

CRF in Study Builder

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1. StudyBuilder and CRF builder vision
2. Present vs. Future
3. CRF Export
4. StudyBuilder live demo
5. Data model
6. Graph DB live demo
7. Exercise

Agenda

OpenStudyBuilder: What is it?

STUDY BUILDER Studies Library ADD NEW STUDY SELECT STUDY JOHN DOE

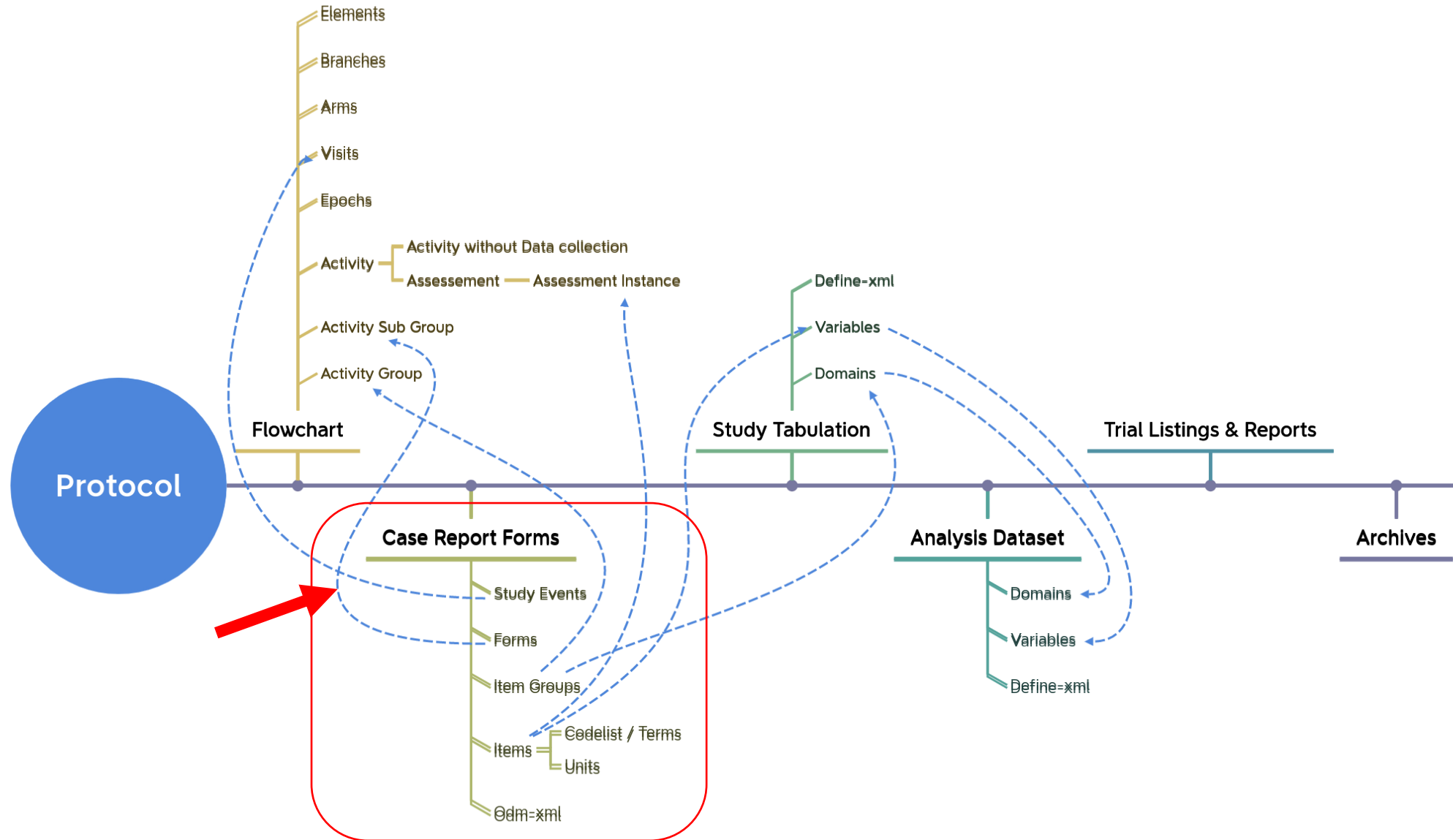
Library

The **Library** helps you manage the standards used in the StudyBuilder

- Process Overview**: Find schematic overviews of th...
- Code Lists**: Find the CDISC controlled term...
- Dictionaries**: Find relevant external diction...
- Concepts**: Find controlled listings of th...
- Syntax Templates**: View (or manage) the different...
- Template Instantiations**: See how the different template...
- Template Collections**: Lorem ipsum dolor sit amet, co...
- Data Exchange Standards**: See the complete master model ...
- List**: Find listings of all codes lis...

<https://studybuilder.clinicalmdr-dev.corp.azure-novonordisk.com/library/crfs>

The OpenStudyBuilder vision - What are we looking for?



CRF concept in the Library

The screenshot shows the 'Library / Concepts / CRFs' page in the Study Builder application. The interface includes a sidebar with navigation options like 'About Library', 'Process Overview', 'Code Lists', 'Dictionaries', 'Concepts', 'Activities', 'Units', and 'CRFs'. The main content area displays a table of CRF Forms with columns for Actions, Name, Repeating, Description, Version, and Status. A 'Select rows' toggle is visible at the top left of the table area.

