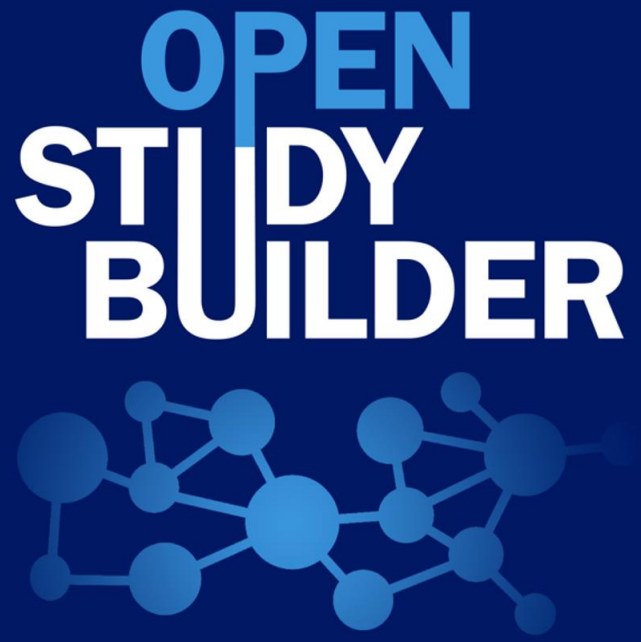
Protocol Automation with OpenStudyBuilder



Birmingham, Monday 6 November 2023

Mikkel Traun

Nicolas de Saint Jorre

What is the OpenStudyBuilder?...

A NEW APPROACH TO STUDY SPECIFICATION

- Compliance with external and internal standards
- Facilitates automation and content reuse
- Ensures a higher degree of end-to-end consistency

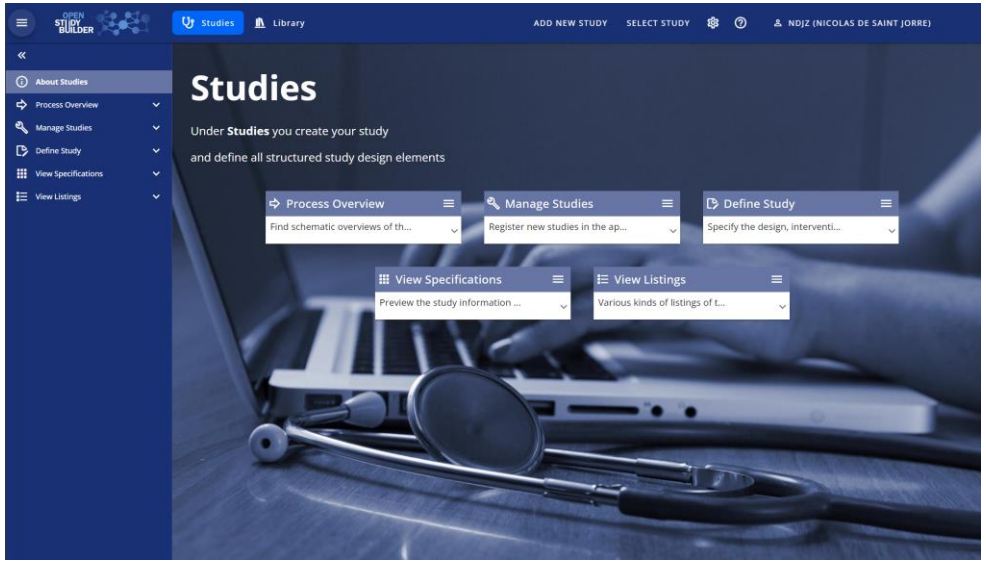
3 ELEMENTS OF OpenStudyBuilder

- **Clinical Metadata Repository (clinical MDR)**
  (central repository for all study specification data)
- **OpenStudyBuilder application / Web UI**
- **API layer**
  (allowing interoperability with other applications)
  (DDF API Adaptor – enabling DDF SDR Compatibility)

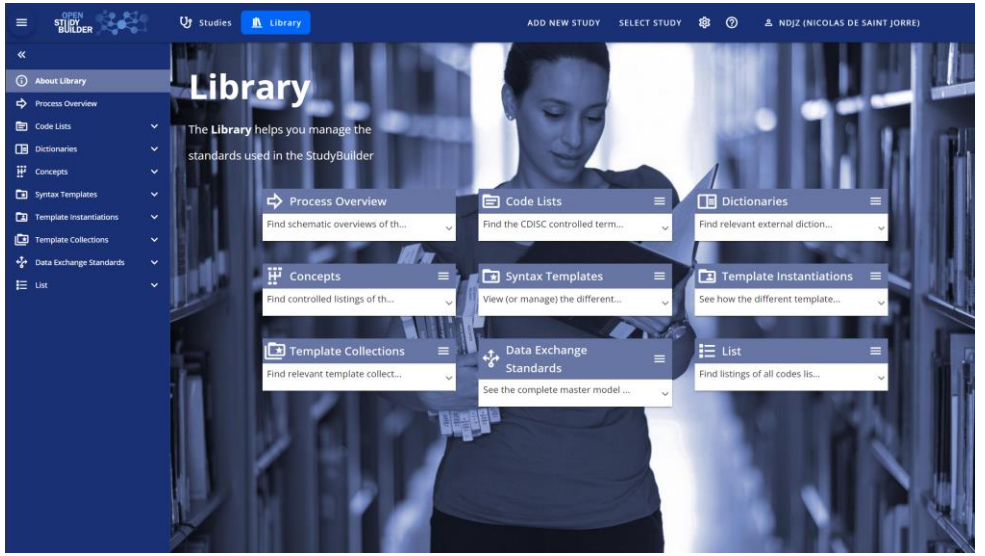
clinical **MDR**

OpenStudyBuilder Components

STUDIES	
TITLE	CRITERIA
REGISTRY IDENTIFERS	INTERVENTIONS
STRUCTURE	PURPOSE
POPULATION	ACTVITIES



LIBRARY	
CONTROLLED TERMINOLOGY	MEDICAL DICTIONARIES (e.g., MedDRA)
CONCEPTS (ACTIVITIES, UNITS, CRFs, COMPOUNDS)	SYNTAX TEMPLATES
DATA EXCHANGE STANDARDS	



What is the key elements of OpenStudyBuilder supporting protocol automation

- **Library module**
  - CDISC and sponsor terminology including sponsor preferred synonyms
  - Biomedical Concepts named as Activity Concepts
  - Syntax templates, to manage human readable structured protocol text
- **Study module**
  - General Study attributes in scope for the protocol
  - Study Design and SoA
  - Objectives and Endpoints
  - In- and Exclusion criteria

clinical **MDR**

About Library
Process Overview
Code Lists
Dashboard
CT Catalogues
CT Packages
CDISC
Sponsor
Dictionaries
Concepts
Syntax Templates
Template Instantiations
Template Collections
Data Exchange Standards
List

