Katja Glass Consulting

Revolutionizing Clinical Trials

The Impact of OpenStudyBuilder on Automation and Insights

Katja Glaß – June 2024

Agenda

- Introduction
- Initiatives & Vision
- Automation
- Insights
- Summary

What is the OpenStudyBuilder?

A Metadata Data and Study Definition Repository

End-to-end automation from structured protocol to submission deliverables using concept-based standards

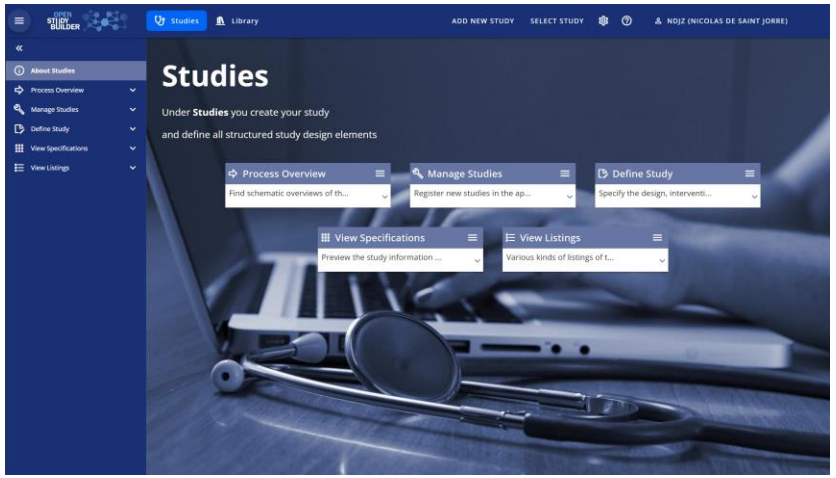
3 Elements

- **Clinical Metadata and Study Definition Repository**
  (central graph repository for all study specification data)
- **OpenStudyBuilder application / Web UI**
- **API layer**
  (allowing interoperability with other applications)
  (DDF API – support USDM)

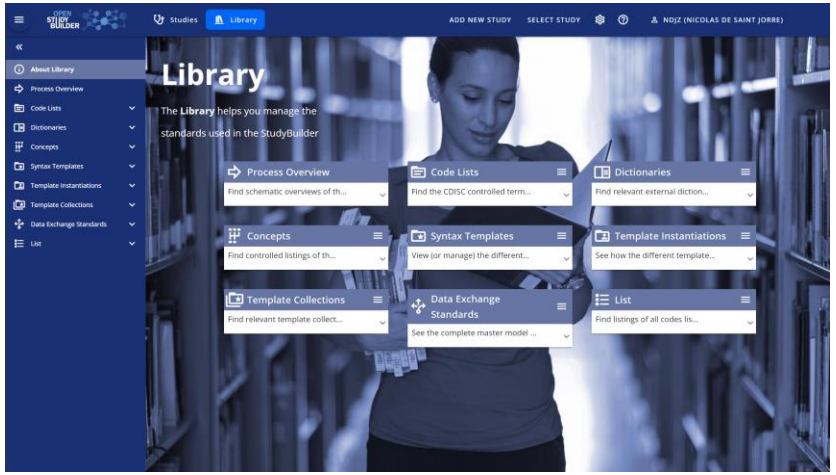
MDR & SDR

OpenStudyBuilder Components

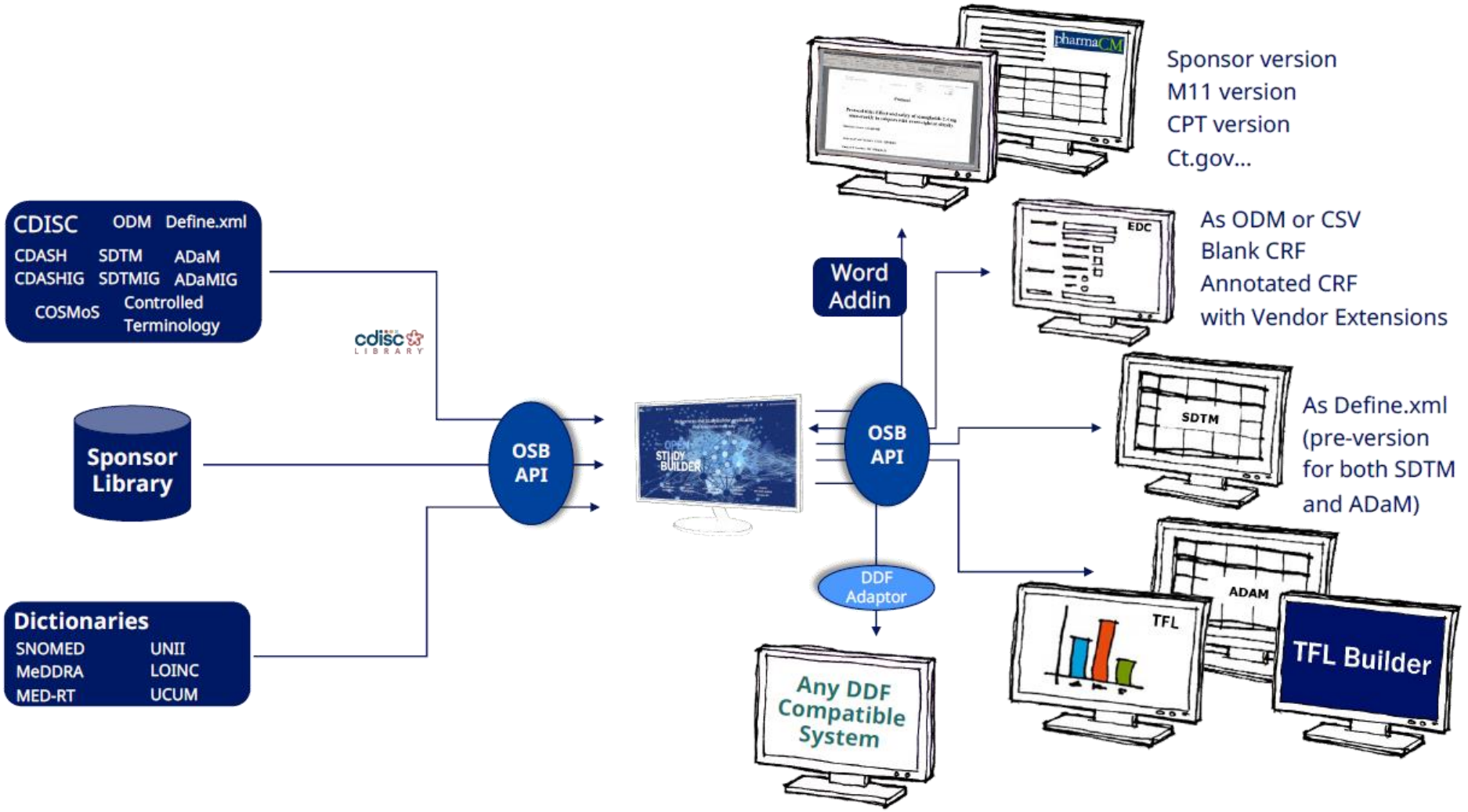
STUDIES	
TITLE	CRITERIA
REGISTRY IDENTIFERS	INTERVENTIONS
STRUCTURE	PURPOSE
POPULATION	ACTVITIES



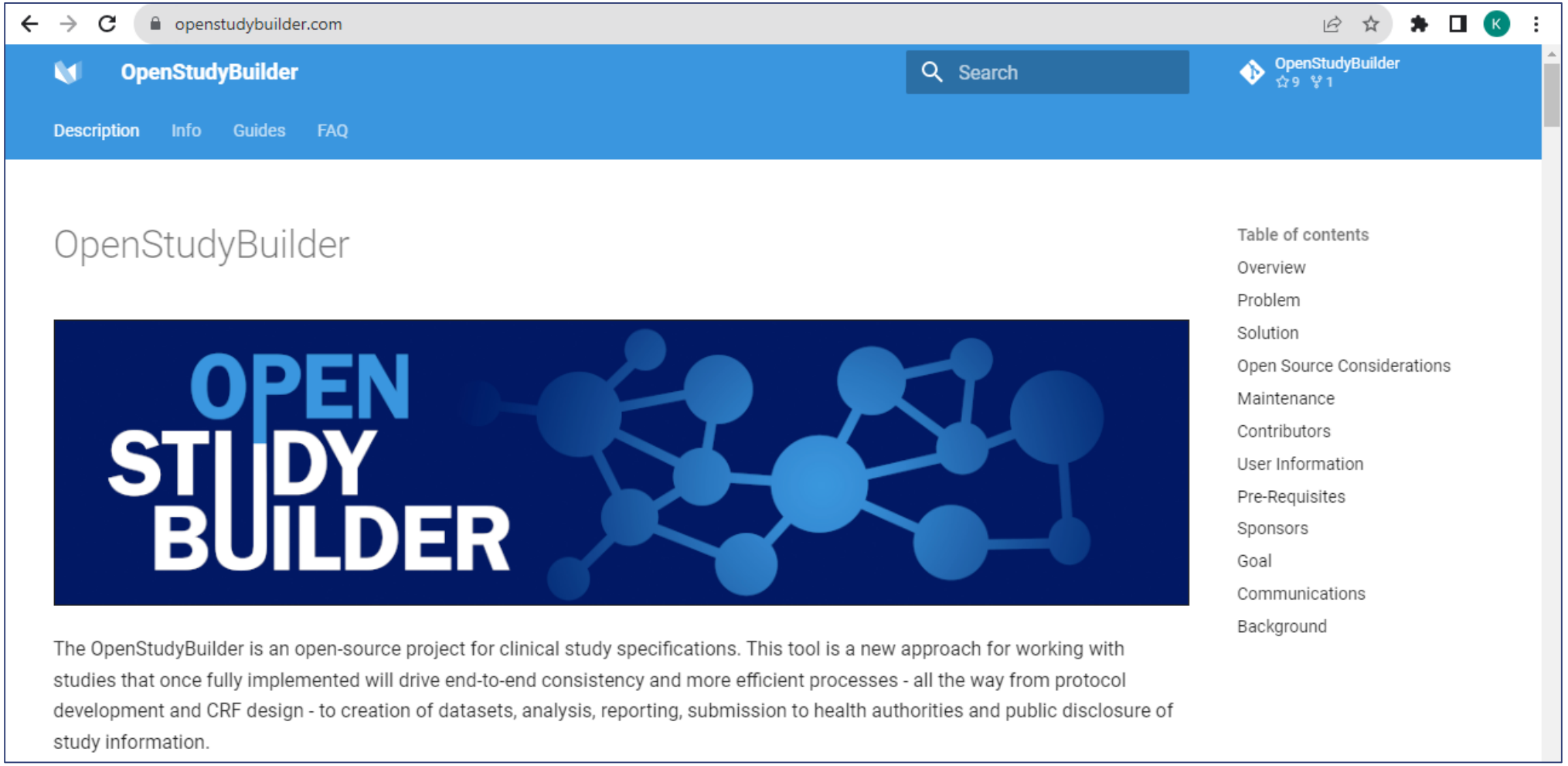
LIBRARY	
CONTROLLED TERMINOLOGY	MEDICAL DICTIONARIES (e.g., MedDRA)
CONCEPTS (ACTIVITIES, UNITS, CRFs, COMPOUNDS)	SYNTAX TEMPLATES
DATA EXCHANGE STANDARDS	



Connectivity is the key



Project Homepage



https://openstudybuilder.com/

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Vision of Automation & Digitalization

