



Automation of SDTM Generation & Artifacts using CDISC 360 enriched standards

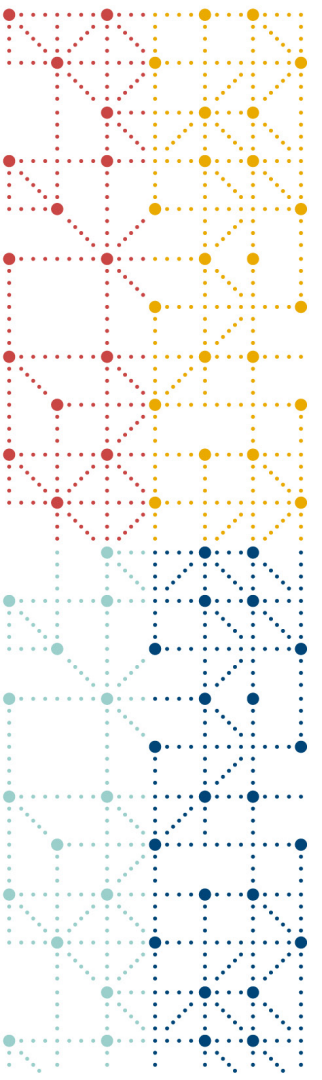
Bhavin Busa (Vita Data Sciences), Jianhui [Jimmy] Zhao (Allergan)
CDISC 360: The Journey So Far and the Road Ahead
April 28, 2020





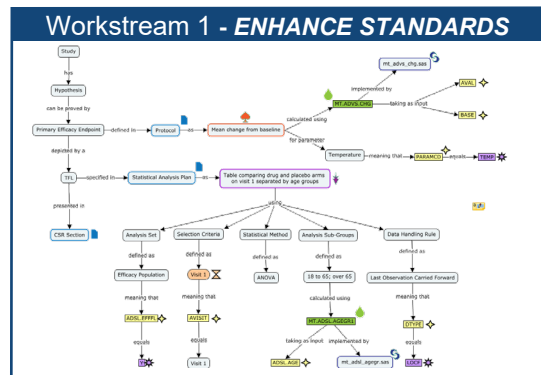
Agenda

1. Workstream 6 Introduction
2. Current State: CDASH to SDTM Execution
3. CDISC 360 Enriched Metadata
4. Future State with Concept-based Standards : CDASH to SDTM Execution
5. Process Flow for CDISC 360 Proof of Concept
6. Machine-readable Mapping Specifications
7. Learnings so far

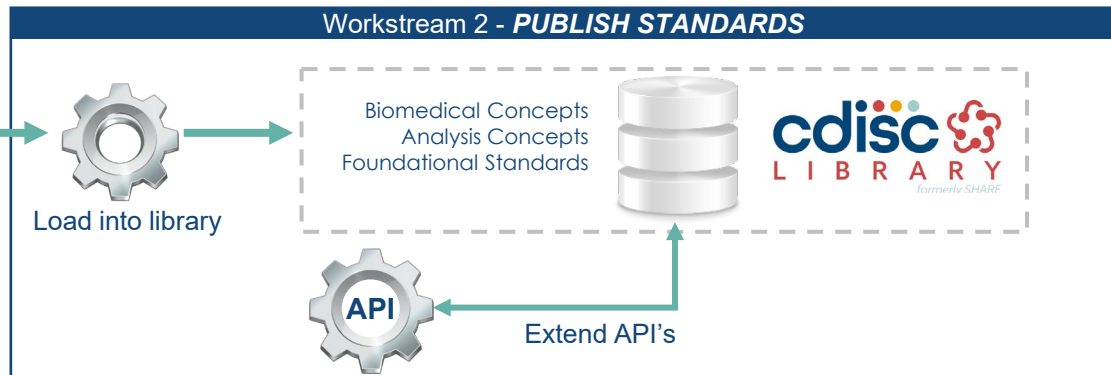


Workstream 6 Introduction

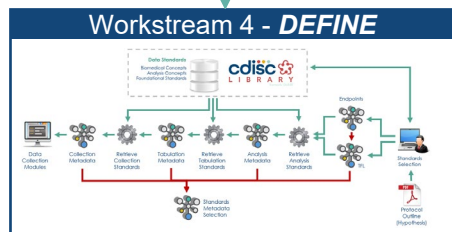
CDISC 360 Workstreams



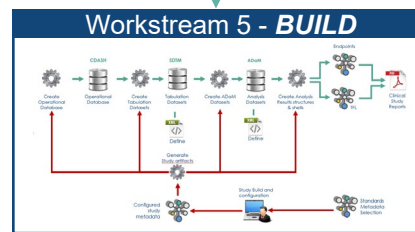
Create concepts in knowledge graphs



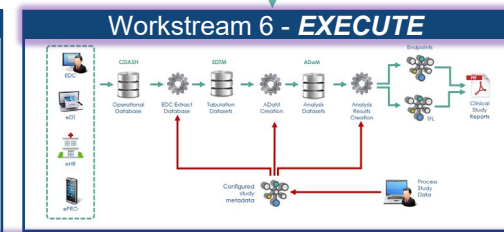
Study
Metadata
Library



Identify and select standards specification (Use Case 1)



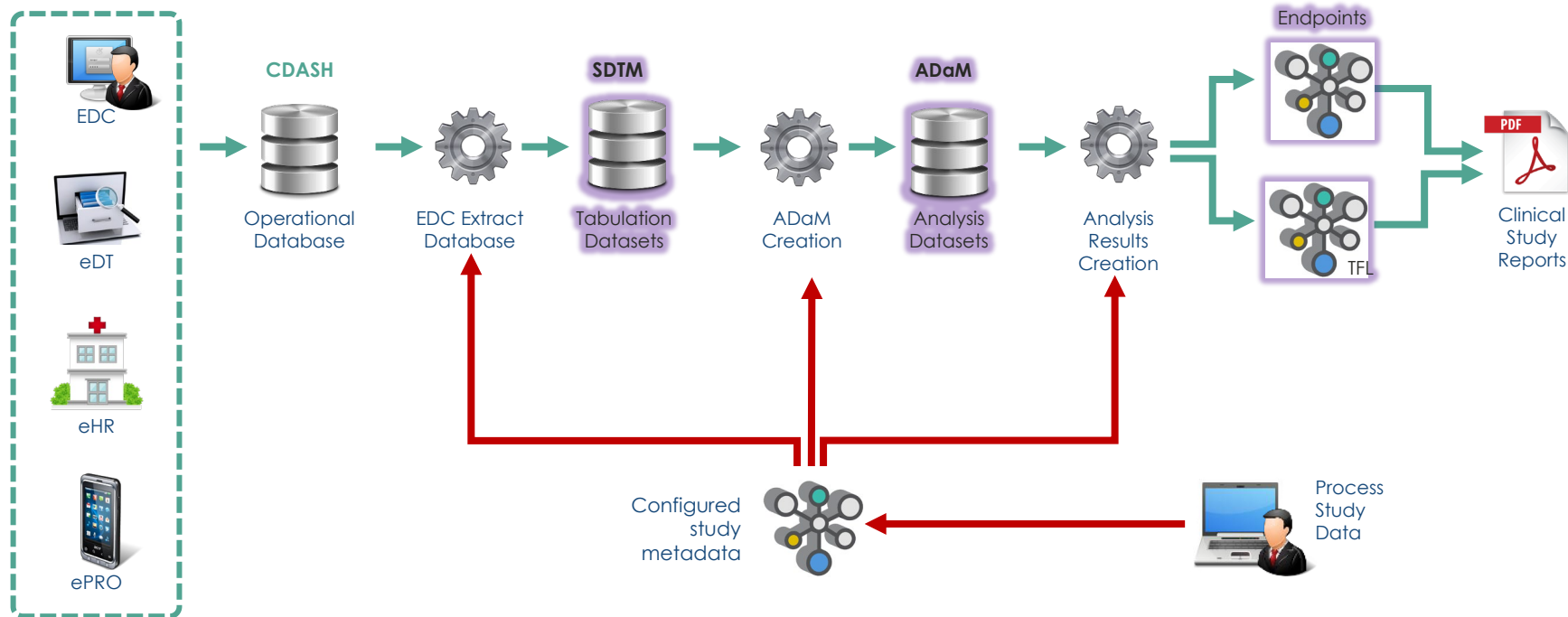
Configure study specification and create artifacts (Use Case 2)



Automatically process and transform data (Use Case 3)

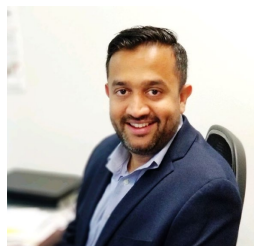
Use Case 3 (Workstream 6): Execute

Automatic population of data into artifacts



Workstream 6 & Task Team Leads

Workstream 6 Lead



Bhavin Busa,
Vita Data Sciences

SDTM/ADaM Automation Task Team Leads

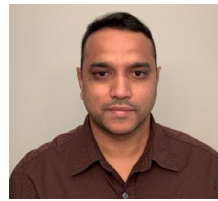


Kaja Najumudeen,
TalentMine



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**Prasanna
Murugesan,**
AstraZeneca



Stuart Malcolm,
Frontier Science

abbvie

 Allergan

AMGEN®

AstraZeneca 

 Bayer HealthCare

 BeiGene

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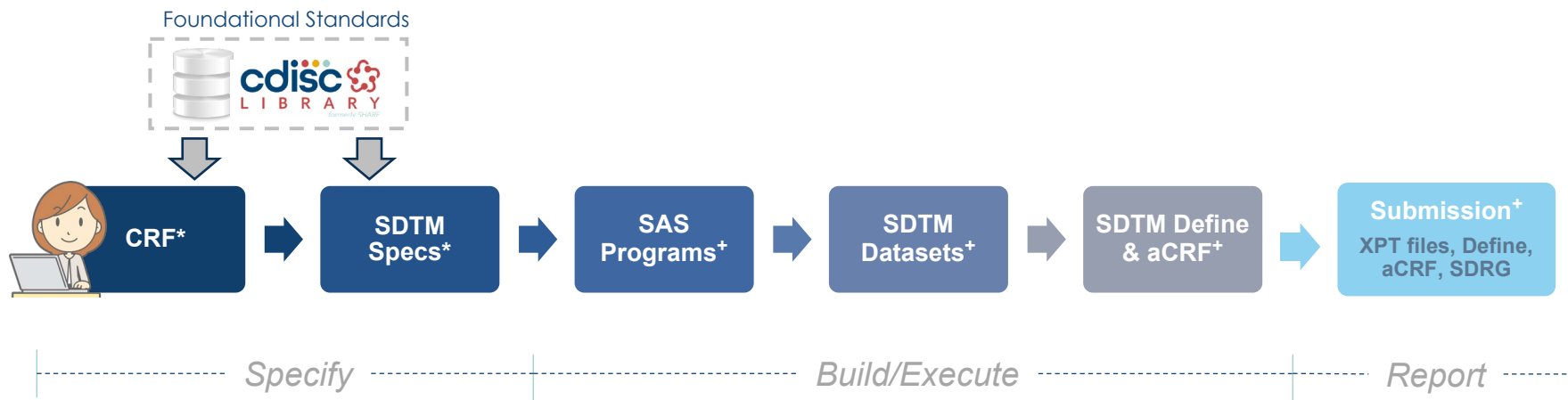
 xclinical