Code list C66737 - TPHASE / Term Detail (Concept ID: C15602_PHASE__III__TRIAL)

For all terminologies we include the option to define the sponsor preferred name, in UK spelling, in Title and sentence case

In this case, we can use Arabic numbers as a synonym in the protocol template for study phase

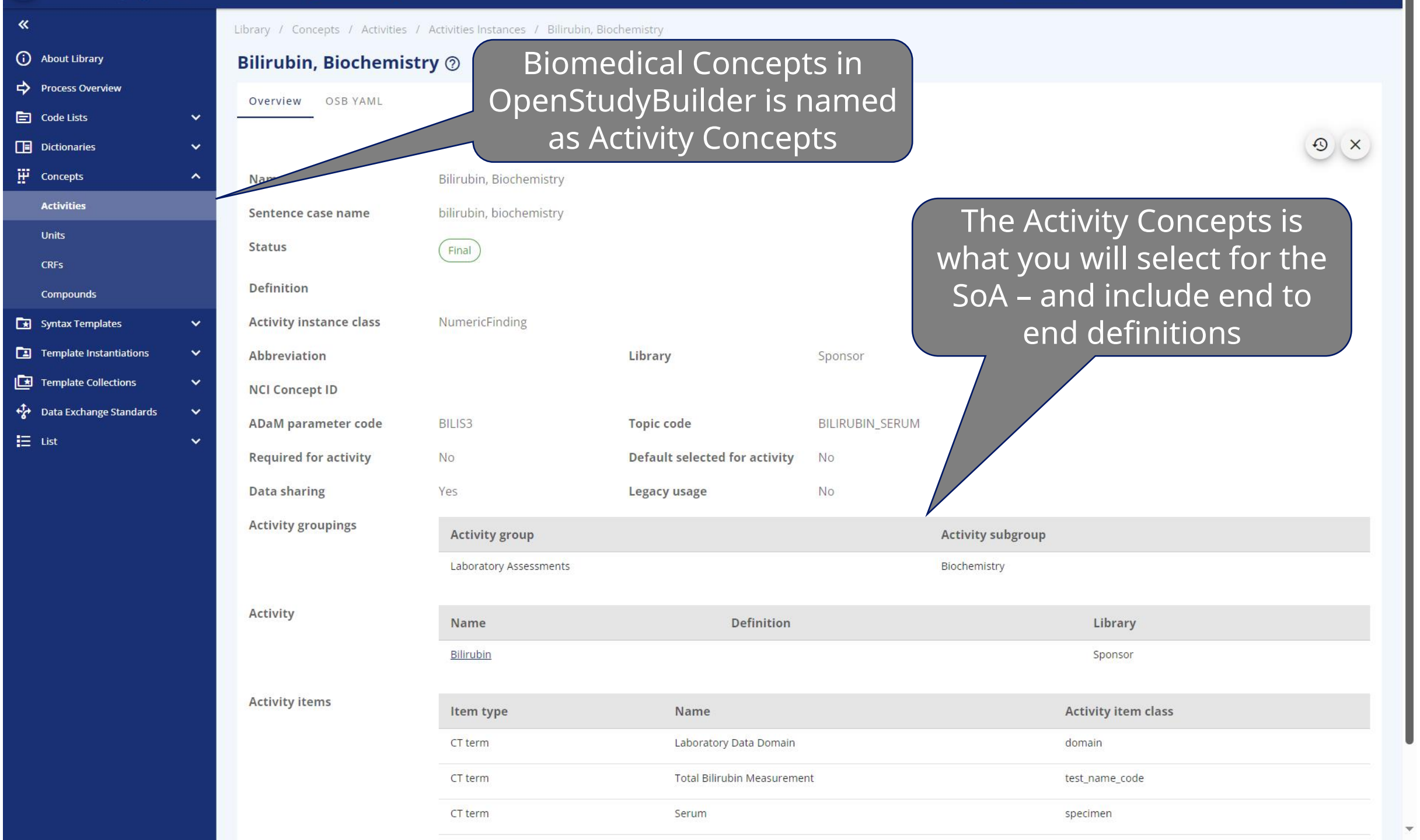
Code List Summary

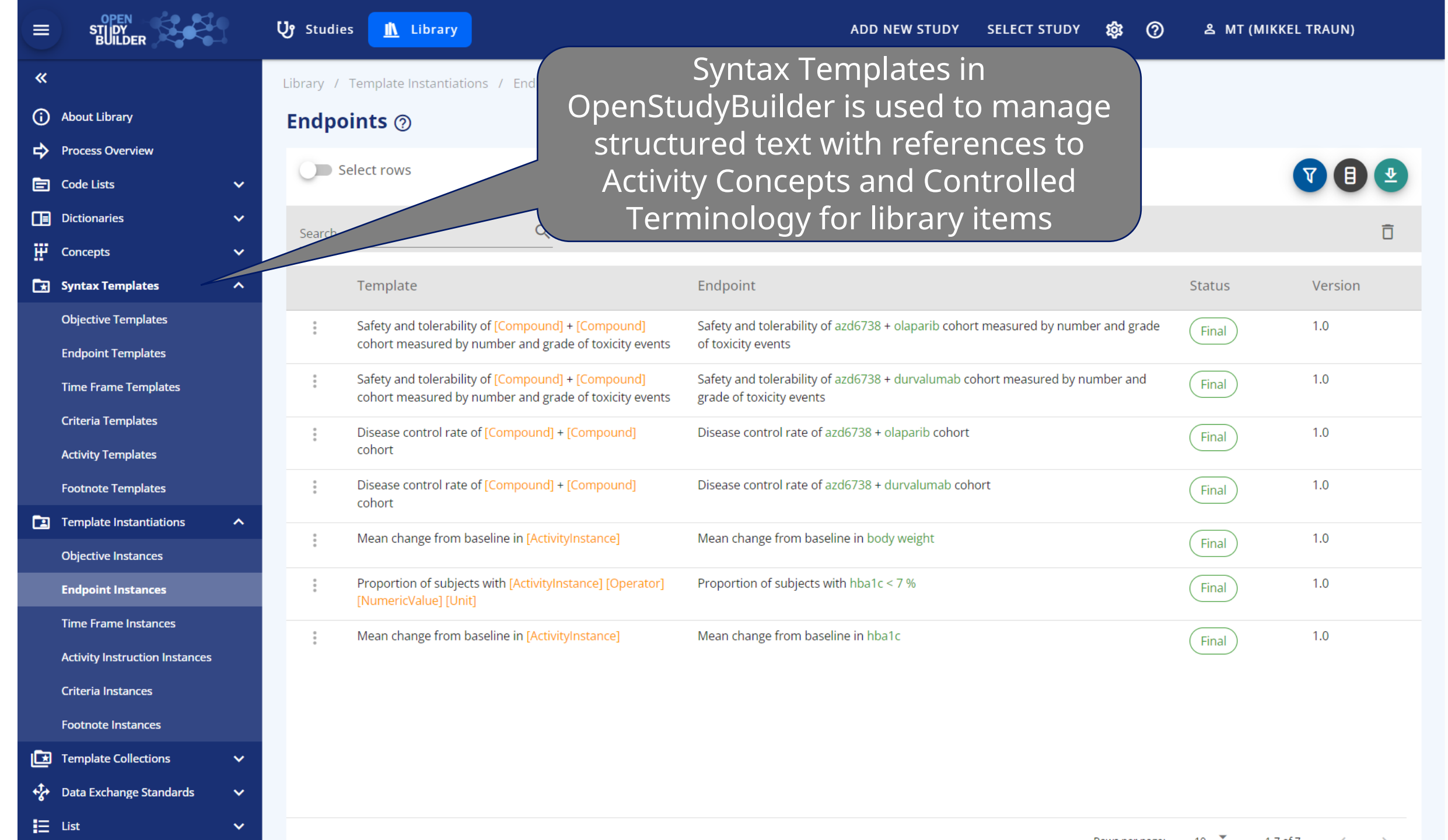
For the term sponsor values

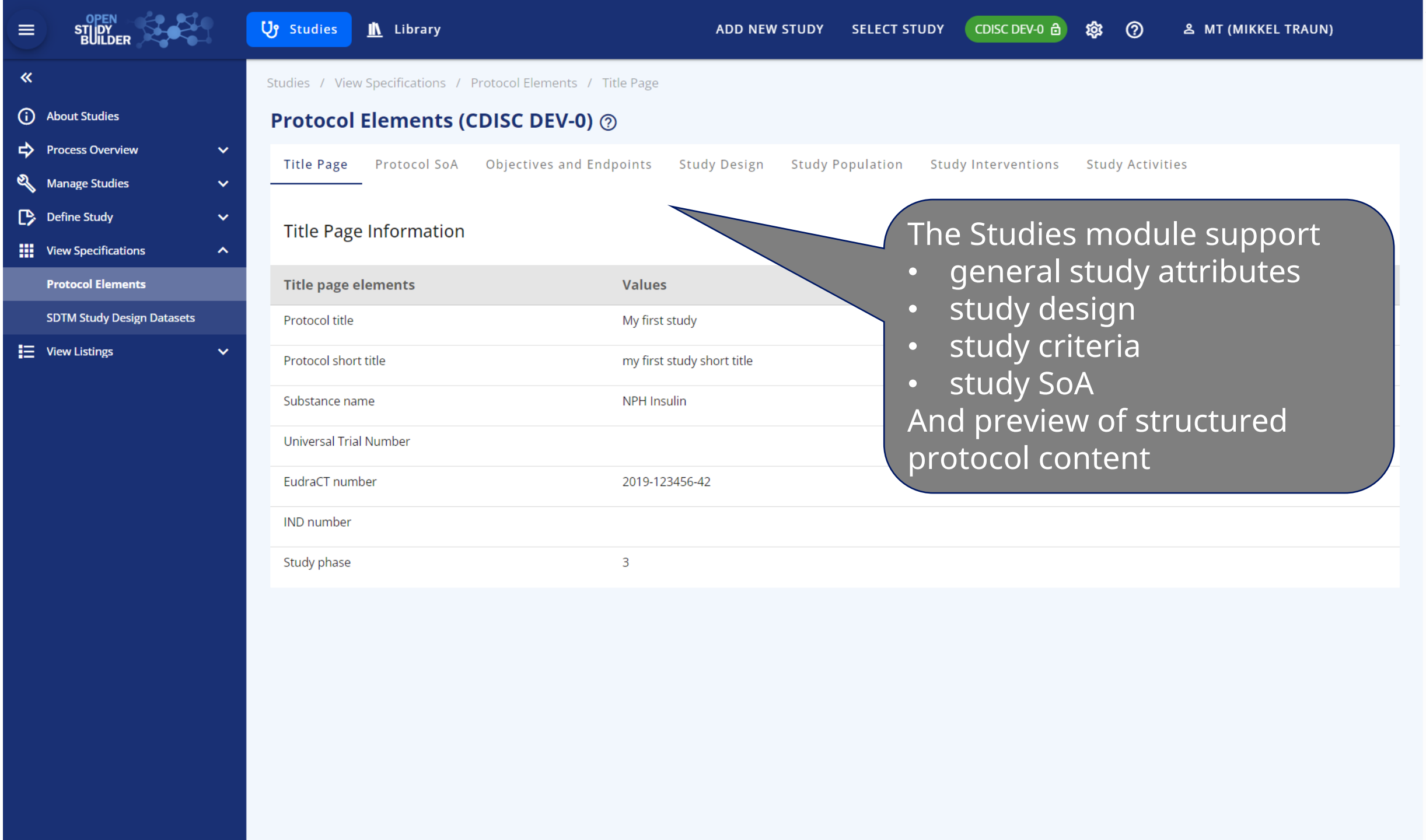
CT identifiers	Selected values	Status	Modified	Version	Actions
Sponsor Preferred Name	3	Final	Oct 19, 2023, 11:06 PM	2.0	
Sentence case name	3				
Order	3				