Actions	Name	Repeating	Description	Version	Status
⋮	Informed Consent and Demography	yes		1.0	Final
⋮	Vital Signs	yes		1.0	Final
⋮	Medical History - Concomitant Illness	no		0.1	Draft
⋮	Administration of Investigational medicinal product	no		0.1	Draft
⋮	Adverse Event	no		0.1	Draft

Elements

CRF
Templates



Forms



Item
Groups



Items

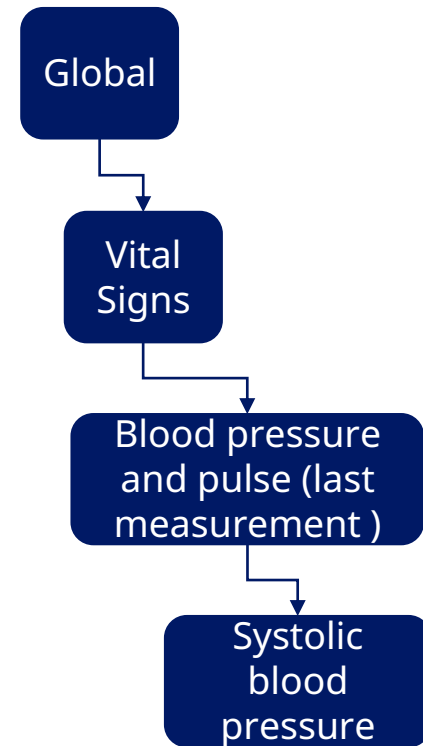
Example

Global

Vital
Signs

Blood pressure
and pulse (last
measurement)

Systolic
blood
pressure



CRF in Study Builder - Vision

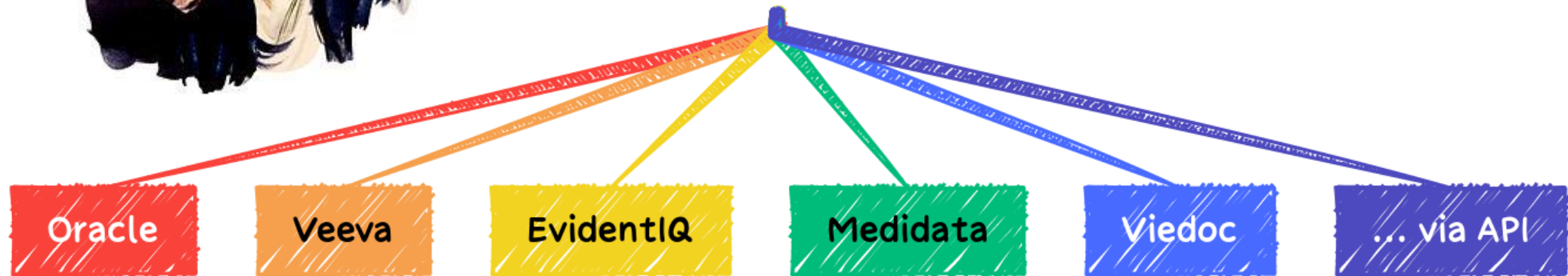
Library

- Re-create CRF library in Study Builder
 - Replacing Word-based CRF standards
 - Creation of trial specific CRF
- CRF export
 - Support creation of CRF library in ClinSpark
- Link CRF to metadata
 - Link CRF element to assessment data model

OpenStudyBuilder interfaces: **we want you!**



OpenStudyBuilder



Examples:

- Module to export to your format that can be imported to EDC
- Interfaces to specific programs

CRF now

Pancreatitis		LB=Laboratory Test Results	FA=Findings About	CE=Clinical Events
Non-Visit Related (AE)		LBCAT=AE REQUIRING ADDITIONAL DATA	FACAT=AE REQUIRING ADDITIONAL DATA	CECAT=AE REQUIRING ADDITIONAL DATA
			FAOBJ=PANCREATITIS	CETERM=PANCREATITIS
Pancreatitis (Pancrea)		[PANCREATITIS] - Repeating		
Study ID: NNXXXX-XXXX		PANCREATITIS		
	Pancreatitis event number [read-only]	0 < N3	CEREFID FAREFID LBREFID	RELREC: CE,FA
*	Related adverse event number	0 < N3	CELNKID FALNKID LBLNKID	RELREC: CE,LB RELREC: CE,AE
*	Did the subject have significant upper abdominal pain?	<input type="radio"/> No <input type="radio"/> Yes	FA PANCREATITIS ABDOMINAL PAIN	PANABPN
*	Were other signs/symptoms present during the course of the event?	<input type="radio"/> No <input type="radio"/> Yes	FAORRES when FATESTCD=PANSYMP FAORRES when FATESTCD=PANSYMP FAORRES when FATESTCD=PANSYMP FAORRES when FATESTCD=PANSYMP	NAUSEA VOMITING FEVER OTHER
		<input type="checkbox"/> Nausea <input type="checkbox"/> Vomiting <input type="checkbox"/> Fever <input type="checkbox"/> Other <input type="radio"/> Unknown	PANCREATITIS VOMITING PANCREATITIS NAUSEA PANCREATITIS FEVER PANCREATITIS OTHER SYMPTOM	FAORRES when FATESTCD=PANFEVER
			FASCAT=PANCREATITIS SIGNS AND SYMP	

- Any change is fully manual
- There is no linkage to metadata
- Possibilities to automate mock-up creation are very limited
- Changes of SDTMIG and CT requires manual impact assessment and corrections
- High risks of wrong annotations

CRF future

The image displays two side-by-side browser windows showing CRF forms for 'Study-4373'. The left window shows a 'Blank CRF' with two main sections: 'FORM : Informed Consent and Den' and 'FORM : General Demography'. The right window shows an 'SDTM Annotated CRF' for the same study, which is populated with data and includes a 'DS' (Data Set) tab. The right form is annotated with various SDTM variables and their relationships, such as 'RFICDTC, DSSTDTC when DSTESTCD = I.RFICTIMLAR1' and 'BRTHDTC when DSTESTCD = I.BRTHDTCARGUS'. The right form also includes a 'DM' (Data Model) tab and a list of radio button options for ethnicity: 'NOT HISPANIC OR LATINO', 'HISPANIC OR LATINO', 'NOT REPORTED', and 'UNKNOWN'.

