



2023

US

INTERCHANGE

FALLS CHURCH, VA | 18-19 OCTOBER



OpenStudyBuilder –
an open-source DDF and COSMoS compatible solution

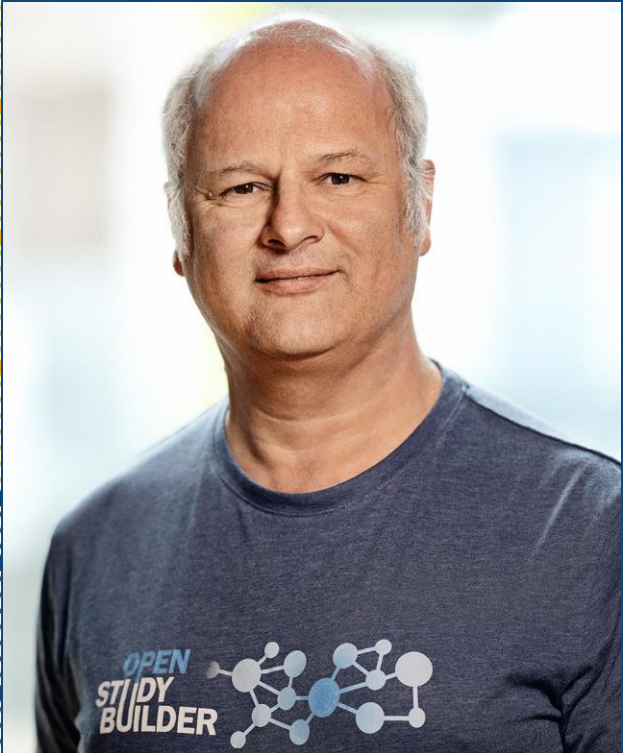
Mikkel Traun, Principal System Developer, Novo Nordisk A/S

Meet the Speakers

Mikkel Traun

Title: Principal System Developer

Organization: Novo Nordisk A/S



Mikkel is one of the product owners for the next generation study builder and data standards repository solution at Novo Nordisk. Mikkel is also an active member of the TransCelerate and CDISC Digital Dataflow project, and previously the CDISC 360 project. He has worked as a principal system developer supporting the clinical data warehouse solution and the CDISC implementation at Novo Nordisk. Previously he has worked on several projects in pre-clinical, clinical and outcome research.

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

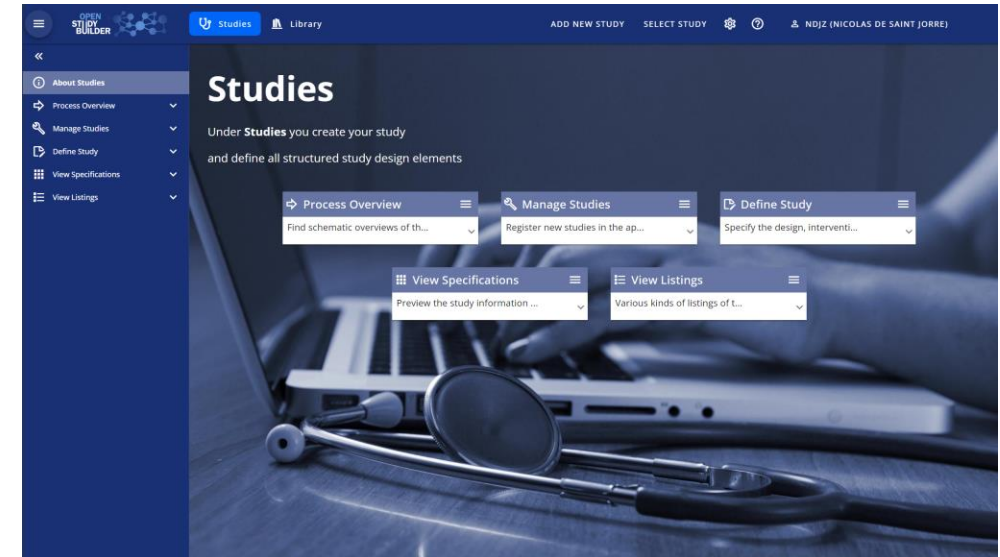
3 ELEMENTS OF OpenStudyBuilder

- **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)

