CDISC 360

Session 4, Track C: CDISC 360, Part II

Bhavin Busa
Vita Data Sciences
VP, Clinical Data Services & Operations

Mikkel Traun
Novo Nordisk
Principal Developer

Nicolas De Saint Jorre
XClinical
Product Owner - Data Manager

Prasanna Murugesan
AstraZeneca
Director

Jianhui Zhao
AbbVie
Associate Director

Stuart Malcolm
Frontier Science (Scotland) Ltd
Senior Programmer

1. Introduction, Future State, Process and Architecture of the PoC – *Bhavin and Mikkel* — 10 mins
2. **PoC for Study Design and Configuration using CDISC 360 Concept-based Standards – Mikkel and Nicolas** — **20 mins**
3. Automation of SDTM & ADaM Generation and Artifacts using CDISC 360 Enriched Metadata – Bhavin and Jimmy — 20 mins
4. Automation of TFL Generation using CDISC 360 Enriched Metadata – *Bhavin, Prasanna & Stuart* — 20 mins
5. Concluding Remarks and Next Steps – *Bhavin and Mikkel* — 5 mins
6. *Q & A session* — 15 mins

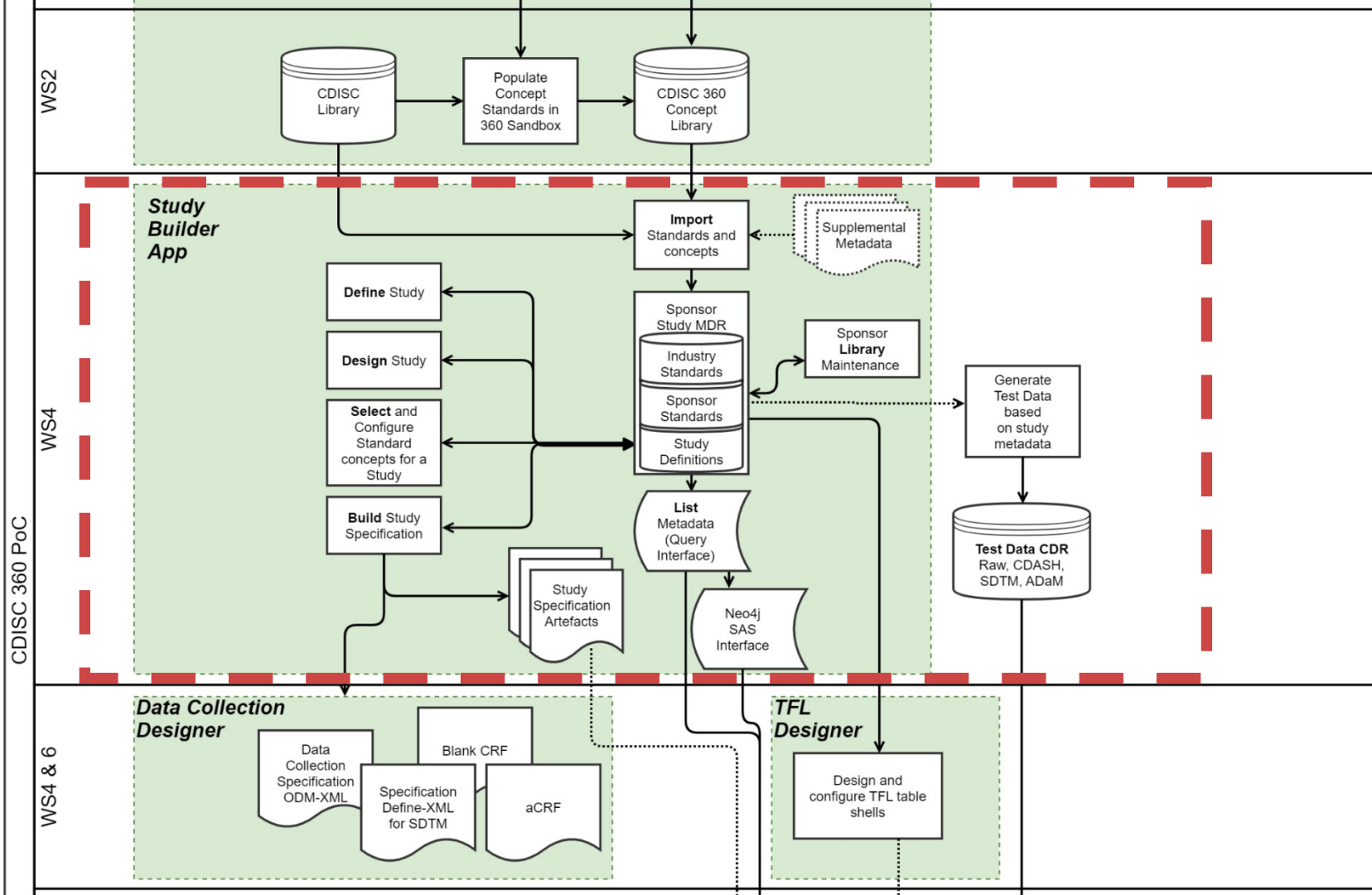
PoC for Study Design and Configuration using CDISC 360 Concept-based Standards

Mikkel Traun, *Novo Nordisk*
Nicolas de Saint Jorre, *XClinical*

CDISC US Interchange, October 2020

Agenda

- General Introduction to Study Builder App & MDR
- Demo
  - Define – Design – Select – Build
  - List and interface study metadata
- BC’s for Activities and Assessment
  - Linked Graph Data Model
- API for Sponsor Study MDR
- Neo4j to SAS Interface


CDISC 360 PoC
WS2
CDISC Library
Populate Concept Standards in 360 Sandbox
CDISC 360 Concept Library
WS4
Study Builder App
Import Standards and concepts
Supplemental Metadata
Define Study
Design Study
Select and Configure Standard concepts for a Study
Build Study Specification
Sponsor Study MDR
Industry Standards
Sponsor Standards
Study Definitions
Sponsor Library Maintenance
Generate Test Data based on study metadata
List Metadata (Query Interface)
Test Data CDR
Raw, CDASH, SDTM, ADaM
Study Specification Artefacts
Neo4j SAS Interface
WS4 & 6
Data Collection Designer
Data Collection Specification ODM-XML
Blank CRF
Specification Define-XML for SDTM
aCRF
TFL Designer
Design and configure TFL table shells

Key features in the Study Designer App

Library

Import definitions from external libraries.

Manage sponsor defined selections and definitions.

Define Identifiers and a general set of trial summary parameters for the study

Design Study design parameters as well as defining study arms, elements, epochs and visits

Select Search and select concept-based standards and define schedule of activities and assessments

Build Generate study specification artefacts that support automation of study setup and execution

List

Extract study metadata in tabular format for down stream usage.

From within the App with export to multiple format as well as direct from SAS.

