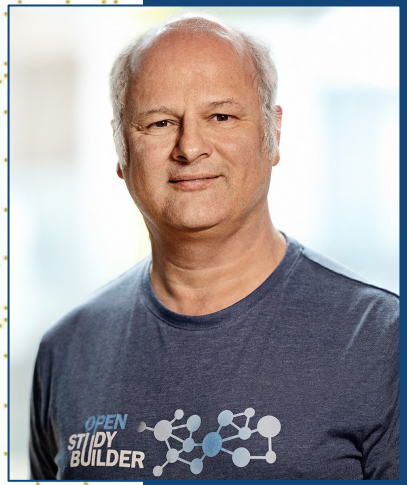
Enhanced Biomedical Concepts: A Design Perspective in OpenStudyBuilder Supporting CDISC 360i

Mikkel Traun, Principal Solution Architect
Nicolas De Saint Jorre, Lead Product Architect
Novo Nordisk A/S

Meet the Speakers



Mikkel Traun

Title: Principal Solution Architect

Organization: Novo Nordisk A/S

Mikkel is solution architect 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.

Nicolas De Saint Jorre

Title: Lead Product Architect

Organization: Novo Nordisk A/S

With over 29 years of experience in the field of Data Management and Clinical Research, I have been working on electronic Case Report Forms (eCRFs) since 2000. From 2005 to 2023, I worked with EvidentIQ, a software publisher specializing in EDC systems. I actively participated in the CDISC 360 project, developing a prototype. Since 2019, I have been collaborating with Novo Nordisk on the OpenStudyBuilder. Since April 2023, I have served as the Lead Product Architect for OpenStudyBuilder at Novo Nordisk, directly connected with the TransCelerate group and the "Digital Data Flow" project.

I am now deeply involved in the CDISC 360i project, as a co-lead in the Build team.

The data landscape is disconnected

Many Data Sources

***MDR and SDR** (Digital Protocol)*
Dictionaries, unit conversion rules, objectives, endpoints, in-/exclusion criteria, schedule of activities, arms, interventions, etc

CTMS
Study ID, sites, investigators, milestones, metrics, protocol deviations

External Standards
CDISC CT, MedDRA, SNOMED CT, WHO Drug, ISO …

IWRS/RTSM
Randomisation number and batch numbers

EDC
Informed consent obtained, subject status, demographics, medical history, concomitant medication, dose and compliance, adverse events, vital signs, body measurements, hypoglycaemic episodes, ECG interpretation, pregnancy test results, queries, etc.

Safety
SAE & pregnancy reporting

Laboratories
Biochemistry, hematology, glucose metabolism, antibodies, trial product concentrations, serology, drug tests, pregnancy test, proteomic and genomic sample tracking, etc.

CGM
Date, time, glucose, visit

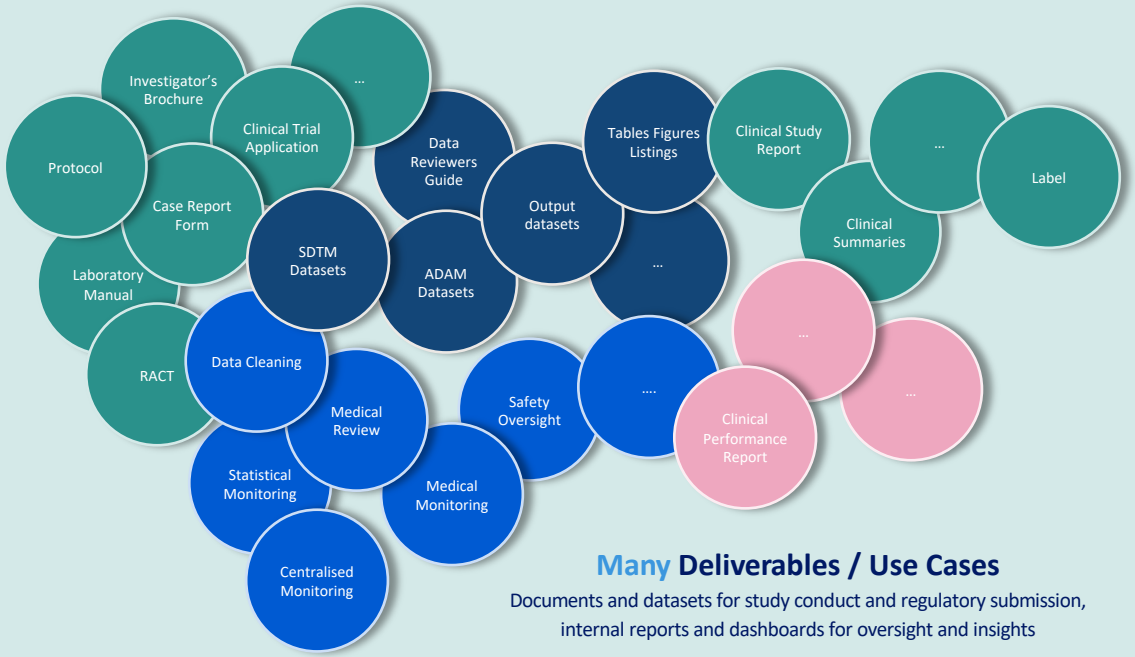
eCOAs
Questionnaires e.g. SF36, CSSRS, PHQ9
Diaries e.g. dose/compliance, hypoglycaemic episode, AE, bleeding event, BG meter readings
Sit and stand test

Imaging
Dexa scan, X-ray, MR

Data Lakes
Harmonized historic study data

Master Data
Medicinal product data

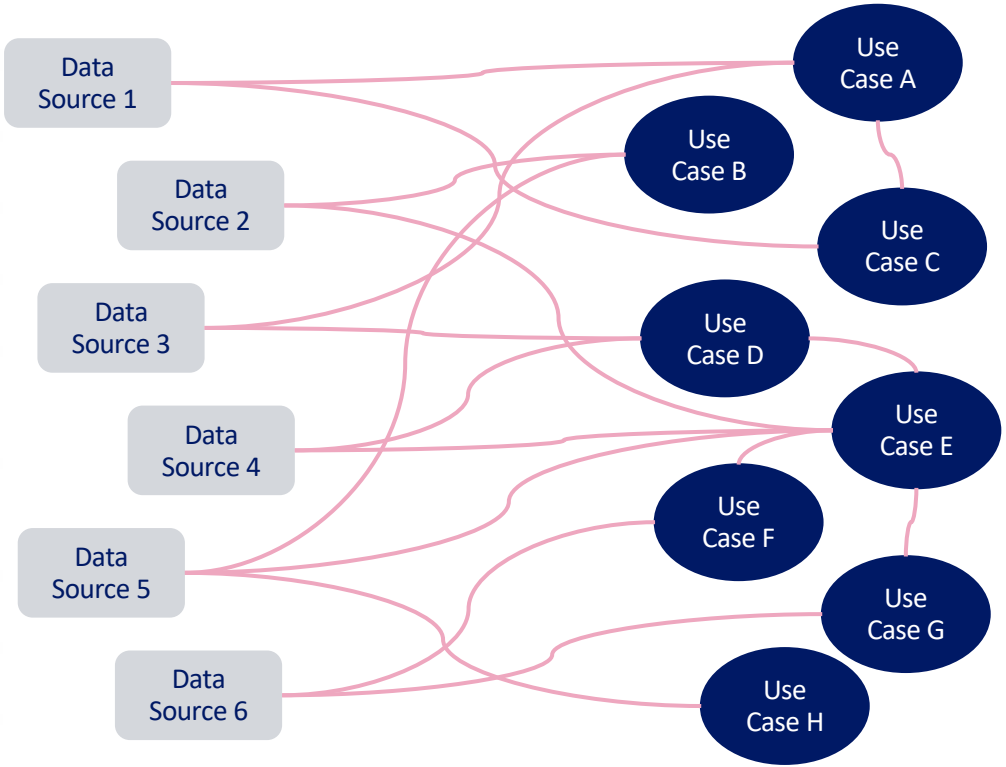
Other data
…



Many Deliverables / Use Cases

Documents and datasets for study conduct and regulatory submission, internal reports and dashboards for oversight and insights

