Next Generation Nonclinical Protocol Development: An OpenStudyBuilder Discussion and Demonstration

Opportunities for Pre-Clinical Protocol Automation

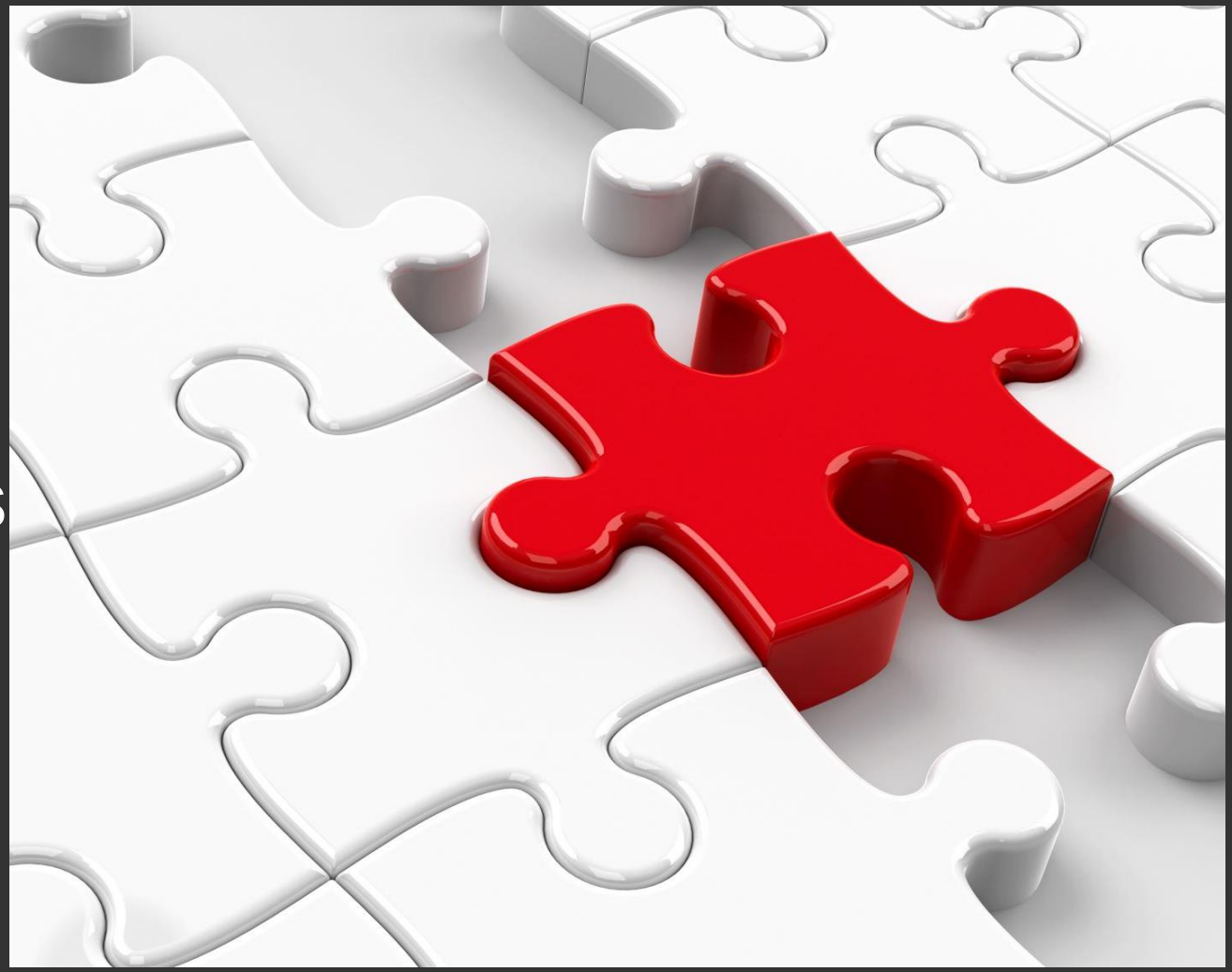
- **Society of Toxicology Meeting**

Bob Friedmann, Xybion
Katja Glaß, Katja Glass Consulting

21 March 2023

Agenda

- Introduction
- Protocol Automation Needs
- Solutions
- Nonclinical vs Clinical
- Collaboration
- Questions & Answers



Introduction

Meet the Presenters

Presenter

Bob Friedman

Chief Technologist &
Chief Solution Architect

Experience

- Over 30 years of experience in life sciences
- Former employee of the New York State Department of Health, Synthes USA, NYU Medical Center

Membership

- Active member of CDISC SEND standards consortium
- Active member of PhUSE / FDA Industry Collaboration

Education

- Master of Engineering, Biomedical Engineering
- Bachelor of Engineering, Biomedical Engineering

Meet the Presenters (online)

Presenter

Katja Glaß

Open Source Consultant

Experience

- Over 15 years of experience in life sciences (SAS, Web Technologies, ADAM, Define.xml and the TLF generation, Study evaluation processes, …)
- Open Source Ambassador (www.glacon.eu/portal)

Membership

- Community Manager of OpenStudyBuilder
- Active member of PHUSE
- Active member of CDISC Open Source Alliance (board member)

Education

- Diploma of Information Technology

Katja Glass Consulting

Protocol Design Automation needs

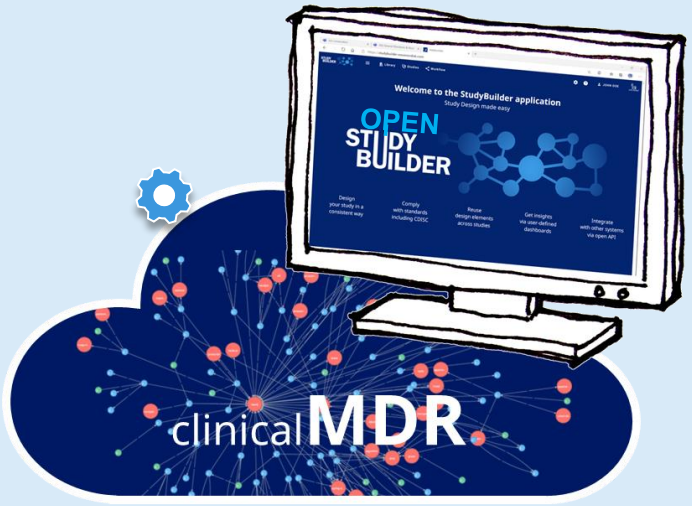
- Ensure a higher degree of end-to-end consistency
- Have built-in compliance with external and internal standards
- Facilitate more automation and content reuse
- Share electronically the nonclinical protocol / study
  - Between Pharma's and CROs
  - To regulatory bodies
- Do so in a manner that is
  - Computer readable for system to system exchange
  - Human readable to turn into approval formal protocol
  - Amendments must be evident

What is the OpenStudyBuilder …

OpenStudyBuilder is an open source solution provided by Novo Nordisk® which is looking for collaborations.

The OpenStudyBuilder comprises three elements:

- **Clinical Metadata Repository (MDR) and Study Definition Repository (SDR)**
  (central repository for all study specification data)
- **OpenStudyBuilder application**
  (web-based user interface)
- **API layer**
  (allowing interoperability with other applications)
  (DDF API Adaptor – enabling DDF SDR Compatibility)