cdisc

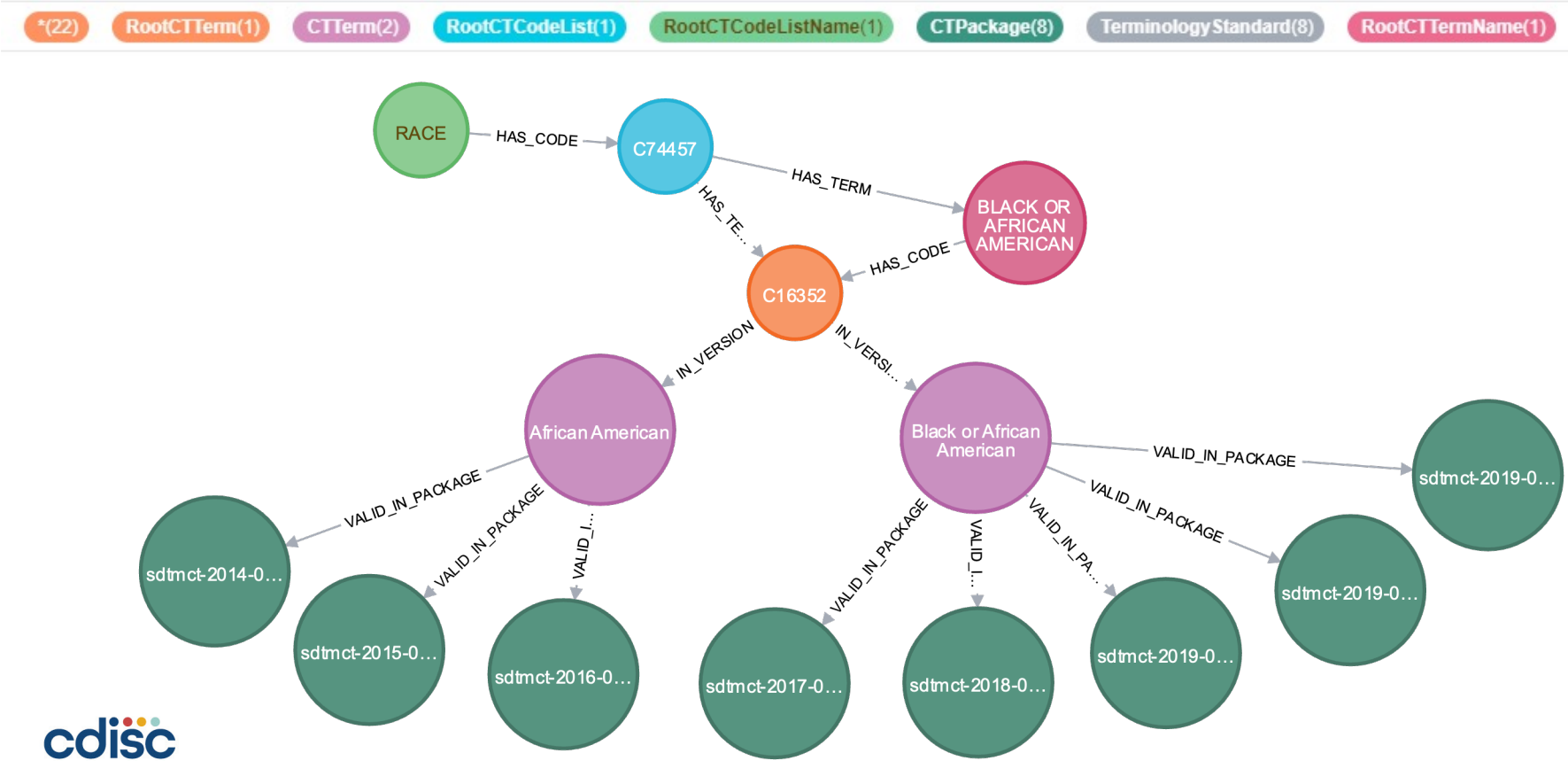
Import Concept Based Standards

- Currently the Concept Based Standards are imported as a combination of data from
  - Current CDISC Library
  - Supplemental Metadata
- This is done in Cypher program scripts loading data into the Neo4j based Study Metadata Library
- Each CT term is stored once and Neo4j enable version tracking over time

```
"https://library.cdisc.org/api/mdr/ct/packages"
```

```
// Load Scope of CT packages
CALL apoc.load.jsonParams("https://library.cdisc.org/api/mdr/ct/packages",{Authorization:
 "Basic Y2xxx", Accept: "application/json"}, null) YIELD value AS link
UNWIND link._links.packages AS package
WITH DISTINCT SPLIT(package.title, ' ')[0] AS model
MERGE (mdl:Model {name: model})
RETURN mdl.name;
```

Linked graph domain model for CDISC CT



Demo

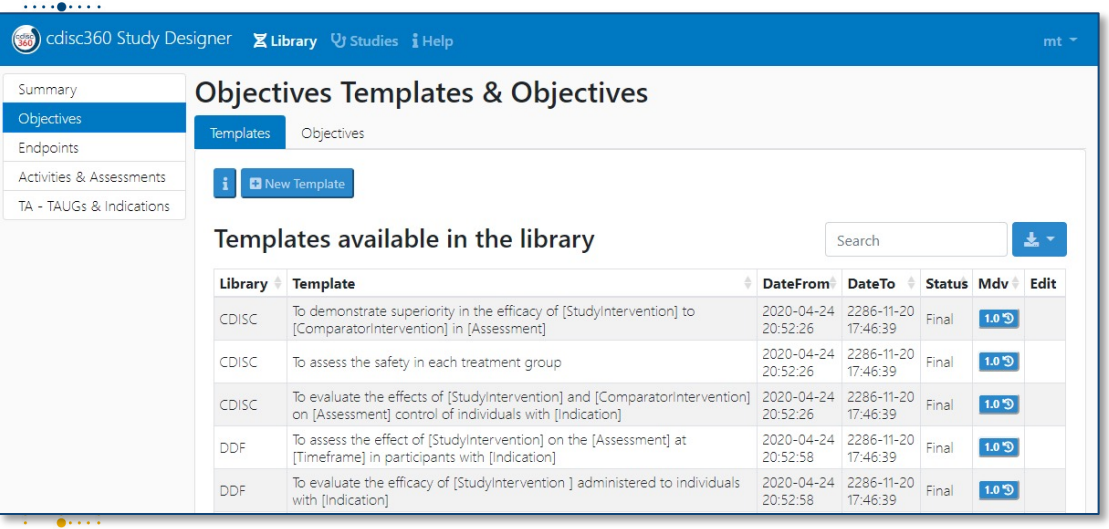
Library – Import and manage sponsor standards

Define – Design – Select – Build

List and interface study metadata

How do you work with a 360 enabled Sponsor Study MDR

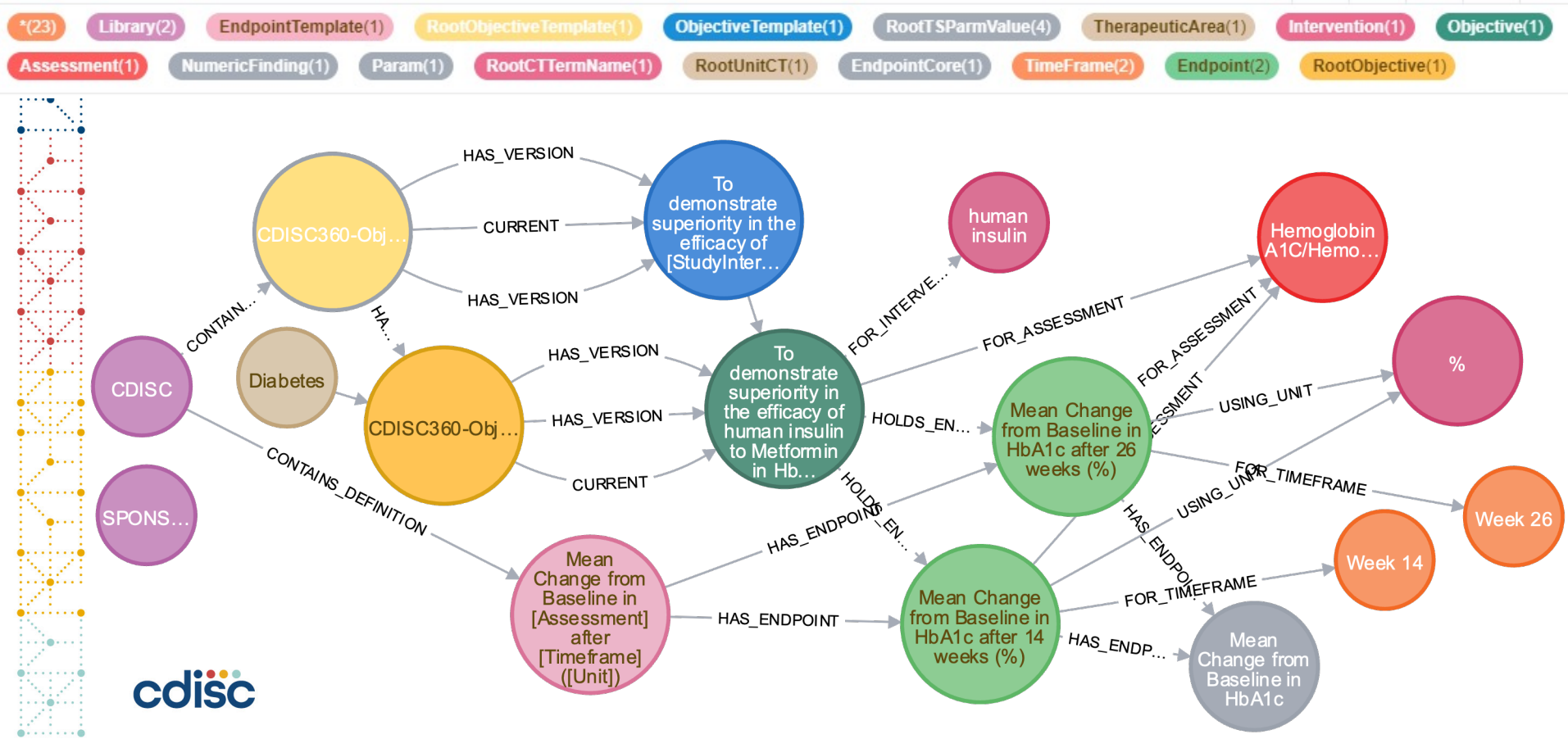
Study Designer App - Library



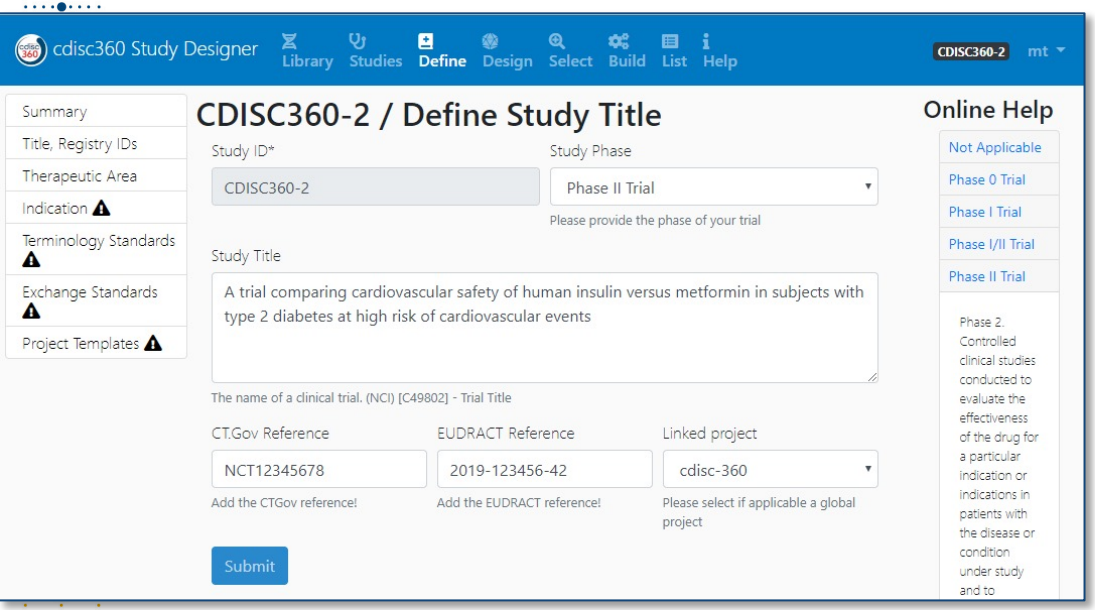
On the **Library** menu the user

- Create additional templates for Objectives and Endpoints
- Create instantiations of imported or sponsor defined templates
- Instances of Objectives and Endpoints include reference to dependent parameters