ODM-XML



Home / Standards / Data Exchange / ODM

ODM-XML

Description Versions Education

ODM-XML is a vendor-neutral, platform-independent administrative data, reference data, and audit the language of choice for representing case r

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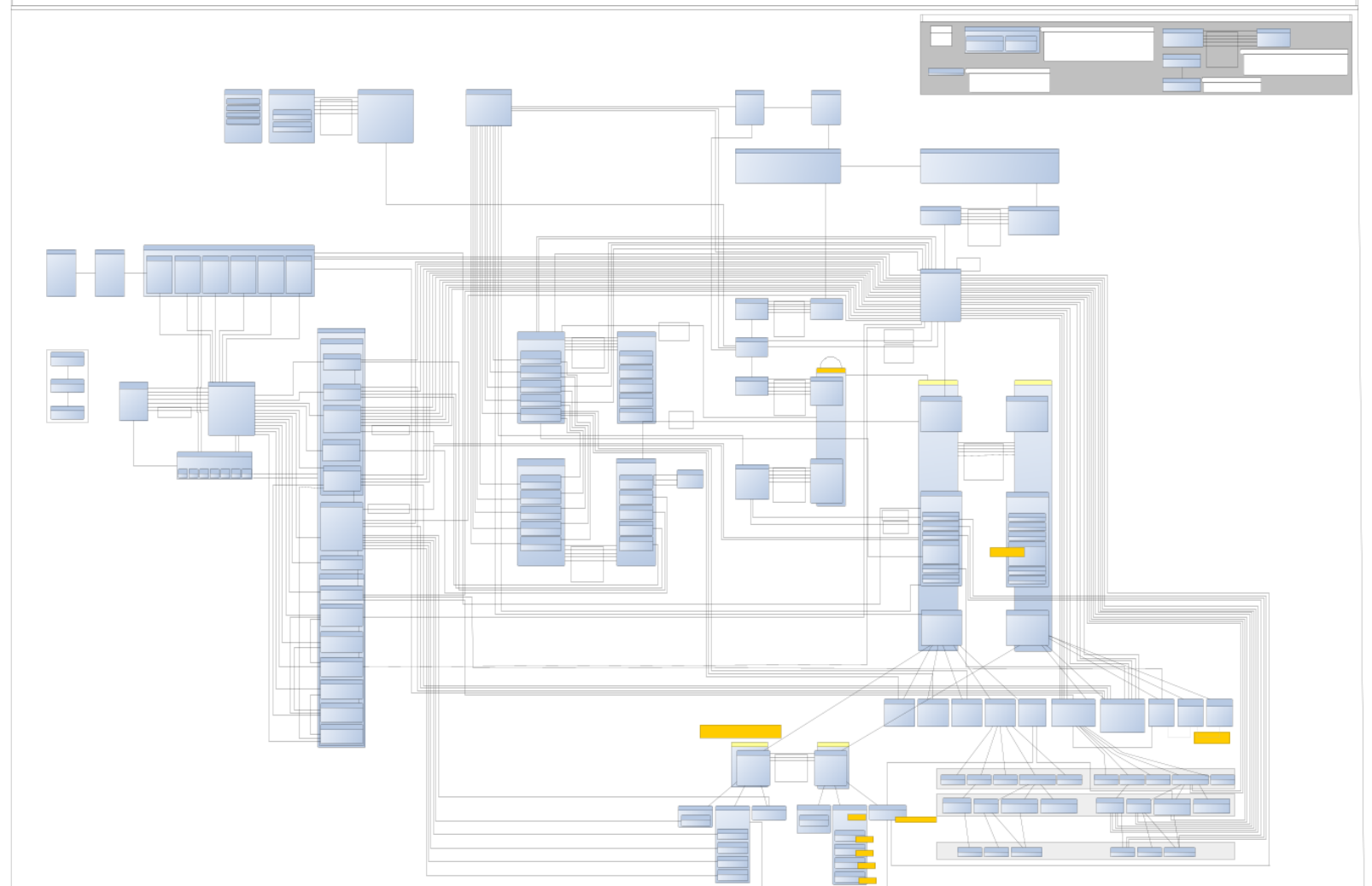
▼<ODM xmlns:odm="http://www.cdisc.org/ns/odm/v1.3" FileType="Snapshot" ODMVersion="1.3">
  ▼<Study OID="Study-4373">
    ▼<MetaDataVersion OID="MDV.0.1" Name="MDV.0.1" Description="Draft version">
      <FormDef OID="F.DM" Name="Demography Form" Repeating="No"/>
      ▼<FormDef OID="F.VS" Name="Vital Signs Form" Repeating="No">
        <ItemGroupRef ItemGroupOID="G.VS.VISDAT" OrderNumber="1" Mandatory="Yes"/>
        <ItemGroupRef ItemGroupOID="G.VS.VSBP" OrderNumber="2" Mandatory="Yes"/>
        <ItemGroupRef ItemGroupOID="G.VS.VS" OrderNumber="3" Mandatory="Yes"/>
      </FormDef>
      ▼<ItemGroupDef OID="G.VS.VISDAT" Name="Visit Date" Repeating="N" Purpose="Tabulation" SDTMDomain="VS">
        <ItemRef ItemOID="I.VISDAT" OrderNumber="1" Mandatory="Yes"/>
      </ItemGroupDef>
      ▼<ItemGroupDef OID="G.VS.VSBP" Name="Vital Signs for Blood Pressure" Repeating="N" Purpose="Tabulation" SDTMDomain="VS">
        <ItemRef ItemOID="I.SYSBP" OrderNumber="2" Mandatory="Yes"/>
        <ItemRef ItemOID="I.DIABP" OrderNumber="3" Mandatory="Yes"/>
        <ItemRef ItemOID="I.POSBP" OrderNumber="4" Mandatory="Yes"/>
        <ItemRef ItemOID="I.LATBP" OrderNumber="5" Mandatory="Yes"/>
        <ItemRef ItemOID="I.LOCBP" OrderNumber="6" Mandatory="Yes"/>
      </ItemGroupDef>