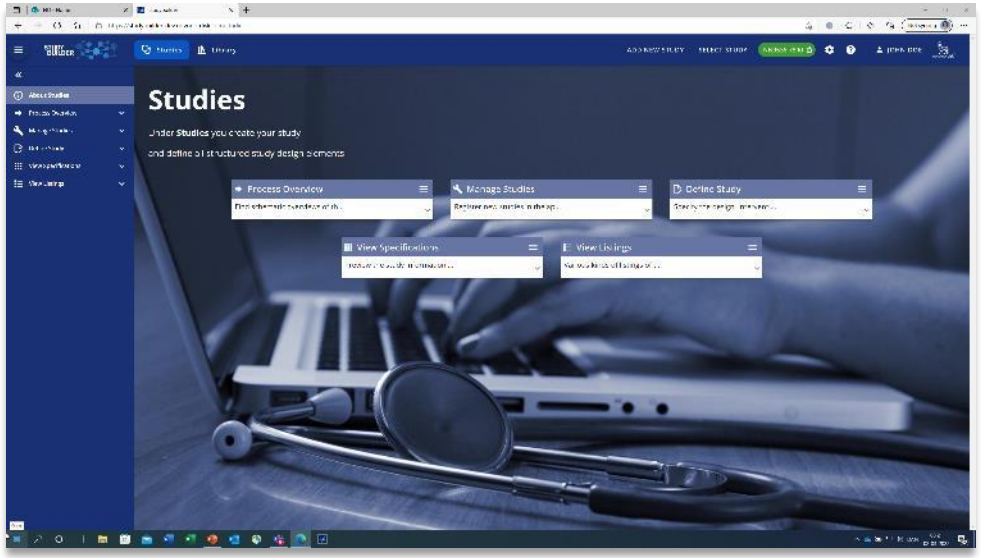


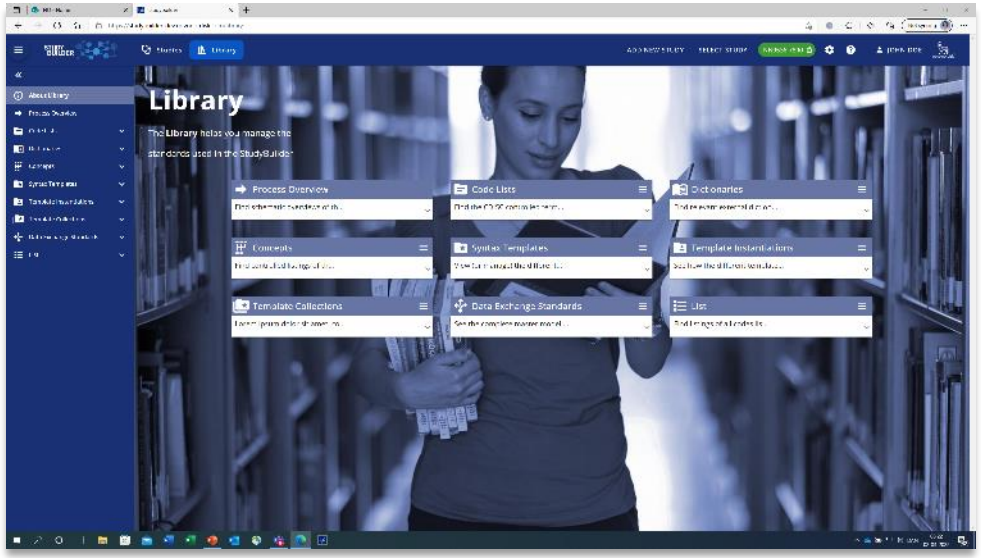
The OpenStudyBuilder includes:

- A **Studies** part for specification of studies
(incl. disease area and study type, objectives and endpoints, population and eligibility criteria, study compounds and other interventions, study design, arms and visits, schedule of activities and associated procedure and assessment instructions)

- A **Library** part for maintenance of terminology standards (incl. CDISC controlled terminology, relevant parts of external dictionaries for medical terms, pharmacological classes, units, a detailed compound library, a granulated library of activity terms) as well as syntax templates for cross-study and cross-project harmonisation)

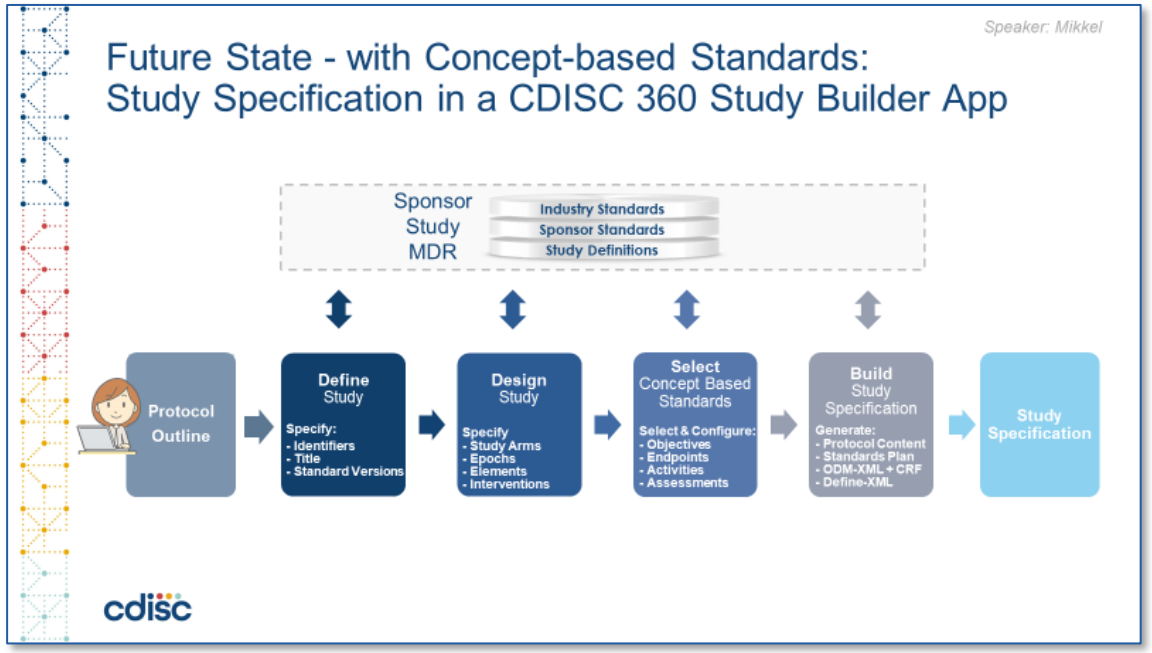
- An underlying **knowledge database**
(enabling complex queries and visualisations for aggregation of information and showing how things are connected end-to-end)

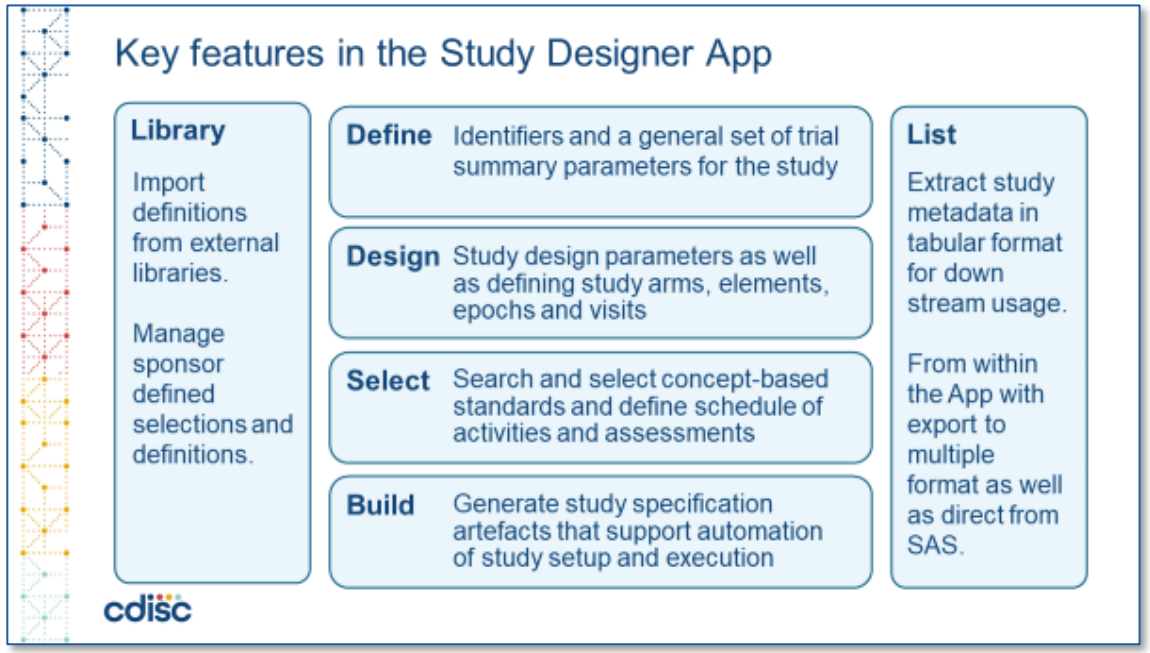




OpenStudyBuilder is being built as an open-source MDR and SDR solution based on the CDISC 360 POC

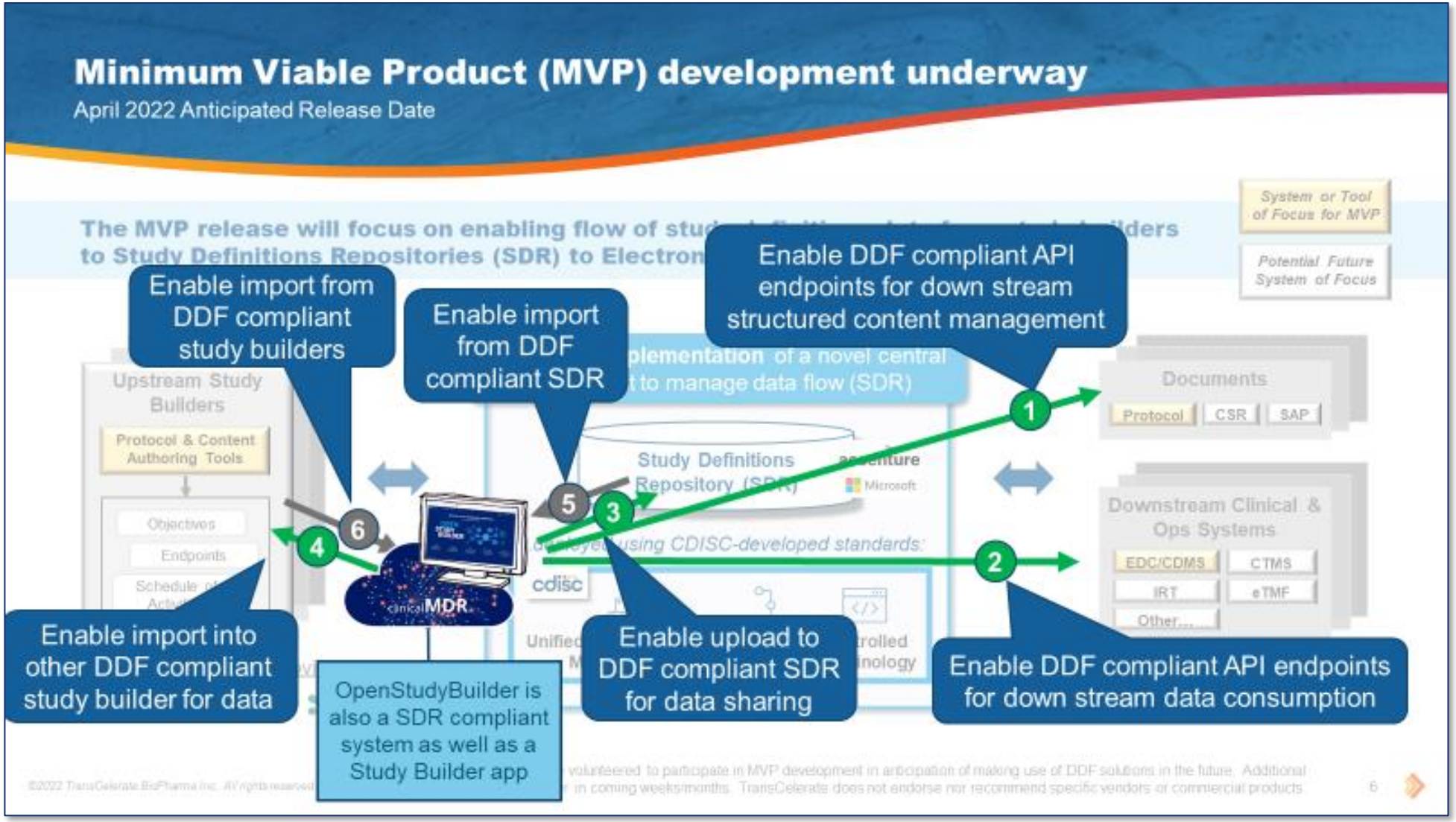
- Project collaborates with CDISC, TransCelerate DDF and suppliers