Linked graph domain model for Library



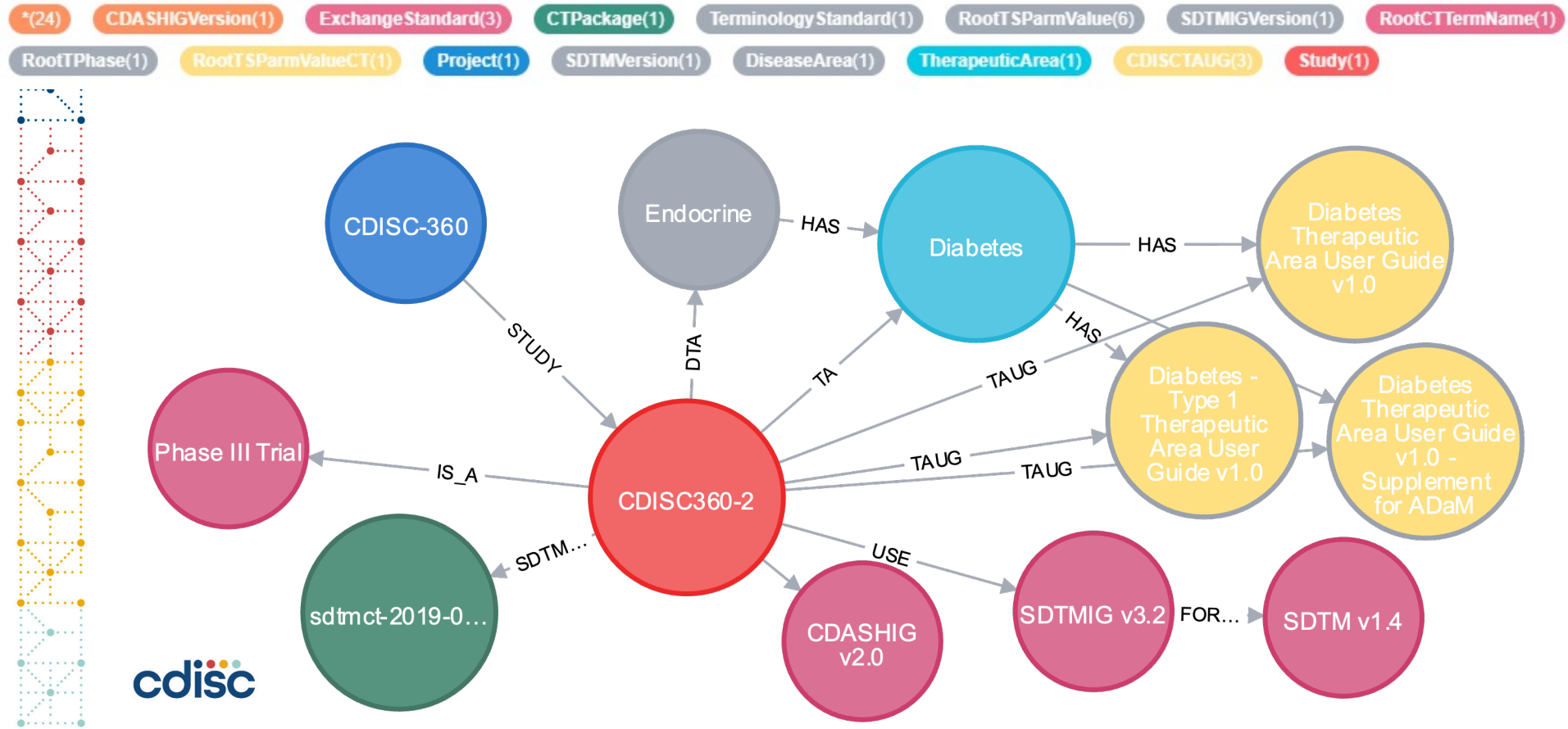
Study Designer App - Define



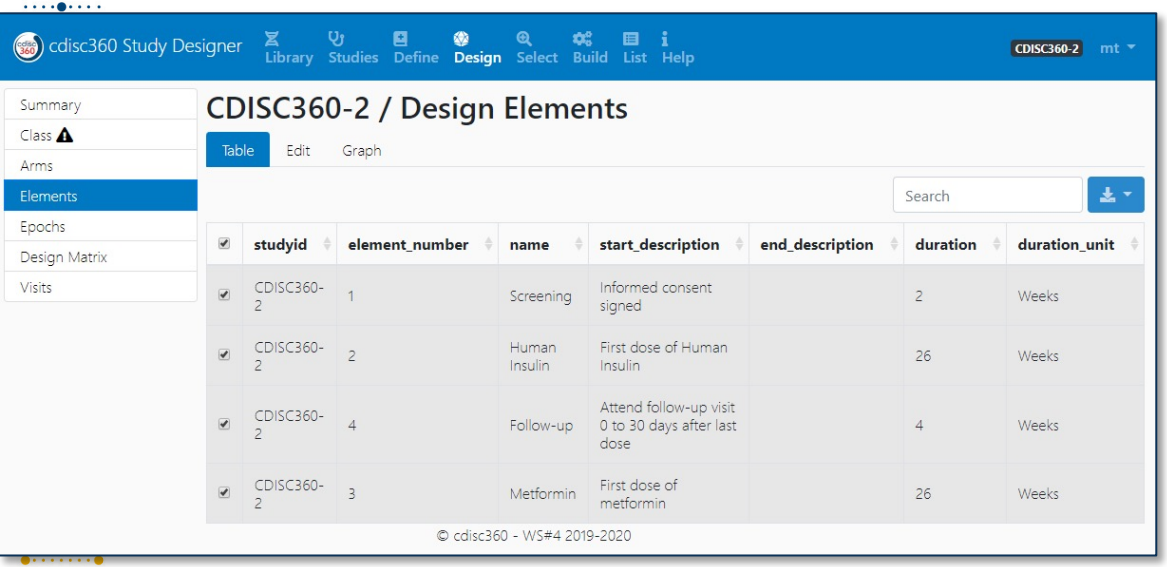
On the **Define** menu the user

- Enter the basic description of the trial like the study phase, title, registry identifiers
- Therapeutic Area of the study and CDISC TAUGs used
- Version of terminology standards
- Version of exchange standards