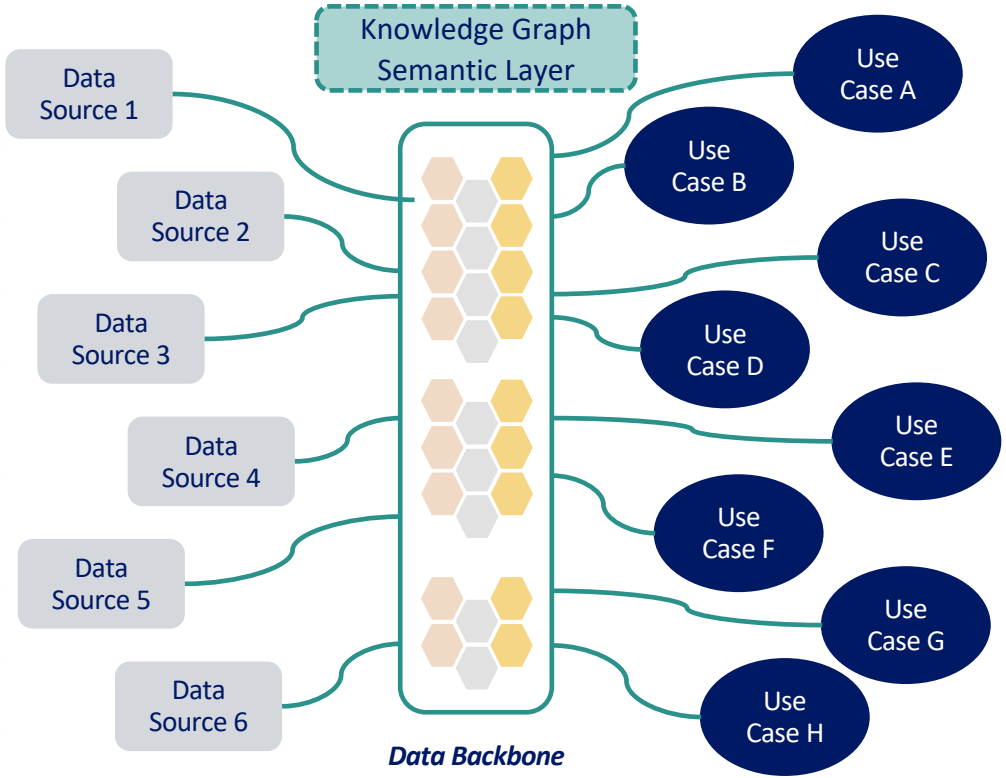
Today's **barrier** for efficiency and speed



Many to **Many** to **Many**

- Limited overview and transparency
- High-risk of inconsistencies
- Inefficiency due to re-do rather than reuse
- Lag-time between data availability and data ready for use

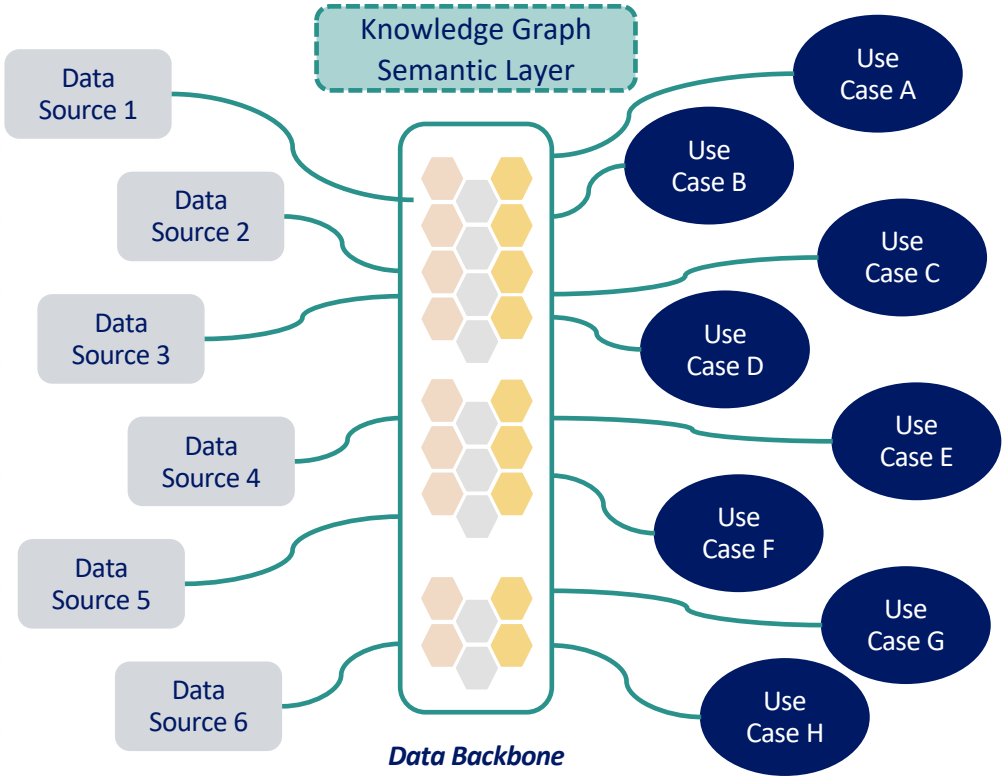
Tomorrow's **opportunity** for efficiency and speed