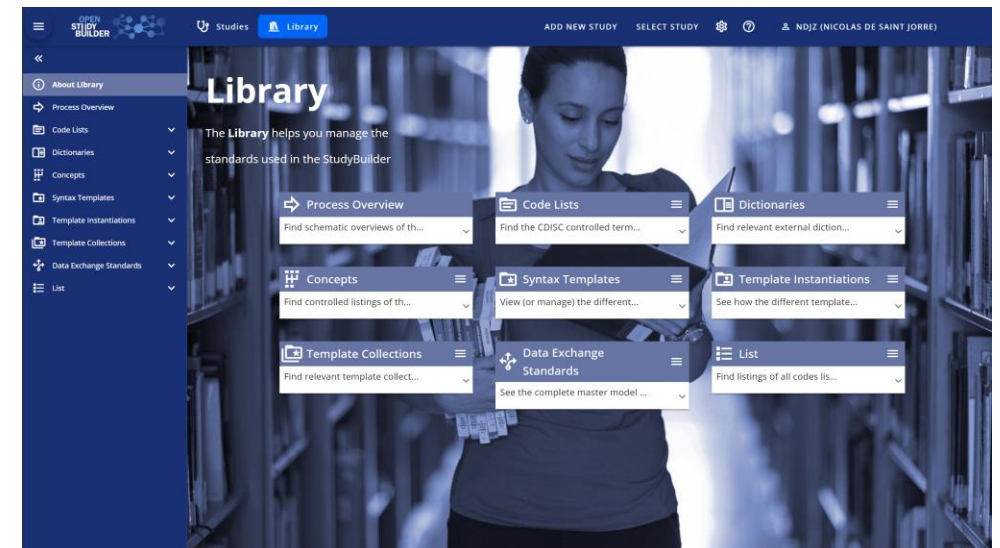


OpenStudyBuilder Components

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	



Digital Data Flow Adaptor (1/2)

The image displays the 'Study Builder' application interface. On the left is a navigation sidebar with options like 'About Studies', 'Process Overview', 'Study List', 'Manage Study', 'Define Study', 'Study Title', 'Registry Identifiers', 'Study Properties', 'Study Structure', 'Study Population', 'Study Criteria', 'Study Interventions', 'Study Purpose', 'Study Activities', 'View Specifications', and 'View Listings'. The main area shows 'Study Properties (CDISC DEV-0)' with a table of 'Selected values':

Property	Value
Study type	Interventional
Trial type	Phase III Trial
Extension study	No
Adaptive design	No
Study stop rules	No
Confirmed response minimum duration	No
Post authorization safety study ind...	No

Below this is a Postman API client window. The URL is `https://ddf-cloud-function-osb-0dot6.azurewebsites.net/api/studyDefinitions?studyId=Study_000001`. The request is a GET with a query parameter `studyId=Study_000001`. The response is a 200 OK with a JSON body:

```
1 {
2   "Study": {
3     "studyId": "9a54489c-6d48-40eb-a4c6-80b3430f662",
4     "studyTitle": "A trial comparing cardiovascular safety of human insulin vexas metformin in subjects with type 2 diabetes at high risk of cardiovascular events",
5     "studyVersion": "0",
6     "studyType": {
7       "codeId": "f85c0e09-a190-4032-8a07-6ad4911979c",
8       "code": "Interventional",
9       "codeSystem": null,
10      "codeSystemVersion": null,
11      "decode": null
12    },
13    "studyPhase": {
14      "standardCode": {
15        "codeId": "97196740-67e3-4e86-a0ea-c1f11fb08ba2",
16        "code": "Phase III Trial",
17        "codeSystem": null,
18        "codeSystemVersion": null,
19        "decode": null
20      },
21      "standardCodeAliases": null
22    },
23    "studyIdentifiers": [ {
24      "studyIdentifierId": "9d93c577-bf86-450e-9496-6e2b848cfad0",
25      "studyIdentifier": "2019-12345678",
26      "studyIdentifierScope": {
27        "organizationId": "8ad08cf7-b80c-4248-a7f6-099790619d48",
28        "organizationIdentifierScheme": null,
29        "organizationIdentifier": "NCT12345678",
30        "organizationName": null,
31        "organizationType": null,
32        "organizationLegalAddress": null
33      }
34    }
35  ]
36 }
```

Annotations include a blue oval around the 'Selected values' table, a blue oval labeled 'OSB API' pointing to the Postman window, and another blue oval labeled 'DDF Adaptor' pointing to the JSON response body.