Linked graph domain model for Study Define



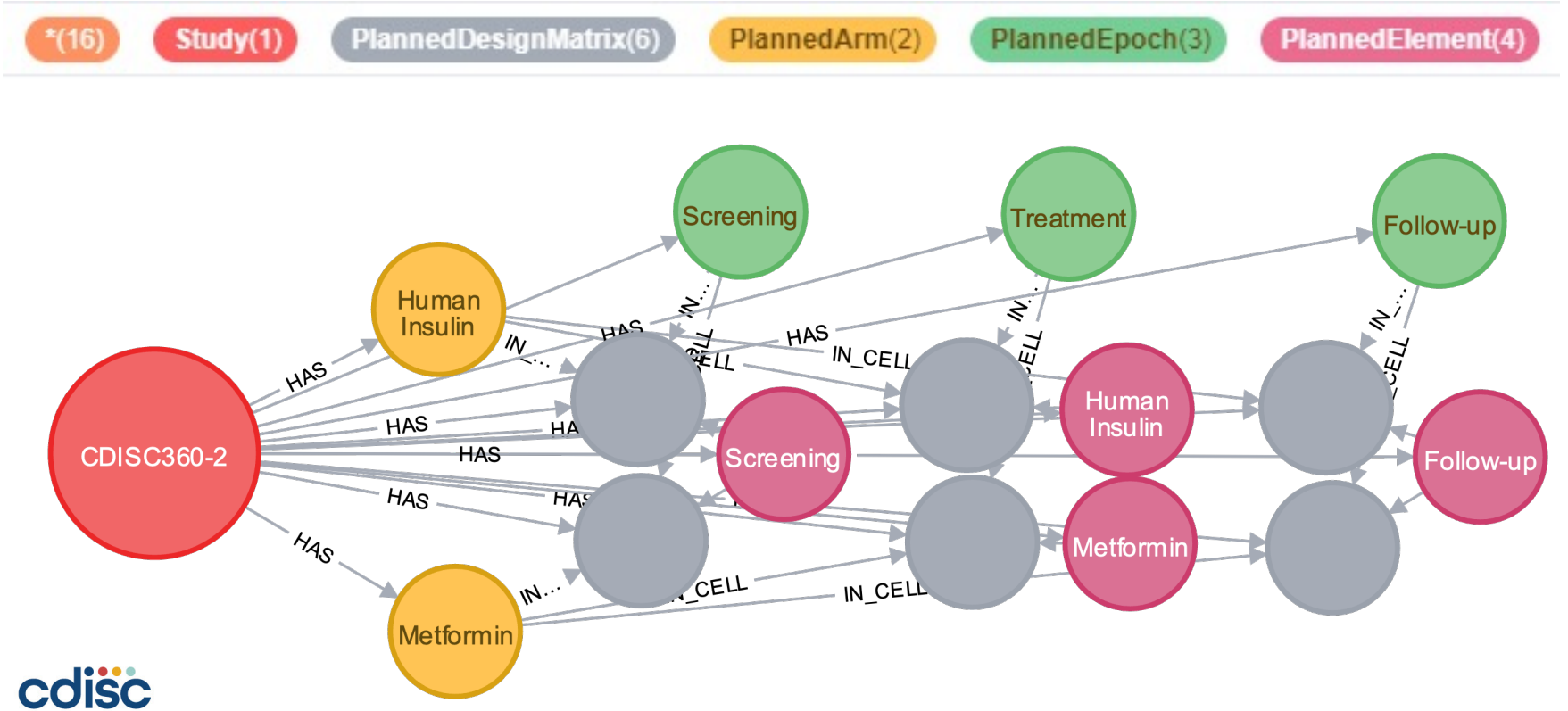
Study Designer App - Design



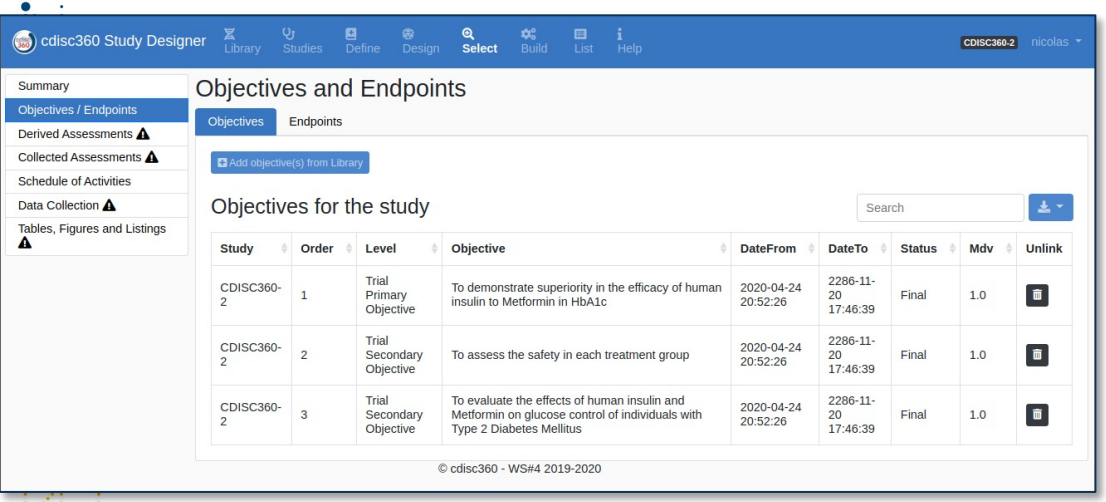
On the **Design** menu the user

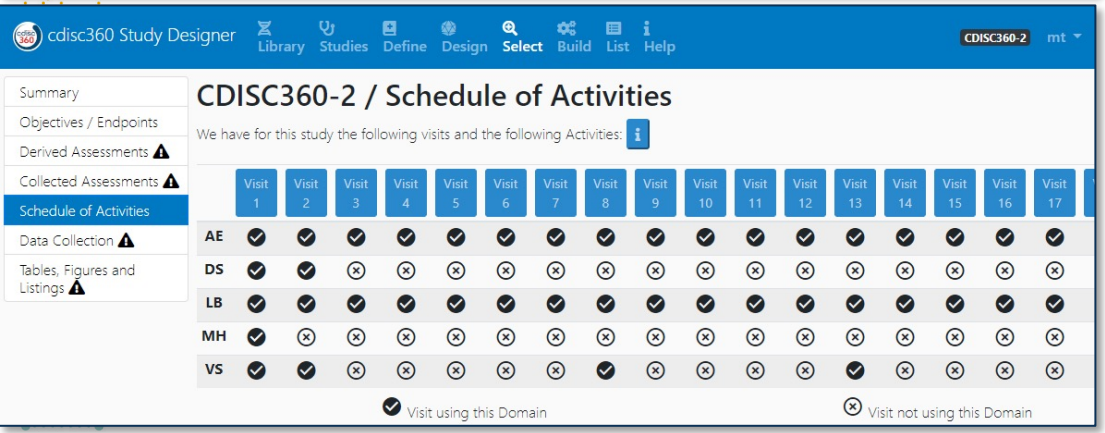
- Make basic selection of trial design related trial summary parameters like Intervention Type, Intervention Model etc.
- Define the Trial Arms, Epochs, Elements and the Design matrix
- Define the visit schedule
- Define the planned interventions