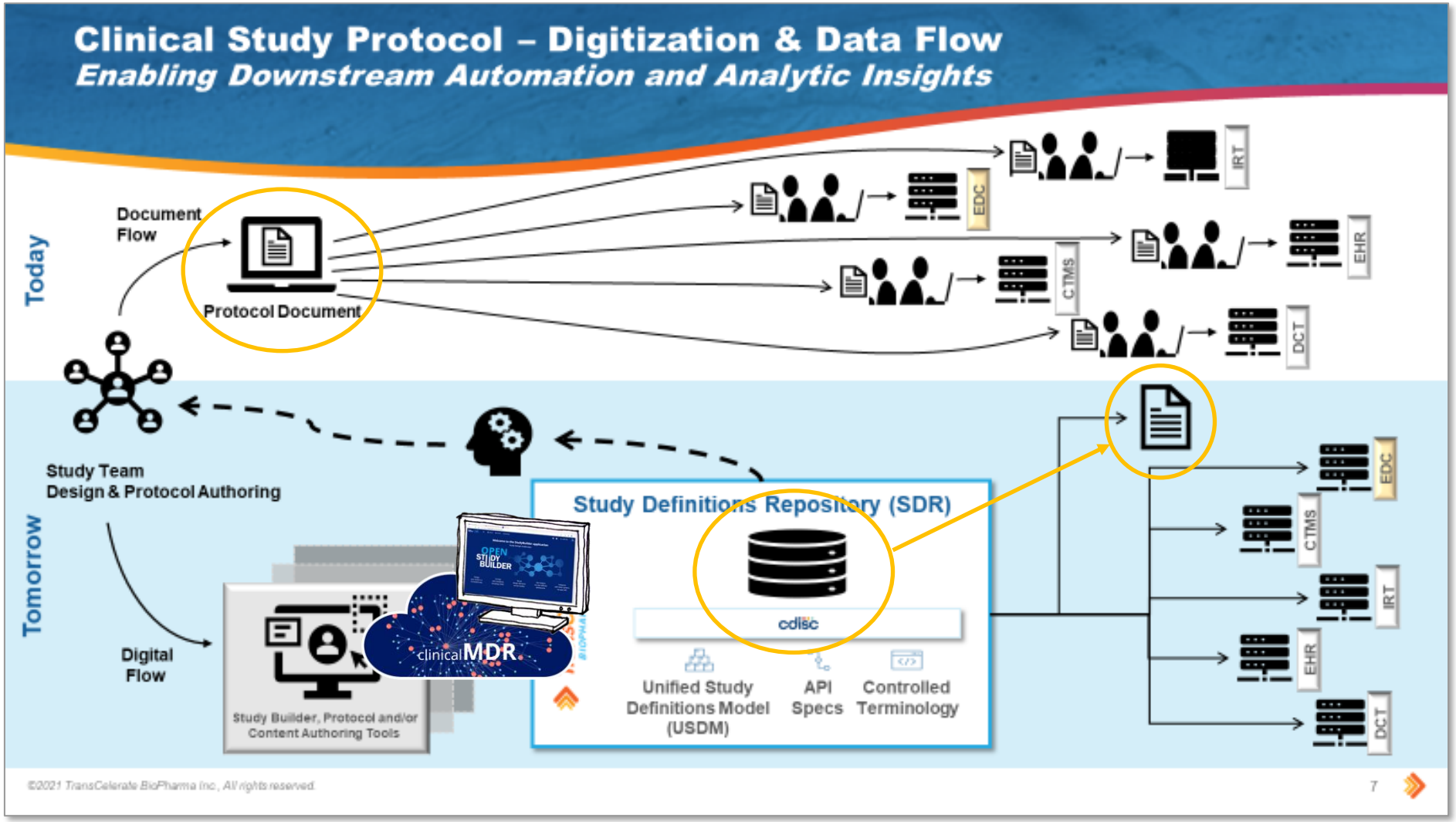
https://www.cdisc.org/cdisc-360

OpenStudyBuilder will also be DDF Compatible



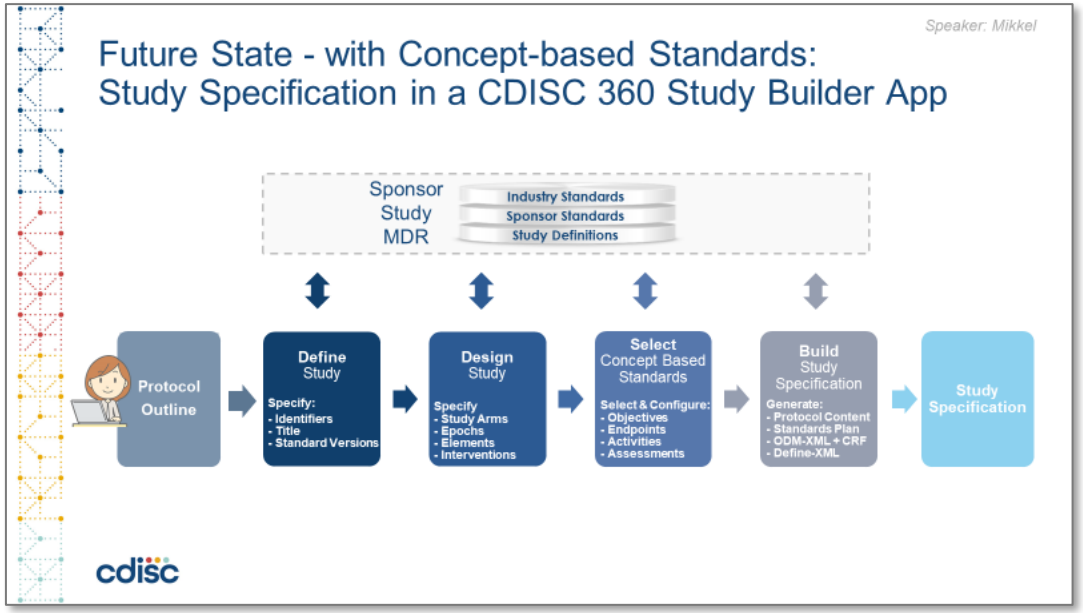
https://transcelerate.github.io/ddf-home/

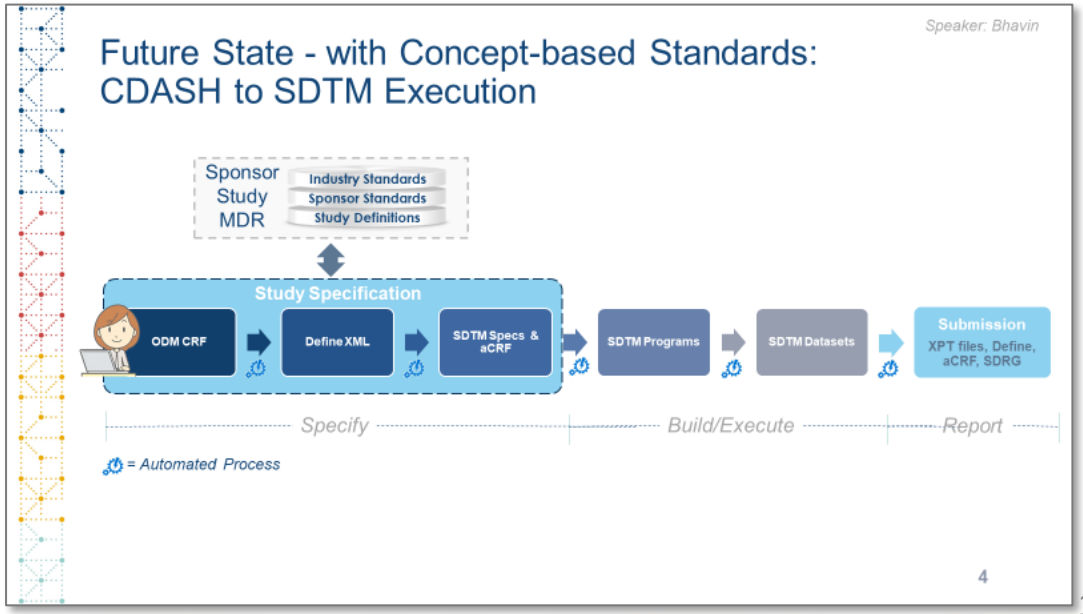
DDF is moving away from Document focused processes to Connected Data Driven processes



