

Digital Data Flow

WITH STANDARDS – UNLOCK THE POWER OF DATA

This initiative aims to move the drug development process from a current state of manual, study start-up asset creation (i.e. Case Report Forms, Procedure Manuals, Statistical Analysis Plans, and Schedule of Activities) to a future state of fully automated, dynamic, study start-up readiness via an open-sourced, vendor-agnostic technical solution that will reduce cycle times and improve data quality for sponsors, third-party providers, sites and regulators.

Links

- Transcelerate Digital Data Flow page
 - <https://www.transceleratebiopharmainc.com/initiatives/digital-data-flow/>
- CDISC DDF Page
 - <https://www.cdisc.org/ddf>
- CDISC Github
 - <https://github.com/cdisc-org/DDF-RA>

Main Elements

- Reference Architecture (CDISC)
 - Unified Study Definitions Model (USDM)
 - Controlled Terminology (CT)
 - Application Programming Interface (API)
 - Implementation Guide (IG)
- Reference Implementation (Accenture), the Study Definitions Repository (SDR)



2022

US

INTERCHANGE

26-27 OCTOBER | AUSTIN



CDISC's Activities on DDF, Benefits for the Community, and Looking Ahead

Presented by D Iberson-Hurst
Partner d4k & CDISC DDF Product Owner

Project Background (see slide deck above)

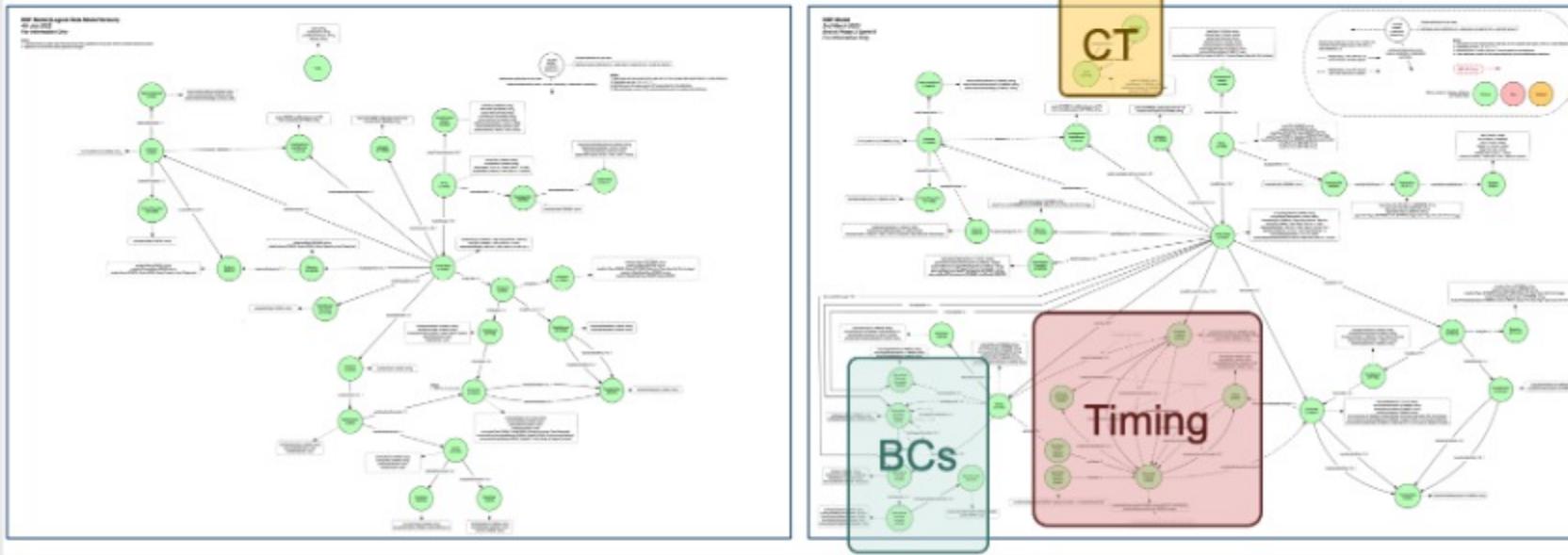
- Phase 1 -> USDM V1
- Phase 2 -> USDM V2
- Phase 3 -> USDM V3
- **In development until end of 2023**
- **V3 to be published April 2024 approx.**

MIRO Board Status

- Used for technical run throughs
- Staging zone for Implementation Guide content
- **Status: Informational. Updated regularly**

Phase One and Two

CDISC DDF Phase One v Two



Phase One & Two

- Small slide deck re Phase One and Two

Changes Between Phase One and Two

- Addition of timing within studies to schedule activities accurately
- Addition of Biomedical Concepts (BCs)
- Improvements to CT handling
- Additional attributes in some classes to support TCB CPT

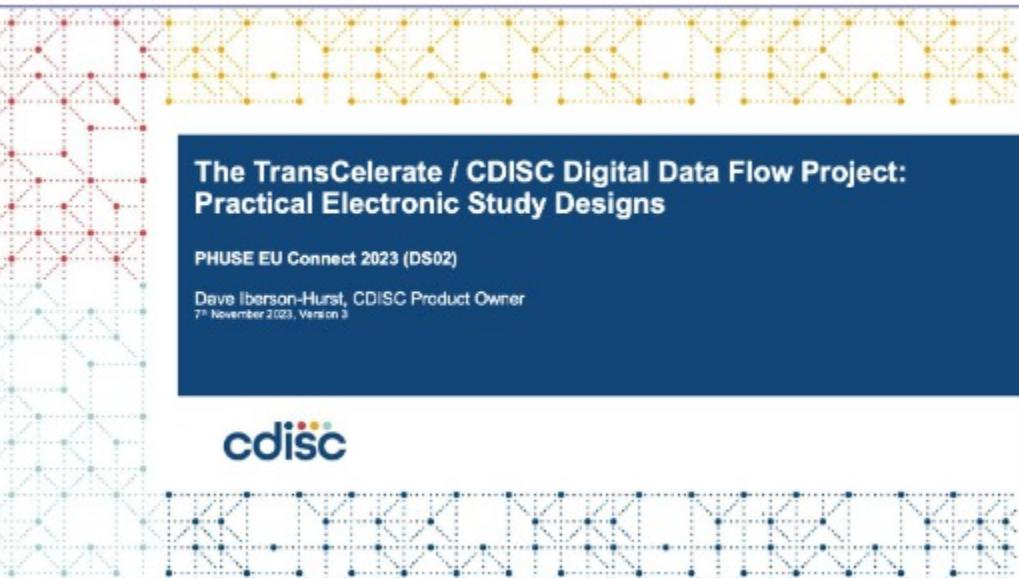
Phase Three

Come to the session at PHUSE EU Connect 2023

- Tuesday 7th November, 11:30am, Hall 10A

Tuesday 7 November

Time (GMT)	Hall 6a	Hall 7	Hall 9	Hall 10A
06:30	PHUSE 5k Run Around Birmingham – Meet Outside the ICC All attendees welcome			
09:00 - 10:00	Keynote Speaker – Gareth Thomas Plenary Room – Hall 1			
10:30-11:00	Morning Break			
11:00-11:30	TT06: Red Pill or Blue Pill? Assessing the Impact of Artificial Intelligence on Pharmaceutical Programming Katalyze Data	PM04: Navigating Unprecedented Challenges: Journey Through a Pandemic and International Conflict Varimed	Panel Discussion Let's Discuss Open Source Openly: A New Path in Pharma	Connect Theme Presentations (DS) Digital Data Flow – From Vision to Reality DS01: ICH M11 Clinical Electronic Structured Harmonized Protocol (CeSHarP) and CDISC: Making the Electronic Protocol a Reality CDISC
11:30-12:00	TT14: Automation and Orchestration of Data Science Applications Using OpenAPI Enimo	PM05: An Agile Approach to Onboarding GSK		DS02: The TransCelerate/CDISC Digital Data Flow Project: Practical Electronic Study Designs data-knowledge & CDISC DS03: The Digital Protocol Is Just the Beginning. Or Is It? Infrom
12:00-12:30	TT16: Taking Down the Fence Between Biostatistics and Medical Writing GSK	PM06: Statistical Programming – Hiring Mission Made Possible Johnson & Johnson		

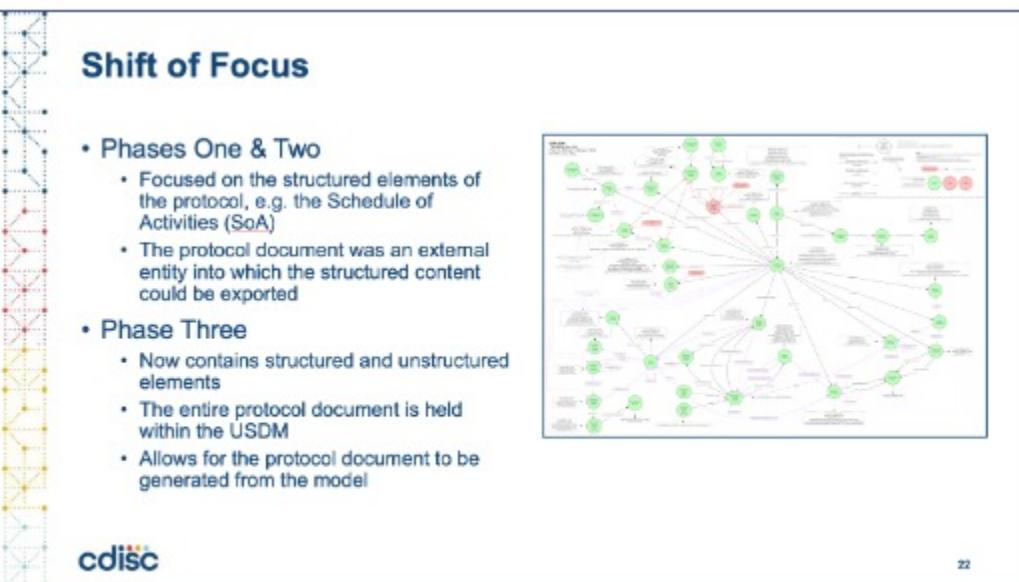


The TransCelerate / CDISC Digital Data Flow Project:
Practical Electronic Study Designs

PHUSE EU Connect 2023 (DS02)

Dave Iberson-Hurst, CDISC Product Owner
7th November 2023, Version 3

cdisc



Shift of Focus

- Phases One & Two
 - Focused on the structured elements of the protocol, e.g. the Schedule of Activities (SoA)
 - The protocol document was an external entity into which the structured content could be exported
- Phase Three
 - Now contains structured and unstructured elements
 - The entire protocol document is held within the USDM
 - Allows for the protocol document to be generated from the model

cdisc

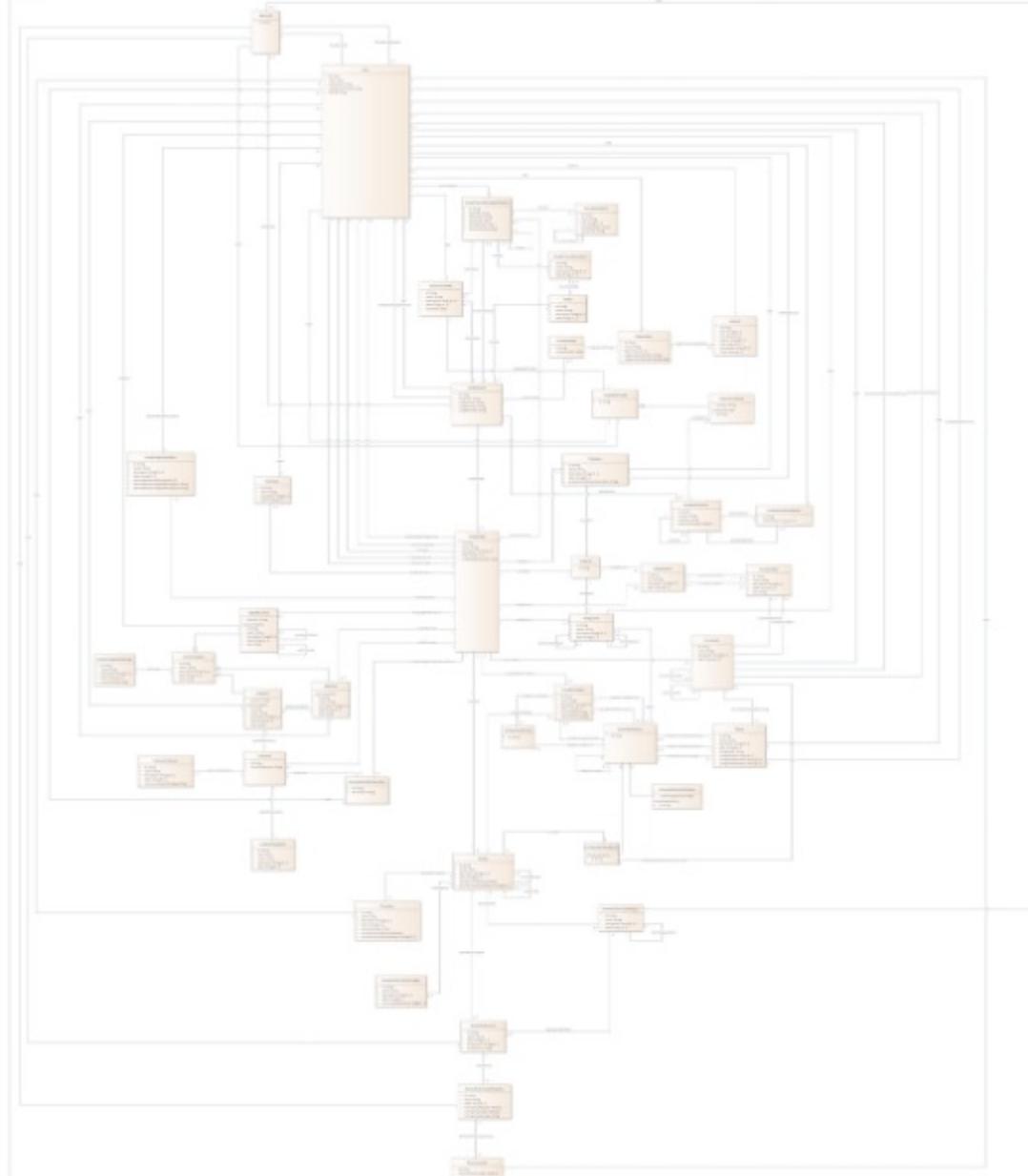
UML Model

UML

- The normative Unified Study Definitions Model (USDM)
- Available from Github

Links

- CDISC Github
 - <https://github.com/cdisc-org/DDF-RA/tree/main/Deliverables/UML>



Controlled Terminology

A	B	C	D	E	F	G	H	I
Row #	Entity Name	Role	Logical Data Model Name	NCI C-code	CT Item Preferred Name	Synonym(s)	Definition	Has Value List
12	StudyProtocolVersion	Entity	StudyProtocolVersion	C83490	Study Protocol Version		A plan at a particular point in time for a formal investigation to assess the utility, impact, pharmacological, physiological, and/or psychological effects of a particular treatment, procedure, drug, device, biologic, food product, cosmetic, care plan, or subject characteristic. (BRIDG)	N
13								
14	StudyProtocolVersion	Attribute	briefTitle	C132345	Brief Protocol Title	Abbreviated Protocol Title	The short descriptive name for the protocol.	N
15	StudyProtocolVersion	Attribute	officialTitle	C132346	Official Protocol Title		The formal descriptive name for the protocol.	N
16	StudyProtocolVersion	Attribute	publicTitle	C94105	Public Protocol Title		The descriptive name of the protocol that is intended for the lay public, written in easily understood language.	N
17	StudyProtocolVersion	Attribute	scientificTitle	C132350	Scientific Protocol Title		A more extensive descriptive name of the protocol that is intended for medical professionals, written using medical and scientific language.	N
18	StudyProtocolVersion	Attribute	protocolVersion	C83490	Study Protocol Version		A plan at a particular point in time for a formal investigation to assess the utility, impact, pharmacological, physiological, and/or psychological effects of a particular treatment, procedure, drug, device, biologic, food product, cosmetic, care plan, or subject characteristic. (BRIDG)	N
19	StudyProtocolVersion	Attribute	protocolAmendment	C132347	Study Protocol Amendment		A written description of a change(s) to, or formal clarification of, a protocol. (ICH E8)	N
20	StudyProtocolVersion	Attribute	protocolEffectiveDate	C188817	Study Protocol Amendment Effective Date		The date and time specifying when the protocol amendment takes effect or becomes operative.	N
21	StudyProtocolVersion	Attribute	protocolStatus	C188818	Protocol Status		A condition of the protocol at a point in time with respect to its state of readiness for implementation.	Y (C188723)

CT

- Provides a list of all classes and attributes
- Provides a definition
- Provides CT references
- Available from Github
- IG now has a UML and CT "merge" summary

Links

- CDISC Github
 - <https://github.com/cdisc-org/DDF-RA/tree/main/Deliverables/CT>

API

Simple API for DDF 1.7 Provisional (0.31) OAS3

openapi.json

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

Production Routes that form the production specification.

^

POST	/v1/studyDefinitions	Create a study
GET	/v1/studyDefinitions/{uuid}	Return a study
PUT	/v1/studyDefinitions/{uuid}	Update a study
GET	/v1/studyDefinitions/{uuid}/history	Returns the study history
GET	/v1/studyDesigns	Study designs for a study

^

API

- OpenAPI specification
- Bulk API
- Available from Github

Links

- CDISC Github
 - <https://github.com/cdisc-org/DDF-RA/tree/main/Deliverables/API>

Implementation Guide

Implementation Guide

- Note that the IG is version 2
- There was no IG with version 1 of the USDM
- Available from Github

Links

- CDISC Github
 - <https://github.com/cdisc-org/DDF-RA/tree/main/Deliverables/IG>

CDISC USDM-IG (Version 2.0 Draft for Internal Review)



**Unified Study Definitions Model
Implementation Guide (USDM-IG)**

Version 2.0 (Draft for Internal Review)

Prepared by the
DDF Team

Notes to Readers

- This is the draft version 2.0 of the Unified Study Definitions Model Implementation Guide (USDM-IG v2.0). It is intended for Internal Review only and is not a final version.

Revision History

Date	Version
2024-04-08	2.0 Draft for Internal Review

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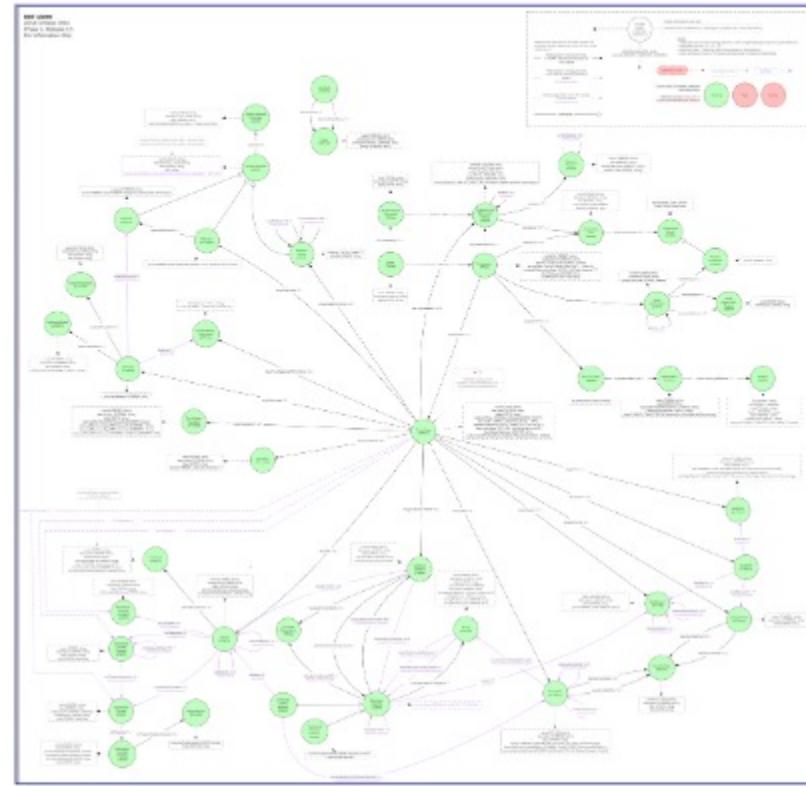
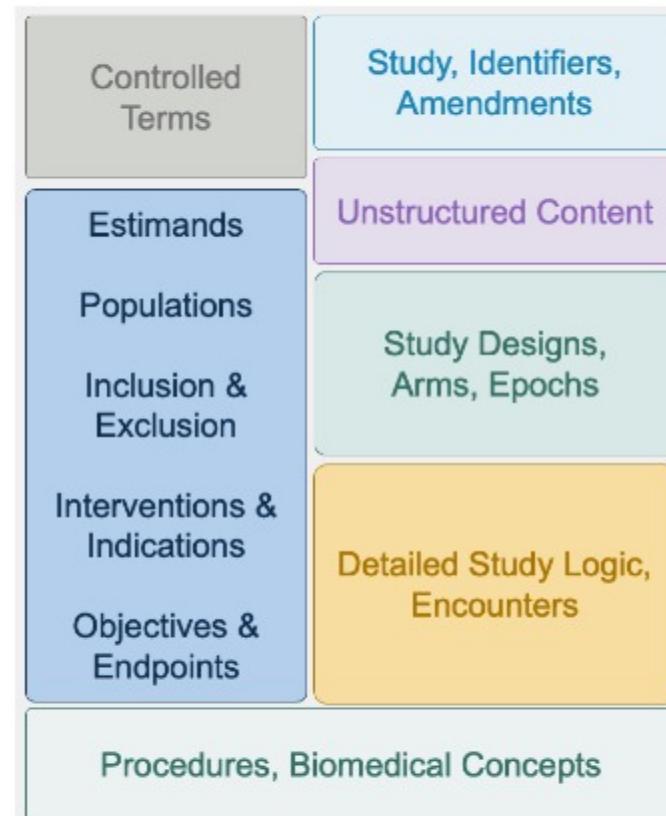
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Draft for Internal Review

Page 1
[Publish Date]