CDISC 360

- 2019-2020
- End-to-end standards-based metadata-driven automated processing

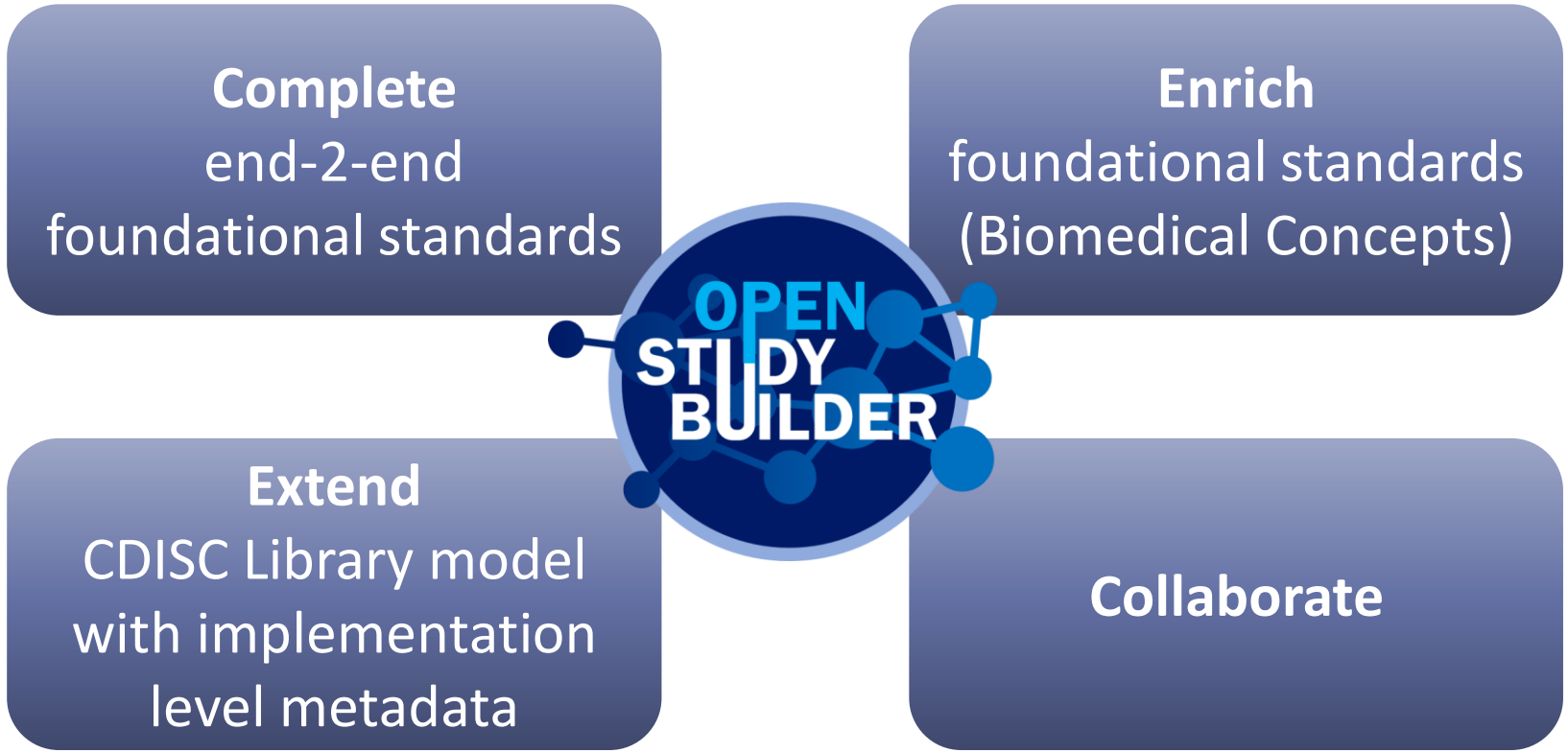
UC1: Create end-to-start specification

UC2: Generate start-to-end metadata

UC3: Transform data start-to-end

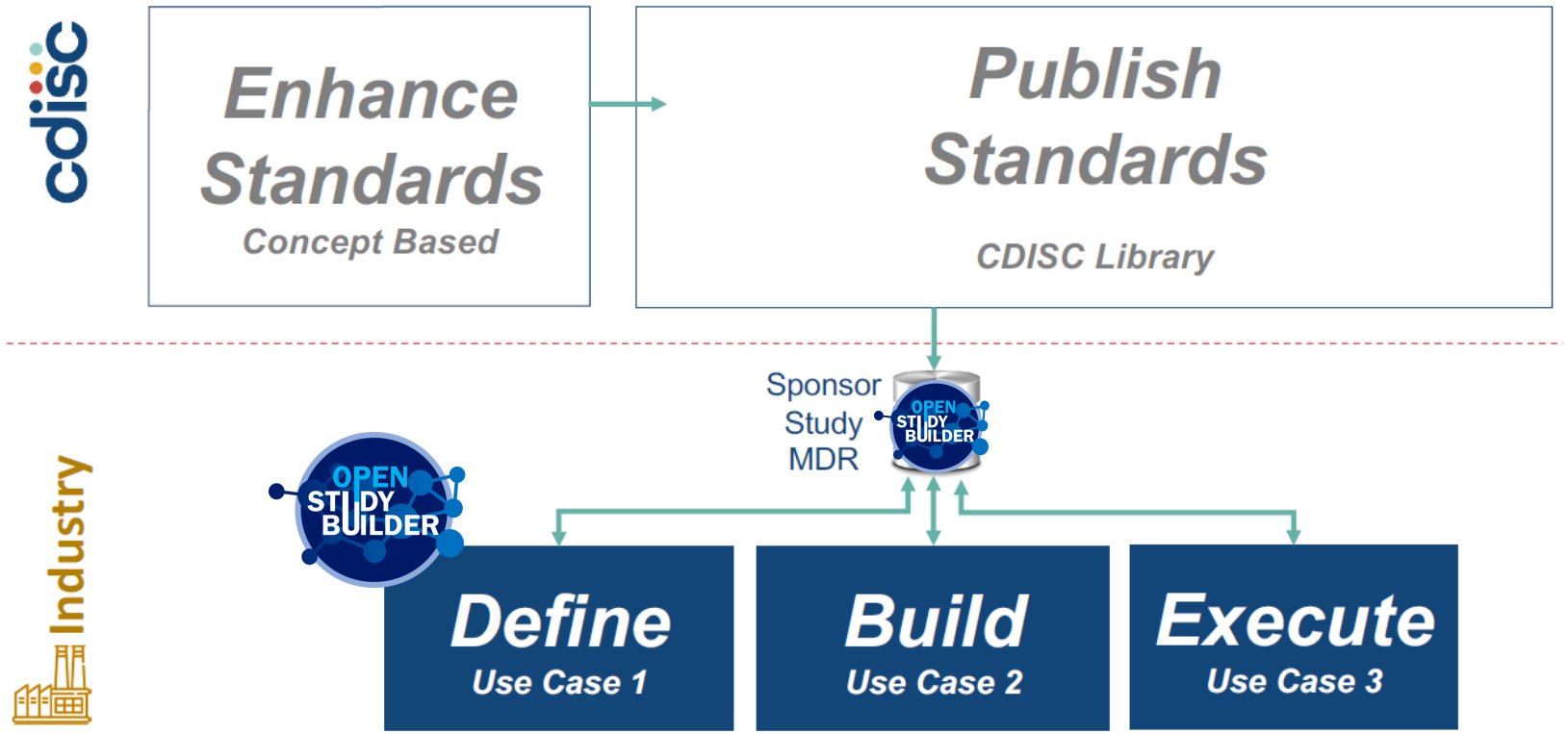
CDISC 360

- Four pillars of 360 implementation[1]



(1) https://www.cdisc.org/sites/default/files/2021-10/CDISC_360_2021_EU_Interchange.pdf

CDISC 360



https://www.cdisc.org/sites/default/files/2021-07/WS4-Prz-360-BreakOut-Session-v02.pdf

CDISC 360

- Outcome

PoC

API

Graph
Model

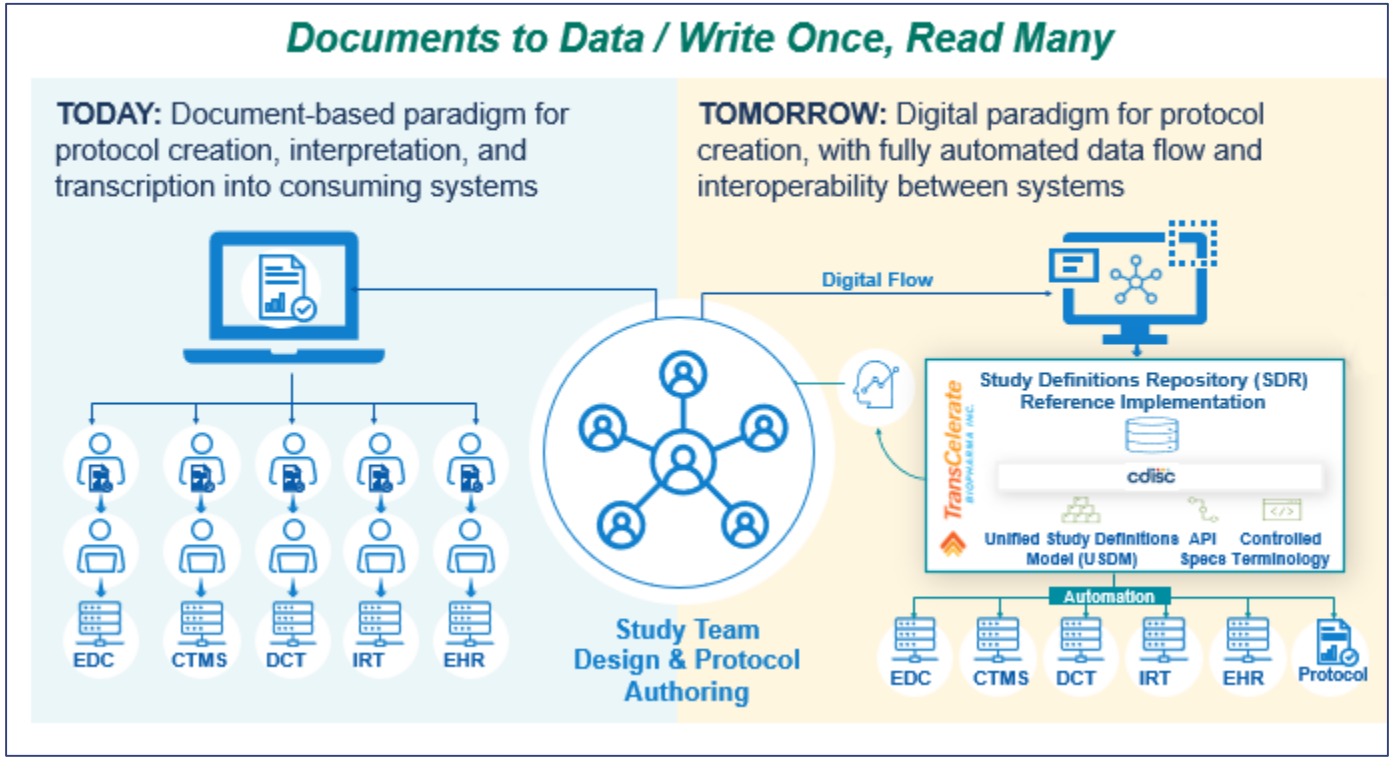
Digital Data Flow (TransCelerate & CDISC)

TransCelerate Digitial Data Flow Project (DDF)

digital workflow that allows for automated creation of study content and configuration of study systems to support clinical trial execution

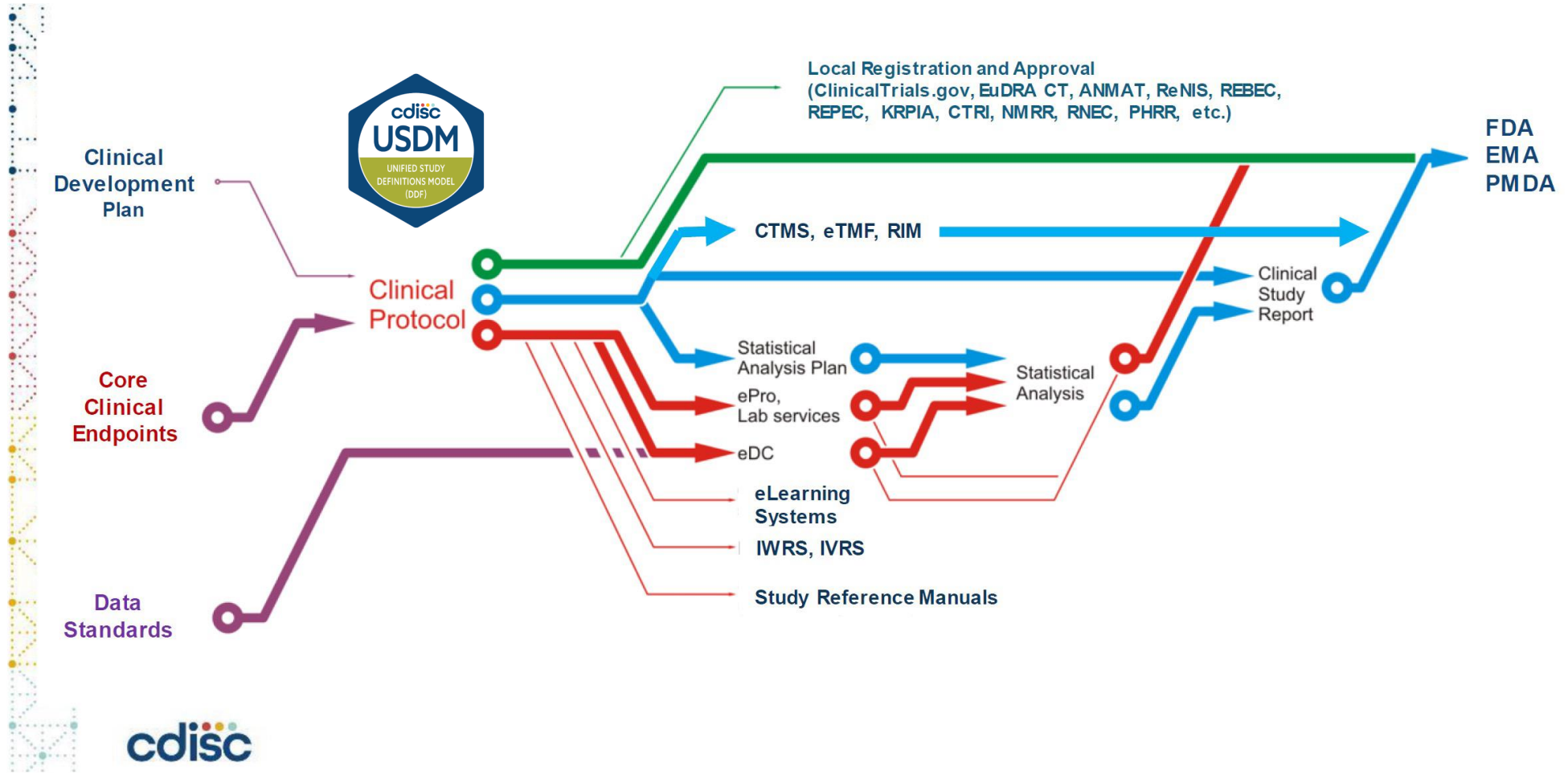
Digital Data Flow (TransCelerate & CDISC)

Digital Data Flow Ambition: Breaking the Document Paradigm



https://phuse.s3.eu-central-1.amazonaws.com/Archive/2024/Connect/US/Bethesda/PRE_SM12.pdf

Digital Data Flow (TransCelerate & CDISC)



https://phuse.s3.eu-central-1.amazonaws.com/Archive/2024/Connect/US/Bethesda/PRE_SM12.pdf

ICH M11

ICH
harmonisation for better health

CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL

(CESHARP)

M11

Term (Variable)	Number of Arms
Data Type	integer
Topic, Value or Header	D
Definition	
User Guidance	Enter the numeric value for the with a different number of arms based on the period with the gr
Conformance	Required

Number of Arms: [Number of Arms]

Enter the numeric value for the number o
of arms in different periods, populate this
of arms.

Blinding: The following roles indicated below will not be made aware of the treatment group assignment during the trial: [blinded roles].

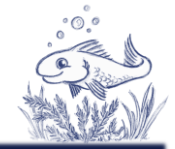
Select from the following blinded roles:

- Participant

Machine Readable Protocol

https://www.ema.europa.eu/en/documents/scientific-guideline/ich-m11-guideline-clinical-study-protocol-template-and-technical-specifications-step-2b_en.pdf

OpenStudyBuilder



cdisc 360

OPEN STUDY BUILDER

TransCelerate BIOPHARMA INC.

Digital Data Flow

+++

Digital Protocol

define.xml

cdisc USDM UNIFIED STUDY DEFINITIONS MODEL (DDF)

ICH M11

ODM.xml

OpenStudyBuilder

- Support industry standards
- Manage sponsor standards
- Protocol standards
- CRF standards

- Study setup
- Protocol information

- Downstream automation (Protocol, EDC, … utilization)

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Automation

Protocol SoA

SoA layout: Protocol SoA

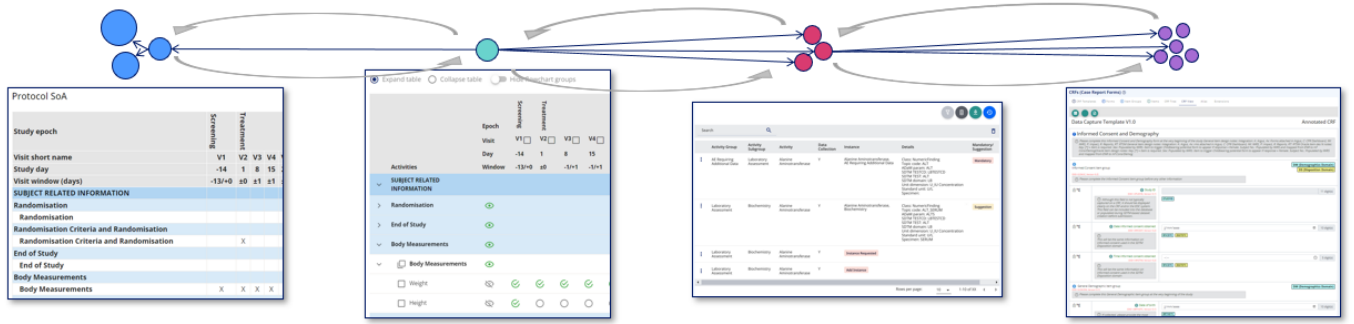
Preferred time unit: Day / Week

	Screening	Treatment									Follow-up
Visit short name	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V9**	**V10**	**V11**	**V8**
Study week	**-2**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**9**	**27**	**6**
Visit window (days)	**-13/+0**	**±0**	**±1**	**±1**	**±1**	**±1**	**±1**	**±1**	**±1**	**±1**	**+0/+35**
Laboratory Assessments											
Lipids	X	X			X			X		X	
Biochemistry	X	X			X			X		X	
Haematology											
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											
Pulse Rate	X	X	X	X		X	X	X	X	X	X
Diastolic Blood Pressure	X	X	X		X	X	X	X	X	X	X
Systolic Blood Pressure	X	X	X	X	X		X	X	X	X	X