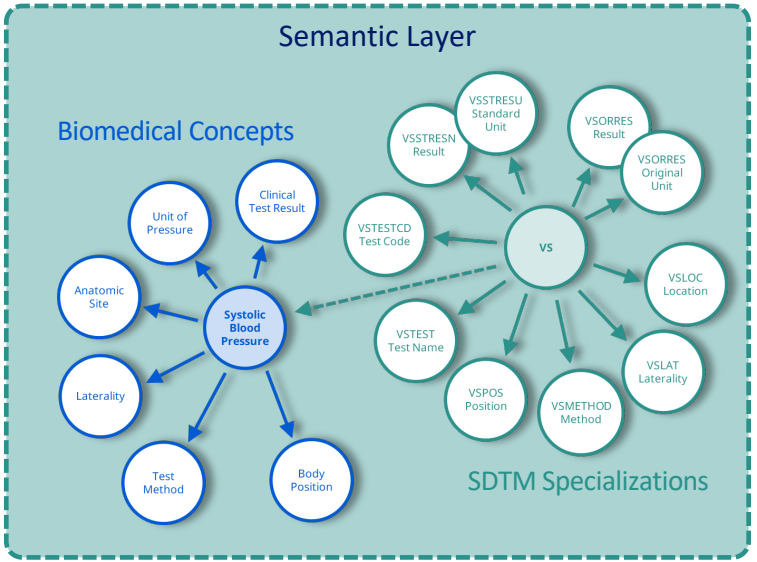


Many to **One** to **Many**

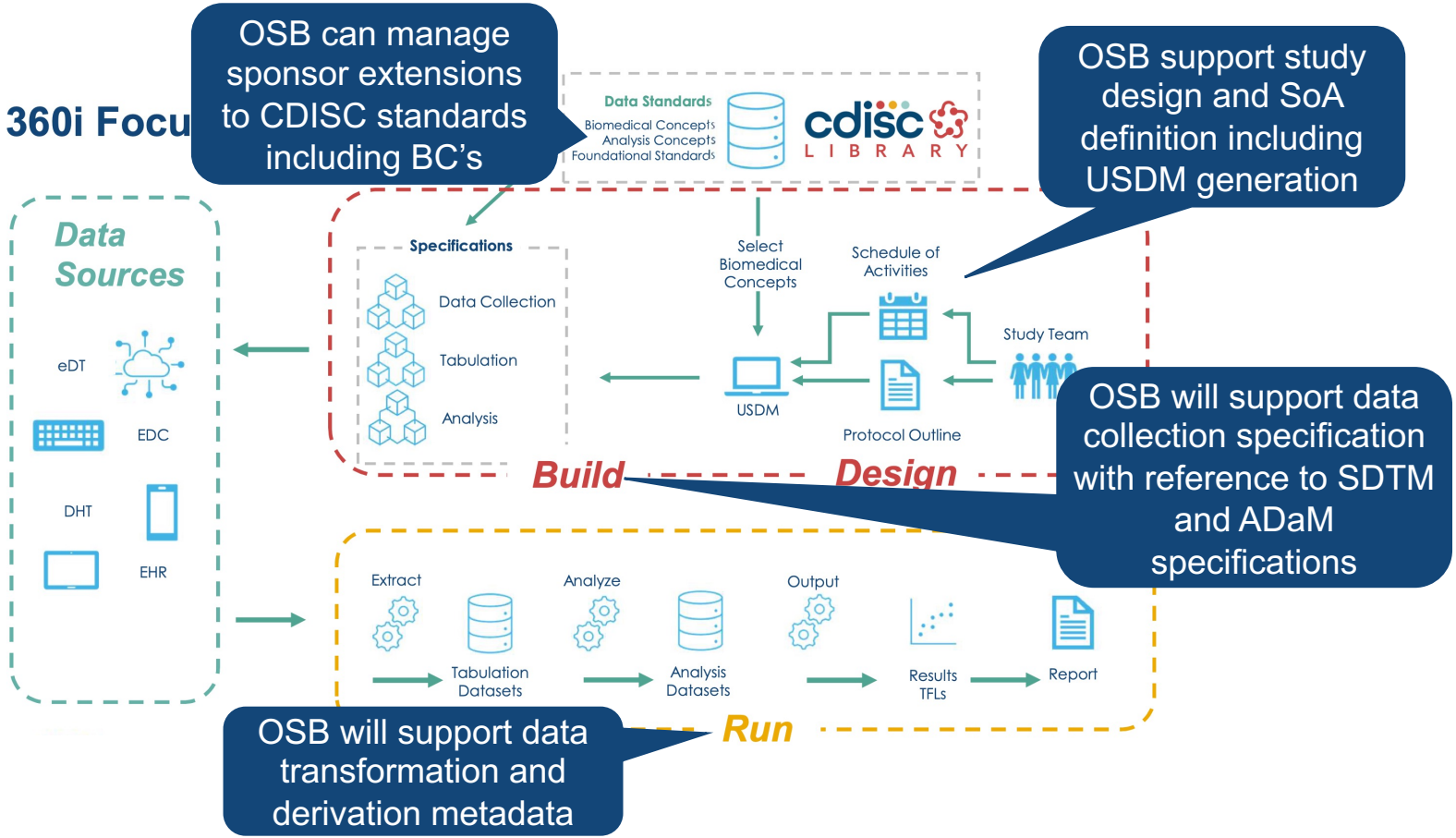
- Overview and transparency
- End-to-end consistency
- Efficiency through reuse
- Faster from data availability to data readiness

Tomorrow's **opportunity** for efficiency and speed





How do OSB fit into 360i vision



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

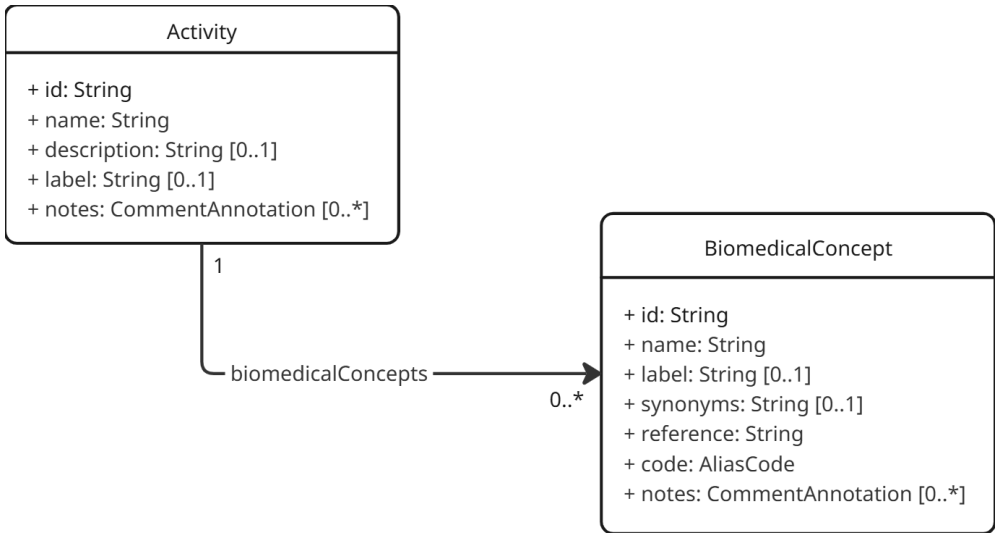
3 ELEMENTS OF OpenStudyBuilder

- **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 Endpoint – enabling DDF SDR Compatibility)

clinical **MDR**

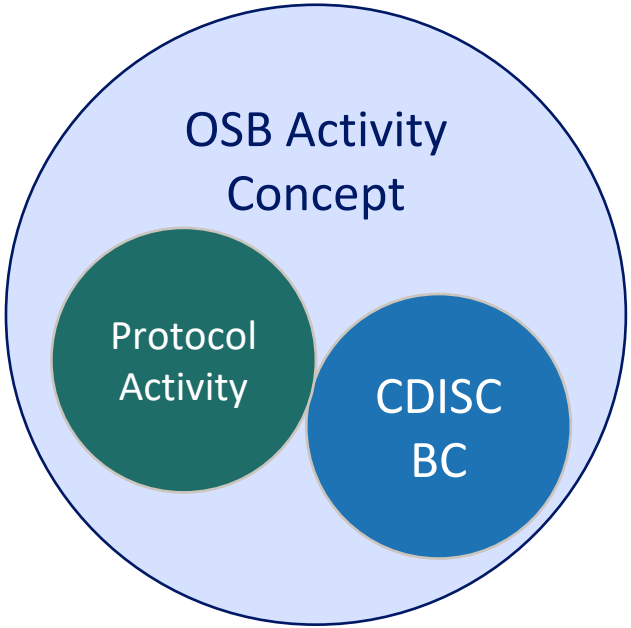
CDISC BCs and Activities in USDM

- **CDISC BCs** cover the semantic definition and SDTM specialisation
  - But do not cover the representation in the protocol nor the Activity in USDM
- **Activities** in USDM is represented as text with study level relationship to BCs
  - i.e. the Activities are not referred to as standard elements
- **CDISC BCs** are defined very broadly
  - But is in reality covering Activities (Clinical Procedures and Assessments)