      ▼<ItemGroupDef OID="G.VS.VS" Name="Vital Signs" Repeating="N" Purpose="Tabulation" SDTMDomain="VS">
        <ItemRef ItemOID="I.PULSE" OrderNumber="7" Mandatory="Yes"/>
        <ItemRef ItemOID="I.WEIGHT" OrderNumber="8" Mandatory="Yes"/>
        <ItemRef ItemOID="I.HEIGHT" OrderNumber="9" Mandatory="Yes"/>
      </ItemGroupDef>
      ▼<ItemDef OID="I.VISDAT" Name="Visit date" DataType="Date" Length="10" SdtmVariable="SVSTDTC">
        ▼<Question>
          <TranslatedText xml:lang="en">Visit date</TranslatedText>
        </Question>
      </ItemDef>
      ▼<ItemDef OID="I.SYSBP" Name="Systolic blood pressure" DataType="integer" Length="3" SdtmVariable="VSORRES">
        ▼<Question>
          <TranslatedText xml:lang="en">Systolic blood pressure</TranslatedText>
        </Question>
        <MeasurementUnitRef MeasurementUnitOID="mmHg"/>
      </ItemDef>
  </Study>
</ODM>

```

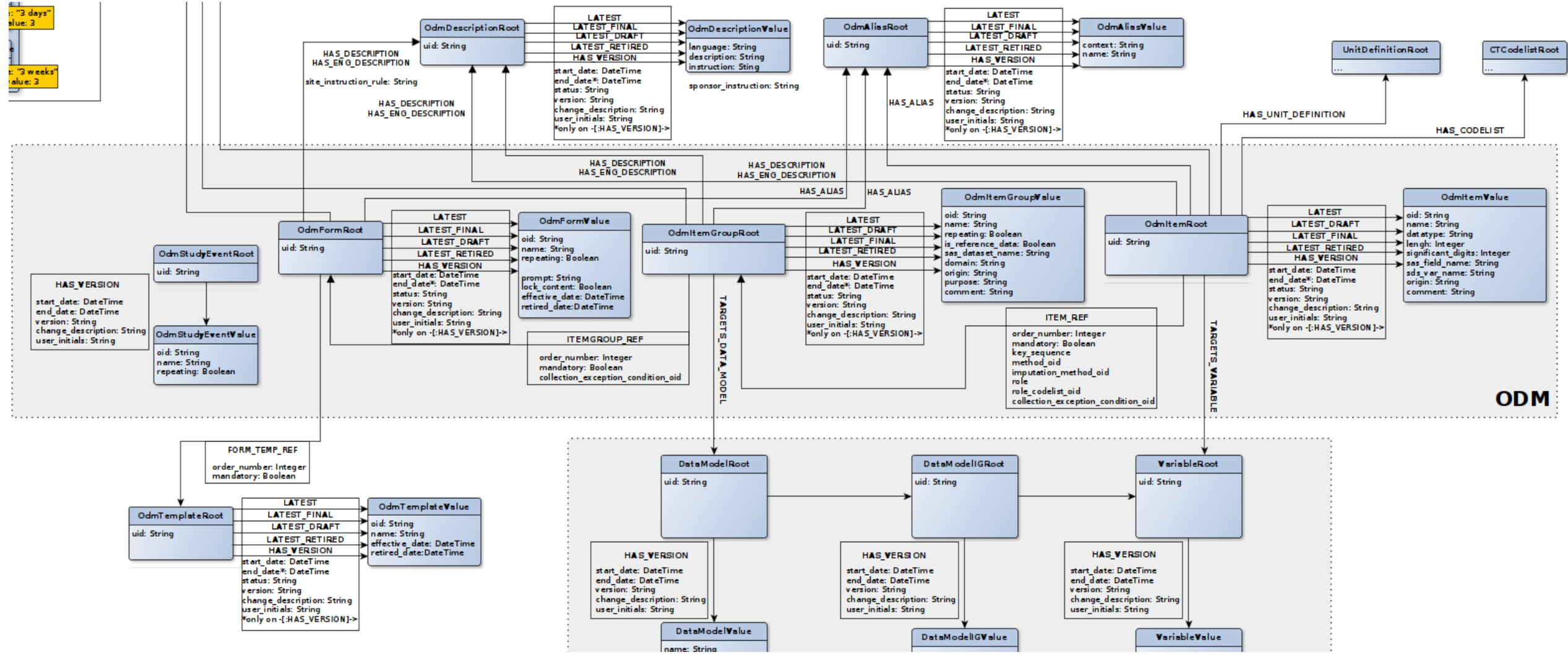
Demo OpenStudyBuilder

Data model

- The engine to ensure compatibility to future releases
- Requires vision since features will be added for years

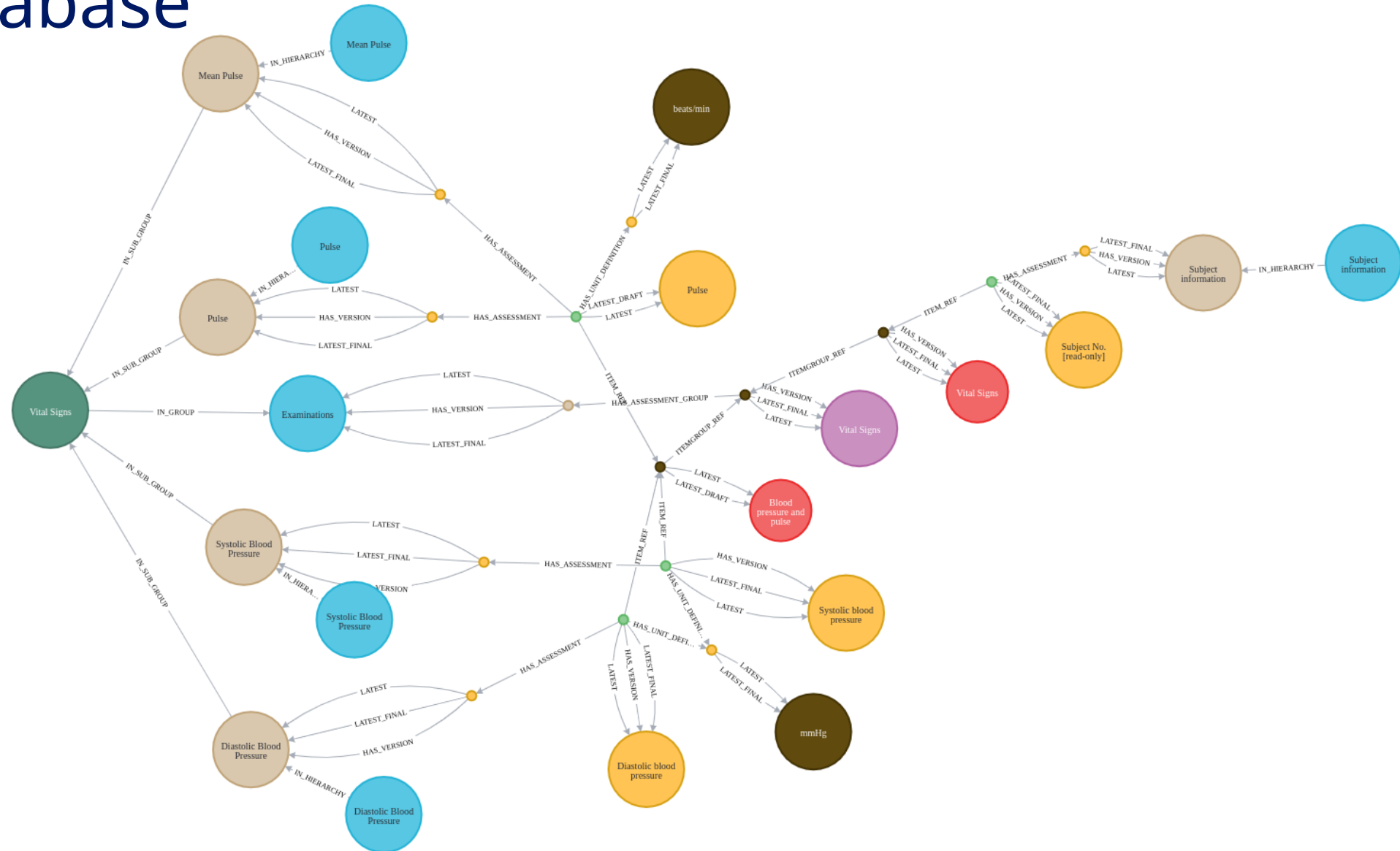


The CRF part...



Graph database

- Using graph database (Neo4j)
- Efficient representation
- Graphical linkage displayed
- Live demo





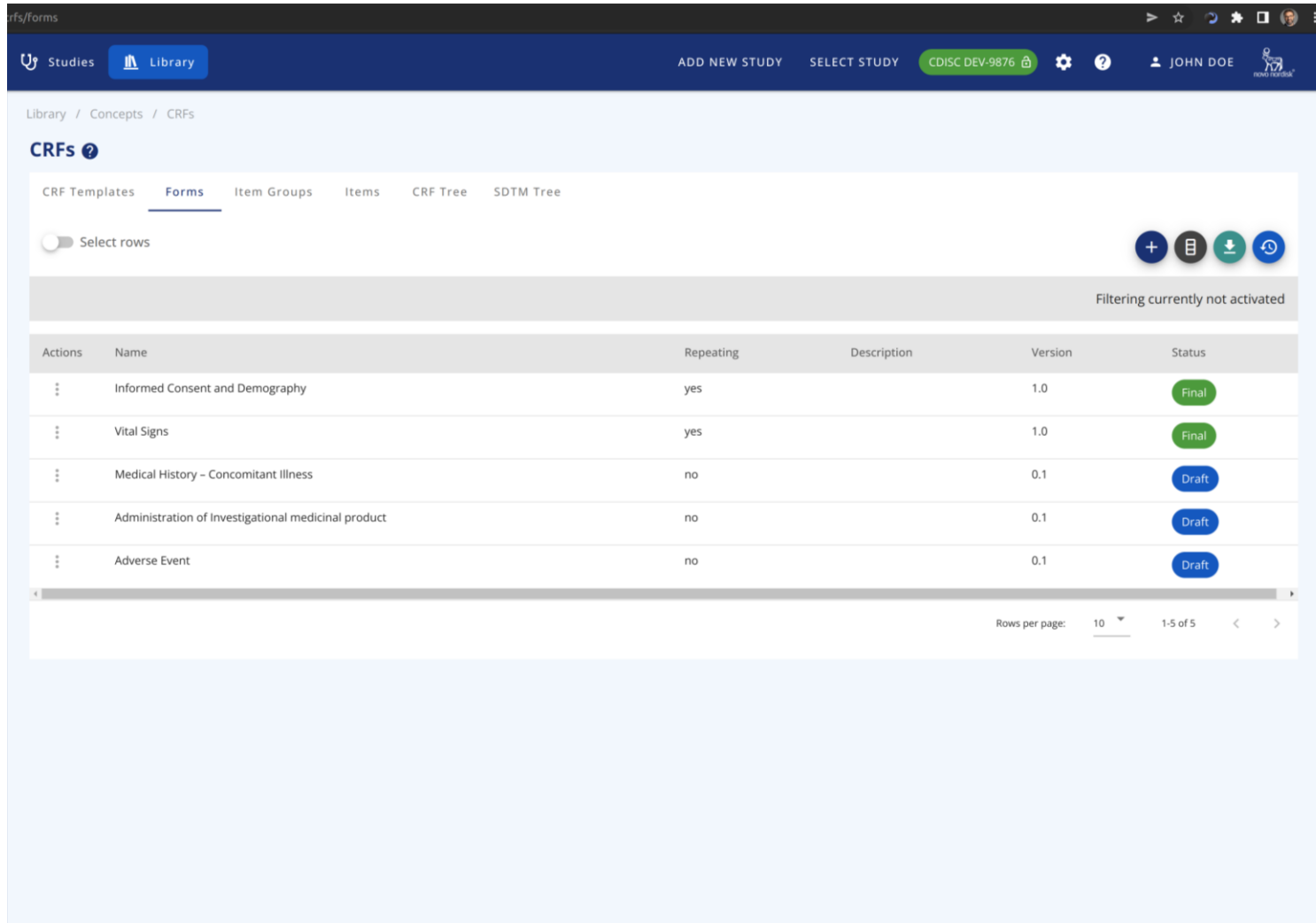
Break

Demo Graph DB

Beyond the CRF...

Linkage to clinical metadata

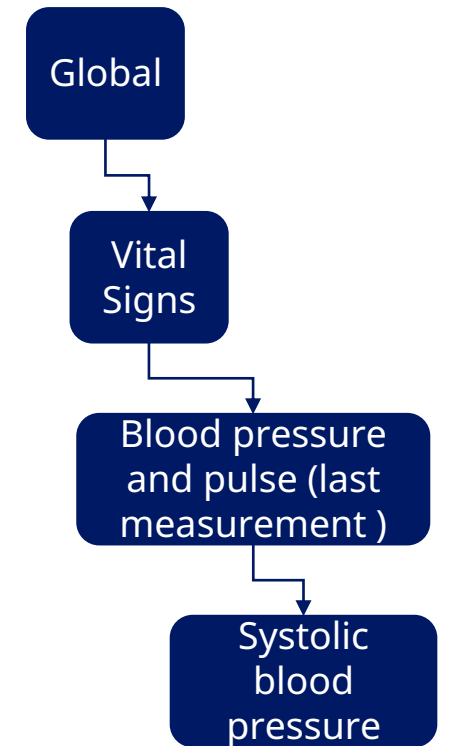
CRF Library to metadata



The screenshot shows the 'CRFs' section of a software interface. It features a navigation bar with 'Studies' and 'Library' tabs, and a header with 'ADD NEW STUDY', 'SELECT STUDY', and a study ID 'CDISC DEV-9876'. Below the navigation, there are tabs