For the code list attributes values

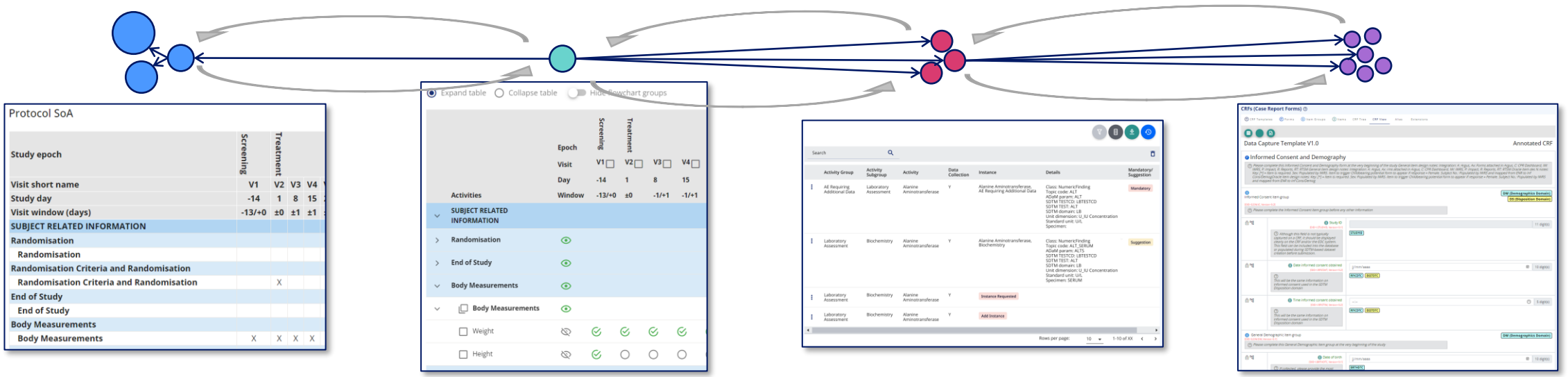
CT identifiers	Selected values	Status	Modified	Version	Actions
Concept ID	C15602_PHASE__III__TRIAL	Final	Mar 31, 2023, 2:00 AM	2.0	
Name submission value					
Code submission value	PHASE III TRIAL				
NCI preferred name	Phase III Trial				
Definition	Phase that includes the controlled clinical trials intended to confirm safety and effectiveness, evaluate the overall benefit-risk relationship, and to provide substantial				


About Library
Process Overview
Code Lists
Dictionaries
Concepts
Activities
Units
CRFs
Compounds
Syntax Templates
Template Instantiations
Template Collections
Data Exchange Standards
List
Library / Concepts / Activities / Activities Instances / Bilirubin, Biochemistry
Bilirubin, Biochemistry
Overview
OSB YAML
Biomedical Concepts in OpenStudyBuilder is named as Activity Concepts
The Activity Concepts is what you will select for the SoA – and include end to end definitions
Name
Bilirubin, Biochemistry
Sentence case name
bilirubin, biochemistry
Status
Final
Definition
Activity instance class
NumericFinding
Abbreviation
Library
Sponsor
NCI Concept ID
ADaM parameter code
BILIS3
Topic code
BILIRUBIN_SERUM
Required for activity
No
Default selected for activity
No
Data sharing
Yes
Legacy usage
No
Activity groupings
Activity group
Activity subgroup
Laboratory Assessments
Biochemistry
Activity
Name
Definition
Library
Bilirubin
Sponsor
Activity items
Item type
Name
Activity item class
CT term
Laboratory Data Domain
domain
CT term
Total Bilirubin Measurement
test_name_code
CT term
Serum
specimen


Studies
Library
ADD NEW STUDY
SELECT STUDY
MT (MIKKEL TRAUN)
Syntax Templates in OpenStudyBuilder is used to manage structured text with references to Activity Concepts and Controlled Terminology for library items
About Library
Process Overview
Code Lists
Dictionaries
Concepts
Syntax Templates
Objective Templates
Endpoint Templates
Time Frame Templates
Criteria Templates
Activity Templates
Footnote Templates
Template Instantiations
Objective Instances
Endpoint Instances
Time Frame Instances
Activity Instruction Instances
Criteria Instances
Footnote Instances
Template Collections
Data Exchange Standards
List
Library / Template Instantiations / End
Endpoints
Select rows
Search
Template
Endpoint
Status
Version
Safety and tolerability of [Compound] + [Compound] cohort measured by number and grade of toxicity events
Safety and tolerability of azd6738 + olaparib cohort measured by number and grade of toxicity events
Final
1.0
Safety and tolerability of [Compound] + [Compound] cohort measured by number and grade of toxicity events
Safety and tolerability of azd6738 + durvalumab cohort measured by number and grade of toxicity events
Final
1.0
Disease control rate of [Compound] + [Compound] cohort
Disease control rate of azd6738 + olaparib cohort
Final
1.0
Disease control rate of [Compound] + [Compound] cohort
Disease control rate of azd6738 + durvalumab cohort
Final
1.0
Mean change from baseline in [ActivityInstance]
Mean change from baseline in body weight
Final
1.0
Proportion of subjects with [ActivityInstance] [Operator] [NumericValue] [Unit]
Proportion of subjects with hba1c < 7 %
Final
1.0
Mean change from baseline in [ActivityInstance]
Mean change from baseline in hba1c
Final
1.0


OPEN STUDY BUILDER
Studies
Library
ADD NEW STUDY
SELECT STUDY
CDISC DEV-0
MT (MIKKEL TRAUN)
About Studies
Process Overview
Manage Studies
Define Study
View Specifications
Protocol Elements
SDTM Study Design Datasets
View Listings
Studies / View Specifications / Protocol Elements / Title Page
Protocol Elements (CDISC DEV-0)
Title Page
Protocol SoA
Objectives and Endpoints
Study Design
Study Population
Study Interventions
Study Activities
Title Page Information
Title page elements
Values
Protocol title
My first study
Protocol short title
my first study short title
Substance name
NPH Insulin
Universal Trial Number
EudraCT number
2019-123456-42
IND number
Study phase
3
The Studies module support
• general study attributes
• study design
• study criteria
• study SoA
And preview of structured protocol content

Schedule of Activities (SoA) at multiple levels



Protocol SoA

- For the high level SoA in protocol section 1.2
- Main purpose is for the investigator and site staff to get an overview of the operational schedule

Detailed SoA

- Specifying the semantic data observations to be collected in the study – but not specific to representation in ADaM, SDTM or data collection
- Will be part of protocol section 8 and appendixes or other supplementary documents

Operational SoA

- The data specification to support data collection specification
- Correspond to our existing legacy BCs (Topic Codes)
- Will also related to specific ADaM PARAM/PARAMCD

Data Capture / Collection Specification

- How data is to be collected in the study and when
- What is pre-set, what is collected and how

Selection process of Activities for SoA

For Protocol Outline / Protocol

- Select Activities in relevant grouping
- When selecting an Activity within a specific grouping, then this will drive ActivityInstance – this should be visible for Protocol Writers (like a COL)
  - Some ActivityInstances can be mark as default for an Activity, and will then be pre-selected
  - Some ActivityInstances can be marked as mandatory – and cannot be un-selected
- Select what to display or hide in high-level Protocol SoA