Digital Data Flow Adaptor (2/2)

Study Structure (CDISC DEV-0)

#	Epoch name	Epoch type	Epoch subtype	Start rule	End rule	Description	Number of visits	Assigned colour
1	Screening	Pre Treatment	Screening	ICF submitted	ICF signed	Screening epoch to start	1	Light Blue
2	Treatment	Treatment	Treatment	RDM ok	Dosing complete	Treatment epoch without dosing esca...	9	Light Green
3	Follow-up	Post Treatment	Follow-up	Treatment ok	Last follow-up ok	Follow-up epoch to follow the subje...	1	Light Red

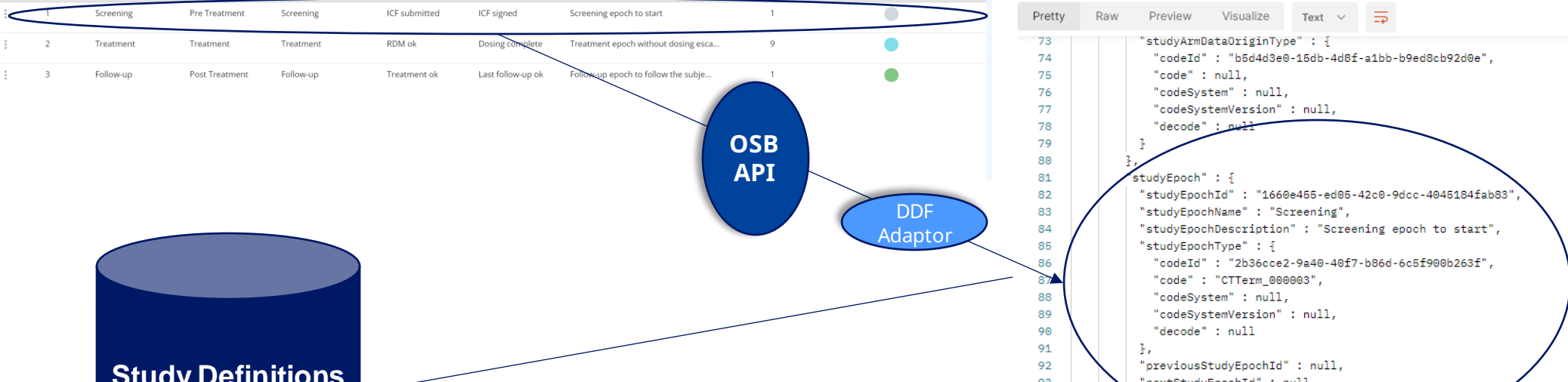
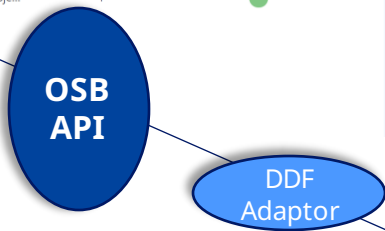
Body Cookies Headers (5) Test Results

Pretty Raw Preview Visualize Text

```

73   "studyArmDataOriginType" : {
74     "codeId" : "b5d4d3e0-15db-4d8f-a1bb-b9ed8cb92d0e",
75     "code" : null,
76     "codeSystem" : null,
77     "codeSystemVersion" : null,
78     "decode" : null
79   },
80
81   "studyEpoch" : {
82     "studyEpochId" : "1660e455-ed05-42c0-9dcc-4045184fab83",
83     "studyEpochName" : "Screening",
84     "studyEpochDescription" : "Screening epoch to start",
85     "studyEpochType" : {
86       "codeId" : "2b36cce2-9a40-40f7-b86d-6c5f900b263f",
87       "code" : "CTTerm_000003",
88       "codeSystem" : null,
89       "codeSystemVersion" : null,
90       "decode" : null
91     },
92     "previousStudyEpochId" : null,
93     "nextStudyEpochId" : null,
94     "encounterIds" : null
95   },
96   "studyElements" : [ {
97     "studyElementId" : "ef36a984-c9b8-48f7-8a9b-6d241169ee62",
98     "studyElementName" : "Screening",
99     "studyElementDescription" : null,
100    "transitionStartRule" : {
101      "transitionRuleId" : "7a0543b7-43ff-48cf-9dd2-c3e65a92b68",
102      "transitionRuleDescription" : "Informed consent signed"
103    },
104    "transitionEndRule" : {