Overview

Basic Hierarchy

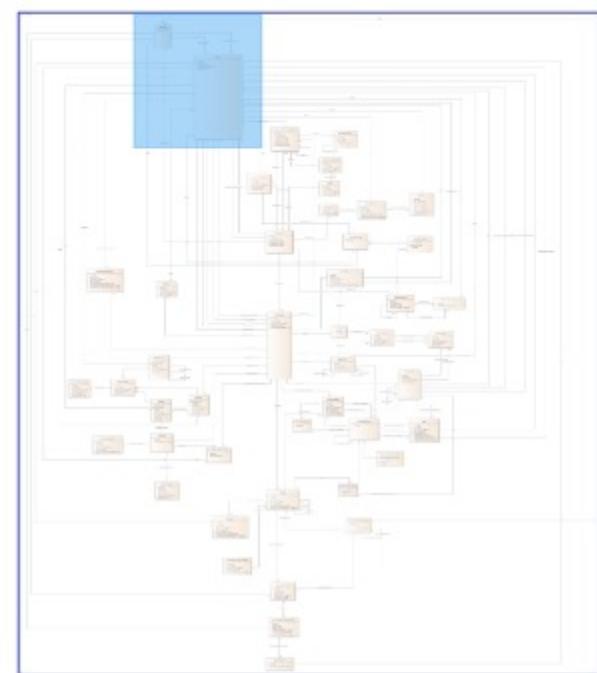
- Study
 - Document
 - Document Versions
 - Narrative Content
 - Study Versions
 - Study Identifiers
 - Amendments
 - 1 or more Study Designs
 - Arms, Epochs ...
 - Study Logic and Timing
 - Biomedical Concepts
 - Populations (Cohorts coming)
 - Objectives & Endpoints
 - Inclusion / Exclusion
 - Estimands
 - Interventions
 - Indications
 - Utility
 - CT References



"Green Blob" Diagram

- **Informative view. The UML is the Normative form**
- Used to discuss ideas before putting into normative UML
- Used as a cross-check of normative deliverables at end of sprints
- <https://github.com/cdisc-org/DDF-RA/blob/main/Documents/DDF%20USDM%20Model%20Informative.png>

AliasCode and Code

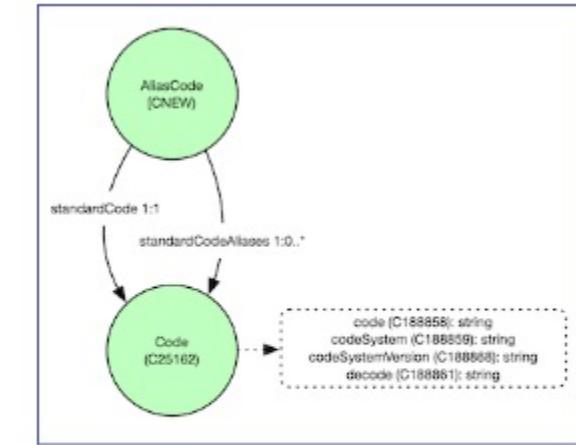


AliasCode and Code

- Code is a standard code reference
 - CDISC CT
 - All other CT
- AliasCode is a mechanism to align a CDISC Code with codes from other CT
 - One standard (CDISC) code
 - Many alternatives

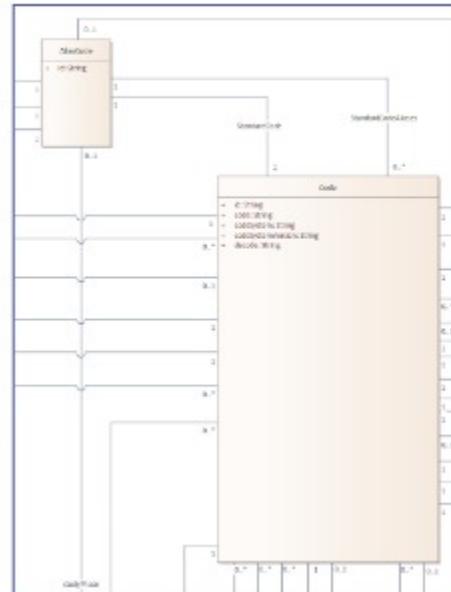
JSON Example

```
{  
  "id": "id_123",  
  "standardCode": {  
    "id": "code_29",  
    "code": "C25299",  
    "codeSystem": "http://www.cdisc.org",  
    "codeSystemVersion": "2022-03-25",  
    "decode": "Diastolic Blood Pressure"  
  },  
  "standardCodeAliases": [  
    {  
      "id": "code_30",  
      "code": "8462-4",  
      "codeSystem": "http://loinc.org/",  
      "codeSystemVersion": "2022-03-25",  
      "decode": "Diastolic Blood Pressure"  
    },  
    {  
      "id": "code_31",  
      "code": "271650006",  
      "codeSystem": "SNOMED-CT",  
      "codeSystemVersion": "2003",  
      "decode": "Diastolic Blood Pressure"  
    },  
    {  
      "id": "code_32",  
      "code": "4154790",  
      "codeSystem": "OHSDI",  
      "codeSystemVersion": "",  
      "decode": "Diastolic Blood Pressure"  
    }  
  ]  
}
```

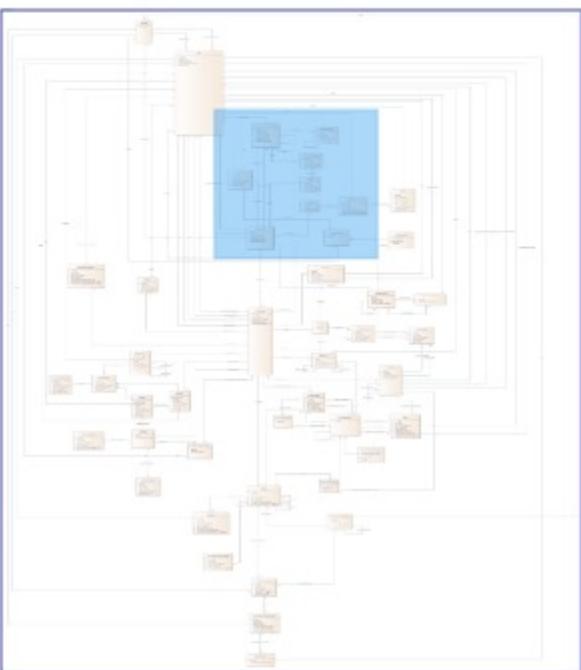


JSON

- Machine readable format but human readable
- Example to the left
 - AliasCode
 - Has an id
 - Has one standardCode
 - A single Code, usually CDISC
 - Has many standardCodeAliases
 - An array of Code
 - All other CT
 - Code has
 - An id
 - code
 - codeSystem
 - codeSystemVersion
 - decode
- Note the indentation and use of '{', '}' and '[', ']' characters

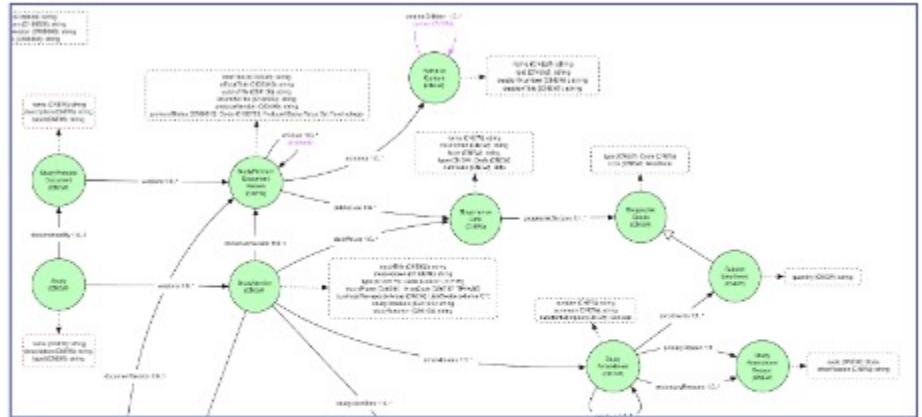


Study

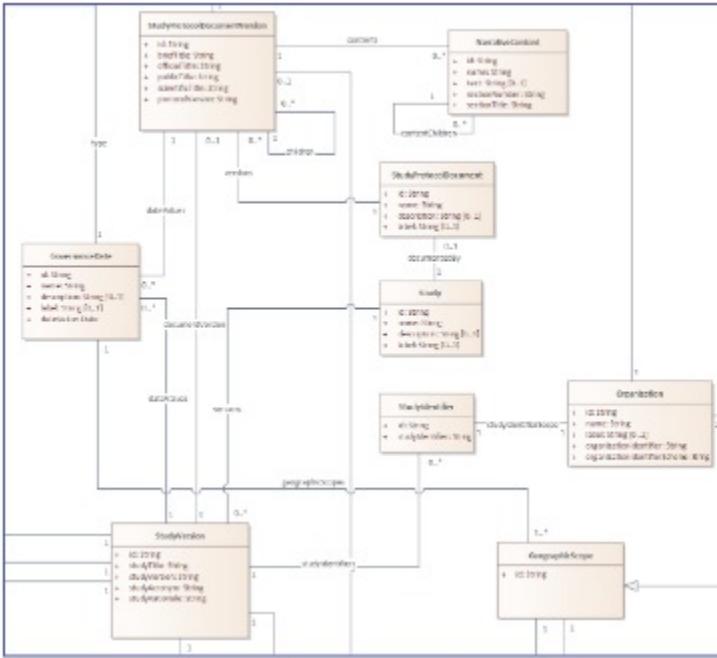


Study

- Study is the root of the whole model
- Study is the overall container that links to many study versions and the protocol document
- Protocol document is a container linking to many protocol document versions



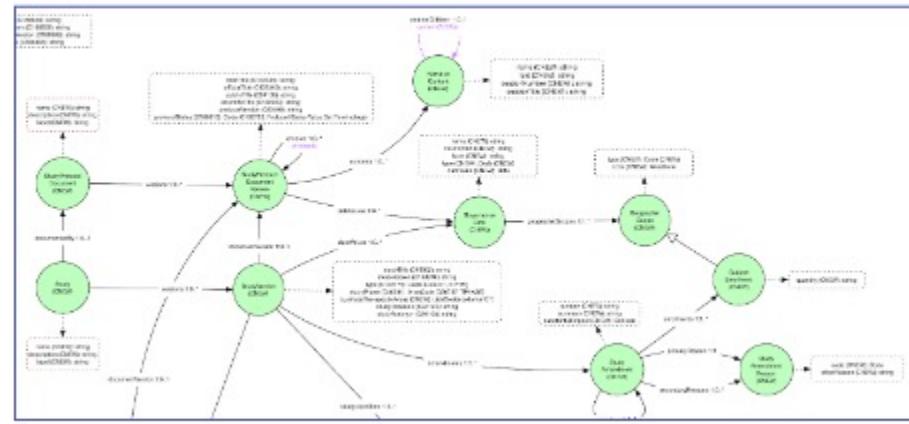
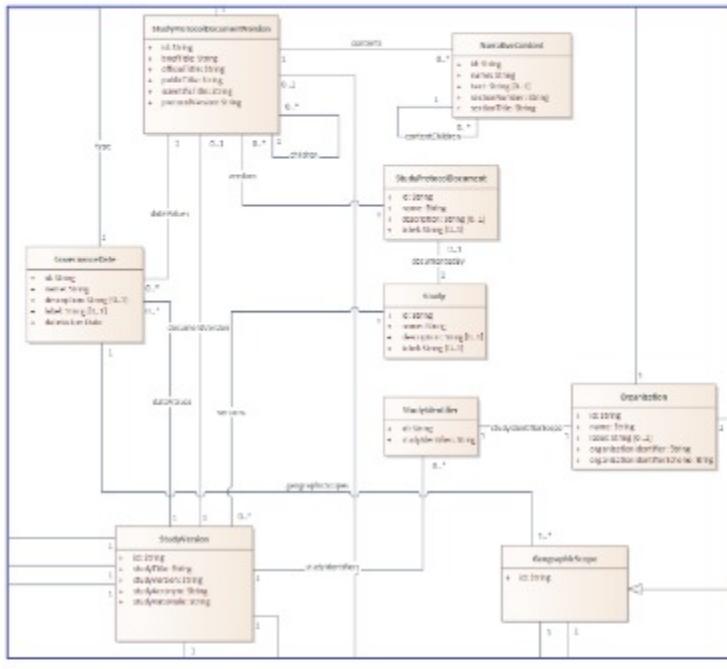
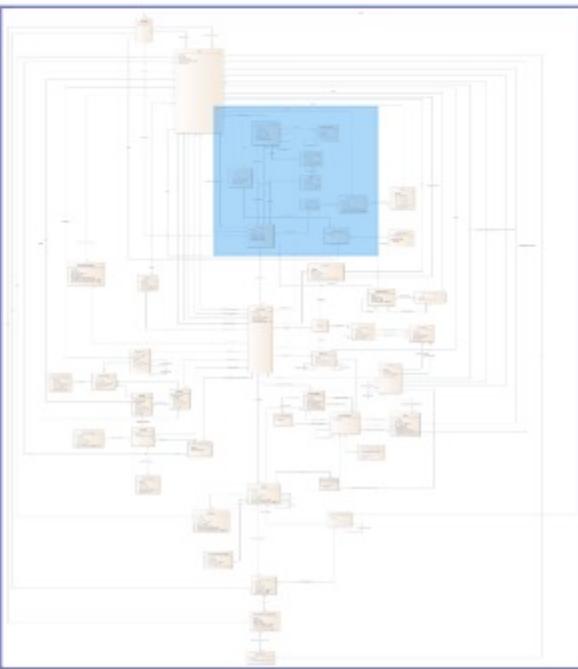
```
{  
  "study": {  
    "id": <UUID HERE>,  
    "name": "Study_SCOPE1",  
    "description": null,  
    "label": null,  
    "versions": [  
      ...  
    ],  
    "documentedBy": {  
      "id": "StudyProtocolDocument_1",  
      "name": "Protocol_Document_SCOPE1",  
      "label": null,  
      "description": null,  
      "versions": [  
        ...  
      ]  
    }  
  }  
}
```



Instance Identifiers

- Study has a UUID (allocated by the SDR for example)
- All other objects have internal ids that should be unique across the study
- Ids are used to
 - Uniquely identify an instance within a study
 - For cross-references such that content is only defined in one place when an entire study is serialised into JSON

Document

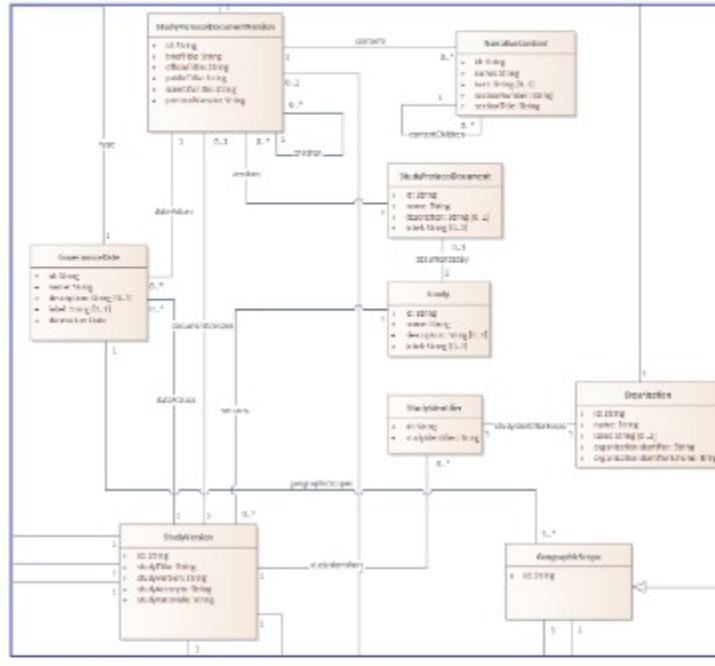
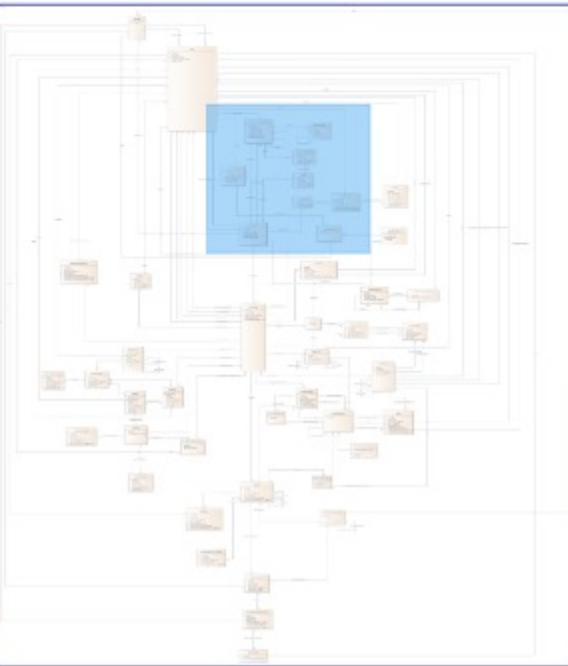


```
{  
  "study": {  
    "id": null,  
    "name": "Study_CDISC PILOT - LZZT",  
    "description": null,  
    "label": null,  
    "versions": [ ... ],  
    "documentedBy": {  
      "id": "StudyProtocolDocument_1",  
      "name": "Protocol_Document_CDISC PILOT - LZZT",  
      "label": null,  
      "description": null,  
      "versions": [  
        { ... }  
      ]  
    }  
  }  
}
```

Document

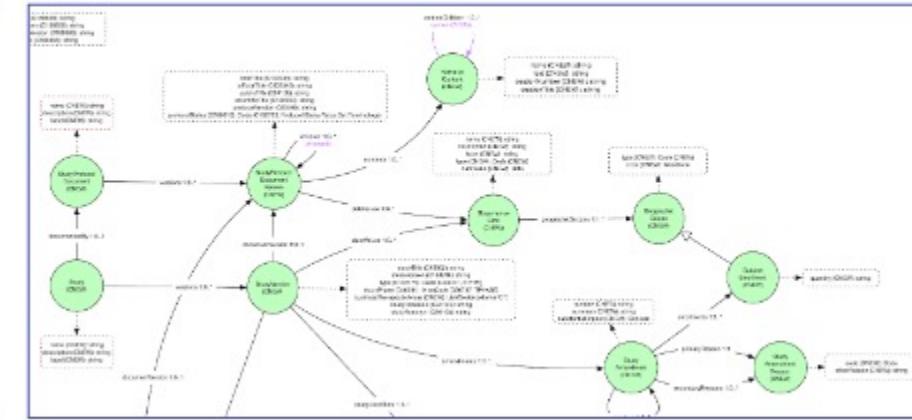
- Container for the document versions
 - Currently envisaged to be the protocol document
 - Could be extended to multiple document types

Document Version



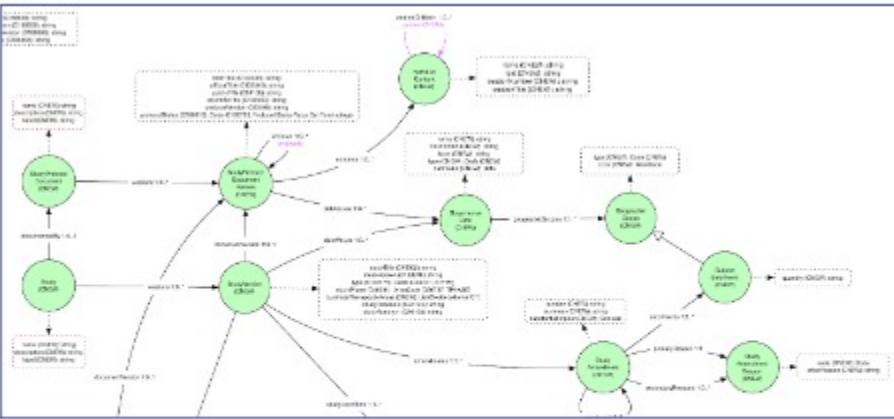
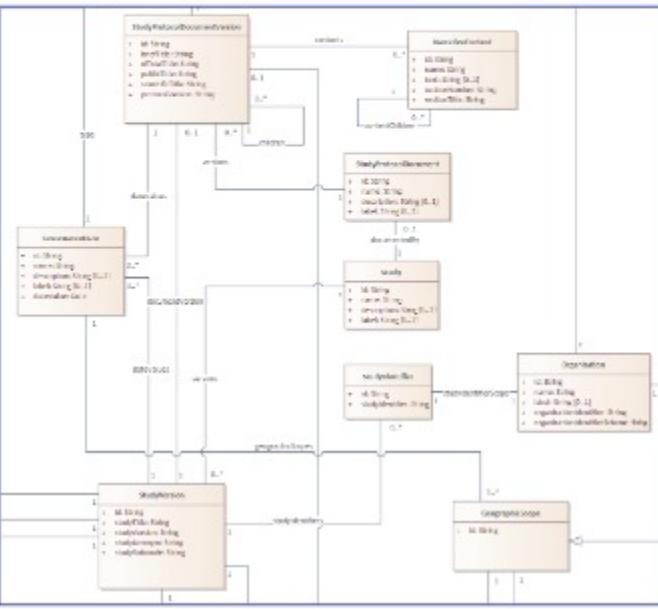
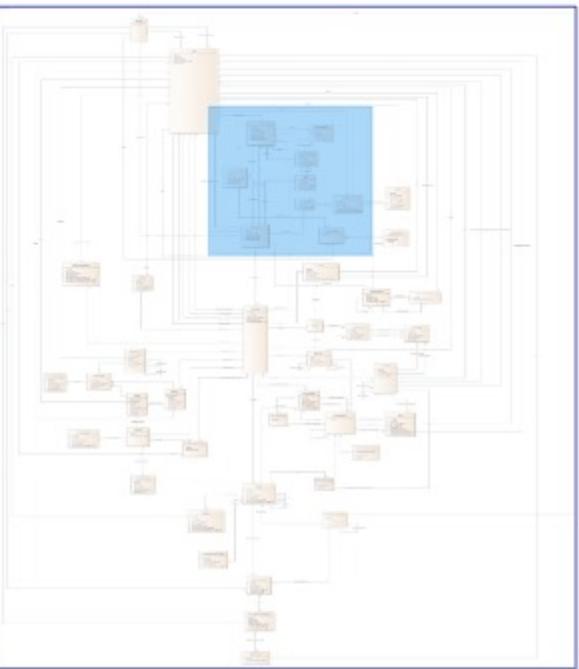
Document Version

- Single version of the protocol document



```
{  
  "id": "StudyProtocolDocumentVersion_1",  
  "briefTitle": "Xanomeline (LY246708)",  
  "officialTitle": "Safety and Efficacy of the Xanomeline Transdermal Therapeutic System (TTS) in Patients with Mild to Moderate Alzheimer's Disease",  
  "publicTitle": "Safety and Efficacy of the Xanomeline Transdermal Therapeutic System (TTS) in Patients with Mild to Moderate Alzheimer's Disease",  
  "scientificTitle": "",  
  "protocolVersion": "2",  
  "protocolStatus": {  
    "id": "Code_4",  
    "code": "C25508",  
    "codeSystem": "http://www.cdisc.org",  
    "codeSystemVersion": "2023-09-29",  
    "decode": "Final"  
  },  
  "dateValues": [ ... ],  
  "contents": [ ... ],  
  "childrenIds": []  
}
```