for 'CRF Templates', 'Forms', 'Item Groups', 'Items', 'CRF Tree', and 'SDTM Tree'. A 'Select rows' toggle is present. The main content is a table with columns: Actions, Name, Repeating, Description, Version, and Status. The table lists five CRF forms. At the bottom right, there is a 'Rows per page' dropdown set to 10 and a page indicator '1-5 of 5'.

Actions	Name	Repeating	Description	Version	Status
⋮	Informed Consent and Demography	yes		1.0	Final
⋮	Vital Signs	yes		1.0	Final
⋮	Medical History - Concomitant Illness	no		0.1	Draft
⋮	Administration of Investigational medicinal product	no		0.1	Draft
⋮	Adverse Event	no		0.1	Draft

Example



Linking to different versions of standard models

⋮ CRFs / Forms / Link Form with Data Model

CRFs

Models

F Demographic Form

M CDASH Model 1.0

IG CDASHIG 2.0

M CDASH Model 1.1

IG CDASHIG 2.1

IG CDASH SAE Supplement 2.0

M CDASH Model 1.2

IG CDASHIG 2.2

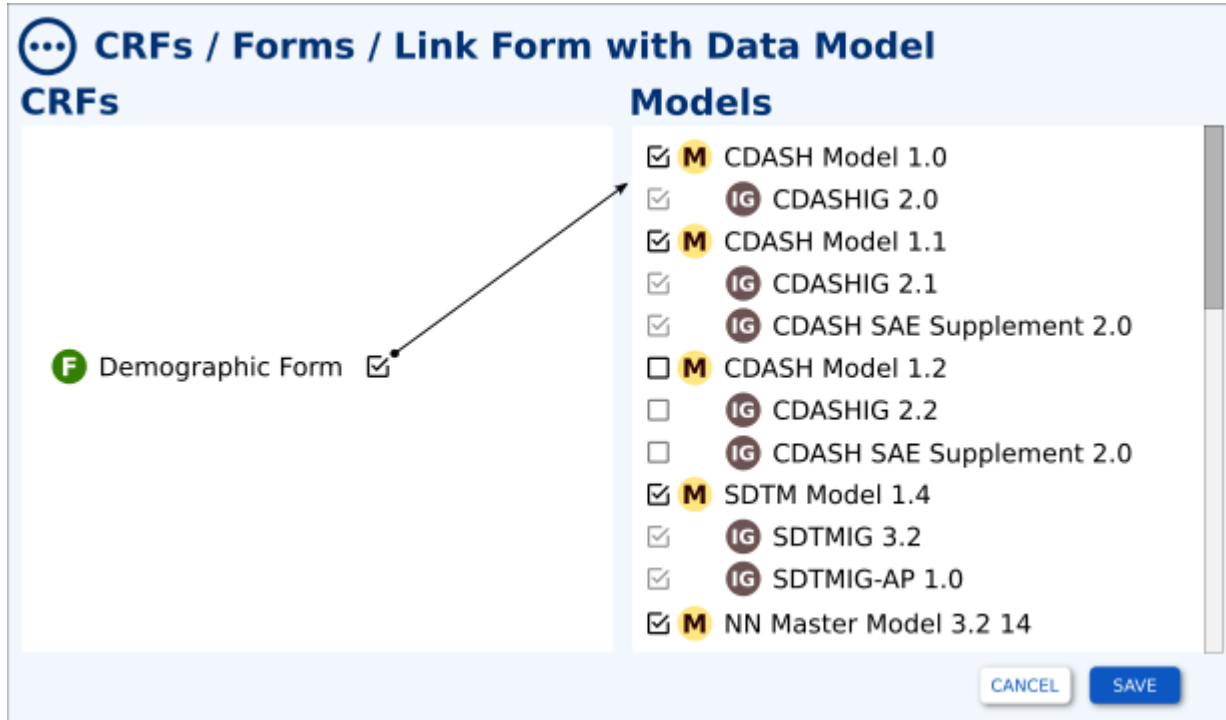
IG CDASH SAE Supplement 2.0

M SDTM Model 1.4

IG SDTMIG 3.2

IG SDTMIG-AP 1.0

M NN Master Model 3.2 14



⋮ CRFs / Item Groups / Link Form with Data Model

CRFs

Models

G Vital Signs Group

M CDASH Model 1.0

IG CDASHIG 2.0

M CDASH Model 1.1

IG CDASHIG 2.1

IG CDASH SAE Supplement 2.0

M CDASH Model 1.2

IG CDASHIG 2.2

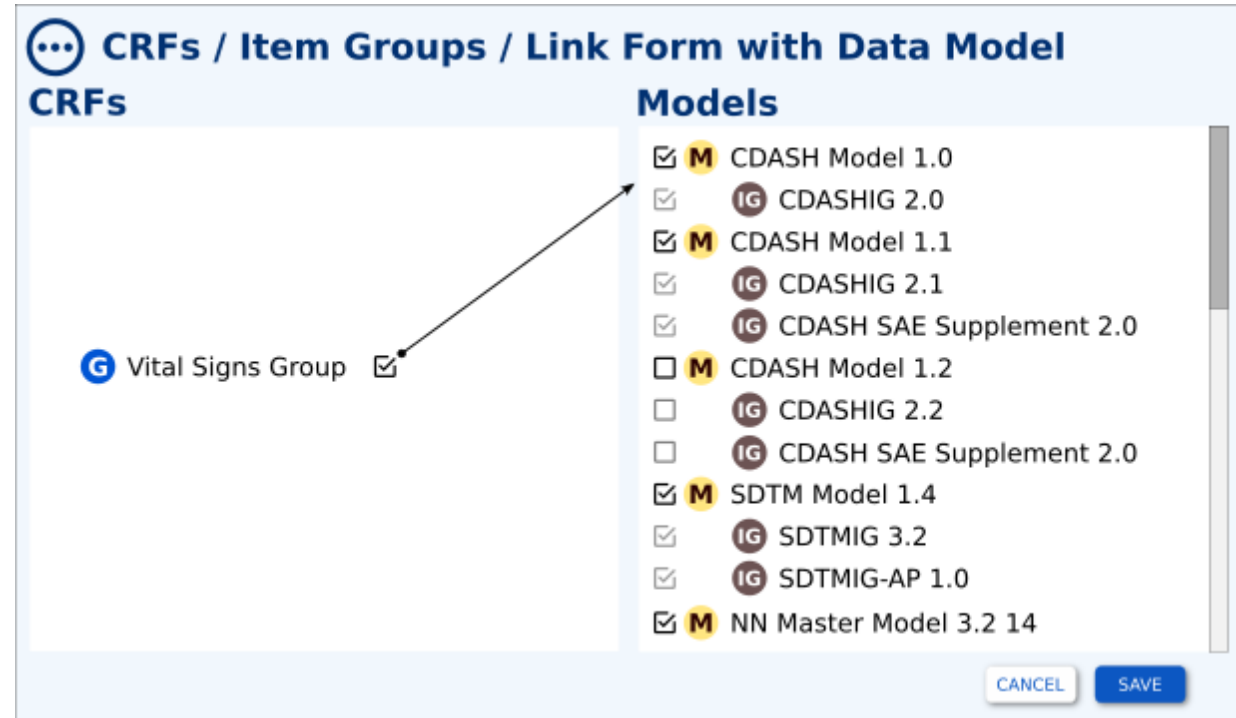
IG CDASH SAE Supplement 2.0

M SDTM Model 1.4

IG SDTMIG 3.2

IG SDTMIG-AP 1.0

M NN Master Model 3.2 14























The SDTM Tree page

Library / Concepts / CRFs / SDTM Tree

CRFs / SDTM Tree

CRF Templates Forms Item Groups Items CRF Tree SDTM Tree Alias

Domains/Variables	Version	Status	Link
V  DM - Demographic Domain	1.0		