```

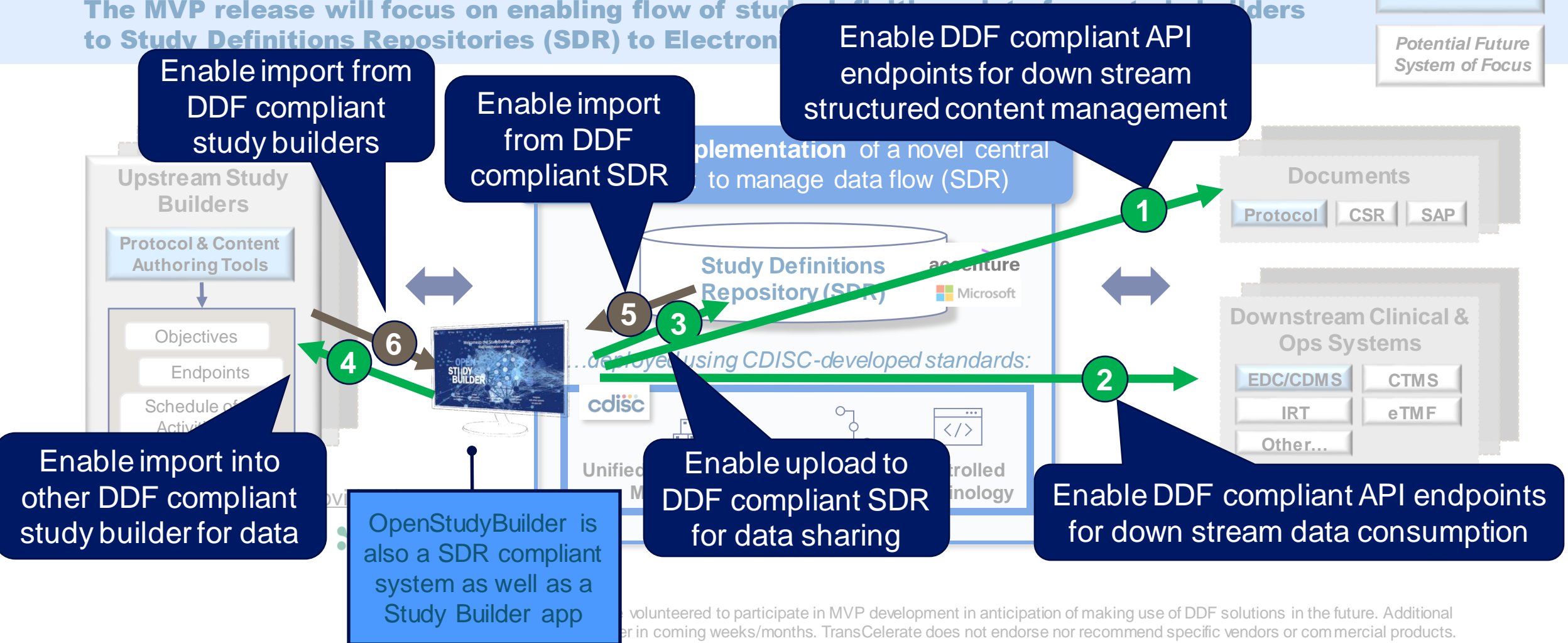


Minimum Viable Product (MVP) development underway

The MVP release will focus on enabling flow of study data from Upstream Study Builders to Study Definitions Repositories (SDR) to Electronic Data Capture (EDC) and Downstream Clinical & Ops Systems

System or Tool of Focus for MVP

Potential Future System of Focus



...volunteered to participate in MVP development in anticipation of making use of DDF solutions in the future. Additional information will be shared in coming weeks/months. TransCelerate does not endorse nor recommend specific vendors or commercial products.

What is a CDISC COSMoS compatible solution

- Conceptual and Operational Standards Metadata Services (COSMoS)
 - Biomedical Concepts (BCs) in a two-layered definition:
 - Conceptual/abstract layer that provides standards-agnostic, unambiguous semantic definition largely based on NCIt concepts.
 - Implementation layer based on valid CDISC dataset specializations that provide value level metadata definitions that facilitate metadata-driven automation.



