Automation of SDTM Generation & Artifacts using CDISC 360 enriched standards

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CDISC 360: The Journey So Far and the Road Ahead

April 28, 2020

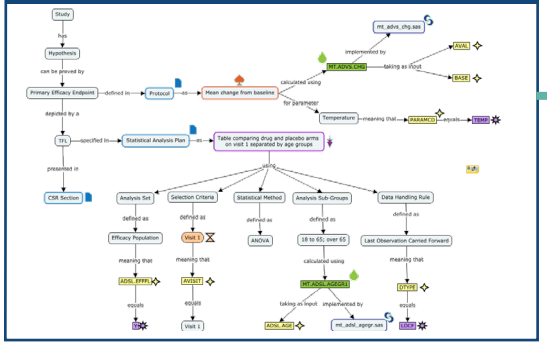
Agenda

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

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

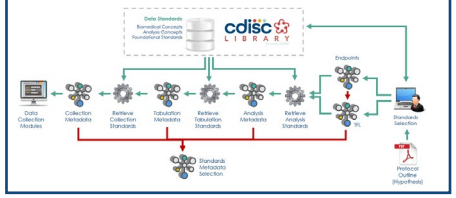
API

Extend API's

Transform concepts in machine readable form

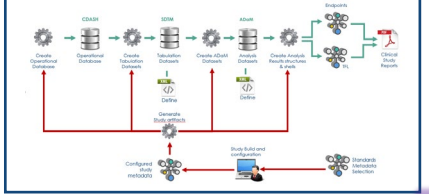
Study Metadata Library

Workstream 4 - *DEFINE*



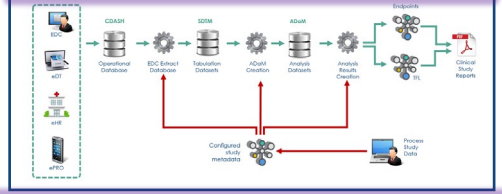
Identify and select standards specification (Use Case 1)

Workstream 5 - *BUILD*



Configure study specification and create artifacts (Use Case 2)

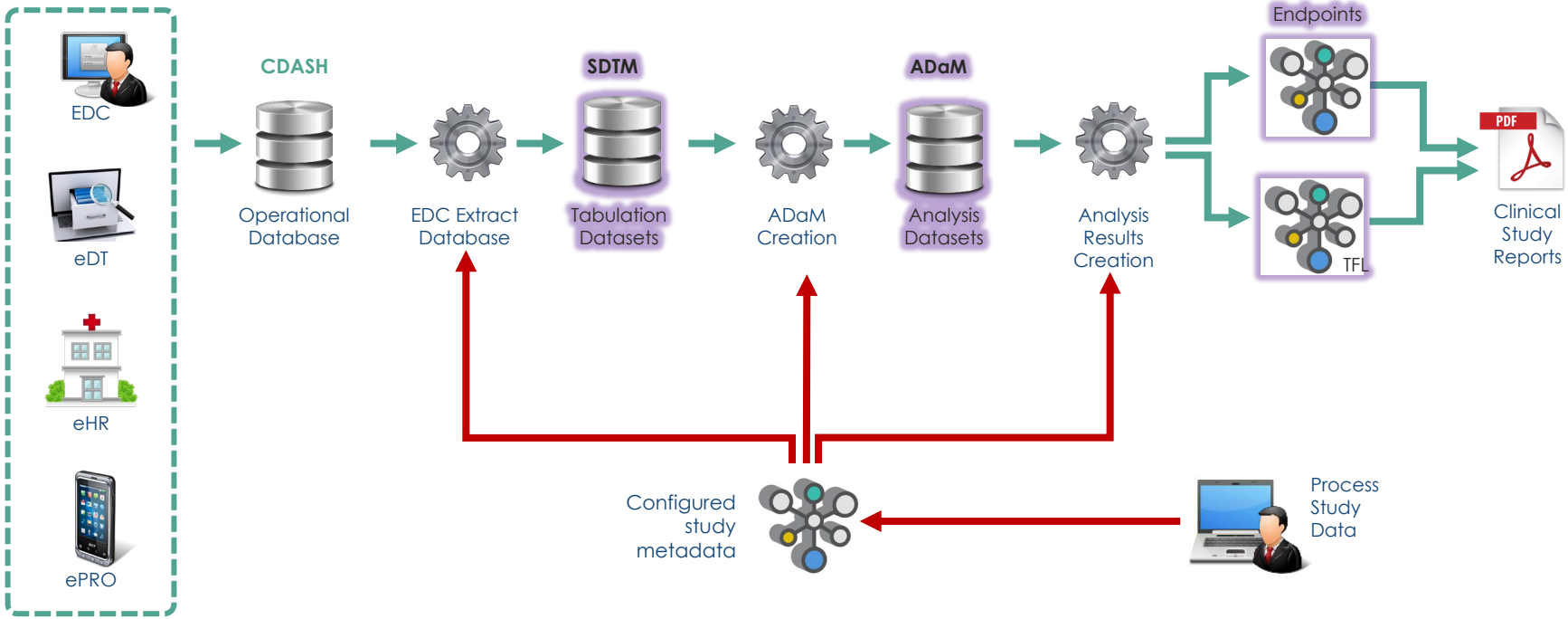
Workstream 6 - *EXECUTE*



Automatically process and transform data (Use Case 3)

Use Case 3 (Workstream 6): Execute

Automatic population of data into artifacts



Workstream 6 & Task Team Leads

Workstream 6 Lead

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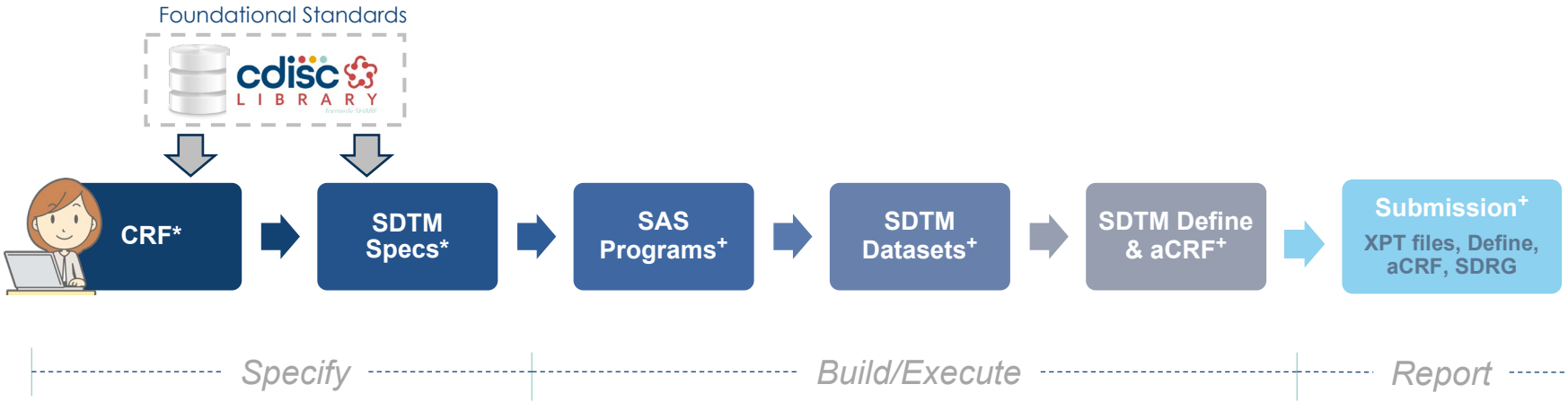
Allergan
AMGEN
AstraZeneca
Bayer HealthCare
BeiGene
Biogen
BIOMARIN
C+R RESEARCH
Celgene
Cytel
STATISTICAL SOFTWARE & SERVICES
Deloitte.
dMed 缔脉
FDA
formedix
frontier science foundation
GILEAD
Inductive Quotient
Research . Bigdata . Analytics
Johnson & Johnson
Lilly
Mel Consulting
MERCK
Microsoft
novo nordisk
ORACLE
Otsuka
Pfizer
PharmaStat
PINNACLE 21
POINT CROSS
S-CUBED
SANOFI
sas
Syneos Health
TALENT MINE
VITA DATA SCIENCES
a division of SOFTWORLD
xclinical
Clinical Solutions Group