Linked graph domain model for Study Design



Study Designer App - Select

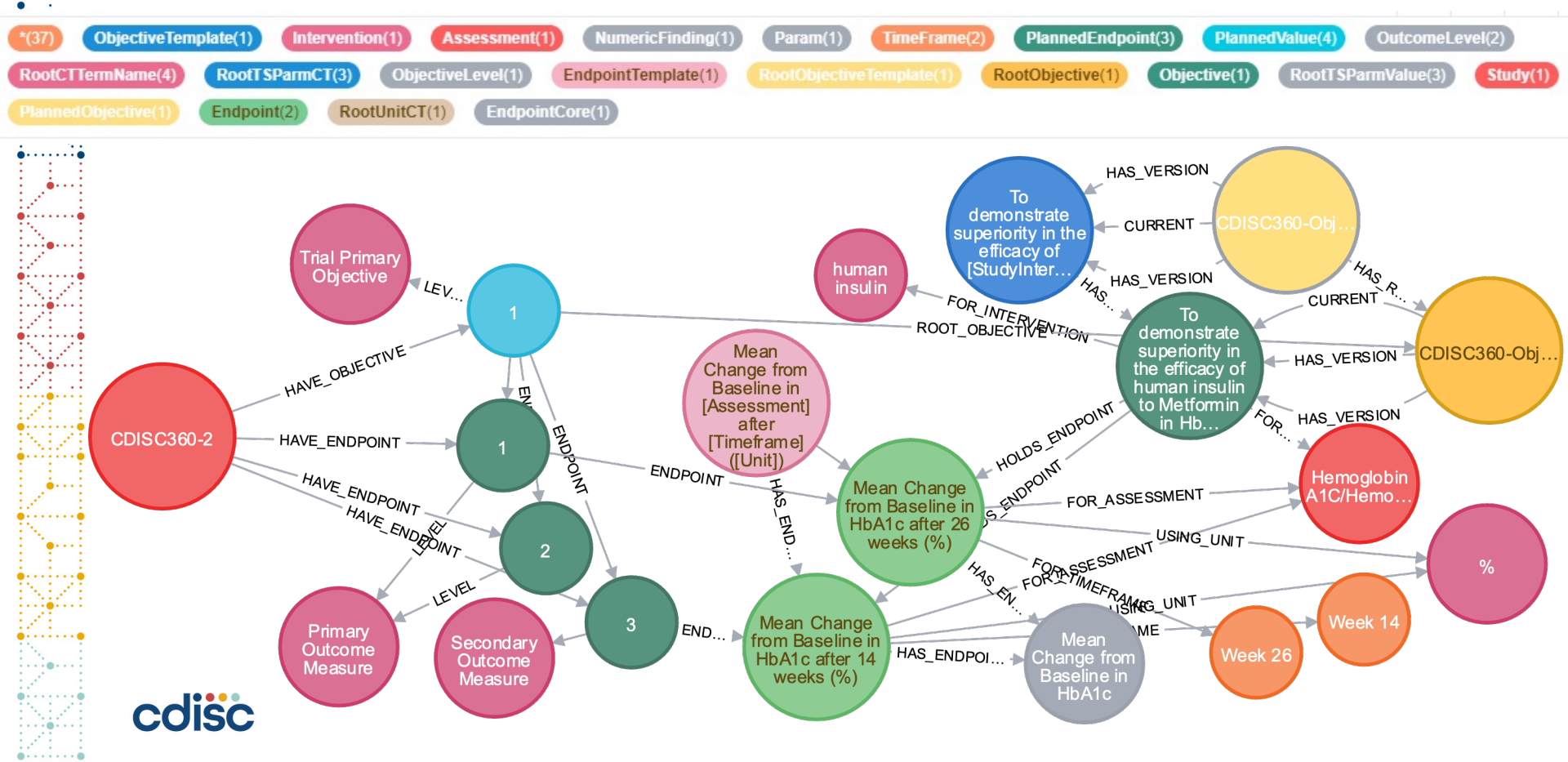




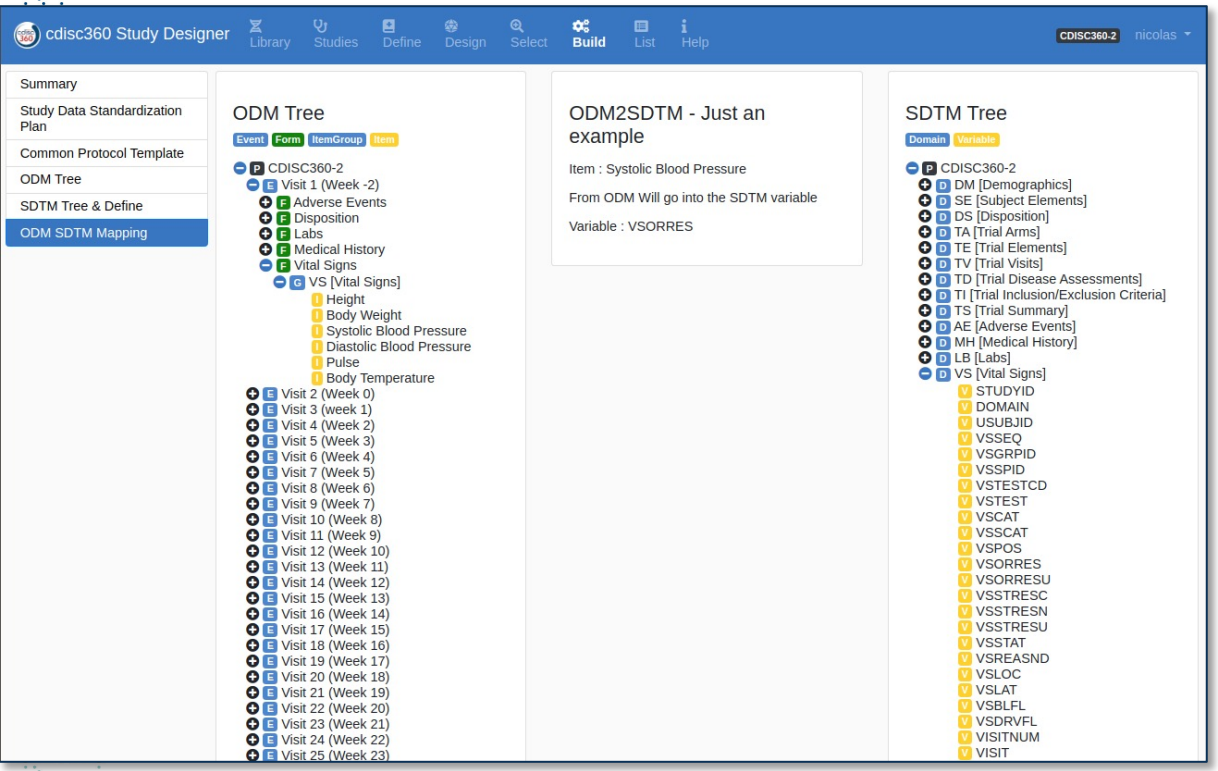
On the **Select** menu the user

- Selects the concept based standards from the libraries that are to be used in the study
  - These can be based on templates that are instantiated in the local library
- Objectives and Endpoints
- Activities and Assessments
- Schedule of Activities and Assessments
- TFL metadata

Linked graph domain model for Study Select



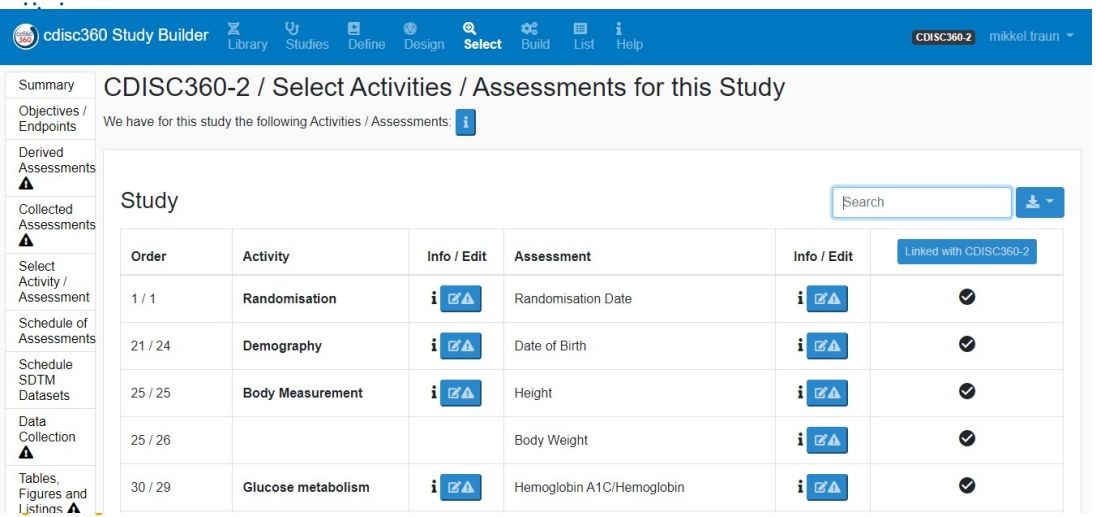
Study Designer App - Build



On the **Build** menu the user can generate:

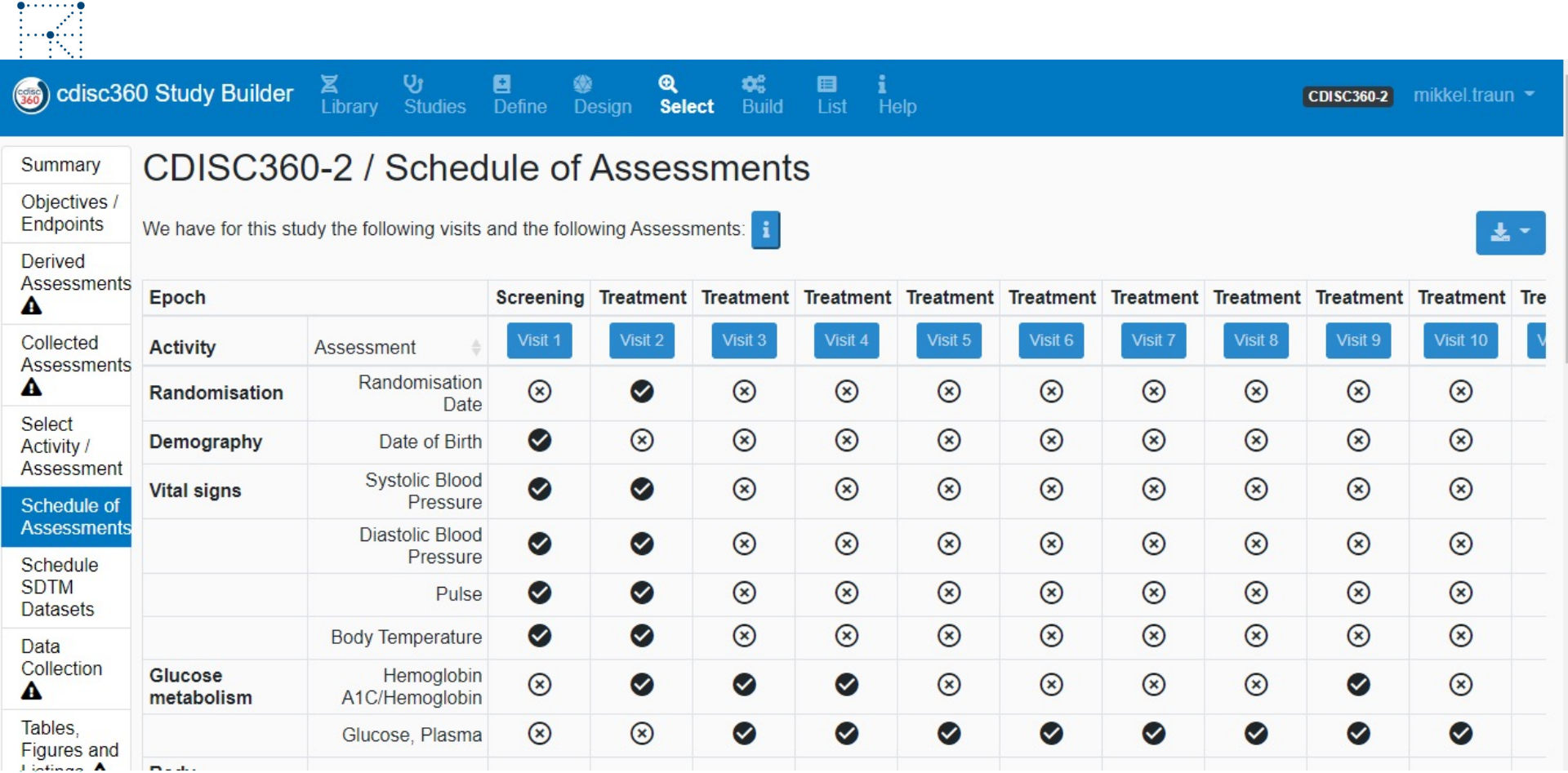
- Study data standards plan
- Protocol metadata report
  - To be copy paste into CPT
  - As XML to be imported into eCPT
  - As tables that can be exported
- Data collection specification
  - ODM-XML
  - Blank CRF, techCRF and aCRF
- Tabulation Specification
  - Define-XML specification
- Analysis Specification