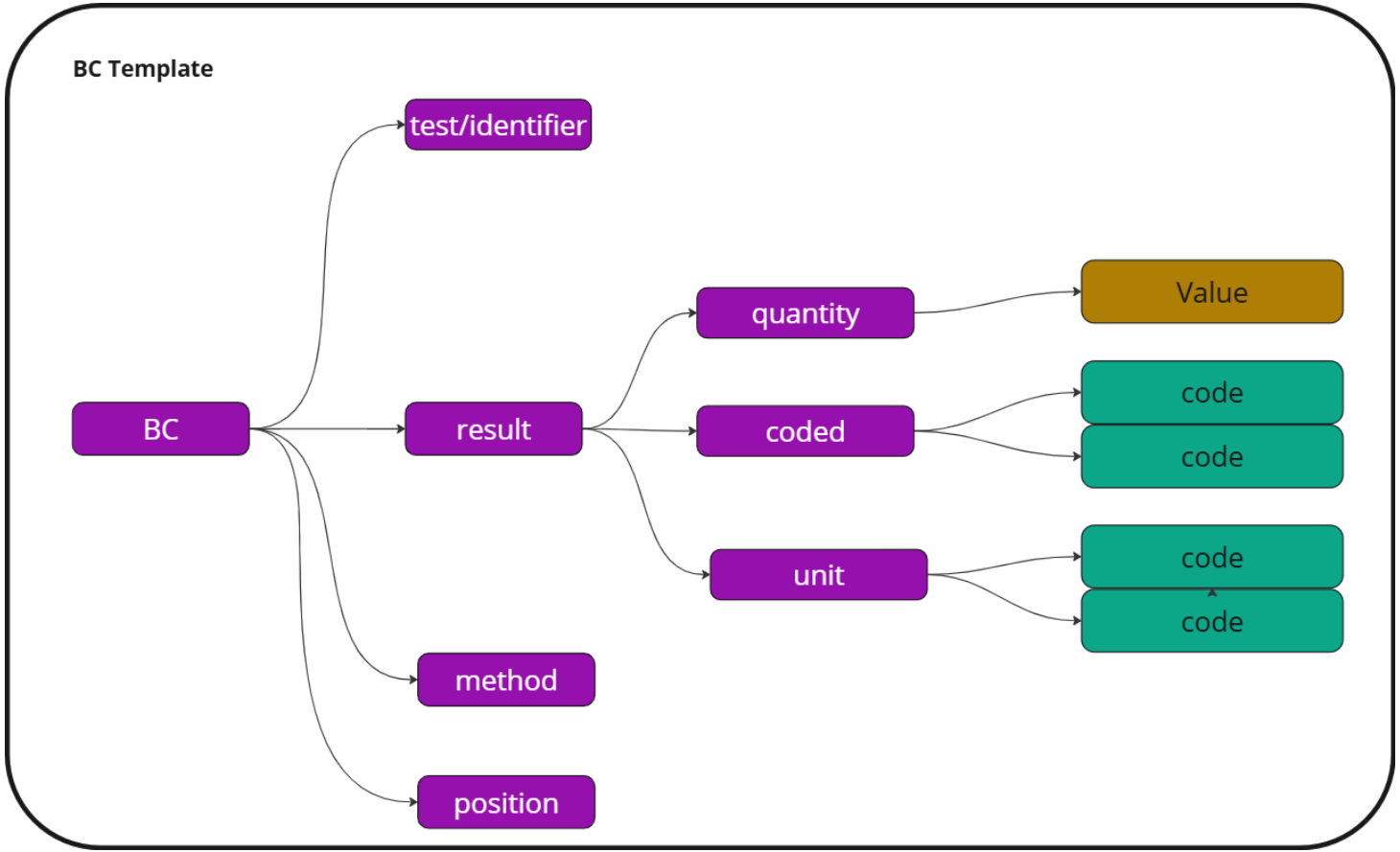


OSB BCs and Activities

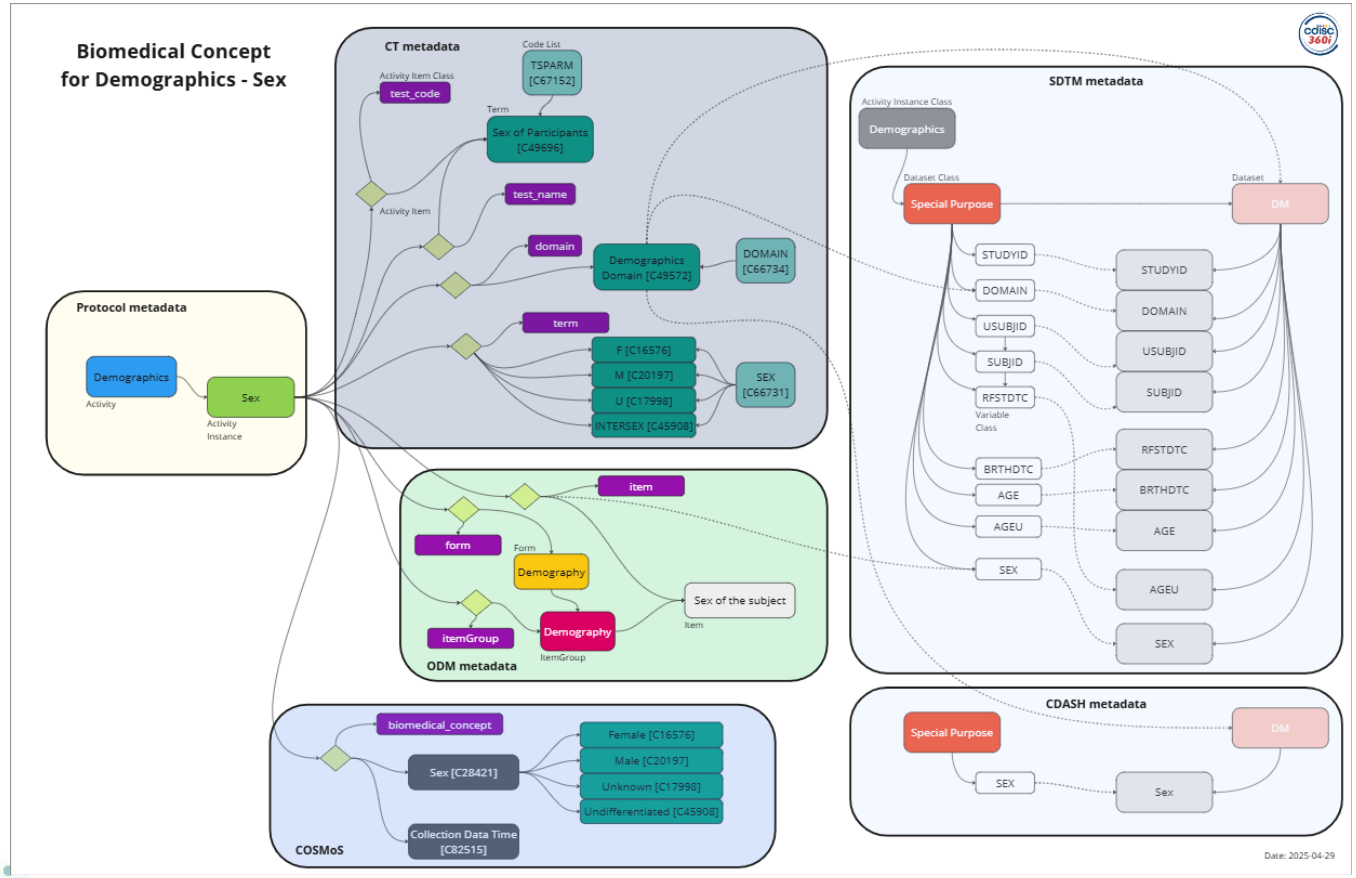
- **OSB BCs** include the semantic definition and SDTM specialisation linked to a **CDISC BC** including NCI.gov term identifiers
- **OSB BC** can be **sponsor defined**
- **OSB BC** include library sponsor definition of the **Activity name** used in protocol including valid **Activity Groupings**
- **OSB BC := Activity Concepts**