To apply concept-based data standards end-to-end

- From protocol preparation through study conduct to reporting and submission of applications to health authorities
  - and with reference to externally-compliant concept-based data standards and terminology



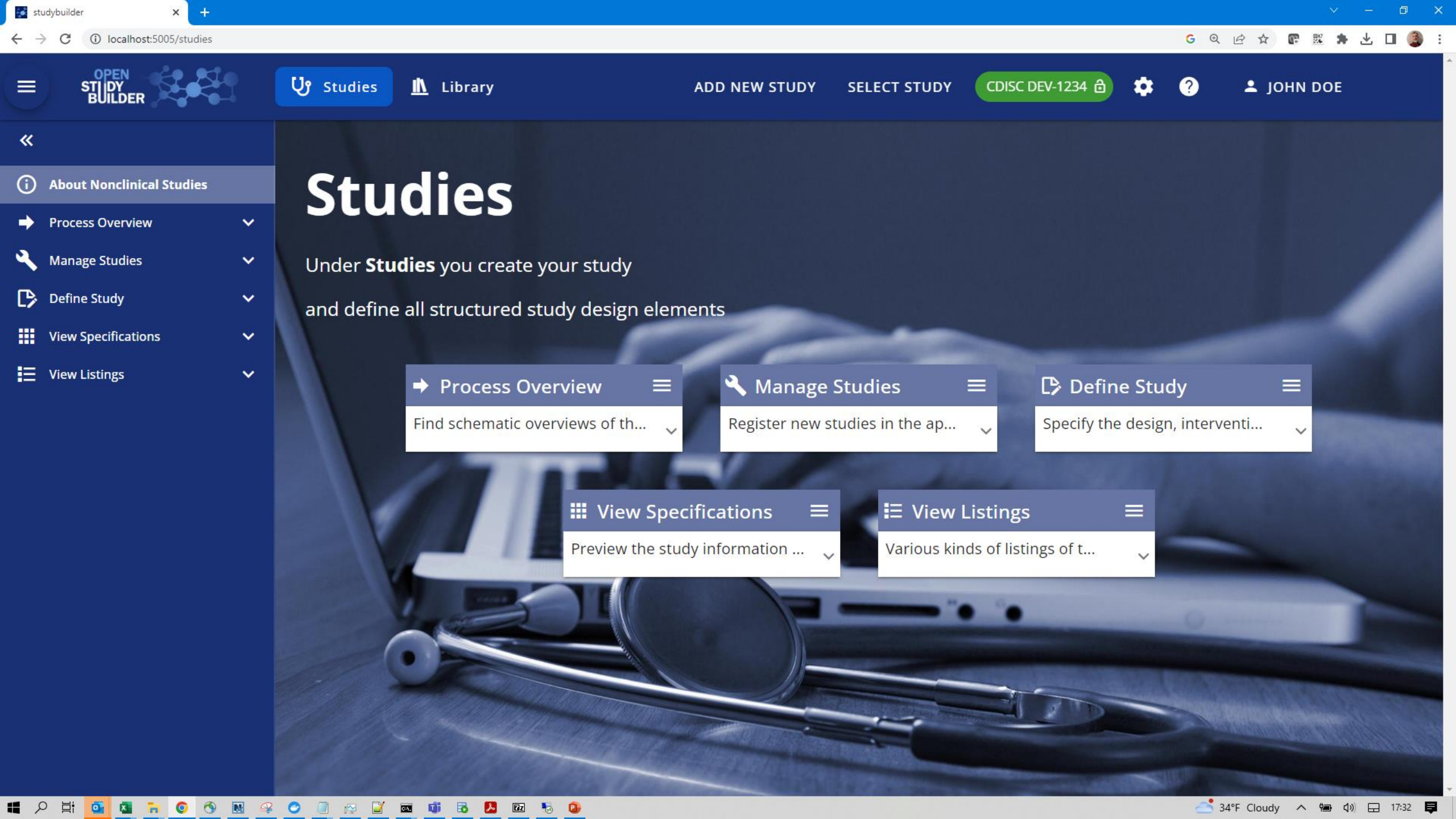


Open-Sourced

- Shared as open source project in Q3 2022
  - https://novo-nordisk.gitlab.io/nn-public/openstudybuilder/project-description/
- Listed in COSA (CDISC Open Source Alliance)
  - https://cosa.cdisc.org/directory/openStudyBuilder
- Seek to actively collaborate with CDISC, TransCelerate DDF, peers and vendors

OpenStudyBuilder Demo

Differences between Non clinical and Clinical


studybuilder
localhost:5005/studies
OPEN STUDY BUILDER
Studies
Library
ADD NEW STUDY
SELECT STUDY
CDISC DEV-1234
JOHN DOE
About Nonclinical Studies
Process Overview
Manage Studies
Define Study
View Specifications
View Listings
Studies
Under Studies you create your study
and define all structured study design elements
Process Overview
Find schematic overviews of th...
Manage Studies
Register new studies in the ap...
Define Study
Specify the design, interventi...
View Specifications
Preview the study information ...
View Listings
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About Nonclinical Studies
Process Overview
Manage Studies
Study List
Study Status
Project Standards
Define Study
View Specifications
View Listings

Study List

Select rows

Search

	Clinical Programme	Project ID	Project name	Brand name	Study number	Study ID	Study acronym
⋮	CDISC Development programme	CDISC DEV	CDISC Dev		0	CDISC DEV-0	CDISC360-2
⋮	CDISC Development programme	CDISC DEV	CDISC Dev		1234	CDISC DEV-1234	Study-1

Process Overview
Manage Studies
Study List
Study Status
Project Standards
Define Study
Specification Overview
Study Title
Registry Identifiers
Study Properties
Study Structure
Study Population
Study Criteria
Study Interventions
Study Purpose
Study Activities
Terminology

Study List

Select rows

Search

	Clinical Programme	Project ID	Project name	Brand name	Study number	Study ID	Study acronym
⋮	CDISC Development programme	CDISC DEV	CDISC Dev		0	CDISC DEV-0	CDISC360-2
⋮	CDISC Development programme	CDISC DEV	CDISC Dev		1234	CDISC DEV-1234	Study-1