Study Designer App – Select Activities & Assessments



On the **Select** menu the user

- Selects BC's in the form of Activities and Assessments
- Configure these in context of the study
- Schedule the Activities and Assessments in Study Design


cdisc360 Study Builder
Library
Studies
Define
Design
Select
Build
List
Help
CDISC360-2
mikkel.traun
Summary
Objectives / Endpoints
Derived Assessments
Collected Assessments
Select Activity / Assessment
Schedule of Assessments
Schedule SDTM Datasets
Data Collection
Tables, Figures and
CDISC360-2 / Schedule of Assessments
We have for this study the following visits and the following Assessments:
Epoch
Screening
Treatment
Activity
Assessment
Visit 1
Visit 2
Visit 3
Visit 4
Visit 5
Visit 6
Visit 7
Visit 8
Visit 9
Visit 10
Randomisation
Randomisation Date
Demography
Date of Birth
Vital signs
Systolic Blood Pressure
Diastolic Blood Pressure
Pulse
Body Temperature
Glucose metabolism
Hemoglobin A1C/Hemoglobin
Glucose, Plasma

swagger

Logout

You are logged in as: **mikkel.traun**

Study Builder API Documentation!!!

[Base URL: cdisc360poc.azurewebsites.net]

Schemes

HTTP

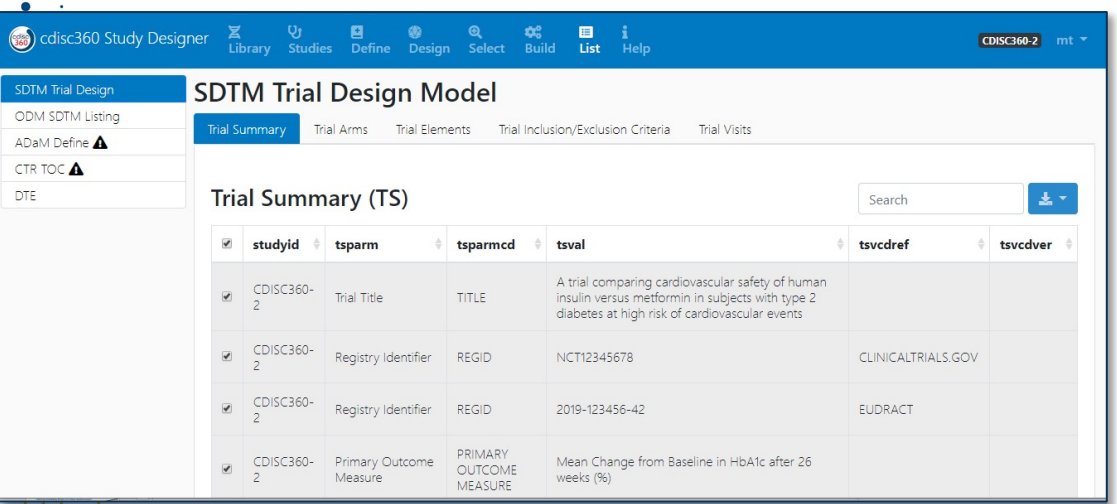
Authorize

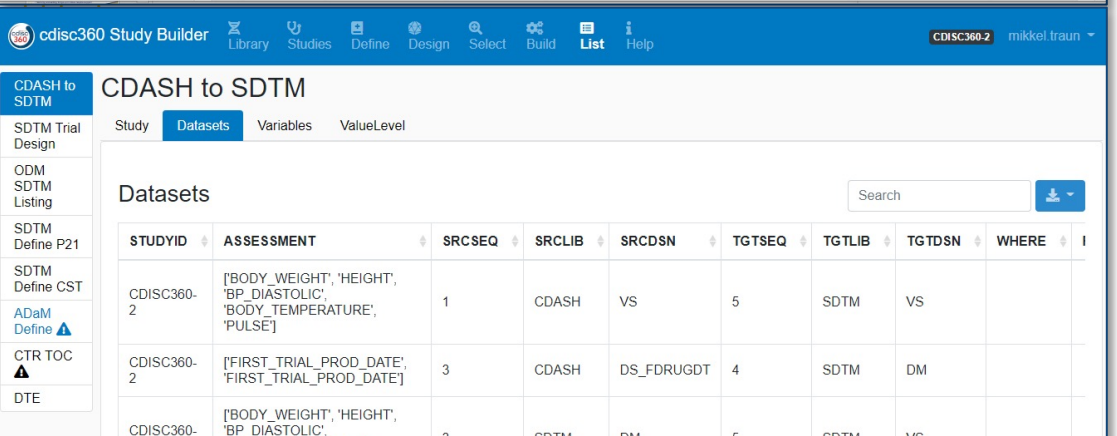
api

GET	/api/objectives-templates/	
GET	/api/objectives/	
GET	/api/schedule-of-assessment/	
POST	/api/schedule-of-assessment/schedule/	Schedule an assessment for a visit.
POST	/api/schedule-of-assessment/unschedule/	Unschedule an assessment for a visit.
GET	/api/studies/	

cdisc

Study Designer App - List





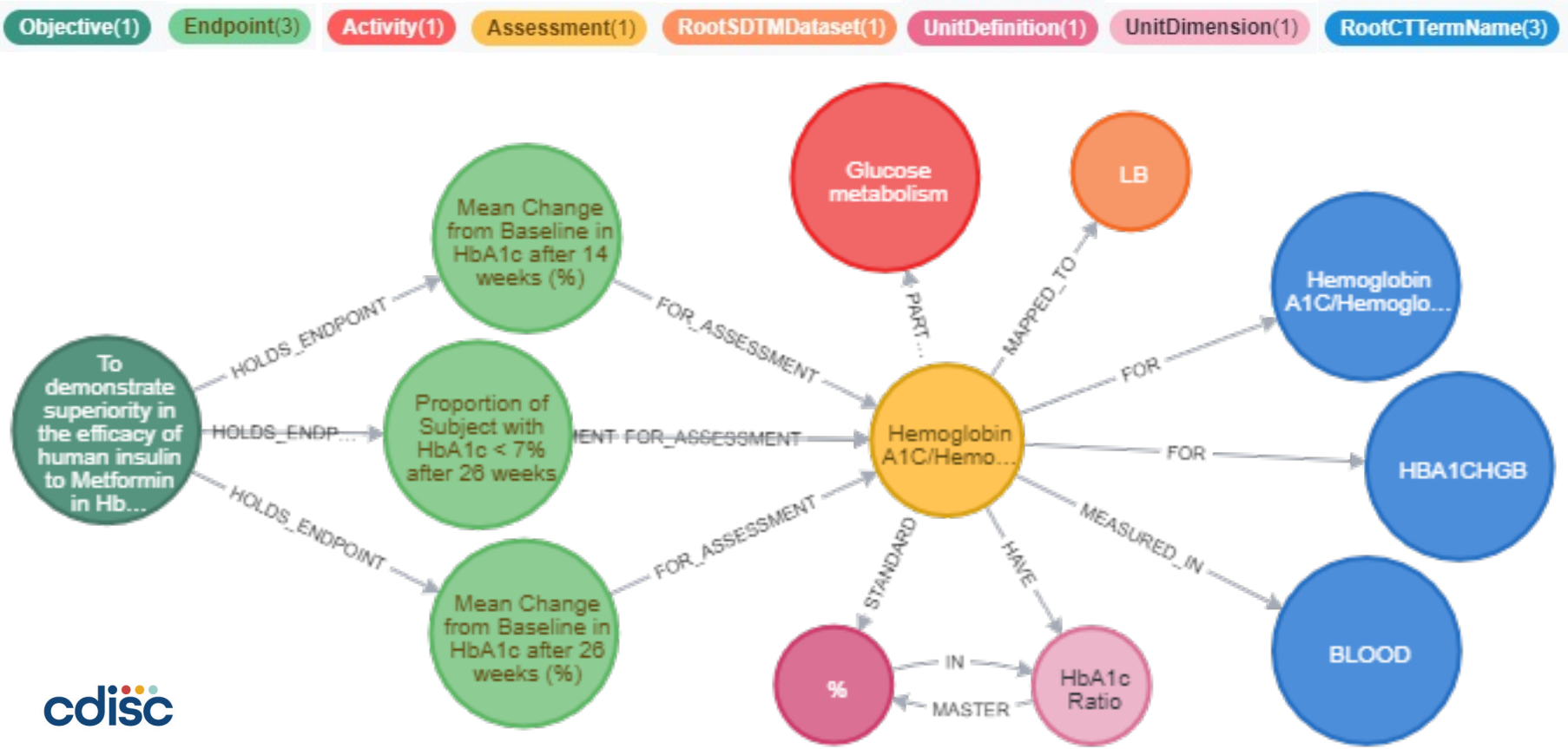
On the **List** menu the user can generate:

