



2024 CDISC + TMF
EUROPE INTERCHANGE

BERLIN

24-25 APRIL: CONFERENCE & EXPO | 22, 23, 26 APRIL: TRAININGS

From OpenStudyBuilder to the Digital Data Flow - USDM Format

Presented by Maurizio Mazzei, Engineer, Neo4j
And Nicolas de Saint Jorre, Lead Product Architect, Novo Nordisk

Meet the Speakers



Maurizio MAZZEI

Title: Consulting Engineer

Organization: Neo4j

Maurizio is a software developer based in Rome, Italy. His career started in academia, where his efforts went towards the creation of a big data integration benchmark, then he moved to the industry, working as a Software Engineer developing APIs and ML models for different products, and now helps people make sense of their data with Neo4j, from database data modeling to web API development. He's currently collaborating with Novo Nordisk on the OpenStudyBuilder as a consulting software engineer.



Nicolas de SAINT JORRE

Title: Lead Product Architect

Organization: Novo Nordisk

29-year career in Data Management and Clinical Research. From pioneering EDC systems in 2000 to advancing CDISC-compliant solutions with EvidentIQ in 2005, I've been at the forefront of innovation in our field. In 2018, I contributed to the CDISC360 project, developing a metadata-centric 'Study Builder' prototype. Furthering this path, I collaborated with Novo Nordisk on the OpenStudyBuilder since 2019 and recently joined their team as Lead Product Architect in 2023.



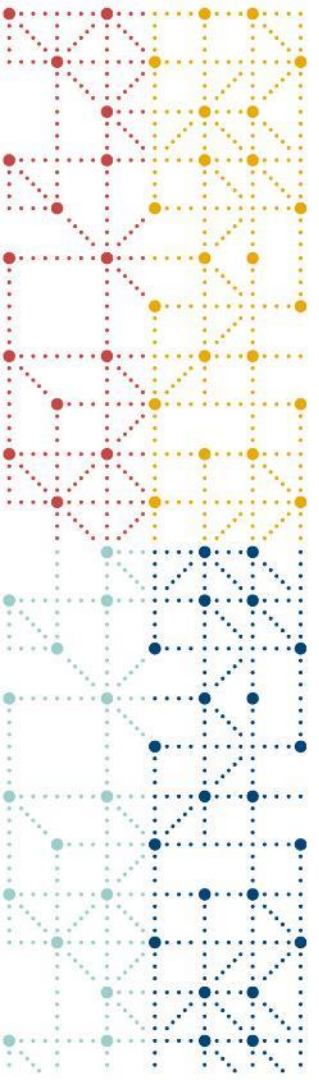
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- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.*



Agenda

1. The OpenStudyBuilder as a Metadata Repository
2. The Word Add-in as a first editing solution
3. The Digital Data Flow Adaptor (DDF Adaptor)
4. Challenges...



The OpenStudyBuilder as a Metadata Repository

How do we create an electronic version of the Protocol?

What is the OpenStudyBuilder?...