 Clinical
Solutions
Group



Current State - without Concept-based Standards

Current State - without Concept-based Standards: CDASH to SDTM Execution



* *Manual Process*

+ *Manual or Semi-automated Execution*



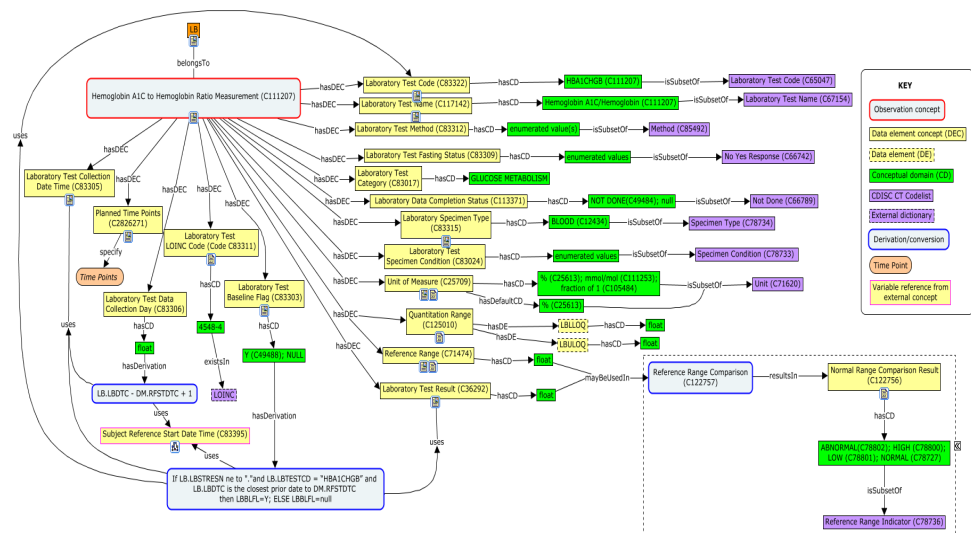
CDISC 360 Enriched Metadata

Machine-readable CDISC 360 Enriched Metadata

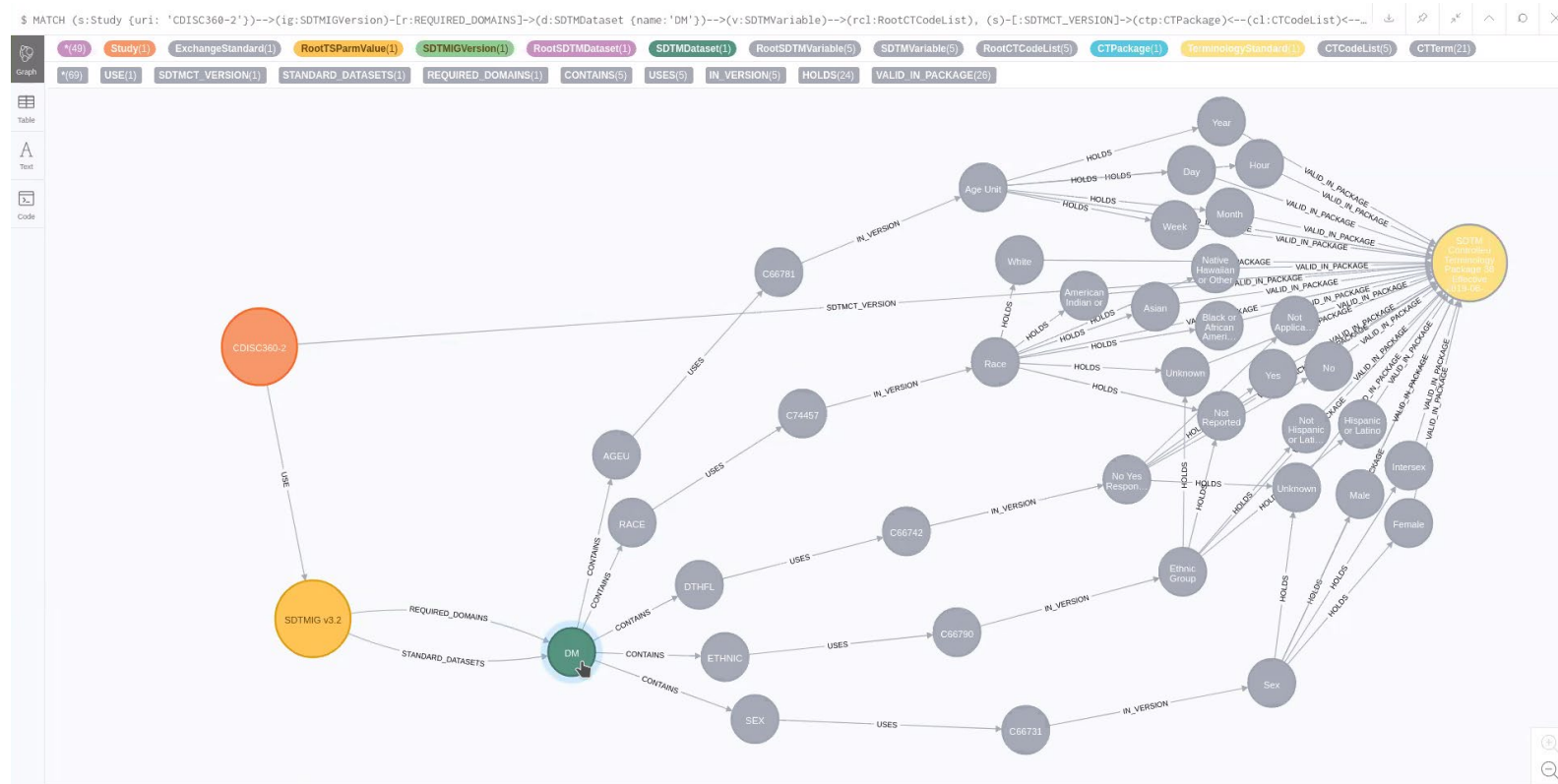


Concept-based Standards: Biomedical Concept

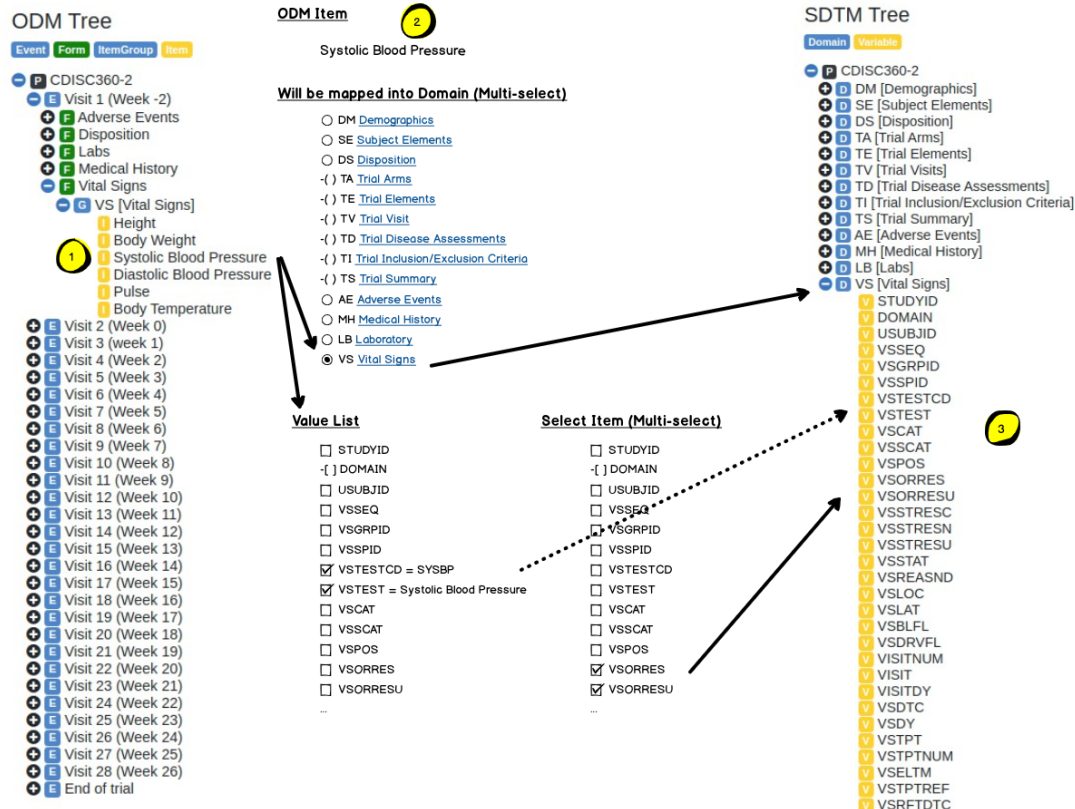
- Triple Store
- Linking controlled terminology to the variable - standardize value level metadata
- Linked derivations and algorithms to variable(s)
- Include process metadata (ETL instructions)
- Machine readable definition of validation rules



Linked Graph Model: Importing Concept-based Standards



Study Build of ODM.XML and Define.XML



ODM CRF Generated using Biomedical Concepts, Bindings, & Standards

ODM-based Vital Signs (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?	<input type="radio"/> Temperature
What was the result of the measurement?	<input type="text"/> . <input type="text"/>
What was the unit of the measurement?	<input type="radio"/> C <input type="radio"/> F

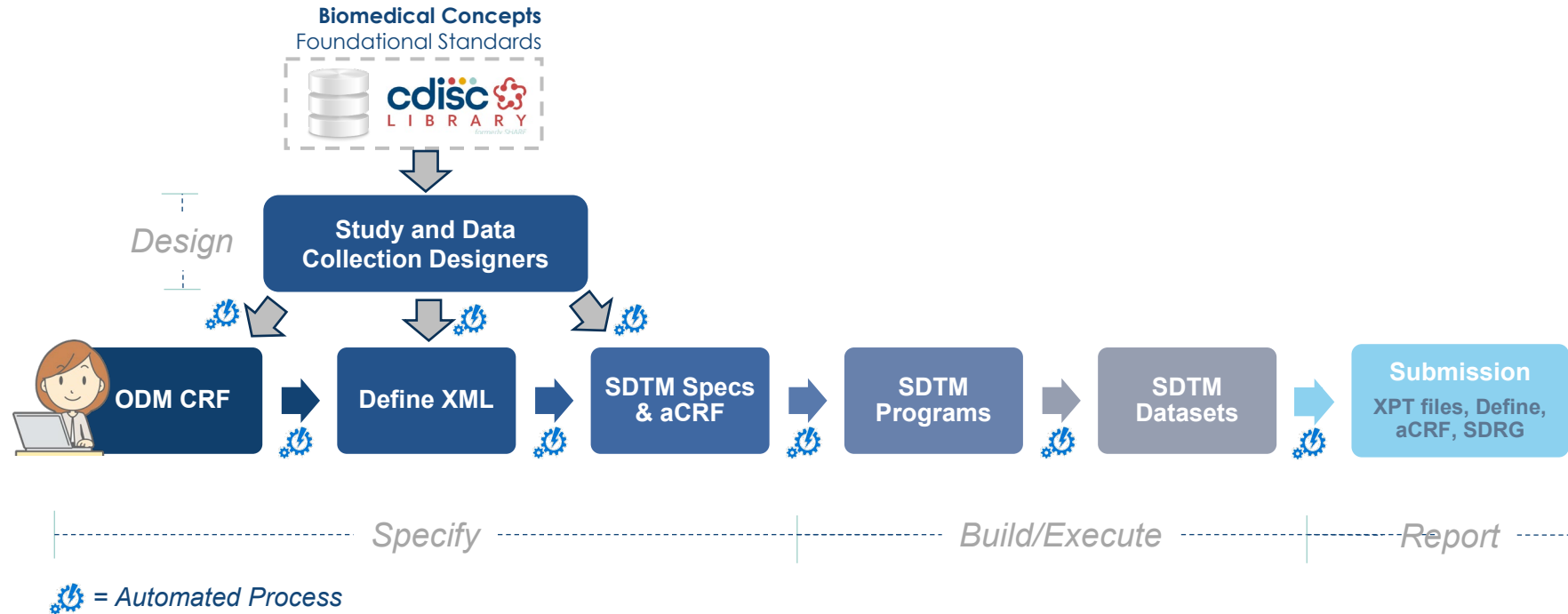
Group: VS Height	
OID=IG.BC.VS.HEIGHT, Repeating=No	
What is the vital sign test name?	<input type="radio"/> Height
What was the result of the measurement?	<input type="text"/> . <input type="text"/>
What was the unit of the measurement?	<input type="radio"/> cm <input type="radio"/> in <input type="radio"/> mm