What is the key elements of OpenStudyBuilder

- Library holding BCs
 - Named as Activity Concepts in OSB
- Study Module supporting Study Design and SoA
- SoA is key component in supporting the Digital Data Flow (DDF) vision
- In OSB we seek to achieve this by defining the SoA at different levels for dedicated parts of the Digital Data Flow



Concepts: Activities and Activity Instances

Library / Concepts / Activities / List of Activities /

Activities

List of Activities | Activities by Grouping | Activities Instances | Requested Activities

Select rows

Search: bilirubin

Library	Activity group	Activity subgroup	Activity Name	Sentence case name	Abbreviation	Modified	Status
Sponsor	Contraceptive Counselling	Contraceptive Counselling	Bilateral Tubal Occlusion	bilateral tubal occlusion		Jul 4, 2023, 2:54 PM	Final
Sponsor	Laboratory Assessments	Biomarkers	Bile Acid	bile acid		Jul 4, 2023, 2:54 PM	Final
Sponsor	Laboratory Assessments	Biochemistry	Bilirubin	bilirubin		Jul 4, 2023, 2:54 PM	Final
Sponsor	AE Requiring Additional Data	Pancreatitis	Dilated Common Bile Duct	dilated common bile duct		Jul 4, 2023, 2:55 PM	Final
Sponsor	Laboratory Assessments	Biochemistry	Direct Bilirubin	direct bilirubin		Jul 4, 2023, 2:54 PM	Final
Sponsor	Eligibility Criteria	Eligibility Criteria	Eligibility Criteria Met	eligibility criteria met			
Sponsor	AE Requiring Additional Data	Gallbladder Disease	Gallbladder Dilated Common Bile Duct	gallbladder dilated common bile duct...			
Sponsor	AE Requiring Additional Data	Gallbladder Disease	Gallstone in Bile	gallstone in bile duct			

Library / Concepts / Activities / List of Activities / Bilirubin

Bilirubin

Overview | COSMoS YAML

Name: Bilirubin

Sentence Case Name: bilirubin

Definition

Abbreviation: Library Sponsor

Activity groupings

Activity group	Activity subgroup
Laboratory Assessments	Biochemistry

Activity instances

Name	Definition	Activity instance class	Topic code	ADaM parameter code
Bilirubin (N)		NumericFinding	BILIRUBIN_N_URINE	BILIU3
Bilirubin Urine		CategoricFinding	BILIRUBIN_URINE	BILIU2
Bilirubin, AE Requiring Additional Data		NumericFinding	BILI	BILI
Bilirubin, Biochemistry		NumericFinding	BILIRUBIN_SERUM	BILIS3

Library / Concepts / Activities / Activities Instances / Bilirubin Urine

Bilirubin Urine

Overview | COSMoS YAML

Name: Bilirubin Urine

Sentence Case Name: bilirubin urine

Definition

Activity instance class: CategoricFinding

Abbreviation: Library Sponsor

ADaM parameter code: BILIU2 Topic code BILIRUBIN_URINE

Activity groupings

Activity group	Activity subgroup
Laboratory Assessments	Biochemistry

Activity

Name	Definition	Library
Bilirubin		Sponsor

Activity items

Name	CT term name	Unit name	Activity item class
BILI	Total Bilirubin Measurement		test_name_code
LB	Laboratory Data Domain		domain
URINALYSIS	Urinalysis		finding_category
URINE	Urine		specimen

Activity

=

Biomedical Concept
(COSMoS project from CDISC)

NeoDash reports to view Activity to SDTM Variables

neo4j Labs neo4j://vm-db-fv7zbjhkegyw.clinicalmldr-dev.corp.azure.novonordisk.com:7687

StudyBuilder Activity Library Dashboard

ReadMe Activity Lib (search top-down) Activity Lib (search bottom-up) **Activity to SDTM** Activity in COSMOS format Activities used in Studies

Select Activity Instance

ActivityGroup	ActivitySubGroup	Activity	ActivityInstance
Adverse Event	Adverse Event	Adverse Event	AE
Laboratory Assessments	Biochemistry	Alanine	ALAP
AE Requiring Additional Data	Laboratory Assessment	Alanine Aminotransferase	ALT
Laboratory Assessments	Biochemistry	Alanine Aminotransferase	ALTS
AE Requiring Additional Data	Laboratory Assessment	Albumin	ALBU2