Diastolic Blood Pressure

Automation - Activity

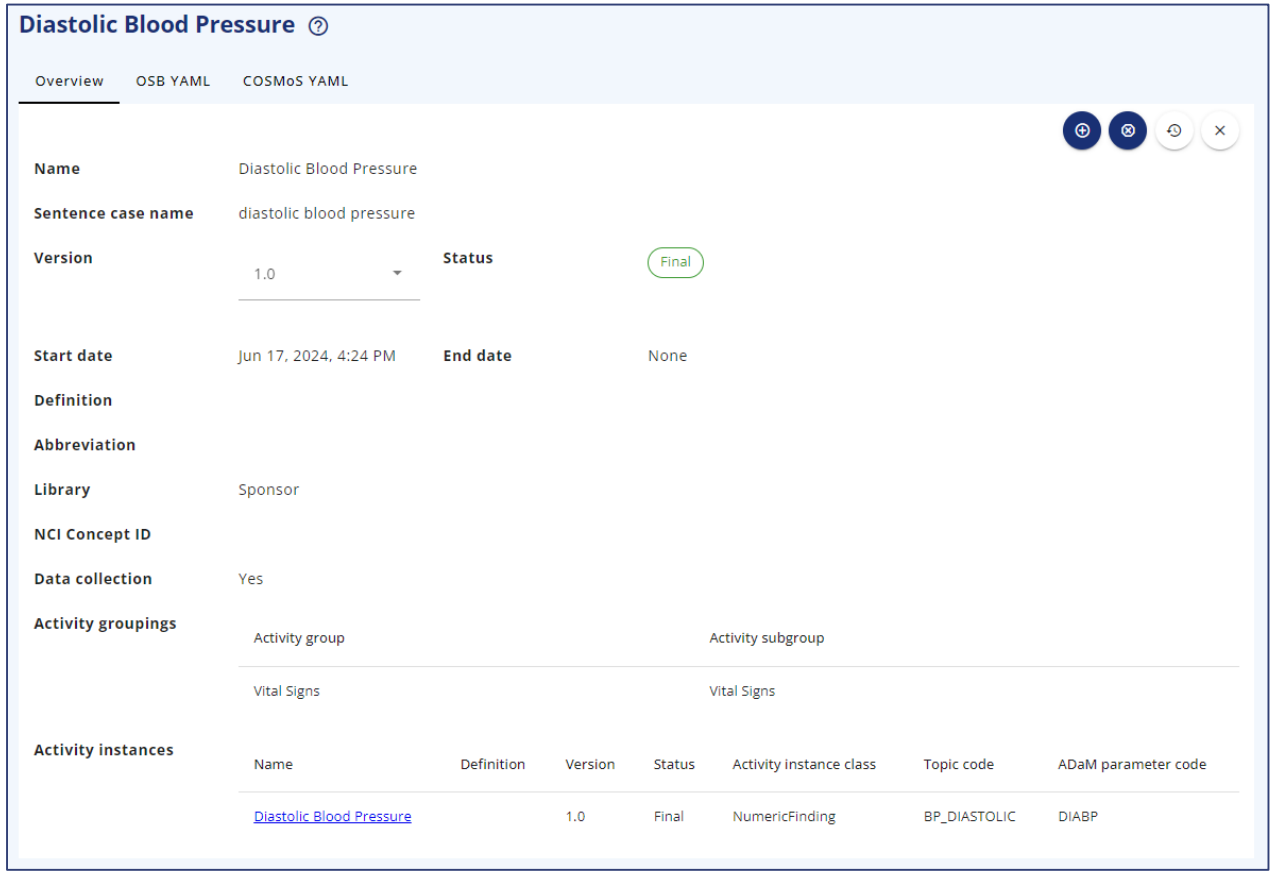
- Steps
  - Define standards / Biomedical Concept
  - Select activities according protocol needs
    - Re-use in protocol
  - Select operational activity (collection specification)
    - Re-use in annotated CRF
    - Re-use in EDC
    - Re-use in mapping



Define Activity

Automation – Define Activity

➢ Step 1: Define Standard / Biomedical Concept



Diastolic Blood Pressure

Overview | OSB YAML | COSMoS YAML

Name	Diastolic Blood Pressure		
Sentence case name	diastolic blood pressure		
Version	1.0	**Status**	Final
Start date	Jun 17, 2024, 4:24 PM	**End date**	None
Definition			
Abbreviation			
Library	Sponsor		
NCI Concept ID			
Data collection	Yes		

Activity groupings

Activity group	Activity subgroup
Vital Signs	Vital Signs

Activity instances

Name	Definition	Version	Status	Activity instance class	Topic code	ADaM parameter code
Diastolic Blood Pressure		1.0	Final	NumericFinding	BP_DIASTOLIC	DIABP

Name: Diastolic Blood Pressure

Activity group / subgroup:
Vital Signs

Class:
NumericFdinding

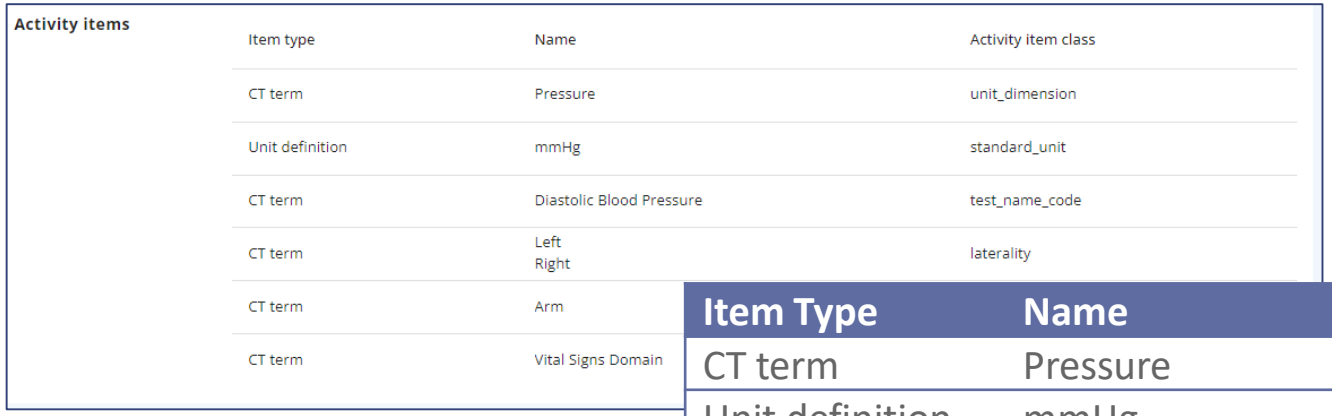
ADaM parameter code:
DIABP

<Instance>

Automation – Define Activity

- Step 1: Define Standard / Biomedical Concept

<Instance>

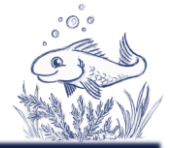


Activity items

Item type	Name	Activity item class
CT term	Pressure	unit_dimension
Unit definition	mmHg	standard_unit
CT term	Diastolic Blood Pressure	test_name_code
CT term	Left Right	laterality
CT term	Arm	
CT term	Vital Signs Domain	

Item Type	Name	Activity item class
CT term	Pressure	unit_dimension
Unit definition	mmHg	standard_unit
CT term	Diastolic Blood Pressure	test_name_code
CT term	Left Right	laterality
CT term	Arm	location
CT term	Vital Signs Domain	domain

Automation – Define Activity

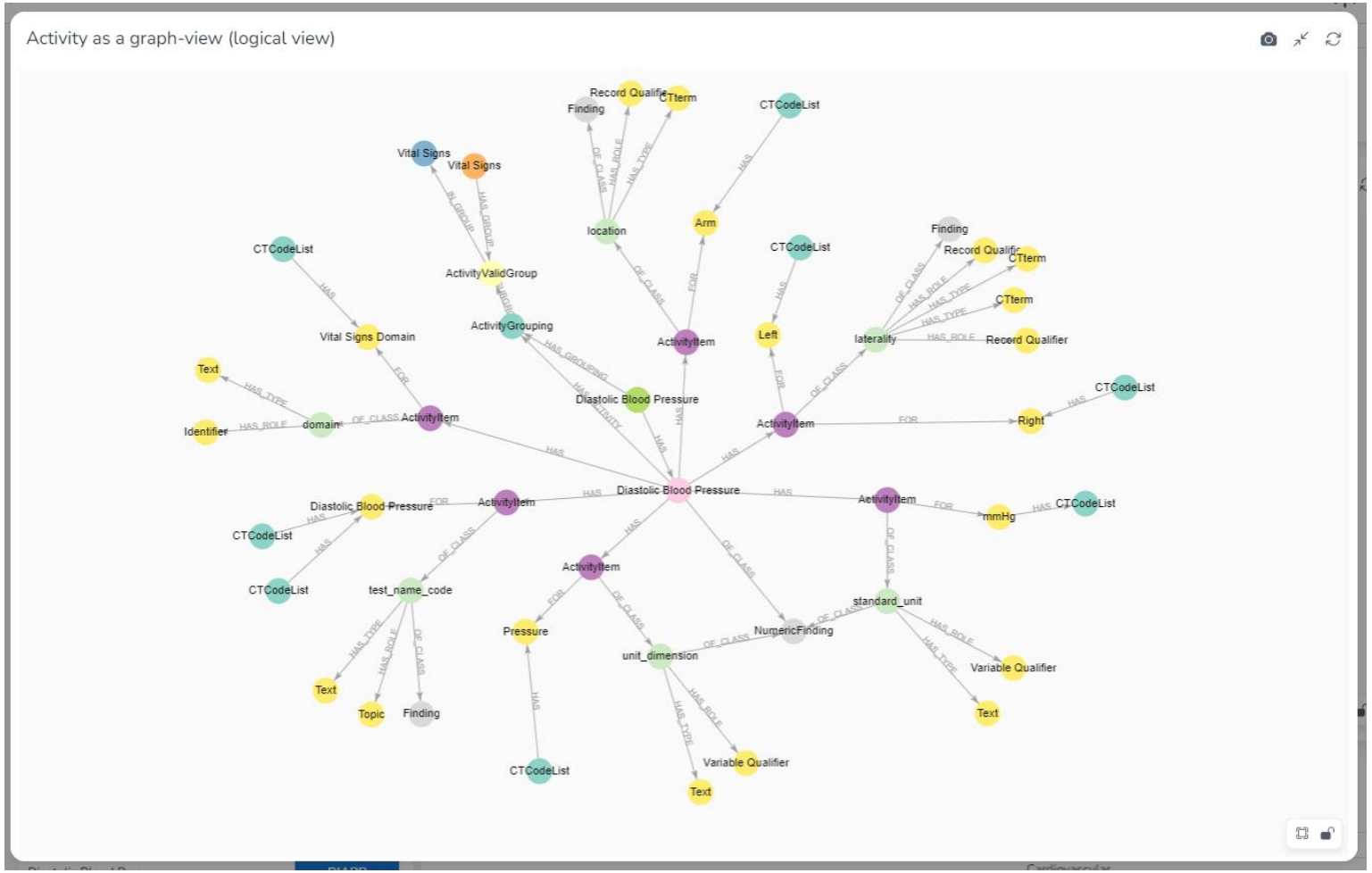


- Same activities, different collection

Acute Kidney Injury Imaging

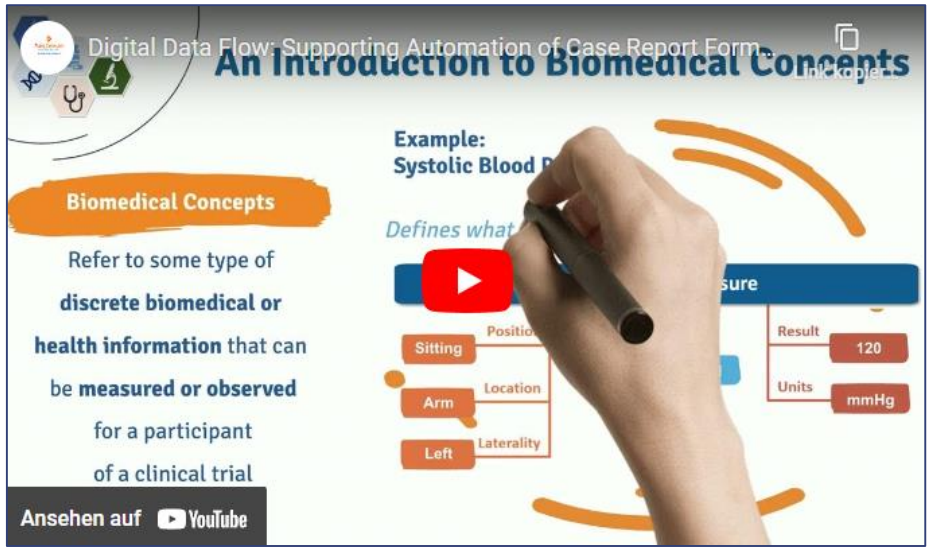
Name	Definition	Version	Status	Activity instance class	Topic code	ADaM parameter code
Acute Kidney Injury - CT Scan Performed		1.0	Final	CategoricFinding	ACUTE_KIDNEY_INJURY_CT_SCAN	AKICTSCA
Acute Kidney Injury - Imaging Performed		1.0	Final	CategoricFinding	ACUTE_KIDNEY_INJURY_IMAGING_PERFORMED	AKIIMAGE
Acute Kidney Injury - Other Imaging Performed		1.0	Final	CategoricFinding	ACUTE_KIDNEY_INJURY_IMAGING_OTHER	AKIIMOTH
Acute Kidney Injury - Renal Angio-Imaging Performed		1.0	Final	CategoricFinding	ACUTE_KIDNEY_INJURY_RENAL_ANGIO-IMAGING	AKIRANIM
Acute Kidney Injury - Summary of Imaging Results		1.0	Final	TextualFinding	ACUTE_KIDNEY_INJURY_IMAGING_RESULTS	AKIHISTO
Acute Kidney Injury - Ultrasound Performed		1.0	Final	CategoricFinding	ACUTE_KIDNEY_INJURY_ULTRASOUND	AKIULTRA

Automation – Define Activity



Automation – Define Activity

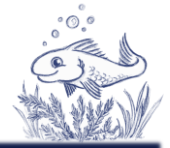
- Define process might be complex
- CDISC Biomedical Concepts
- Additional OpenStudyBuilder Biomedical Concepts



