Study Design and Configuration using CDISC 360 concept based standards

Mikkel Traun, Novo Nordisk
Nicolas de Saint Jorre, XClinical

CDISC EU Interchange, April 2020
Study Design and Configuration using CDISC 360 concept based standards

- CDISC 360 Use Case 1 & 2
  - Using a Study Metadata Library
- Approach for the Proof of Concept prototype
- Demo
  - Import Concept Based Standards
  - Define – Design – Select – Build
  - List and interface study metadata
- Learnings so far
  - Linked Graph Data Model for Study Metadata Library
- Next Step
CDISC 360 Use Case 1 & 2
Using a Study Metadata Library

How the Study Metadata Library fit in the overall CDISC360 vision
CDISC 360 Use Case 1 and 2

**Enhance Standards**
Concept Based

**Publish Standards**
CDISC Library

- **Define**
  Use Case 1

- **Build**
  Use Case 2

- **Execute**
  Use Case 3

Study Metadata Library
Goal for Study Metadata Library PoC prototype

• Import Concept Based standards
  • Including end-to-end definitions

• Select Concept Based standards to be used in a study
  • Search and select concept standards for a study

• Deliver selection of Concept standards to support study configuration
  • Concepts will drive CDASH-SDTM-ADaM-Output automation

• To limit scope
  • Started in the middle with SDTM, adding relationship downstream to ADaM and TFL’s
  • Added upstream relationship to Endpoints, Objectives and Trial Design
  • Next add relationship to data collection and specifications for study setup
Process flow for Study Metadata Library PoC prototype

**Study Designer App**
- Define Study
- Design Study
- Select and Configure Standard concepts for a Study
- Build Study Specification

**Import**
- Standards and concepts

**Study Metadata Library**

**List**
- Metadata (Query Interface)

**Ne04j SAS Interface**

**Sponsor Library Maintenance**

**Supplemental Metadata**
Approach for the Study Metadata Library
Proof of Concept prototype

What is the main design elements of a Study Metadata Library solution
Study Metadata Library in Label Property Graph Model

• What is a Label Property Graph
  • A linked graph model where nodes have labels, relationships and properties
  • Invented by Neo4j

• Why
  • Representing study metadata close to our logical model
  • Enable dynamic linking between study definition and standards metadata
  • Cypher Query language very efficient for PoC development

• How
  • In program scripts
  • Simple listing exports in CSV files
  • Simple Browser Guide Apps
  • Generic GUI (Bloom)
  • Interface with Python and SAS
  • Rapid application developments for prototyping
<table>
<thead>
<tr>
<th>Library</th>
<th>Define</th>
<th>Design</th>
<th>Select</th>
<th>Build</th>
<th>List</th>
</tr>
</thead>
<tbody>
<tr>
<td>Import definitions from external libraries.</td>
<td>Identifiers and a general set of trial summary parameters for the study</td>
<td>Study design parameters as well as defining study arms, elements, epochs and visits</td>
<td>Search and select concept-based standards and define schedule of activities and assessments</td>
<td>Generate study specification artefacts that support automation of study setup and execution</td>
<td>Extract study metadata in tabular format for downstream usage. From within the App with export to multiple format as well as direct from SAS.</td>
</tr>
</tbody>
</table>
Demo
Import Concept Based Standards

Library – manage templates and standards
Define – Design – Select – Build
List and interface study metadata

*How do you work with a Study Metadata Library*
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

```
// Load Scope of CT packages
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
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

CDISC360-Obj...

CDISC

Diabetes

Mean Change from Baseline in [Assessment] after [Timeframe] (([Unit]))

Mean Change from Baseline in [Assessment] after [Timeframe] (([Unit]))

Mean Change from Baseline in HbA1c after 14 weeks (%)

Mean Change from Baseline in HbA1c after 26 weeks (%)

Week 14

Week 26

Hemoglobin A1C/Hemo...

human insulin

To demonstrate superiority in the efficacy of insulin to Metformin in Hb...
Linked graph domain model for Objective with versioning
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
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
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
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
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
**Neo4j to SAS Interface – Engine CST**

Using SAS PROC LUA to easily interface with the Neo4j REST API from SAS

Credit: Lex Jansen, SAS Institute
Learnings so far

*Experience using Linked Graph Data Model for Study Metadata Library*
Learnings from initial implementation of Study Library in a Property Label Graph database (Neo4j)

- Very efficient to load JSON data from API’s into Neo4j with no duplication of metadata
- Intuitive to represent BCs in a Property Label Graph Model linked with metadata from the CDISC Library
- Intuitive to define and query standards selections for a study in Property Label Graph Model
- Difficult to articulate and agree on what a BC is
  - Iterations are needed to learn and evolve definitions of a BC
- Learning new tools takes time
- Working and setting things up in Azure require support
  - Big thanks to Microsoft, Neo4j and CDISC IT
Next Steps

Our plans for remaining part of PoC
Next Steps in Study Design and Configuration

- Configuring BCs as Assessments and Activities in Study
- Data Collection Specification as ODM.XML
- Metadata for transformations
- Metadata for TFLs
Thank You!

Mikkel Traun, Novo Nordisk
Nicolas de Saint Jorre, XClinical