86-90 of 1000

Select SDTM version

Click	IG	Description	Effective Date	Version Number
SELECT	SDTMIG v3.4	This is the implementation guide for human clinical trials corresponding to Version 2.0 of the CDISC Study Data Tabulation Model.	2021-11-29	3.4
SELECT	SDTMIG v3.3	CDISC Version 3.3 (V3.3) Study Data Tabulation Model Implementation Guide for Human Clinical Trials (SDTMIG) is intended to guide t	2018-11-20	3.3
SELECT	SDTMIG v3.2	CDISC Version 3.2 (V3.2) Study Data Tabulation Model Implementation Guide for Human Clinical Trials (SDTMIG) is intended to guide t	2013-11-26	3.2
SELECT	SDTMIG v3.1.3	CDISC Version 3.1.3 (V3.1.3) Study Data Tabulation Model Implementation Guide for Human Clinical Trials (SDTMIG) is intended to gu	2012-07-16	3.1.3
SELECT	SDTMIG v3.1.2	CDISC Version 3.1.2 (V3.1.2) Study Data Tabulation Model Implementation Guide for Human Clinical Trials (SDTMIG) is intended to gu	2008-11-12	3.1.2

1-5 of 5

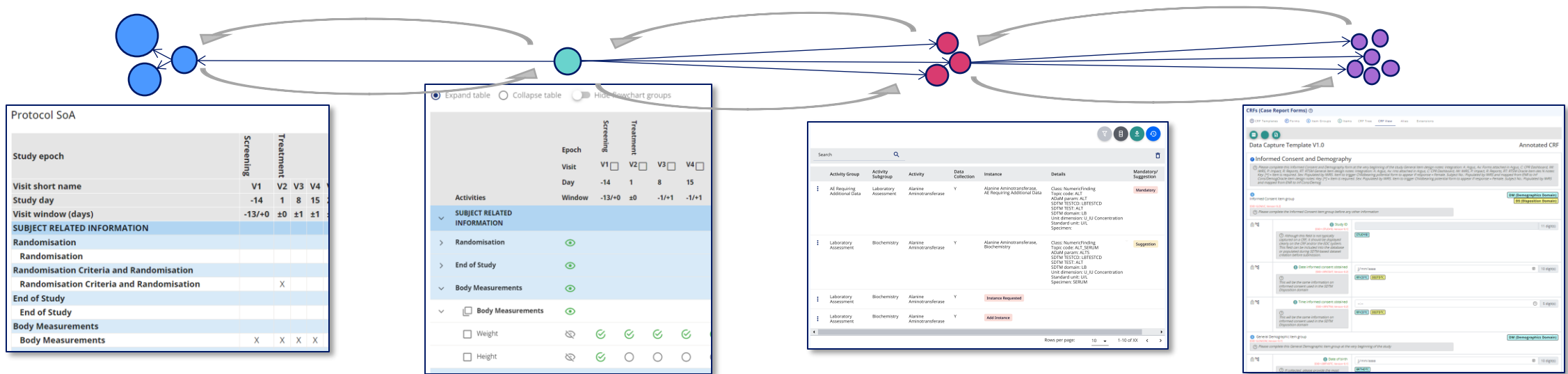
Activity mapped to SDTM

Activity	Activity Instance	Activity Item Class	Variable Class	SDTMIG Variable	SDTMIG Dataset
Albumin	Urinary Albumin Excretion	domain	DOMAIN	Domain Abbreviation	Labs
Albumin	Urinary Albumin Excretion	test_name_code	--TESTCD	Lab Test or Examination Short	Labs
Albumin	Urinary Albumin Excretion	test_name_code	--TEST	Lab Test or Examination Name	Labs
Albumin	Urinary Albumin Excretion	specimen	--SPEC	Specimen Type	Labs

