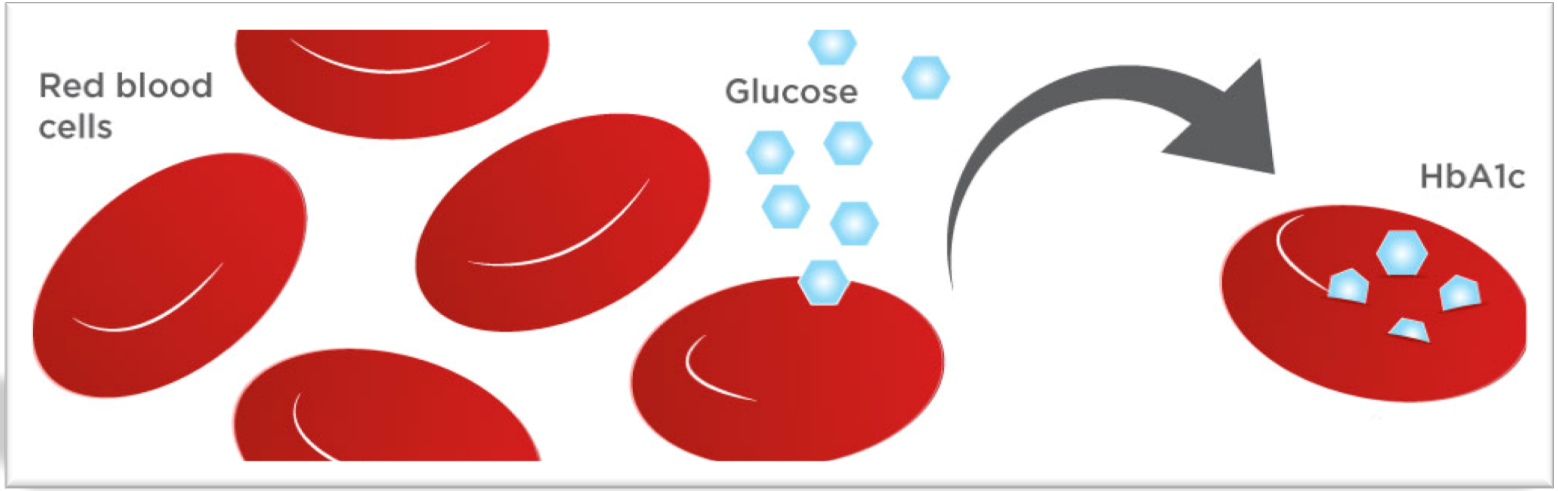
360 Sprint Cycles for 2019



4. Concepts Development - status

Organizing a Global Team

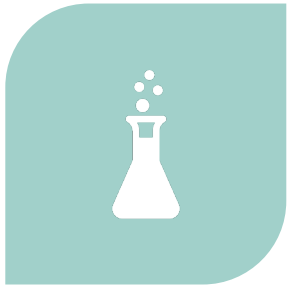
What is HbA1c?



Glycosylated Hemoglobin

Image source: https://www.ekfdiagnostics.com/res/HbA1c-Hemoglobin-banner

HbA1c, What's In a Name?



