1. Introduction, Future State, Process and Architecture of the PoC – Bhavin and Mikkel

2. PoC for Study Design and Configuration using CDISC 360 Concept-based Standards – Mikkel and Nicolas

3. Automation of SDTM & ADaM Generation and Artifacts using CDISC 360 Enriched Metadata – Bhavin and Jimmy

4. Automation of TFL Generation using CDISC 360 Enriched Metadata – Bhavin, Prasanna & Stuart

5. Concluding Remarks and Next Steps – Bhavin and Mikkel

6. Q & A session
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
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 downstream usage.
From within the App with export to multiple format as well as direct from SAS.
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 enables 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
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*
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
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
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**
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
# CDISC360-2 / Schedule of Assessments

We have for this study the following visits and the following Assessments.

<table>
<thead>
<tr>
<th>Epoch</th>
<th>Activity</th>
<th>Assessment</th>
<th>Visit 1</th>
<th>Visit 2</th>
<th>Visit 3</th>
<th>Visit 4</th>
<th>Visit 5</th>
<th>Visit 6</th>
<th>Visit 7</th>
<th>Visit 8</th>
<th>Visit 9</th>
<th>Visit 10</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Randomisation</td>
<td>Randomisation Date</td>
<td>![X]</td>
<td>![X]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Demography</td>
<td>Date of Birth</td>
<td>![X]</td>
<td>![X]</td>
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<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Pulse</td>
<td>![X]</td>
<td>![X]</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Body Temperature</td>
<td>![X]</td>
<td>![X]</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glucose, Plasma</td>
<td>![X]</td>
<td>![X]</td>
<td></td>
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<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
# Study Builder API Documentation!!!

[ Base URL: cdisc360doc.azurewebsites.net ]

## Schemes

| HTTP |

## api

<table>
<thead>
<tr>
<th>Method</th>
<th>Endpoint</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>GET</td>
<td>/api/objectives-templates/</td>
<td></td>
</tr>
<tr>
<td>GET</td>
<td>/api/objectives/</td>
<td></td>
</tr>
<tr>
<td>GET</td>
<td>/api/schedule-of-assessment/</td>
<td></td>
</tr>
<tr>
<td>POST</td>
<td>/api/schedule-of-assessment/schedule/</td>
<td>Schedule an assessment for a visit.</td>
</tr>
<tr>
<td>POST</td>
<td>/api/schedule-of-assessment/unschedule/</td>
<td>Unschedule an assessment for a visit.</td>
</tr>
<tr>
<td>GET</td>
<td>/api/studies/</td>
<td></td>
</tr>
</tbody>
</table>
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

- Objective
- Endpoint
- Activity
- Assessment
- RootSDTMDataset
- UnitDefinition
- UnitDimension
- RootCTTermName

To demonstrate superiority in the efficacy of human insulin to Metformin in Hb...

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

- Proportion of Subject with HbA1c < 7% after 26 weeks

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

Glucose metabolism

Hemoglobin A1C/Hemoglobin

HBA1CHGB

LB

Blood

CDISC
The CDISC 360 Bindings from CDASH -> SDTM
Linked graph domain model for Schedule of Assessment
// 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 accessed 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
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!

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