 Birth Date	1.0		
 Sex	2.0		
 Age	1.0		
.....			
V  VS - Vital Signs Domain	1.0		
 VSORRES	1.0		
 VSORRESU	2.0		
 VSLOC	1.0		
.....			

Linking to study metadata – Protocol to CRFs

The image displays three screenshots of a software interface for linking study metadata to CRFs. Each screenshot shows a list of CRFs on the left and a list of activities on the right, with checkboxes for selection.

Top Left Screenshot: CRFs / Forms / Link Form with Activities Group

- CRFs:** Demographic Form (checked)
- Activities Group:**
 - Demographic (checked)
 - General Demography (checked)
 - Examinations (unchecked)
 - Vitals Signs (unchecked)
 - Body Measurements (unchecked)
 - ECG (unchecked)
 - Physical Examination (unchecked)
 - Glucose Metabolism (unchecked)
 - Study Compounds (unchecked)
 - Laboratory Assessments (unchecked)

Top Right Screenshot: CRFs / Item Groups / Link Item Group with Activities

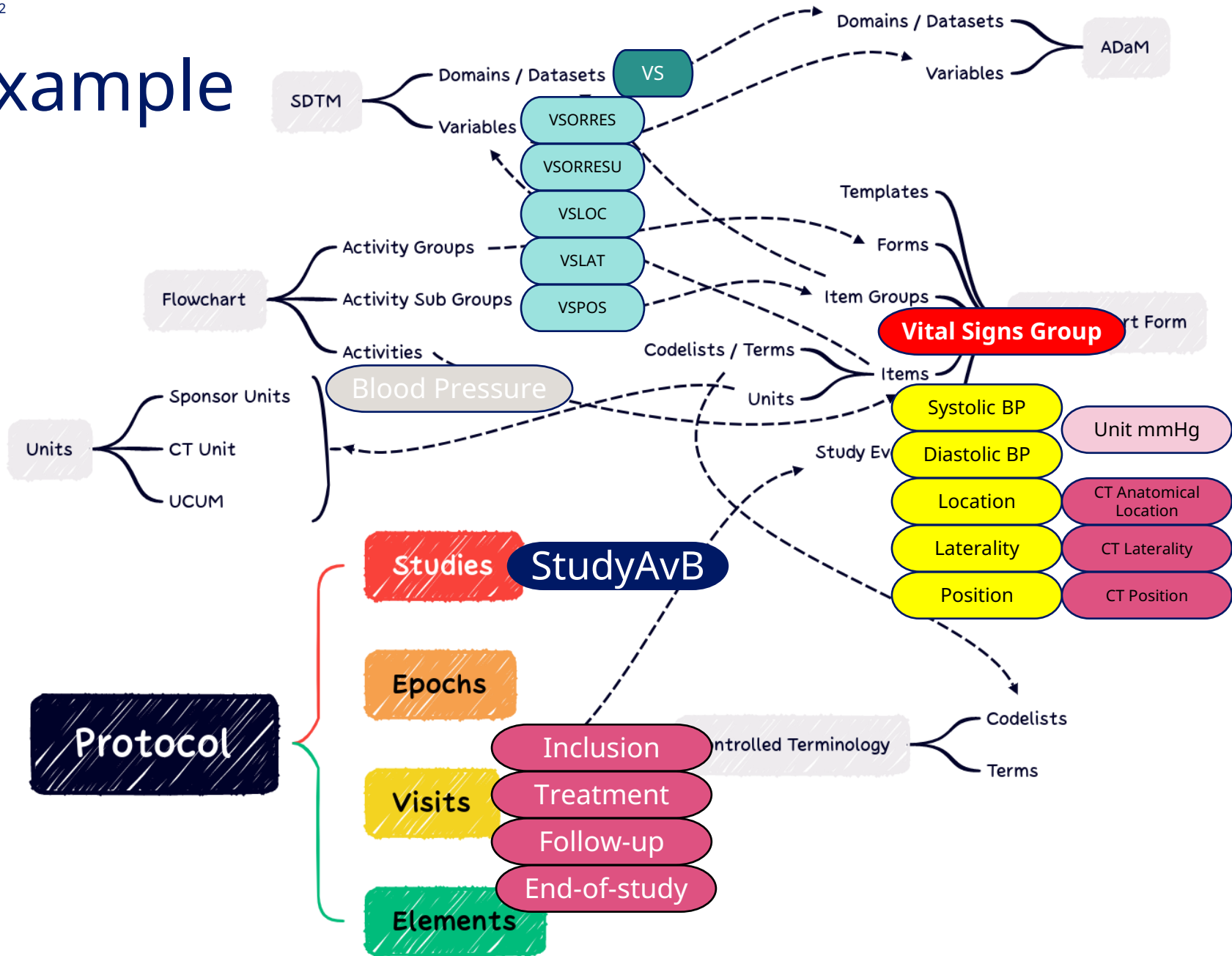
- CRFs:** Vital Signs Group (checked)
- Activities Sub-group:**
 - Demographic (unchecked)
 - General Demography (unchecked)
 - Examinations (checked)
 - Vitals Signs (checked)
 - Body Measurements (unchecked)
 - ECG (unchecked)
 - Physical Examination (unchecked)
 - Glucose Metabolism (unchecked)
 - Study Compounds (unchecked)
 - Laboratory Assessments (unchecked)

Bottom Screenshot: CRFs / Items / Link Item with Activities

- CRFs:** Birth Date (checked)
- Activities:**
 - Date of birth (checked)
 - Appearance in U-wave (unchecked)
 - Sex (unchecked)
 - Conduction finding (unchecked)
 - ECG Overall Interpretation (unchecked)
 - ECG abnormality (unchecked)
 - ECG infarction location (unchecked)