For Operational Data Specification

- Confirm or Select Activity Instances for each selected Activity
- If the correct ActivityInstance will change Grouping – this will require a change to the Protocol SoA – this will then

For Data Collection Specification

- The data collection specification
  - Lab specs
  - CRF
  - Other eSources
  - What is pre-set

Studies / Define Study / Study Activities / Detailed SoA

About Studies
Process Overview
Manage Studies
Define Study
Study Title
Registry Identifiers
Study Properties
Study Structure
Study Population
Study Criteria
Study Interventions
Study Purpose
Study Activities
View Specifications
View Listings

Study Activities (CDISC DEV-0)

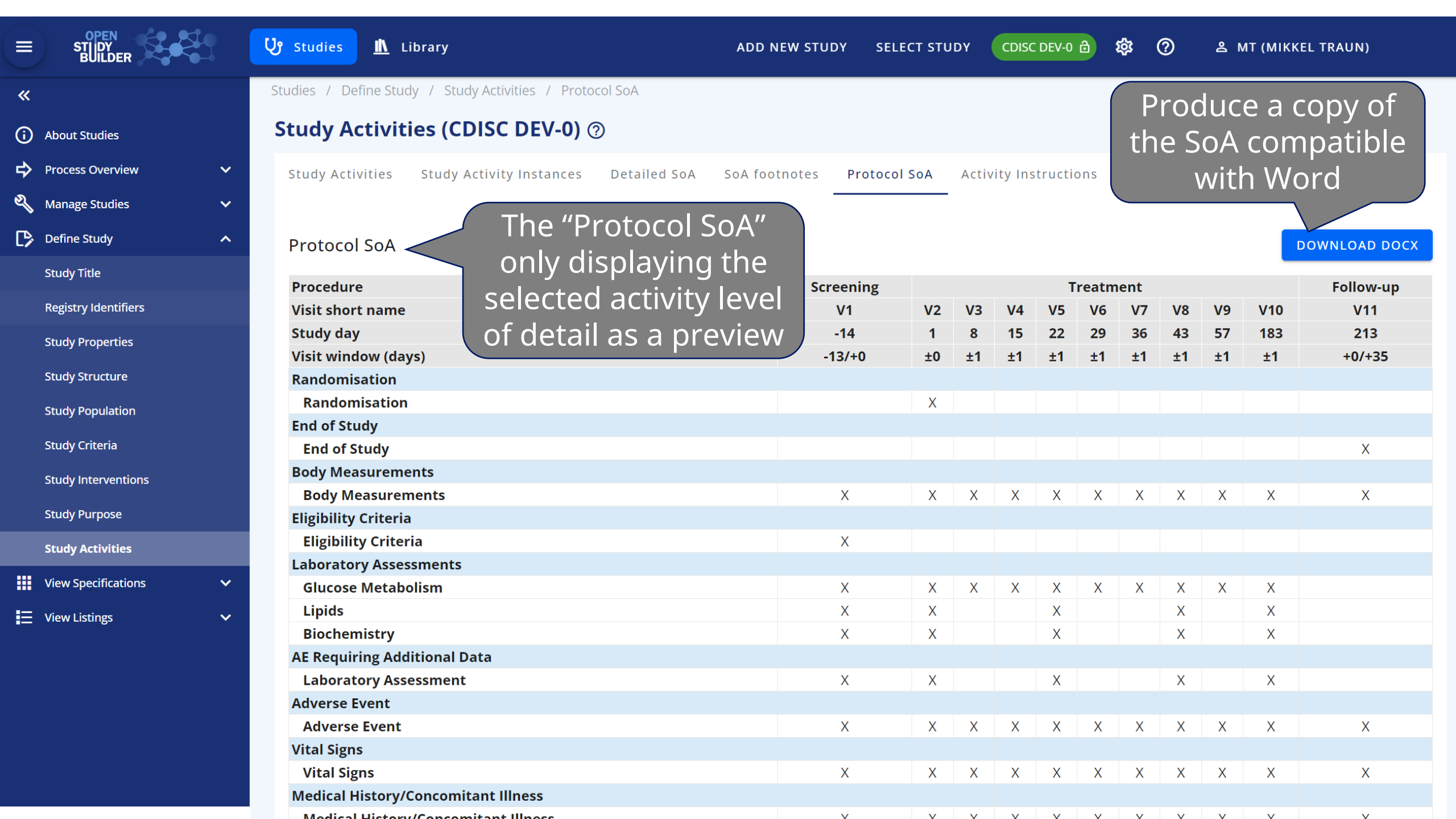
Study Activities | Study Activity Instances | Detailed SoA | SoA footnotes | Protocol SoA | Activity Instructions

The detailed SoA describe scheduling of the specific Activities and their grouping for the study

roups

Activities	Window	Screening V1	Treatment V2	V3	V4	V5	V6	V7	V8	V9	V10	Follow-up V11
		-14	1	8	15	22	29	36	43	57	183	213
		-13/+0	±0	-1/+1	-1/+1	-1/+1	-1/+1	-1/+1	-1/+1	-1/+1	-1/+1	0/+35
SUBJECT RELATED INFORMATION												
EFFICACY												
Laboratory Assessments												
Glucose Metabolism												
HbA1c		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	○
Self Measured Plasma Glucose												
Self Measured Plasma Glucose												
Mean Plasma Glucose		○	○	○	○	○	○	○	○	○	○	○
SAFETY												

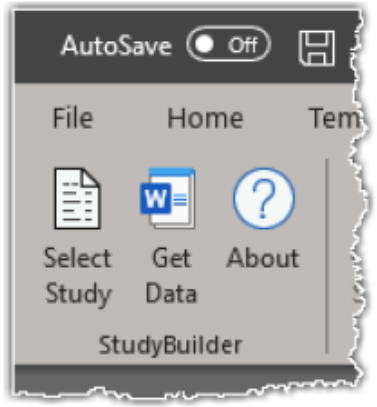
Each level in the Activity hierarchy can be selected for display in the “Protocol SoA”