Current State - without Concept-based Standards

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



* *Manual Process*

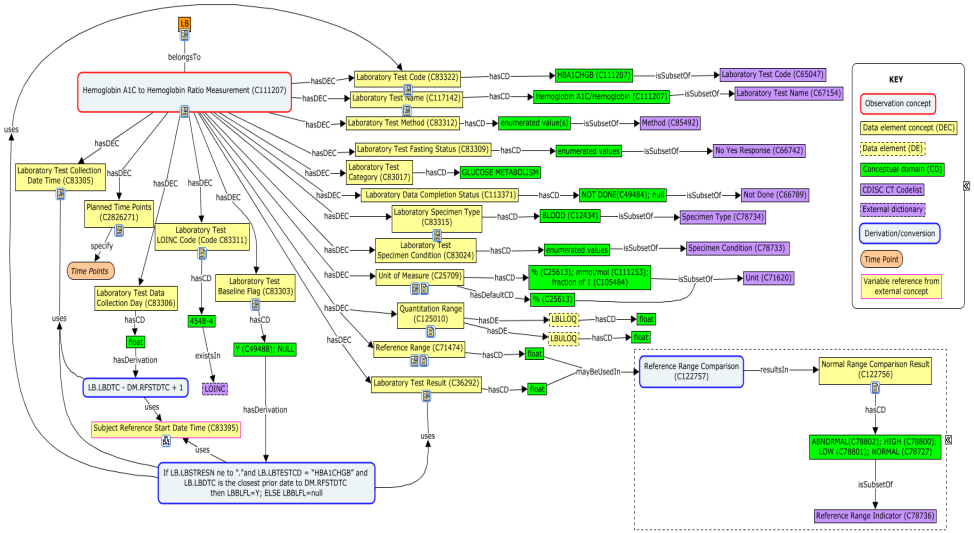
+ Manual or Semi-automated Execution

CDISC 360 Enriched Metadata

Machine-readable CDISC 360 Enriched Metadata

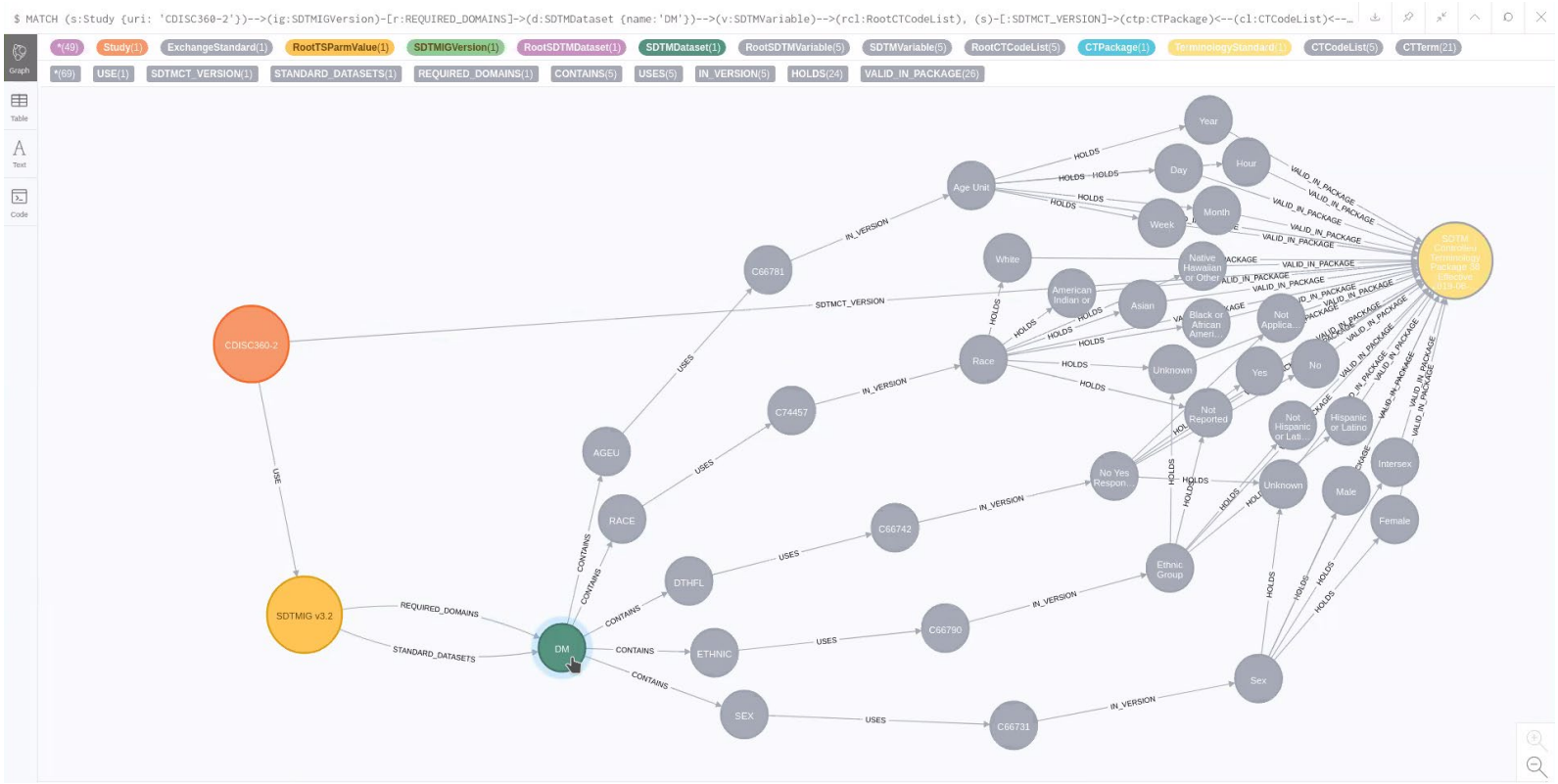
Concept-based Standards: Biomedical Concept

- 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



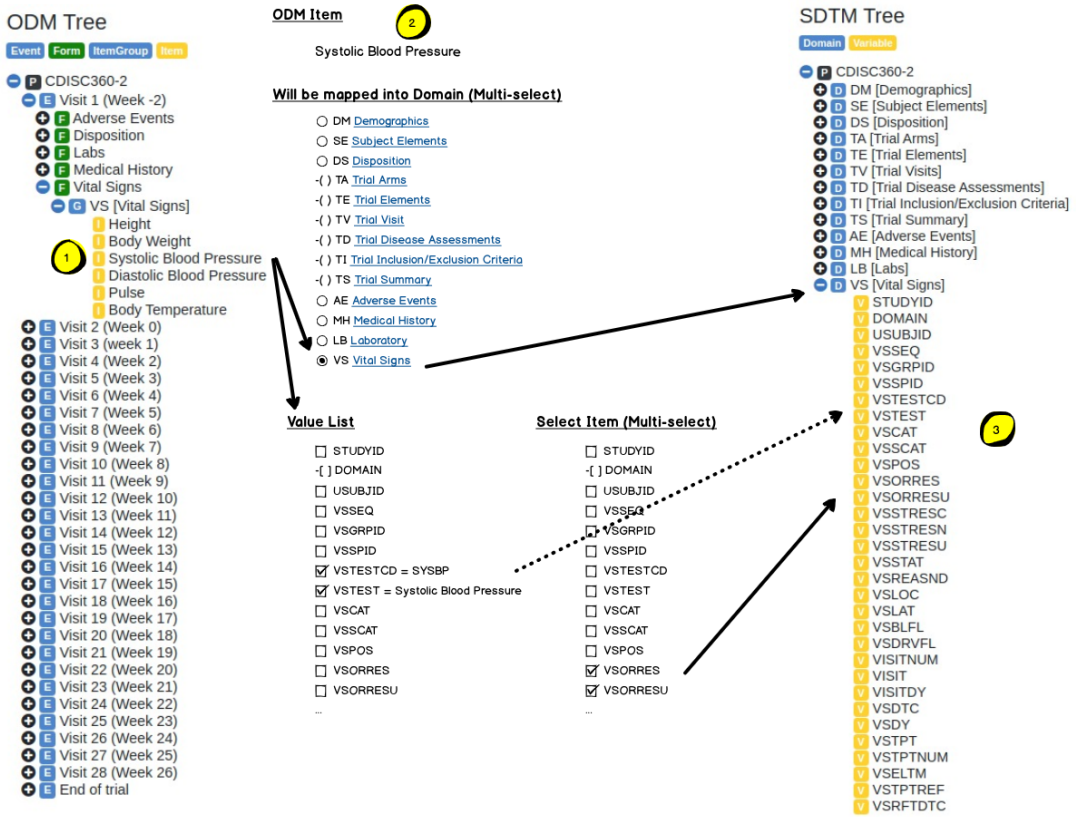
Reference: '*CDISC 360 - The Journey so Far and the Road Ahead', Peter Van Reusel, 28th April 2020*