Study Amendments



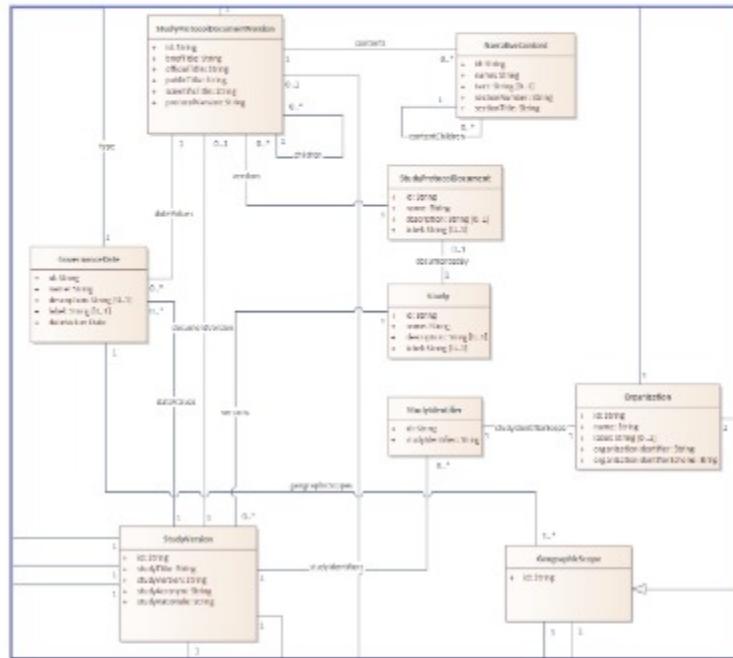
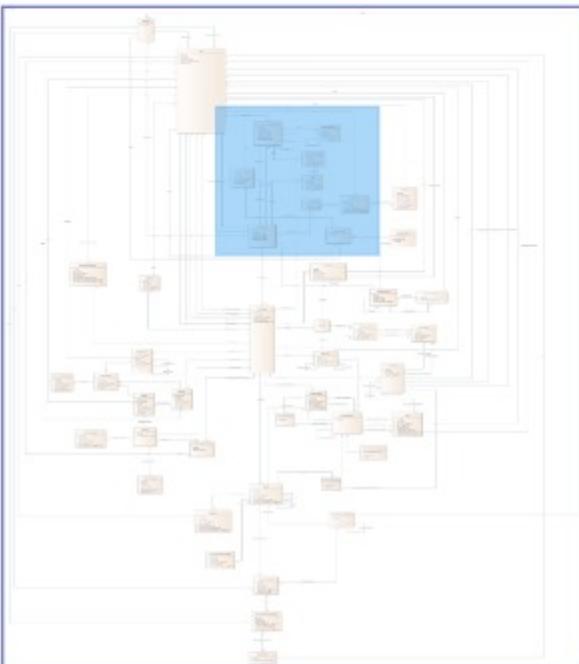
```
{  
    "id": "StudyAmendment_1",  
    "number": "1",  
    "summary": "Updated inclusion criteria",  
    "substantialImpact": true,  
    "primaryReason": {  
        "id": "StudyAmendmentReason_1",  
        "code": {  
            "id": "Code_10",  
            "code": "C99904x3",  
            "codeSystem": "http://www.cdisc.org",  
            "codeSystemVersion": "2023-09-29",  
            "decode": "IRB/IEC Feedback"  
        },  
        "otherReason": null  
    },  
    "secondaryReasons": [  
        ... as per primary, 0,1 or more ...  
    ],  
    "enrollments": [ ... ]  
    "previousId": null  
}
```

```
{  
    "enrollments": [  
        {  
            "id": "SubjectEnrollment_1",  
            "type": {  
                "id": "Code_13",  
                "code": "C41129",  
                "codeSystem": "http://www.cdisc.org",  
                "codeSystemVersion": "2023-09-29",  
                "decode": "Region"  
            },  
            "code": {  
                "id": "AliasCode_3",  
                "standardCode": {  
                    "id": "Code_12",  
                    "code": "150",  
                    "codeSystem": "ISO 3166 1 alpha3",  
                    "codeSystemVersion": "2020-08",  
                    "decode": "Europe"  
                },  
                "standardCodeAliases": []  
            },  
            "quantity": "15"  
        },  
        {...}  
    ],  
    "...
```

Amendments

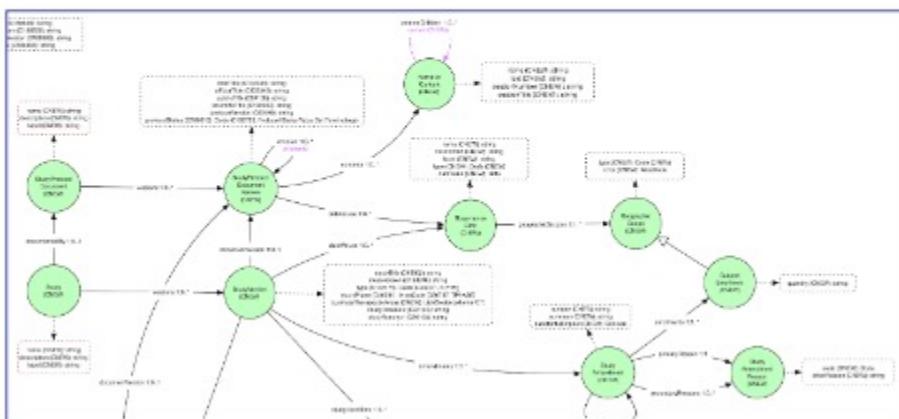
- A study can have zero, one or more amendments
- Hangs off the Study Design not the document, the design is amended not the document, the document reflects the design
- Amendment must have a single primary reason with zero, one or more secondary reasons
- A reason can be a code (M11 defined) or a free text "other" reason
- Also records the enrollment at time of amendment which can be geographically scoped

Dates



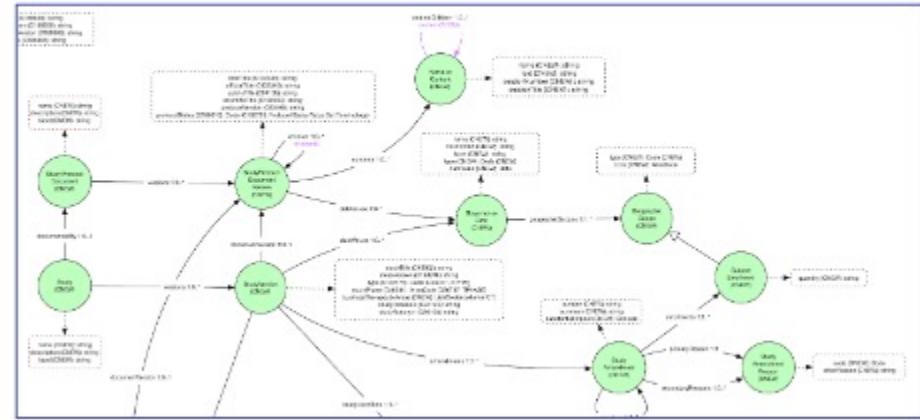
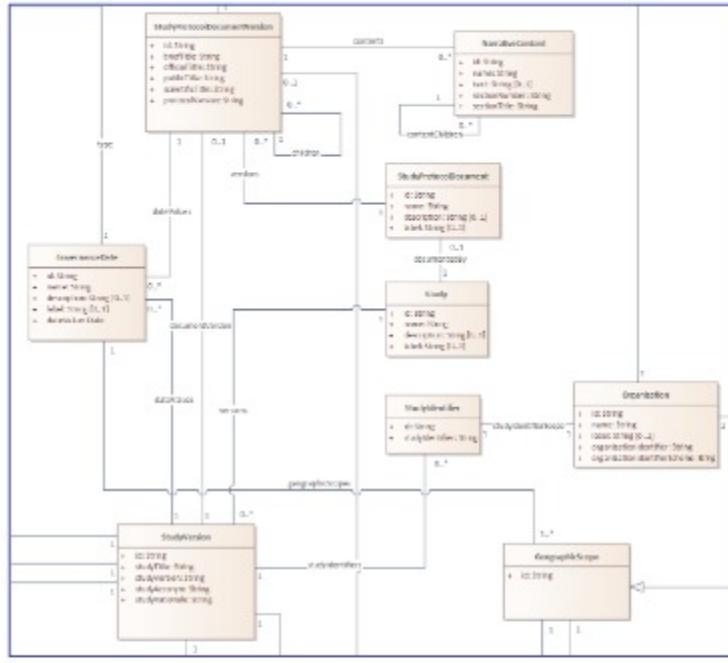
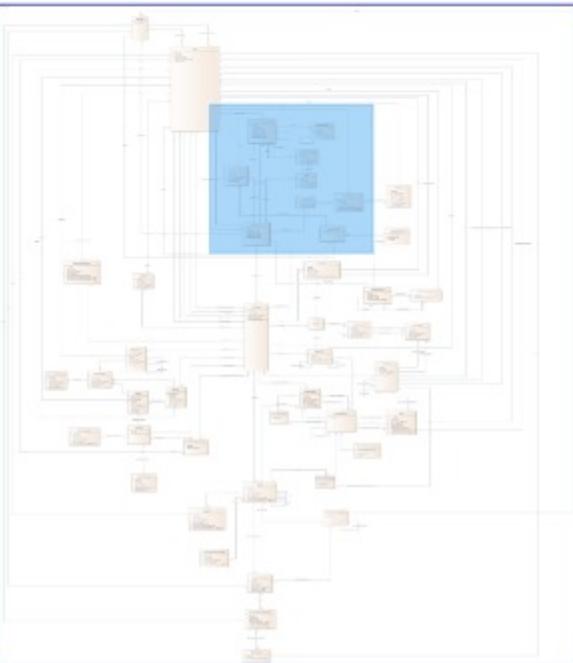
Dates

- Used for documents
- Used for amendments
- Dates have geographic scope (Global, Regional, Country)



```
*dateValues*: [
  {
    "id": "GovernanceDate_1",
    "name": "Approval",
    "label": "Design Approval",
    "description": "Design approval date",
    "type": {
      "id": "Code_5",
      "code": "C132352",
      "codeSystem": "http://www.cdisc.org",
      "codeSystemVersion": "2023-09-29",
      "decode": "Sponsor Approval Date"
    },
    "dataValue": "2006-07-01",
    "geographicScopes": [
      {
        "id": "GeographicScope_1",
        "type": {
          "id": "Code_6",
          "code": "C68846",
          "codeSystem": "http://www.cdisc.org",
          "codeSystemVersion": "2023-09-29",
          "decode": "Global"
        }
      },
      "code": null
    ]
  }
]
```

Geographic Scope

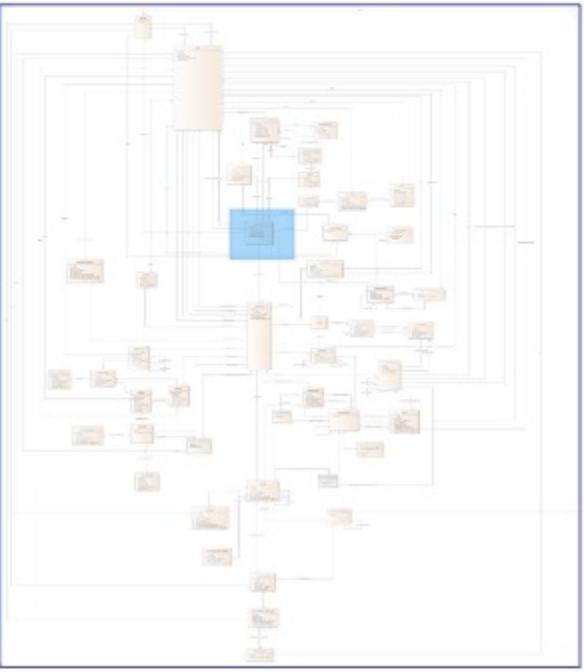


```
{  
    "id": "GeographicScope_2",  
    "type": {  
        "id": "Code_9",  
        "code": "C41129",  
        "codeSystem": "http://www.cdisc.org",  
        "codeSystemVersion": "2023-09-29",  
        "decode": "Region"  
    },  
    "code": {  
        "id": "AliasCode_2",  
        "standardCode": {  
            "id": "Code_8",  
            "code": "150",  
            "codeSystem": "ISO 3166 1 alpha3",  
            "codeSystemVersion": "2020-08",  
            "decode": "Europe"  
        },  
        "standardCodeAliases": []  
    }  
}
```

Document Version

- Allows for a date or an enrollment figure to be constrained to a Geographic Scope
- Scopes are Global, Regional, Country

Study Version

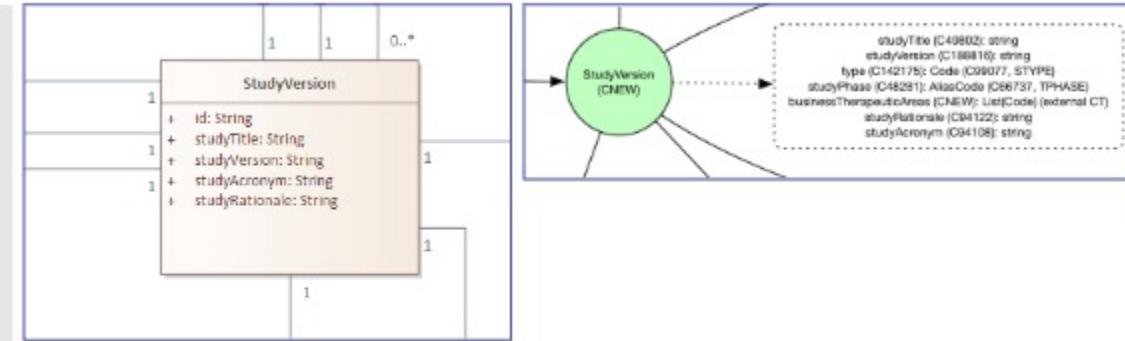


Study Version

- A single version of the study
- One study version links to many study designs
- Study version also links to the study identifiers

```
{  
  "study": {  
    "id": null,  
    "name": "Study_SCOPE1",  
    "description": null,  
    "label": null,  
    "versions": [  
      {  
        "id": "StudyVersion_1",  
        "studyTitle": "Simple Test 1",  
        "studyVersion": "1",  
        "studyRationale": "A simple test",  
        "studyAcronym": "SIMPLE",  
        "type": {  
          "id": "Code_1",  
          "code": "C98388",  
          "codeSystem": "http://www.cdisc.org",  
          "codeSystemVersion": "2023-09-29",  
          "decode": "Interventional Study"  
        },  
        "studyPhase": {  
          "id": "AliasCode_1",  
          "standardCode": {  
            "id": "Code_2",  
            "code": "C15602",  
            "codeSystem": "http://www.cdisc.org",  
            "codeSystemVersion": "2023-09-29",  
            "decode": "Phase III Trial"  
          },  
          "standardCodeAliases": []  
        },  
        "documentVersionId": "StudyProtocolDocumentVersion_1",  
        "dateValues": [...],  
        "amendments": [...],  
        "businessTherapeuticAreas": [...],  
        "studyIdentifiers": [...],  
        "studyDesigns": [...]  
      }  

```



Business Therapeutic Area

- Sponsor requested. More for downstream processes
- Not the same as StudyDesign therapeuticAreas attribute

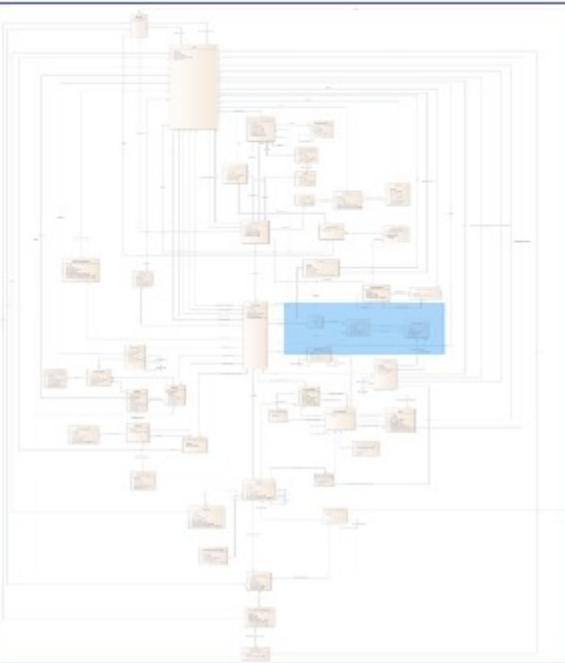
One Study Version, Many Study Designs

- USDM allows for many study designs within a single study
- This accommodates master, umbrella studies etc.

Notes:

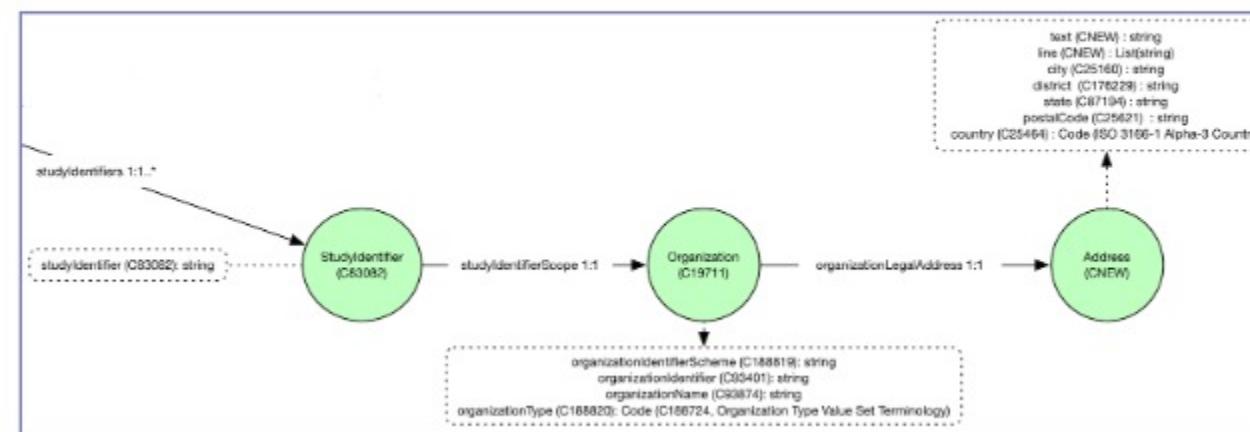
- [FDA guidance](#) talks about master protocols
- [Master Protocols for Precision Medicine in Oncology: Overcoming Methodology of Randomized Clinical Trials](#)

Study Identifiers



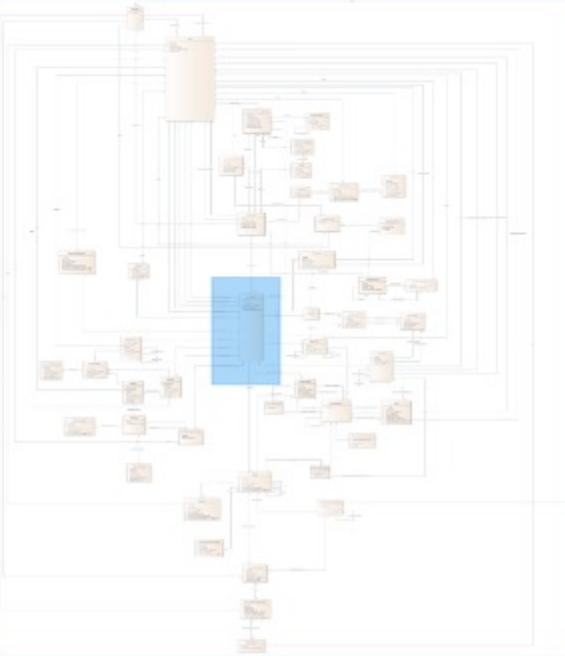
Study Identifiers

- Multiple identifiers permitted, various types
 - Sponsor
 - Registry
 - Regulatory Authority
- Should have a Sponsor Id
- Should only have one Sponsor Id
- Note the country code (ISO 3166-1)



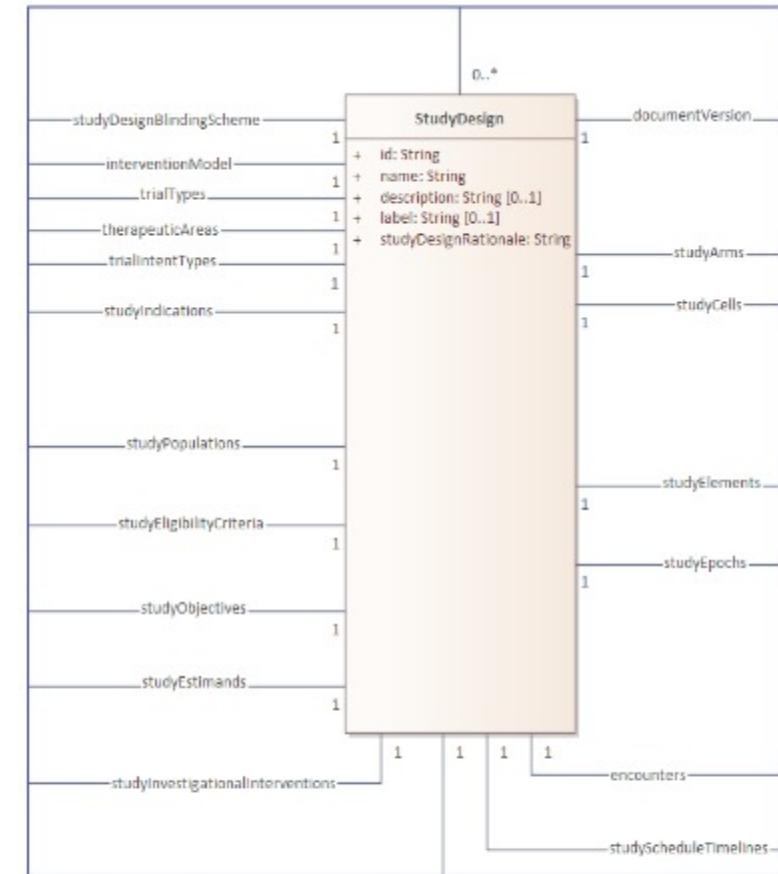
```
{
    "id": "StudyIdentifier_1",
    "studyIdentifier": "H2Q-MC-LZZT",
    "studyIdentifierScope": {
        "id": "Organization_1",
        "name": "Eli Lilly",
        "label": "",
        "type": {
            "id": "Code_16",
            "code": "C70793",
            "codeSystem": "http://www.cdisc.org",
            "codeSystemVersion": "2023-09-29",
            "decode": "Clinical Study Sponsor"
        },
        "organizationIdentifierScheme": "DUNS",
        "organizationIdentifier": "00-642-1325",
        "organizationLegalAddress": {
            "id": "Address_1",
            "text": "Lilly Corporate Ctr, Indianapolis, -, IN, 4628, United States of America",
            "line": "Lilly Corporate Ctr",
            "city": "Indianapolis",
            "district": "-",
            "state": "IN",
            "postalCode": "4628",
            "country": {
                "id": "Code_17",
                "code": "USA",
                "codeSystem": "ISO 3166 1 alpha3",
                "codeSystemVersion": "2020-08",
                "decode": "United States of America"
            }
        }
    }
}
```