 - Systolic blood pressure (unchecked)
 - Diastolic blood pressure (unchecked)
 - Body Length (unchecked)
 - Body Weight (unchecked)

Buttons for CANCEL and SAVE are visible at the bottom right of each screenshot.

Example



Example:
To demonstrate the superiority of Drug A relative to Drug B on Blood Pressure (BP)

Exercise

- CRF annotations
 - FORM
 - ITEMGROUP
 - ITEM
- SDTM linkage
 - Topic variables
 - Qualifiers variables
- Exercise

Vital Signs (VS)	
Trial ID: NNXXXX-XXXX	
<Visits A, B>: If abnormal, clinically significant, record in the Medical History/Concomitant Illness form (MedHx/ConIll). If medication is taken remember to record in the Concomitant Medication form (CM).	
<Visits X to Y>: Any clinically significant deterioration of a pre-existing condition as well as any new clinically significant sign, symptom or illness is considered an adverse event. Complete an Adverse Event form (AE). If medication is taken remember to record in the Concomitant Medication form (CM).	
* Date of examination	Req☑/Req☑/Req☑ (2020-2030)
Blood pressure and pulse – Second last measurement	
* Blood pressure	Systolic / Diastolic N3 mmHg / N3 mmHg
Arm used to measure blood pressure	<input type="radio"/> Right arm <input type="radio"/> Left arm
* Pulse	N3 beats/min
Blood pressure and pulse – Last measurement	
* Blood pressure	Systolic / Diastolic N3 mmHg / N3 mmHg
Arm used to measure blood pressure	<input type="radio"/> Right arm <input type="radio"/> Left arm
Mean of blood pressure and pulse	
* Mean blood pressure (System calculated)	Systolic / Diastolic N3 mmHg / N3 mmHg
Mean blood pressure	Systolic / Diastolic N3 mmHg / N3 mmHg