Group: VS DiastolicBP	
OID=IG.BC.VS.DIASTOLICBP, Repeating=No	
What is the vital sign test name?	<input type="radio"/> Diastolic Blood Pressure
What was the result of the measurement?	<input type="text"/>
What was the unit of the measurement?	<input type="radio"/> mmHg <input type="radio"/> cmHg
What was the position of the subject during the measurement?	<input type="radio"/> SITTING <input type="radio"/> STANDING <input type="radio"/> SUPINE



Future State - with Concept-based Standards

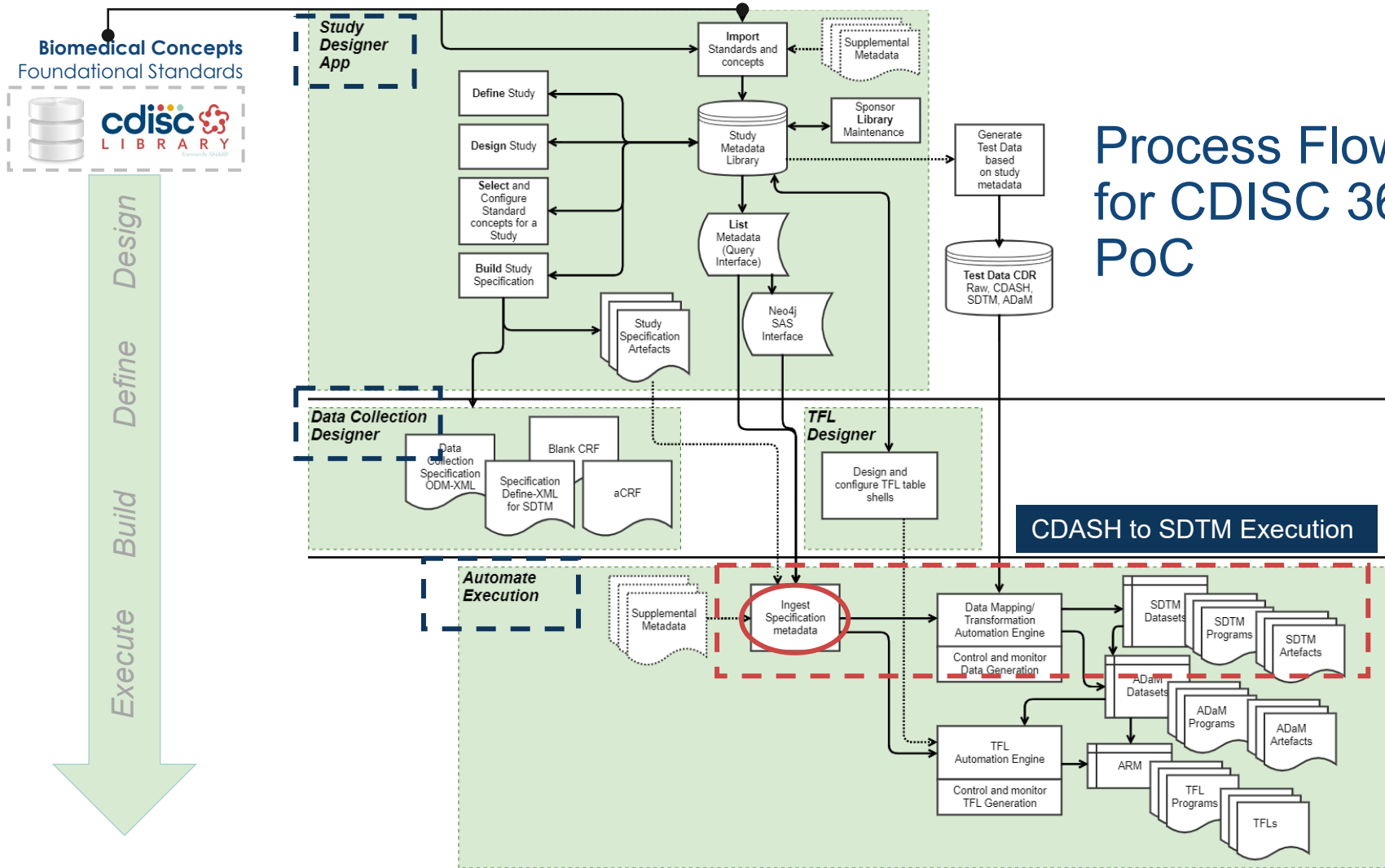
Future State - with Concept-based Standards: CDASH to SDTM Execution

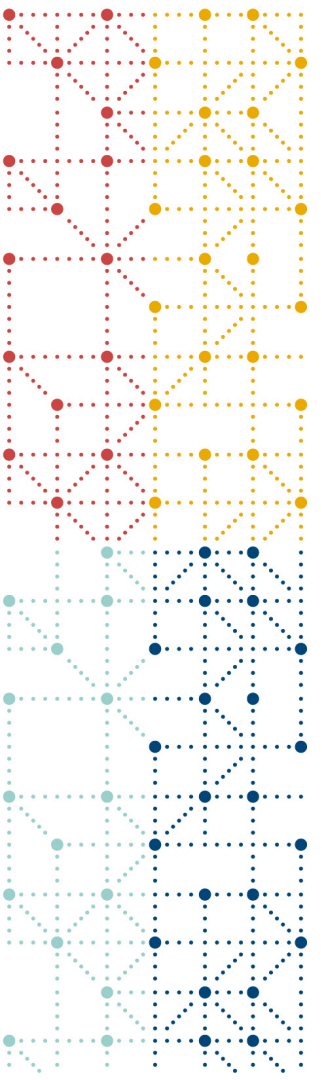




Process Flow for CDISC 360 Proof of Concept (PoC)

Process Flow for CDISC 360 PoC





Machine-readable Mapping Specifications



Essential Elements for Machine-readable Mapping Specifications

We break down the essential elements in 2 dimensions to meet the 4 key aspects of the machine readability

Dimension 1

- Source: location (library name), datasets, processing sequence
- Mapping: fields needed to describe how source transits to target
- Target: location (library name), datasets, processing sequence, attributes (label, class, structure, purpose, etc.)

Dimension 2

- Dataset Level: Transit datasets from source to target
- Variable Level: Map variables from source to target
- Value Level: Map variables from source to target under different conditions

Mapping Specifications: Dimension 1

Source	Mapping	Target
--------	---------	--------

A	B	C	D	F	G	H	I	J	K	L	M	N	O	P	Q
Source Sequence	Source Library	Source Dataset	Source Variable	Map Sequence	Origin	Method	Comment	Code List	Target Library	Target Dataset	Target Variable	Target Description	Target Data Type	Target Length	Target Sorting Order
1	CDASH	VS			Assigned		CDISC360-2		SDTM	VS	STUDYID	Study Identifier	text	10	1
1	CDASH	VS			Assigned		VS	DOMAIN	SDTM	VS	DOMAIN	Domain Abbreviation	text	2	2
1	CDASH	VS	SUBJID		Assigned	ALL.SUBJID			SDTM	VS	USUBJID	Unique Subject Identifier	text	14	3
1	CDASH	VS			Assigned	VS.VSSPID			SDTM	VS	VSSPID	Sponsor-Defined Identifier	text	4	5
1	CDASH	VS	VISIT		Convert			VISITNUM	SDTM	VS	VISITNUM	Visit Number	integer	8	16
1	CDASH	VS	VISIT		Predecessor			VISIT	SDTM	VS	VISIT	Visit Name	text	18	17
1	CDASH	VS	VSDAT		Assigned	VS.VSDTC			SDTM	VS	VSDTC	Date/Time of Measurements	date	10	19
1	CDASH	VS	VISDAT		Assigned	VS.VSDTC			SDTM	VS	VSDTC	Date/Time of Measurements	date	10	19
1	CDASH	VS			Derived	VS.VSBLFL			SDTM	VS	VSBLFL	Baseline Flag	text	1	14
2	SDTM	DM	RFSTDTC		Derived	VS.VSDY			SDTM	VS	VSDY	Study Day of Vital Signs	integer	8	20
2			VSDTC		Derived	VS.VSDY			SDTM	VS	VSDY	Study Day of Vital Signs	integer	8	20
3	SDTM	SV	VISITDY	1	Predecessor				SDTM	VS	VISITDY	Planned Study Day of Visit	integer	8	18
3	SDTM	SV	EPOCH	2	Predecessor			EPOCH	SDTM	VS	EPOCH	Epoch	text	9	15
4				3	Assigned	VS.VSTESTCD		VSTESTCD	SDTM	VS	VSTESTCD	Vital Signs Test Short Name	text	6	6
4				4	Derived	VS.VSORRES			SDTM	VS	VSORRES	Result or Finding in Original Units	text	4	9
4				5	Derived	VS.VSORRESU		VSUNIT	SDTM	VS	VSORRESU	Original Units	text	9	10
4				6	Assigned	VS.VSSTRESU		VSUNIT	SDTM	VS	VSSTRESU	Standard Units	text	9	13
4				7	Derived	VS.VSSTRESN			SDTM	VS	VSSTRESN	Numeric Result/Finding in Standard Units	float	8	12
4				8	Derived	VS.VSSTRESC			SDTM	VS	VSSTRESC	Character Result/Finding in Std Format	text	4	11
4				9	Assigned	VS.VSPOS		VSPOS	SDTM	VS	VSPOS	Position	text	7	13
5			VSTESTCD		Convert			VSTEST	SDTM	VS	VSTEST	Vital Signs Test Name	text	24	7
5			VSTESTCD		Convert			VSCAT	SDTM	VS	VSCAT	Category for Vital Signs	text	16	8
5					Derived	VS.VSSEQ			SDTM	VS	VSSEQ	Sequence Number	integer	8	4