Linked Graph Model: Importing Concept-based Standards



Reference: 'Study Design and Configuration using CDISC 360 concept-based standards', *Mikkel Traun,* Nicolas de Saint Jorre, *28th April 2020*

Study Build of ODM.XML and Define.XML



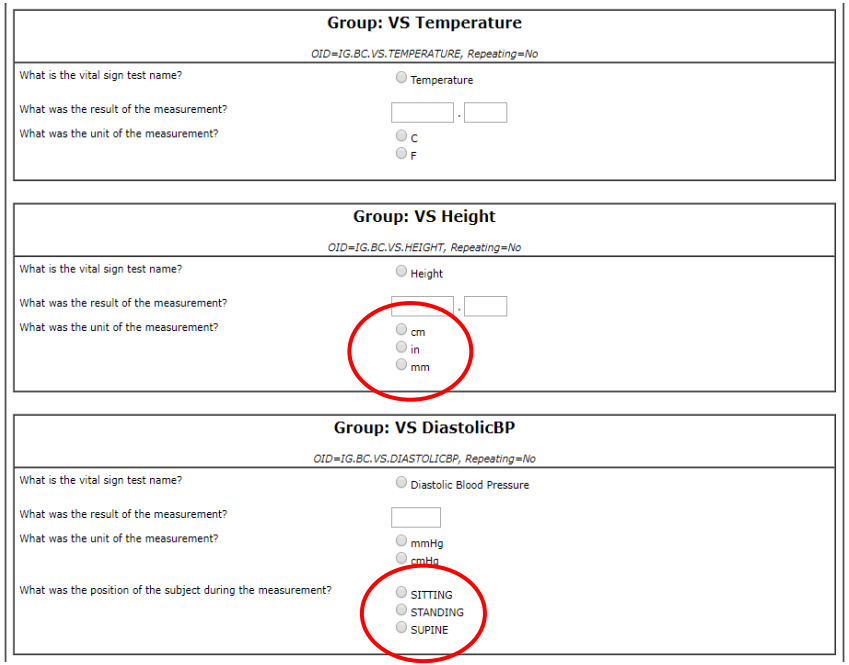
Reference: 'Study Design and Configuration using CDISC 360 concept-based standards', *Mikkel Traun,* Nicolas de Saint Jorre, *28th April 2020*

