

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)



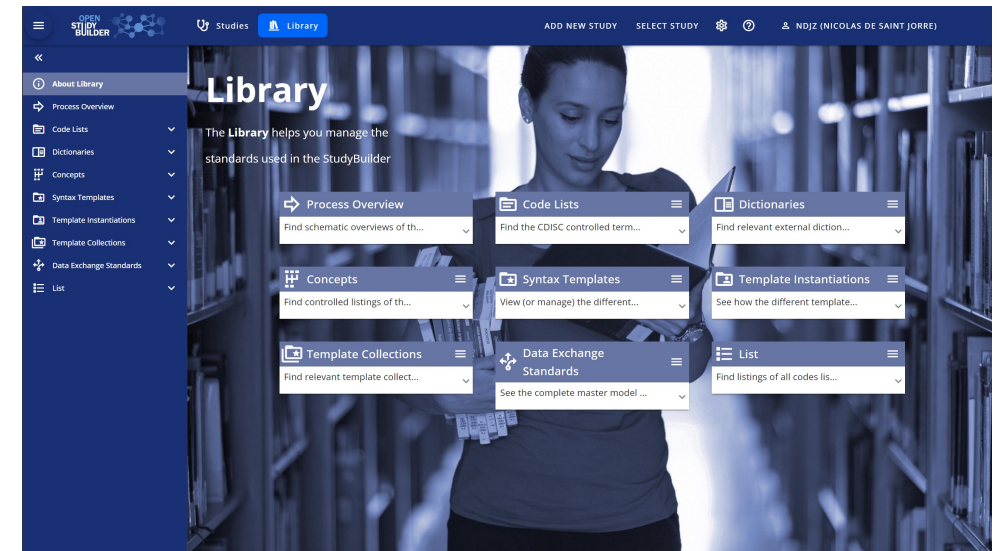
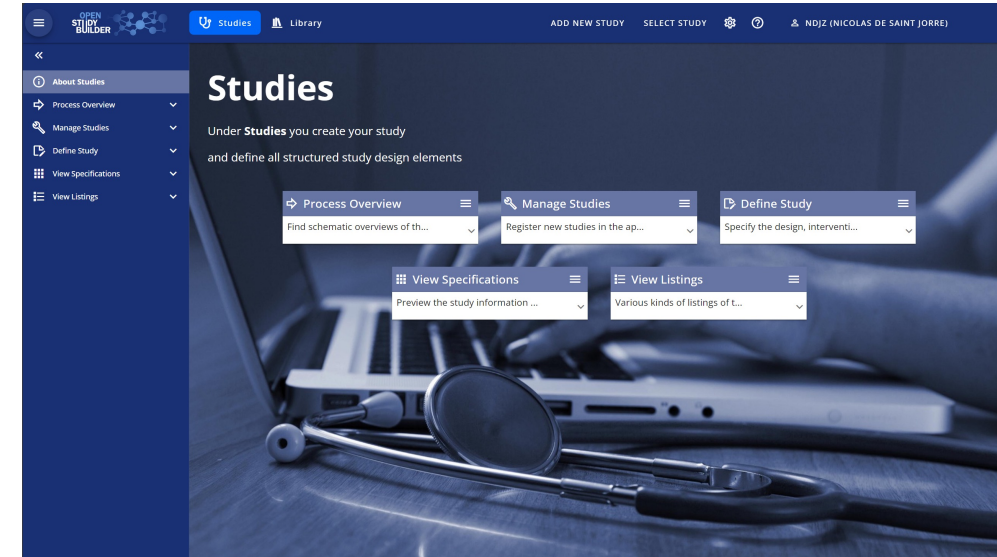
OpenStudyBuilder Components

STUDIES

TITLE	CRITERIA
REGISTRY IDENTIFIERS	INTERVENTIONS
STRUCTURE	PURPOSE
POPULATION	ACTIVITIES

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



OPEN
STUDY
BUILDER

Studies

Library

ADD NEW STUDY

SELECT STUDY

MT (MIKKEL TRAUN)

<<

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

Library / Code Lists / CT Catalogues / / C66737 / Terms / C15602_PHASE_III_TRIAL

Code list C66737 - TPHASE / Term Detail (Concept ID: C15602_PHASE_III_TRIAL)

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 evidence for regulatory approval and labeling. NOTE: Phase 2 studies usually include a form				