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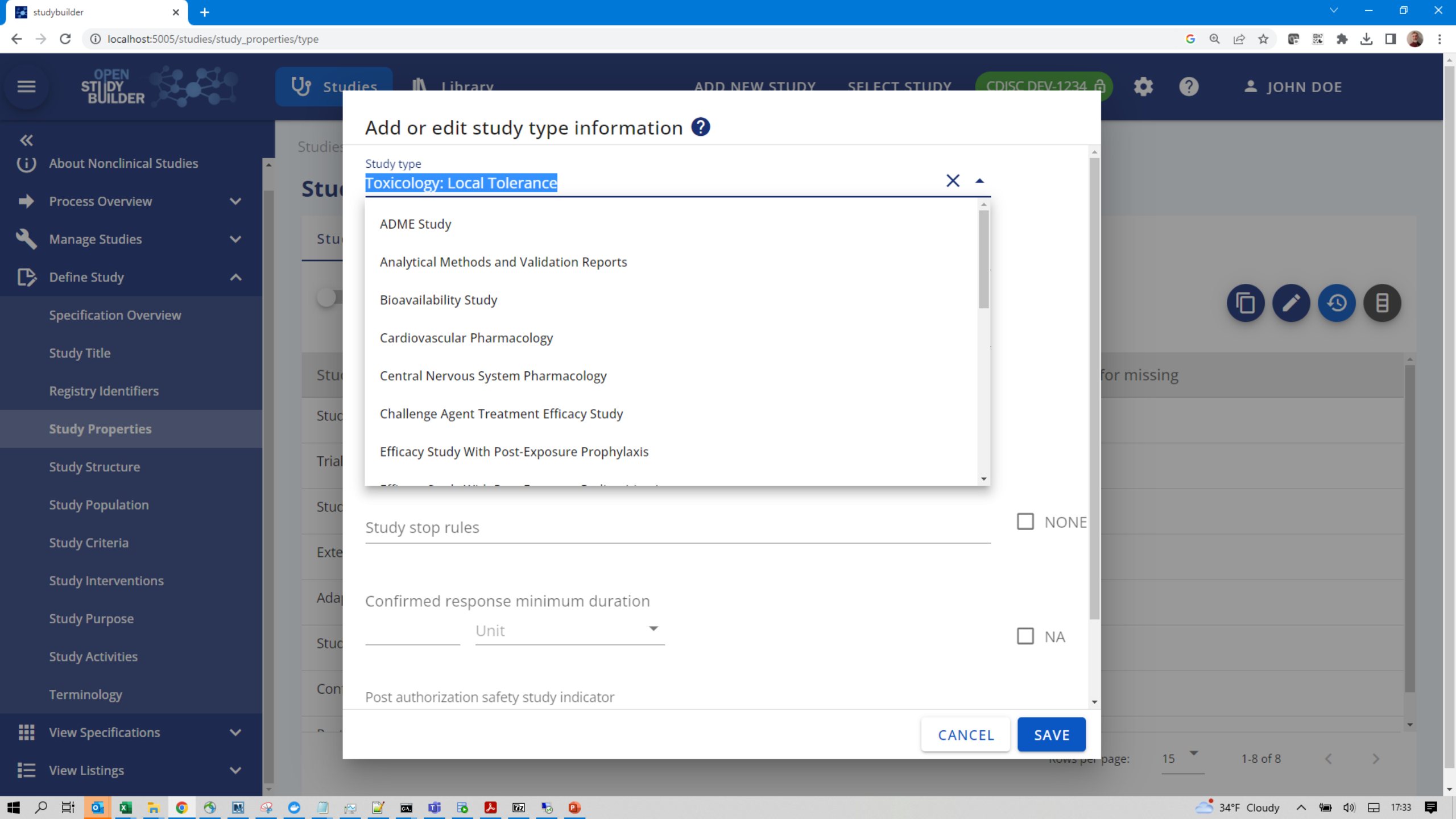
studybuilder
localhost:5005/studies/study_properties/type
OPEN STUDY BUILDER
Studies
Library
ADD NEW STUDY
SELECT STUDY
CDISC DEV-1234
JOHN DOE
About Nonclinical Studies
Process Overview
Manage Studies
Define Study
Specification Overview
Study Title
Registry Identifiers
Study Properties
Study Structure
Study Population
Study Criteria
Study Interventions
Study Purpose
Study Activities
Terminology
View Specifications
View Listings
Add or edit study type information
Study type
Toxicology: Local Tolerance
ADME Study
Analytical Methods and Validation Reports
Bioavailability Study
Cardiovascular Pharmacology
Central Nervous System Pharmacology
Challenge Agent Treatment Efficacy Study
Efficacy Study With Post-Exposure Prophylaxis
Study stop rules
NONE
Confirmed response minimum duration
Unit
NA
Post authorization safety study indicator
CANCEL
SAVE
Rows per page:
15
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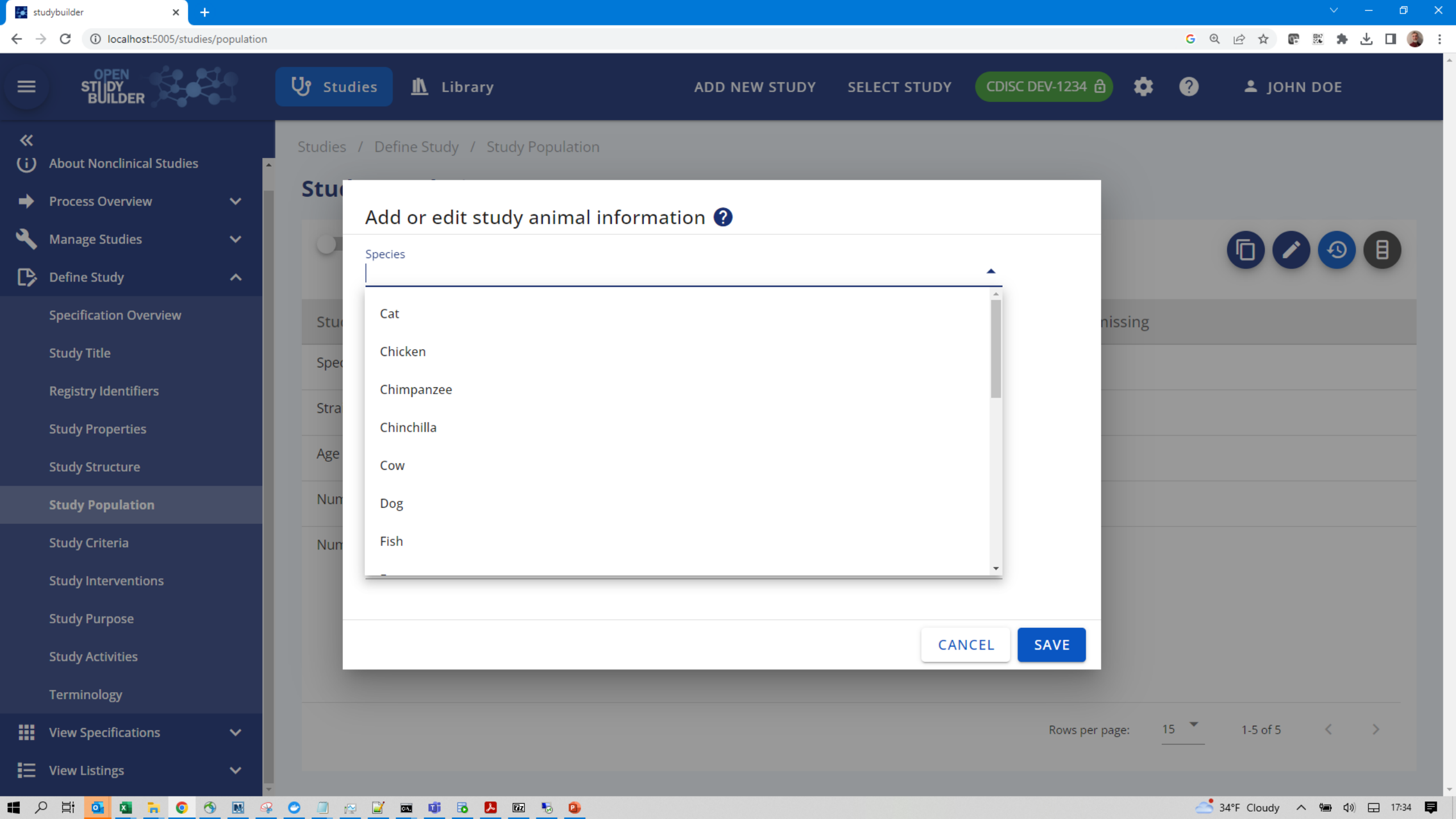
About Nonclinical Studies
Process Overview
Manage Studies
Define Study
Specification Overview
Study Title
Registry Identifiers
Study Properties
Study Structure
Study Population
Study Criteria
Study Interventions
Study Purpose
Study Activities
Terminology
View Specifications
View Listings

Study Population (CDISC DEV-1234)

Select rows

Study population information	Selected values	Reason for missing
Species		
Strain		
Age range of animals		
Number of Males		
Number of Females		


studybuilder
localhost:5005/studies/population
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Studies
Library
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SELECT STUDY
CDISC DEV-1234
JOHN DOE
About Nonclinical Studies
Process Overview
Manage Studies
Define Study
Specification Overview
Study Title
Registry Identifiers
Study Properties
Study Structure
Study Population
Study Criteria
Study Interventions
Study Purpose
Study Activities
Terminology
View Specifications
View Listings
Studies / Define Study / Study Population
Add or edit study animal information
Species
Cat
Chicken
Chimpanzee
Chinchilla
Cow
Dog
Fish
CANCEL
SAVE
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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