Study Design



Study Design

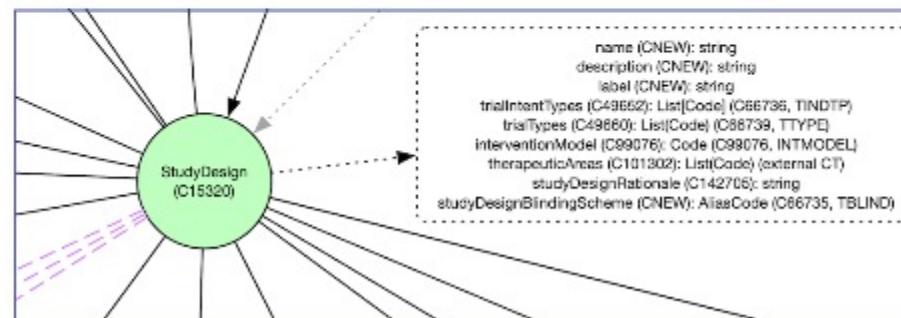
- Root of a single design
- Links all the pieces together using relationships



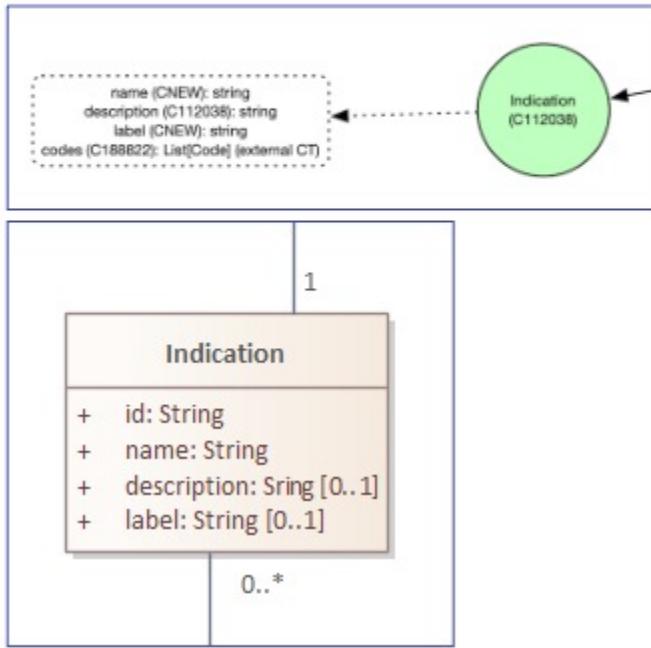
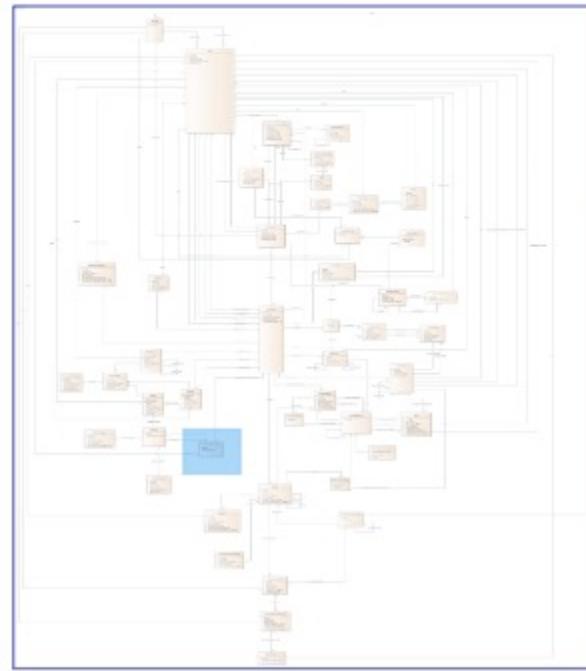
```
"studyDesigns": [
  {
    "id": "StudyDesign_1",
    "name": "Study Design 1",
    "label": "",
    "description": "The main design for the study",
    "trialIntentTypes": [...],
    "trialTypes": [...],
    "therapeuticAreas": [...],
    "interventionModel": {...},
    "encounters": [...],
    "activities": [...],
    "biomedicalConcepts": [...],
    "bcCategories": [],
    "bcSurrogates": [...],
    "studyArms": [...],
    "studyCells": [...],
    "studyDesignBlindingScheme": {...},
    "studyDesignRationale": "Basic study",
    "studyEpochs": [...],
    "studyElements": [...],
    "studyEstimands": [...],
    "studyIndications": [...],
    "studyInvestigationalInterventions": [...],
    "studyObjectives": [...],
    "studyPopulations": [...],
    "studyScheduleTimelines": [...],
    "documentVersion": null,
    "studyEligibilityCritieria": [...],
    "dictionaries": [...]
  }
]
```

Therapeutic Areas

Dictionary / Terminology Name	URL
EUDRACT	https://eudract.emea.europa.eu/docs/technical/EUDRACT_Eutect_Pick_Lists_and_coded_values_v1_0.xls
ICD-10	https://www.icd10data.com/ICD10CM/Codes
MEDDRA	https://www.meddra.org/
MeSH	https://www.ncbi.nlm.nih.gov/mesh/
NCI Thesaurus	https://ncit.nci.nih.gov/ncitbrowser/
SNOMEDCT	https://www.ncbi.nlm.nih.gov/healthit/snomedct/index.html
US FDA	https://www.fda.gov/drugs/development-resources/spectrum-diseasesconditions

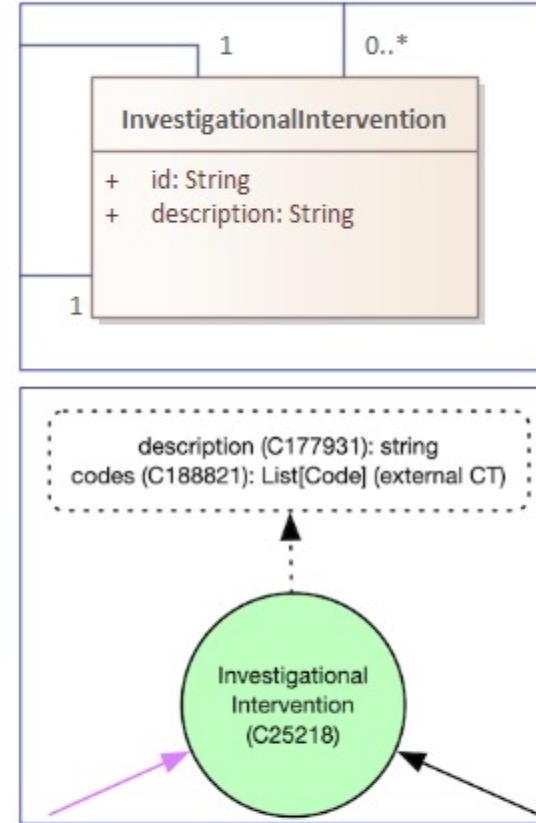
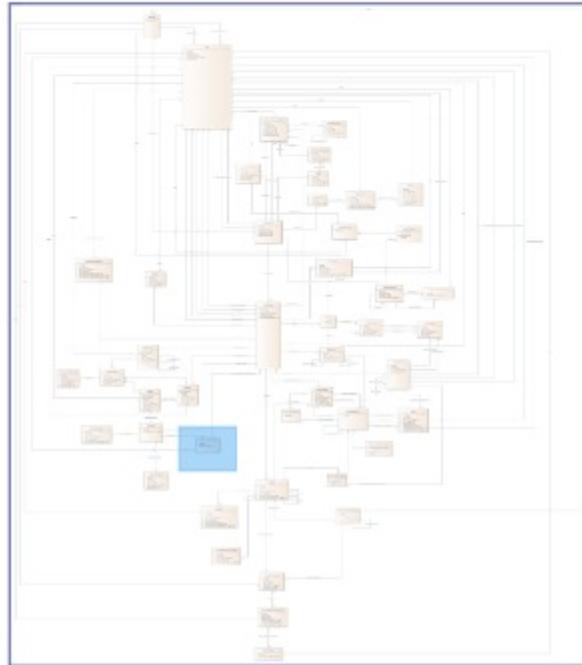


Indications

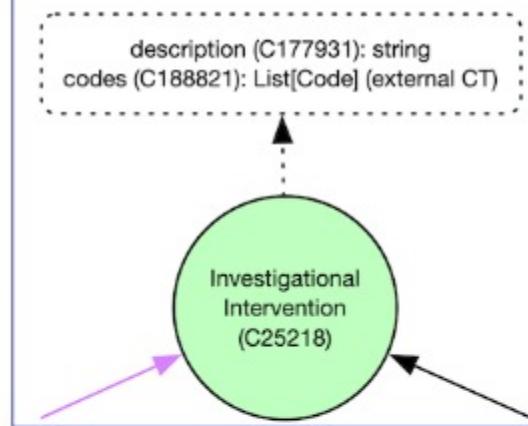


```
"studyIndications": [
  {
    "id": "Indication_1",
    "codes": [
      {
        "code": "E11",
        "codeSystem": "ICD-10-CM",
        "codeSystemVersion": "10",
        "decode": "Type 2 diabetes mellitus"
      },
      {
        "code": "44054006",
        "codeSystem": "SNOMED",
        "codeSystemVersion": "2022",
        "decode": "Diabetes mellitus type 2 (disorder)"
      }
    ],
    "description": "Diabetes Type II"
  },
  {
    "id": "Indication_2",
    "codes": [
      {
        "code": "E10",
        "codeSystem": "ICD-10-CM",
        "codeSystemVersion": "10",
        "decode": "Type 1 diabetes mellitus"
      },
      {
        "code": "44635009",
        "codeSystem": "SNOMED",
        "codeSystemVersion": "2022",
        "decode": "Diabetes mellitus type 1 (disorder)"
      }
    ],
    "description": "Diabetes Type I"
  }
]
```

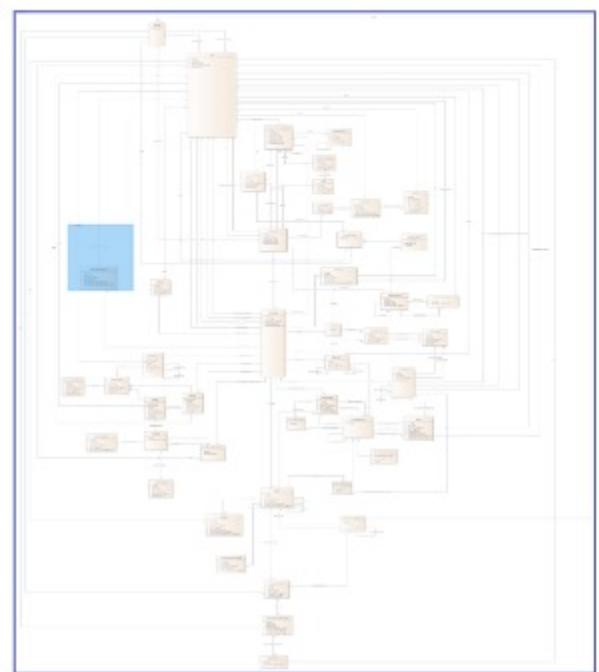
Interventions



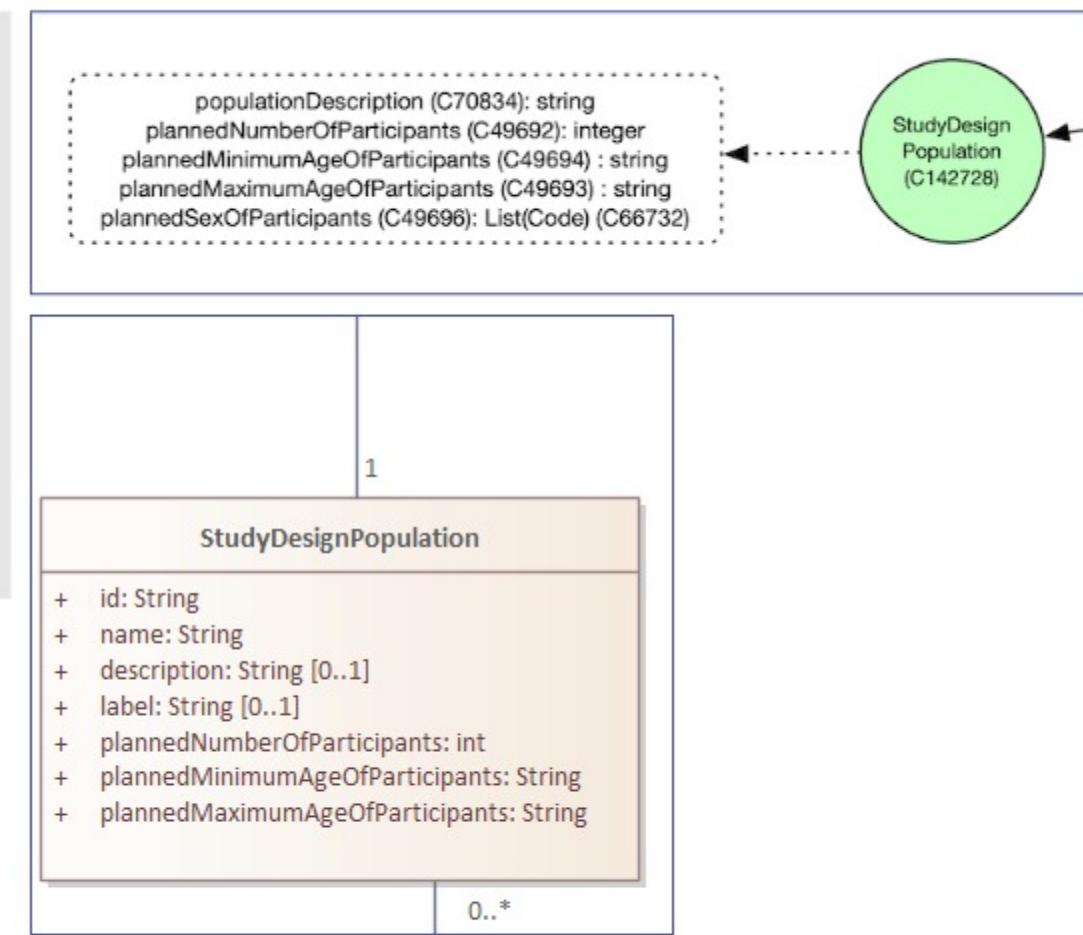
```
"studyInvestigationalInterventions": [
  {
    "id": "InvestigationalIntervention_1",
    "codes": [
      {
        "code": "XX031ZA",
        "codeSystem": "ATC",
        "codeSystemVersion": "2021",
        "decode": "SubstX"
      }
    ],
    "description": "Treatment with substX"
  }
]
```



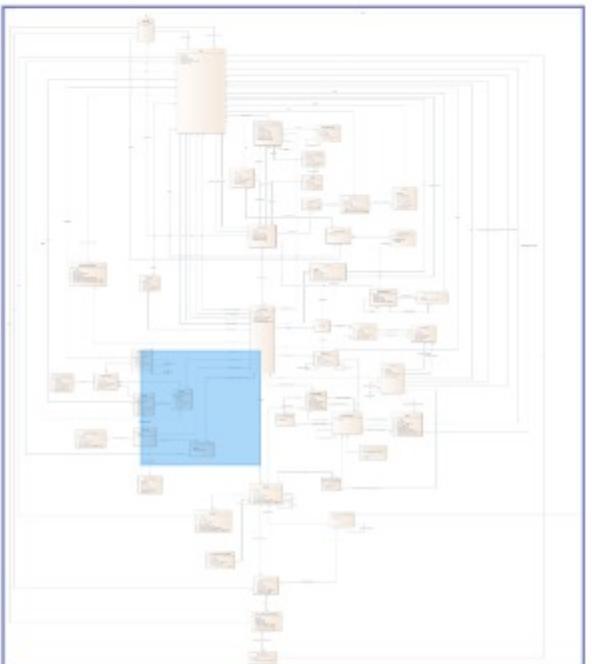
Study Populations



```
{  
  "id": "StudyDesignPopulation_1",  
  "name": "POP1",  
  "label": "",  
  "description": "Population One, low age group",  
  "plannedNumberOfParticipants": 100,  
  "plannedMaximumAgeOfParticipants": "40 years",  
  "plannedMinimumAgeOfParticipants": "18 years",  
  "plannedSexOfParticipants": [  
    {  
      "id": "Code_104",  
      "code": "C49636",  
      "codeSystem": "http://www.cdisc.org",  
      "codeSystemVersion": "2023-09-29",  
      "decode": "Both"  
    }  
  ]  
}
```



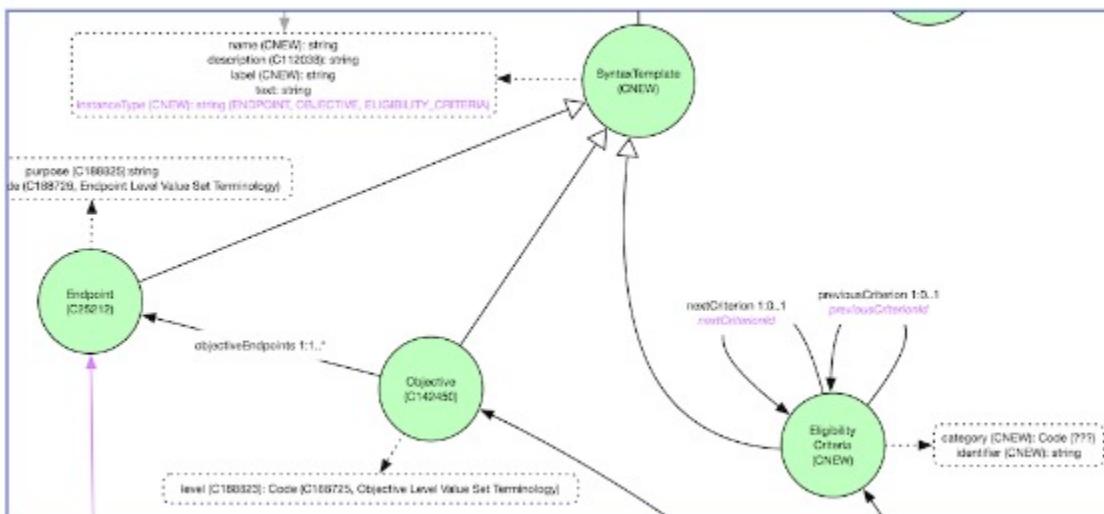
Eligibility Criteria



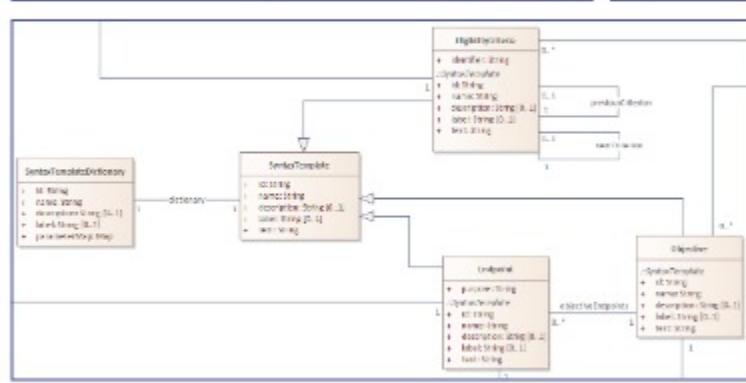
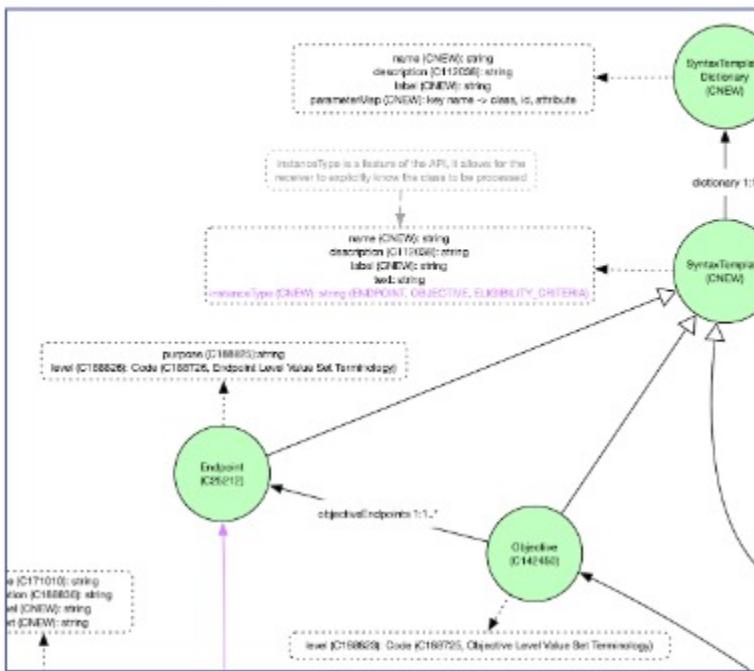
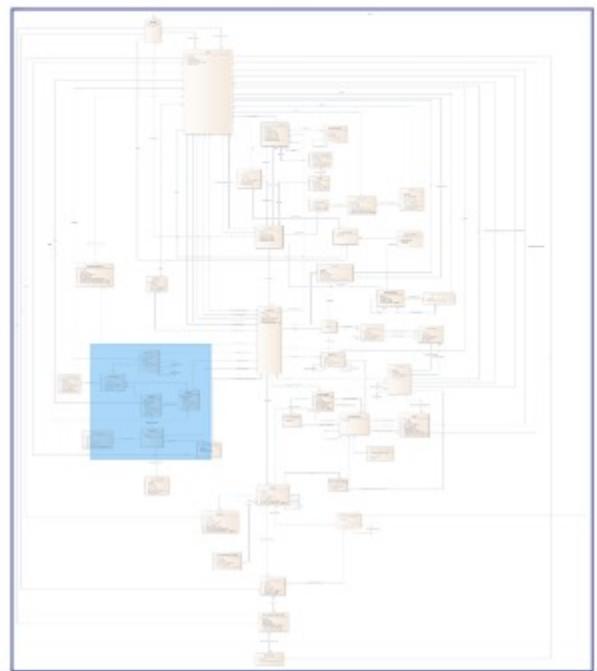
Eligibility Criteria