Mapping Specifications: Dimension 2

Source			Mapping					Target		
Source Sequence	Source Library	Source Dataset	Subset Condition	Pre Processing	Join Type	Join Timing	Merge Key	Target Sequence	Target Library	Target Dataset
1	CDASH	VS						5	SDTM	VS
2	SDTM	DM			TARGET	PRE	USUBJID	5	SDTM	VS
3	SDTM	SV			TARGET	PRE	USUBJID, VISITNUM	5	SDTM	VS
4					SORT		USUBJID, VISITNUM, VSDTC	5	SDTM	VS
5					SORT		USUBJID, VSTESTCD, VISITNUM, VSDTC	5	SDTM	VS

Source Sequence	Source Library	Source Dataset	Source Variable	Map Sequence	Origin	Method	Comment	Code List	Target Library	Target Dataset	Target Variable	Target Description	Target Data Type	Target Length	Target Sorting Order
4				3	Assigned	VS.VSTESTCD		VSTESTCD	SDTM	VS	VSTESTCD	Vital Signs Test Short Name	text	6	6
4				4	Derived	VS.VSORRES		VSORRES	SDTM	VS	VSORRES	Result or Finding in Original Units	text	4	9
4				5	Derived	VS.VSORRESU		VSUNIT	SDTM	VS	VSORRESU	Original Units	text	9	10
4				6	Assigned	VS.VSSTRESU		VSUNIT	SDTM	VS	VSSTRESU	Standard Units	text	9	13
4				7	Derived	VS.VSSTRESN			SDTM	VS	VSSTRESN	Numeric Result/Finding in Standard Units	float	8	12
4				8	Derived	VS.VSSTRESC			SDTM	VS	VSSTRESC	Character Result/Finding in Std Format	text	4	11
4				9	Assigned	VS.VSPOS		VSPOS	SDTM	VS	VSPOS	Position	text	7	13

Source Sequence	Source Library	Source Dataset	Source Variable	Where Clause	Condition	Output	Map Sequence	Origin	Method	Comment	Code List	Target Library	Target Dataset	Target Variable	Target Data Type	Target Length	Significant Digits
3	WORK		VSORRES	VS.VSTESTCD.EQ.DIABP	DIABP_VSPERF = "Y"	Y	7	Convert		best.		SDTM	VS	VSSTRESN	float	8	0
3	CDASH	VS	SYSBP_VSORRES	VS.VSTESTCD.EQ.SYSBP	SYSBP_VSPERF = "Y"	Y	7	Convert		best.		SDTM	VS	VSSTRESN	float	8	0
3	CDASH	VS	HR_VSORRES	VS.VSTESTCD.EQ.PULSE	HR_VSPERF = "Y"	Y	7	Convert		best.		SDTM	VS	VSSTRESN	float	8	0
3	CDASH	VS	TEMP_VSORRES	VS.VSTESTCD.EQ.TEMP	TEMP_VSPERF = "Y"	Y	7	Convert		best.		SDTM	VS	VSSTRESN	float	8	1
3	CDASH	VS	HEIGHT_VSORRES	VS.VSTESTCD.EQ.HEIGHT	HEIGHT_VSPERF = "Y"	Y	7	Derived	VS.VSSTRESN.item1			SDTM	VS	VSSTRESN	float	8	2
3	CDASH	VS	WEIGHT_VSORRES	VS.VSTESTCD.EQ.WEIGHT	WEIGHT_VSPERF = "Y"	Y	7	Convert		best.		SDTM	VS	VSSTRESN	float	8	0

Mapping Specifications: Dataset Level

	Source Sequence	Source Library	Source Dataset	Pre Subset Condition	Pre Processing	Join Type	Join Timing	Join Merge Key	Target Sequence	Target Library	Target Dataset
1	1	CDASH	VS						5	SDTM	VS
2	2	SDTM	DM			TARGET	PRE	USUBJID	5	SDTM	VS
3	3	SDTM	SV			TARGET	PRE	USUBJID, VISITNUM	5	SDTM	VS
4	4					SORT		USUBJID, VISITNUM, VSDTC	5	SDTM	VS
5	5					SORT		USUBJID, VSTESTCD, VISITNUM, VSDTC	5	SDTM	VS

```
data VS1;
  set CDASH.VS;
  /*****
    variable level: Source Sequence = 1
  *****/
run;
```

```
proc sort data=VS1; by SUBJID;
proc sort data=CDASH.DM OUT=DM2; by USUBJID;

data VS2;
  merge DM2 (in=a) VS1 (in=b);
  by USUBJID;
  if b;
  /*****
    variable level: Source Sequence = 2
  *****/
run;
```

... Sequence 3, 4

```
proc sort data=VS4;
  by USUBJID VSTESTCD VISITNUM VSDTC;
run;

data SDTM.VS;
  set VS4;
  by USUBJID VSTESTCD VISITNUM VSDTC;

  /*****
    variable level: Source Sequence = 6
  *****/

run;
```


Mapping Specifications: Variable Level

Source Sequence	Source Library	Source Dataset	Source Variable	Map Sequence	Origin	Method	Comment	Code List	Target Library	Target Dataset	Target Variable	Target Description	Target Data Type	Target Length	Target Sorting Order
1	CDASH	VS			Assigned		VS	DOMAIN	SDTM	VS 1	DOMAIN	Domain Abbreviation	text	2	2
1	CDASH	VS	SUBJID		Assigned	ALL.USUBJID			SDTM	VS 2	USUBJID	Unique Subject Identifier	text	14	3
1	CDASH	VS	VISIT		Convert			VISITNUM	SDTM	VS 3	VISITNUM	Visit Number	integer	8	16
1	CDASH	VS	VISIT		Predecessor			VISIT	SDTM	VS 4	VISIT	Visit Name	text	18	17
1	CDASH	VS	VSDAT		Assigned	VS.VSDTC			SDTM	VS 5	VSDTC	Date/Time of Measurements	date	10	19
1	CDASH	VS			Derived	VS.VSBLFL			SDTM	VS 6	VSBLFL	Baseline Flag	text	1	14

ID	Description	Function	Parameter
2	Concatenation of STUDYID and SUBJID	Concatenate	dot/STUDYID/SUBJID
5	Convert assessment date (VISDAT/VSDAT) to ISO8601 date format.	ISODTC	VISDAT/VSDAT
6	Baseline flag set to Y when the assessment is collected at the visit marked as baseline in the trial flowchart.	Baseline	"VISIT/VISIT 2 (WEEK 0)"

SAS Code
2
USUBJID = catx('.', STUDYID, SUBJID); if not missing(VISDAT) then
5
VSDTC = put(VISDAT, e8601da.); else if not missing(VSDAT) then VSDTC = put(VSDAT, e8601da.);
6
if VISIT = "VISIT 2 (WEEK 0)" then VSBLFL = 'Y';

```

data VS1;
    set CDASH.VS;

    *** Variable level processing ;

    1 DOMAIN    = 'VS';
    2 USUBJID   = catx('.', STUDYID, SUBJID);
    3 VISITNUM  = input(put(VISIT, $VISITNUM.), BEST.);

    4 [origin = Predecessor, do nothing];

    5 if      not missing(VISDAT) then
        VSDTC = put(VISDAT, E8601DA.);
    else if not missing(VSDAT) then
        VSDTC = put(VSDAT, E8601DA.);

    6 if VISIT = "VISIT 2 (WEEK 0)" then VSBLFL = 'Y';
run;

```

Mapping Specifications: Value Level

Source Sequence	Source Library	Source Dataset	Source Variable	Where Clause	Condition	Output	Map Sequence	Origin	Method	Comment	Code List	Target Library	Target Dataset	Target Variable	Target Data Type	Target Length	Significant Digits
3	CDASH	VS		VS.VSTESTCD.EQ.DIABP	DIABP_VSPERF = 'Y'	Y	3	Assigned		DIABP		SDTM	VS	VSTESTCD	text	6	
3	CDASH	VS	DIABP_VSORRES	VS.VSTESTCD.EQ.DIABP	DIABP_VSPERF = 'Y'	Y	4	Predecessor				SDTM	VS	VSORRES	text	4	
3	CDASH	VS	DIABP_VSORRESU	VS.VSTESTCD.EQ.DIABP	DIABP_VSPERF = 'Y'	Y	5	Predecessor				SDTM	VS	VSORRESU	text	9	
3	CDASH	VS		VS.VSTESTCD.EQ.DIABP	DIABP_VSPERF = 'Y'	Y	6	Assigned		mmHg		SDTM	VS	VSSTRESU	text	9	
3	WORK		VSORRES	VS.VSTESTCD.EQ.DIABP	DIABP_VSPERF = 'Y'	Y	7	Convert			best.	SDTM	VS	VSSTRESN	float	8	0
3	WORK		VSSTRESN	VS.VSTESTCD.EQ.DIABP	DIABP_VSPERF = 'Y'	Y	8	Convert			4.0	SDTM	VS	VSSTRESC	text	6	
3	CDASH	VS	DIABP_VSPOS	VS.VSTESTCD.EQ.DIABP	DIABP_VSPERF = 'Y'	Y	9	Predecessor				SDTM	VS	VSPOS	text	7	
3	CDASH	VS		VS.VSTESTCD.EQ.HEIGHT	HEIGHT_VSPERF = 'Y'	Y	3	Assigned		HEIGHT		SDTM	VS	VSTESTCD	text	6	
3	CDASH	VS	HEIGHT_VSORRES	VS.VSTESTCD.EQ.HEIGHT	HEIGHT_VSPERF = 'Y'	Y	4	Predecessor				SDTM	VS	VSORRES	text	4	
3	CDASH	VS	HEIGHT_VSORRESU	VS.VSTESTCD.EQ.HEIGHT	HEIGHT_VSPERF = 'Y'	Y	5	Predecessor				SDTM	VS	VSORRESU	text	9	
3	CDASH	VS		VS.VSTESTCD.EQ.HEIGHT	HEIGHT_VSPERF = 'Y'	Y	6	Assigned		m		SDTM	VS	VSSTRESU	text	9	
3	CDASH	VS	HEIGHT_VSORRES	VS.VSTESTCD.EQ.HEIGHT	HEIGHT_VSPERF = 'Y'	Y	7	Derived	VS.VSSTRESN.item1			SDTM	VS	VSSTRESN	float	8	2
3	CDASH	VS	VSSTRESN	VS.VSTESTCD.EQ.HEIGHT	HEIGHT_VSPERF = 'Y'	Y	8	Convert			4.2	SDTM	VS	VSSTRESC	text	6	
3	CDASH	VS		VS.VSTESTCD.EQ.HEIGHT	HEIGHT_VSPERF = 'Y'	Y	9	Assigned		NULL		SDTM	VS	VSPOS	text	7	

```

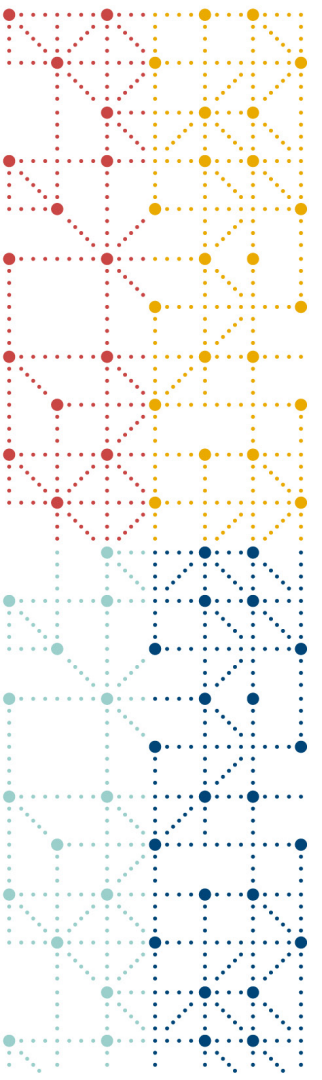
data VS3;
  set CDASH.VS;

  if DIABP_VSPREF = 'Y' then do;
    VSTESTCD = 'DIABP';
    VSORRES = DIABP_VSORRES;
    VSORRESU = DIABP_VSORRESU;
    VSSTRESN = 'mmHg';
    VSSTRESN = INPUT(VSORRES, BEST.);
    VSSTRESC = PUT(VSSTRESN, 4.0);
    VSPOS = DIABP_VSPOS;
    OUTPUT;
  end;
  