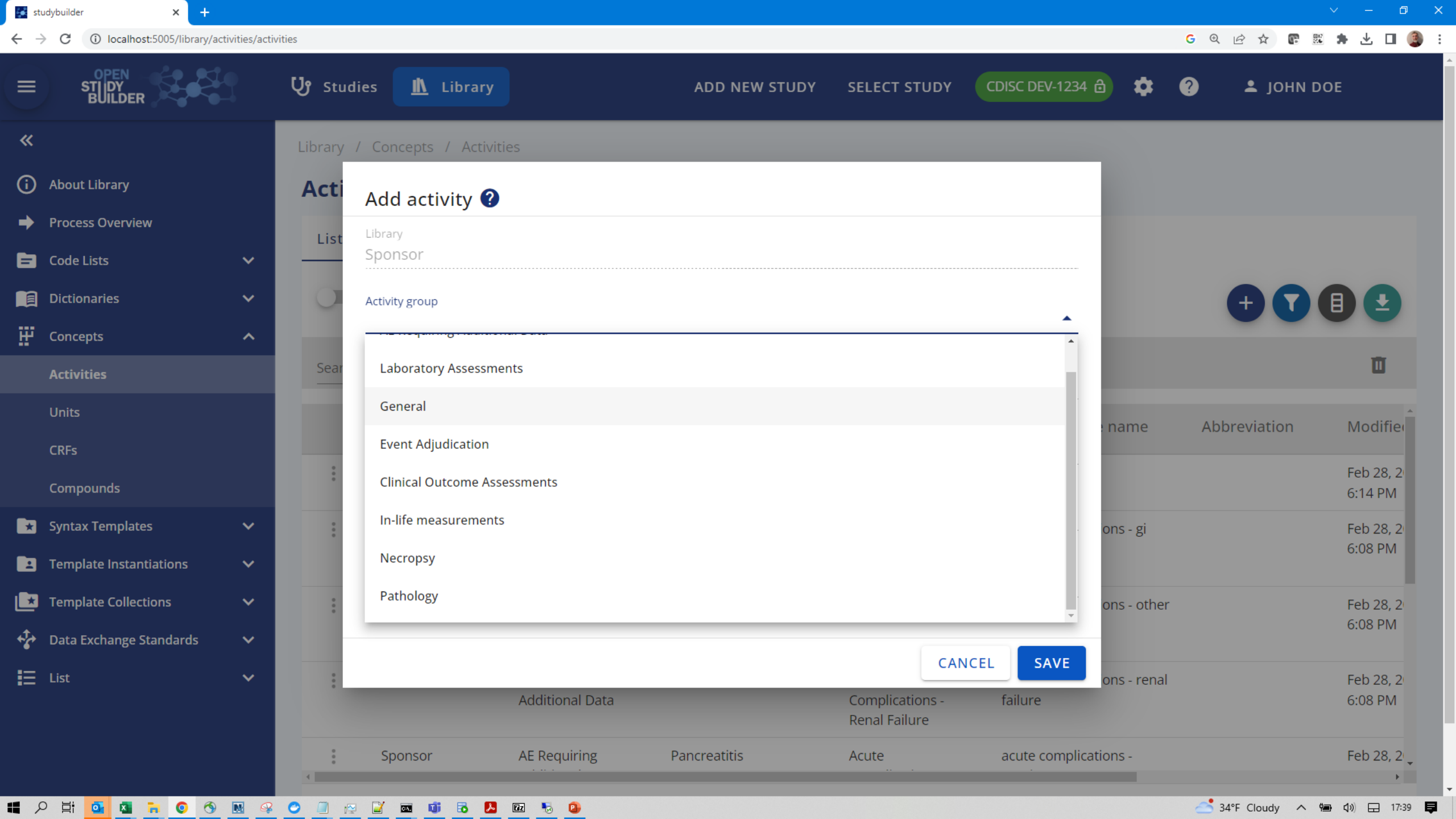
CT Catalogues

All | ADAM CT | CDASH CT | DEFINE-XML CT | SDTM CT | SEND CT

Select rows

Search

Library	Sponsor preferred name	Template parameter	Code list status	Name modified	Concept ID
CDISC	SEND Domain Abbreviation	No	Final	Mar 3, 2023, 11:10 AM	C111113
CDISC	Chronicity	No	Final	Mar 3, 2023, 11:11 AM	C120529
CDISC	Distribution	No	Final	Mar 3, 2023, 11:12 AM	C120530
CDISC	Non-Neoplastic Finding Type	No	Final	Mar 3, 2023, 11:11 AM	C120531
CDISC	SEND Cardiovascular Test Code	No	Final	Mar 3, 2023, 11:10 AM	C120532


studybuilder
localhost:5005/library/activities/activities
OPEN STUDY BUILDER
Studies
Library
ADD NEW STUDY
SELECT STUDY
CDISC DEV-1234
JOHN DOE
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
Add activity
Library
Sponsor
Activity group
Laboratory Assessments
General
Event Adjudication
Clinical Outcome Assessments
In-life measurements
Necropsy
Pathology
CANCEL
SAVE
name
Abbreviation
Modifie
Feb 28, 2
6:14 PM
ons - gi
Feb 28, 2
6:08 PM
ons - other
Feb 28, 2
6:08 PM
ons - renal
failure
Additional Data
Complications - Renal Failure
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Sponsor
AE Requiring
Pancreatitis
Acute
acute complications -
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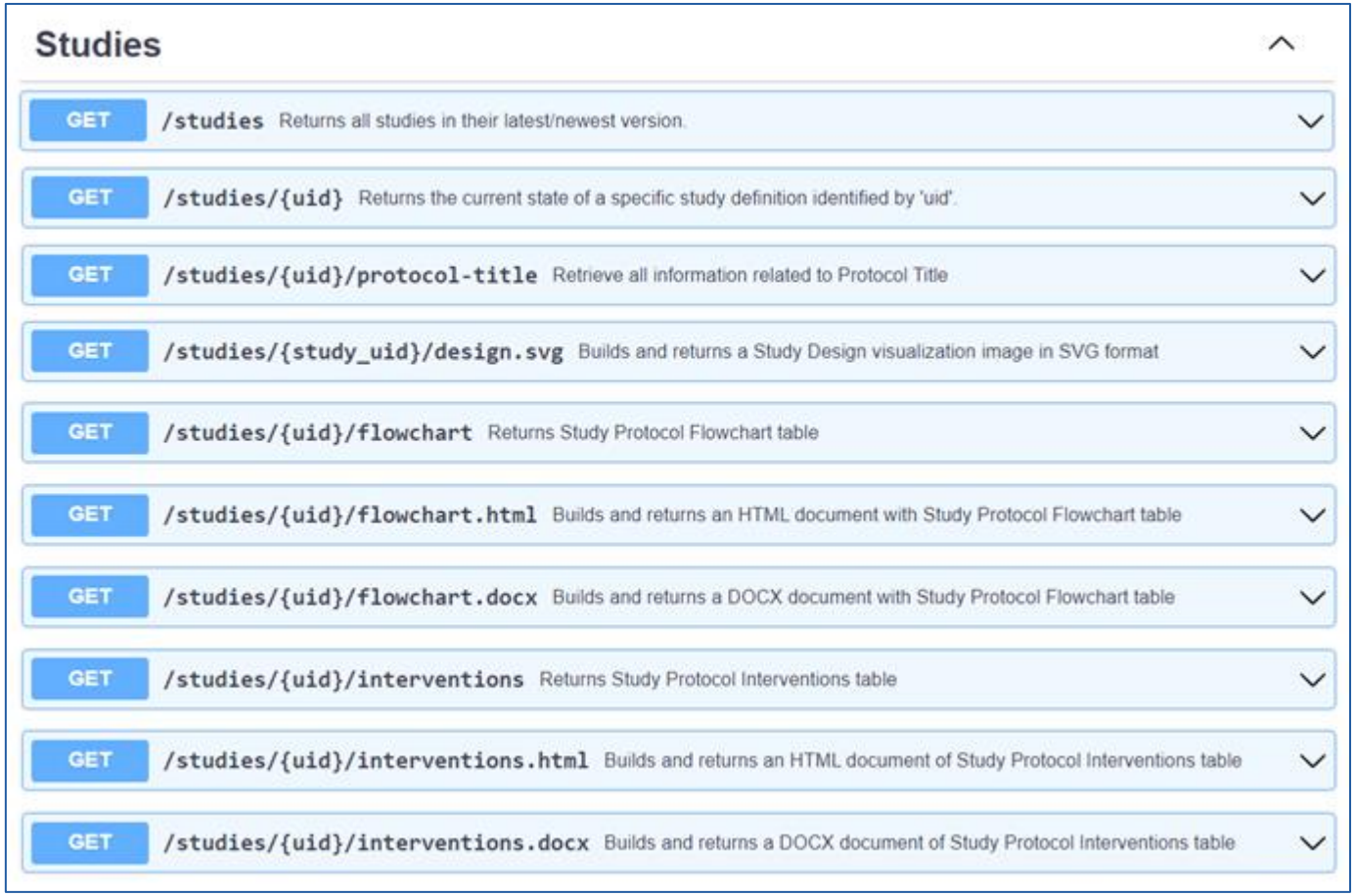
Automation Opportunities

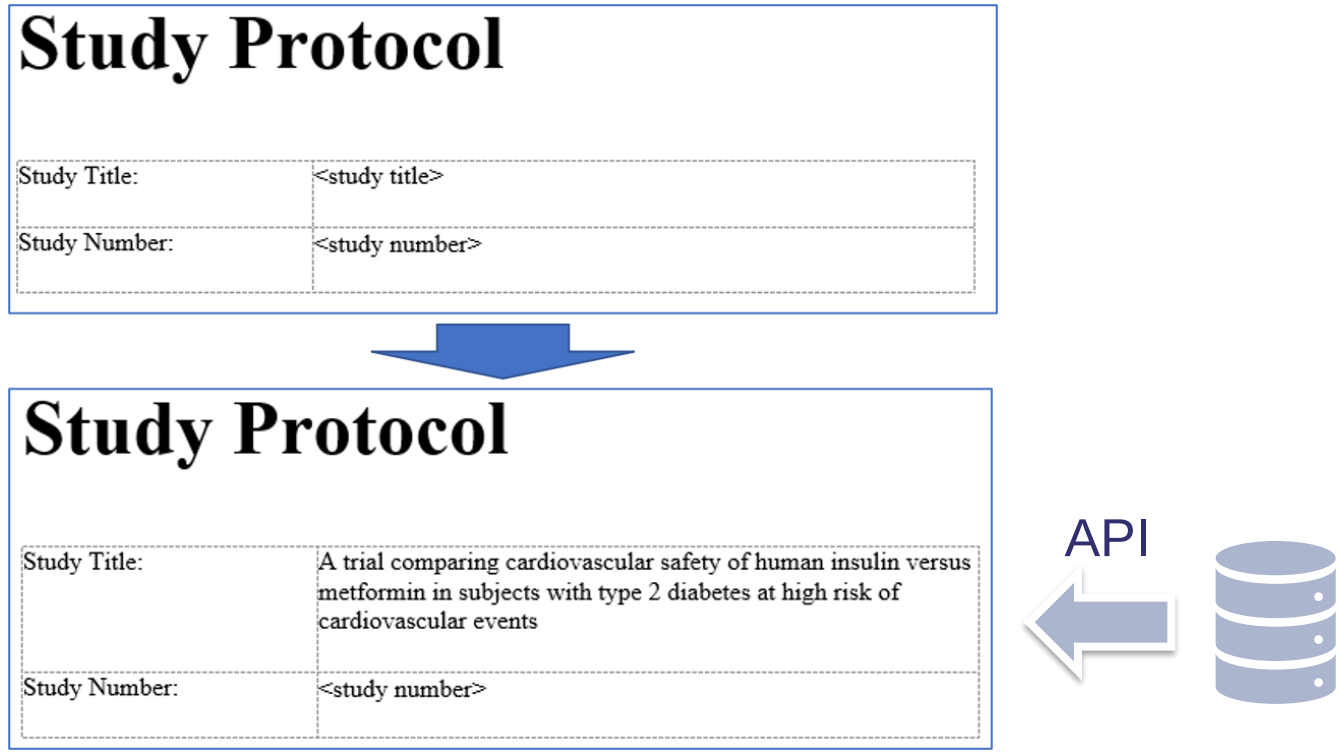
Getting Data

- All data accessible through APIs
- Tools can be automated



Protocol Automation

- Example:
  - Word-Programming in VBA
  - Word-Programming in R
  - Word-Programming in Python
  - …
- API to get
  - Study Design as SVG
  - Flowchart as HTML or DOCX
  - Interventions as HTML or DOCX