Rows per page: 5 1-4 of 4

Activity with links to SDTM

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

- ←
- 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

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

Activities	Window	Screening										Follow-up
		V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	
		-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	👁️											
> <input type="checkbox"/> Glucose Metabolism	👁️											
> <input type="checkbox"/> HbA1c	🔒	✅	✅	✅	✅	✅	✅	✅	✅	✅	✅	○
> Self Measured Plasma Glucose	👁️											
> <input type="checkbox"/> Self Measured Plasma Glucose	🔒											
> <input type="checkbox"/> Mean Plasma Glucose	🔒	○	○	○	○	○	○	○	○	○	○	○
> SAFETY	🔒											

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

Select Study & Version | Get Data | Start/End tags visible | About

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
	V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	
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

- ←
- 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

Selection is made to specific Activity Instance level

Activity Group	Activity Subgroup	Activity	Data Collection	Instance	Details	Mandatory/Suggestion	
⋮	AE Requiring Additional Data	Laboratory Assessment	Alanine Aminotransferase	Y	Alanine Aminotransferase, AE Requiring Additional Data	Class: NumericFinding Topic code: ALT ADaM param: ALT SDTM TESTCD: LBTESTCD SDTM TEST: ALT SDTM domain: LB Unit dimension: U_IU Concentration Standard unit: U/L Specimen:	Mandatory
⋮	Laboratory Assessment	Biochemistry	Alanine Aminotransferase	Y	Alanine Aminotransferase, Biochemistry	Class: NumericFinding Topic code: ALT_SERUM ADaM param: ALTS SDTM TESTCD: LBTESTCD SDTM TEST: ALT SDTM domain: LB Unit dimension: U_IU Concentration Standard unit: U/L Specimen: SERUM	Suggestion
⋮	Laboratory Assessment	Biochemistry	Alanine Aminotransferase	Y			Instance Requested

Concept: CRFs

Library / Concepts / CRFs / CRF Tree

CRFs (Case Report Forms) ⓘ

CRF Templates Forms Item Groups Items CRF Tree CRF View Alias Extensions

Reorder content

Templates / Forms / ItemGroups / Items	Reference attributes	Definition attributes	Status	Version	Link
Template NN V1			Draft	0.1	+ FORMS
Informed Consent and Demography			Draft	0.1	+ ITEM GROUPS
Informed Consent			Draft	0.2	+ ITEMS
Study ID			Draft	0.1	
Date informed consent obtained			Draft	0.2	
Time informed consent obtained			Draft	0.2	
General Demography			Draft	0.1	
Date of birth			Draft	0.1	
Sex (read-only)			Draft	0.1	
Ethnicity			Draft	0.1	
Race			Draft	0.1	
Age		123	Draft	0.1	
Race other			Draft	0.1	
Vital Signs			Draft	0.1	

Templates used to defined multiple CRF version

PDF format

Annotated CRF following MSG 2.0 standard

ODM.xml with vendor extensions (or CSV)

Library / Concepts / CRFs / CRF View

CRFs (Case Report Forms) ⓘ

CRF Templates Forms Item Groups Items CRF Tree CRF View Alias Extensions

Template NN V1 Annotated CRF

Informed Consent and Demography

Please complete this Informed Consent and Demography form at the very beginning of the study General Item design notes: Integration: A: Argus, Ax: Forms attached in Argus, C: CPR Dashboard, IW: IWRS, P: Impact, R: Reports, RT: RTSM General item design notes: Integration: A: Argus, Ax: rms attached in Argus, C: CPR Dashboard, IW: IWRS, P: Impact, R: Reports, RT: RTSM Oracle item des N notes: Key: [*] = Item is required. Sex: Populated by IWRS. Item to trigger Childbearing potential form to appear if response = Female. Subject No.: Populated by IWRS and mapped from ENR to Inf Cons/Demog Oracle item design notes: Key: [*] = Item is required. Sex: Populated by IWRS. Item to trigger Childbearing potential form to appear if response = Female. Subject No.: Populated by IWRS and mapped from ENR to Inf Cons/Demog

Informed Consent item group DM (Demographics Domain) DS (Disposition Domain)

[OID=GDM.IC, Version=0.2]