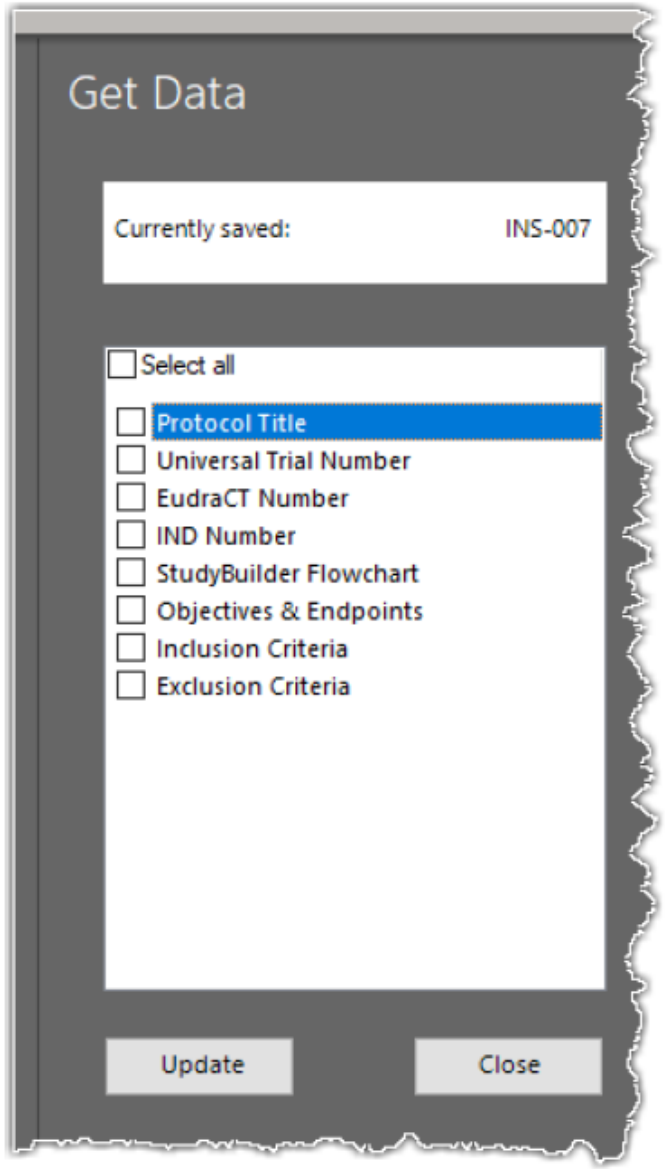
Procedure	Screening	Treatment									Follow-up
Visit short name	V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11
Study day	-14	1	8	15	22	29	36	43	57	183	213
Visit window (days)	-13/+0	±0	±1	±1	±1	±1	±1	±1	±1	±1	+0/+35
Randomisation											
Randomisation		X									
End of Study											
End of Study											X
Body Measurements											
Body Measurements	X	X	X	X	X	X	X	X	X	X	X
Eligibility Criteria											
Eligibility Criteria	X										
Laboratory Assessments											
Glucose Metabolism	X	X	X	X	X	X	X	X	X	X	
Lipids	X	X			X			X		X	
Biochemistry	X	X			X			X		X	
AE Requiring Additional Data											
Laboratory Assessment	X	X			X			X		X	
Adverse Event											
Adverse Event	X	X	X	X	X	X	X	X	X	X	X
Vital Signs											
Vital Signs	X	X	X	X	X	X	X	X	X	X	X
Medical History/Concomitant Illness											

StudyBuilder ribbon
(Word add-in)

- ✓ One-way connection
- ✓ Code recognizes the document type
- ✓ User-friendly ribbon and ‘fly-out’ in Word
- ✓ Styles ensure proper formatting in Word



Protocol



Protocol

This template is based on the *NN Authoring Master Template* and requires the **NN Authoring ribbon,** which you install (once) from the Software portal.

*To remove this guidance text, click it and tap Delete **twice**. To bulk remove all guidance text boxes in the document, use the NN Authoring ribbon: Document Fix > Remove Guidance Text.*

For template support and more information type: TemplateSupport/ in your browser

For explanation of the formatting and text conventions, see Instructions for Protocol Templates on page 2.

*To remove this guidance text box, click it and tap Delete **twice**.*

Protocol Title: Insert via the StudyBuilder ribbon.

The title must include the name of the investigational intervention(s), the condition being studied, the study population included and the primary purpose, and should not be longer than 300 characters, including spaces. Two studies must not have identical titles.

Study intervention name(s) must be consistent throughout the protocol and protocol-related documents. The investigational medicinal product name must comply with document *Q145046*. Consult HQ Regulatory Affairs and/or project vice president/project director for correct use of product/substance name(s)/devices.

*To remove this guidance text box, click it and tap Delete **twice**.*

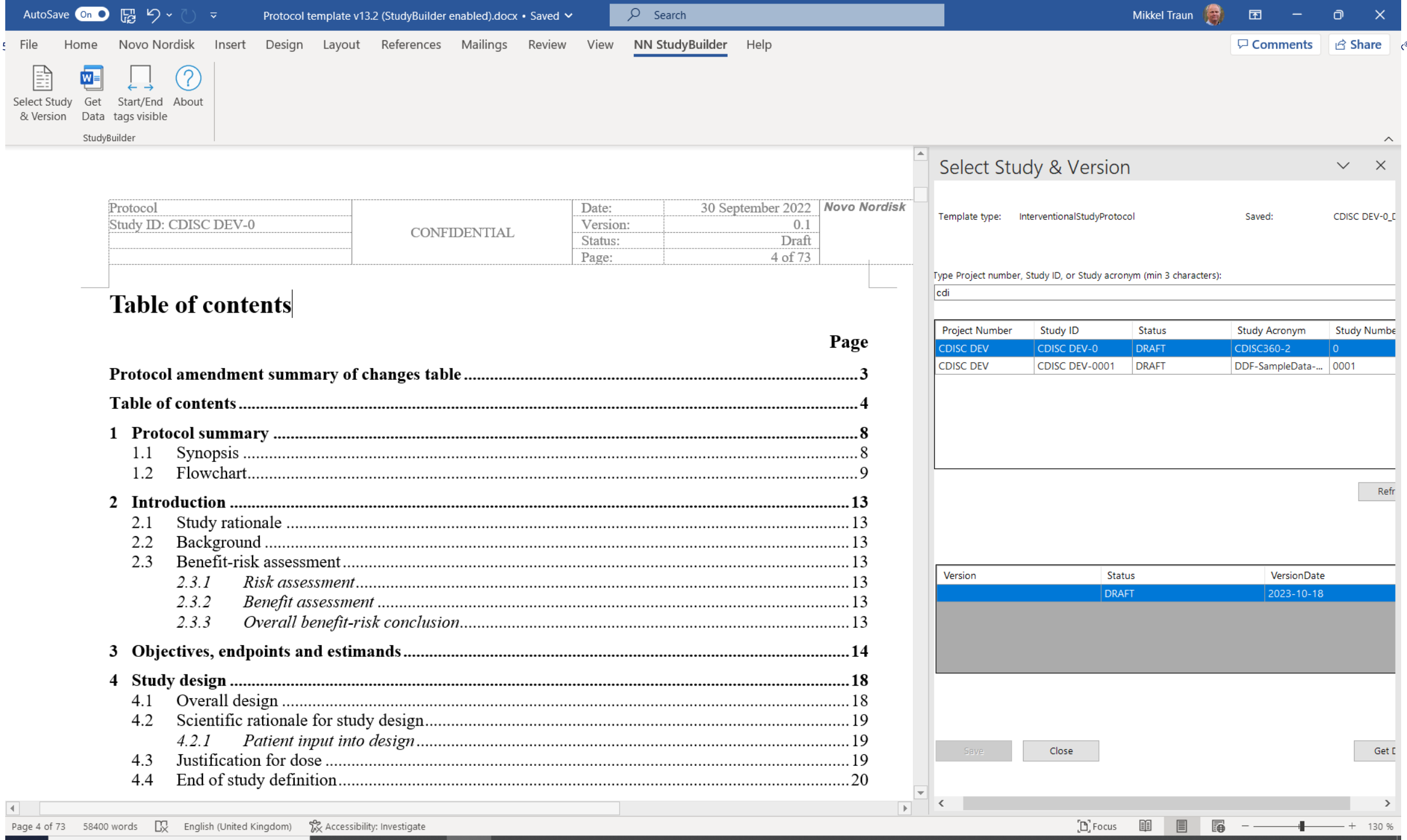
Short Title: Insert via the StudyBuilder ribbon.