```

```

*** CONTINUE ***;

if HEIGHT_VSPREF = 'Y' then do;
  VSTESTCD = 'HEIGHT';
  VSORRES = HEIGHT_VSORRES;
  VSORRESU = HEIGHT_VSORRESU;
  VSSTRESN = 'm';
  VSSTRESN = INPUT(VSORRES, BEST.);
  VSSTRESC = PUT(VSSTRESN, 4.0);
  OUTPUT;
end;
run;
  
```

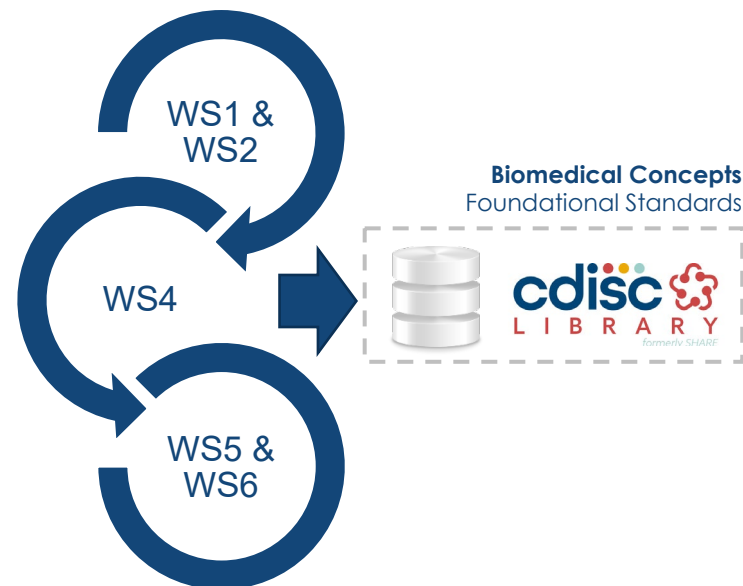


Learnings so far

Machine-readable Metadata

Machine-readable Metadata

- CDISC 360 Enriched Metadata = Structural + Conceptual + Semantic + Process [Key to Automation]
 - Content is part of the standards (CDISC library)
 - ETL Metadata (mapping inference & derivation)
- System agnostic standards, concepts and elements
 - Can be consumed by any tool
 - Organization can build an automation engine their own way
- Iterations are needed to learn and evolve
 - Strong workstream collaboration: CDISC, Industry volunteers & Microsoft



Automation of ADaM & TLF Generation using CDISC 360 enriched standards

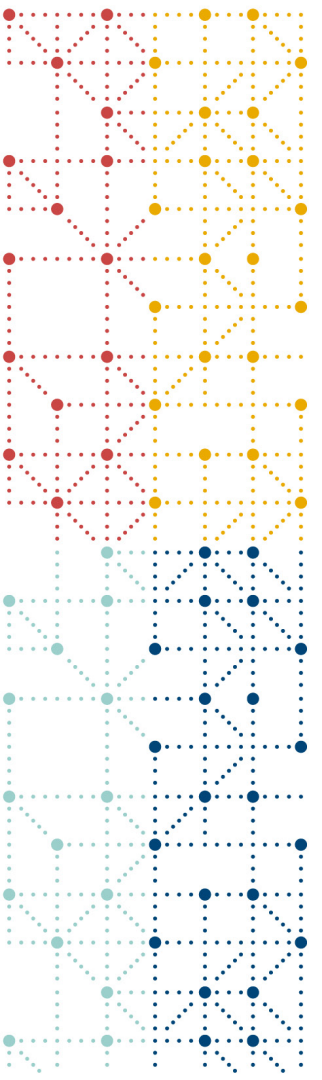
Bhavin Busa (Vita Data Sciences), Prasanna Murugesan (AstraZeneca)
CDISC 360: The Journey So Far and the Road Ahead
April 28, 2020





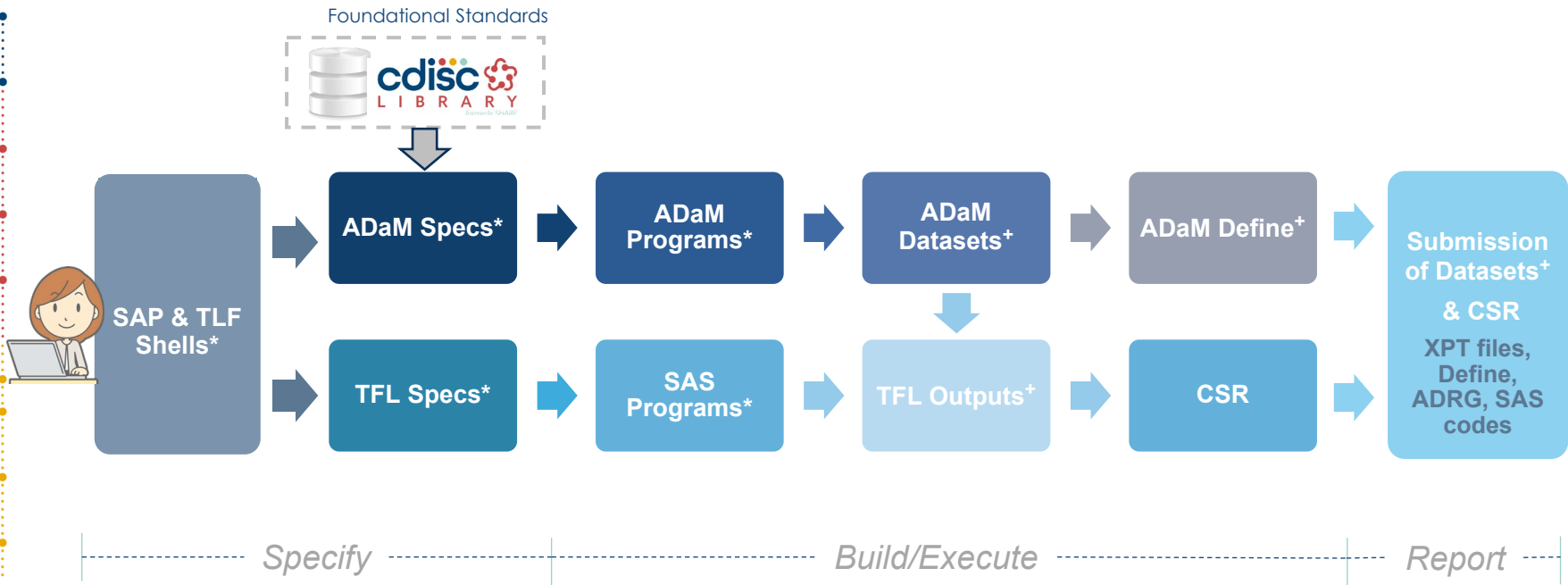
Agenda

1. Current State: Analysis Datasets & TFL Execution
2. CDISC 360 Enriched Metadata
 - CDISC 360 Enriched (Machine-readable) TFL Metadata
3. Future State with Concept-based Standards: Analysis Datasets & TFL Execution
4. Process Flow for CDISC 360 Proof of Concept (PoC)
5. TFL Automation Engine – PoC Design
6. TFL Automation Engine – Live Demo
7. Learnings so far
8. Next Steps



Current State - without Concept-based Standards

Current State - without Concept-based Standards: Analysis Datasets and TFL Generation





CDISC 360 Enriched Metadata

CDISC 360: The Art of the Possible

The screenshot displays the CDISC 360 web application interface. The top navigation bar is blue and includes the CDISC 360 logo, the text "Powered by Microsoft", a search bar labeled "Search the CDISC Library", and icons for refresh, user profile, settings, and a user avatar. The left sidebar contains a vertical list of six selection steps, each with a numbered circle and a checkmark: 1. Disease Area (Endocrine), 2. Therapeutic Area (Diabetes - Type 2), 3. Standards Focus (Study Endpoint), 4. Study Endpoint (Analysis of Glycated Hemoglobin), 5. Standard Analyses (Mean Change from Baseline in HbA1c (%) Over Time), and 6. Selection Summary (highlighted with a blue circle). The main content area is titled "Selection Summary" and is divided into three columns. The first column, "Study Endpoint", contains a box for "Analysis of Glycated Hemoglobin" with a description of a Phase III study and a "View details" link. The second column, "Analysis", contains a box for "Mean Change from Baseline in HbA1c (%) Over Time" featuring a line graph showing mean change over time for two groups (Control and Treatment) and "View details" and "View analysis results metadata" links. The third column, "Analysis Datasets", contains two boxes: "ADSL" (Analysis Data Subject Level) with links for metadata, sample data, and structure, and "ADHBA1C" (DBS - Structured Dataset) with similar links. At the bottom, there is a "Back" button and a "Save Selection" button.

CDISC 360

Powered by Microsoft

Search the CDISC Library

1 Disease Area
✓ Endocrine

2 Therapeutic Area
✓ Diabetes - Type 2

3 Standards Focus
✓ Study Endpoint

4 Study Endpoint
✓ Analysis of Glycated Hemoglobin

5 Standard Analyses
✓ Mean Change from Baseline in HbA1c (%) Over Time

6 Selection Summary
Endocrine
Diabetes - Type 2
Study Endpoint
Analysis of Glycated Hemoglobin
Mean Change from Baseline in HbA1c (%) Over Time

Selection Summary

Study Endpoint

Analysis of Glycated Hemoglobin

Analysis of the continuous clinical endpoint of HbA1c. Example: a Phase III, parallel-group study designed to determine efficacy of Drug A for patients with Type II diabetes. The primary endpoint defined as the change in HbA1c from baseline.

[View details](#)

Analysis

Mean Change from Baseline in HbA1c (%) Over Time

Figure 1: Mean Change from Baseline in HbA1c (%) Over Time. The graph shows the mean change from baseline in HbA1c (%) over time for two groups: Control (n=100) and Treatment (n=100). The y-axis ranges from -10 to 10. The x-axis shows time points: Baseline, Week 1, Week 2, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, Week 28, Week 32, Week 36, Week 40, Week 44, Week 48, Week 52, Week 56, Week 60, Week 64, Week 68, Week 72, Week 76, Week 80, Week 84, Week 88, Week 92, Week 96, Week 100. The Control group shows a steady increase in HbA1c, while the Treatment group shows a steady decrease.