A NEW APPROACH TO STUDY SPECIFICATION

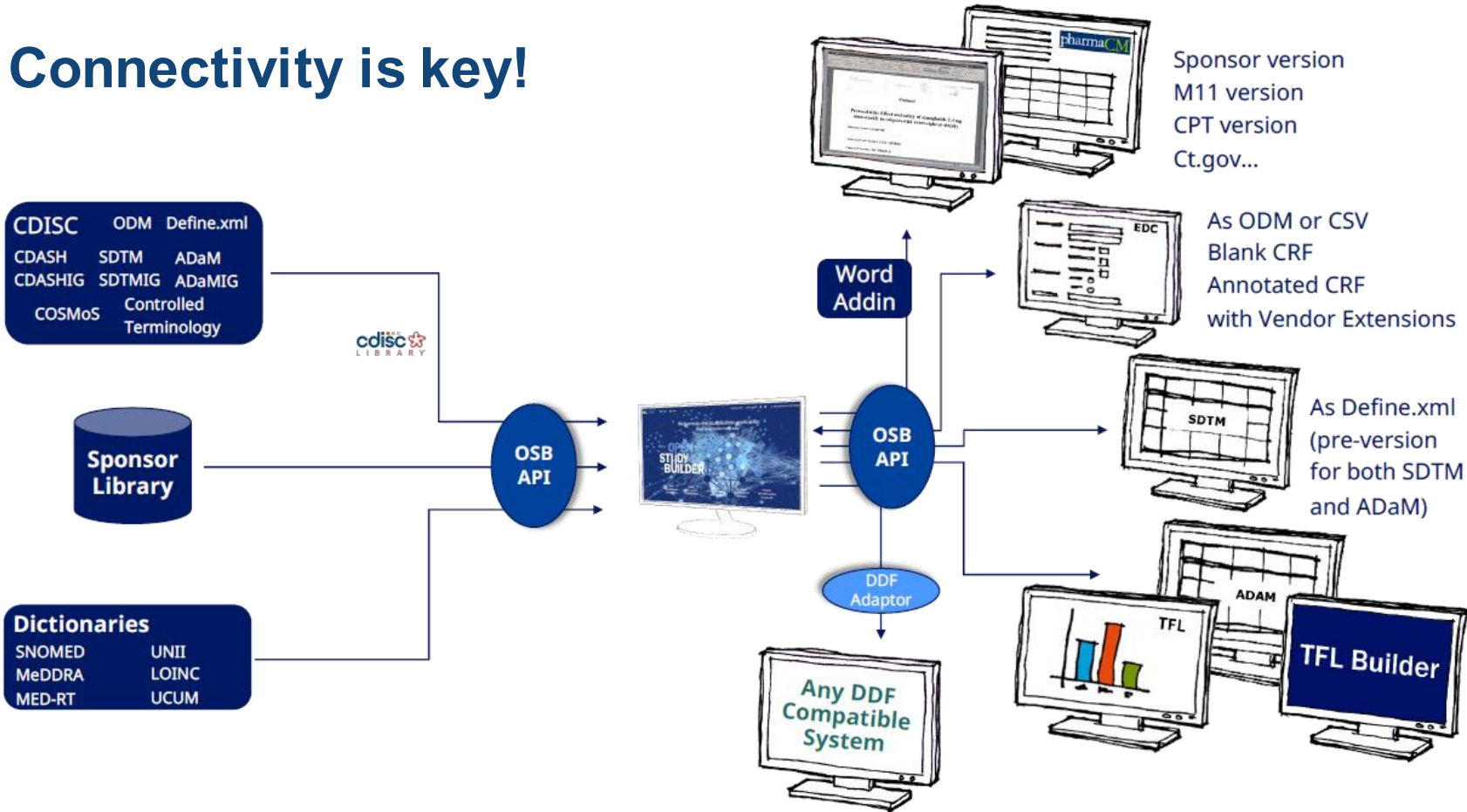
- Compliance with external and internal standards
- Facilitates automation and content reuse
- Ensures a higher degree of end-to-end consistency

3 ELEMENTS OF OpenStudyBuilder

- **Clinical Metadata and Study Definition Repository**
(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)



Connectivity is key!



How to Specify our Electronic Protocol?

- In the « Studies »:

- Study title
- Registry Identifiers
- Study Properties
- Study Structure
- Study Population
- Study Criteria
- Study Interventions
- Study Purpose
- Study Activities

- Many data are using the metadata coming from the Library

Study Activities (CDISC DEV-0) Ⓞ

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

Expand table Collapse table Show SoA groups

Activities	Epoch Visit Day	Screening Treatment										Follow-up	
		V1	V2	V3	V4	V5	V6	V7	V8	V9	V10		V11
Window		-2	1	2	3	4	5	6	7	9	27	31	
Randomisation	Window	-13/+0	±0	±1	±1	±1	±1	±1	±1	±1	±1	±1	+0/+35
Randomisation	Randomized	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
End of Study	End of Study	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Body Measurements	Weight	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Body Measurements	Height	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Eligibility Criteria	Eligibility Criteria Met	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Laboratory Assessments	HbA1c	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

SoA Footnotes

OPEN STI DY BUILDER

Studies Library

ADD NEW

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

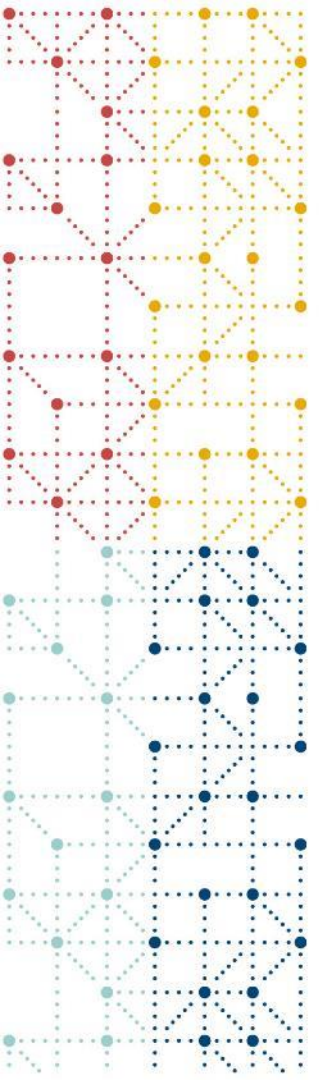
CT identifiers	Selected values	Status	Modified	Version	Actions
Sponsor Preferred Name	3	Final	Oct 19, 2023, 11:06 PM	2.0	+ ⊗ ⌵
Sentence case name	3				
Order	3				