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>
```

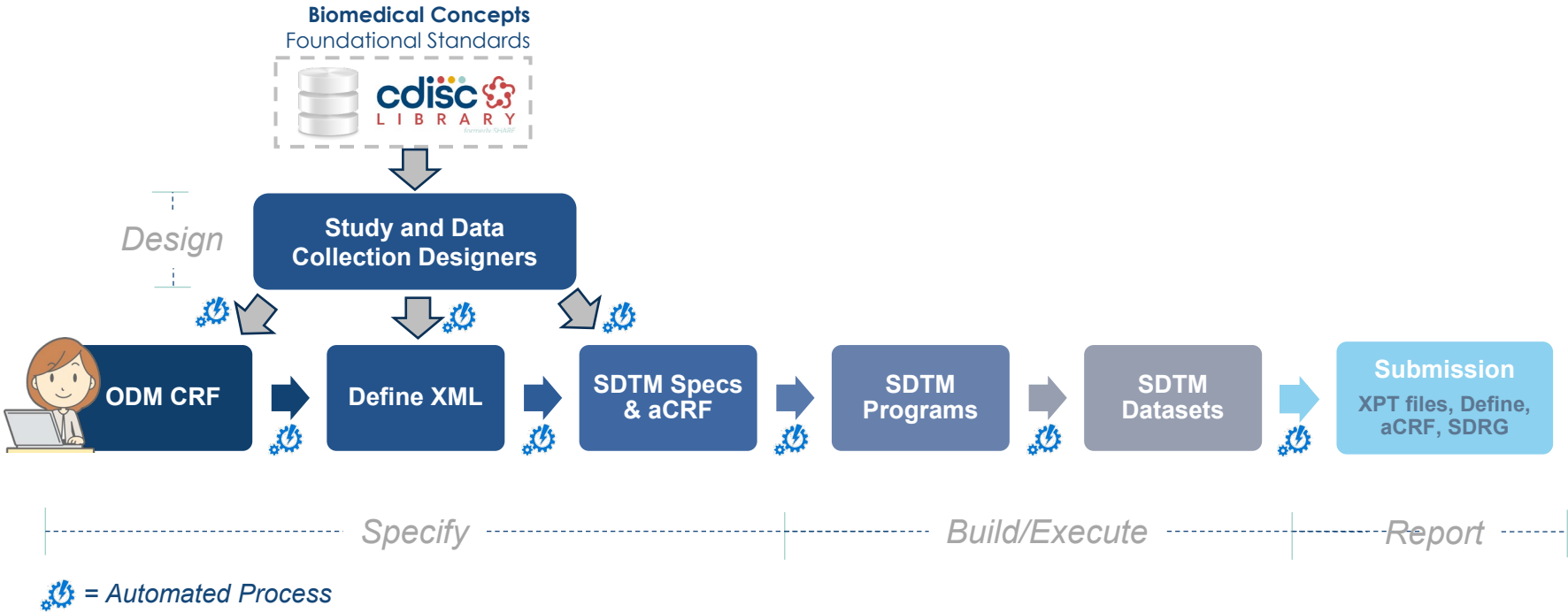
Stylesheet rendering of ODM VS CRF



Reference: 'CDISC Library: Integrating and Surfacing 360 Content', Sam Hume, October 16, 2019

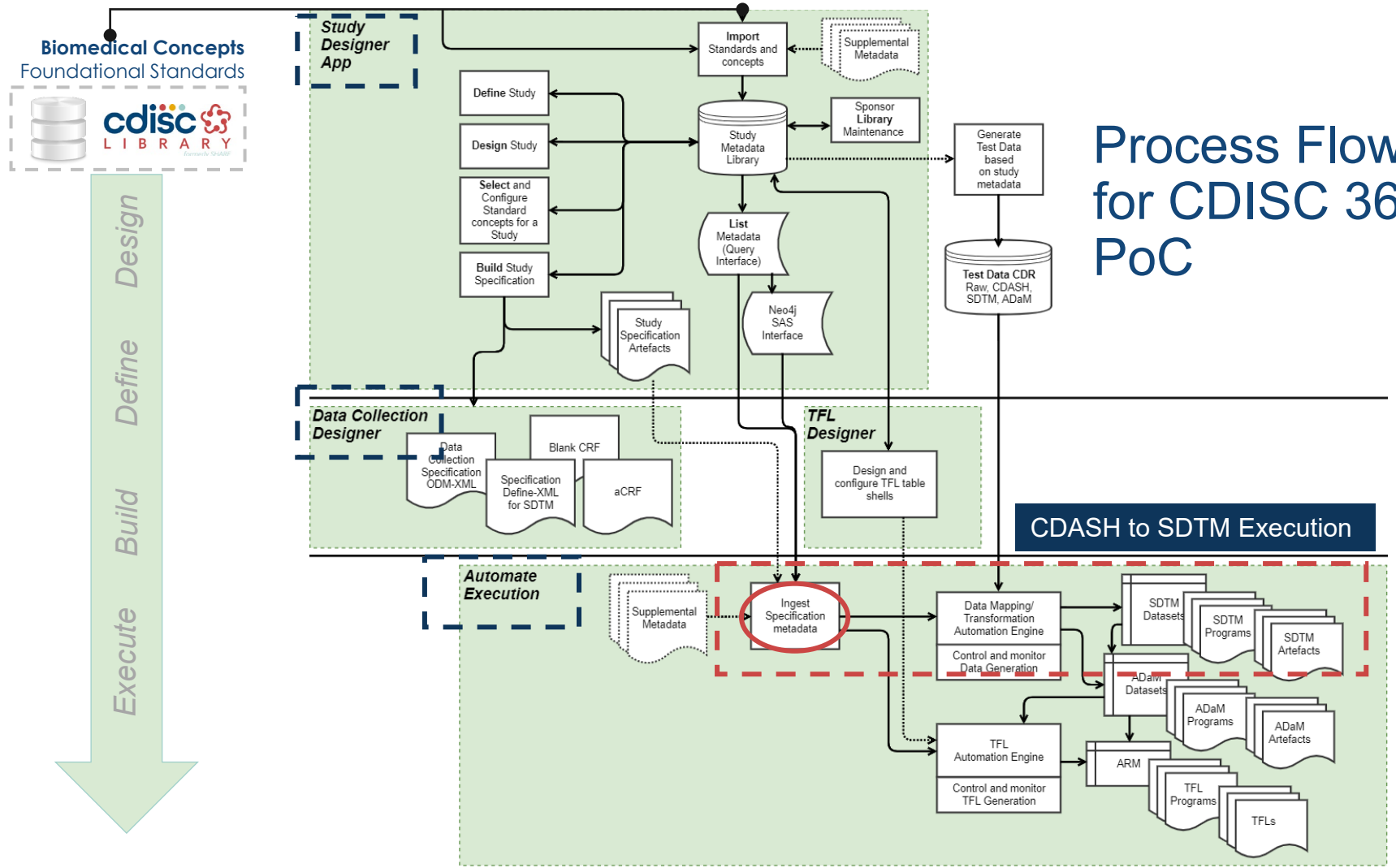
Future State - with Concept-based Standards

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

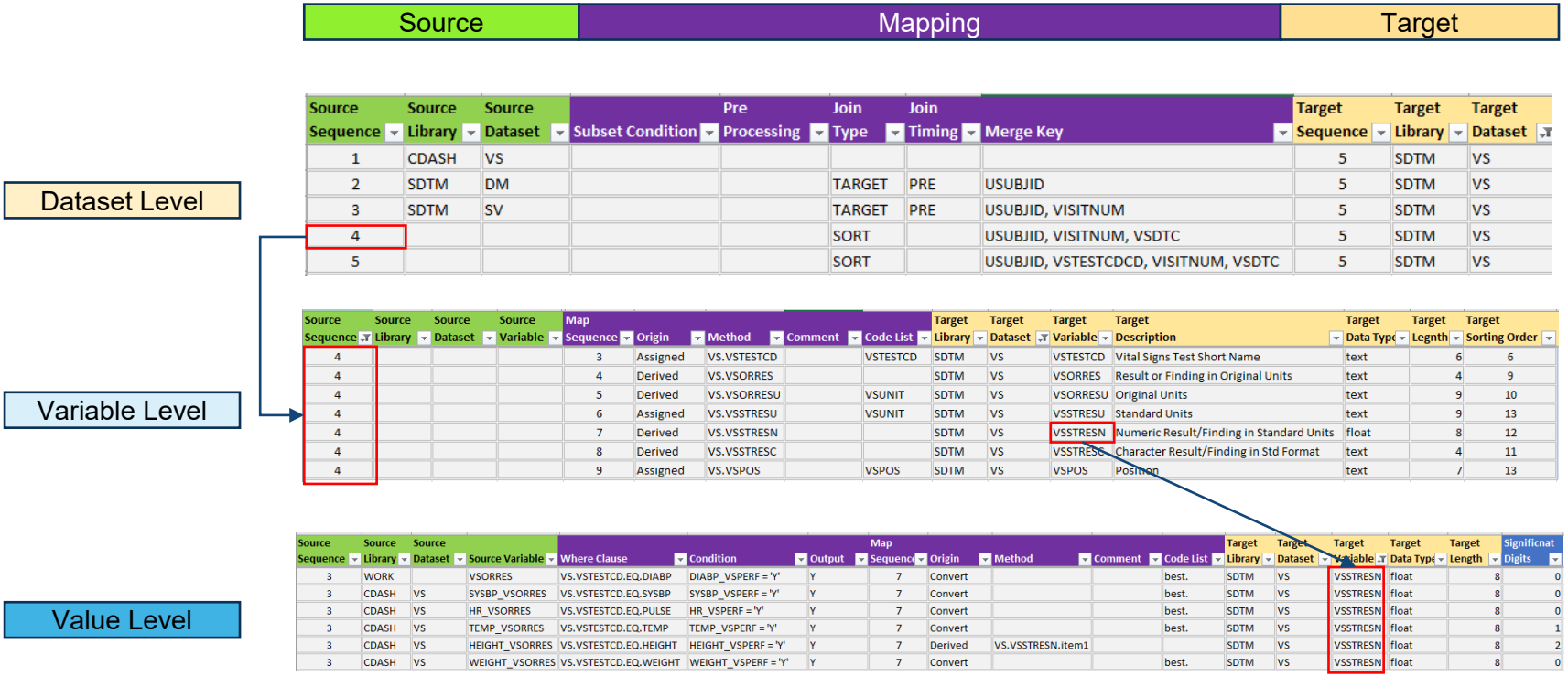
- Dataset Level: Transit datasets from source to target
- Variable Level: Map variables from source to target
- Value Level: Map variables from source to target under different conditions

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 Legnth	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.USUBJID			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 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, VSTESTCDCD, 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			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	Map Output	Map Sequence	Map Origin	Map Method	Map Comment	Map 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	Subset Condition	Pre Processing	Join Type	Join Timing	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, VSTESTCDCD, VISITNUM, VSDTC	5	SDTM	VS

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

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

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

```
... Sequence 3, 4                                   3  4
```

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

data SDTM.VS;
   set VS4;                                         5
   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	ALL.USUBJID	Concatenation of STUDYID and SUBJID	Concatenate	dot/STUDYID/SUBJID
5	VS.VSDTC	Convert assessnent date (VISDAT/VSDAT) to ISO8601 date format.	ISODTC	VISDAT/VSDAT
6	VS.VSBLFL	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);

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';