- Employs the syntax template mechanism
 - Embedded tags within the text attribute
- "text": "Subjects shall be between [min_age] and [max_age]"

```
{  
  "id": "EligibilityCriteria_1",  
  "name": "Age Criteria",  
  "label": "",  
  "description": "The study age criterion",  
  "instanceType": "ELIGIBILITY_CRITERIA",  
  "text": "Subjects shall be between [min_age] and [max_age]",  
  "dictionaryId": "SyntaxTemplateDictionary_1",  
  "category": {  
    "id": "Code_112",  
    "code": "C25532",  
    "codeSystem": "http://www.cdisc.org",  
    "codeSystemVersion": "2023-09-29",  
    "decode": "Inclusion Criteria"  
  },  
  "identifier": "1",  
  "nextCriterionId": null,  
  "previousCriterionId": null  
}
```

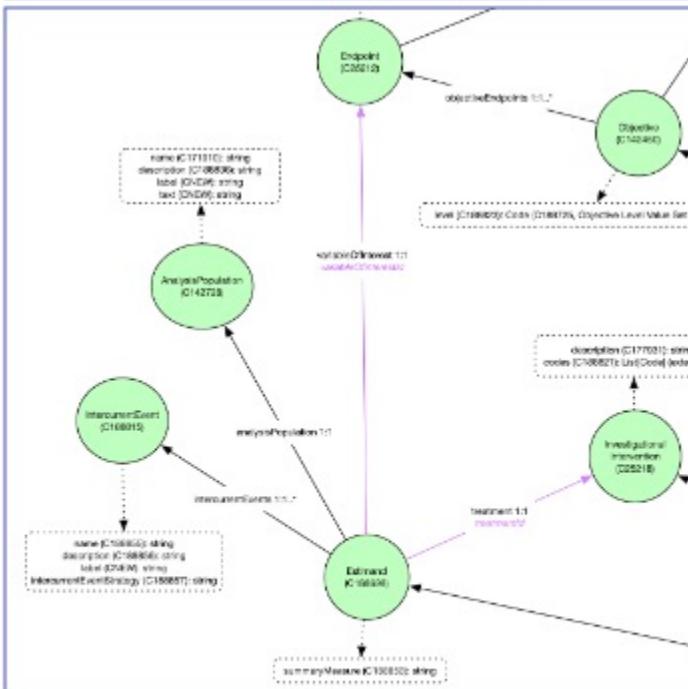
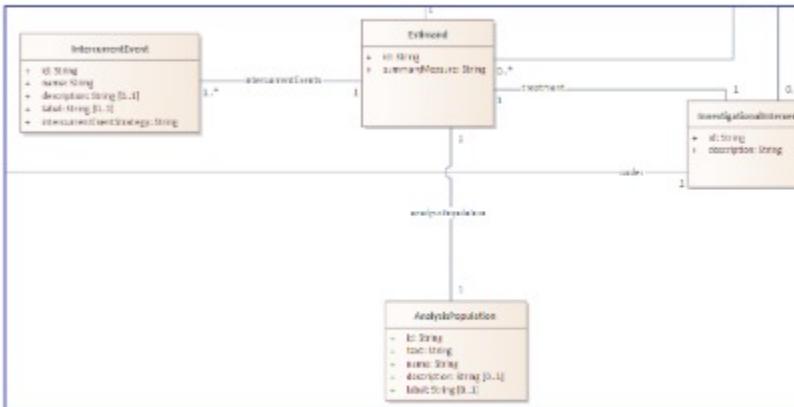
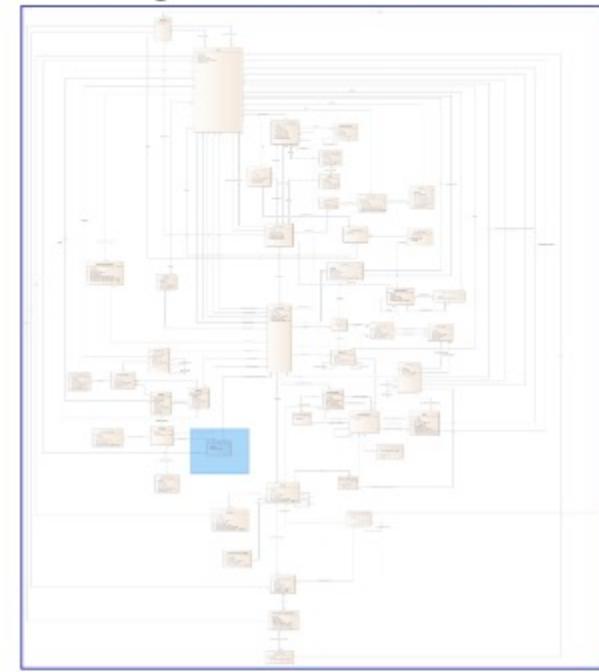


Study Objectives and Endpoints



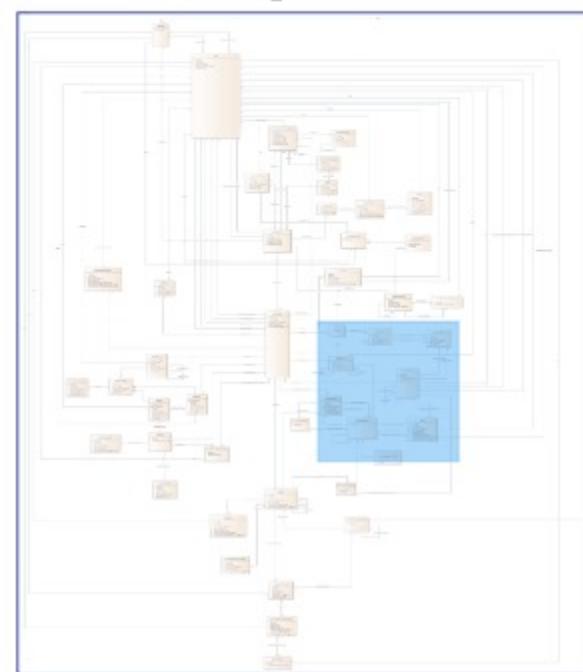
```
{  
    "id": "Objective_1",  
    "name": "OBJ1",  
    "label": "",  
    "description": "Primary",  
    "instanceType": "OBJECTIVE",  
    "text": "The primary efficacy objective for this study is to evaluate the efficacy of TCZ compared with placebo in combination with SOC for the treatment of severe COVID-19 pneumonia",  
    "dictionaryId": null,  
    "level": {  
        "id": "Code_108",  
        "code": "C85B26",  
        "codeSystem": "http://www.cdisc.org",  
        "codeSystemVersion": "2023-09-29",  
        "decode": "Trial Primary Objective"  
    },  
    "objectiveEndpoints": [  
        {  
            "id": "Endpoint_1",  
            "name": "END1",  
            "label": "",  
            "description": "Day 28, 7 category scale",  
            "instanceType": "ENDPOINT",  
            "text": "Clinical status assessed using a 7-category ordinal scale at Day 28",  
            "dictionaryId": null,  
            "purpose": "",  
            "level": {  
                "id": "Code_107",  
                "code": "C94496",  
                "codeSystem": "http://www.cdisc.org",  
                "codeSystemVersion": "2023-09-29",  
                "decode": "Primary Endpoint"  
            }  
        }  
    ]  
}
```

Study Estimands



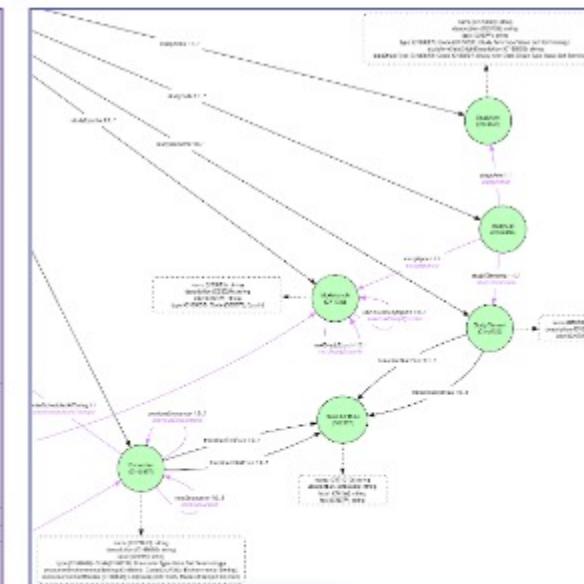
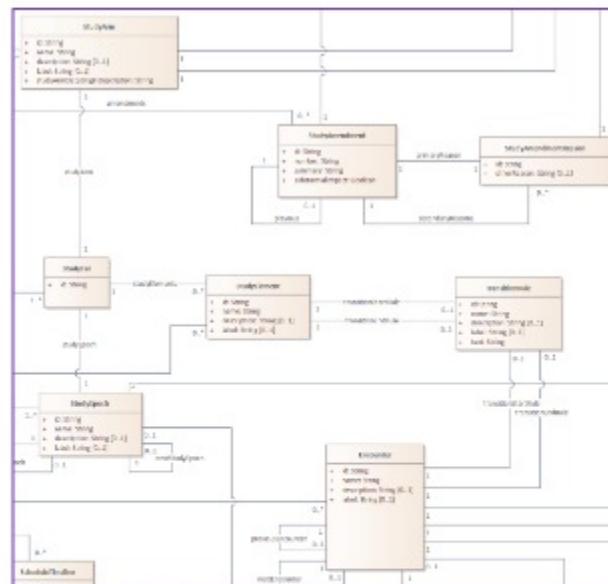
```
{
    "id": "Estimand_1",
    "summaryMeasure": "Survival of all patients",
    "analysisPopulation": {
        "id": "AnalysisPopulation_1",
        "name": "AP_1",
        "label": null,
        "description": null,
        "text": "ITT"
    },
    "treatmentId": "InvestigationalIntervention_1",
    "variableOfInterestId": "Endpoint_1",
    "intercurrentEvents": [
        {
            "id": "IntercurrentEvent_1",
            "name": "termination",
            "label": "",
            "description": "IC Event Description",
            "intercurrentEventStrategy": "Patients with out of range lab values before dosing will be excluded"
        }
    ]
}
```

Arms, Epoch etc



High Level Study Design

- Arms & Epochs
- Cells
- Elements
- Encounters (Visits)
- Entry and Exit Rules
- Can be used as a start of SDTM Trial Design Domain population
- Also T domains can be imported to build a study design "framework"



```
{  
  "id": "StudyArm_1",  
  "name": "Active",  
  "label": "Active Substance",  
  "description": "Active Substance",  
  "type": {  
    "id": "Code_57",  
    "code": "C174267",  
    "codeSystem": "http://www.cdisc.org",  
    "codeSystemVersion": "2023-09-29",  
    "decode": "Active Comparator Arm"  
  },  
  "studyArmDataOriginDescription": "Data collected from subjects",  
  "dataOriginType": {  
    "id": "Code_58",  
    "code": "C188866",  
    "codeSystem": "http://www.cdisc.org",  
    "codeSystemVersion": "2023-09-29",  
    "decode": "Data Generated Within Study"  
  }  
},  
  
{  
  "id": "StudyEpoch_1",  
  "name": "Screening",  
  "label": "Screening",  
  "description": "Screening Epoch",  
  "type": {  
    "id": "Code_61",  
    "code": "C48262",  
    "codeSystem": "http://www.cdisc.org",  
    "codeSystemVersion": "2023-09-29",  
    "decode": "Trial Screening"  
  },  
  "previousStudyEpochId": null,  
  "nextStudyEpochId": "StudyEpoch_2"  
}
```

Trial Summary Domain

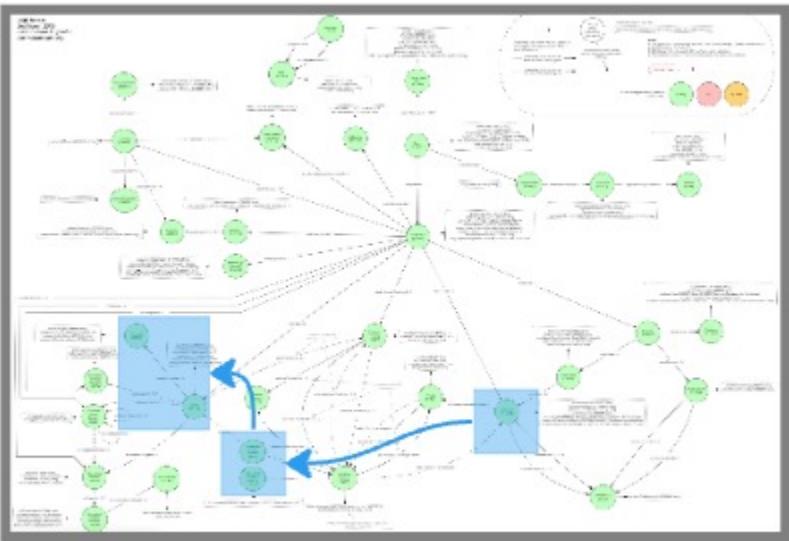
Trial Summary (TS) Domain

- Initial mapping
- In the IG

VERSION 2.0

Will be updated for
Version 3

Code	CDISC Submission Value	CDISC Synonym(s)	NCI Preferred Term	USDM Entity Name	USDM Role	USDM Item Name	
C101302	THERAREA	Therapeutic Area	Therapeutic Area	StudyDesign	Attribute	therapeuticAreas	
C112038	INDIC	Trial Disease/Condition Disease/Condition Inv	Trial Indication	Indication	Entity	Indication	
C112038	INDIC	Trial Disease/Cond/ Disease/Condition	Trial Indication	Indication	Attribute	indicationDescription	
C142175	STYPE	Study Type; Stud	Study Type	Study	Attribute	studyType	
C48281	TPHASE	Trial Phase; Trial Phase ..	Trial Phase	Study	Attribute	studyPhase	
		[After ICH E6, WHO, 21 CFR 50.3 (e), and after IDMP]					
C49852	TINTDP	Trial Intent Type	The planned purpose of the study under study in the clinical trial.	Clinical Study by Intent	StudyDesign	Attribute	trialIntentType
C49858	TBLIND	Study Blinding Design; Study Blinding Schema; Study Masking Design; Trial Blinding Design; Trial Blinding Schema; Trial Masking Design	The type of experimental design used to control the level of awareness of the study subjects and/or study personnel as it relates to the respective intervention(s) or assessments being observed, received or administered.	Trial Blinding Schema	StudyDesign	Attribute	studyDesignBlindingScheme
C49860	TTYPE	Trial Scope; Trial Type	The nature of the interventional study for which information is being collected.	Trial Type	StudyDesign	Attribute	trialType
C49892	PLANSUB	Anticipated Enrollment; Planned Enrollment; Planned Number of Subjects; Target Enrollment	The planned number of subjects to be entered in a clinical trial. (NCI)	Planned Subject Number	StudyDesignPopulation	Attribute	plannedNumberOfParticipants
C49893	AGEMIN	Planned Minimum Age of Subjects	The anticipated minimum age of the subjects to be entered in a clinical trial. (NCI)	Planned Minimum Age of Subjects	StudyDesignPopulation	Attribute	plannedMinimumAgeOfParticipants
C49894	AGEMAX	Planned Maximum Age of Subjects	The anticipated maximum age of the subjects to be entered in a clinical trial. (NCI)	Planned Maximum Age of Subjects	StudyDesignPopulation	Attribute	plannedMaximumAgeOfParticipants
C49896	SEXPOP	Sex of Participants	The specific sex, either male, female, or mixed of the subject group being studied. (NCI)	Sex of Study Group	StudyDesignPopulation	Attribute	plannedSexOfParticipants
C49802	TITLE	Official Study Title; Study Title; Trial Title	The sponsor-defined name of the clinical study.	Trial Title	Study	Attribute	studyTitle
C98746	INTMODEL	Intervention Model	The general design of the strategy for assigning interventions to participants in a clinical study. (clinicaltrials.gov)	Intervention Model	StudyDesign	Attribute	interventionModel
C70793	SPONSOR	Clinical Study Sponsor; Sponsor; Study Sponsor	An individual, company, institution, or organization that takes responsibility for the initiation, management, and/or financing of a clinical study. [After ICH E6, WHO, 21 CFR 50.3 (e), and after IDMP]	Clinical Study Sponsor	Organization	Valid Value	Valid Value Set for Attribute organizationType
C85826	OBJPRIM	Study Primary Objective; Trial Primary Objective	A principle objective of the study.	Trial Primary Objective	Objective	Valid Value	Valid Value Set for Attribute objectiveLevel
C85827	OBJSEC	Study Secondary Objective; Trial Secondary Objective	An auxiliary objective of the study.	Trial Secondary Objective	Objective	Valid Value	Valid Value Set for Attribute objectiveLevel



Linking Encounters with Activities

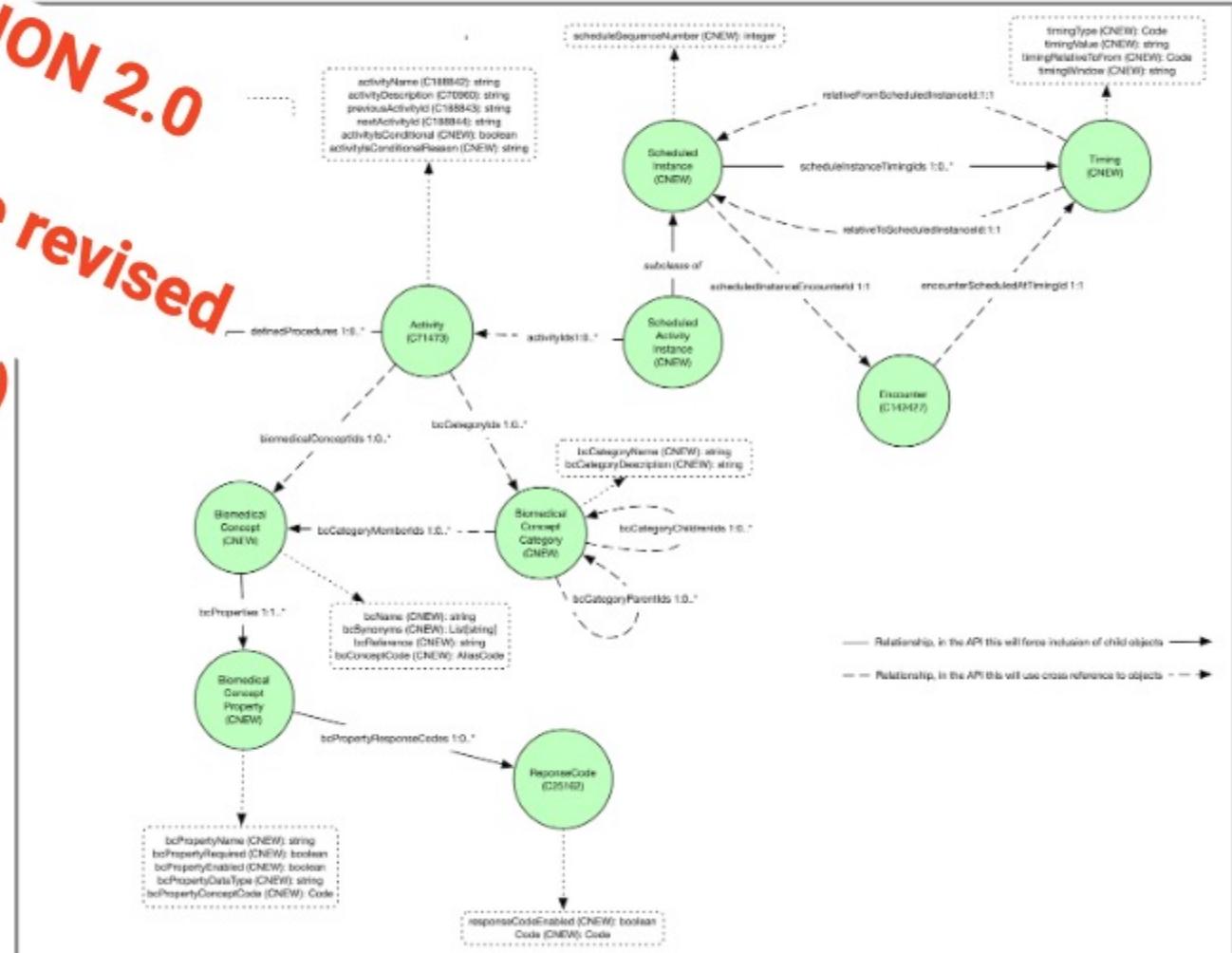
- Scheduled Activity Instance links encounters with Activities
- Timing also provided by linking Scheduled Activity Instance to Timing
- Activity links onto Procedures and BCs
- Important piece is the Activity <-> "timing" <-> Encounter linkage

Activities, Encounters & "Glue"

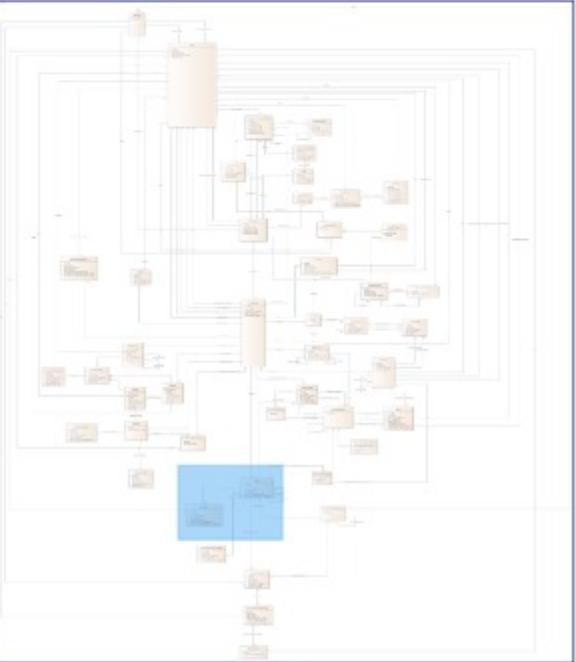
VERSION 2.0

Needs to be revised

Ignore! :)