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 3 studies usually include from several hundred to several thousand subjects. [After ICH E8: Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products Draft Guidance for Industry, December 2019] See also phase, phase 3b. (CDISC Glossary)				

Sponsorvms

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



The Word Add-in as a first editing solution

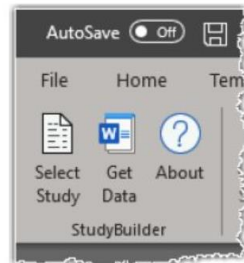
Authors can work in the Word editor to complete the Protocol...

Protocol Generation

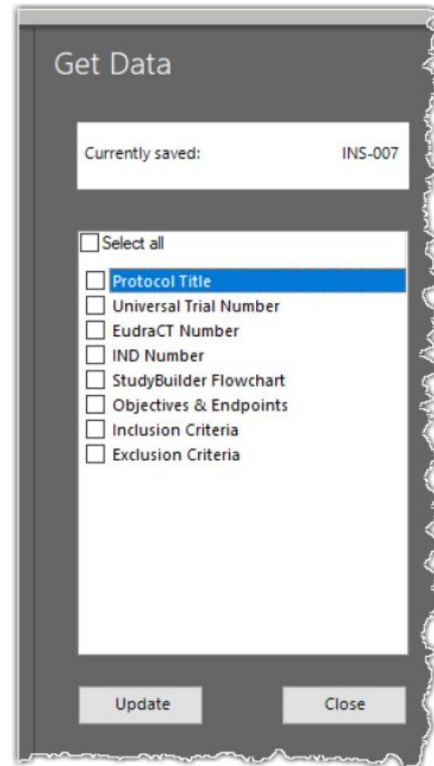
StudyBuilder ribbon (Word add-in)



- ✓ One-way connection
- ✓ Code recognizes the document type
- ✓ User-friendly ribbon and 'fly-out' in Word
- ✓ Style ensure proper formatting in Word
- ✓ Using the API to generate the Word content



Protocol



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

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

1.2 Flowchart

Schedule of Activities

Procedure	Screening		Treatment								Follow-up
	V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11
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											