An Introduction to Biomedical Concepts

https://youtu.be/0tGpj8g5gxY

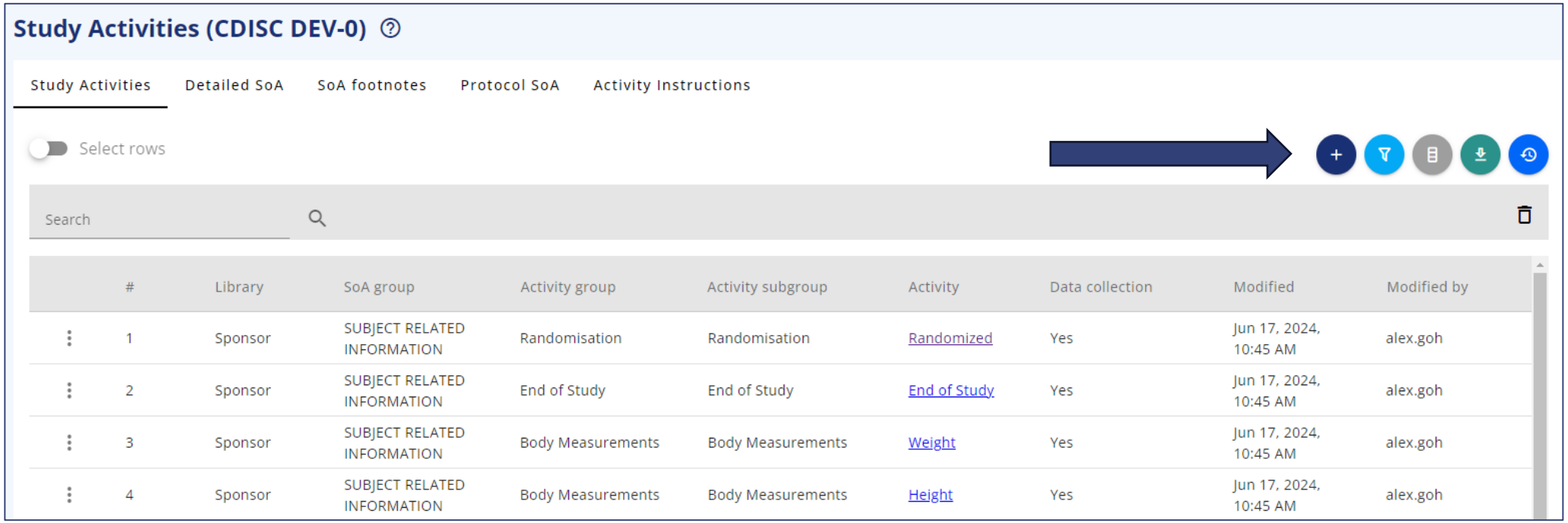
Automation - Activity



Select Activity

Automation – Select Activity

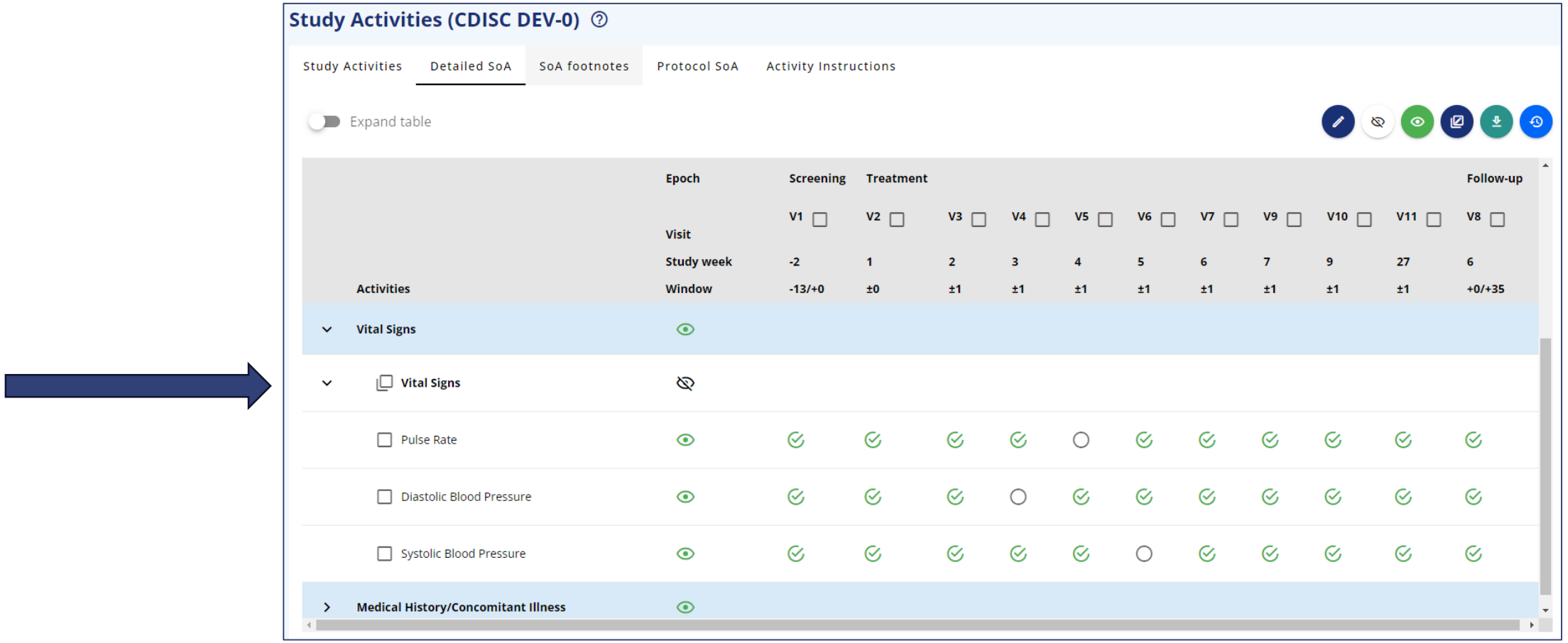
- Select activities according protocol needs (Medical Writer)



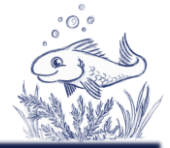
#	Library	SoA group	Activity group	Activity subgroup	Activity	Data collection	Modified	Modified by
1	Sponsor	SUBJECT RELATED INFORMATION	Randomisation	Randomisation	Randomized	Yes	Jun 17, 2024, 10:45 AM	alex.goh
2	Sponsor	SUBJECT RELATED INFORMATION	End of Study	End of Study	End of Study	Yes	Jun 17, 2024, 10:45 AM	alex.goh
3	Sponsor	SUBJECT RELATED INFORMATION	Body Measurements	Body Measurements	Weight	Yes	Jun 17, 2024, 10:45 AM	alex.goh
4	Sponsor	SUBJECT RELATED INFORMATION	Body Measurements	Body Measurements	Height	Yes	Jun 17, 2024, 10:45 AM	alex.goh

Automation – Select Activity

- Select activities according protocol needs (Medical Writer)



Automation - Activity

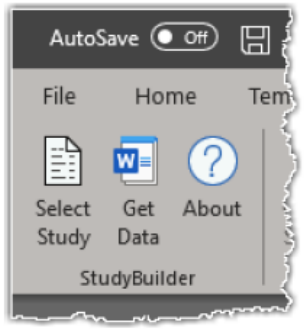


Apply in Protocol

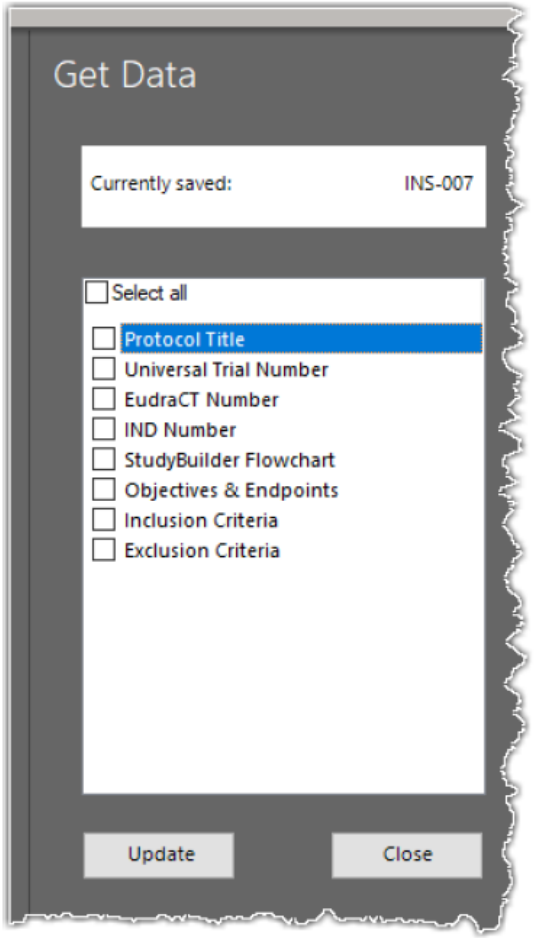
Automation – Apply Activity

StudyBuilder ribbon
(Word add-in)

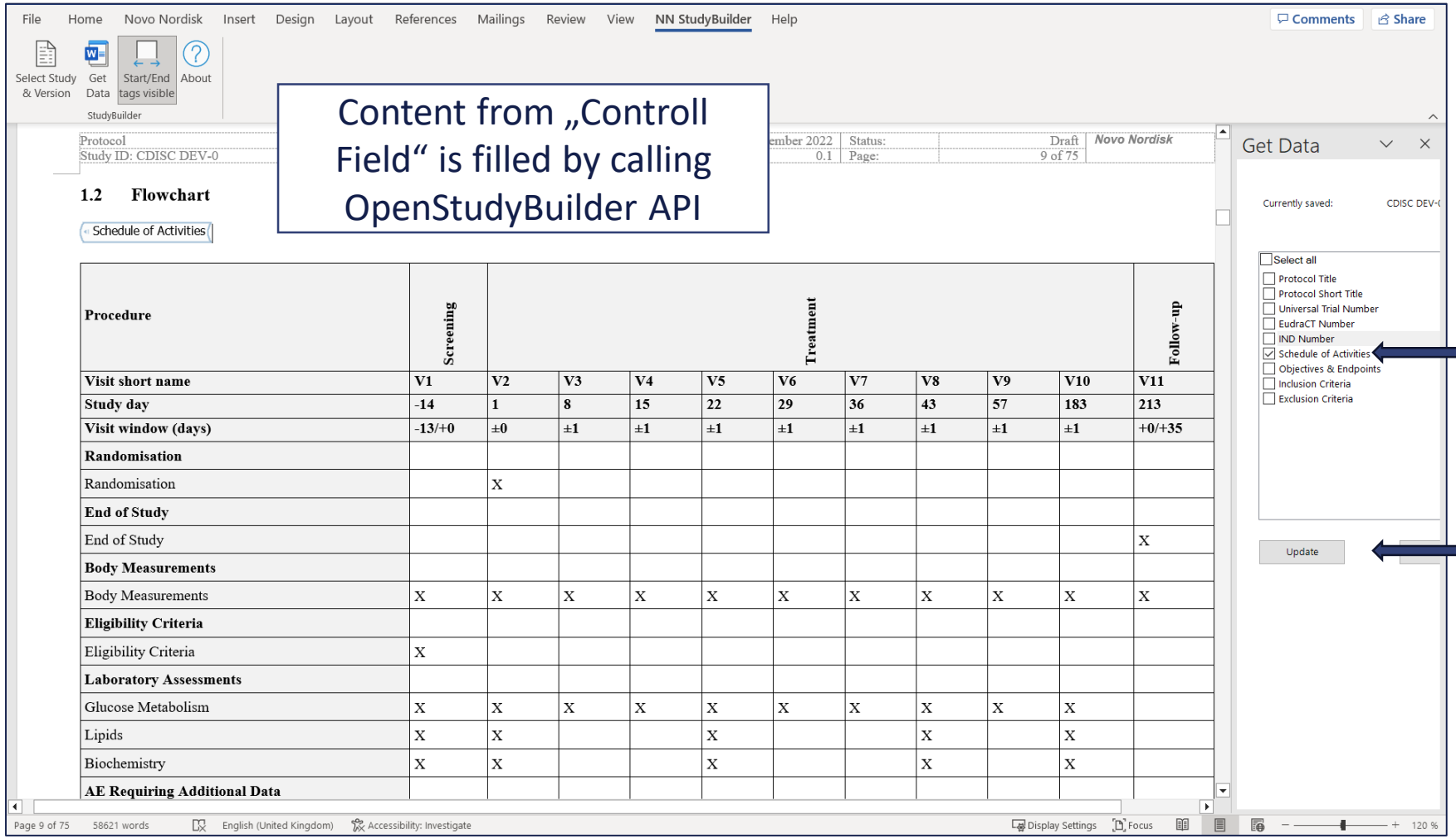
- ✓ One-way connection
- ✓ Code recognizes the document type
- ✓ User-friendly ribbon and 'fly-out' in Word
- ✓ Styles ensure proper formatting in Word



Protocol



Automation – Apply Activity

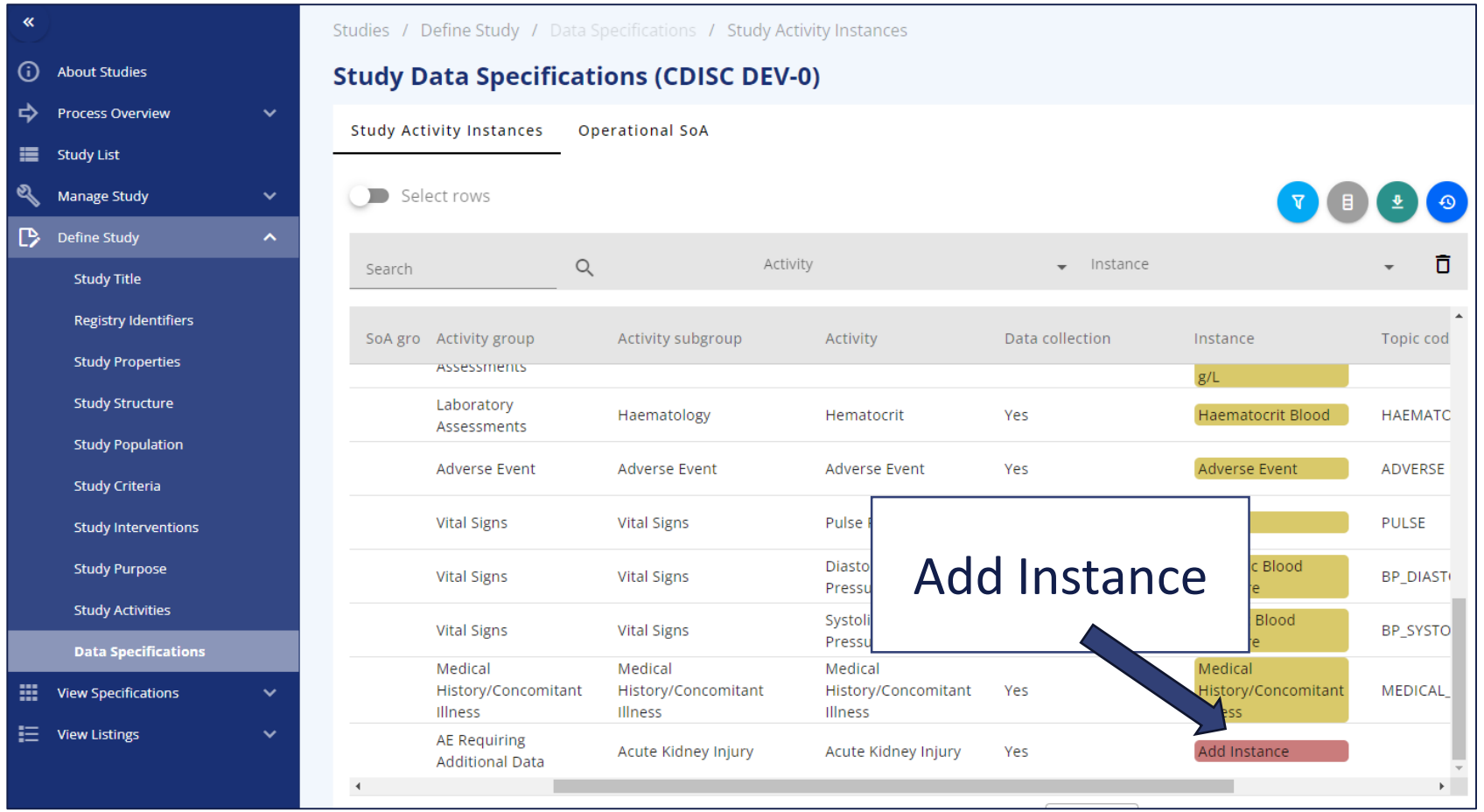


Procedure	Screening	Treatment									Follow-up
Visit short name	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**	**V10**	**V11**
Study day	**-14**	**1**	**8**	**15**	**22**	**29**	**36**	**43**	**57**	**183**	**213**
Visit window (days)	**-13/+0**	**±0**	**±1**	**±1**	**±1**	**±1**	**±1**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

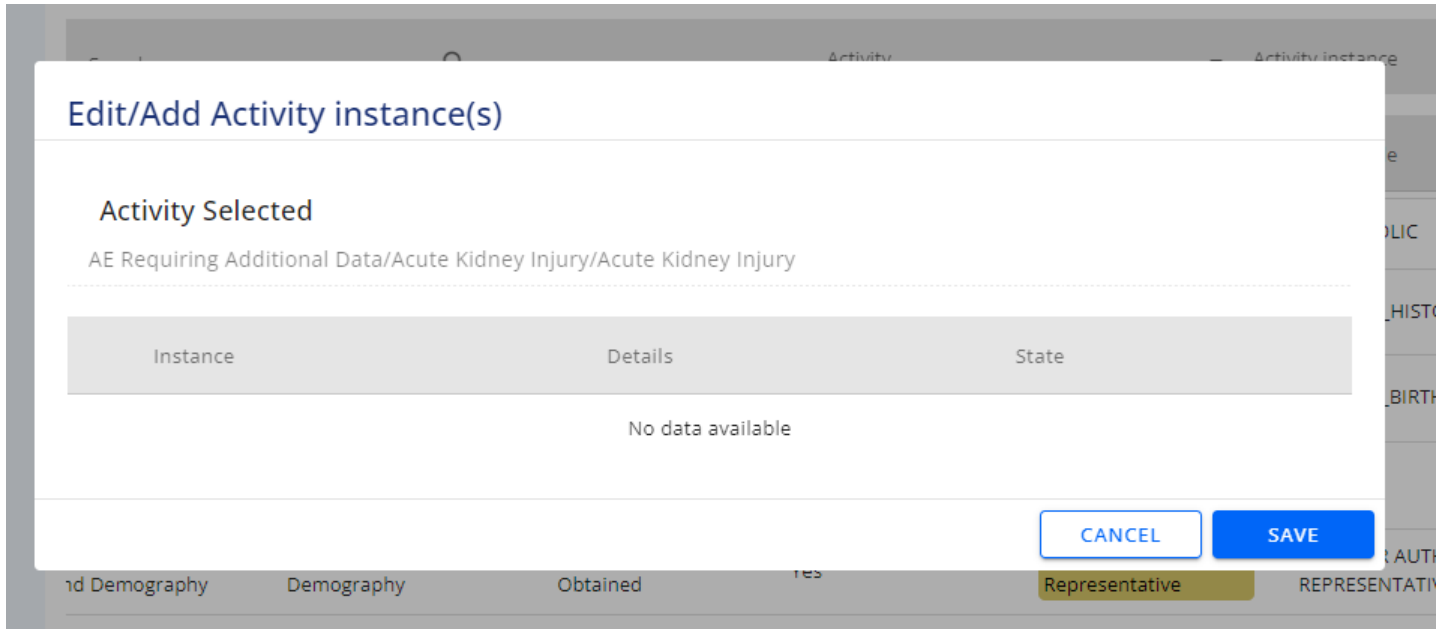
Define Collection Details

Automation – Define Activity Instance

Data Specifications



Automation – Define Activity Instance



Work in Progress

Use Activity Information

Automation – Use Activity

- CRF & aCRF & ODM.xml

Vital signs [ItemGroup] — VS (Vital Signs Domain)