Include a short title in lay language, to be aligned with the participant information/informed consent (PI/IC) title. Maximum 300 characters. For guidance on lay language titles please refer to the User guide on lay language titles in the PI/IC toolbox on SharePoint.

*To remove this guidance text box, click it and tap Delete **twice**.*

***Substance** Number / Name (as applicable):*

Protocol Version Number: Version *X*.0 *(add the version number that the protocol ultimately will*


AutoSave On
Protocol template v13.2 (StudyBuilder enabled).docx • Saved
Search
Mikkel Traun
File Home Novo Nordisk Insert Design Layout References Mailings Review View NN StudyBuilder Help
Comments Share
Select Study & Version
Get Data
Start/End tags visible
About
StudyBuilder
Protocol
Study ID: CDISC DEV-0
CONFIDENTIAL
Date: 30 September 2022
Version: 0.1
Status: Draft
Page: 4 of 73
Novo Nordisk
Table of contents
Page
Protocol amendment summary of changes table 3
Table of contents 4
1 Protocol summary 8
1.1 Synopsis 8
1.2 Flowchart 9
2 Introduction 13
2.1 Study rationale 13
2.2 Background 13
2.3 Benefit-risk assessment 13
2.3.1 Risk assessment 13
2.3.2 Benefit assessment 13
2.3.3 Overall benefit-risk conclusion 13
3 Objectives, endpoints and estimands 14
4 Study design 18
4.1 Overall design 18
4.2 Scientific rationale for study design 19
4.2.1 Patient input into design 19
4.3 Justification for dose 19
4.4 End of study definition 20
Select Study & Version
Template type: InterventionalStudyProtocol
Saved: CDISC DEV-0_D
Type Project number, Study ID, or Study acronym (min 3 characters):
cdi
Project Number Study ID Status Study Acronym Study Numbe
CDISC DEV CDISC DEV-0 DRAFT CDISC360-2 0
CDISC DEV CDISC DEV-0001 DRAFT DDF-SampleData-... 0001
Refr
Version Status VersionDate
DRAFT 2023-10-18
Save
Close
Get D
Page 4 of 73 58400 words English (United Kingdom) Accessibility: Investigate
Focus
130 %

Structured content including SoA will be transferred to the content controls Word based Protocol Template

1.2 Flowchart

Schedule of Activities

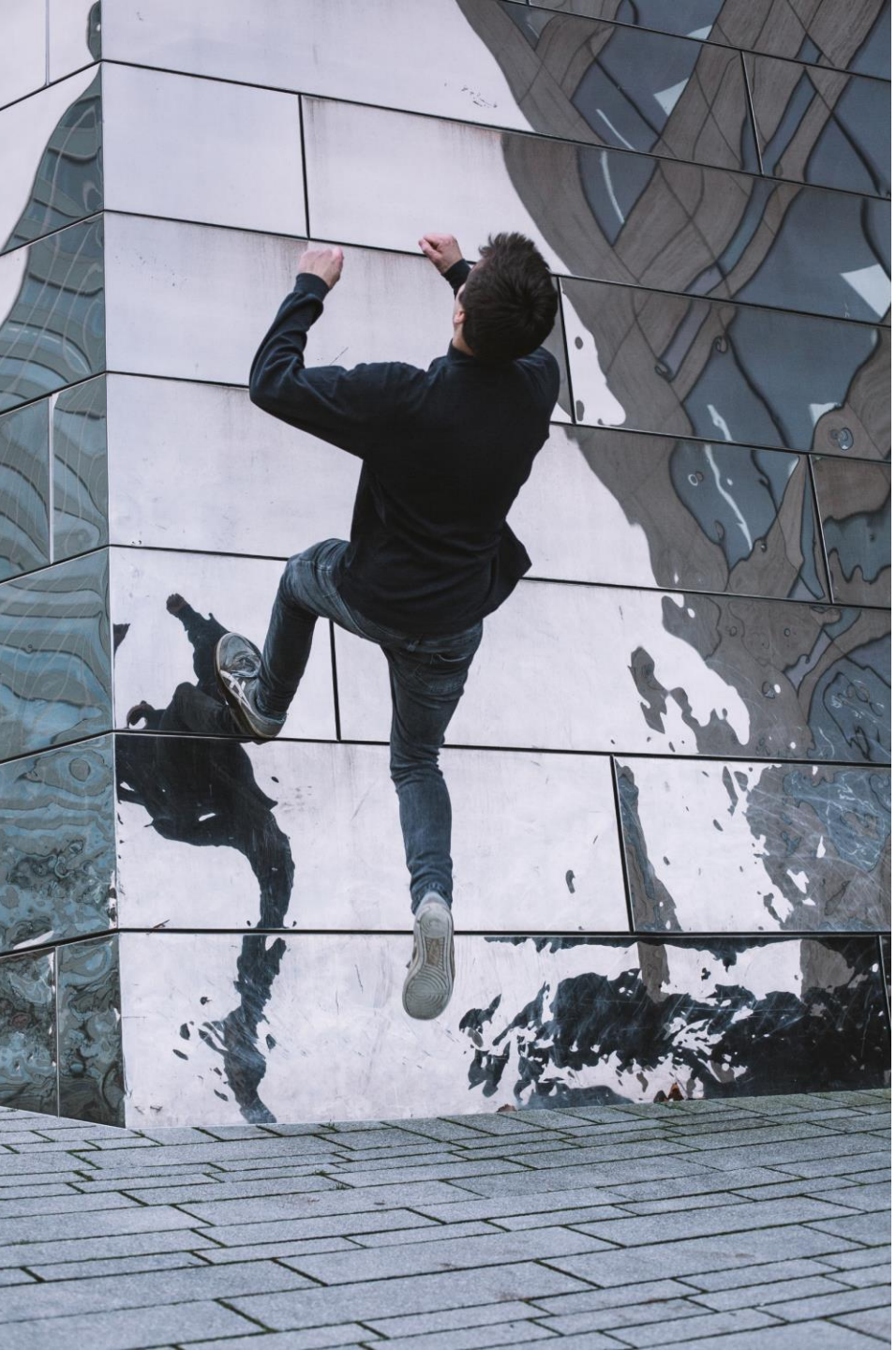
Procedure	Screening	Treatment									Follow-up
Visit short name	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**	**V10**	**V11**
Study day	**-14**	**1**	**8**	**15**	**22**	**29**	**36**	**43**	**57**	**183**	**213**
Visit window (days)	**-13/+0**	**±0**	**±1**	**±1**	**±1**	**±1**	**±1**	**±1**	**±1**	**±1**	**+0/+35**
Randomisation											
Randomisation		X									
End of Study											
End of Study											X
Body Measurements											
Body Measurements	X	X	X	X	X	X	X	X	X	X	X
Eligibility Criteria											
Eligibility Criteria	X										
Laboratory Assessments											
Glucose Metabolism	X	X	X	X	X	X	X	X	X	X	
Lipids	X	X			X			X		X	
Biochemistry	X	X			X			X		X	
AE Requiring Additional Data											