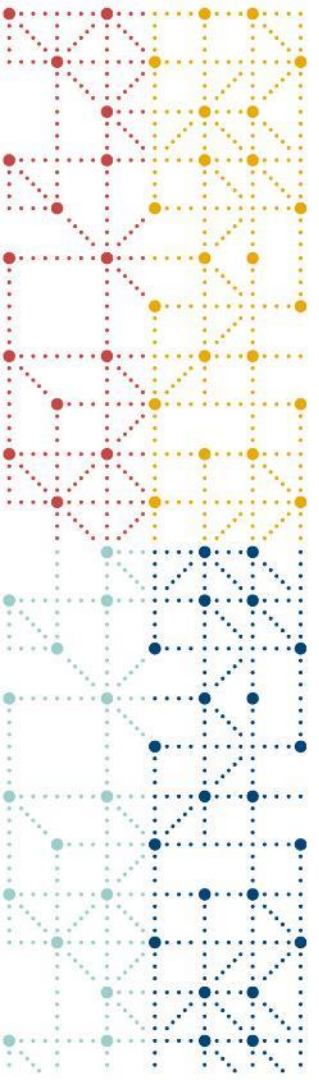
Get Data X

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 Close





The Digital Data Flow Adaptor

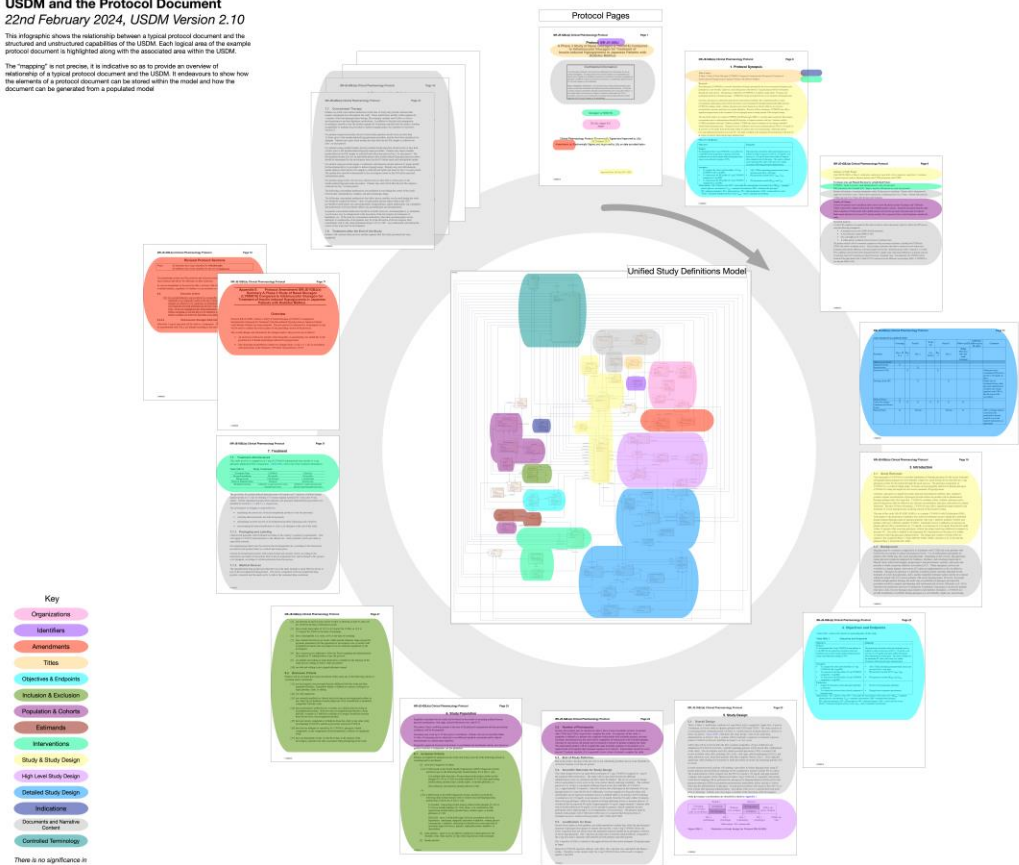
A dedicated module enables OpenStudyBuilder to convert our metadata into the Unified Study Definition Model (USDM) and exposes the result through DDF-compliant API

USDM: The big Protocol Picture

USDM and the Protocol Document 22nd February 2024, USDM Version 2.10

This infographic shows the relationship between a typical protocol document and the structured and unstructured capabilities of the USDM. Each logical area of the example protocol document is highlighted along with the associated area within the USDM.

The "mapping" is not precise, it is indicative so as to provide an overview of relationships of a typical protocol document and the USDM. It is intended to show how the elements of a protocol document can be stored within the model and how the document can be generated from a populated model.



- Key**
- Organizations
 - Identifiers
 - Amendments
 - Titles
 - Objectives & Endpoints
 - Inclusion & Exclusion
 - Population & Cohorts
 - Estimands
 - Interventions
 - Study & Study Design
 - High Level Study Design
 - Detailed Study Design
 - Indications
 - Documents and Narrative Content
 - Controlled Terminology

There is no significance in the choice of colour for a logical area of the USDM

Key

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There is no significance in the choice of colour for a logical area of the USDM

DDF Adaptor enables new use cases

- The DDF Adaptor enables:
 - Downstream structured content management
 - For documents: Protocol, SAP...
 - Downstream data consumption
 - Clinical & Ops Systems
 - EDC/CDMS, CTMS, ...
 - Upload to DDF-compliant SDR for data sharing