- Browse all study metadata in tabular form
- Export these into various file formats
- Will correspond to the SAS based interface to the Study Metadata Library enabling extract of study metadata into SAS datasets
- This include CDASH2SDTM and SDTM2ADaM Bindings

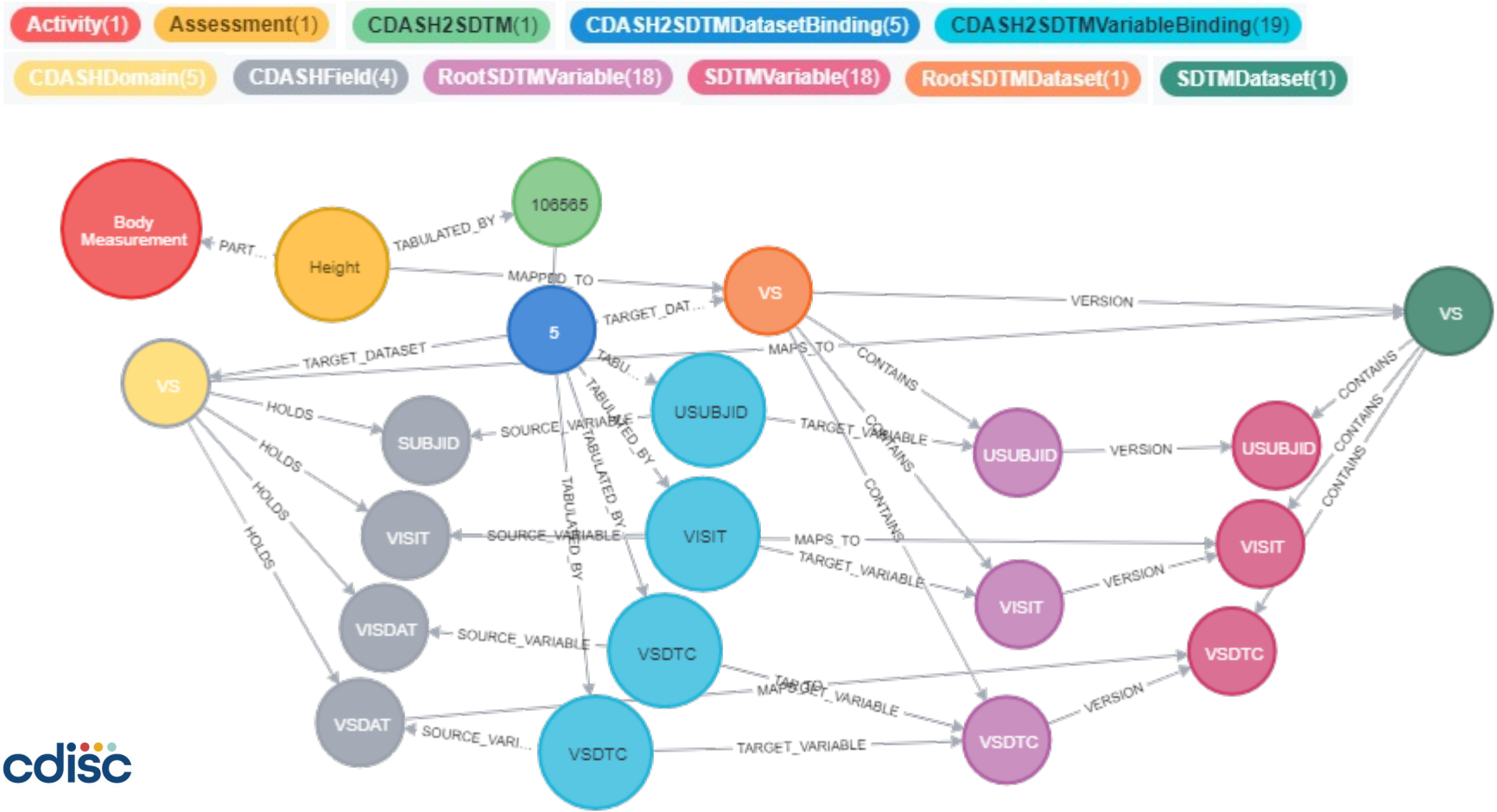
BC’s for Activities and Assessment

Linked Graph Data Model

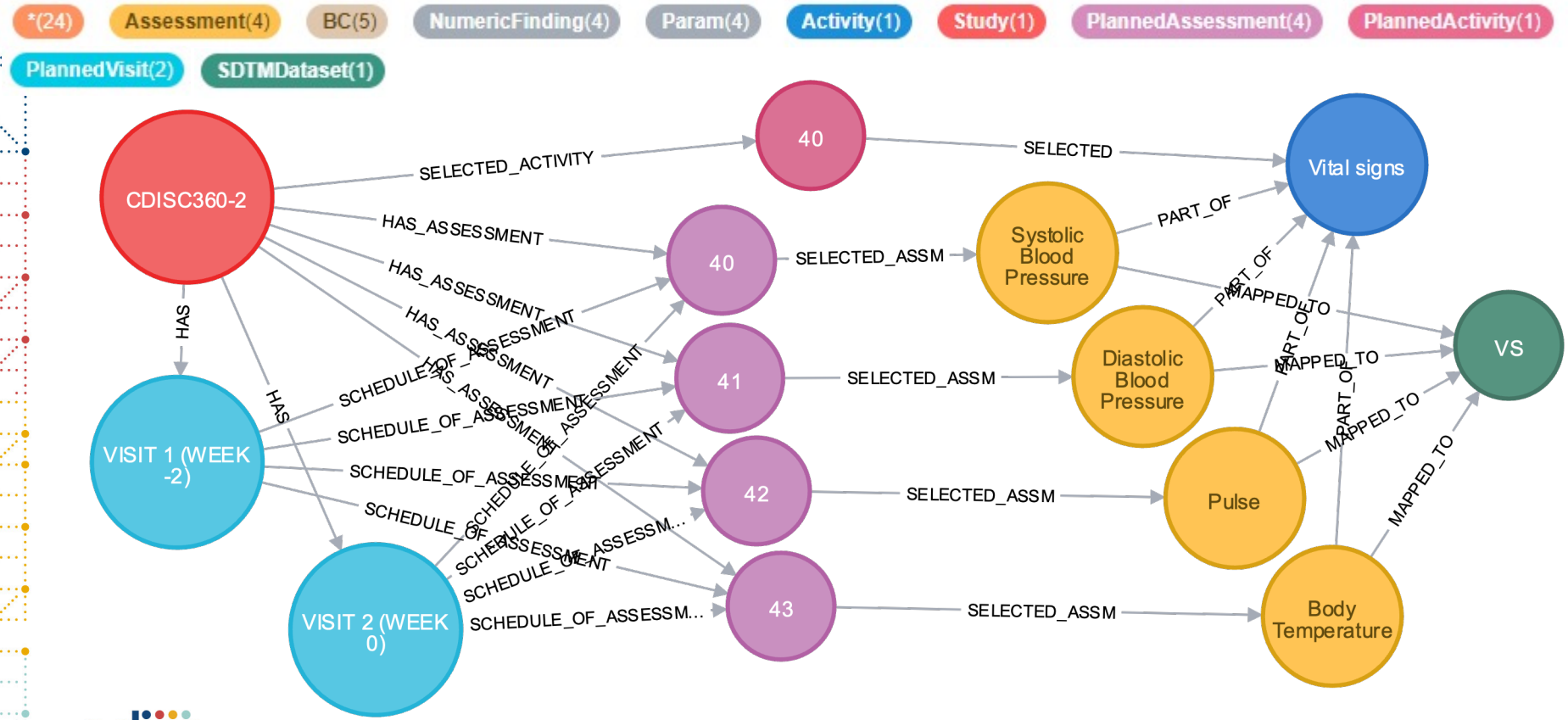
Linked graph domain model for Activities and Assessments The Concept Definition