HBA1C

OR

HBA1C / HEMOGLOBIN

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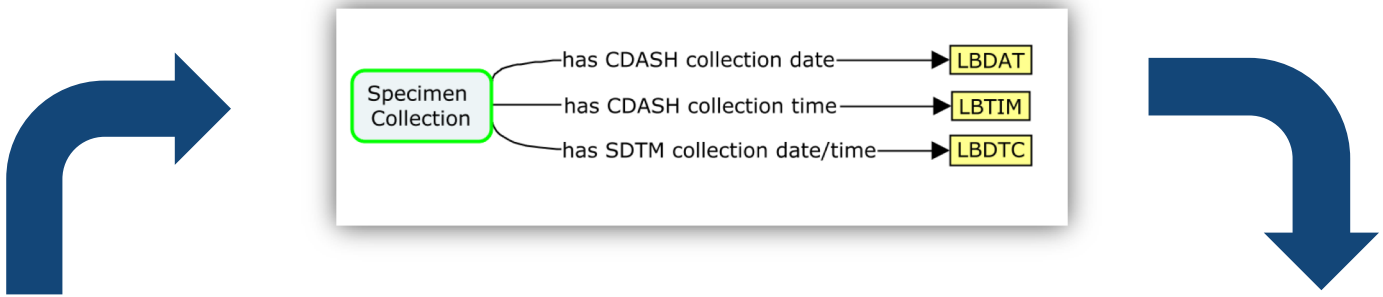
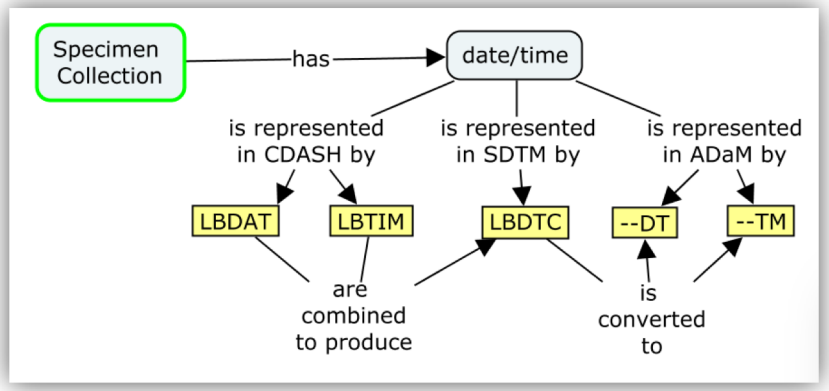
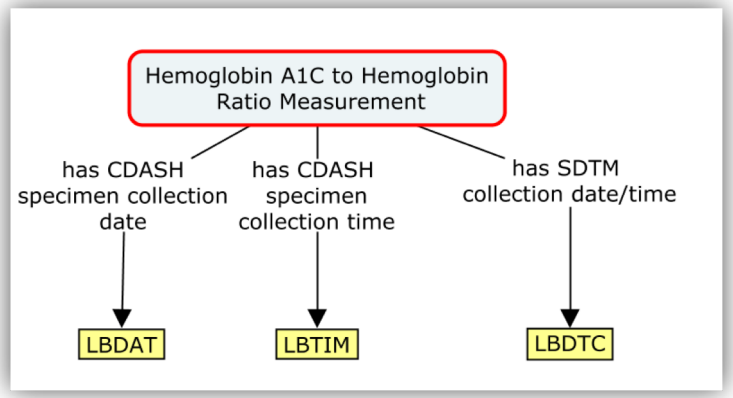
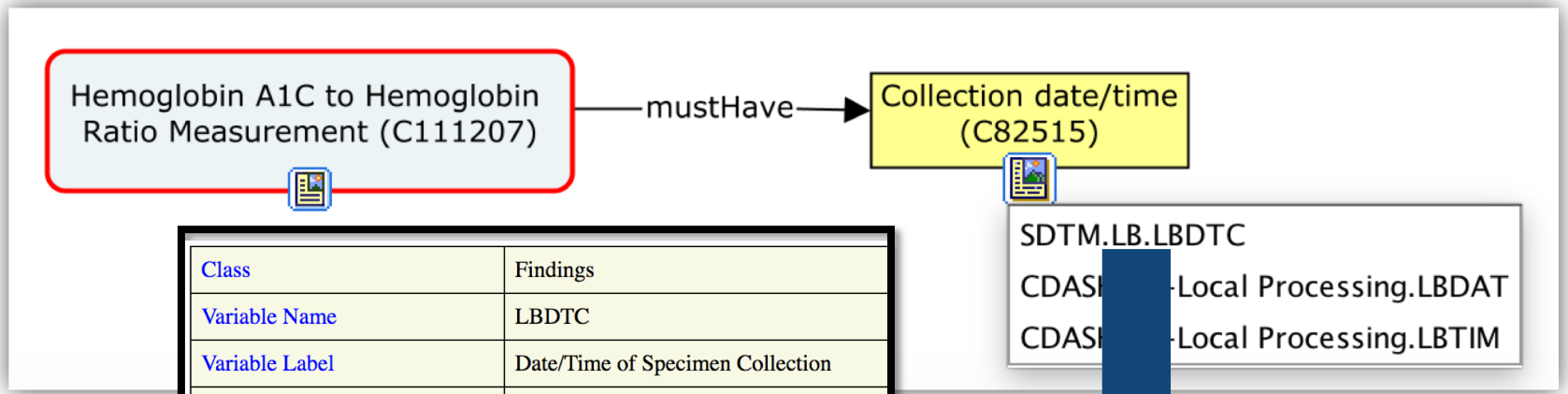
Finding Balance Between Linking Phrases and Elements