```
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	

1

2

```
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;                                    1
```

```
 *** CONTINUTE ***;

   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;                                    2
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

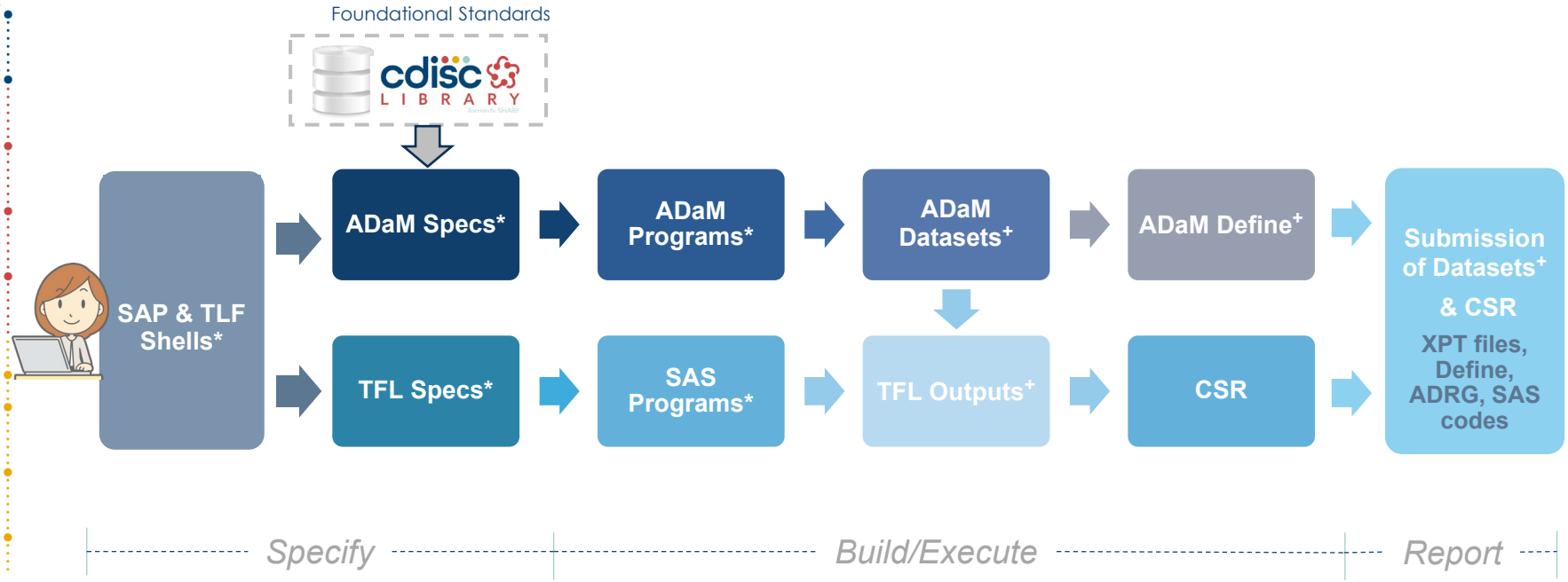
April 28, 2020

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

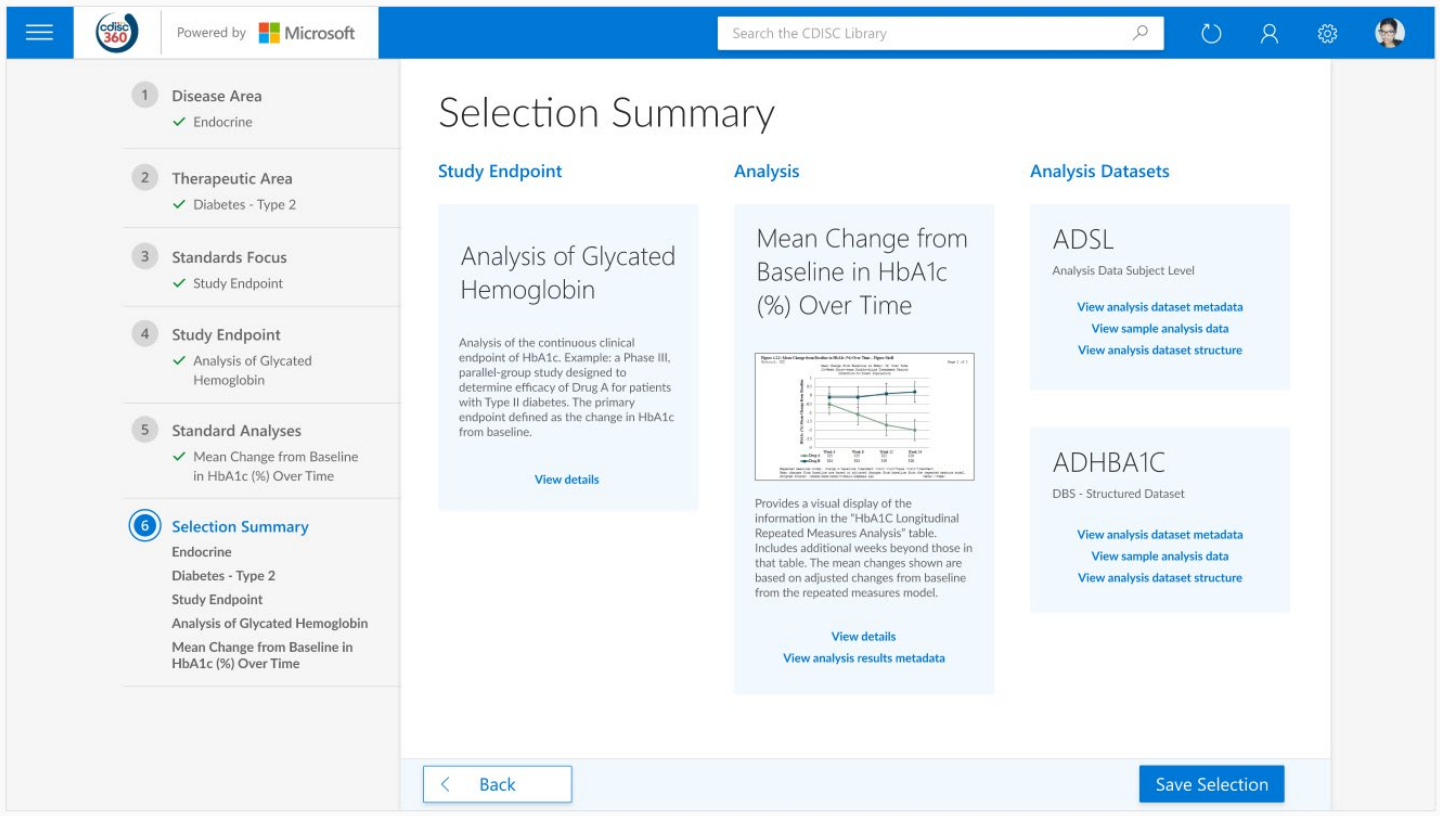


* *Manual Process*

\+ *Manual or Semi-automated Execution*

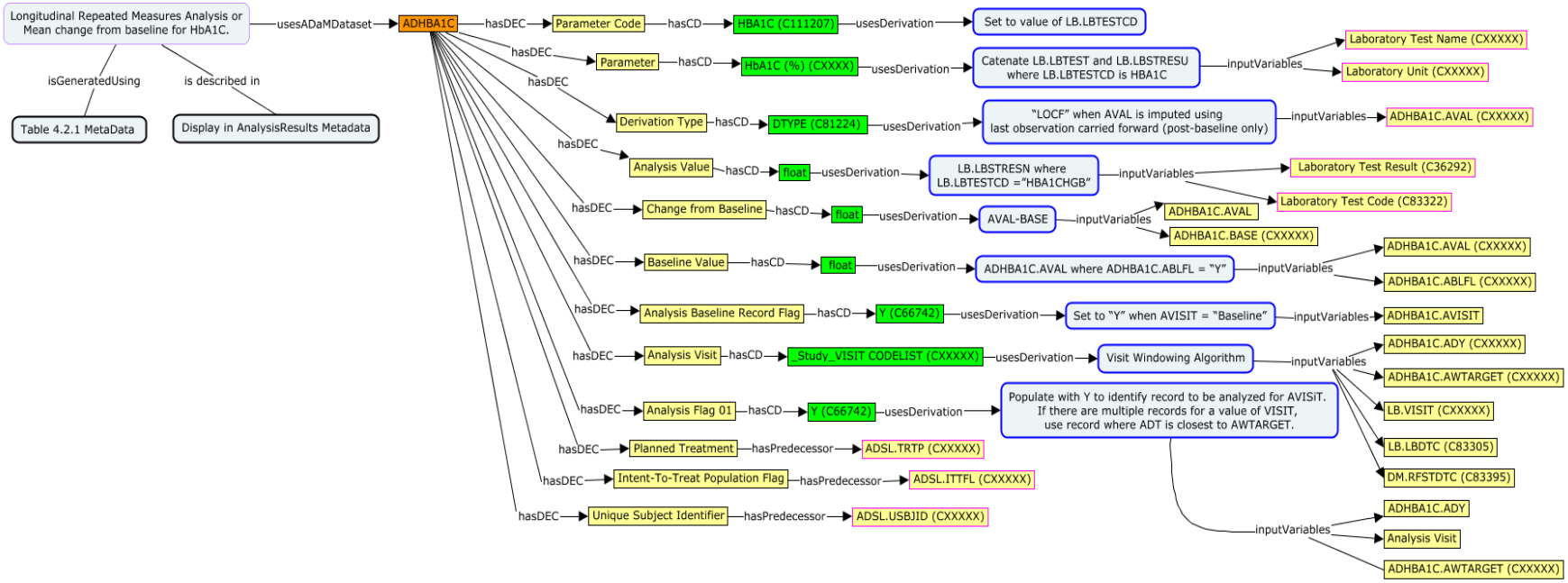
CDISC 360 Enriched Metadata

CDISC 360: The Art of the Possible



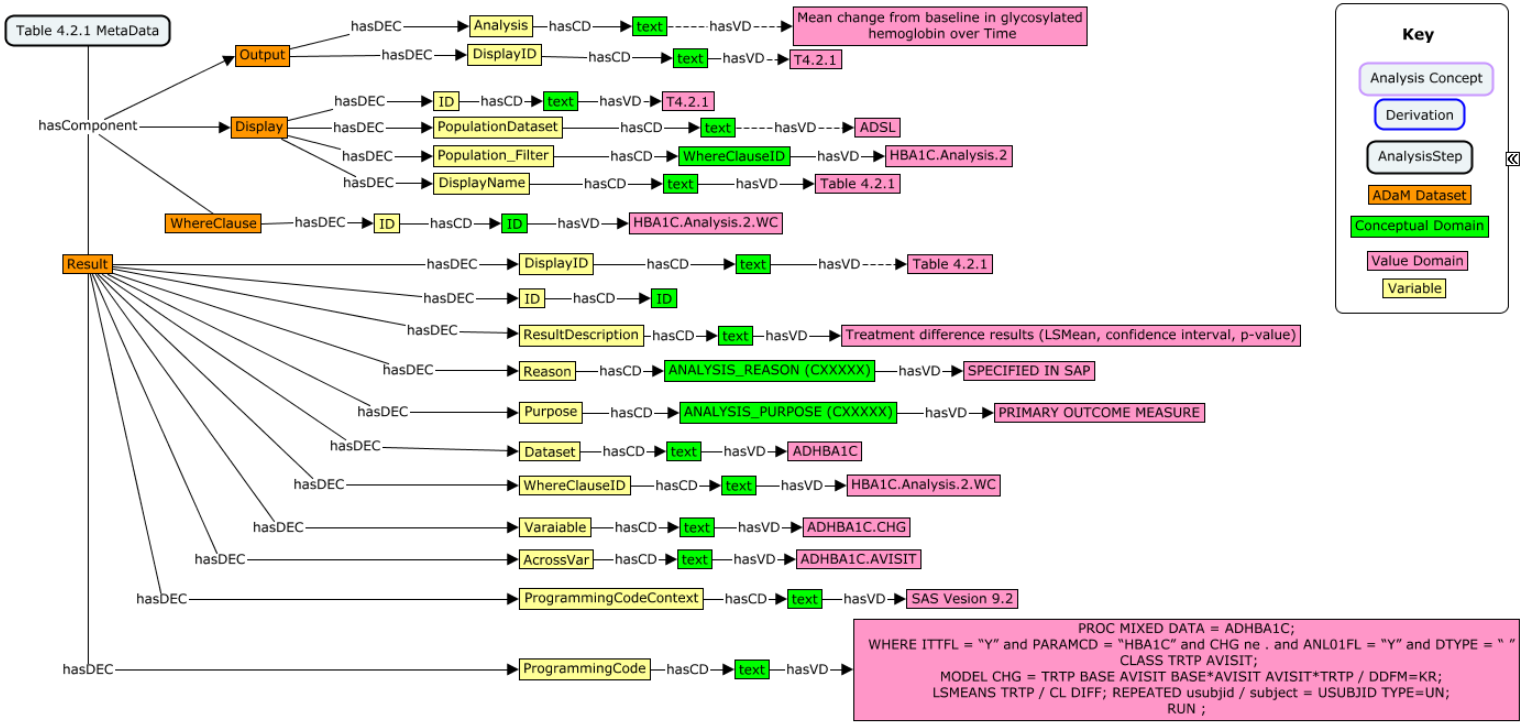