[OID=G.VS.VS, Version=0.1]

Please complete the Vital Signs item group at each expected time point

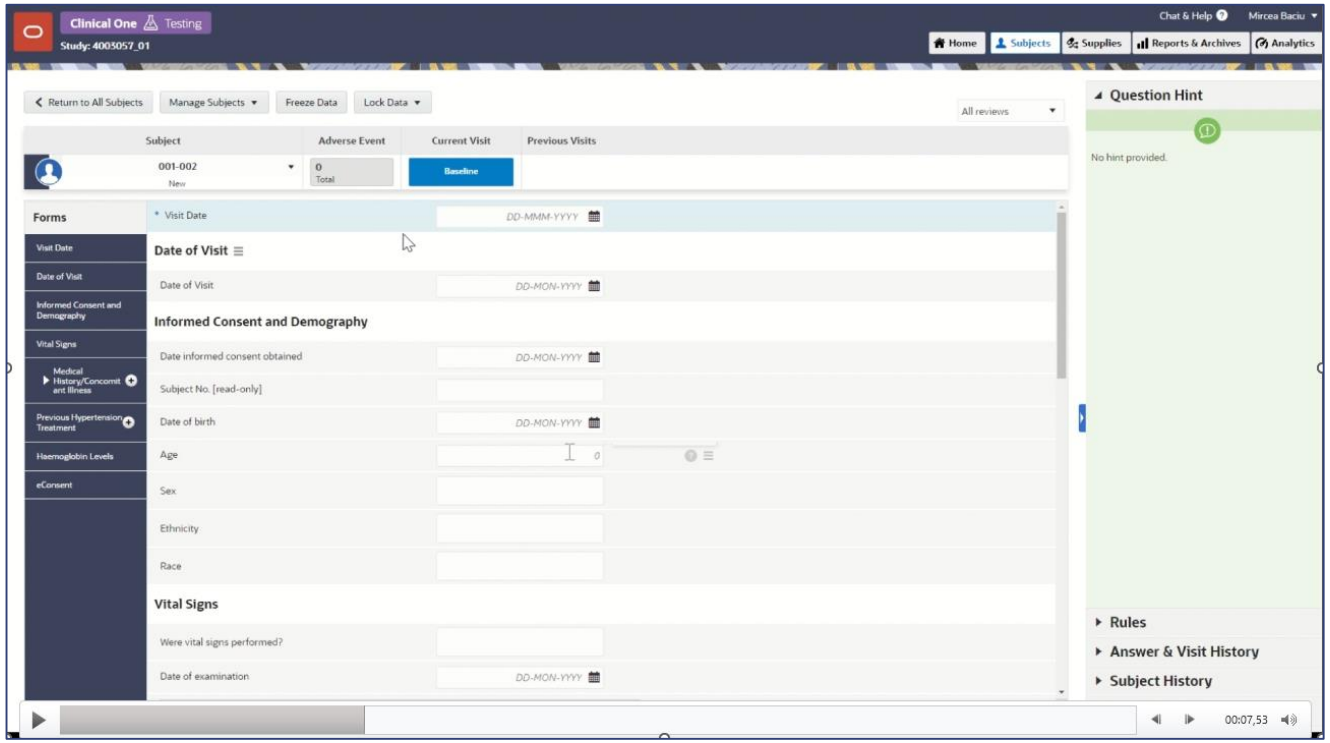
Date of examination [OID=I.VSDAT, Version=0.1]	tt.mm.jjjj	10 digit(s)		
	VSDTC			
Systolic blood pressure [OID=I.SYSBP, Version=0.1]		3 digit(s)	Unit	mmHg [OID=mmHg, Version=1.0]
Please collect the systolic blood pressure of the subject	VSORRES where VSTESTCD=SYSBP, VSORRESU where VSTESTCD=SYSBP			
Diastolic blood pressure [OID=I.DIABP, Version=0.1]		3 digit(s)	Unit	mmHg [OID=mmHg, Version=1.0]
Please collect the diastolic blood pressure of the subject	VSORRES where VSTESTCD=DIABP, VSORRESU where VSTESTCD=DIABP			

```
<ItemDef OID="I.DIABP" Name="Diastolic blood pressure" Origin="Collected Value" DataType="integer" Length="3" SASFieldName="BP_DIASTOLIC"
    <Question>
        <TranslatedText xml:lang="en" osb:version="0.1">Diastolic blood pressure</TranslatedText>
    </Question>
    <Description>
        <TranslatedText xml:lang="en" osb:version="0.1">Diastolic blood pressure</TranslatedText>
    </Description>
    <MeasurementUnitRef MeasurementUnitOID="mmHg"/>
</ItemDef>
```

Partially working, additional work in Progress

Automation – Use Activity

- EDC Automation
  - Create items / visits based on Schedule of Activities



Proof of Concepts available

https://youtu.be/4-33kqSTdeY

Automation – Use Activity

- Download mapping specification (define.xml)

CDISC SDTM 3.2

Date of Define-XML document generation: 2018-11-19T08:39:20

Stylesheet version: 2015-01-16

- Annotated Case Report Form
- Tabulation Datasets
- Value Level Metadata
- Controlled Terminology
- Computational Algorithms
- Comments

Standard	CDISC SDTM 3.2
Study Name	TDF_SDTM
Study Description	Test datasets created by updating existing CDISCPILOT SDTM datasets
Protocol Name	TDF_Datasets
Metadata Name	Study TDF_SDTM Data Definitions
Metadata Description	Test datasets created by updating existing CDISCPILOT SDTM datasets

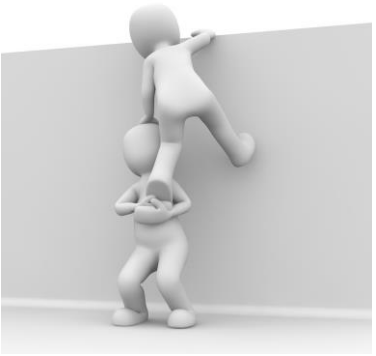
Tabulation Datasets for Study TDF_SDTM (CDISC SDTM 3.2)

Dataset	Description	Class	Structure	Purpose	Keys	Location	Documentation
TA	Trial Arms	TRIAL DESIGN	One record per planned Element per Arm	Tabulation	STUDYID, ARMCD, TAETORD	ta.xpt	
TE	Trial Elements	TRIAL DESIGN	One record per planned Element	Tabulation	STUDYID, ETCD	te.xpt	
TI	Trial Inclusion/ Exclusion Criteria	TRIAL DESIGN	One record per I/E criterion	Tabulation	STUDYID, IETESTCD	ti.xpt	
TS	Trial Summary	TRIAL DESIGN	One record per trial summary parameter value	Tabulation	STUDYID, TSPARMCD, TSSEQ	ts.xpt	
TV	Trial Visits	TRIAL DESIGN	One record per planned Visit per Arm	Tabulation	STUDYID, VISITNUM	tv.xpt	
DM	Demographics	SPECIAL PURPOSE	One record per subject	Tabulation	STUDYID, USUBJID	dm.xpt	
SE	Subject Elements	SPECIAL PURPOSE	One record per actual Element per subject	Tabulation	STUDYID, USUBJID, ETCD	se.xpt	
SV	Subject Visits	SPECIAL PURPOSE	One record per actual visit per subject	Tabulation	STUDYID, USUBJID, VISITNUM	sv.xpt	

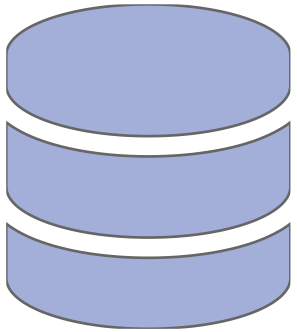
Work in Progress

Automation – Use Activity

- Use to generate Test Data
  - Possible units, standard units, PARAMCD
  - Enhance with additional information
    - Reference Ranges



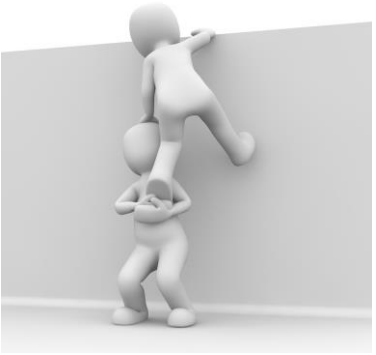
TestData

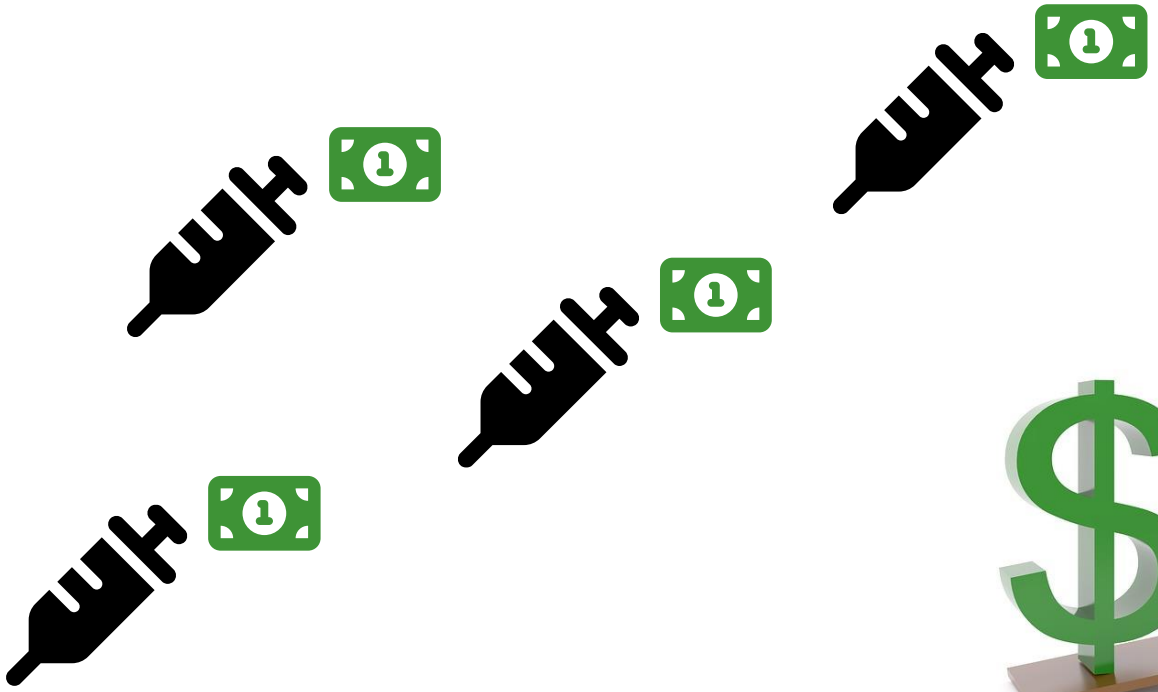


Out of Scope for OpenStudyBuilder

Automation – Use Activity

- Use to Cost / Patient Burden
  - Enhance with additional information
    - Cost per test per visit





Out of Scope for OpenStudyBuilder

Agenda

- Introduction
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- **Insights**
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Insights

One-Stop-Shop

Study Information

Trial Domains

CRF/EDC Specification

Standards & Harmonization

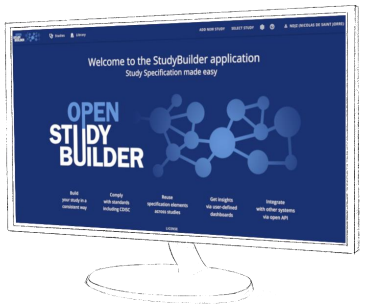
Mapping Specification

Biomedical Concepts

Data Models

...