Mapping matrix between OSB and DDF

	A	B	C	D	E	F	G	H	I	J	K
1	Row	Entity Name	Role	Logical Data Model Name	NCI C-code	CT Item Preferred Name	Synonym(s)	Definition	Has Value List	Codelist URL	OpenStudyBuilder Mapping
112	111	Encounter	Entity	Encounter	C142427	Clinical Encounter		Contact between subject/patient and healthcare practitioner/researcher, during	N		uuid4
113	112	Encounter	Relationship	transitionStartRule					N/A		entity "TransitionRule" (id: uuid4, name: 'TransitionStartRule', text: StudyVisit->start_rule)
114	113	Encounter	Relationship	transitionEndRule					N/A		entity "TransitionRule" (id: uuid4, name: 'TransitionEndRule', text: StudyVisit->end_rule)
115	114	Encounter	Relationship	scheduledAt					N/A	/	
116	115	Encounter	Attribute	name	C171010	Clinical Encounter Name		The literal identifier (i.e., distinctive designation) for a protocol-defined clinical encounter.	N		StudyVisit->visit_name
117	116	Encounter	Attribute	description	C188836	Clinical Encounter Description		A narrative representation of the protocol-defined clinical encounter.	N		StudyVisit->description
118	117	Encounter	Attribute	label	CNEW	Encounter Label		The short descriptive designation for the encounter.	N		/
119	118	Encounter	Relationship	previous					N/A		
120	119	Encounter	Relationship	next					N/A		
121	120	Encounter	Attribute	type	C188839	Clinical Encounter Type		A characterization or classification of contact between subject/patient and healthcare practitioner/researcher, during which an assessment or activity is performed.	Y (C188728)	https://ncit.nci.nih.gov/ncitbrowse/r/ajax?action=create_src_vs_tree	entity "Code" (id: uuid4, code: StudyVisit->visit_type_uid, codeSystem: 'openstudybuilder.org', decode: StudyVisit->visit_type_name)
122	121	Encounter	Attribute	environmentalSetting	C188840	Environmental Setting		The environment/setting where the event, intervention, or finding occurred.	Y (SDTM Terminology C171445)	https://ncit.nci.nih.gov/ncitbrowse/r/ajax?action=create_src_vs_tree&vstd_uri=http://	/
123	122	Encounter	Attribute	contactModes	C188841	Contact Mode		The means by which an interaction occurs between the subject/participant and person or entity (e.g., a device).	Y (SDTM Terminology C171445)	https://ncit.nci.nih.gov/ncitbrowse/r/ajax?action=create_src_vs_tree&vstd_uri=http://	list of entity "Code" (id: uuid4, code: StudyVisit->visit_contact_mode_uid, codeSystem: 'openstudybuilder.org', decode: StudyVisit->visit_contact_mode_uid)

DDF API specification

Simple API for DDF

2.7.1

OAS 3.1

<https://raw.githubusercontent.com/asynccapi/spec/v2.6.0/examples/streetlights-kafka.yml>

A simple TransCelerate Digital Data Flow (DDF) Study Definitions Repository API.

Production Routes that form the production specification.



POST

/v3/studyDefinitions Create a study



PUT

/v3/studyDefinitions/{studyId} Update a study



GET

/v3/studyDefinitions/{studyId} Return a study



GET

/v3/studyDefinitions/{studyId}/history Returns the study history



GET

/v3/studyDesigns Study designs for a study



Schemas



DDF API specification

GET /v3/studyDefinitions/{studyId} Return a study

Return an entire study including all child elements

Parameters Try it out

Name	Description
studyId * required string (path)	<input type="text" value="studyId"/>

Responses

Code	Description	Links
200	Successful Response	No links

Media type

Controls Accept header.

Example Value | Schema

```
Wrapper-Output ^ Collapse all object
study* ^ Collapse all object
  id > Expand all (string | null)
  name* string >= 1 characters
  description > Expand all (string | null)
  label > Expand all (string | null)
  versions > Expand all array<object>
  documentedBy > Expand all (object | null)
```

DDF is now in the OpenStudyBuilder API!

Dataset classes ∨

Datasets ∨

Dataset scenarios ∨

Class variables ∨

Dataset variables ∨

MS Graph API integrations ∨

DDF endpoints ∧

GET /ddf/v3/studyDefinitions/{study_id} Return an entire study in DDF USDM format ∧

State before:

- Study must exist.

State after:

- no change.

Possible errors:

- Invalid study-uid.

Parameters Cancel

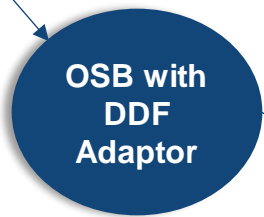
Name	Description
study_id <small>required</small> string <small>(path)</small>	The unique id of the study.
<input type="text" value="Study_000001"/>	
x-test-user-id string <small>(header)</small>	A value to be injected into User object as user id.
<input type="text" value="x-test-user-id"/>	

Execute Clear

Digital Data Flow Adaptor (in the OpenStudyBuilder)