Reference: '*CDISC 360 - The Journey so Far and the Road Ahead', Peter Van Reusel, 28th April 2020*

Analysis Concept



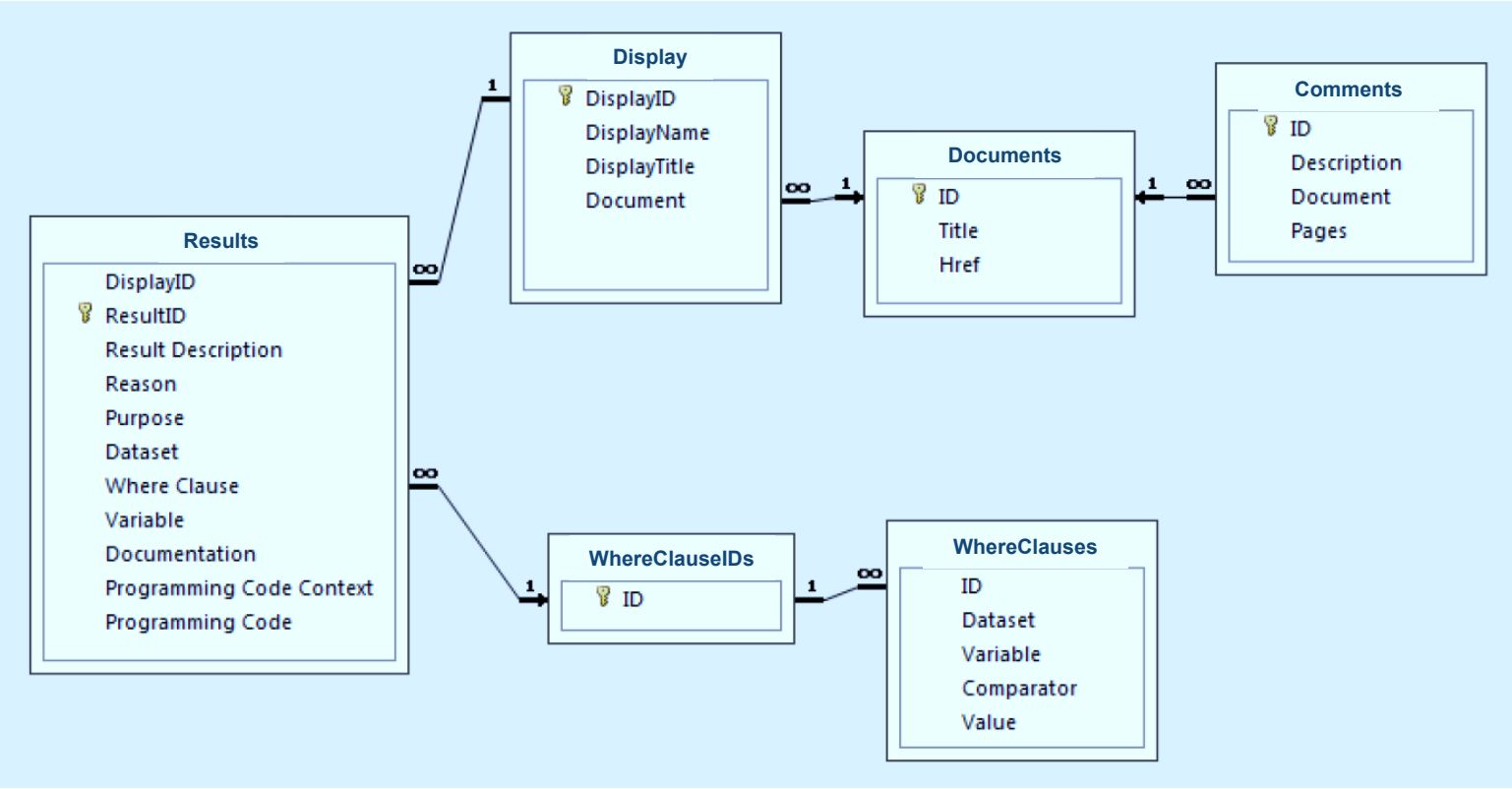
Reference: '*CDISC 360 - The Journey so Far and the Road Ahead', Peter Van Reusel, 28th April 2020*

Analysis Result Concept



Reference: '*CDISC 360 - The Journey so Far and the Road Ahead', Peter Van Reusel, 28th April 2020*

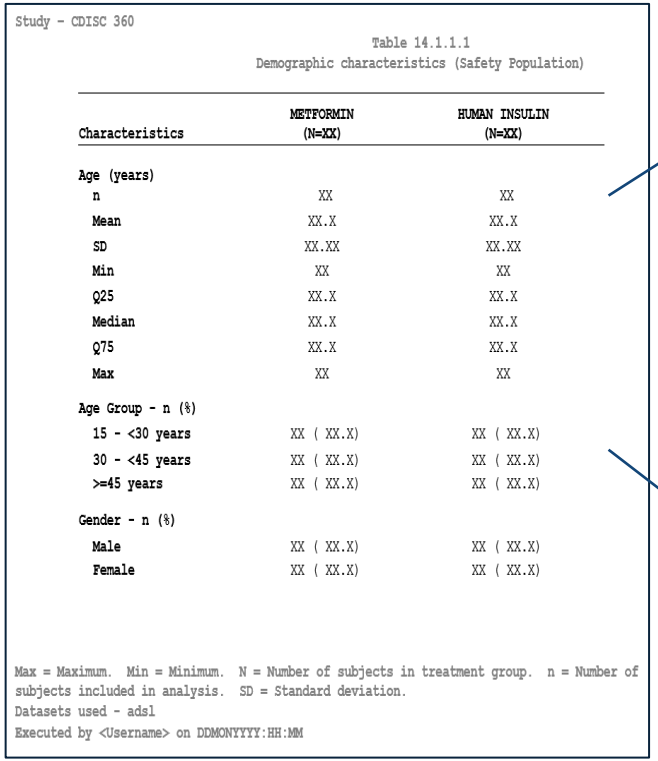
CDISC ARM Metadata



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

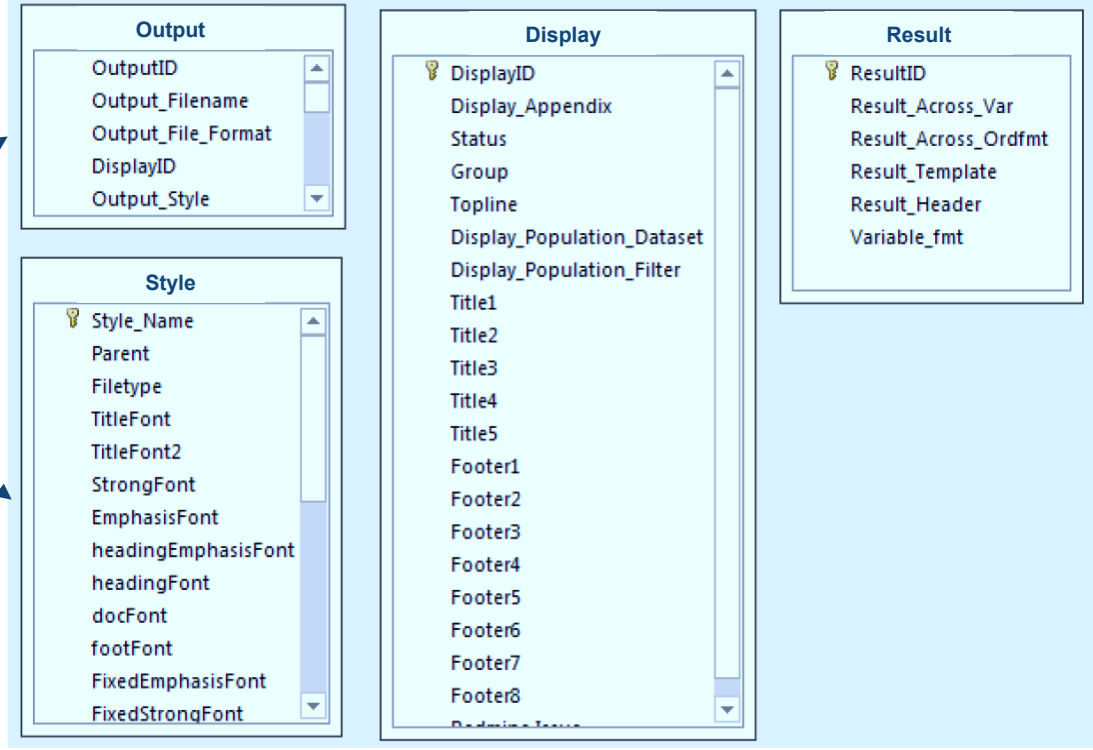


Study - CDISC 360

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 DDMONYYYY:HH:MM



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

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