Provides a visual display of the information in the "HbA1C Longitudinal Repeated Measures Analysis" table. Includes additional weeks beyond those in that table. The mean changes shown are based on adjusted changes from baseline from the repeated measures model.

[View details](#)
[View analysis results metadata](#)

Analysis Datasets

ADSL

Analysis Data Subject Level

[View analysis dataset metadata](#)
[View sample analysis data](#)
[View analysis dataset structure](#)

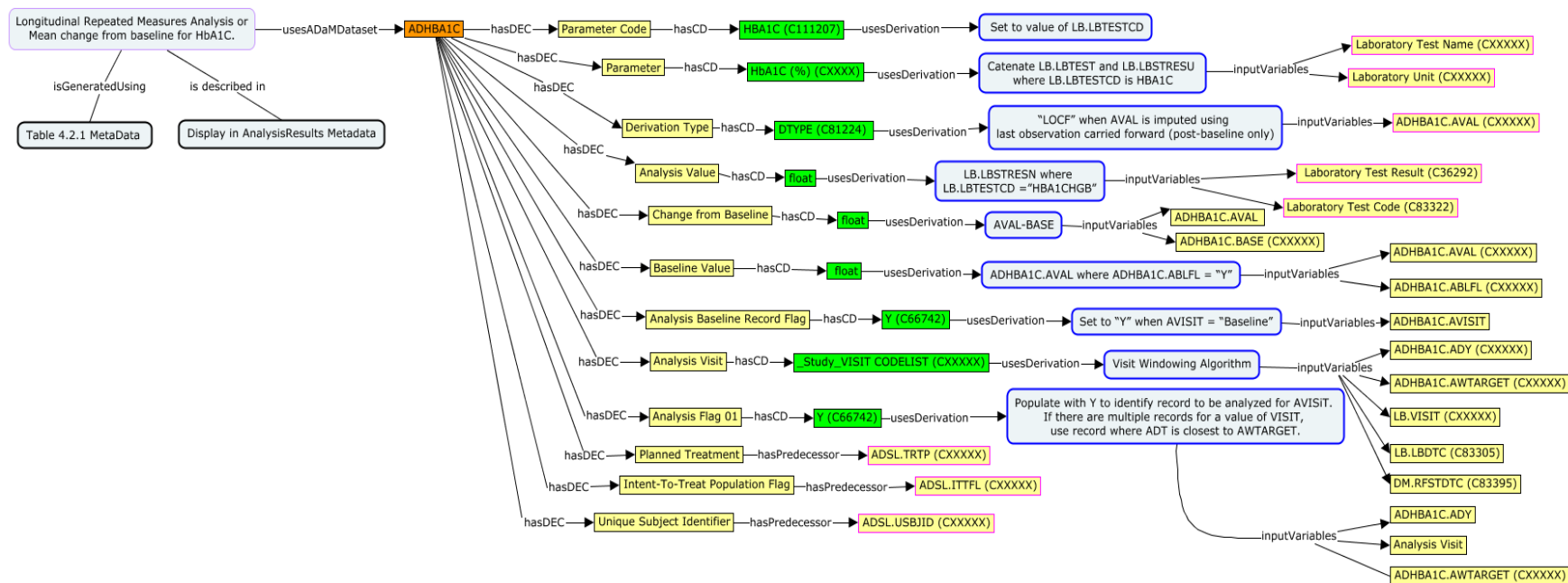
ADHBA1C

DBS - Structured Dataset

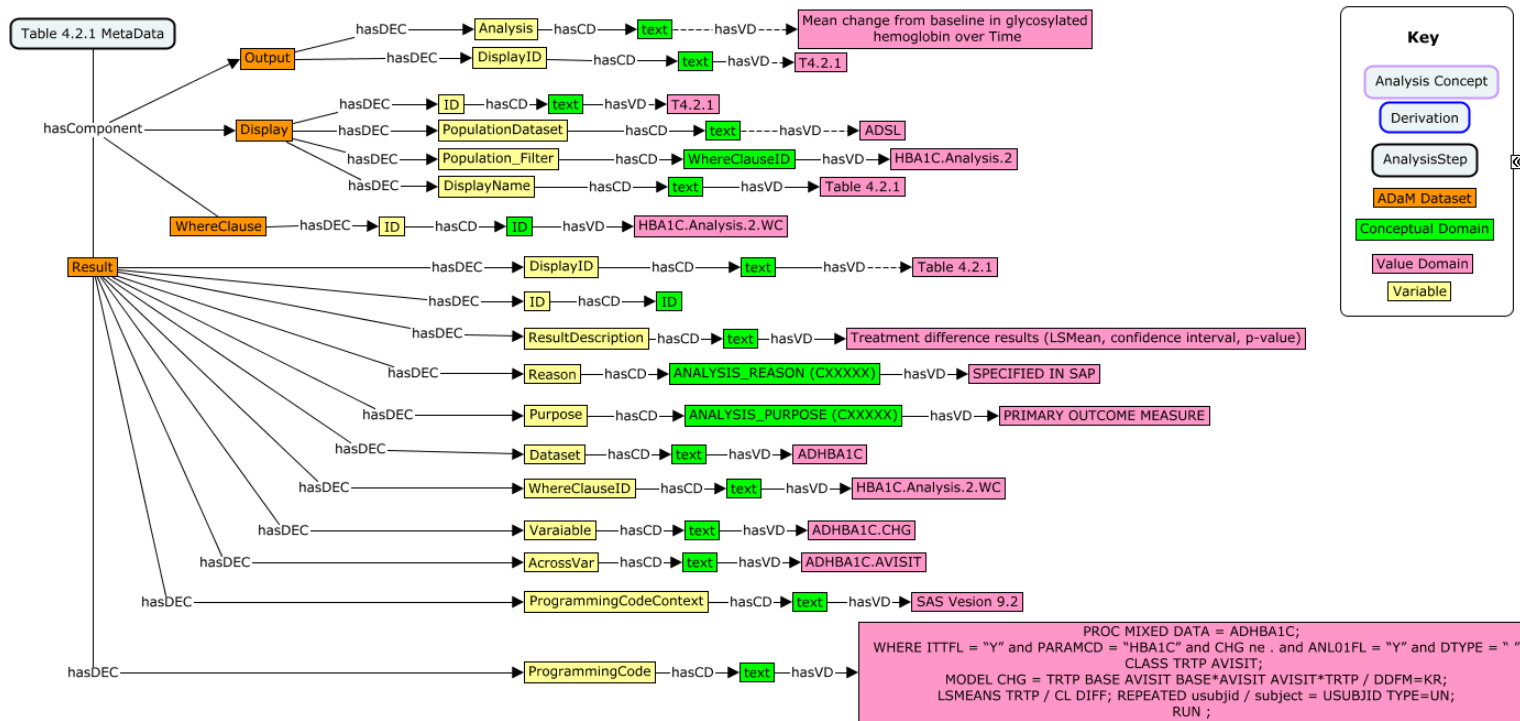
[View analysis dataset metadata](#)
[View sample analysis data](#)
[View analysis dataset structure](#)

[Back](#) [Save Selection](#)

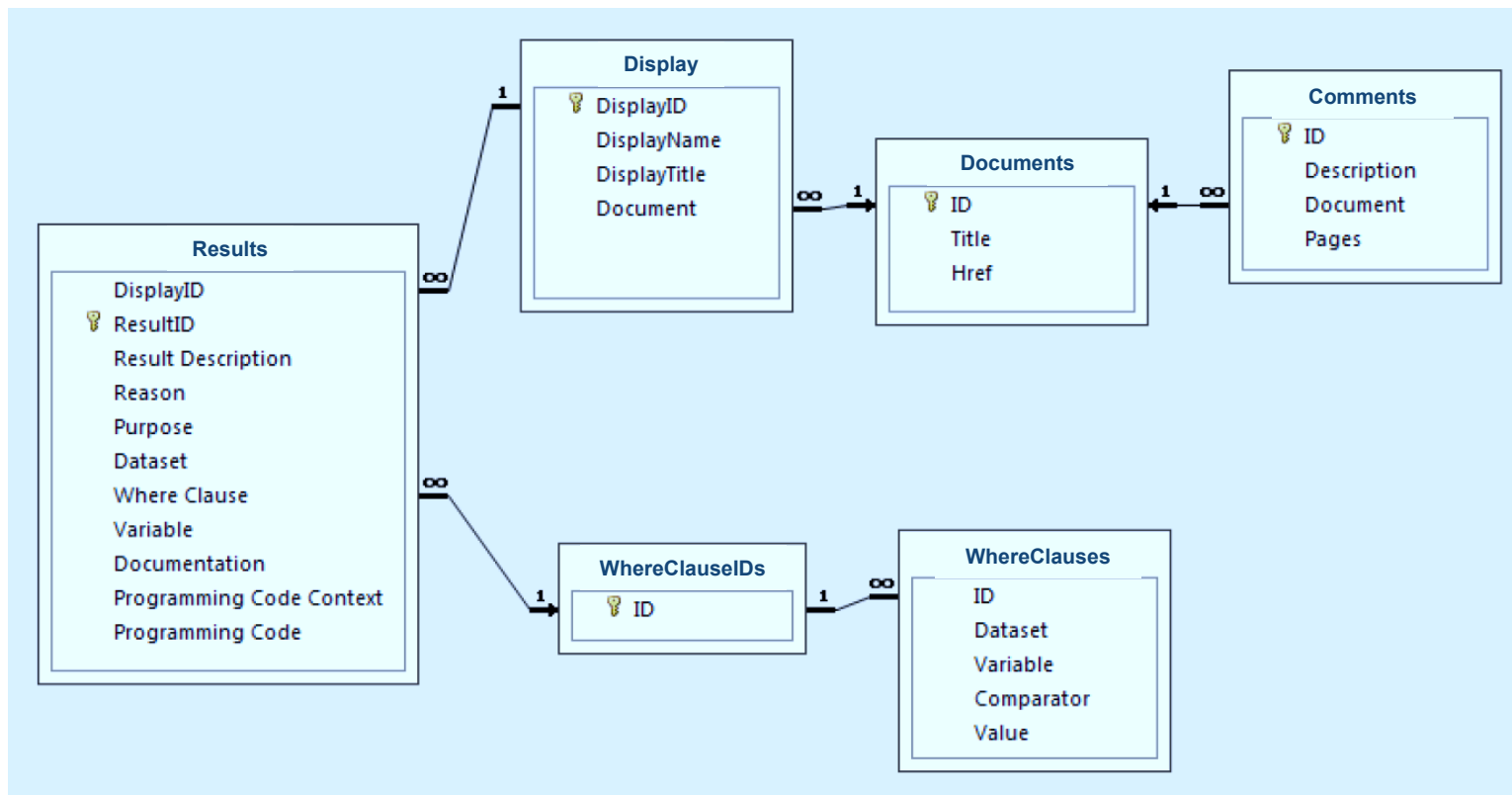
Analysis Concept



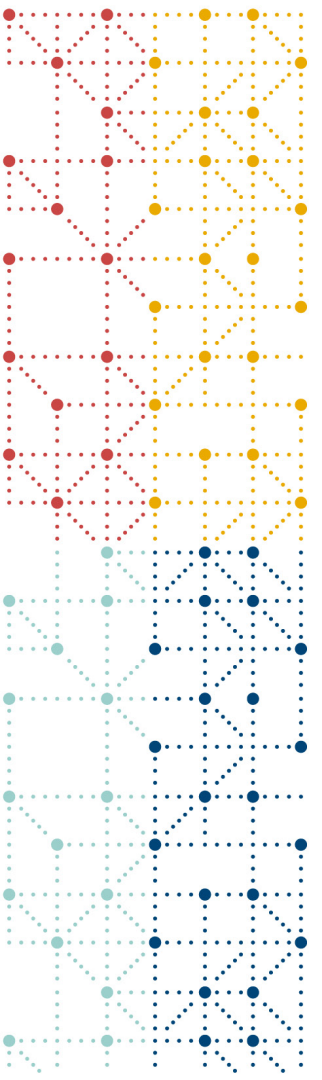
Analysis Result Concept



CDISC ARM Metadata



Reference: 'Large-scale TFL Automation for regulated Pharmaceutical trials using CDISC ARM', Stuart Malcolm, AD203, PharmaSUG 2019