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



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

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

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

- «
- ⓘ

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 / Endpoints

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

Down per page: 10 1 of 7

Syntax Templates in OpenStudyBuilder is used to manage structured text with references to Activity Concepts and Controlled Terminology for library items

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

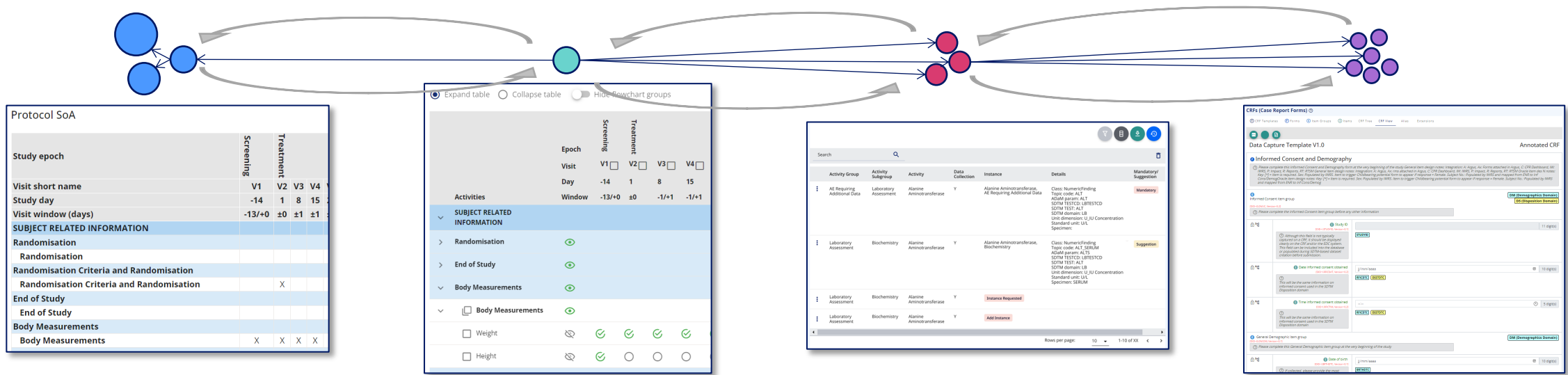
3

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

11

OPEN STUDY BUILDER

Studies

Library

ADD NEW STUDY

SELECT STUDY

CDISC DEV-0

MT (MIKKEL TRAUN)

<<

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

Studies / Define Study / Study Activities / Detailed SoA

Study Activities (CDISC DEV-0)

Study Activities

Study Activity Instances

Detailed SoA

SoA footnotes

Protocol SoA

Activity Instructions

		Screening	Treatment								Follow-up	
		V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11
		-14	1	8	15	22	29	36	43	57	183	213
Activities	Window	-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												

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

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

OPENSTUDYBUILDER

StudiesLibrary

ADD NEW STUDYSELECT STUDYCDISC DEV-0⏏⚙️❓👤 MT (MIKKEL TRAUN)

«

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

Studies / Define Study / Study Activities / Protocol SoA

Study Activities (CDISC DEV-0) ?

Study ActivitiesStudy Activity InstancesDetailed SoASoA footnotesProtocol SoAActivity Instructions

Protocol SoA

The "Protocol SoA" only displaying the selected activity level of detail as a preview

Produce a copy of the SoA compatible with Word

DOWNLOAD DOCX

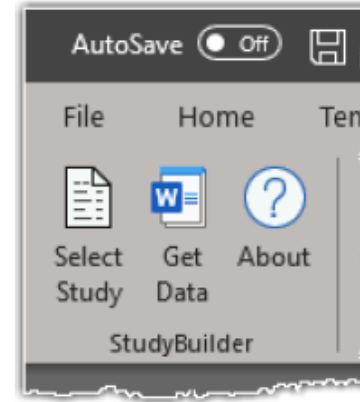
Procedure	Screening	Treatment										Follow-up
Visit short name	V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11	
Study day	-14	1	8	15	22	29	36	43	57	183	213	
Visit window (days)	-13/+0	±0	±1	±1	±1	±1	±1	±1	±1	±1		+0/+35
Randomisation												
Randomisation		X										
End of Study												
End of Study												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												
Medical History/Concomitant Illness	X	X	X	X	X	X	X	X	X	X		X