Get Data

Currently saved: CDISC DEV-(

Select all
- Protocol Title
- Protocol Short Title
- Universal Trial Number
- EudraCT Number
- IND Number
- Schedule of Activities
- Objectives & Endpoints
- Inclusion Criteria
- Exclusion Criteria

Update

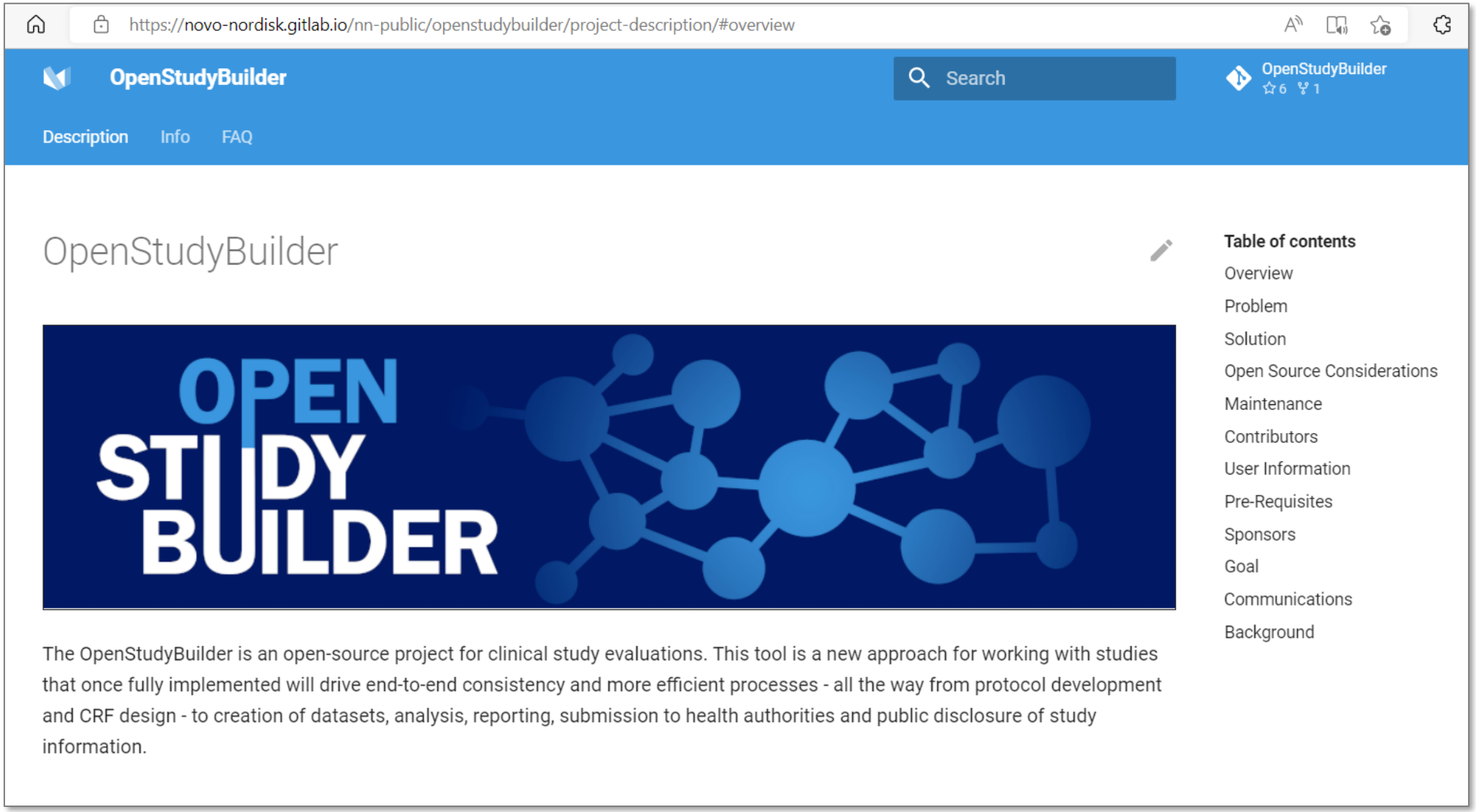


OpenStudyBuilder next steps

- Non-GCP MVP released internally at Novo Nordisk in September 2022 for pilots
- Business go-live November 2023 for phase 2-4 studies with protocol outline kickoff
- Share as open source project under COSA
  - https://cosa.cdisc.org/directory/openStudyBuilder
  - https://openstudybuilder.com/

  Currently only containing a project description
- Seek to actively collaborate with CDISC, TransCelerate DDF, peers and vendors

How do I get started on OpenStudyBuilder?



https://novo-nordisk.gitlab.io/nn-public/openstudybuilder/project-description/

Thanks!
Questions?