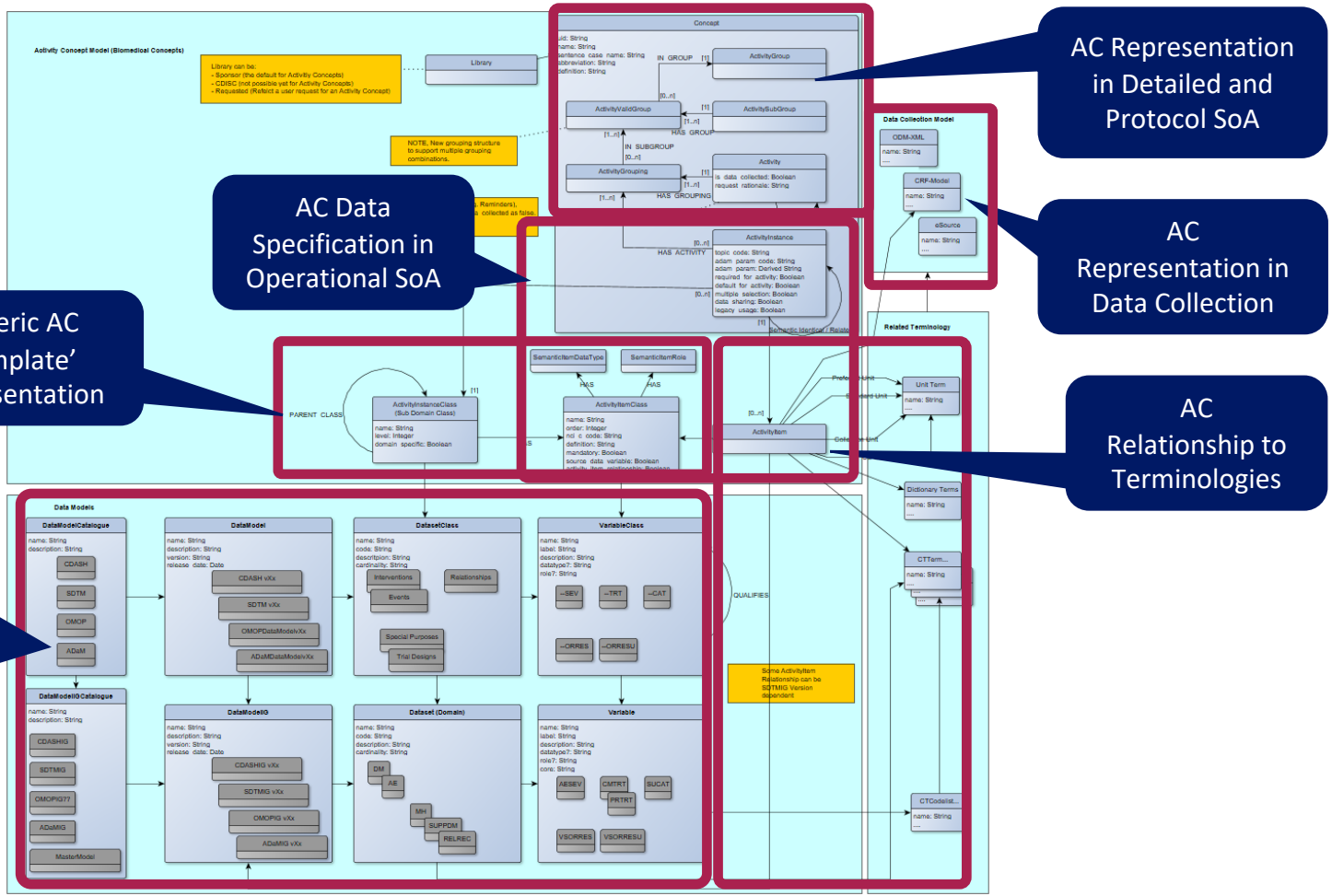
BC idea


BC Template
BC
test/identifier
result
quantity
coded
unit
method
position
Value
code
code
code
code

BC vision in OSB



Activity Concept (AC) data model in StudyBuilder



OpenStudyBuilder Activity Concept data model (BC)

ActivityGroup ActivitySubgroup	***CDISC BC:*** Seem to be similar a parent BC at a high level. Often demoed as a CRF form name. ***OSB AC:*** Grouping of activities. The activity group or subgroup level can be what you decide to show in the protocol schedule of activities. May be like a CRF form names, but not necessarily, the clinical term relevant to show in the protocol.
Activity	***CDISC BC:*** An action, undertaking, or event, which is anticipated to be performed or observed, or was performed or observed, according to the study protocol during the execution of the study. ***OSB AC:*** If relating to data collection, resulting in a semantic logical observation, this can depend on context and qualifiers have different identifications. If not related to data collection, then to a semantic specific activity. At the most detailed level as needed in protocol SoA
ActivityInstance	***CDISC BC:*** Similar to a SDTM specialisation (but for an ADaM PARAM). ***OSB AC:*** The specific identification of the semantic logical observation, this includes reference to context and qualifier values. Primary identification is for ADaM BDS PARAM/PARAMCD or column name in ADSL. Also include internal uid identification as well as internal topic code.
ActivityItem	***CDISC BC:*** Similar to SDTM Variable but can be connected to any data exchange standards. ***OSB AC:*** Linking to related data model variables as well as terminology codes.