CDISC 360 Enriched (Machine-readable) TFL Metadata

Additional TFL Metadata Required for Automation

Study - CDISC 360

Table 14.1.1.1
Demographic characteristics (Safety Population)

Characteristics	METFORMIN (N=XX)	HUMAN INSULIN (N=XX)
Age (years)		
n	XX	XX
Mean	XX.X	XX.X
SD	XX.XX	XX.XX
Min	XX	XX
Q25	XX.X	XX.X
Median	XX.X	XX.X
Q75	XX.X	XX.X
Max	XX	XX
Age Group - n (%)		
15 - <30 years	XX (XX.X)	XX (XX.X)
30 - <45 years	XX (XX.X)	XX (XX.X)
>=45 years	XX (XX.X)	XX (XX.X)
Gender - n (%)		
Male	XX (XX.X)	XX (XX.X)
Female	XX (XX.X)	XX (XX.X)

Max = Maximum. Min = Minimum. N = Number of subjects in treatment group. n = Number of subjects included in analysis. SD = Standard deviation.
 Datasets used - adsl
 Executed by <Username> on DDMMYYYY:HH:MM

Output

- OutputID
- Output_Filename
- Output_File_Format
- DisplayID
- Output_Style

Display

- DisplayID
- Display_Appendix
- Status
- Group
- Topline
- Display_Population_Dataset
- Display_Population_Filter
- Title1
- Title2
- Title3
- Title4
- Title5
- Footer1
- Footer2
- Footer3
- Footer4
- Footer5
- Footer6
- Footer7
- Footer8

Style

- Style_Name
- Parent
- Filetype
- TitleFont
- TitleFont2
- StrongFont
- EmphasisFont
- headingEmphasisFont
- headingFont
- docFont
- footFont
- FixedEmphasisFont
- FixedStrongFont

Result

- ResultID
- Result_Across_Var
- Result_Across_OrdFmt
- Result_Template
- Result_Header
- Variable_fmt

CDISC 360 Enriched TFL Metadata Tables

Metadata View Table	Description	Structure
Output	The contents and format of each output (which displays, file format, etc.)	One record per Output per Display
Display	List of all Displays - both generic library Display and study-specific (using in 1 or more Output)	One record per Display per Version
Result	All result metadata required to describe the analysis and create display in output	One record per Result
WhereClause	All the component parts of a where clause used to filter data	One record per where clause component
Style	Stylesheet parameters associated with Outputs	One record per Style per parameter

CDISC 360 Enriched TFL Metadata Tables – Sample

Study - CDISC 360

Table 14.1.1.1
Demographic characteristics (Safety Population)

Characteristics	METFORMIN (N=XX)	HUMAN INSULIN (N=XX)
Age (years)		
n	XX	XX
Mean	XX.X	XX.X
SD	XX.XX	XX.XX
Min	XX	XX
Q25	XX.X	XX.X
Median	XX.X	XX.X
Q75	XX.X	XX.X
Max	XX	XX
Age Group - n (%)		
15 - <30 years	XX (XX.X)	XX (XX.X)
30 - <45 years	XX (XX.X)	XX (XX.X)
>=45 years	XX (XX.X)	XX (XX.X)
Gender - n (%)		
Male	XX (XX.X)	XX (XX.X)
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Max = Maximum. Min = Minimum. N = Number of subjects in treatment group. n = Number of subjects included in analysis. SD = Standard deviation.
Datasets used - adsl
Executed by <Username> on DDMMYYYY:HH:MM

Study	Analysis	Group	Filename	Type	Order	DisplayID	DisplayVersion	StyleID
CDISC	CDISC 360	Safety	tdemog_saf	rtf	1	T14111_SAF_DEMOG	1	table_rtf
CDISC	CDISC 360	Safety	tae_soc_pt_saf	rtf	2	T14131_SAF_AE2TIER	1	table_rtf
CDISC	CDISC 360	Safety	tmace_edpt_fas	rtf	2	T1421_FAS_EFF	1	table_rtf

DisplayID	DisplayVersion	Population_Dataset	Population_Variable	Population_Comparator	Population_Value	AcrossVar	AcrossOrdFmt	DisplayName	DisplayTitle
T14111_SAF_DEMOG	1	adsl	SAFFL	EQ	Y	TRTA	trtord	Table 14.1.1.1	Demographic characteristics (SAF)

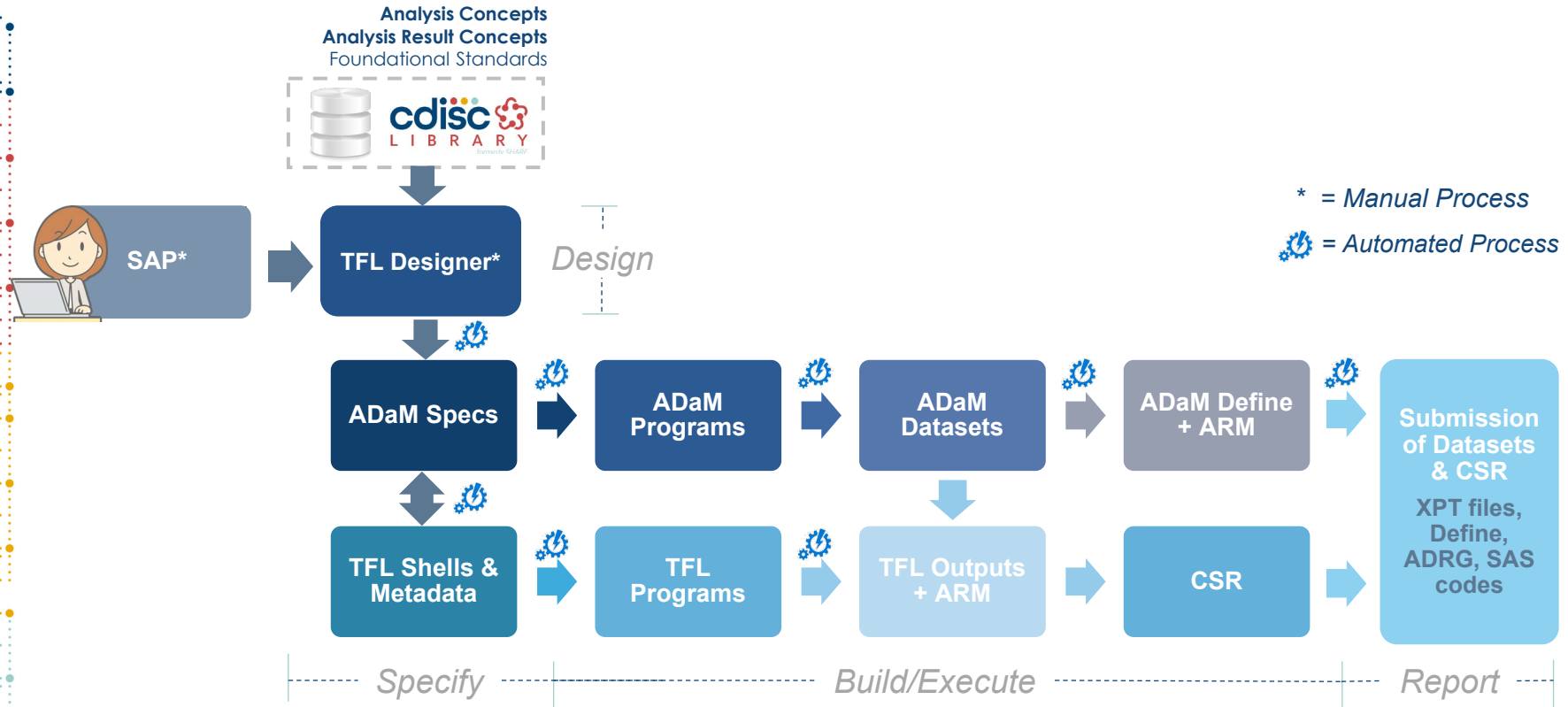
DisplayID	ID	Version	ResultDescription	ResultFmt
T14111_SAF_DEMOG	T14111_01_SAF_DEMOG	1	"Age (years)"	
T14111_SAF_DEMOG	T14111_01_SAF_DEMOG	1	n	XXX
T14111_SAF_DEMOG	T14111_01_SAF_DEMOG	1	Mean	XX.X
T14111_SAF_DEMOG	T14111_01_SAF_DEMOG	1	SD	XX.XX
T14111_SAF_DEMOG	T14111_01_SAF_DEMOG	1	Min	XX
T14111_SAF_DEMOG	T14111_01_SAF_DEMOG	1	Q25	XX.X

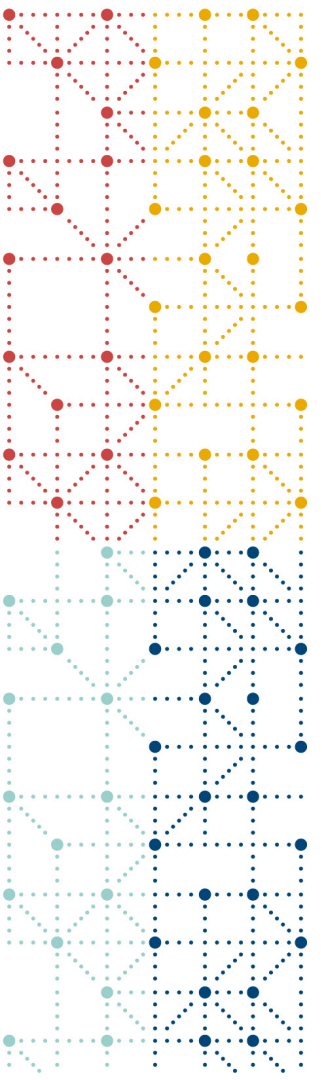
DisplayName	WhereClauseID	Dataset	WhereClause_Variable	WhereClause_Comparator	WhereClause_Value
Table 14.1.1.1	_01_SAF_DEMOG_01	adsl	AGE		
Table 14.1.1.1	_02_SAF_DEMOG_01	adsl	AGEGR1	eq	15<= to <30 years
Table 14.1.1.1	_02_SAF_DEMOG_02	adsl	AGEGR1	eq	30<= to <45 years
Table 14.1.1.1	_02_SAF_DEMOG_03	adsl	AGEGR1	eq	>=45 years
Table 14.1.1.1	_03_SAF_DEMOG_01	adsl	SEX	eq	M
Table 14.1.1.1	_03_SAF_DEMOG_02	adsl	SEX	eq	F