Binding Variables and Attributes to Concepts



Class	Findings
Variable Name	LBDTC
Variable Label	Date/Time of Specimen Collection
Type	Char
Core	Exp
Controlled Terms	ISO 8601
Role	Timing
Core	Exp
Sourced from SDTM 1.4 SDTMIG 3.2	

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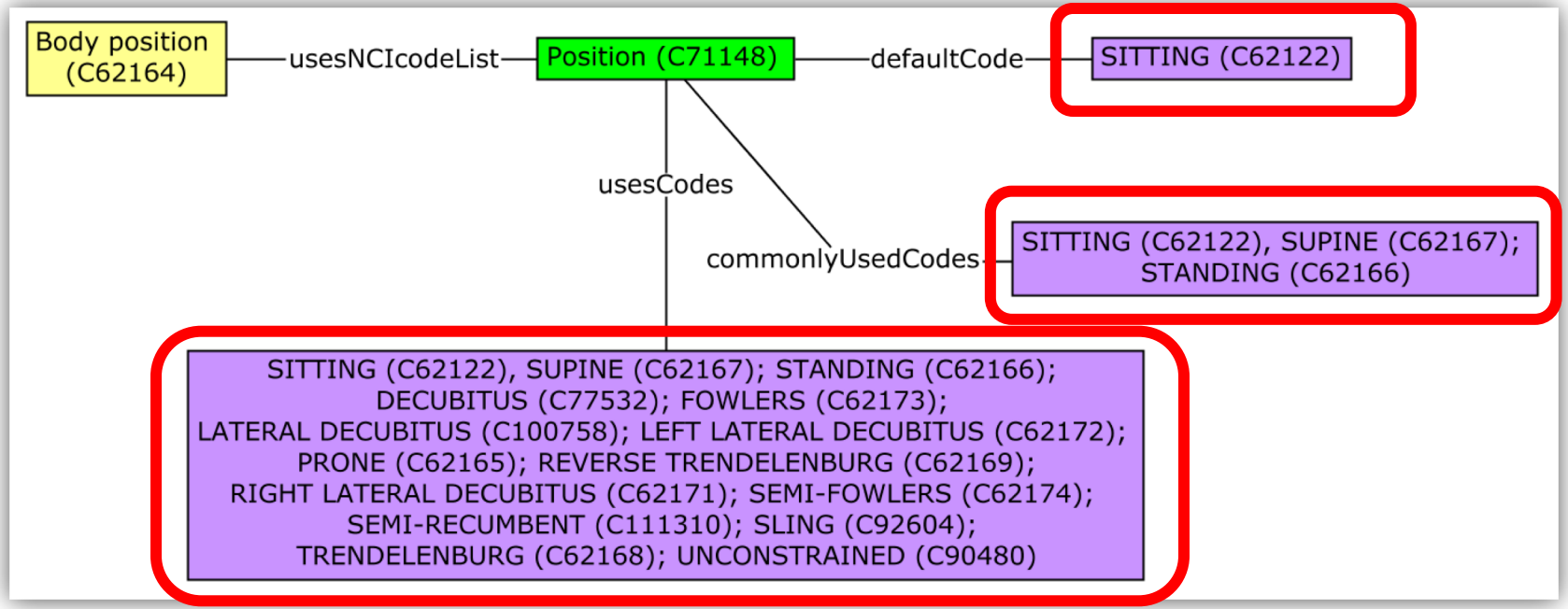
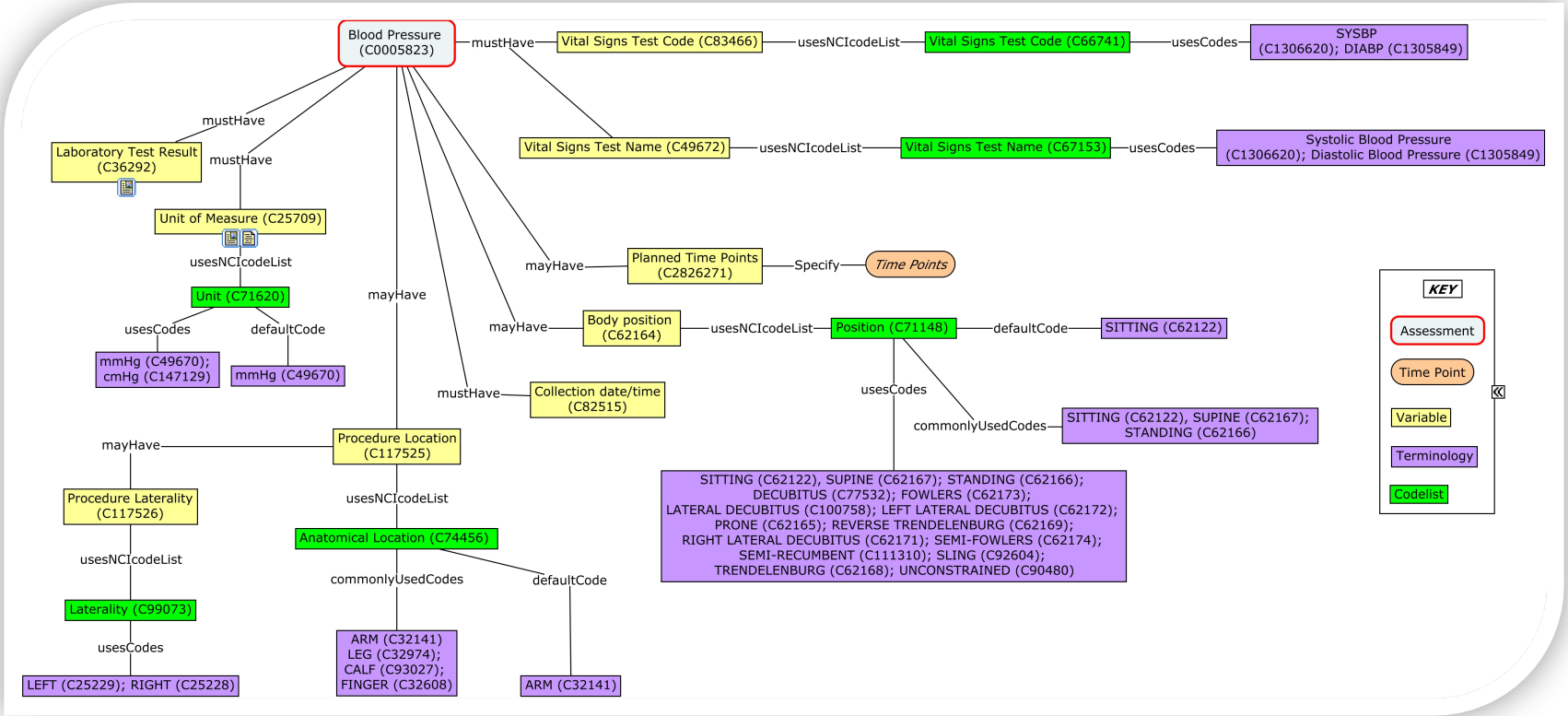
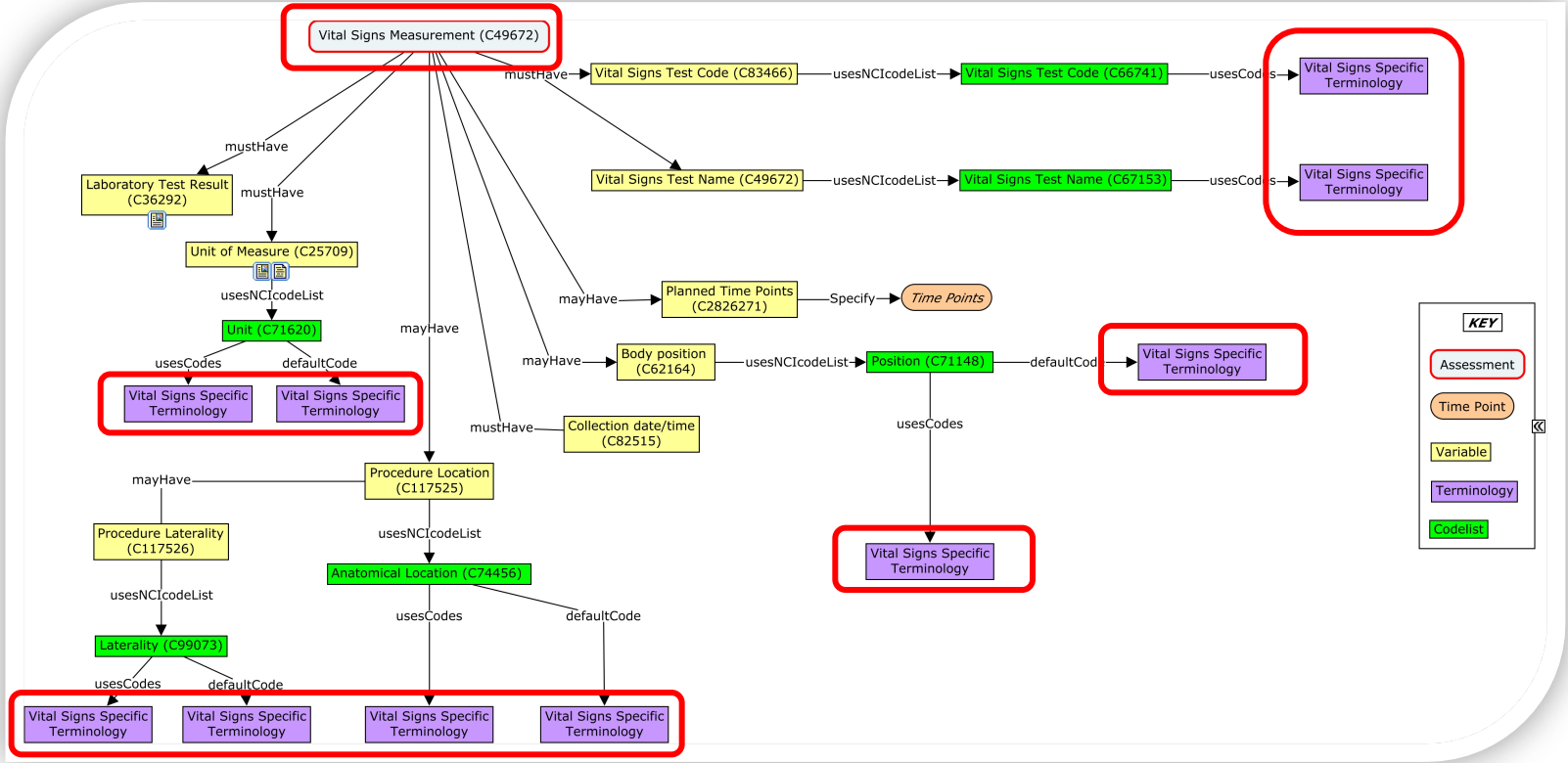
Configuration Options for Controlled Terminology



Biomedical Concept Specific Maps vs. Reference Maps



Biomedical Concept Specific Maps vs. Reference Maps



Next Steps for Concept Development

- Complete end-to-end metadata mapping
  - Collection
  - Analysis
  - Additional concepts (e.g., demographics, study drug exposure, etc.)
- Decide on the amount of study specific metadata that should be represented in the map
- Incorporate FDA safety end-point use-cases

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5. 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

- Scope of the User Experience:
  - Use the CDISC Library to create a simple study specification
  - Use concepts to generate an eCRF and Define-XML

➔ *These automations reflect what CDISC 360 achieved to date*

- After this User Experience, we will show how the back end works today

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Thank You!

Peter Van Reusel
Sam Hume