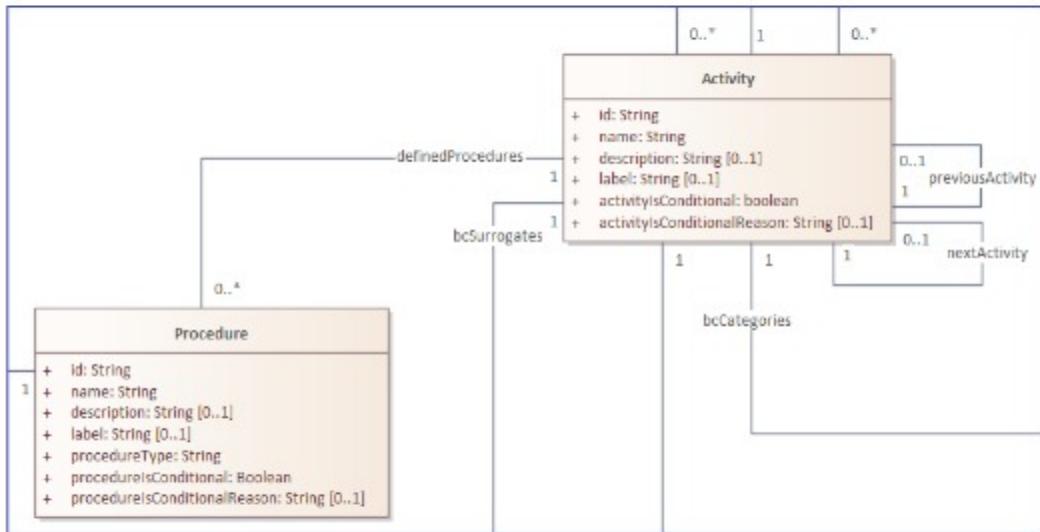


Procedures

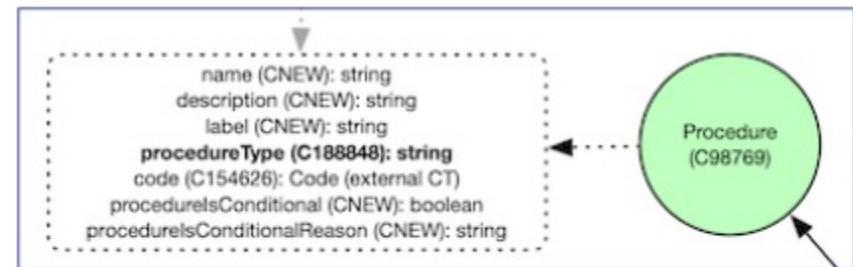


Procedures

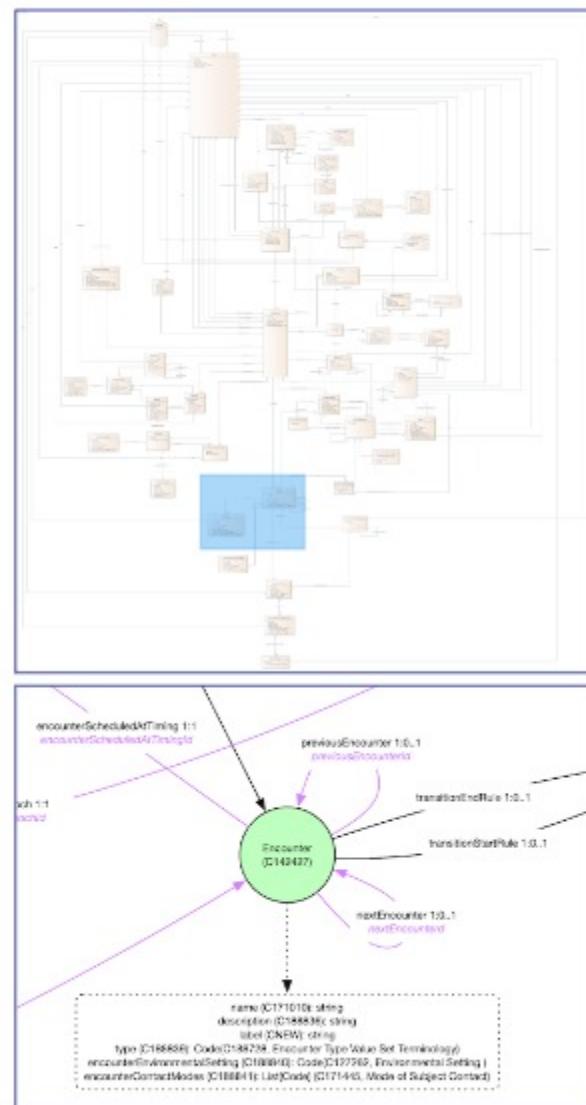
- Linked from activities with multiple procedures per activity
- Name and description added during internal review
- Can be conditional with condition expressed as text



```
{
  "id": "Procedure_2",
  "name": "PR2",
  "label": "6MWT",
  "description": "6min Walk Test conducted after the stress test",
  "procedureType": "Stress",
  "code": {
    "id": "Code_38",
    "code": "12345679",
    "codeSystem": "SNOMED",
    "codeSystemVersion": "January 31, 2018",
    "decode": "Test"
  },
  "procedureIsConditional": true,
  "procedureIsConditionalReason": "Only if stress test passed"
}
```

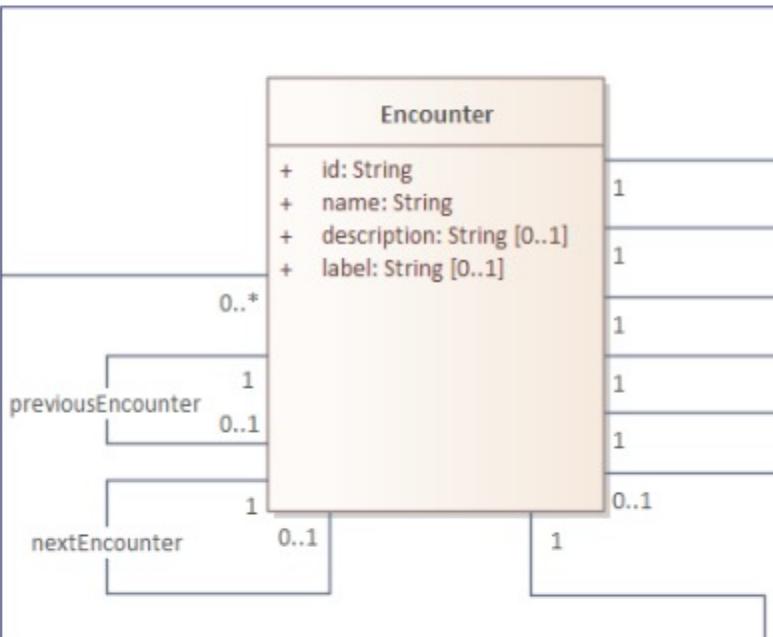


Encounters



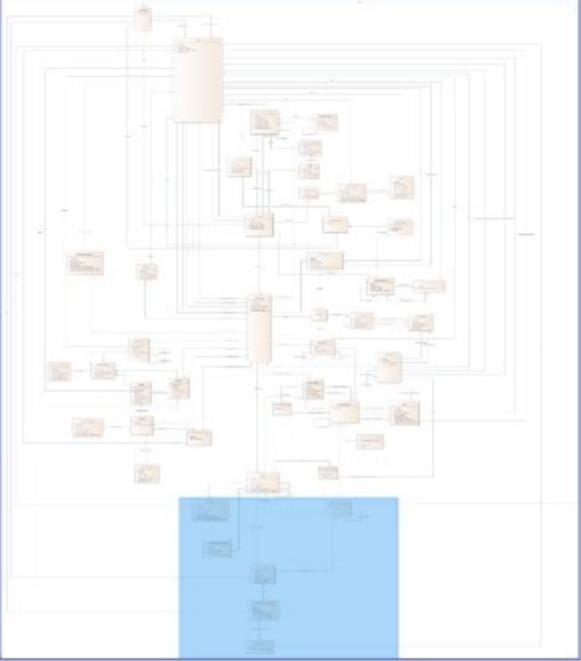
Encounters

- Definition of an encounter
- Cross referenced from Epochs
- References timing to detail the encounter window
- Note encounter type, currently only value is "Visit"



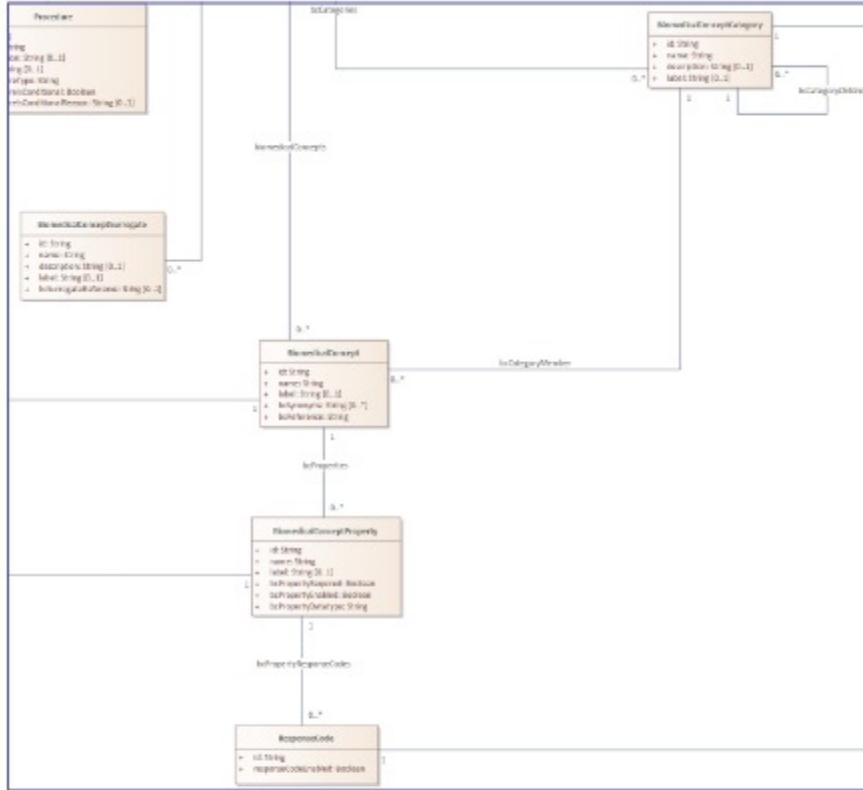
```
{  
  "id": "Encounter_1",  
  "name": "E1",  
  "label": "Screening",  
  "description": "Screening encounter",  
  "type": {  
    "id": "Code_39",  
    "code": "C25716",  
    "codeSystem": "http://www.cdisc.org",  
    "codeSystemVersion": "2023-09-29",  
    "decode": "Visit"  
  },  
  "previousEncounterId": null,  
  "nextEncounterId": "Encounter_2",  
  "encoderScheduledAtTimingId": null,  
  "encoderEnvironmentalSetting": {  
    "id": "Code_40",  
    "code": "C51282",  
    "codeSystem": "http://www.cdisc.org",  
    "codeSystemVersion": "2023-09-29",  
    "decode": "Clinic"  
  },  
  "encoderContactModes": [  
    {  
      "id": "Code_41",  
      "code": "C175574",  
      "codeSystem": "http://www.cdisc.org",  
      "codeSystemVersion": "2023-09-29",  
      "decode": "In Person"  
    }  
,  
    "transitionStartRule": {  
      "id": "TransitionRule_1",  
      "name": "ENCOUNTER_START_RULE_1",  
      "label": null,  
      "description": null,  
      "text": "Subject identified"  
    },  
    "transitionEndRule": {  
      "id": "TransitionRule_2",  
      "name": "ENCOUNTER_START_RULE_1",  
      "label": null,  
      "description": null,  
      "text": "IEs passed"  
    }  
  ]  
}
```

Biomedical Concepts I



Biomedical Concepts

- Allows for
 - Single BC
 - Hierarchy of BCs
 - Surrogate BCs
- Based on CDISC BC Model
- See example of simple BC to the right



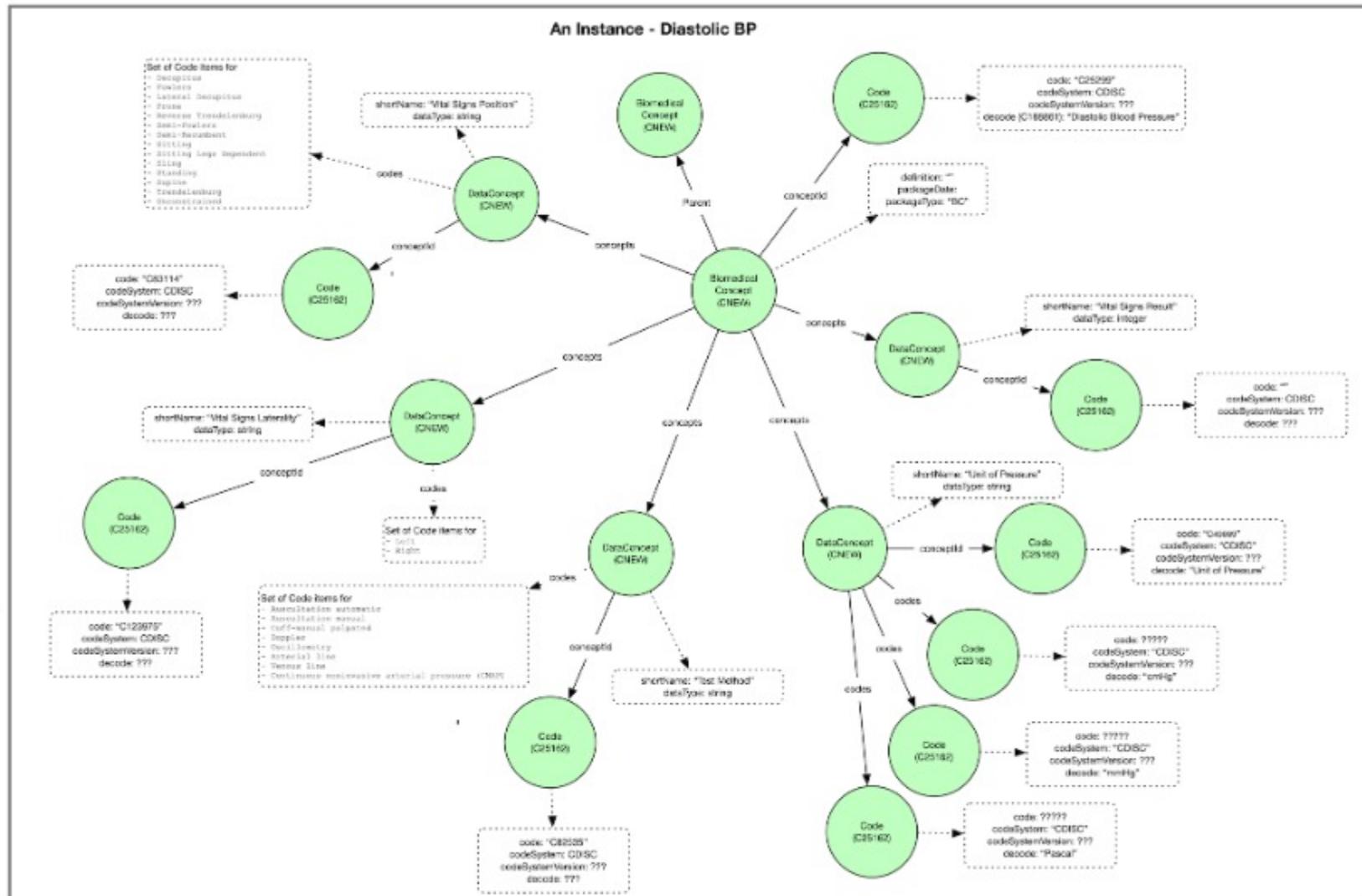
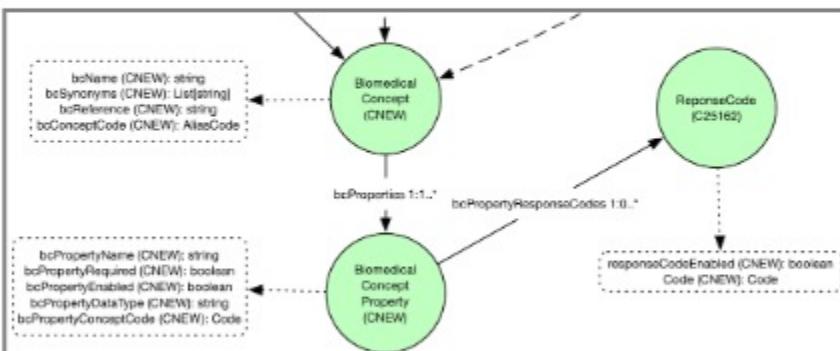
Slide Deck

- Sets the scene for BCs
- Used several times to provide the background around BCs

Biomedical Concepts II

View of an CDISC API Instance

- Image is a little old now but useful if you are not familiar with the idea of BCs
 - Note
 - Central note and the multiple "data concept" or "property" nodes
 - Code responses or definition, e.g.
 - identification is a single code
 - units has multiple codes
 - USDM BCs have three levels, see model below



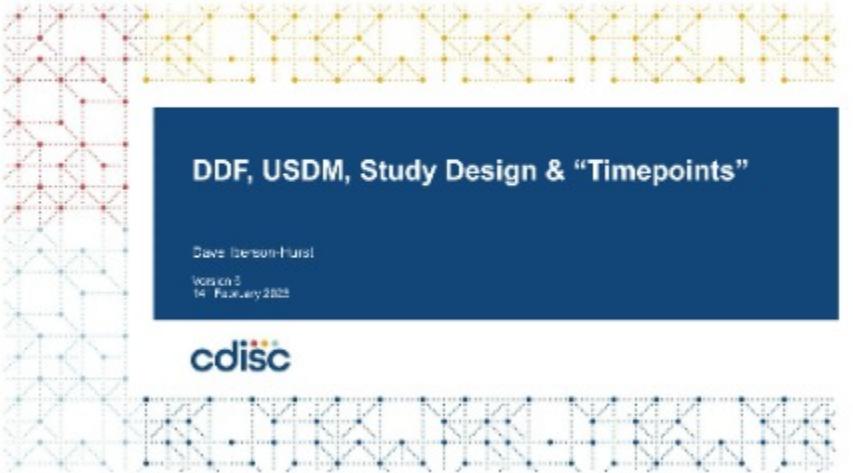
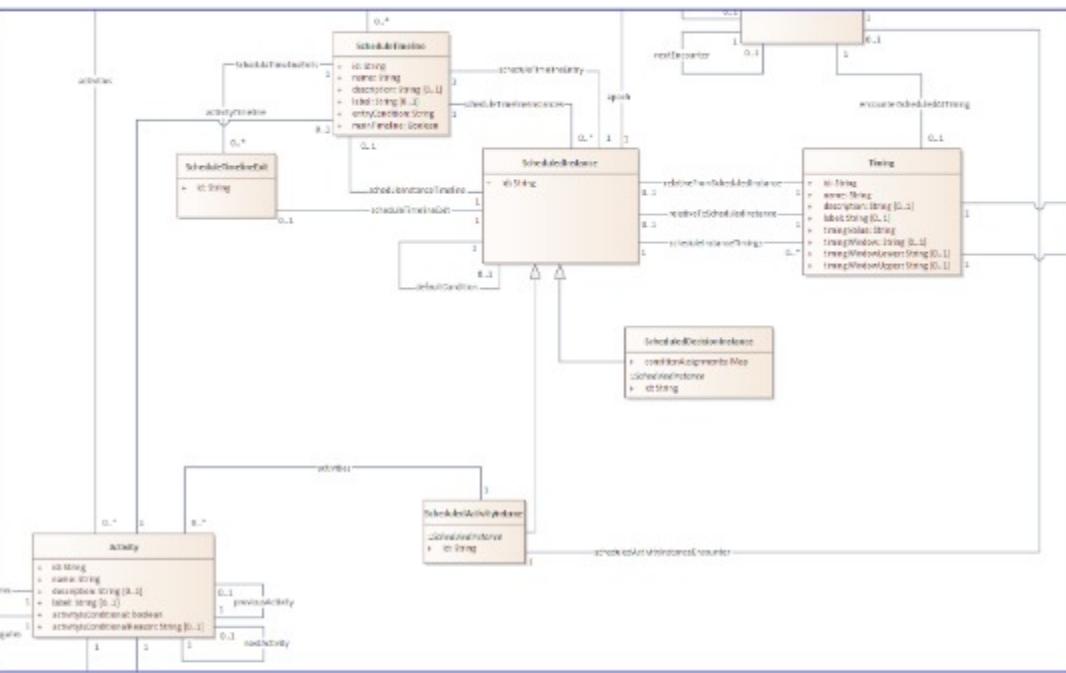
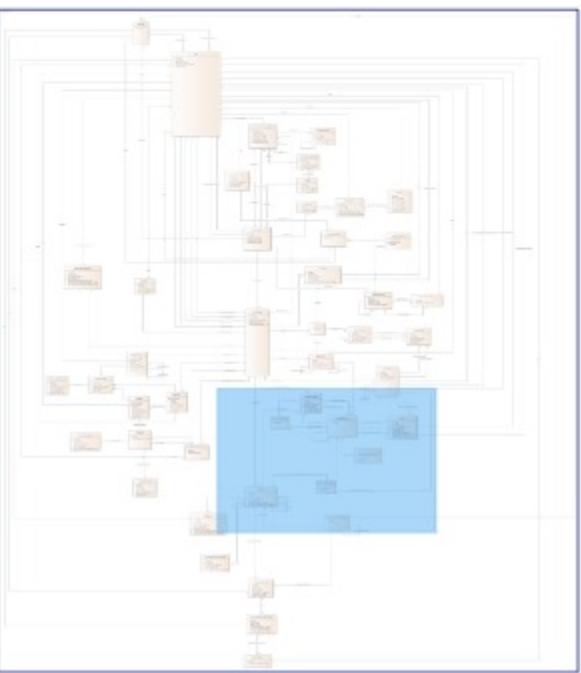
Biomedical Concepts III

Example BC Content

- Work ongoing to improve ISDM examples to use CDISC SDTM specializations
- Use these to fully populate USDM BC definitions

```
---
BiomedicalConcept:
  bcName: Diastolic Blood Pressure
  bcConceptId:
    standardCode:
      code: C25299
      codeSystem: http://www.cdisc.org
      codeSystemVersion: "2022-03-25"
      decode: Diastolic Blood Pressure
    standardCodeAliases:
    -
      code: 8462-4
      codeSystem: http://loinc.org/
      codeSystemVersion: "2022-03-25"
      decode: Diastolic Blood Pressure
    -
      code: 271650006
      codeSystem: SNOMED-CT
      codeSystemVersion: "2003"
      decode: Diastolic blood pressure
    -
      code: 4154790
      codeSystem: OHSDI
      codeSystemVersion:
      decode: Diastolic blood pressure
    -
      bcSynonyms:
        - DIABP
        - DIA BP
        - Blood pressure diastolic
    ...
  bcProperties:
  -
    ...
bcProperties:
-
  bcPropertyName: Vital Signs Result
  bcPropertyEnabled: true
  bcPropertyRequired: true
  bcPropertyDataType: integer
  bcPropertyConceptId:
    code: C173522
    codeSystem: http://www.cdisc.org
    codeSystemVersion: "2022-03-25"
    decode: Vital Signs Result
  bcPropertyResponseCodes: []
-
  bcPropertyName: Unit of Pressure
  bcPropertyEnabled: true
  bcPropertyRequired: true
  bcPropertyDataType: string
  bcPropertyConceptId:
    code: C49669
    codeSystem: http://www.cdisc.org
    codeSystemVersion: "2022-03-25"
    decode: Unit of Pressure
  bcPropertyResponseCodes:
  -
    responseCodeEnabled: true
    code:
      code: C49670
      codeSystem: http://www.cdisc.org
      codeSystemVersion: "2022-03-25"
      decode: mmHg
  -
    responseCodeEnabled: true
    code:
      code: C42547
      codeSystem: http://www.cdisc.org
      codeSystemVersion: "2022-03-25"
      decode: Pascal
```