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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
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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)
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>=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 DDMONYYYY: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

Output | Display | Style | Results | WhereClause | TFL Metadata View list

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)

Output | Display | Style | Results | WhereClause | TFL M ...

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

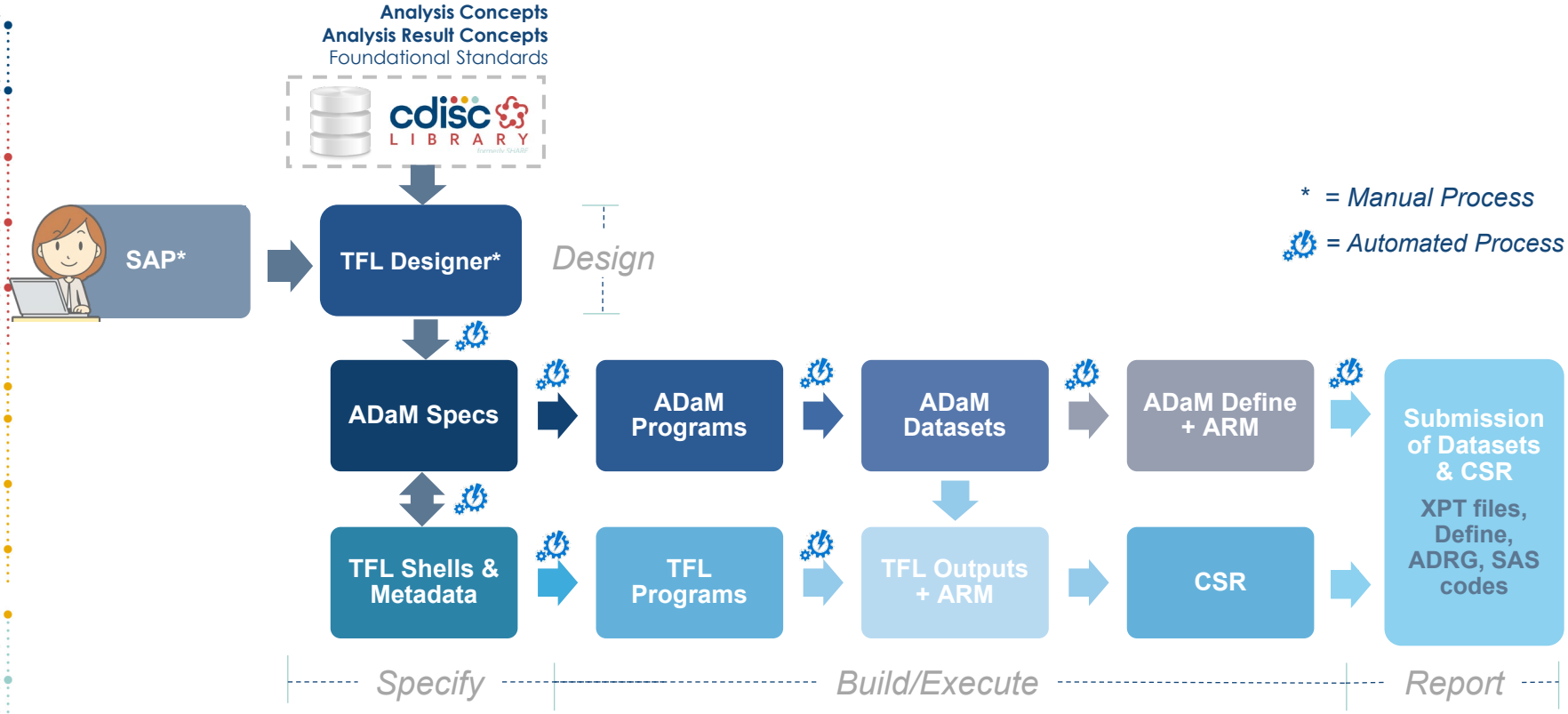
Output | Display | Style | Results | Whe ...

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