Protocol Automation

- Examples available

```r
library(httr)
library(officer)

# Switch to the corresponding working directory
setwd(".../OpenStudyBuilderScripts/scripts")

api_url <- "http://localhost:5003"
response <- GET(paste(api_url,"studies", "Study_000001", "protocol-title", sep = "/"))
study_1_prot_title <- jsonlite::fromJSON(rawToChar(response$content))
study_title = toString(study_1_prot_title["study_title"])

print(study_title)

protocol_doc <- read_docx(path = "./files/protocol_example_input.docx")
body_replace_all_text(
  protocol_doc,
  "<study title>",
  study_title)
print(protocol_doc, target = "./files/protocol_example_output_r.docx")
```

Protocol filled in from underlying data

1. Objective

The author may choose to add more or less detail based on expectations of Sponsor/CRO or other local requirements (class of compound, potential disease area, etc).

The purpose of this study is to evaluate the toxicity **[and determine toxicokinetics]** of the test item/article, **[TRT]**, when administered **[PDOSFRQ], [ROUTE], [SPECIES], [DOSDUR]** (e.g. once daily by oral gavage to rats for at least 4 weeks)], and to provide data to support the use of **[TRT]** in humans.

2. Proposed Study Schedule

Schedule detail may vary based on study/sponsor/CRO needs. The black text in brackets may be included for studies requiring SEND.

Experimental Start Date (date of first data collection):	**[EXPSTDTC]**
Dosing Start Date:	**[DOSSTDTC]**
Dosing End Date:	**[DOSENDTC]**
Experimental Completion Date (date of last data collected):	**[EXPENDTC]**
Audited Draft Report Date:	**[DATE]**

3. Sponsor/Test Facility/Test Site Information

Sponsor:	**[SSPONSOR]**
Test Facility:	**[TSTFNAM]**
Test Site:	**[TSNAM]**

Repeat as needed for additional test sites. The black text in brackets may be included for

1. Objective

The author may choose to add more or less detail based on expectations of Sponsor/CRO or other local requirements (class of compound, potential disease area, etc.).

The purpose of this study is to evaluate the toxicity **[and determine toxicokinetics]** of the test item/article, **MyDrug**, when administered **ONCE, INTRAVENOUS, RAT, P29D** (e.g. once daily by oral gavage to rats for at least 4 weeks)], and to provide data to support the use of **MyDrug** in humans.

2. Proposed Study Schedule

Schedule detail may vary based on study/sponsor/CRO needs. The black text in brackets may be included for studies requiring SEND.

Experimental Start Date (date of first data collection):	**2019-08-03**
Dosing Start Date:	**2019-08-03**
Dosing End Date:	**2019-09-01**
Experimental Completion Date (date of last data collected):	**2019-09-01**
Audited Draft Report Date:	**[DATE]**

3. Sponsor/Test Facility/Test Site Information

Sponsor:	**The sponsor**
Test Facility:	**Test facility B**
Test Site:	**Test Site A**

Repeat as needed for additional test sites. The black text in brackets may be included for studies requiring SEND.

Study Protocol

Study Title:

Study ID:

Study Acronym

Project

Program

Table of Contents

1. Objective

…

Get Study Title & ID

Study Protocol

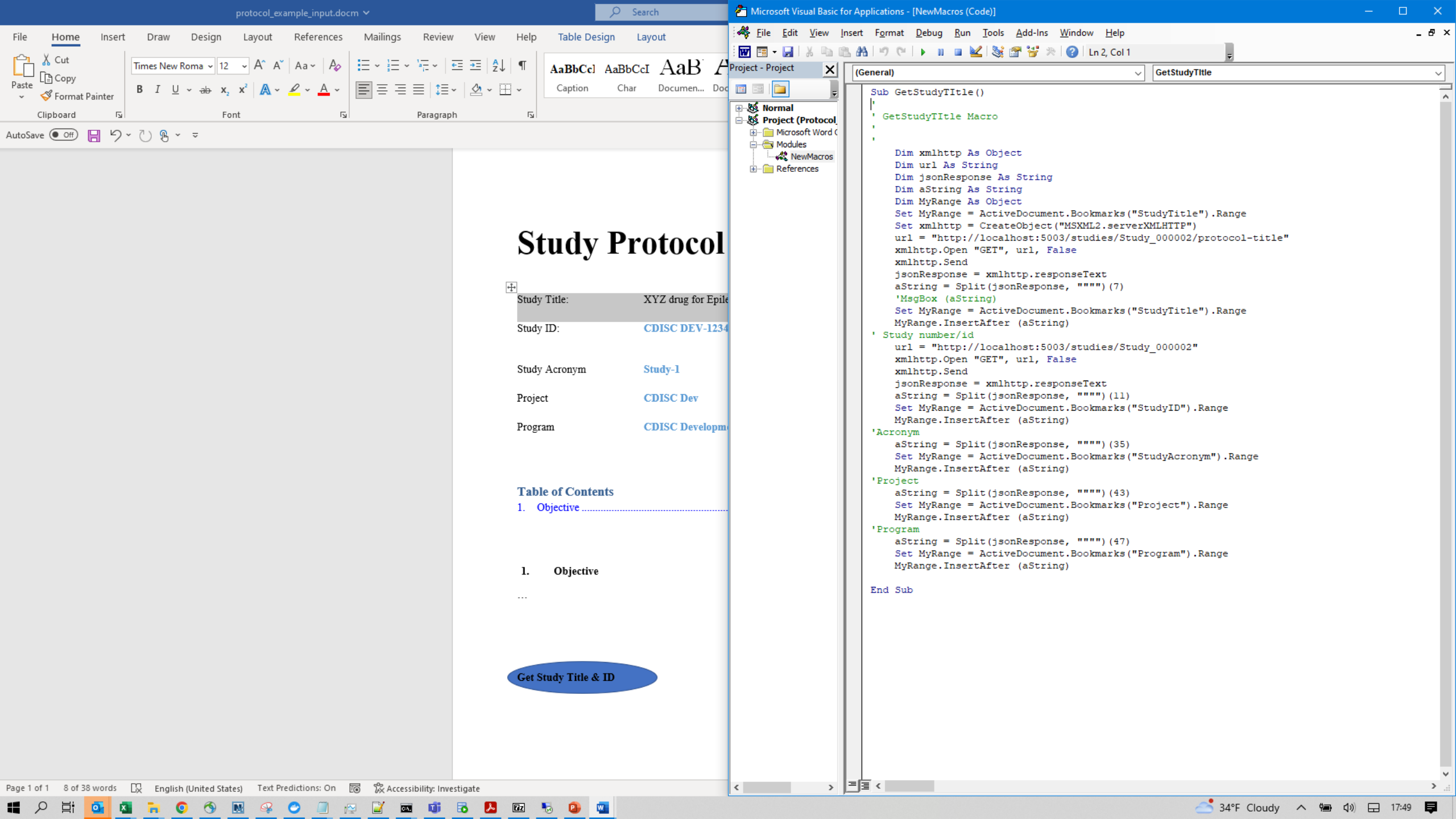
Study Title:	XYZ drug for Epilepsy, rat study
Study ID:	CDISC DEV-1234
Study Acronym	Study-1
Project	CDISC Dev
Program	CDISC Development programme