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Process Overview
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Activities
Units
CRFs
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Template Instantiations
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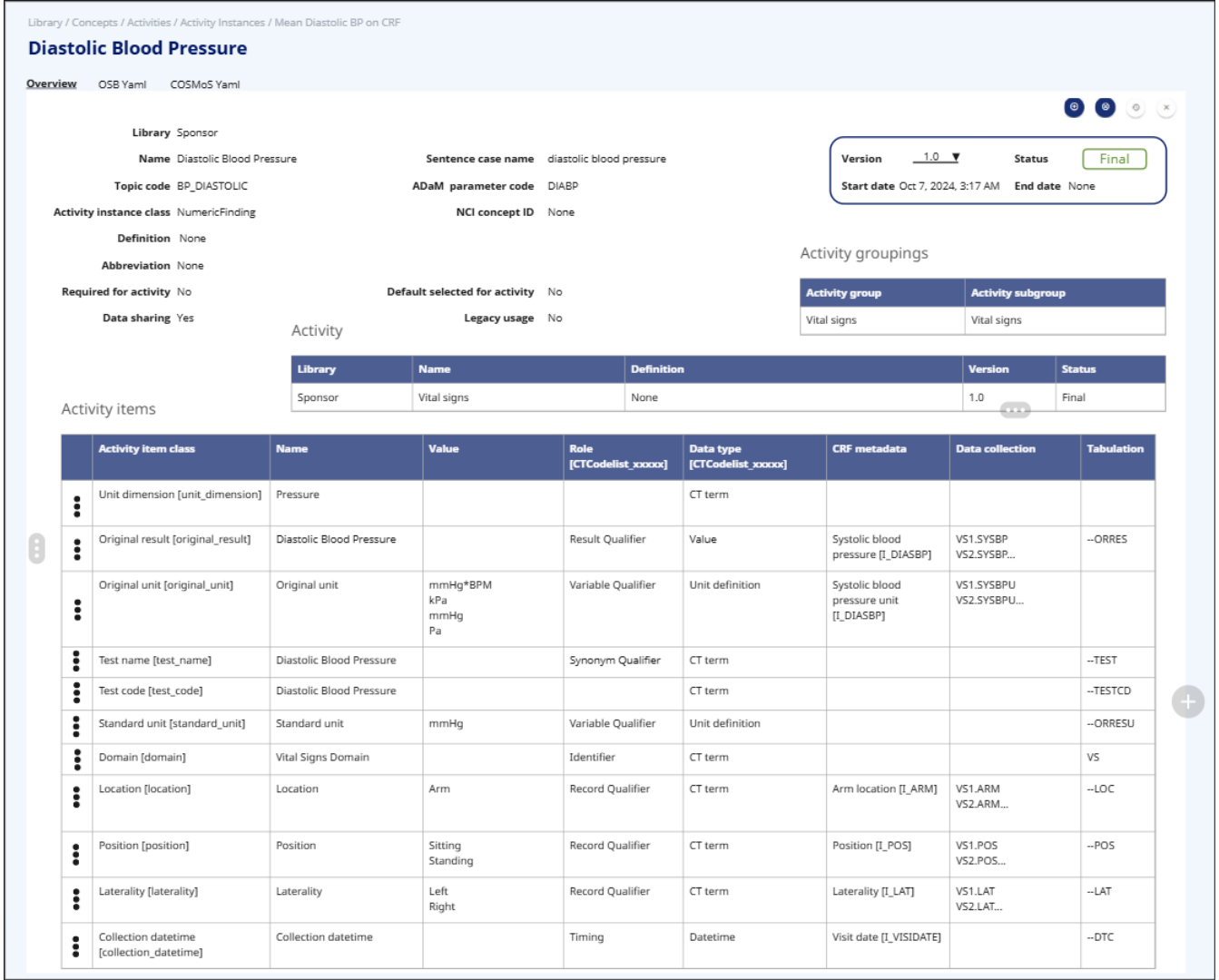
List

Systolic Blood Pressure

Overview | OSB YAML | COSMoS YAML

Name	Systolic Blood Pressure		
Sentence case name	systolic blood pressure		
Version	1.0	**Status**	Final
Start date	Apr 22, 2024, 1:15 PM	**End date**	None
Definition			
Activity instance class	NumericFinding		
Abbreviation		**Library**	Sponsor
NCI Concept ID			
ADaM parameter code	SYSBP	**Topic code**	BP_SYSTOLIC



Library / Concepts / Activities / Activity Instances / Mean Diastolic BP on CRF

Diastolic Blood Pressure

Overview | OSB Yaml | COSMoS Yaml

Library Sponsor
Name Diastolic Blood Pressure
Topic code BP_DIASTOLIC
Activity instance class NumericFinding
Definition None
Abbreviation None
Required for activity No
Data sharing Yes

Sentence case name diastolic blood pressure
ADaM parameter code DIABP
NCI concept ID None
Default selected for activity No
Legacy usage No

Version 1.0 **Status** Final
Start date Oct 7, 2024, 3:17 AM **End date** None

Activity groupings

Activity group	Activity subgroup
Vital signs	Vital signs

Activity

Library	Name	Definition	Version	Status
Sponsor	Vital signs	None	1.0	Final

Activity items

Activity item class	Name	Value	Role [CTCodelist_xxxxx]	Data type [CTCodelist_xxxxx]	CRF metadata	Data collection	Tabulation
Unit dimension [unit_dimension]	Pressure			CT term			
Original result [original_result]	Diastolic Blood Pressure		Result Qualifier	Value	Systolic blood pressure [I_DIASBP]	VS1.SYSBP VS2.SYSBP...	--ORRES
Original unit [original_unit]	Original unit	mmHg*BPM kPa mmHg Pa	Variable Qualifier	Unit definition	Systolic blood pressure unit [I_DIASBP]	VS1.SYSBPU VS2.SYSBPU...	
Test name [test_name]	Diastolic Blood Pressure		Synonym Qualifier	CT term			--TEST
Test code [test_code]	Diastolic Blood Pressure			CT term			--TESTCD
Standard unit [standard_unit]	Standard unit	mmHg	Variable Qualifier	Unit definition			--ORRESU
Domain [domain]	Vital Signs Domain		Identifier	CT term			VS
Location [location]	Location	Arm	Record Qualifier	CT term	Arm location [I_ARM]	VS1.ARM VS2.ARM...	--LOC
Position [position]	Position	Sitting Standing	Record Qualifier	CT term	Position [I_POS]	VS1.POS VS2.POS...	--POS
Laterality [laterality]	Laterality	Left Right	Record Qualifier	CT term	Laterality [I_LAT]	VS1.LAT VS2.LAT...	--LAT
Collection datetime [collection_datetime]	Collection datetime		Timing	Datetime	Visit date [I_VISIDATE]		--DTC

NeoDash reports to view Activity to SDTM Variables

neo4j Labs — neo4j://vm-db-fv7zbjhkehgyw.clinicalmdr-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

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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

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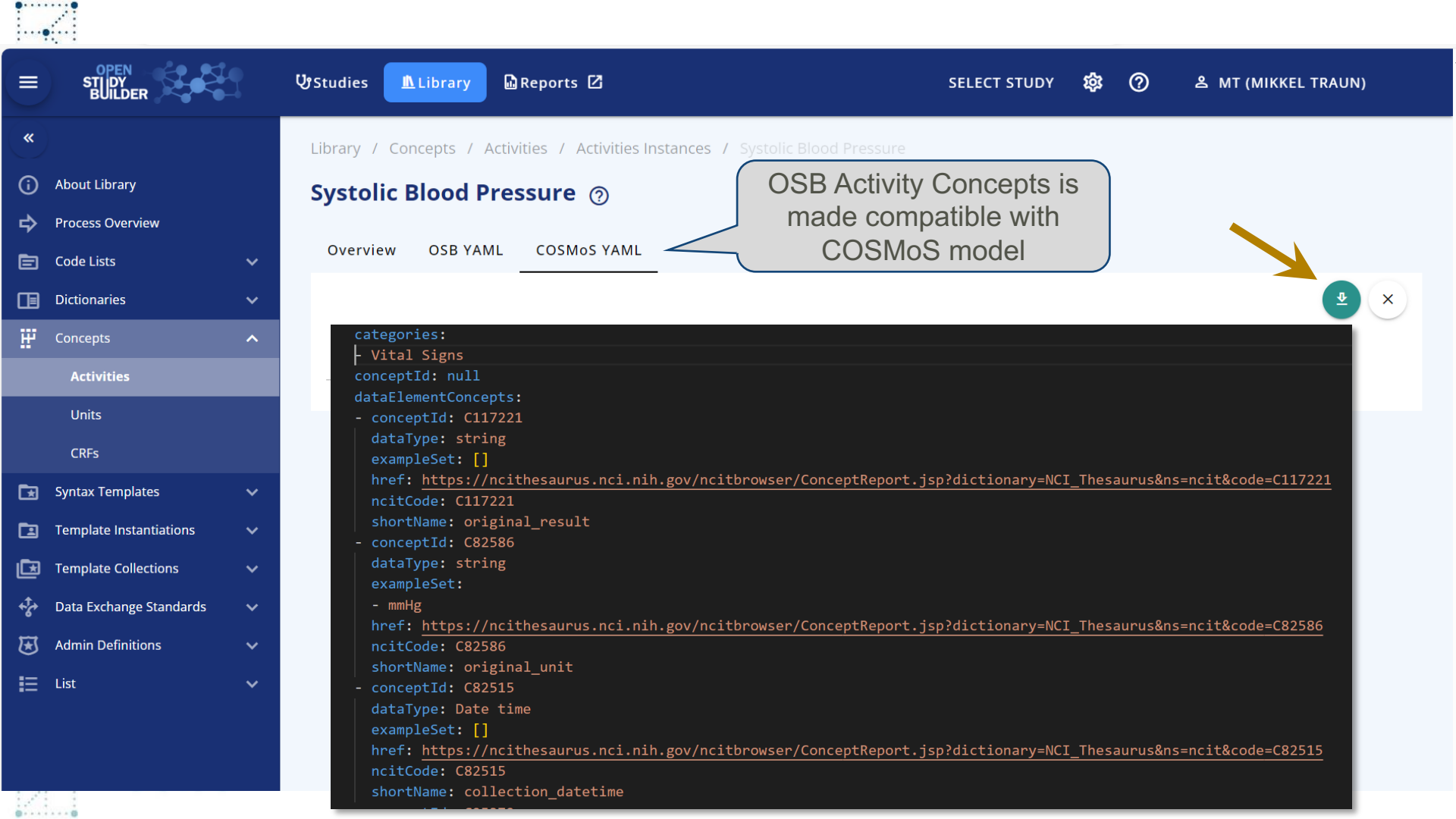
Activity mapped to SDTM