Future State - with Concept-based Standards

Future State - with Concept-based Standards: Analysis Datasets and TFL Generation





Process Flow for CDISC 360 Proof of Concept (PoC)

Analysis Concepts
Analysis Result Concepts
Foundational Standards



Design

Define

Build

Execute

Study
Designer
App

Define Study
Design Study
Select and Configure
Standard concepts for a
Study
Build Study
Specification

Import
Standards and
concepts

Supplemental
Metadata

Study
Metadata
Library

Sponsor
Library
Maintenance

Generate
Test Data
based
on study
metadata

Test Data CDR
Raw, CDASH,
SDTM, ADaM

Process Flow for CDISC 360 PoC

List
Metadata
(Query
Interface)
Neodj
SAS
Interface

Study
Specification
Artefacts

Data Collection
Designer

Data
Collection
Specification
ODM-XML

Blank CRF
Specification
Define-XML
for SDTM

aCRF

TFL
Designer

Design and
configure TFL
table shells

SDTM to ADaM to TFL

Automate
Execution

Supplemental
Metadata

Ingest
Specification
metadata

Data Mapping/
Transformation
Automation Engine
Control and monitor
Data Generation

TFL
Automation Engine
Control and monitor
TFL Generation

SDTM
Datasets

SDTM
Programs

SDTM
Artefacts

ADaM
Datasets

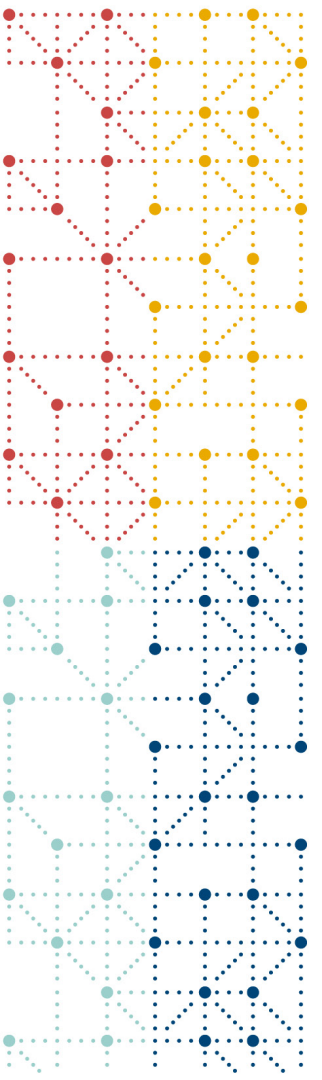
ADaM
Programs

ADaM
Artefacts

ARM

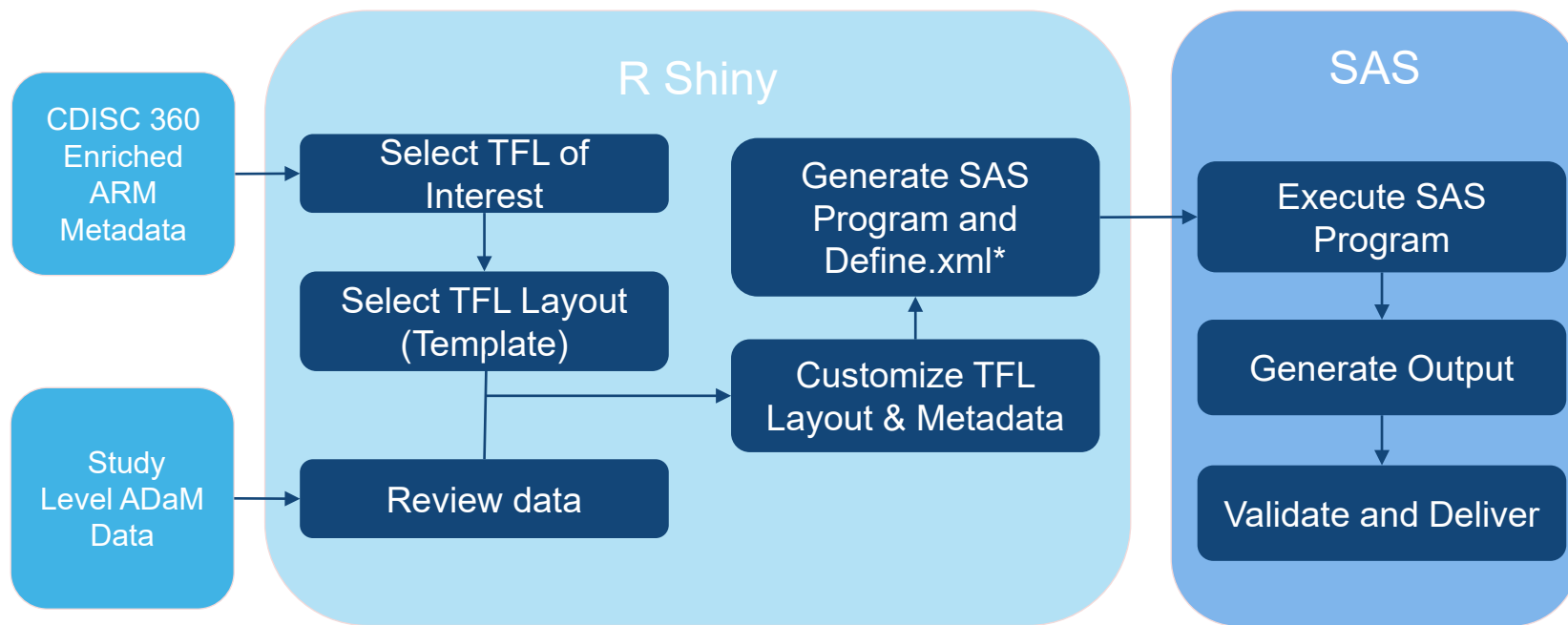
TFL
Programs

TFLs

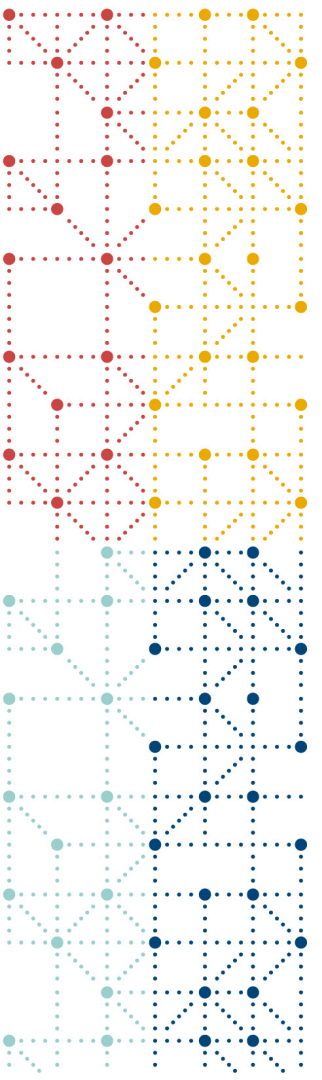


TFL Automation Engine – Proof of Concept Design

CDISC 360 – TFL Automation Engine PoC Design



* ARM to be combined with ADaM Define



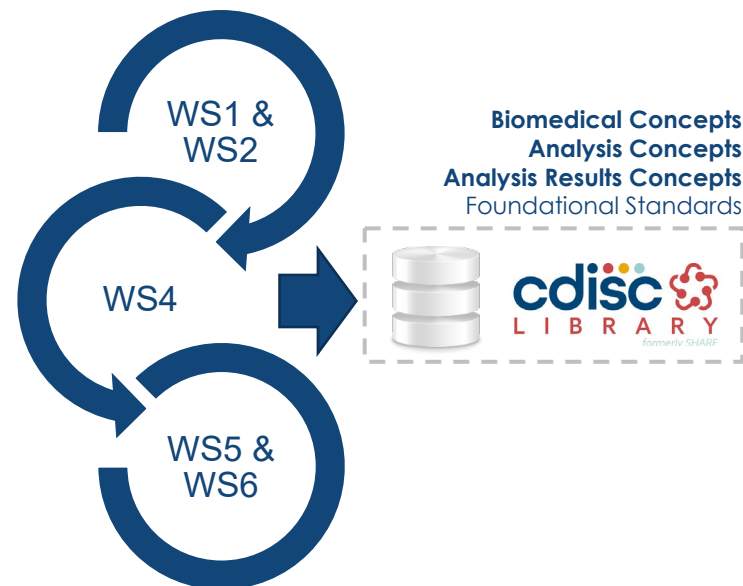
TFL Automation Engine – Live Demo!

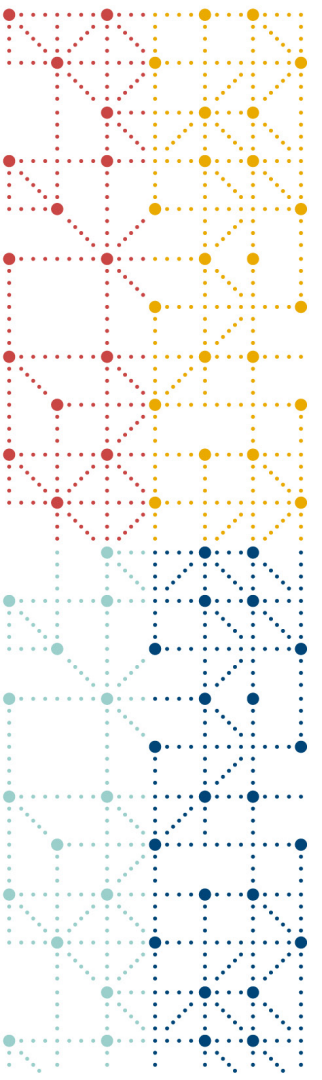


Learnings so far

Machine-readable TFL Metadata

- ARM + additional TFL Metadata
 - Use case tested with enriched metadata
 - Can be consumed by any tool
- TFL Automation Engine PoC
 - Demonstrated execution of TFL & generation of Define.xml + ARM
 - Organization can build an automation engine their own way
- TFL Designer
 - Will help build TFL Shells and ADaM Specs
- CDISC currently does not support TFL standards – can templates be developed?





Next Steps

Our plans for remaining part of PoC



Next Steps in Automate Execution [CDASH → SDTM → ADaM → TLFs]

- Collaborate with other workstreams to develop concept-based standards, ODM CRF, and Define-XML [per CDISC 360 defined scope]
- CDASH to SDTM
 - Test & finalize machine-readable metadata elements for mapping specifications
 - Autogenerate SDTM artifacts from CDASH via CDISC 360 Process Flow for PoC [*DM, EX, LB, VS, and trial design domains*]
- SDTM to ADaM
 - Define, test & finalize machine-readable metadata elements for mapping specifications
 - Autogenerate ADaM artifacts from SDTM via CDISC 360 Process Flow for PoC [*ADSL*]
- ADaM to TFL
 - Adjust TFL metadata to meet CDISC ARM v1.0 for Define-XML v2.0 standards
 - TFL Designer – will be conceptualize but team to hold on further development of PoC



Thank You!

Bhavin Busa, *Vita Data Sciences*

Jianhui [Jimmy] Zhao, *Allergan*

Prasanna Murugesan, *AstraZeneca*



Courtesy: Mahi Busa