Insights

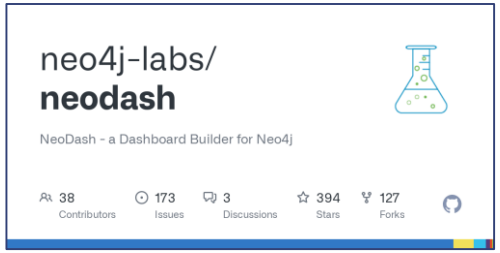


User Interface

neo4j

Cypher queries

API

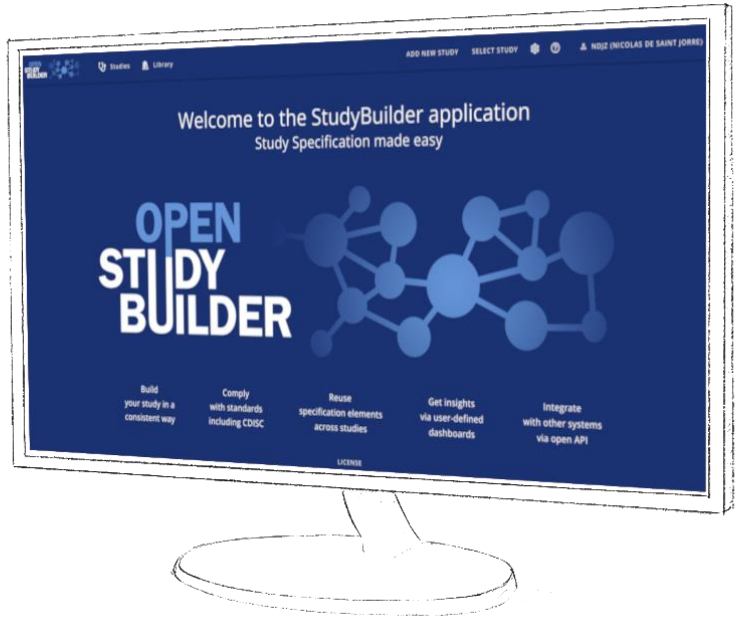


Dashboard

AI
Training & Chat

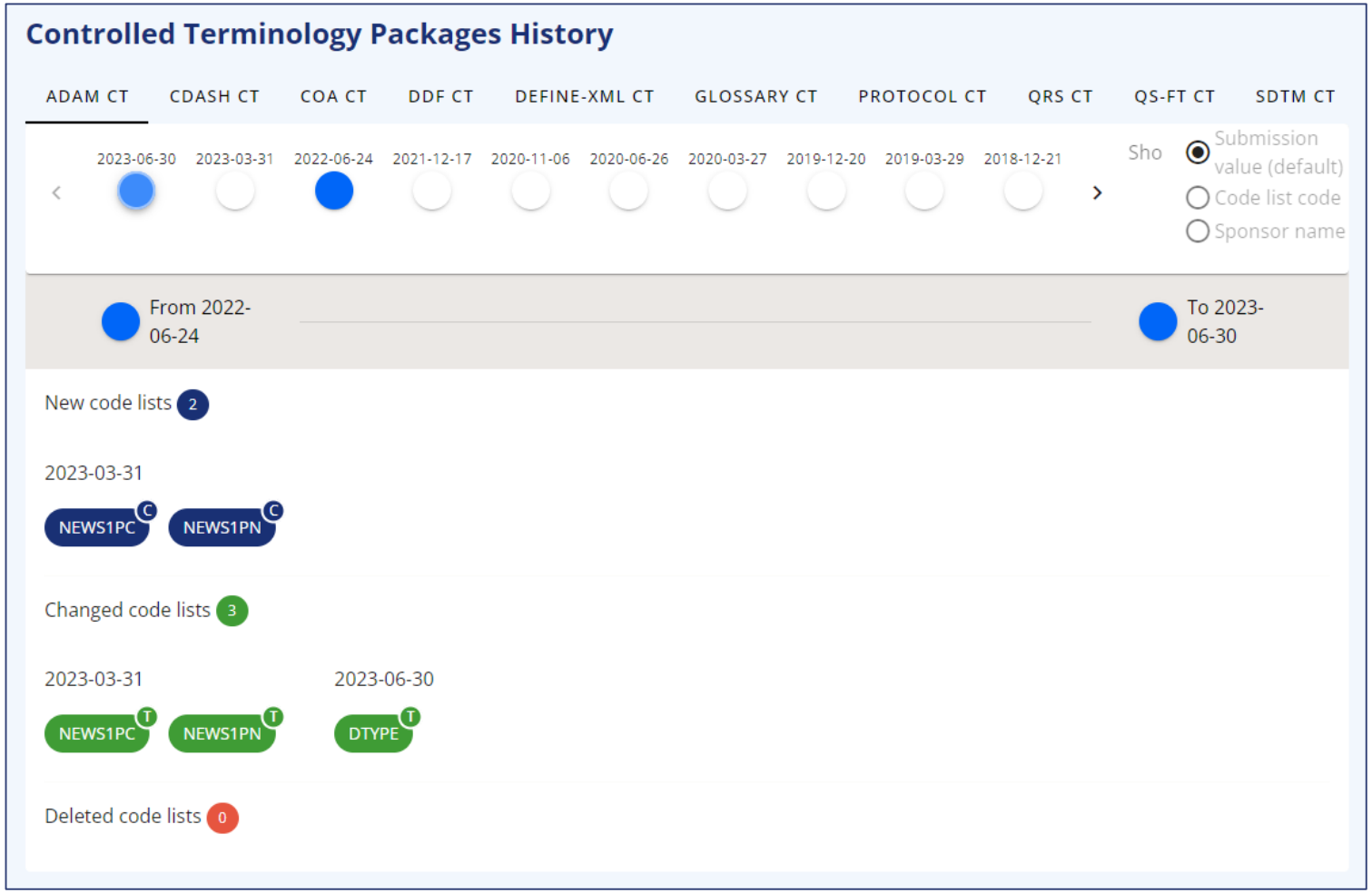
Insights
Programming

Insights – User Interface



Insights – User Interface

Changes for CDISC CT Packages



Insights – User Interface

History

Sponsor values history for code list [CTCodelist_000001]

Library	Name	Template parameter	Change description	Status	Version	Change type	User	From	To
Sponsor	**Unit Dimension**	**No**	**Approved version**	**Final**	**1.0**		**unknown-user**	**Apr 22, 2024, 1:09 PM**	
Sponsor	Unit Dimension	No	Initial version	Draft	0.1		unknown-user	Apr 22, 2024, 1:09 PM	Apr 22, 2024, 1:09 PM

Items per page: 10 0-0 of 0

Study (CDISC DEV-0)

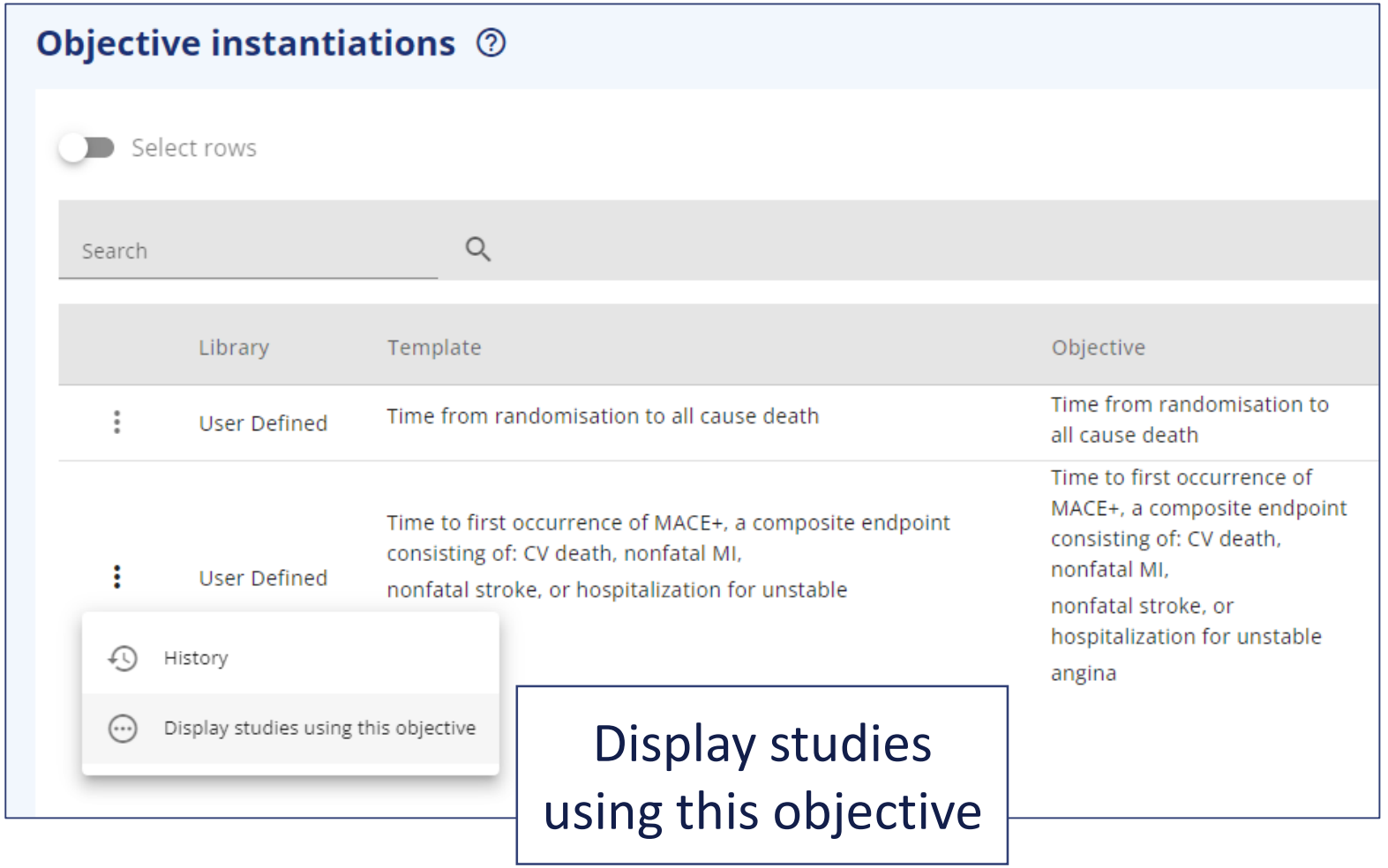
Study Core Attributes | Study Status | Study Subparts | Protocol Version

Study status	Version	Release description	Modified	Modified by
DRAFT			Jun 23, 2024, 10:45 AM	unknown-user
LOCKED	3	add tempareature visit	Jun 23, 2024, 10:45 AM	unknown-user
RELEASED	3	add tempareature visit	Jun 23, 2024, 10:45 AM	unknown-user
LOCKED	2	new release	Jun 23, 2024, 10:40 AM	unknown-user
RELEASED	2	new release	Jun 23, 2024, 10:40 AM	unknown-user
LOCKED	1	Initial version	Jun 23, 2024, 10:23 AM	unknown-user
RELEASED	1	Initial version	Jun 23, 2024, 10:23 AM	unknown-user

Insights – User Interface

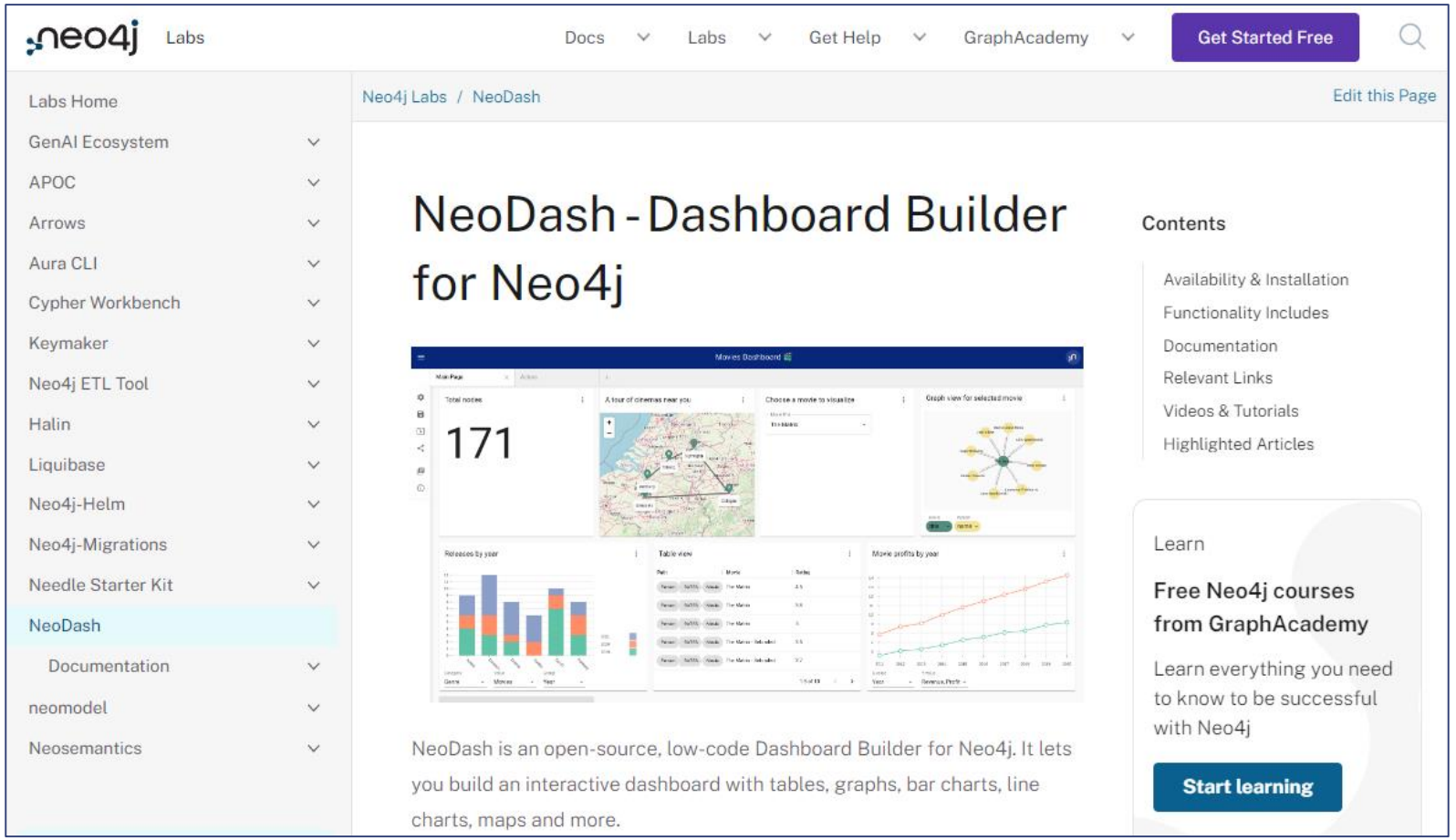
Investigate Studies

- Objectives
- Endpoints
- Time Frames
- Criteria
- Activity Instructions
- Footnotes