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


OPEN STUDY BUILDER
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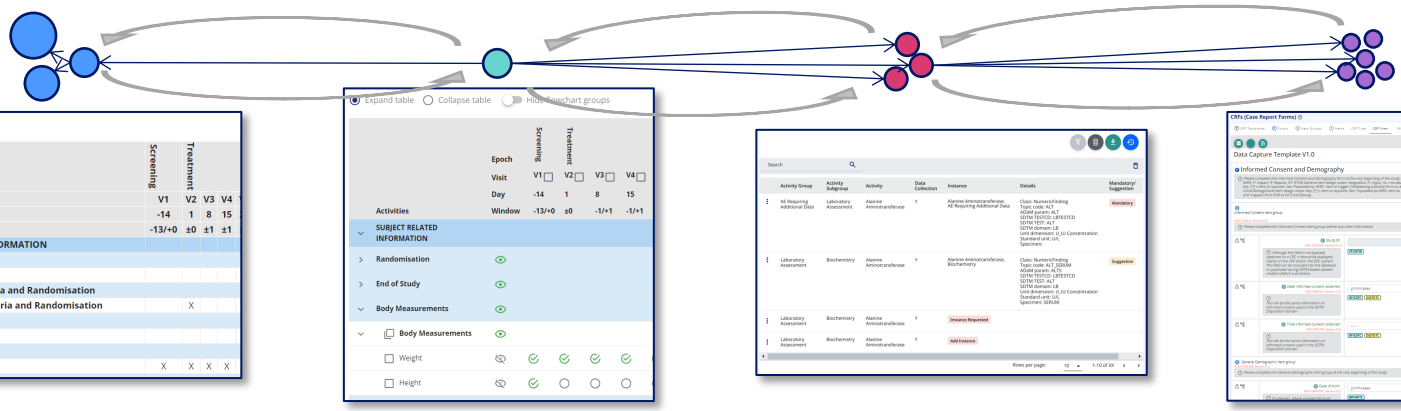
Library / Concepts / Activities / Activities Instances / Systolic Blood Pressure
Systolic Blood Pressure
Overview
OSB YAML
COSMoS YAML
OSB Activity Concepts is made compatible with COSMoS model
categories:
- Vital Signs
conceptId: null
dataElementConcepts:
- conceptId: C117221
dataType: string
exampleSet: []
href: https://ncithesaurus.nci.nih.gov/ncitbrowser/ConceptReport.jsp?dictionary=NCI_Thesaurus&ns=ncit&code=C117221
ncitCode: C117221
shortName: original_result
- conceptId: C82586
dataType: string
exampleSet:
- mmHg
href: https://ncithesaurus.nci.nih.gov/ncitbrowser/ConceptReport.jsp?dictionary=NCI_Thesaurus&ns=ncit&code=C82586
ncitCode: C82586
shortName: original_unit
- conceptId: C82515
dataType: Date time
exampleSet: []
href: https://ncithesaurus.nci.nih.gov/ncitbrowser/ConceptReport.jsp?dictionary=NCI_Thesaurus&ns=ncit&code=C82515
ncitCode: C82515
shortName: collection_datetime

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

Activity Concepts := Biomedical Concepts

- **Can be linked to from:**
  - Objectives
  - Endpoints
  - Criteria
  - Analysis Concepts
- **Will link to**
  - Protocol representation
  - Data Specification
  - Data Collection Specification

- **Will support automation in**
  - Protocol Document Generation
  - Data Collection system setup
  - Data ingestion verification
  - SDTM generation
  - ADaM generation