Table of Contents

1. Objective

…

Get Study Title & ID


protocol_example_input.docm
Search
File Home Insert Draw Design Layout References Mailings Review View Help Table Design Layout
Paste Cut Copy Format Painter
Clipboard
Times New Roma 12
Font
Caption Char Documen...
Paragraph
AutoSave Off
Study Protocol
Study Title: XYZ drug for Epile
Study ID: CDISC DEV-1234
Study Acronym Study-1
Project CDISC Dev
Program CDISC Developm
Table of Contents
1. Objective .....
1. Objective
...
Get Study Title & ID
Page 1 of 1 8 of 38 words English (United States) Text Predictions: On Accessibility: Investigate
Microsoft Visual Basic for Applications - [NewMacros (Code)]
File Edit View Insert Format Debug Run Tools Add-Ins Window Help
Ln 2, Col 1
Project - Project
Normal
Project (Protocol
Microsoft Word
Modules
NewMacros
References
(General)
GetStudyTitle
Sub GetStudyTItle()
'
' GetStudyTItle Macro
'
'
Dim xmlhttp As Object
Dim url As String
Dim jsonResponse As String
Dim aString As String
Dim MyRange As Object
Set MyRange = ActiveDocument.Bookmarks("StudyTitle").Range
Set xmlhttp = CreateObject("MSXML2.serverXMLHTTP")
url = "http://localhost:5003/studies/Study_000002/protocol-title"
xmlhttp.Open "GET", url, False
xmlhttp.Send
jsonResponse = xmlhttp.responseText
aString = Split(jsonResponse, """)(7)
'MsgBox (aString)
Set MyRange = ActiveDocument.Bookmarks("StudyTitle").Range
MyRange.InsertAfter (aString)
' Study number/id
url = "http://localhost:5003/studies/Study_000002"
xmlhttp.Open "GET", url, False
xmlhttp.Send
jsonResponse = xmlhttp.responseText
aString = Split(jsonResponse, """)(11)
Set MyRange = ActiveDocument.Bookmarks("StudyID").Range
MyRange.InsertAfter (aString)
'Acronym
aString = Split(jsonResponse, """)(35)
Set MyRange = ActiveDocument.Bookmarks("StudyAcronym").Range
MyRange.InsertAfter (aString)
'Project
aString = Split(jsonResponse, """)(43)
Set MyRange = ActiveDocument.Bookmarks("Project").Range
MyRange.InsertAfter (aString)
'Program
aString = Split(jsonResponse, """)(47)
Set MyRange = ActiveDocument.Bookmarks("Program").Range
MyRange.InsertAfter (aString)
End Sub
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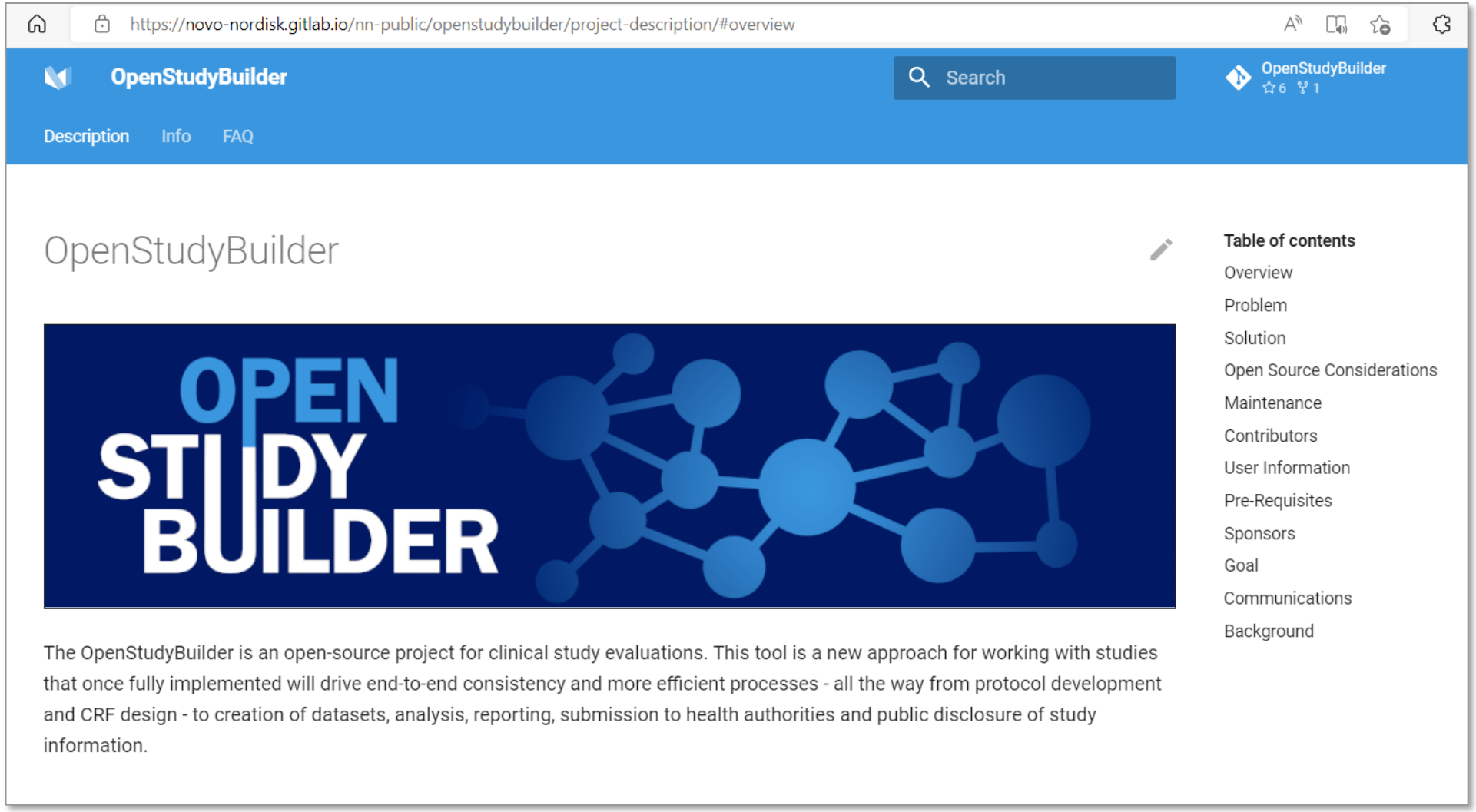
Getting Started

How do I get started on OpenStudyBuilder?



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

Starting with OpenStudyBuilder

- Neo4j Sandbox to play around
  - Browse, test and investigate functionality
  - Checkout Biomedical Concept (linked data browser)

- Local installation (free) or Custom/dedicated environment
  - API usage to upload/download custom data
  - Load trial domains
  - Browse “your” data

Collaboration Opportunities

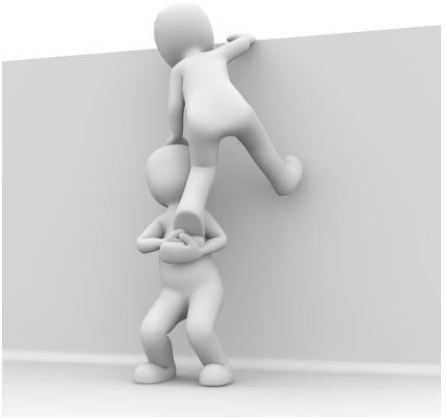
- BioCelerate Protocol Template Project
- OpenStudyBuilder community
- PHUSE eProtocol project
- Metadata standards

Collaboration Opportunities

- Enhance OpenStudyBuilder for NonClinical usage
- Create common additional standards “templates”, e.g. for endpoints, scope
- Common tools, processes and guides
  - Protocol automation
  - CRF
  - What to do on distressed animals
  - How to describe statistical planning

Expectation & Reality

- Novo Nordisk is continuously enhancing the tool and is looking for collaborations
- Pre-clinical does not have priority on internal development, don’t expect specific updates by them
- Support only through community or vendors
  - Appreciate and include documentation from everyone
  - If you want quick progress on developments, you have to invest, either personal or vendors

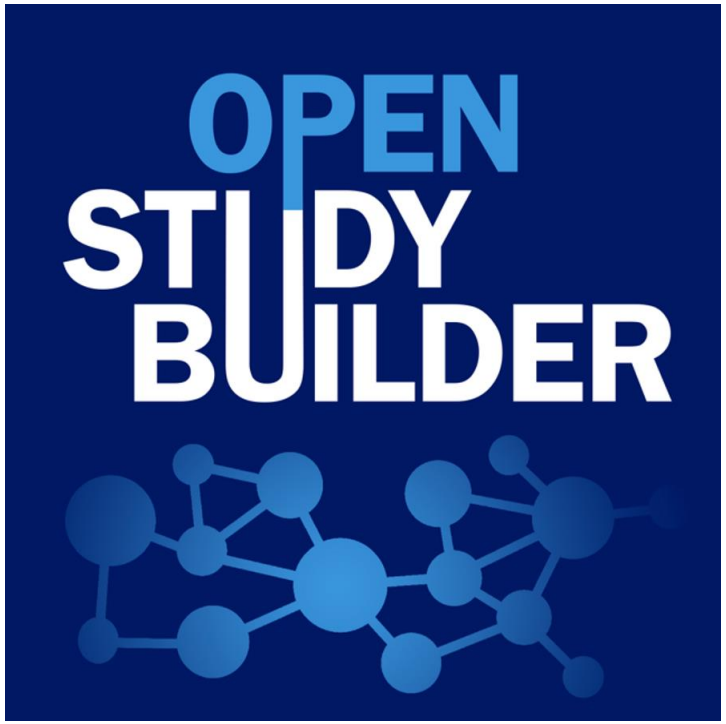


- Pre-clinical version:
  - Ideally there would be a “configuration” for pre-clinical, no additional parallel development

Links

- Project Homepage
  - https://novo-nordisk.gitlab.io/nn-public/openstudybuilder/project-description/
- Source Repository
  - https://gitlab.com/Novo-Nordisk/nn-public/openstudybuilder/OpenStudyBuilder-Solution
- COSA Homepage
  - https://cosa.cdisc.org/
- Newsletter (LinkedIn)
  - https://www.linkedin.com/newsletters/openstudybuilder-6990328054849916928/
- Sandbox to request access
  - Mail openstudybuilder@neotechnology.com – Subject “Request Sandbox access”
- User Scripts & Experiences Documentation
  - https://github.com/KatjaGlassConsulting/OpenStudyBuilderScripts

Thanks!
Questions?



Thank You

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Chief Technology Officer, Xybion
Email: bfriedman@xybion.com

Katja Glaß
Katja Glass Consulting
Email: katja.glass@glacon.eu

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

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+1-418-525-0606

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Old Mahabalipuram Road,
Chennai, 600097
+91-44-4283-3115

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Plot No-44, Phase I Kavuri Hills,
Hyderabad, Telangana 500033.

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