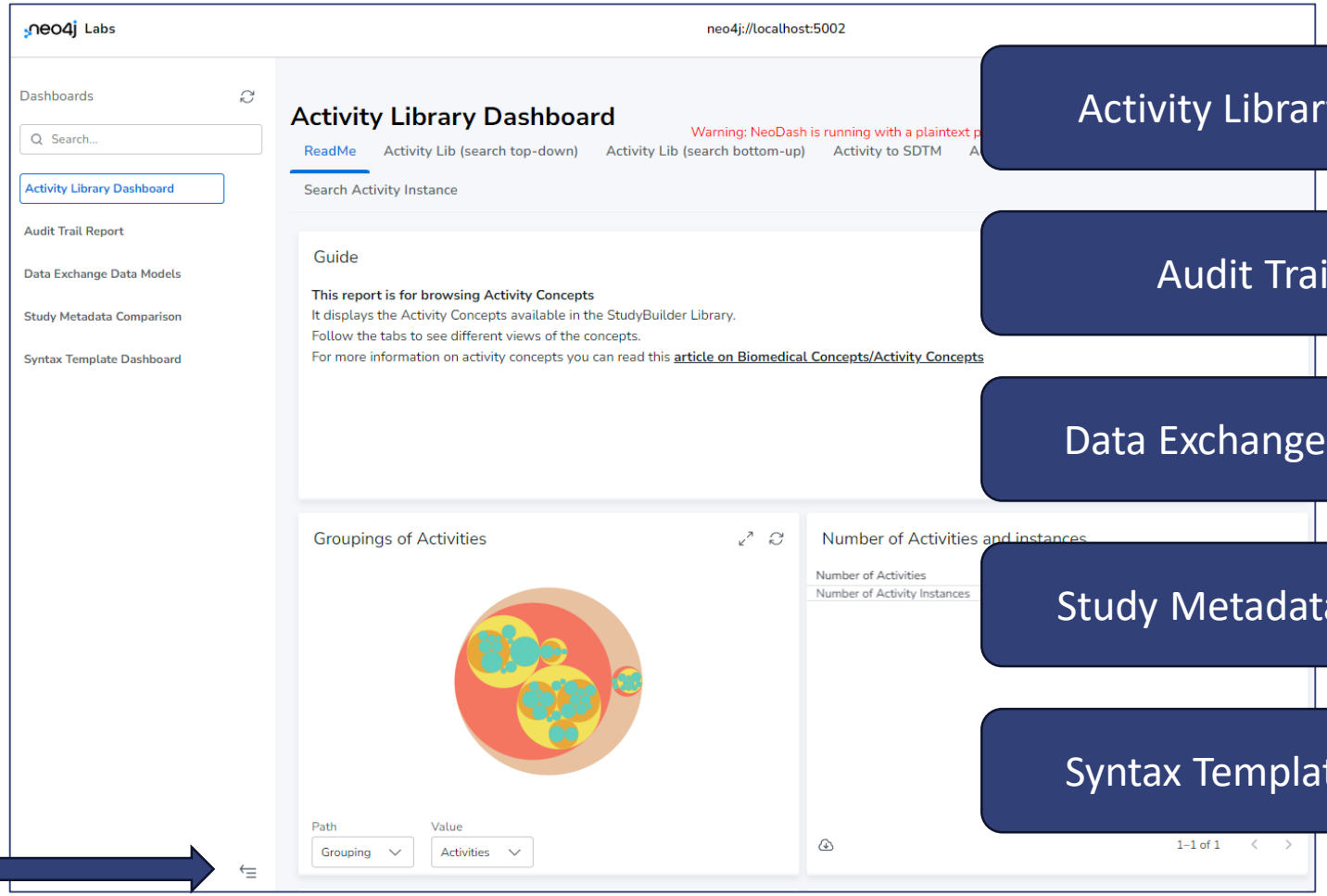
Display studies using this objective

Insights - NeoDash



https://neo4j.com/labs/neodash/

Insights - NeoDash



Activity Library Dashboard

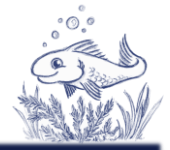
Audit Trail Report

Data Exchange Data Models

Study Metadata Comparison

Syntax Template Dashboard

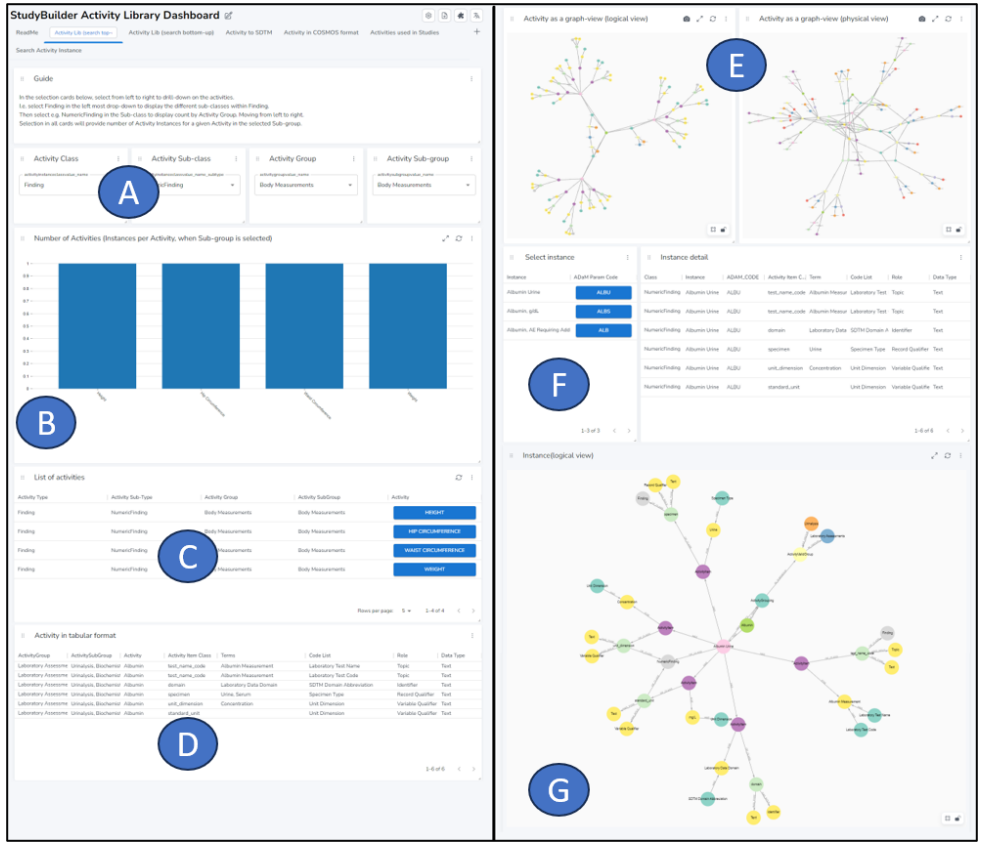
Menu

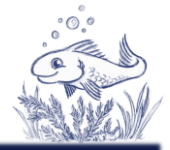


Activities

Insights – NeoDash - Activities

- Which biomedical concepts exist?
- Which activities are used?
- How map activities in SDTM?





Audit Trail

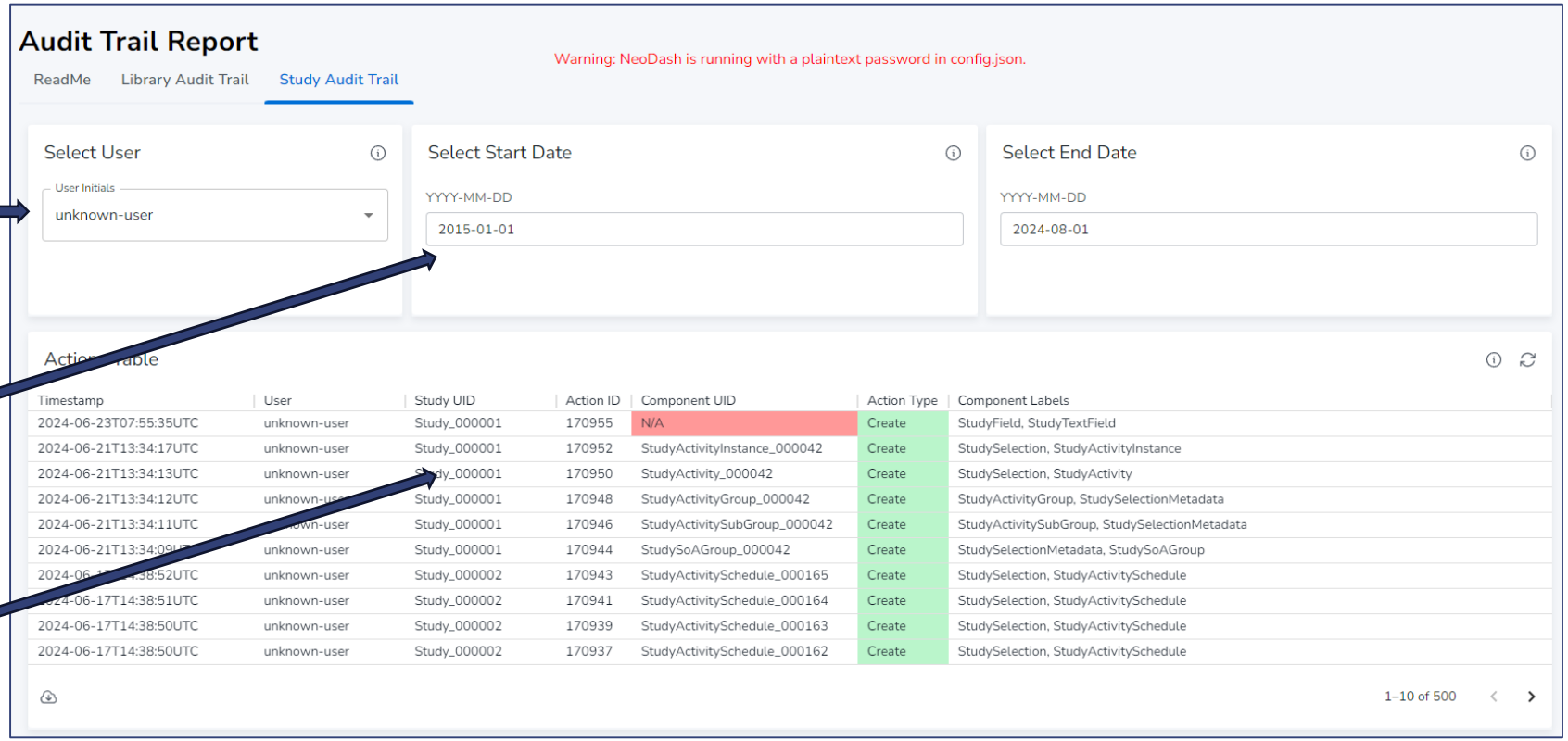
Insights – NeoDash – Audit Trail

- Who changed what when?
  - Library
  - Study

Who

When

Changes



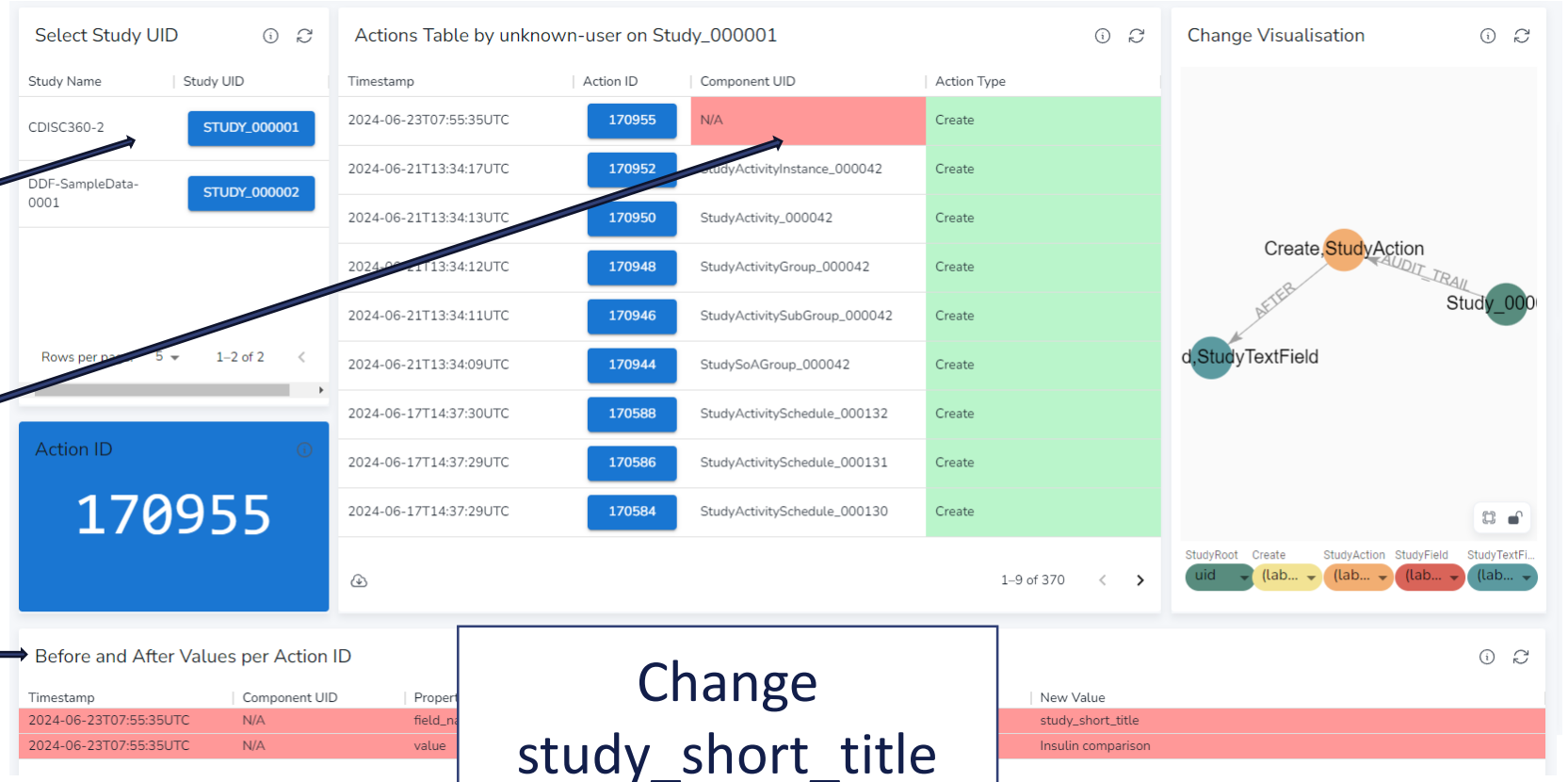
Insights – NeoDash – Audit Trail

- Who changed what when?
  - Library
  - Study

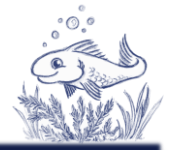
Study

Changes

From-To



Change
study_short_title
Insulin comparison



Data Models

Insights – NeoDash – Data Models

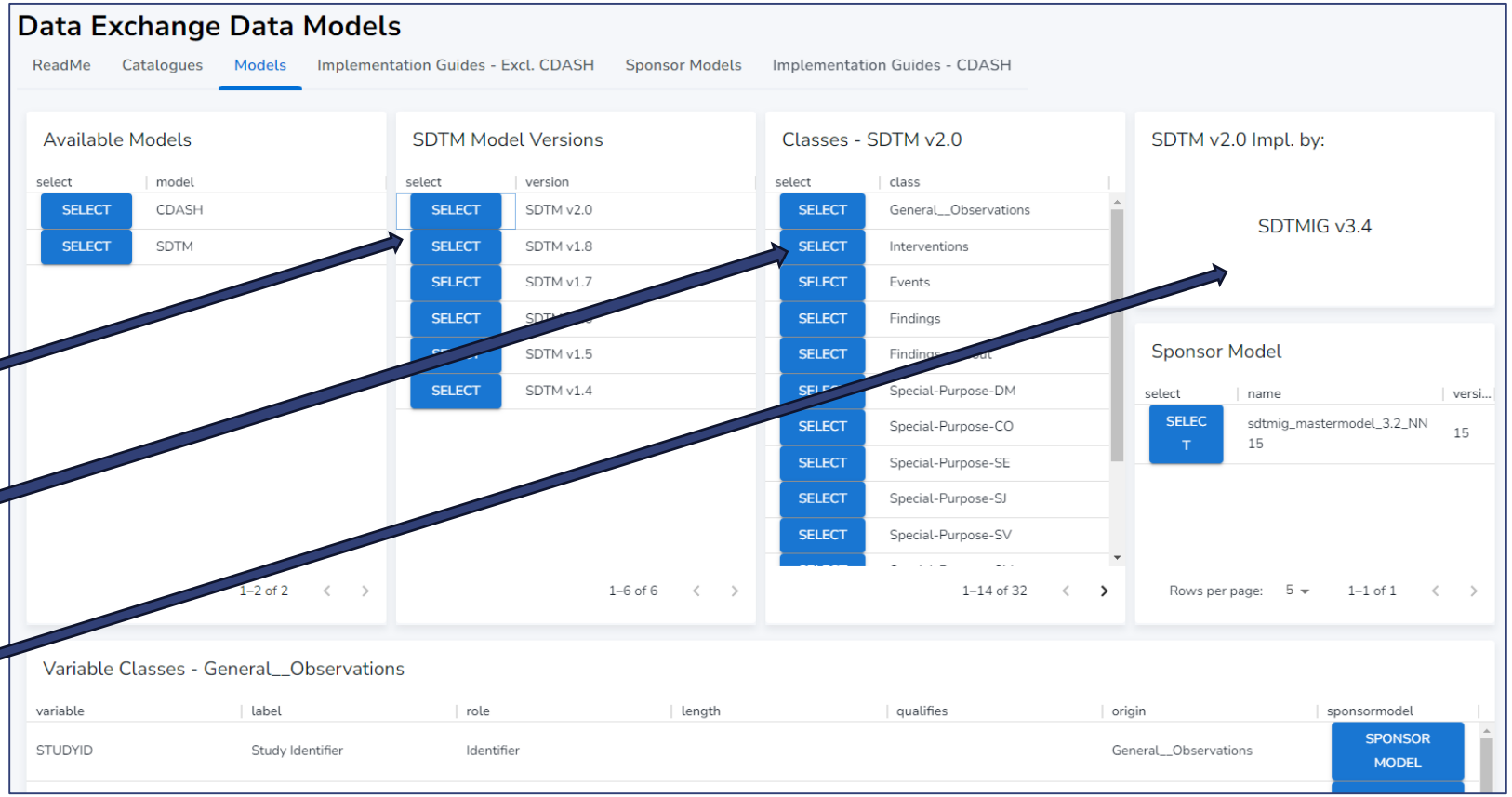
- Investigate Data Models
  - SDTM
  - Versions