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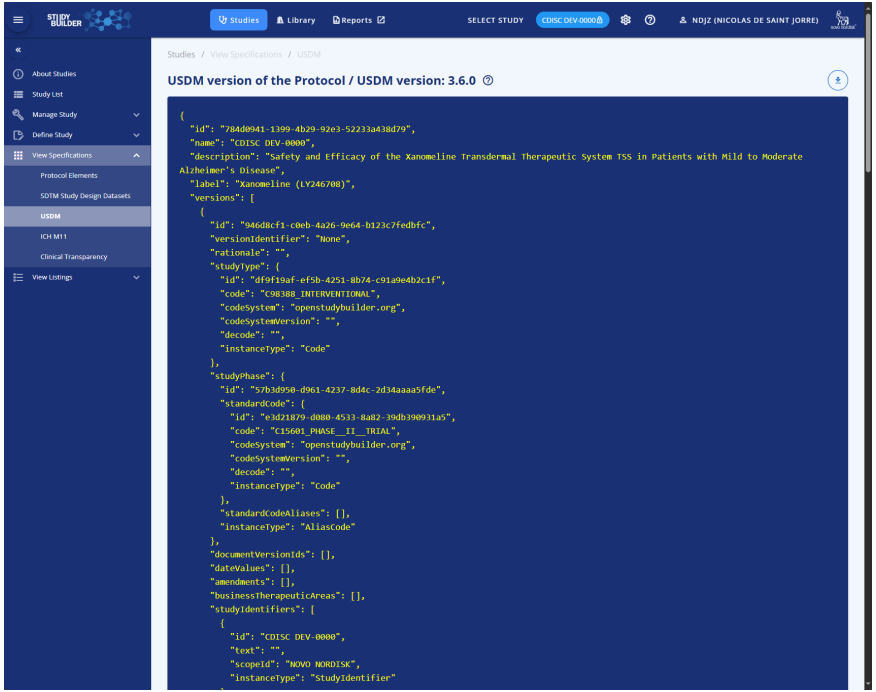
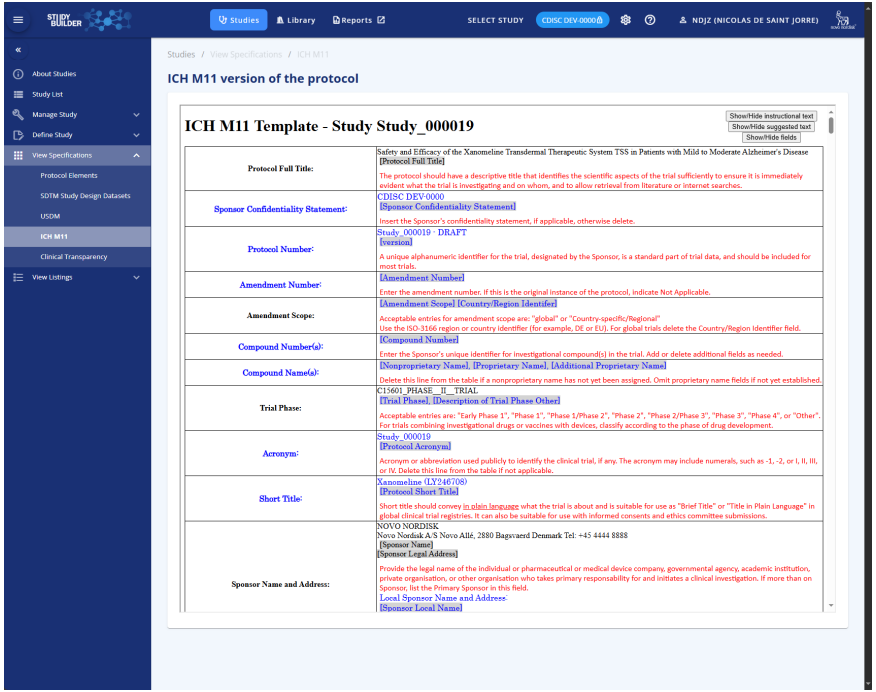
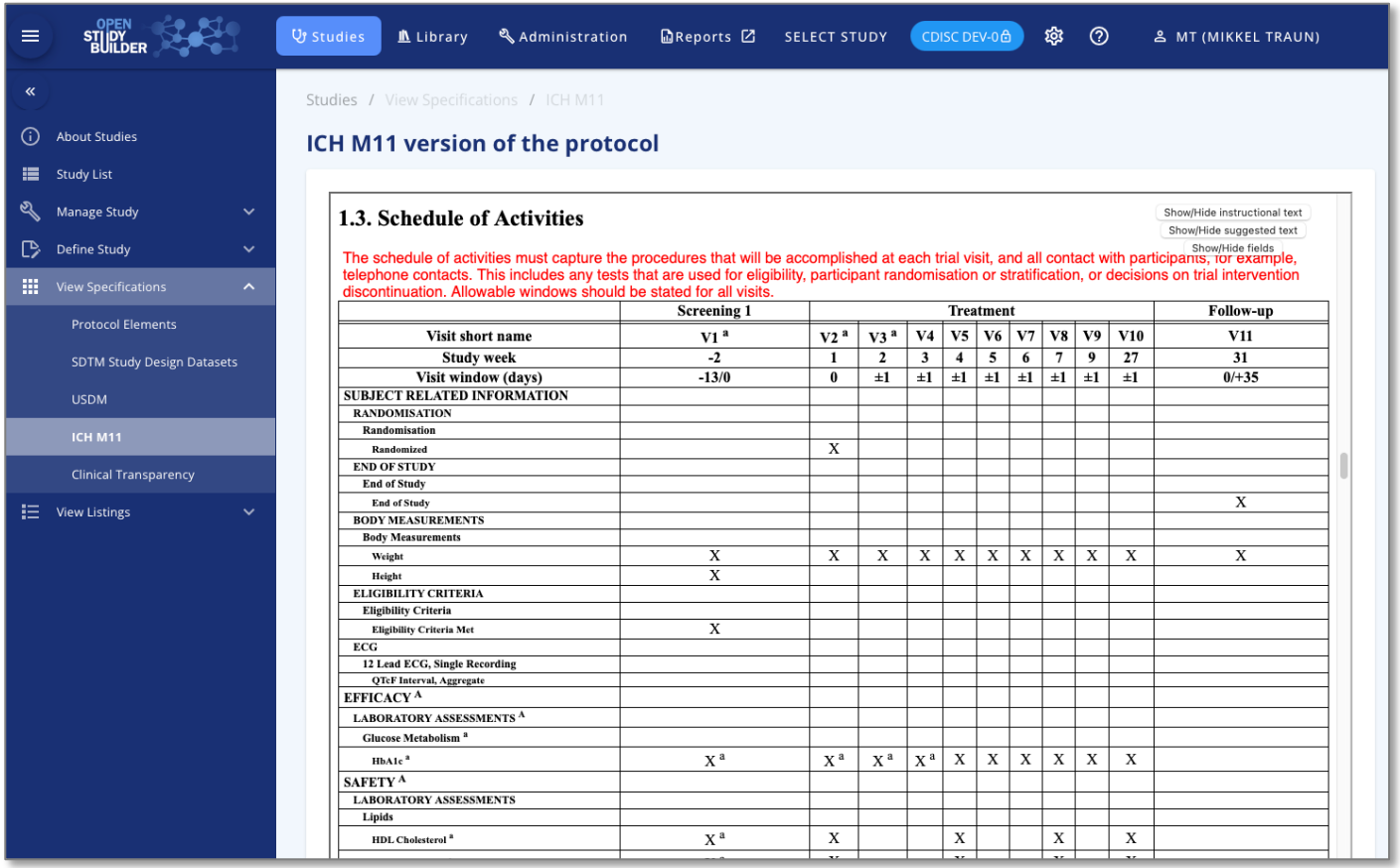
USDM and M11 as an export format





USDM and M11 as an export format - with SoA



	Screening 1	Treatment									Follow-up
Visit short name	V1 [a]	V2 [a]	V3 [a]	V4	V5	V6	V7	V8	V9	V10	V11
Study week	-2	1	2	3	4	5	6	7	9	27	31
Visit window (days)	-13/0	0	±1	±1	±1	±1	±1	±1	±1	±1	0/+35
SUBJECT RELATED INFORMATION											
RANDOMISATION											
Randomisation											
Randomized		X									
END OF STUDY											
End of Study											
End of Study											X
BODY MEASUREMENTS											
Body Measurements											
Weight	X	X	X	X	X	X	X	X	X	X	X
Height	X										
ELIGIBILITY CRITERIA											
Eligibility Criteria											
Eligibility Criteria Met	X										
ECG											
12 Lead ECG, Single Recording											
QTcF Interval, Aggregate											
EFFICACY [A]											
LABORATORY ASSESSMENTS [A]											
Glucose Metabolism [a]											
HbA1c [a]	X [a]	X [a]	X [a]	X [a]	X	X	X	X	X	X	
SAFETY [A]											
LABORATORY ASSESSMENTS											
Lipids											
HDL Cholesterol [a]	X [a]	X			X			X		X	

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Plans for OSB in CDISC 360i

Sponsor end-to-end Standards

- Import from CDISC Library
- Extensions, including sponsor BC's
- Share Sponsor BC's to CDISC curation

Build

- ODM.XML data collection specification including SDTM annotations
- Lab data specifications

Design

- Define Study Design and SoA
- Generate USDM
- Preview structured study design content in ICH M11 template

Run

- SDTM and ADaM data metadata specifications
- Data transformation and derivation metadata specification

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Thank You!

Questions or need more information

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OpenStudyBuilder contact: OpenStudyBuilder@gmail.com