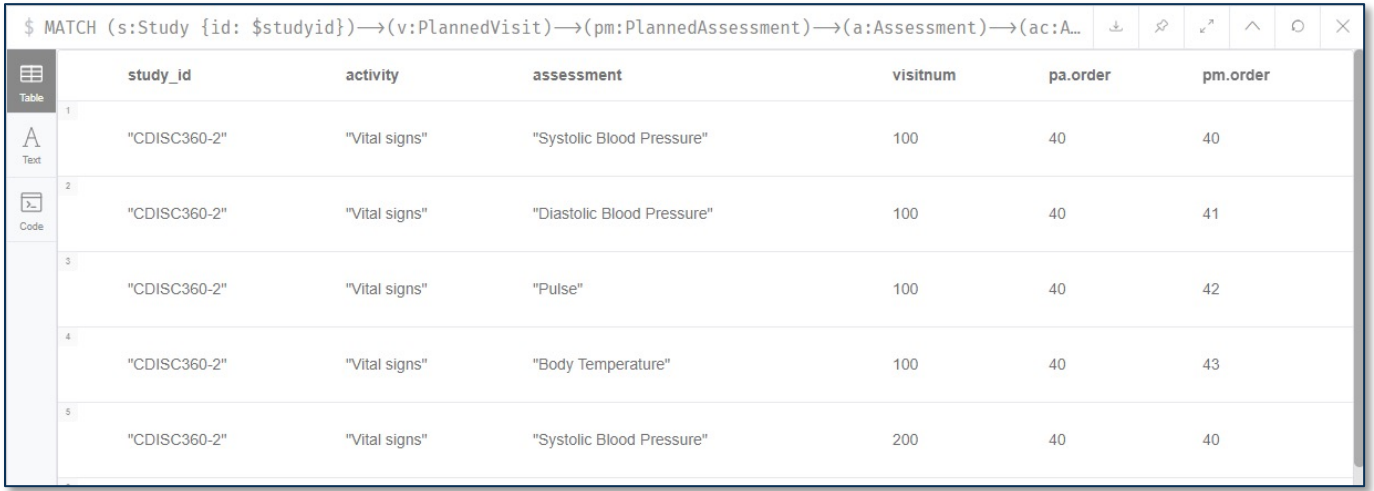
The CDISC 360 Bindings from CDASH -> SDTM



Linked graph domain model for Schedule of Assessment



Sample Cypher Query Schedule of Assessments



	study_id	activity	assessment	visitnum	pa.order	pm.order
1	"CDISC360-2"	"Vital signs"	"Systolic Blood Pressure"	100	40	40
2	"CDISC360-2"	"Vital signs"	"Diastolic Blood Pressure"	100	40	41
3	"CDISC360-2"	"Vital signs"	"Pulse"	100	40	42
4	"CDISC360-2"	"Vital signs"	"Body Temperature"	100	40	43
5	"CDISC360-2"	"Vital signs"	"Systolic Blood Pressure"	200	40	40

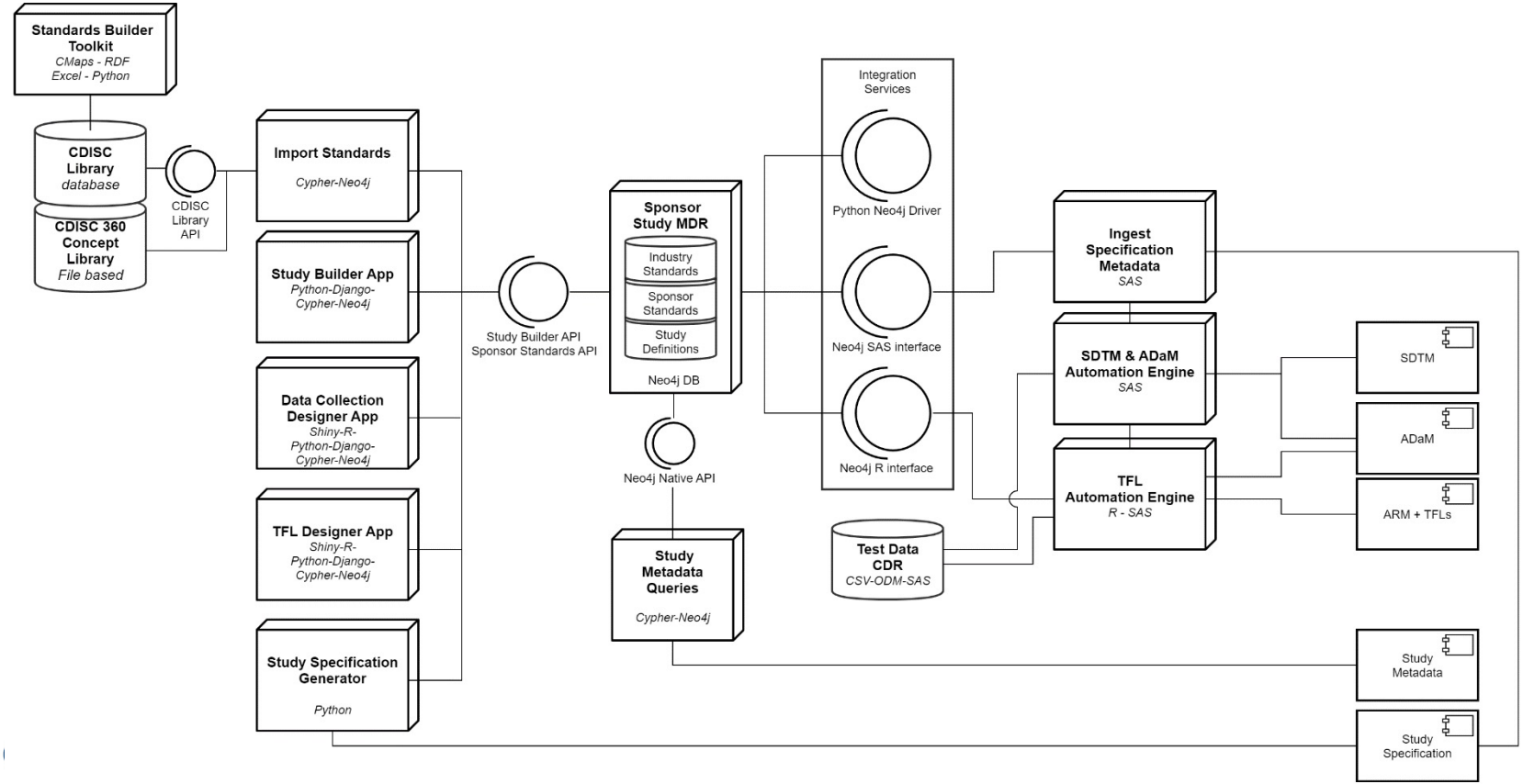
```
// List Schedule of Activity and Assessment for a Study
MATCH (s:Study {id: $studyid})-->(v:PlannedVisit)-->
(pm:PlannedAssessment)-->(a:Assessment)-->(ac:Activity)<--
(pa:PlannedActivity)<--(s)
RETURN  s.id as study_id, ac.name as activity, a.name as assessment,
        v.visitnum as visitnum, pa.order, pm.order
ORDER BY s.id, v.visitnum, pa.order, pm.order;
```

API for Sponsor Study MDR

PoC implementation of API endpoints

API for Sponsor MDR managing the Study Metadata

This component diagram will be described in the CDISC 360 PoC Yellow-paper



Neo4j to SAS Interface

All metadata in Sponsor Study MDR Neo4j database can be access directly from SAS

Access Neo4j Sponsor Study MDR from SAS

- The Neo4j transactional HTTP endpoint allows you to execute Cypher statements
- Using SAS PROC LUA to easily interface with the Neo4j REST API from SAS
- Neo4j to SAS Interface manage SAS Dataset metadata

ASSESSMENT	SRCSEQ	SRCLIB	SRCDSN	SRCVAR	SRCTYPE	ORIGIN	METHOD	CODELIST	TGTLIB
["BODY_WEIGHT", "HEIGHT", "BP_DIASTOLIC", "BODY_TEMPERATURE", "PULSE"]	1	CDASH	VS	SUBJID	text	Assigned	ALL.USUBJID		SDTM
["BODY_WEIGHT", "HEIGHT", "BP_DIASTOLIC", "BODY_TEMPERATURE", "PULSE"]	1	CDASH	VS	VISIT	text	Predecessor		VISIT	SDTM
["BODY_WEIGHT", "HEIGHT", "BP_DIASTOLIC", "BODY_TEMPERATURE", "PULSE"]	1	CDASH	VS	VSDAT	text	Assigned	VS.VSDTC		SDTM
["BODY_WEIGHT", "HEIGHT", "BP_DIASTOLIC", "BODY_TEMPERATURE", "PULSE"]	1	CDASH	VS	VISDAT	text	Assigned	VS.VSDTC		SDTM
["BODY_WEIGHT", "HEIGHT", "BP_DIASTOLIC", "BODY_TEMPERATURE", "PULSE"]	1	CDASH	DM	SUBJID	text	Assigned	ALL.USUBJID		SDTM
["BODY_WEIGHT", "HEIGHT", "BP_DIASTOLIC", "BODY_TEMPERATURE", "PULSE"]	1	CDASH	DM	RACE	text	Predecessor		RACE	SDTM
2" ["FIRST_TRIAL_PROD_DATE", "FIRST_TRIAL_PROD_DATE"]	3	CDASH	DS_FDRUGDT	DSSTDAT	date	Assigned	DM.RFSTDTC	ISO 8601	SDTM

Reflections from WS4

What have we accomplished in the cdisc360 PoC

Machine-readable Study Specification Metadata

- Study Design
  - Implemented basic Study Definition and Design in Study Repository linked to Schedule of Assessment
- CDASH & SDTM
  - Implemented Assessment BC's in a Label Property Graph Model linked with versioned metadata from the CDISC Library
  - Including sample CDASH2SDTM bindings
- ADaM
  - Implemented basic ADaM Sponsor model in a Label Property Graph Model linked with versioned metadata from the CDISC Library
  - Including sample SDTM2ADaM bindings
- Study Builder & Sponsor Study MDR
  - Standard API based to enable tool and vendor agnostic system integrations

Thank You!

Mikkel Traun, *Novo Nordisk*

Nicolas de Saint Jorre, *XClinical*