Models

Version

Classes

IG



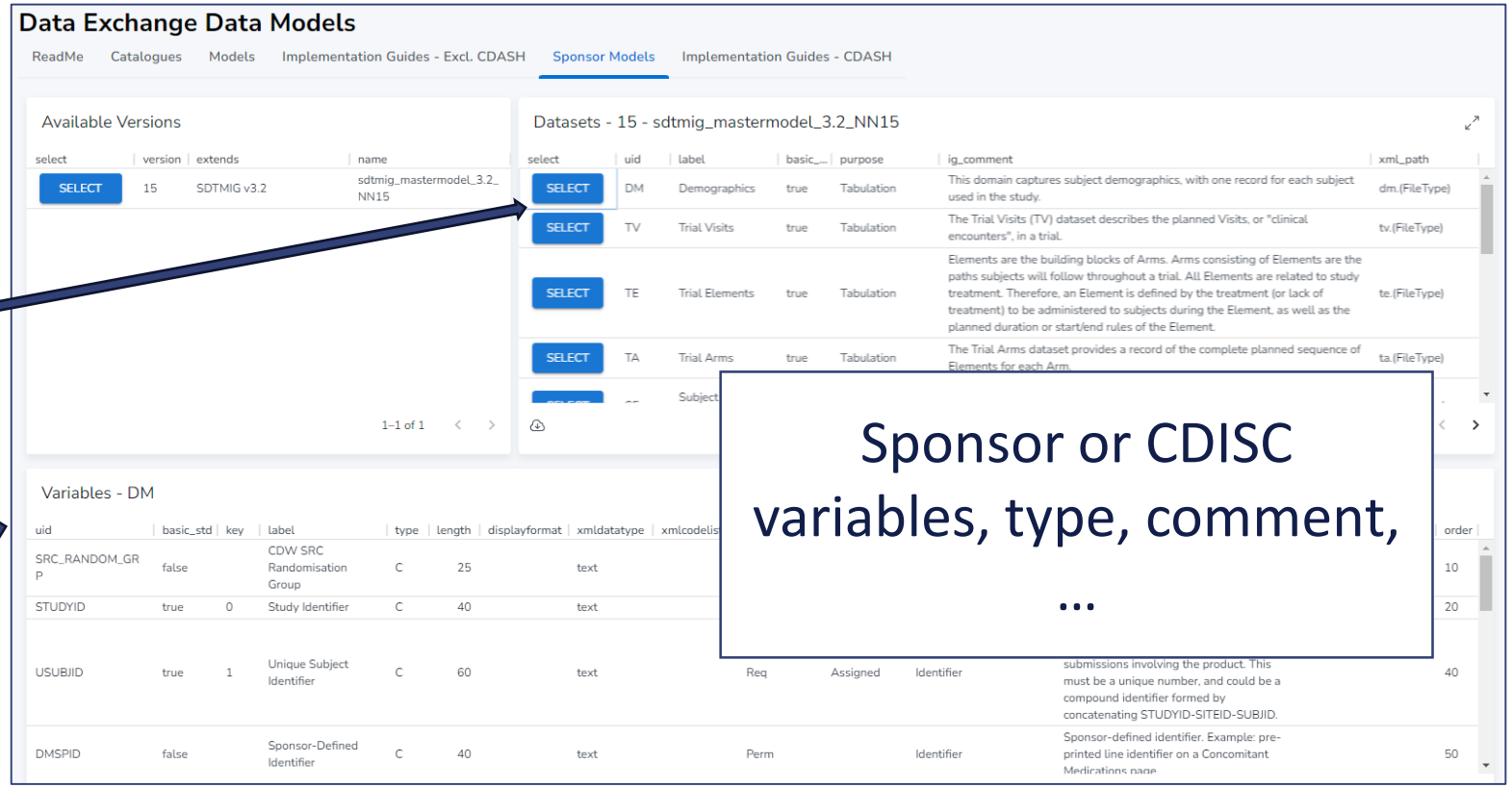
Insights – NeoDash – Data Models

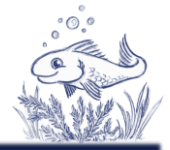
- Investigate Data Models
  - Sponsor Model

Implementation Guide

Domain

Variables





Study Metadata

Insights – NeoDash – Study Metadata

- Compare Study Metadata

Select Study & Version

Select Base

Trial ID	Date	Version	Status	Select
CDISC DEV-0	2024-06-17T14:30:30		DRAFT	BASE
CDISC DEV-0	2024-06-17T14:31:47	1	LOCKED	BASE
CDISC DEV-0	2024-06-23T08:23:26	2	LOCKED	BASE
CDISC DEV-0	2024-06-23T08:40:37		DRAFT	BASE
CDISC DEV-0001	2024-06-17T14:37:30		DRAFT	BASE

Select Compare

Trial ID	Date	Version	Status	Select
CDISC DEV-0	2024-06-17T14:30:30		DRAFT	COMPARE
CDISC DEV-0	2024-06-17T14:31:47	1	LOCKED	COMPARE
CDISC DEV-0	2024-06-23T08:23:26	2	LOCKED	COMPARE
CDISC DEV-0	2024-06-23T08:40:37		DRAFT	COMPARE
CDISC DEV-0001	2024-06-17T14:37:30		DRAFT	COMPARE

Insights – NeoDash – Study Metadata

- Compare Study Metadata

Study field comparison

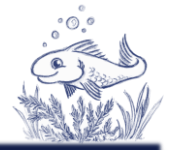
Study Field	Base	Compare	Diff
Study short title	Insulin comparison	Human insulin comparison	yes

Objectives

```
No differences found
```

Detailed Flowchart compare between base and compare study

Change Type	Flowchart Group (Base)	Activity Group (Base)	Activity Subgroup (Base)	Flowchart Group (Compare)	Activity Group (Compare)	Activity Subgroup (Compa...)	Activity Detail
Activity added	SAFETY	Vital Signs	Vital Signs				Temperature(Data collection: true)
No change	SUBJECT RELATED INFORMATION	Randomisation	Randomisation	SUBJECT RELATED INFORMATION	Randomisation	Randomisation	Randomized(Data collection: true)
No change	SUBJECT RELATED INFORMATION	End of Study	End of Study	SUBJECT RELATED INFORMATION	End of Study	End of Study	End of Study(Data collection: true)
No change	SUBJECT RELATED INFORMATION	Body Measurements	Body Measurements	SUBJECT RELATED INFORMATION	Body Measurements	Body Measurements	Height(Data collection: true)



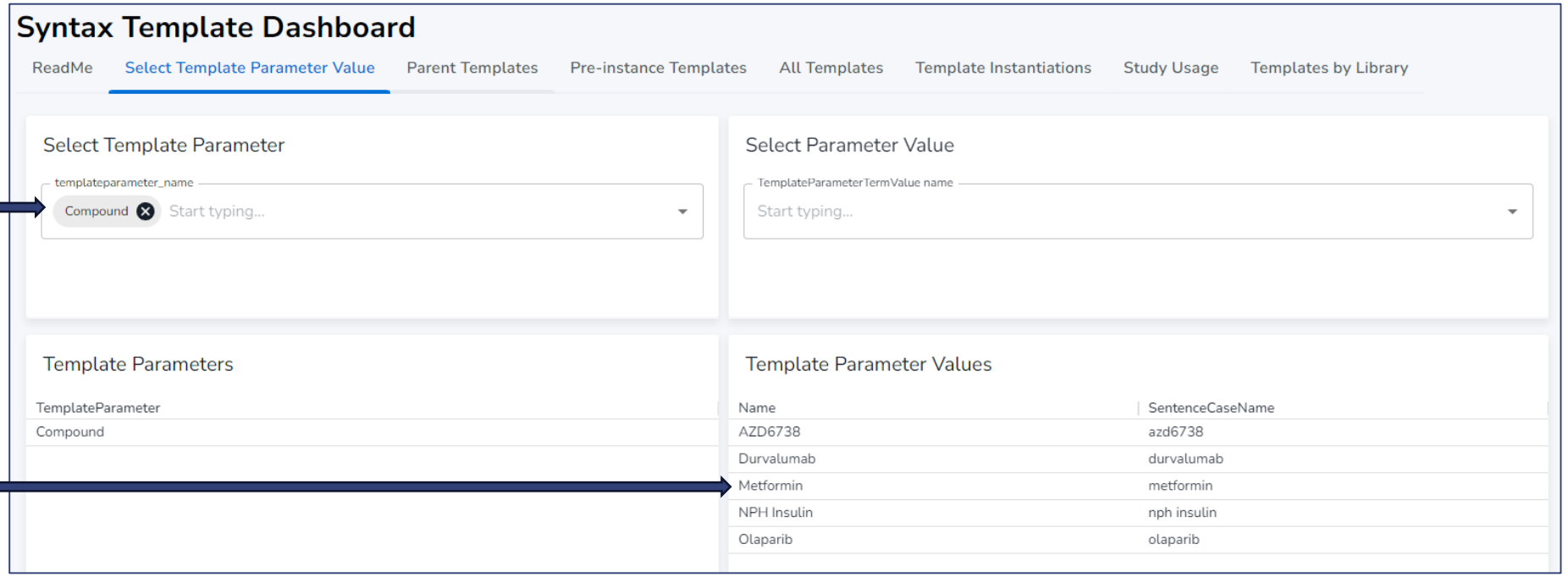
Syntax Templates

Insights – NeoDash – Syntax Templates

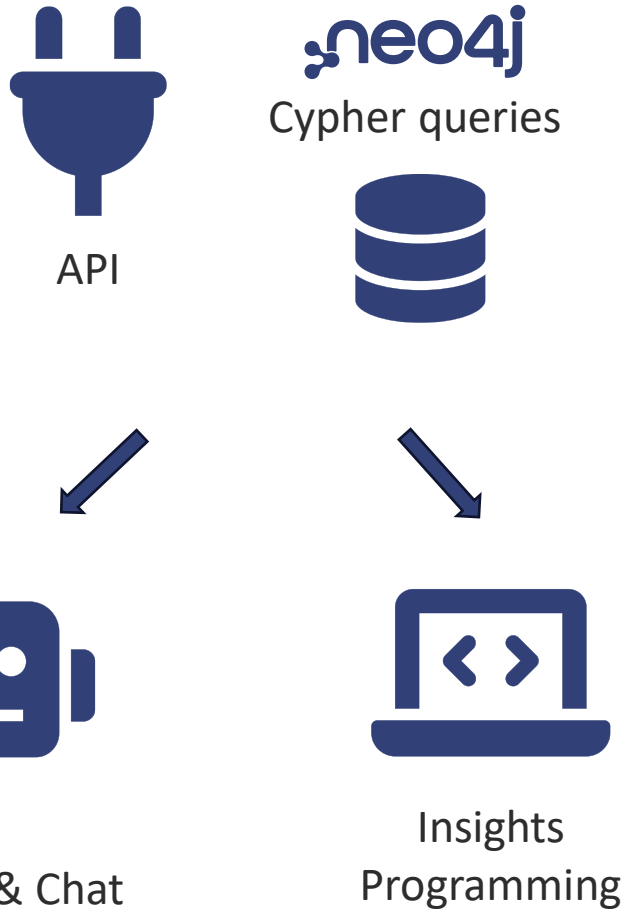
- Which templates components are in use?

Parameter Template "Compound"

Used Values

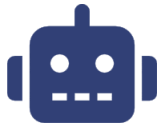


Insights - Options



Insights - Options

- Which studies had been using the questionnaire XY?
- Which studies used XY as endpoint?
- Overview of study designs
- Which studies used domain XY?
- How many Placebo studies do we have?
- What are the most common endpoints?
- …



AI
Training & Chat

Insights
Programming

Agenda

- Introduction
- Initiatives & Vision
- Automation
- Insights
- **Summary**

Summary

- Various automation and insights opportunities available
- Standard initiatives aiming for automation
  - CDISC 360 Revived
  - TransCelerate Digital Data Flow
  - CDISC CoSMOS (Biomedical Concepts)
- Standardization for Interoperability
  - USDM
  - ICH M11
  - API standards

cdisc 360

TransCelerate BIOPHARMA INC.

Digital Data Flow

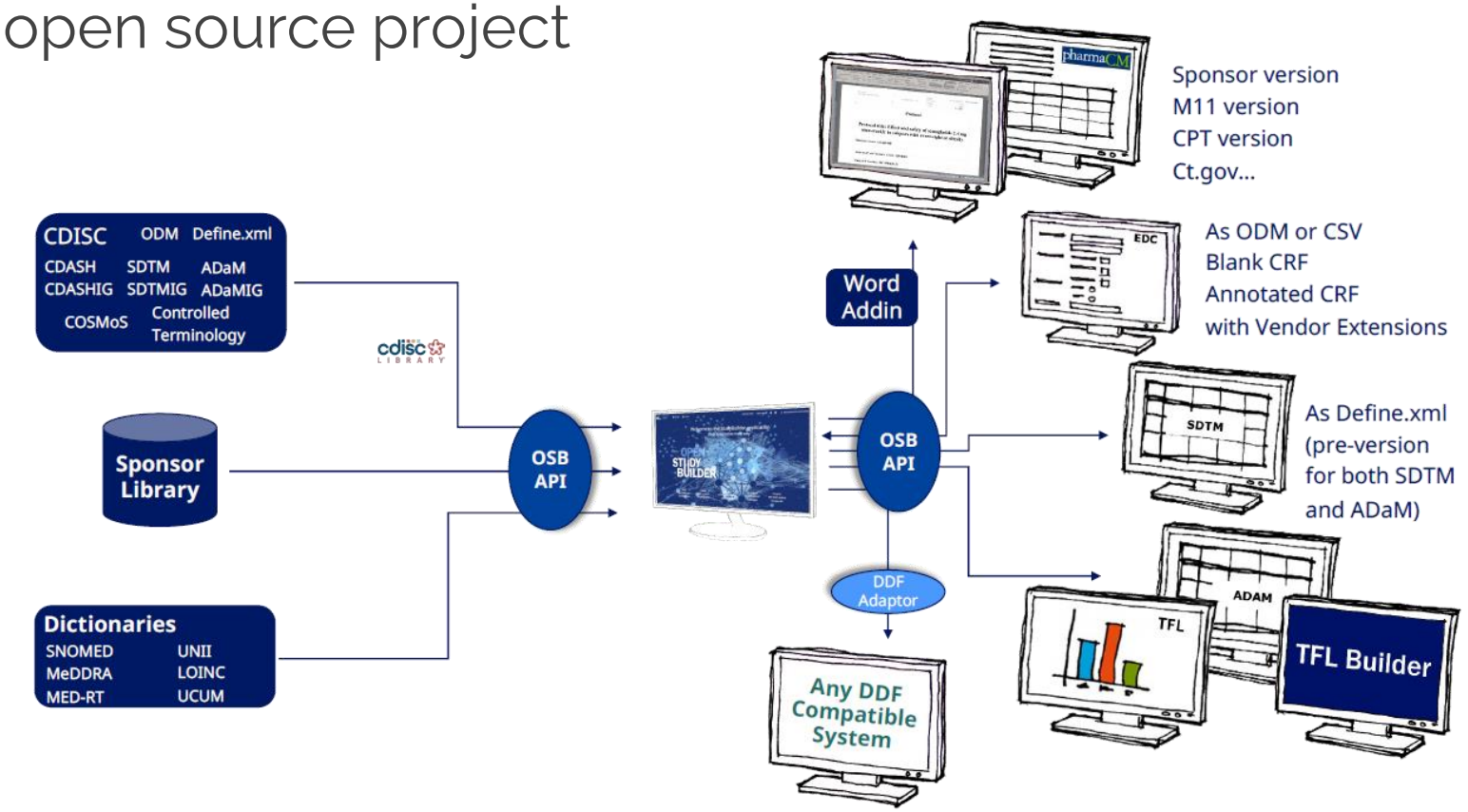
cdisc USDM UNIFIED STUDY DEFINITIONS MODEL (DDF)

Summary

- Cannot be done by one alone
- Need collaborations & initiatives
- Must come from industry & partners

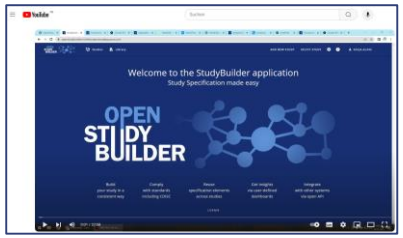
Summary

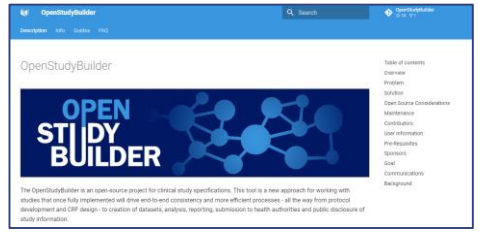
- OpenStudyBuilder is one way forward!
  - Benefit from open source project
  - Collaborate

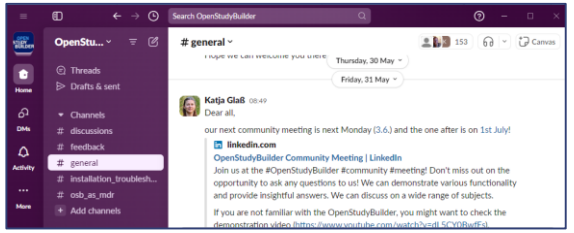


Links

- Project Homepage
- Newsletter
- YouTube Demonstration
- GitLab (Solution, Description)
- Slack
- E-Mail - openstudybuilder@gmail.com







- Sandbox environment
  - Mail openstudybuilder@neotechnology.com – Subject “Request Sandbox access”

Questions?

Katja Glass Consulting

info@glacon.eu

www.glacon.eu

www.glacon.eu/portal