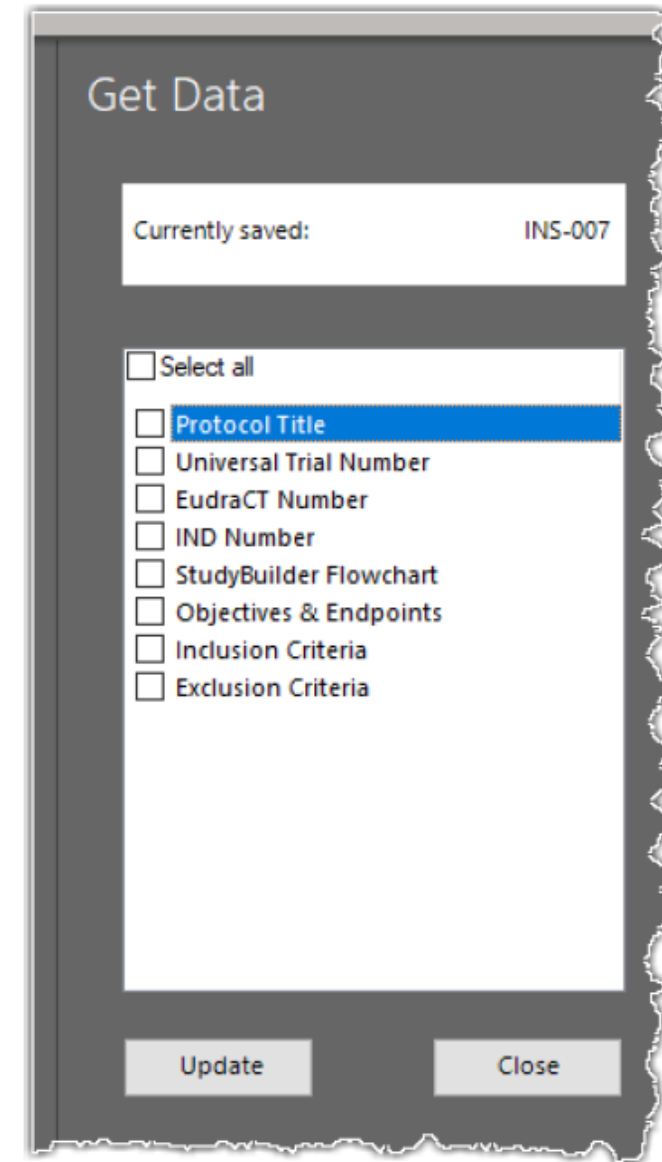
StudyBuilder ribbon (Word add-in)

✓ One-way
connection

- ✓ Code recognizes the document type
- ✓ User-friendly ribbon and 'fly-out' in Word
- ✓ Styles ensure proper formatting in Word



Protocol



Protocol	CONFIDENTIAL	Date:	30 September 2022	Novo Nordisk
Study ID:		Version:	0.1	
		Status:	Draft	
		Page:	1 of 73	

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

Page 1 of 7358395 wordsEnglish (United Kingdom)Accessibility: Investigate

Display SettingsFocus120%

Select Study & VersionGet DataStart/End tags visibleAbout

StudyBuilder

Protocol	CONFIDENTIAL	Date:	30 September 2022	Novo Nordisk
Study ID: CDISC DEV-0		Version:	0.1	
		Status:	Draft	
		Page:	4 of 73	

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_C

Type Project number, Study ID, or Study acronym (min 3 characters):

cdi

Project Number	Study ID	Status	Study Acronym	Study Number
CDISC DEV	CDISC DEV-0	DRAFT	CDISC360-2	0
CDISC DEV	CDISC DEV-0001	DRAFT	DDF-SampleData-...	0001

Version	Status	VersionDate
	DRAFT	2023-10-18

Protocol		Date:	30 September 2022	Status:	Draft	Novo Nordisk
Study ID: CDISC DEV-0		Version:	0.1	Page:	9 of 75	