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	
2	Treatment	Treatment	Treatment	RDM ok	Dosing complete	Treatment epoch without dosing escalation	9	
3	Follow-up	Post Treatment	Follow-up	Treatment ok	Last follow-up ok	Follow-up epoch to follow the subject	1	



```
1251 "epochs": [  
1252   {  
1253     "id": "StudyEpoch_000001",  
1254     "name": "Screening",  
1255     "label": null,  
1256     "description": "Screening epoch to start",  
1257     "type": {  
1258       "id": "2785a39f-c632-490e-9dea-d8ede4b6e5ca",  
1259       "code": "CTTerm_000003",  
1260       "codeSystem": "openstudybuilder.org",  
1261       "codeSystemVersion": "",  
1262       "decode": "Pre Treatment"  
1263     },  
1264     "previousId": null,  
1265     "nextId": "StudyEpoch_000002"  
1266   },  
1267   {  
1268     "id": "StudyEpoch_000002",  
1269     "name": "Treatment",  
1270     "label": null,  
1271     "description": "Treatment epoch without dosing escalation",  
1272     "type": {  
1273       "id": "f04010d7-7c95-4b18-94f0-a6391fb7a190",  
1274       "code": "C101526_TREATMENT",
```



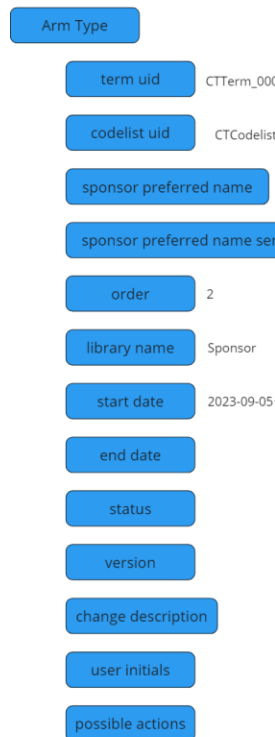


Challenges?

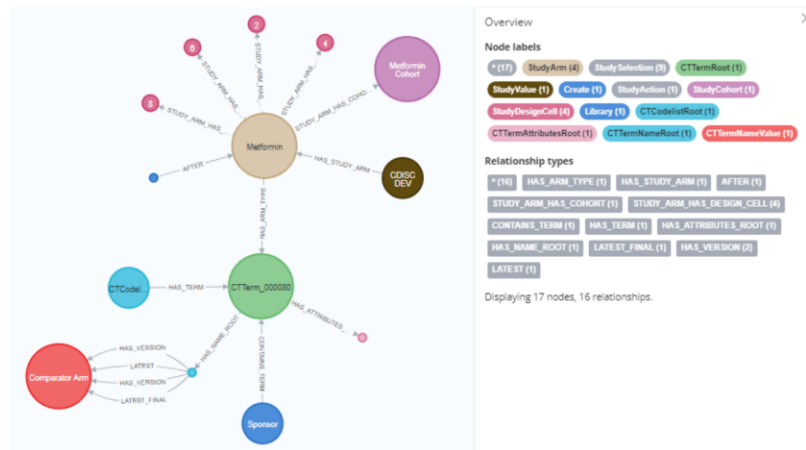
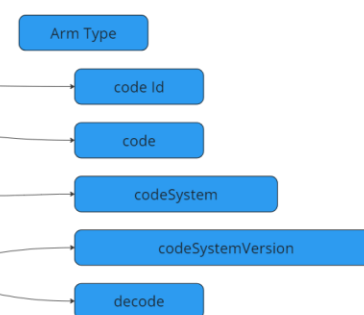
Evolution of the OpenStudyBuilder and the DDF-USDM

- OpenStudyBuilder started before DDF...
- OpenStudyBuilder is still in version 0.8.1 / DDF is looking at version 3.0...
- OpenStudyBuilder is defining metadata differently

StudyBuilder



USDM



Objectives using Template versus Blob Text...

Study Purpose (CDISC DEV-0) ?