Please complete the Informed Consent item group before any other information

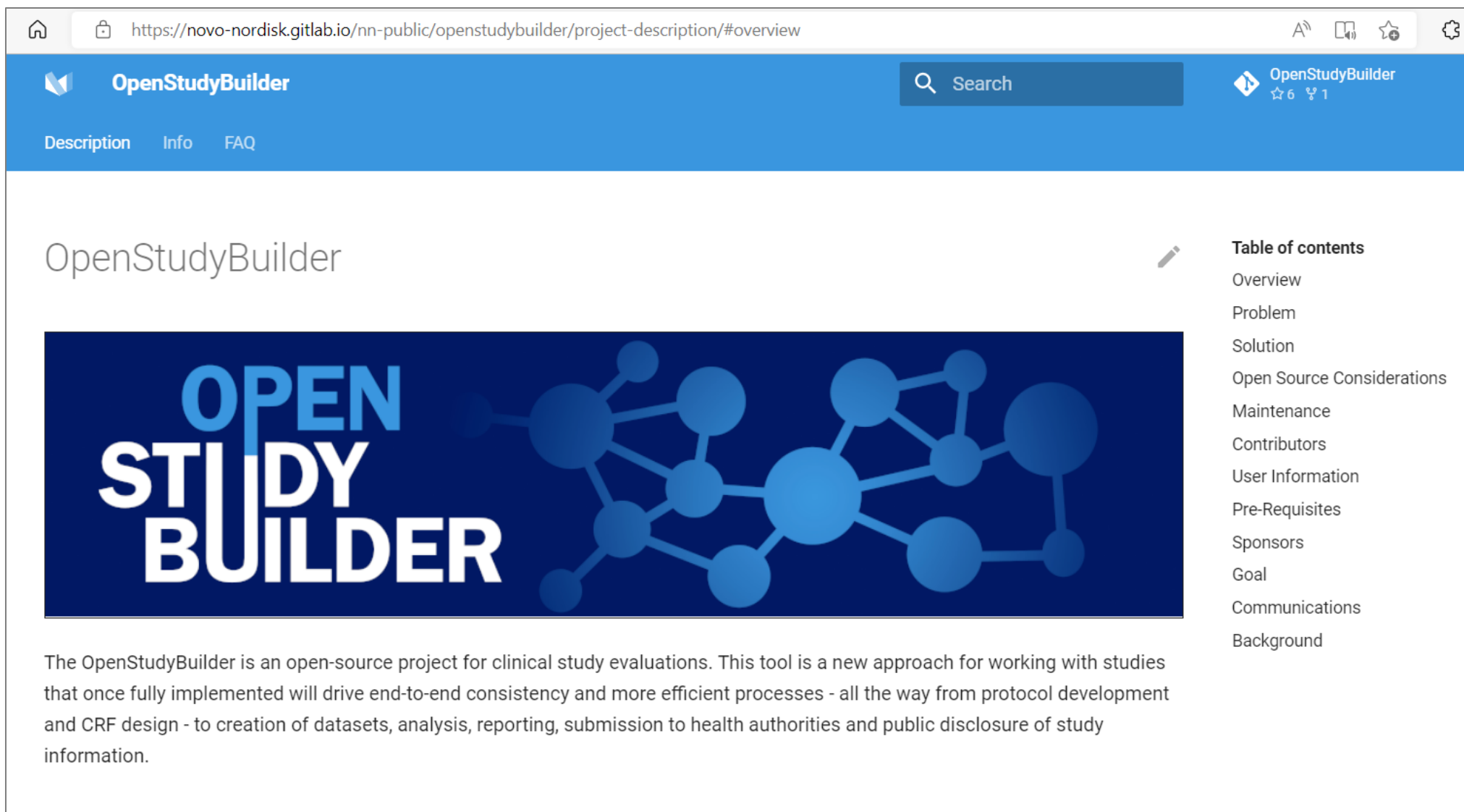
Study ID [OID=LSTUDID, Version=0.1]	11 digit(s)
Date informed consent obtained [OID=LRFICDAT, Version=0.2]	jj/mm/aaaa 10 digit(s)

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://novo-nordisk.gitlab.io/nn-public/openstudybuilder/project-description/>
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 project description for OpenStudyBuilder. The browser's address bar shows the URL: <https://novo-nordisk.gitlab.io/nn-public/openstudybuilder/project-description/#overview>. The page header features the OpenStudyBuilder logo, a search bar, and navigation links for Description, Info, and FAQ. The main content area includes the title "OpenStudyBuilder" and a large banner image with the text "OPEN STUDY BUILDER" and a network diagram. A table of contents is visible on the right side of the page.

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?

OPEN
STUDY
BUILDER