Study Design and Timing



Slide Deck

- Outlines requirements (slides 7-26)
 - Complex timing
 - Branching
 - Cycles
- Slides 28-44 provide "instance" examples to explain the ideas
- Things have moved on since the slide set was written
 - For example, class naming has changed
 - Still useful for overall concept

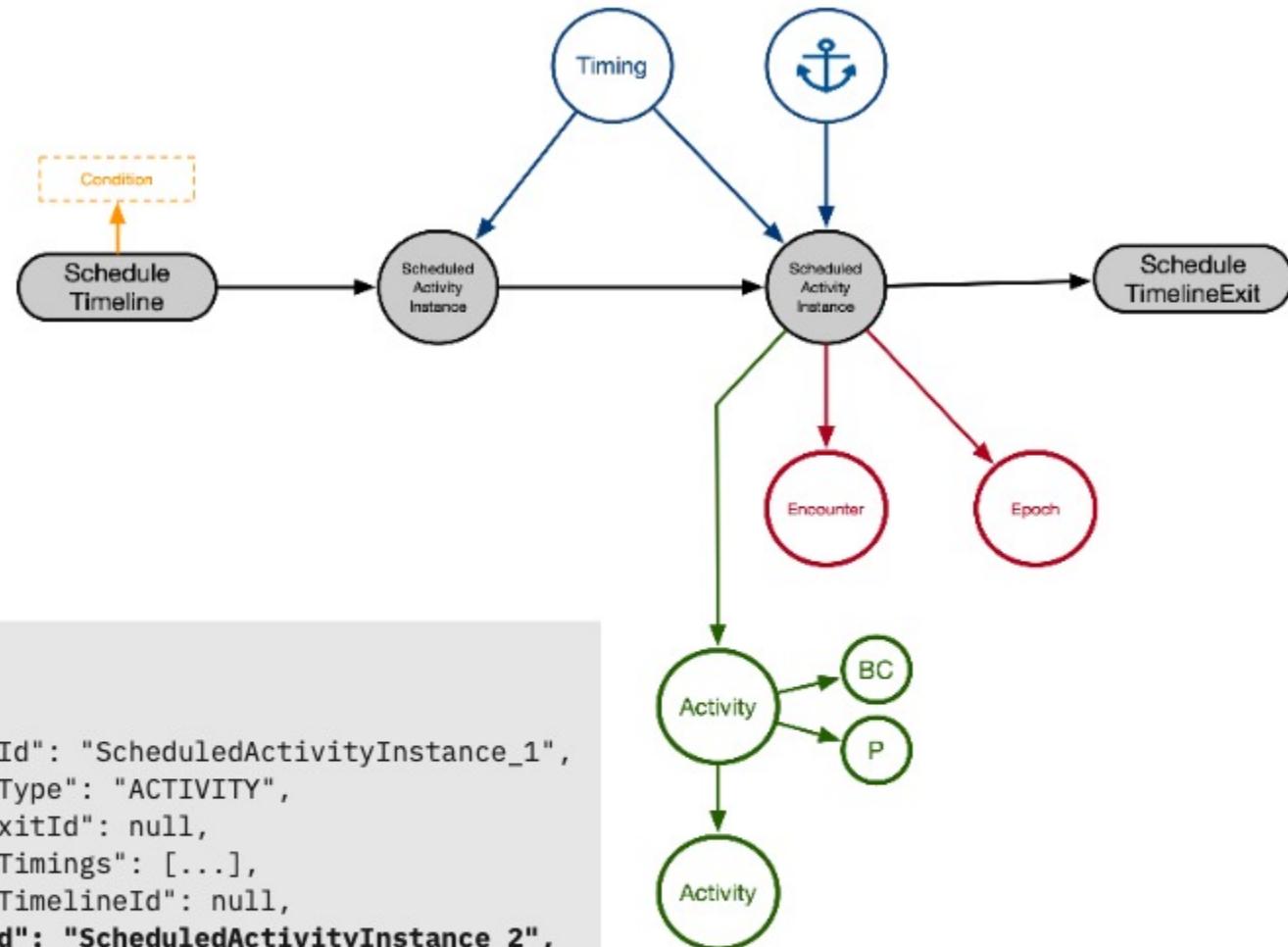
"Timepoints"

- "Timepoints" was a label given to this area on the DDF project just for easy identification of an area of work.
- It is all about study timing

Timeline

Basics

- Based upon a “timeline” that uses
 - Entry and Exit
 - Conditions
 - Activity Instances
 - Condition Instances
 - Timing
- Activity Instances are linked by Timing information to position the instances in the timeline
- Linked to encounters, activities as per the current USDM
- Timelines can be referenced and reused



```
{  
  ...  
  {  
    "scheduledInstanceId": "ScheduledActivityInstance_1",  
    "scheduledInstanceType": "ACTIVITY",  
    "scheduleTimelineExitId": null,  
    "scheduledInstanceTimings": [...],  
    "scheduledInstanceTimelineId": null,  
    "defaultConditionId": "ScheduledActivityInstance_2",  
    "epochId": "StudyEpoch_1",  
    "activityIds": [...],  
    "scheduledActivityInstanceEncounterId": "Encounter_1"  
  },  
  ...  
}
```

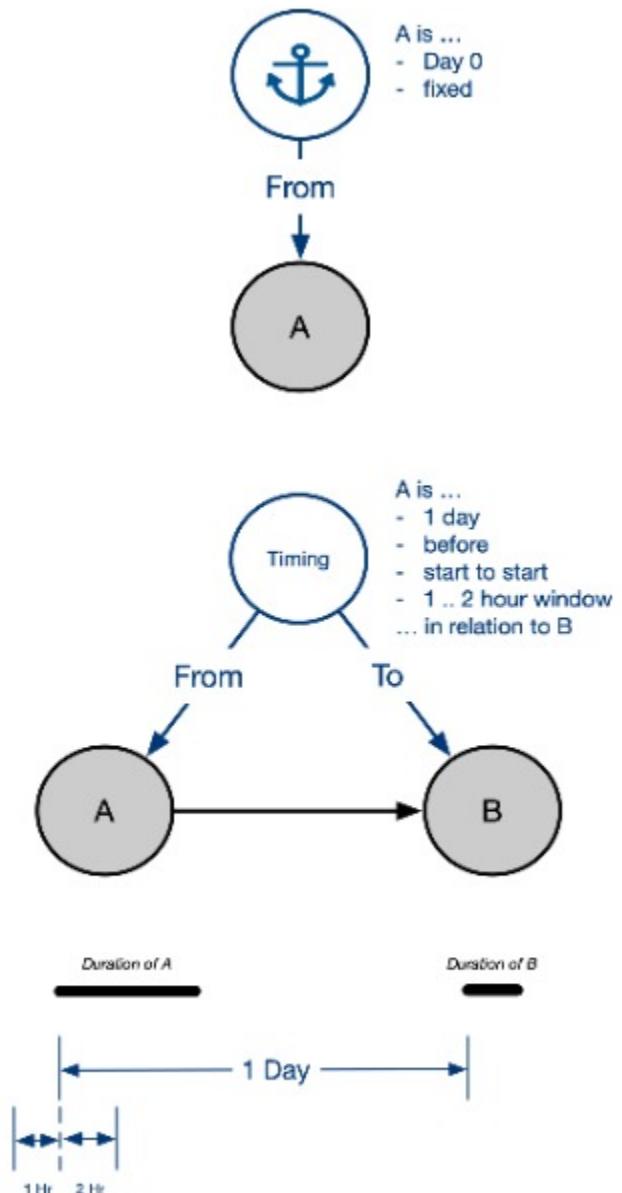
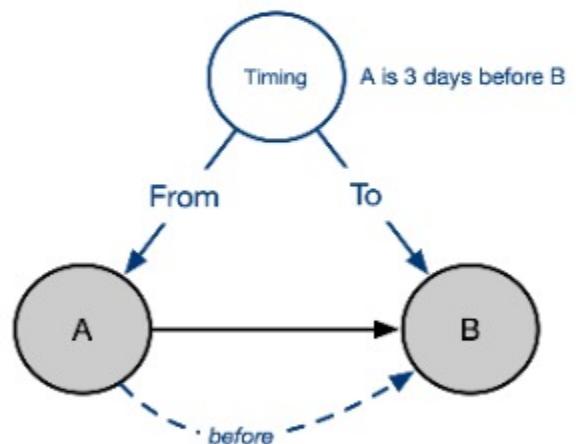
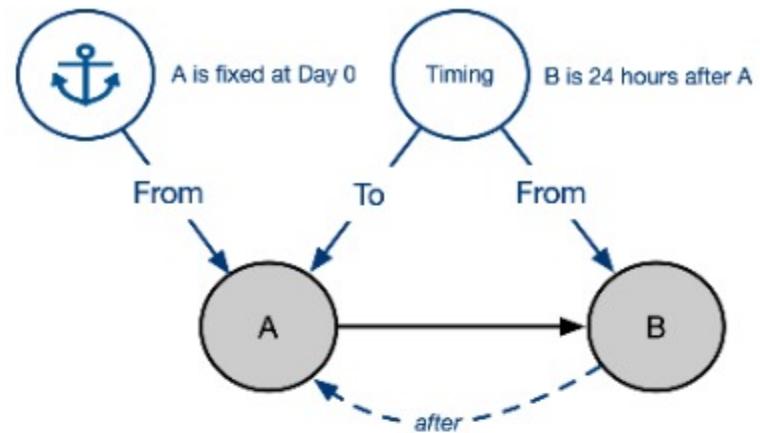
A **ScheduledActivityInstance** Example.
Colour coding to match diagram

Timing

Basics

- Two types of relationship
 - Anchor - A fixed point
 - Before or After - A relative point
- Window can be defined
- Descriptive and coded timing values
- Coded values are ISO8601 Durations

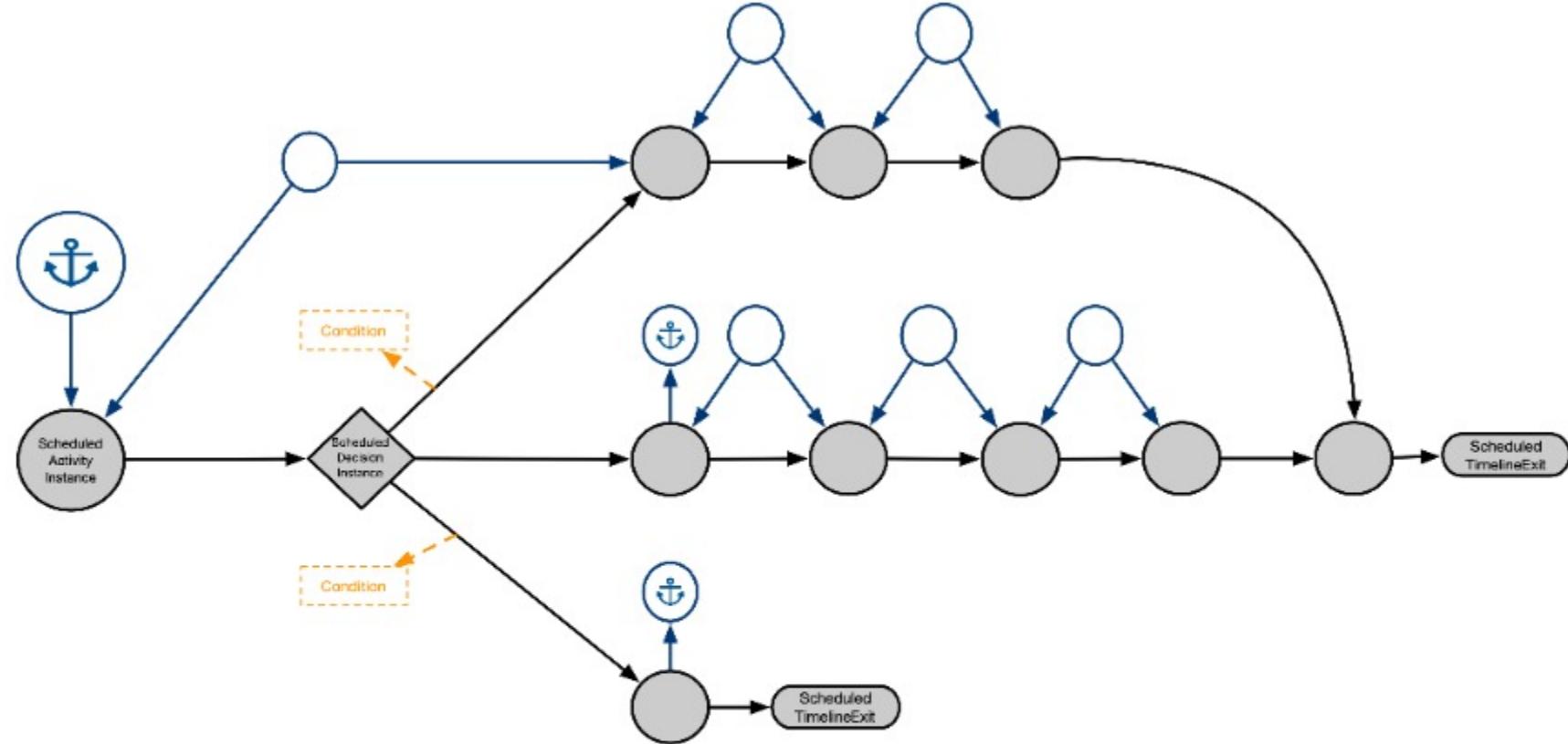
```
{  
  "id": "Timing_2",  
  "name": "TIM2",  
  "label": "Pre dose",  
  "description": "Pre dose timing",  
  "type": {  
    "id": "Code_67",  
    "code": "C201264",  
    "codeSystem": "http://www.cdisc.org",  
    "codeSystemVersion": "2023-09-29",  
    "decode": "Before"  
  },  
  "timingValue": "PT15M",  
  "timingRelativeToFrom": {  
    "id": "Code_68",  
    "code": "C201265",  
    "codeSystem": "http://www.cdisc.org",  
    "codeSystemVersion": "2023-09-29",  
    "decode": "Start to Start"  
  },  
  "relativeFromScheduledInstanceId": "ScheduledActivityInstance_2",  
  "relativeToScheduledInstanceId": "ScheduledActivityInstance_3",  
  "timingWindowLower": "PT4H",  
  "timingWindowUpper": "PT0H",  
  "timingWindow": "-4..0 hours"  
}
```



Branching

Basics

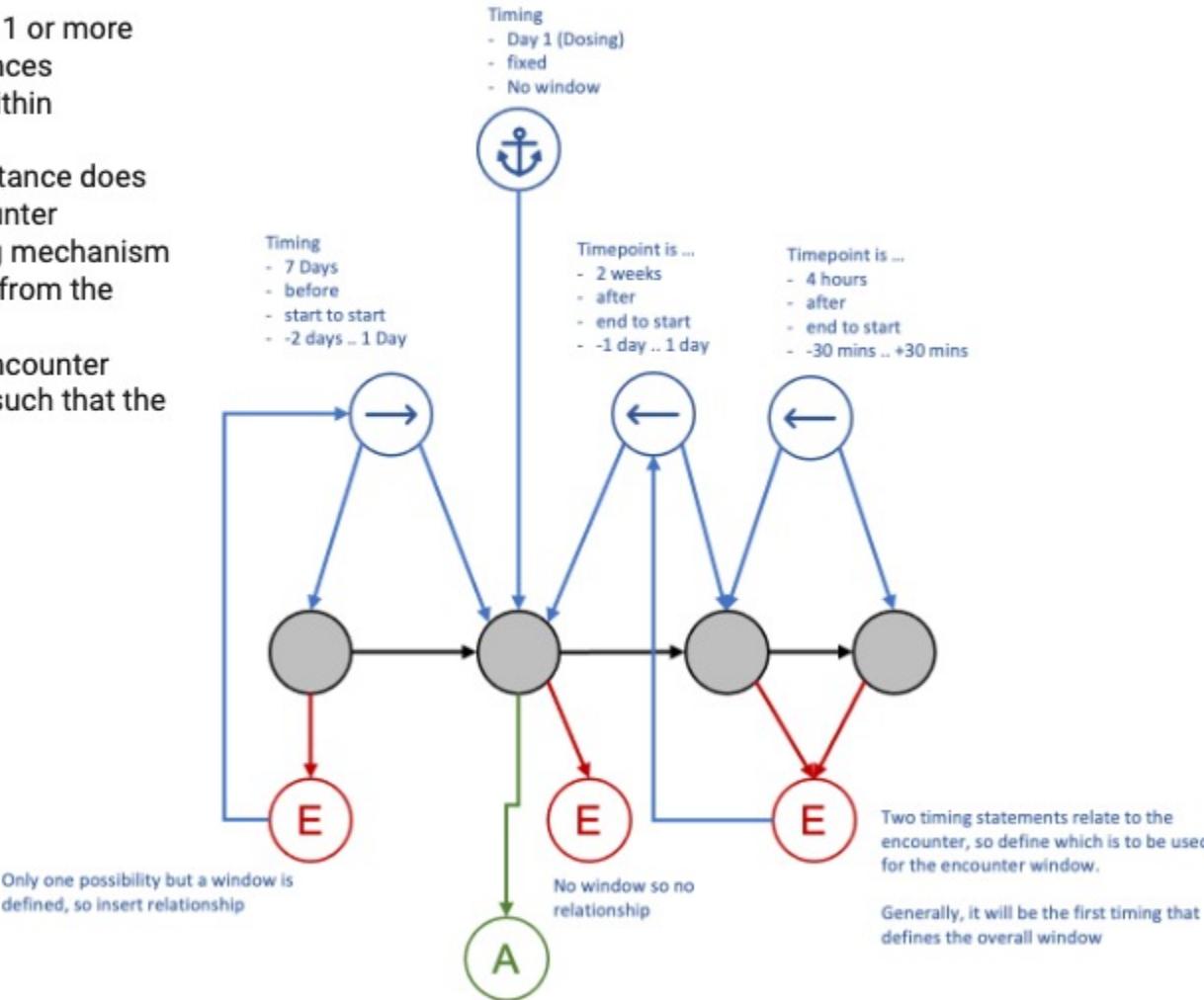
- Uses the Decision Instance
- Defined as a switch
- A set of (condition, destination) pairs
- A default link (if no condition is met)



Encounters and Timing Windows

Basics

- An encounter can be linked from 1 or more ScheduledActivityInstance instances
- This allows for detailed timing within encounters when needed
- Note that a ScheduledActivityInstance does not need to be linked to an encounter
- The timeline is the precise timing mechanism
- The encounter derives its timing from the timeline.
- A relationship is inserted from Encounter instance to the Timing instance such that the encounter window is defined

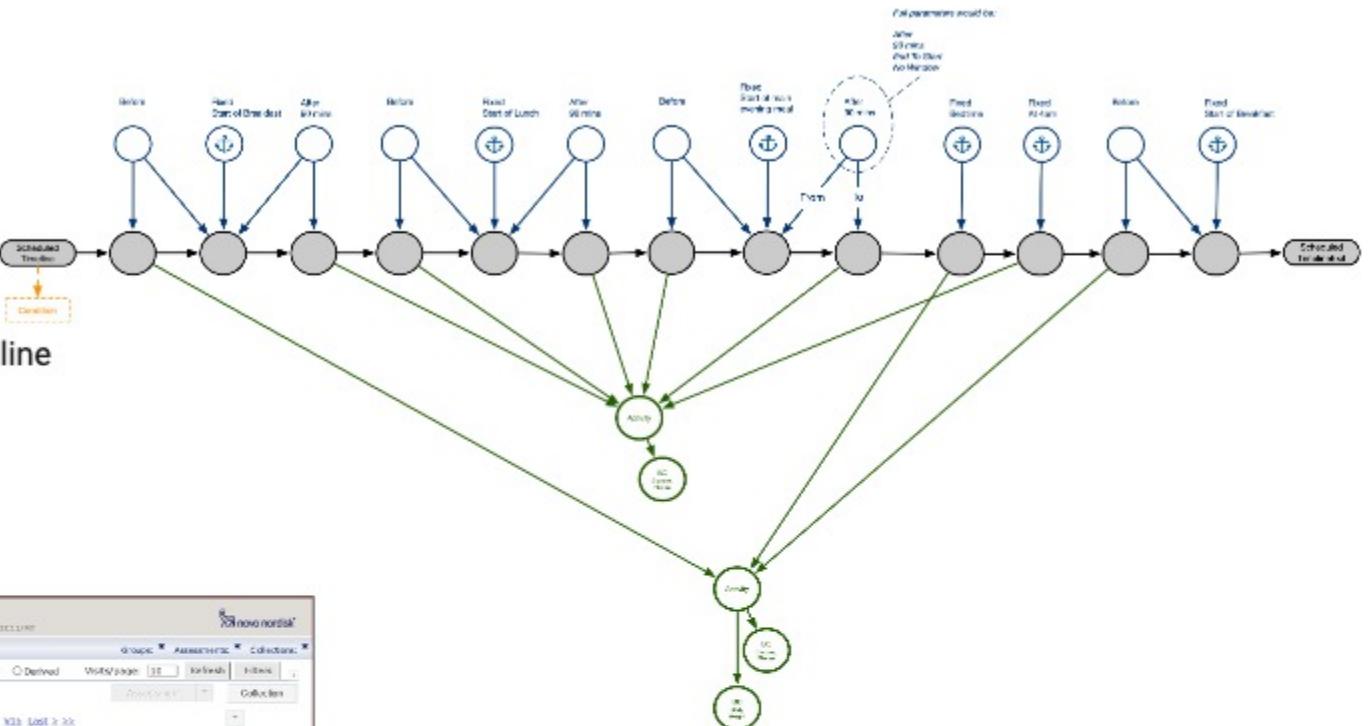


```
{  
  "id": "Encounter_1",  
  "name": "E1",  
  "label": "Screening",  
  "description": "Screening encounter",  
  "type": {  
    "id": "Code_51",  
    "code": "C25716",  
    "codeSystem": "http://www.cdisc.org",  
    "codeSystemVersion": "2023-09-29",  
    "decode": "Visit"  
  },  
  "previousEncounterId": null,  
  "nextEncounterId": "Encounter_2",  
  "encounterScheduledAtTimingId": "Timing_1",  
  "encounterEnvironmentalSetting": {  
    "id": "Code_52",  
    "code": "C51282",  
    "codeSystem": "http://www.cdisc.org",  
    "codeSystemVersion": "2023-09-29",  
    "decode": "Clinic"  
  },  
  "encounterContactModes": [  
    {  
      "id": "Code_53",  
      "code": "C175574",  
      "codeSystem": "http://www.cdisc.org",  
      "codeSystemVersion": "2023-09-29",  
      "decode": "In Person"  
    }  
  ],  
  "transitionStartRule": {  
    "id": "TransitionRule_1",  
    "name": "ENCOUNTER_START_RULE_1",  
    "label": null,  
    "description": null,  
    "text": "Subject identified"  
  },  
  "transitionEndRule": {  
    "id": "TransitionRule_2",  
    "name": "ENCOUNTER_START_RULE_1",  
    "label": null,  
    "description": null,  
    "text": "IEs passed"  
  }  
}
```