* Mean pulse (System calculated)	N3 beats/min
Mean pulse	N3 beats/min

Discussion about exercise and what to bring to plenum

Comments taken during the Workshop

- Challenge: How can we have ODM as the default EDC format?
- Visit matrix can be defined differently between Vendors... How can we address that?
- A setup for Vendor Extension in the ODM format is needed
- Amendments need to be considered at the level of the CRFs with link with the Protocol
- The ODM definition should allow very specific display options (like using bold in clinical questions...) -> This should work with html
- The ODM version 2.0 should be managed by the OpenStudyBuilder – This will allow the creation of more complex Study Definition

Considerations for MDR-CRFs next steps

Strengths

Project

- Integration between Protocol and CRFs makes a lot of sense
- Link between CRF and assessment model enabling for example the generation of define.xml was considered very promising

System

- Amendments need to be considered at the level of the CRFs with link to the Protocol

Opportunities

Project

- The ODM version 2.0 should be managed by the StudyBuilder – This will allow the creation of more complex Study Definition

System

- A setup for Vendor Extension in the ODM format is needed
- Add Edit Checks rule in the ODM

Weaknesses

Project

- Formal Biomedical Concept is not established fully

System

- The ODM definition should allow very specific display options (like using bold in clinical questions...)

Threats

Project

- How can we make ODM the default CRF format

System

- Visit matrix can be defined differently between Vendors... How can we address that?

Questions