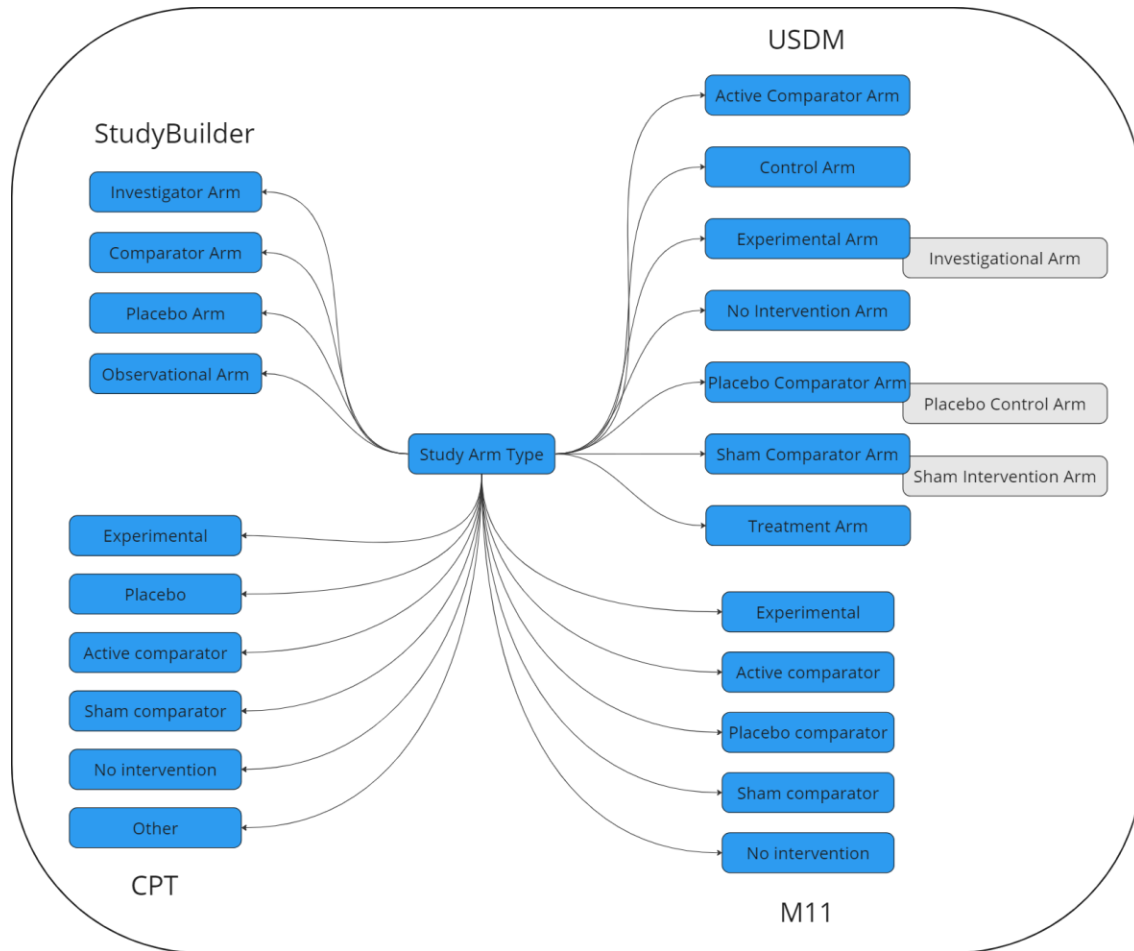
Study Objectives Study Endpoints Study Estimands