... | Display | Style | Results | WhereClause | TFL M ...

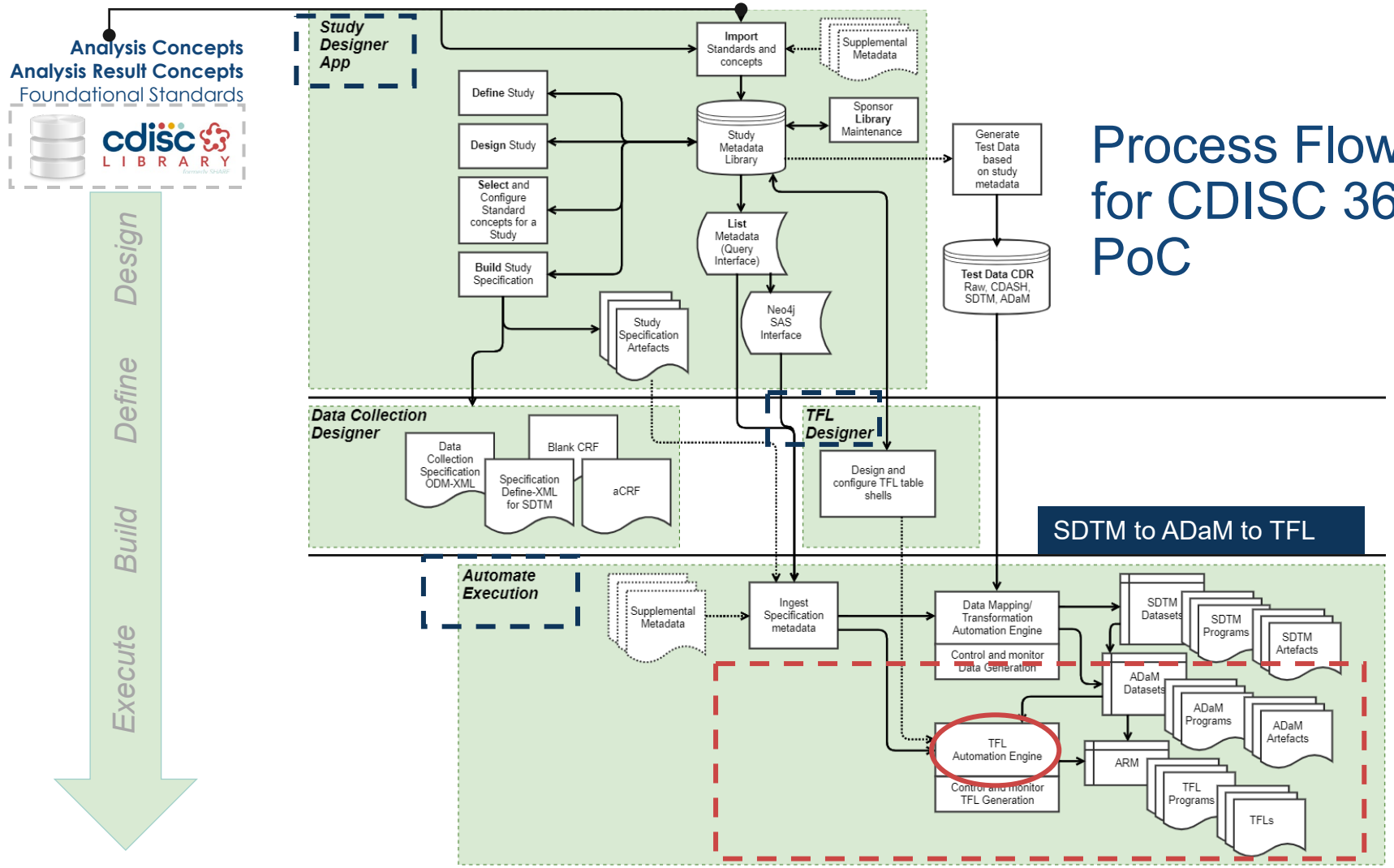
Future State - with Concept-based Standards

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



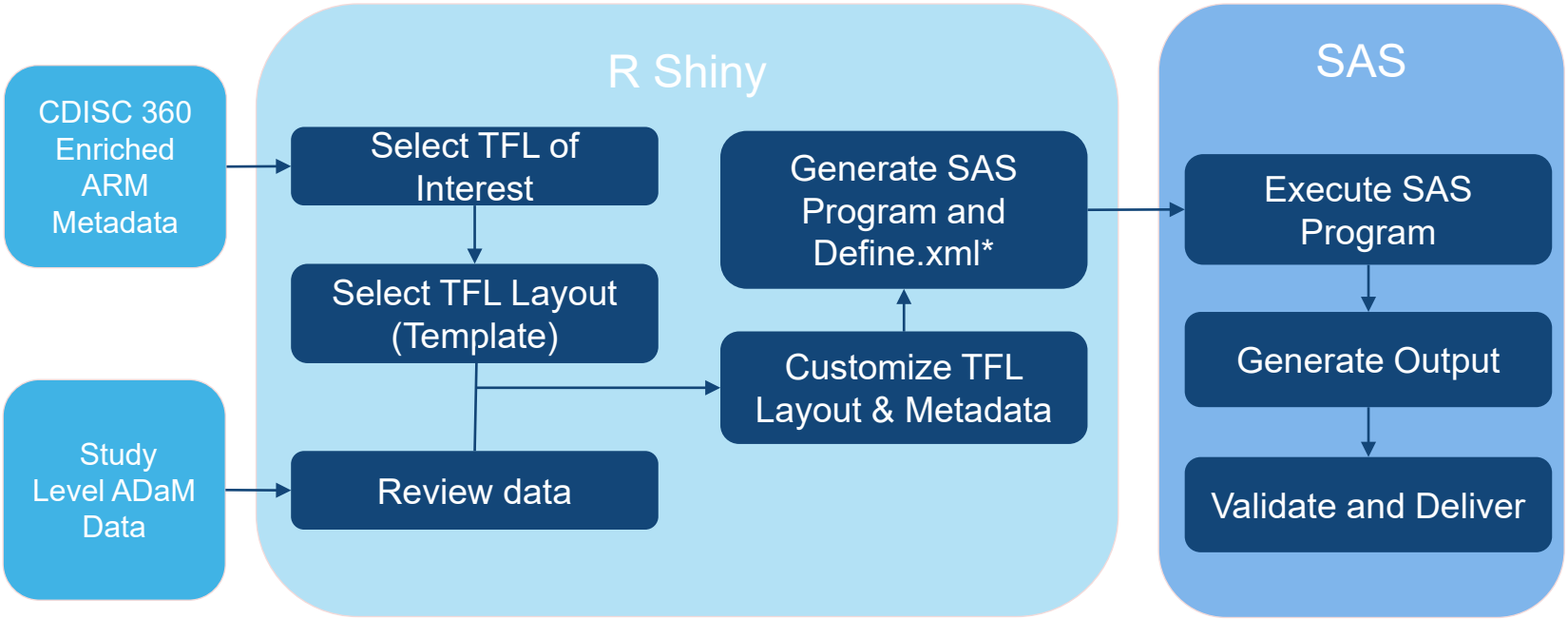
Process Flow for CDISC 360 Proof of Concept (PoC)

Process Flow for CDISC 360 PoC



TFL Automation Engine – Proof of Concept Design

CDISC 360 – TFL Automation Engine PoC Design



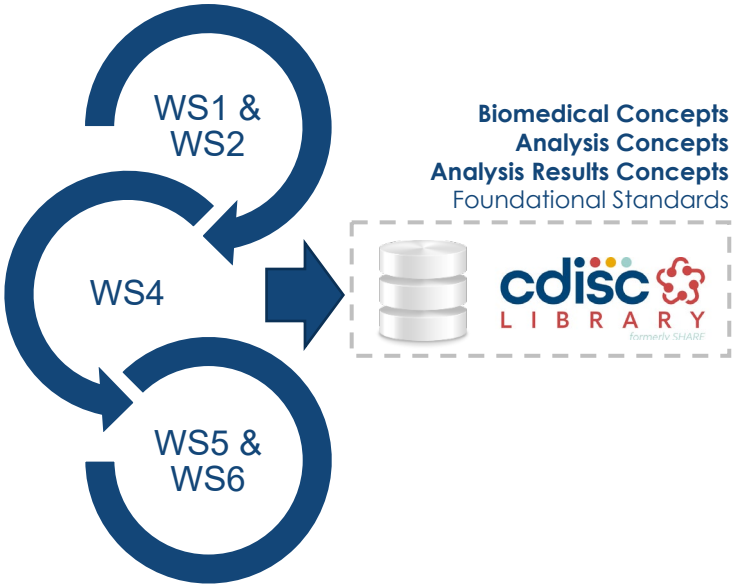
** ARM to be combined with ADaM Define*

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

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Thank You!

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Jianhui [Jimmy] Zhao, *Allergan*
Prasanna Murugesan, *AstraZeneca*

Courtesy: Mahi Busa