1.2 Flowchart

Schedule of Activities

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

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-0

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

Update

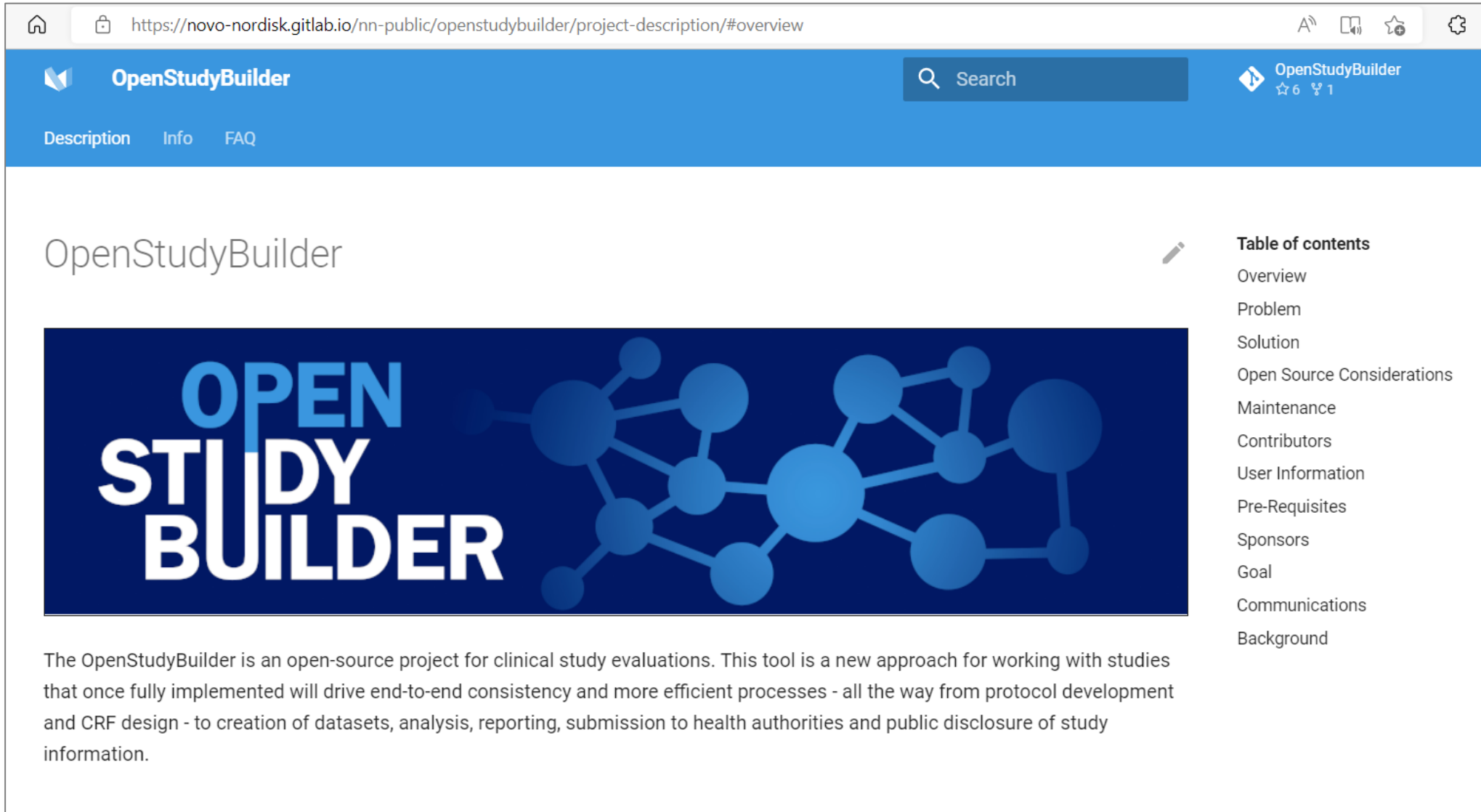
Cancel

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?



The screenshot shows a web browser window displaying the OpenStudyBuilder project description on GitLab. The browser's address bar shows the URL: <https://novo-nordisk.gitlab.io/nn-public/openstudybuilder/project-description/#overview>. The page has a blue header with the OpenStudyBuilder logo, a search bar, and navigation links for Description, Info, and FAQ. The main content area features the title "OpenStudyBuilder" and a large blue banner with the text "OPEN STUDY BUILDER" and a network diagram. Below the banner, a paragraph describes the project as an open-source tool for clinical study evaluations. On the right side, a "Table of contents" lists various sections of the project description.

OpenStudyBuilder

OPEN STUDY BUILDER

The OpenStudyBuilder is an open-source project for clinical study evaluations. This tool is a new approach for working with studies that once fully implemented will drive end-to-end consistency and more efficient processes - all the way from protocol development and CRF design - to creation of datasets, analysis, reporting, submission to health authorities and public disclosure of study information.

Table of contents

- Overview
- Problem
- Solution
- Open Source Considerations
- Maintenance
- Contributors
- User Information
- Pre-Requisites
- Sponsors
- Goal
- Communications
- Background

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

Thanks!
Questions?