Profile

Basics

- Uses the timeline pattern
- Reusable
- Linked to an activity or timeline



CDW Operations Trial Flowchart

Trial ID: CDISC360-2 **Assessments:** All Non-derived Derived

	V1	V2	V3	V4	V5	V6	V7	V8	V9	V10
Screening	X									
Baseline		X	X	X	X	X	X	X	X	X
Treatment			X	X	X	X	X	X	X	X
Treatment				X	X	X	X	X	X	X
Treatment					X	X	X	X	X	X
Treatment						X	X	X	X	X
Treatment							X	X	X	X
Treatment								X	X	X
Treatment									X	X
Treatment										X

Time Point Sequence

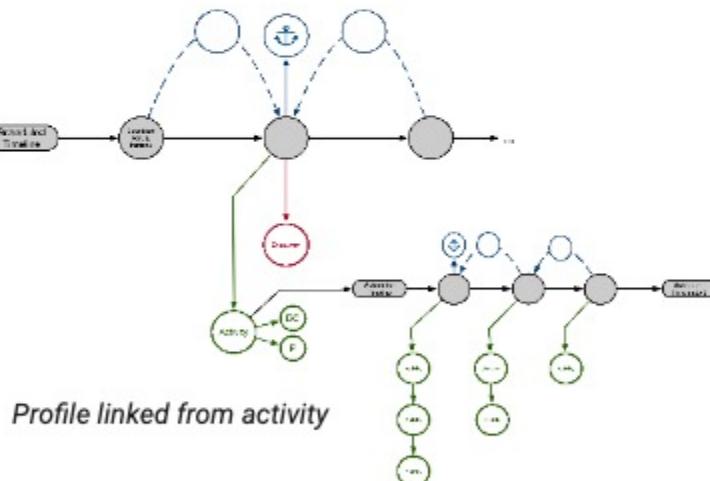
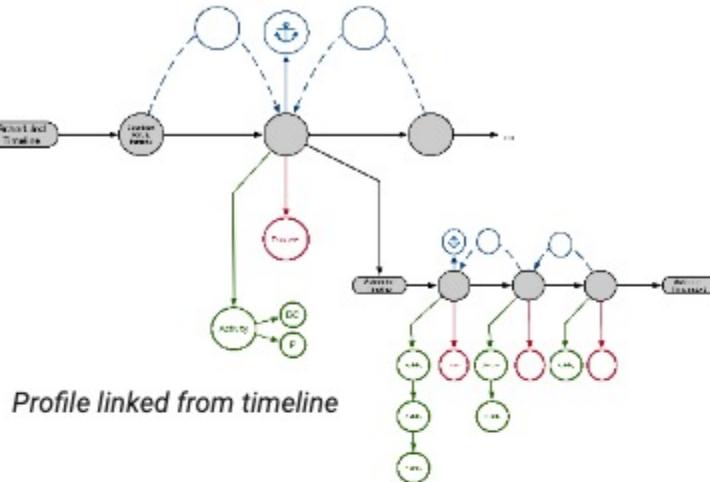
Sequence Time
1. Before breakfast
2. 90 minutes after start of breakfast
3. Before lunch
4. 90 minutes after start of lunch
5. Before main evening meal
6. 90 min after main evening meal
7. Bedtime
8. At 04:00 A.M.
9. Before breakfast the following day

Buttons: Add Time Point, Delete Time Point, Save

Trial ID: CDISC360-2 **Trial Definition ID:** CTR
Trial Metadata: 4 **Version:**
Trial Definition: Draft **Status:** Draft
Profile Name: 9-point profile **Profile Type:** Sequence Profile

Time Point Sequence	Sequence Time
1.	Before breakfast
2.	90 minutes after start of breakfast
3.	Before lunch
4.	90 minutes after start of lunch
5.	Before main evening meal
6.	90 min after main evening meal
7.	Bedtime
8.	At 04:00 A.M.
9.	Before breakfast the following day

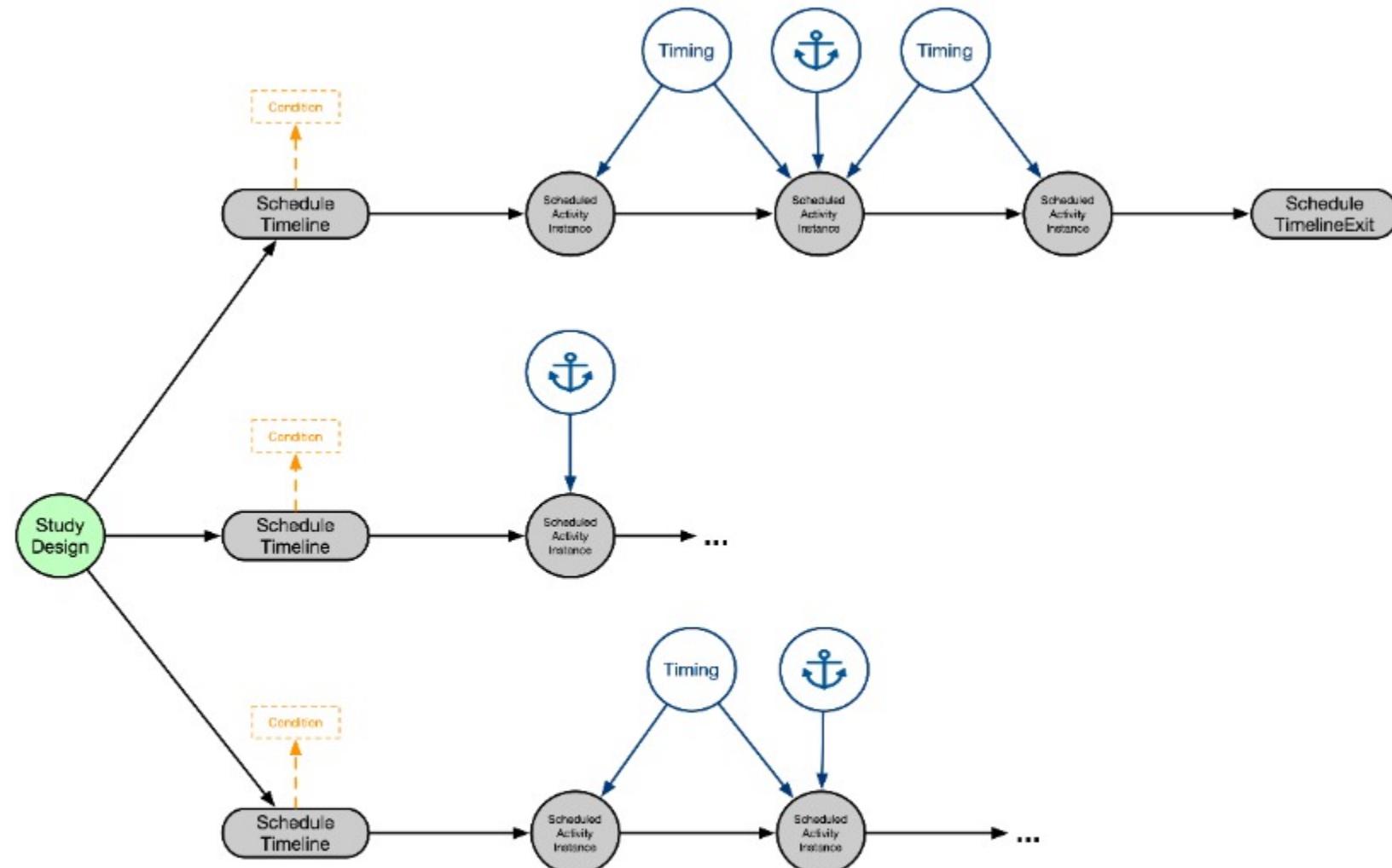
Buttons: Add Time Point, Delete Time Point, Save



Unscheduled

Basics

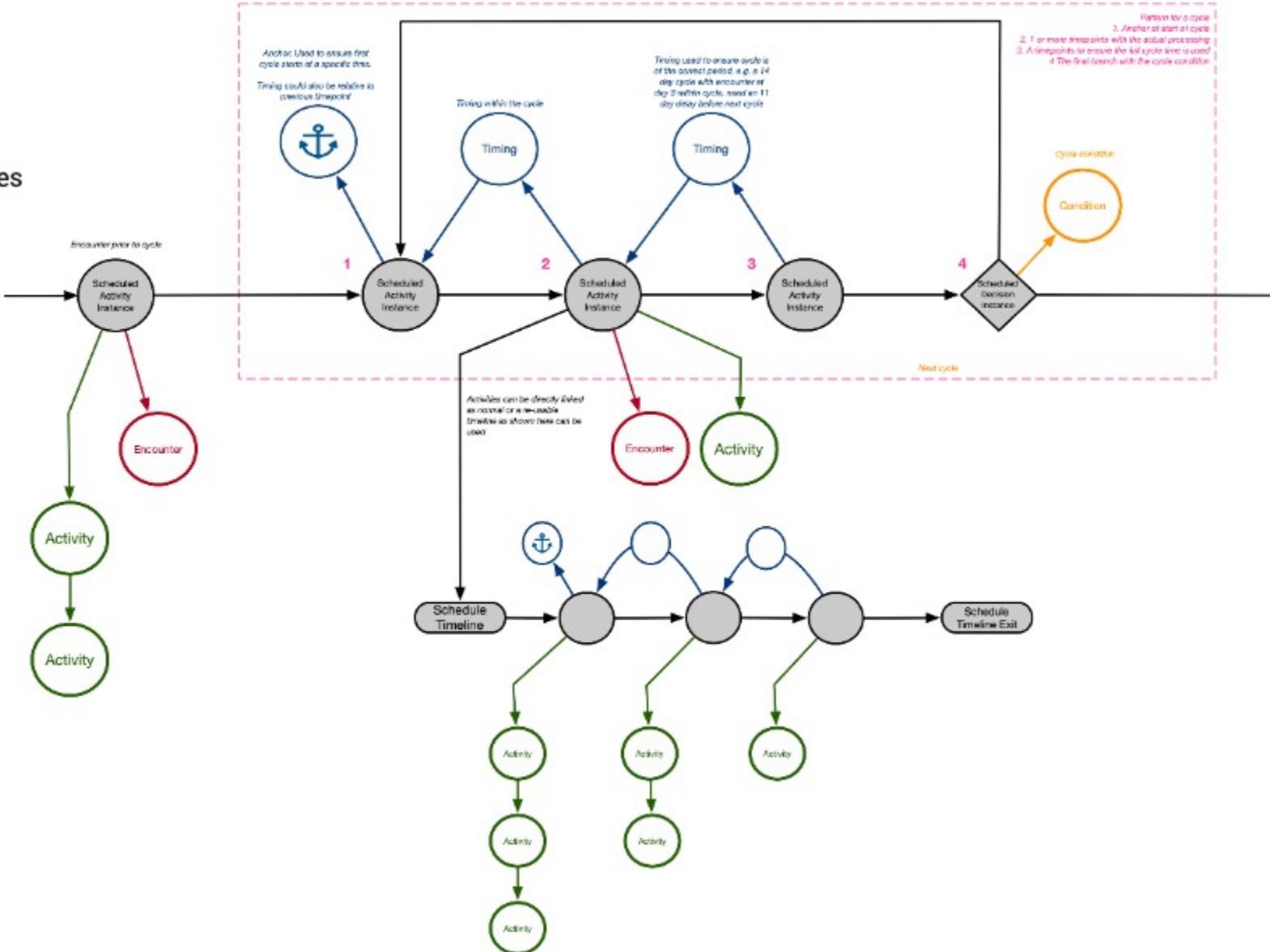
- Each potential unscheduled event handled as a timeline
- One main path
- Several child paths for unscheduled events
- A condition for each
- As many instances and timing as needed
- Linked to activities, encounters as needed
- Some instances need not be linked to encounters



Cycles

Basics

- One mechanism for implementing cycles
- Other patterns could be implemented



USDM Examples I

Test Utility

- Developing a test utility:
 - Multi-sheet Excel file containing a full USDM definition (bar one or two pieces)
 - Intended to build the full USDM JSON
 - Also builds a visualisation
- Will be available as a python package

Github Examples

See JSON examples
[main branch](#)

The screenshot shows a GitHub repository named 'ddf-ra/Documentation/Examples'. It lists several files and their commit history:

- ... (commit 2 months ago)
- CDISC_Pilot (commit 2 months ago)
- NCT03421379 (commit 2 months ago)
- NCT04320095 (commit 2 months ago)
- Other (commit 2 months ago)
- README.md (commit 5 months ago)

Examples Currently Being Updated to V2.5

Note

- No BC category example as yet

Current Examples

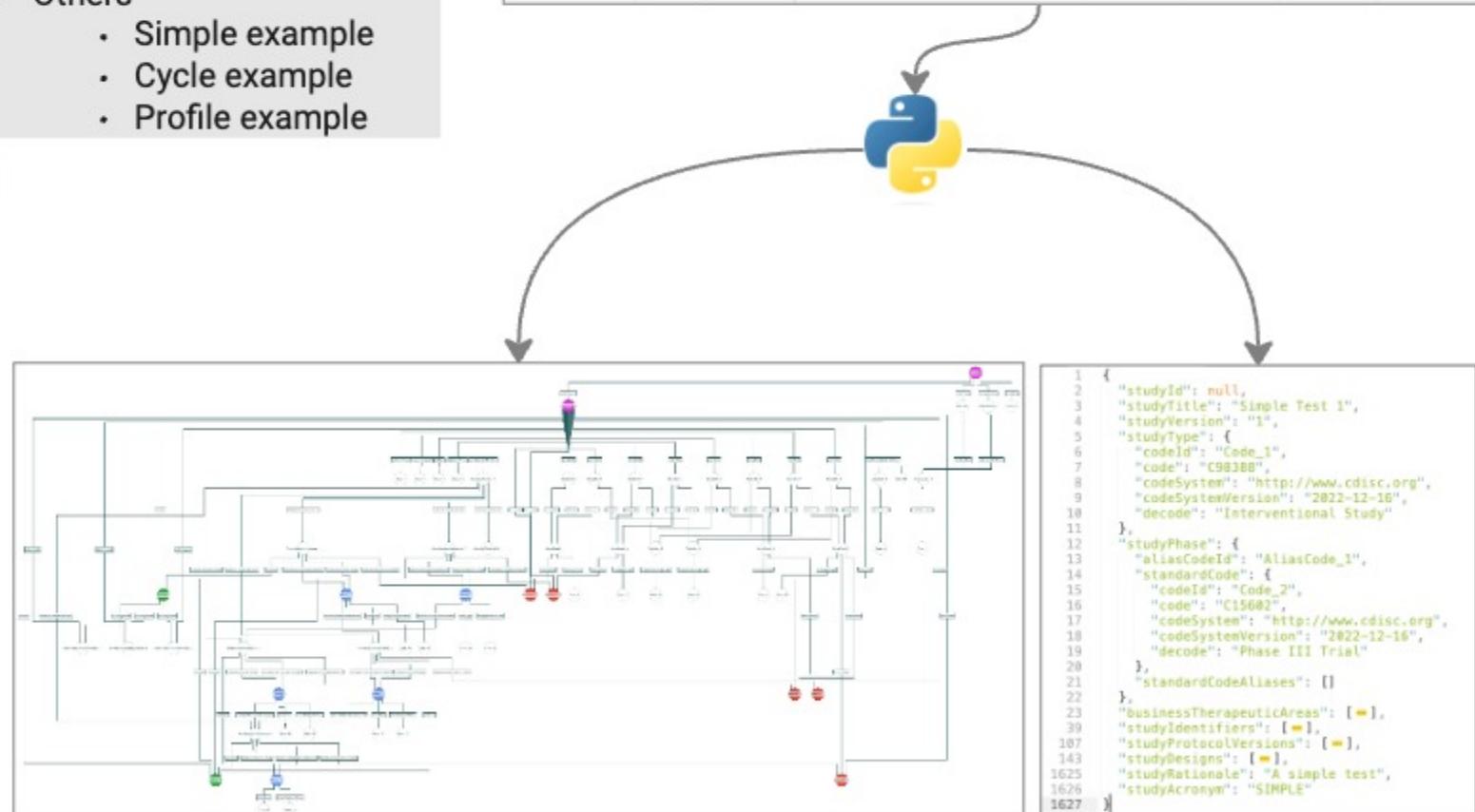
- A Roche Study
- CDISC Pilot Study
- Eli Lilly Study
- Others
 - Simple example
 - Cycle example
 - Profile example

Epoch	Screening	Baseline	Treatment	Follow-Up
Cycle	-	-	-	-
First Cycle Start	-	-	-	-
Cycle Period	-	-	-	-
Cycle End Rule	-	-	-	-
Timing	N: 0..2 Days	N: Pre Dose	A: P: +24 Hours	P: +7 Days
Visit Label	Screening	Baseline	15 min	Day 24
Visit Window	0..4 Hours	0..1 Hours		-3..3 Days

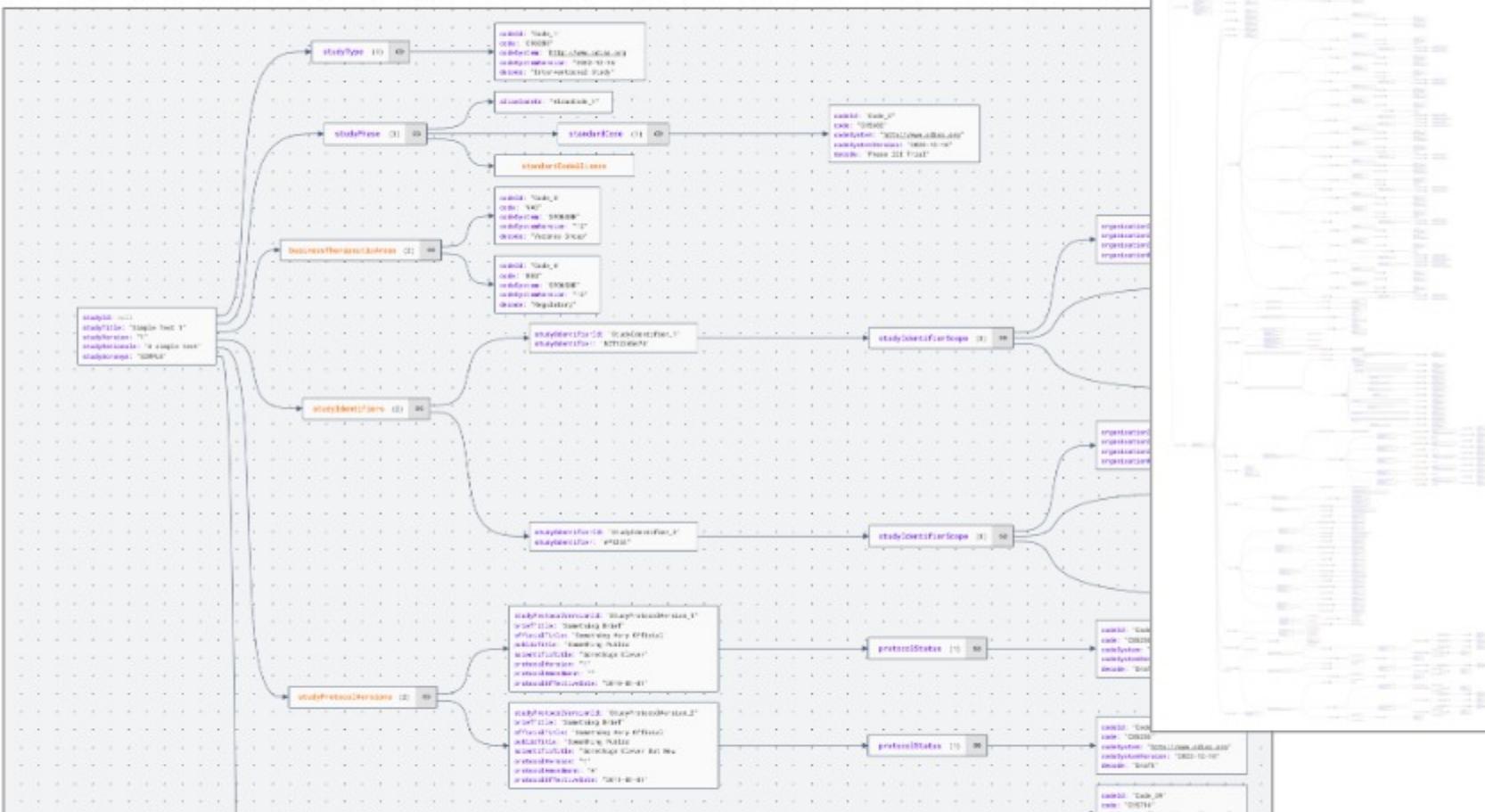
Parent Activity Child Activity BC/Profile

- Demographics BC:Age, BC:Sex, BC:Race

- Something Else -



USDM Examples II



Visualise Examples

Useful JSON tool, [JSON Crack Editor](#)

Online Utility

- Useful visualisation
- Does NOT do cross references
- **Limit on size of file**

Web Version

Online conversion [tool here](#).

The screenshot shows a web-based utility for converting USDM Excel files to JSON. It includes a header 'USDM Excel to JSON Utility STATUS', a section for 'Excel File List' displaying three files, and a 'File List' table. At the bottom, there's an 'Upload New Excel File' section with a 'CLICK TO UPLOAD NEW FILE' button.

File	Last Modified	Status
Roche Phase 3 NCT04320615.xlsx	2023-04-14	X G
cycles_1.xlsx	2023-04-14	X G
example_3.xlsx	2023-04-14	X G

Online Utility

- Saves installing any software
- Will upload Excel file and return JSON equivalent
- No login as yet but will be added

USDM Examples III

Infographic

Download high resolution [version here](#)
Further info will be added