Select rows

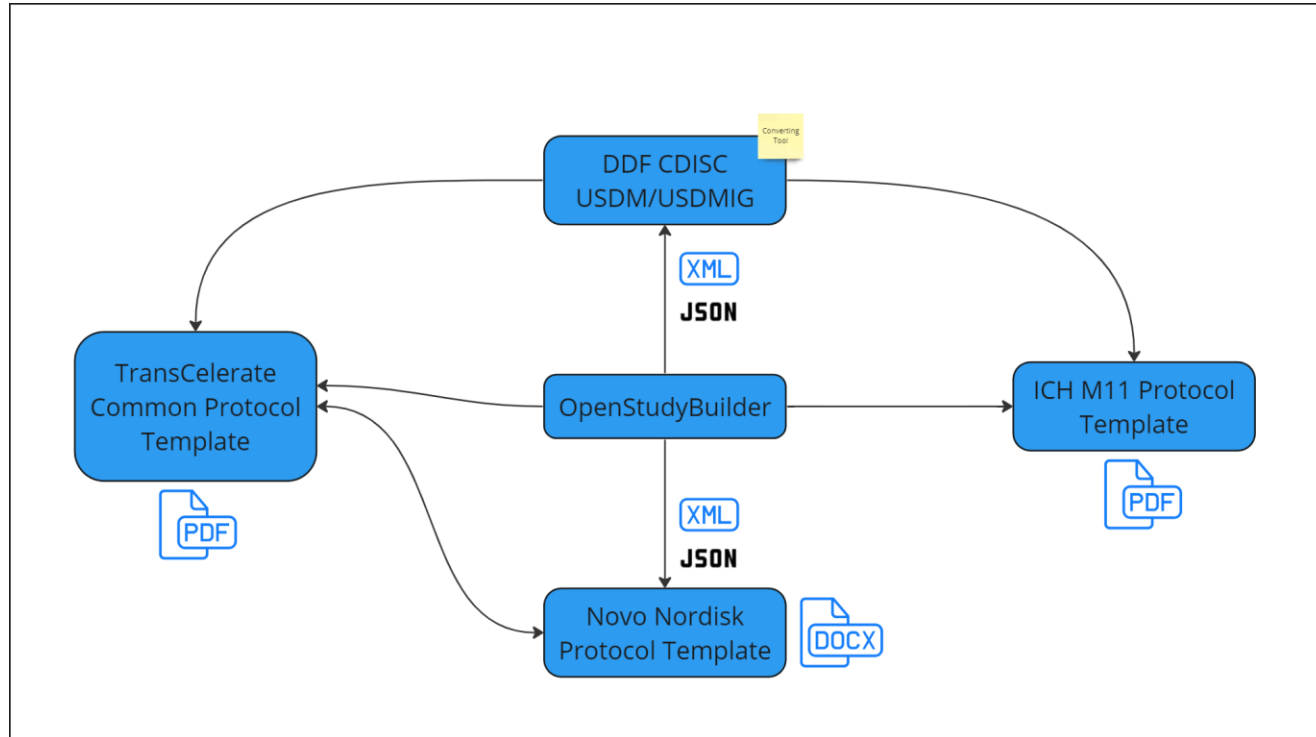
Search

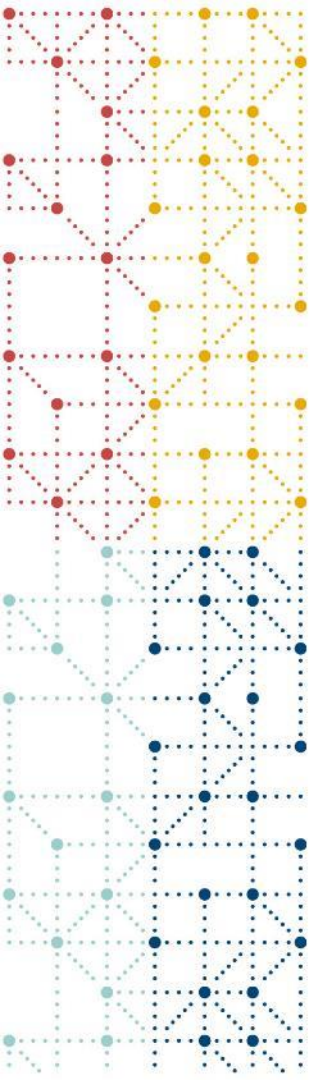
#	Objective level	Objective
⋮	1	Primary Objective
		Time to first occurrence of MACE+, a composite endpoint consisting of: CV death, nonfatal MI, nonfatal stroke, or hospitalization for unstable angina
⋮	2	Secondary Objective
		Time from randomisation to all cause death

```
"objectives": [
  {
    "id": "2bc878b4-3317-42c5-b51c-be23fcd43679",
    "name": "Objective_000004",
    "label": null,
    "description": "<p>Time to first occurrence of MACE+, a composite endpoint consisting of: CV death, nonfatal MI,</p><p>nonfatal stroke, or hospitalization for unstable&nbsp;</p><p>angina</p>",
    "instanceType": "OBJECTIVE",
    "text": "",
    "dictionaryId": null,
    "level": {
      "id": "2c71d89c-47b6-48c8-bf9a-43350ce4bd0b",
      "code": "C85826_OBJPRIM",
      "codeSystem": "openstudybuilder.org",
      "codeSystemVersion": "",
      "decode": "Primary Objective"
    },
    "endpoints": [
      {
        "id": "cb9a5d33-6863-4551-8190-40e6da8958ac",
        "name": "Endpoint_000001",
        "label": null,
        "description": "<p>Mean change from baseline in hbalc</p>",
        "instanceType": "ENDPOINT",
        "text": "",
        "dictionaryId": null,
        "purpose": "",
        "level": {
          "id": "c6076db7-708c-42a0-9b4a-4e39bfc96023",
          "code": "C98772_OUTMSPRI",
          "codeSystem": "openstudybuilder.org",
          "codeSystemVersion": "",
          "decode": "Primary Endpoint"
        }
      }
    ]
  }
],
]
```



OpenStudyBuilder as a multisource system





Thank You!

You can contact us:

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- Nicolas DE SAINT JORRE - ndj@novonordisk.com

cdisc