Digital Data Flow

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)

WITH STANDARDS – UNLOCK THE POWER OF DATA

cdisc

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)
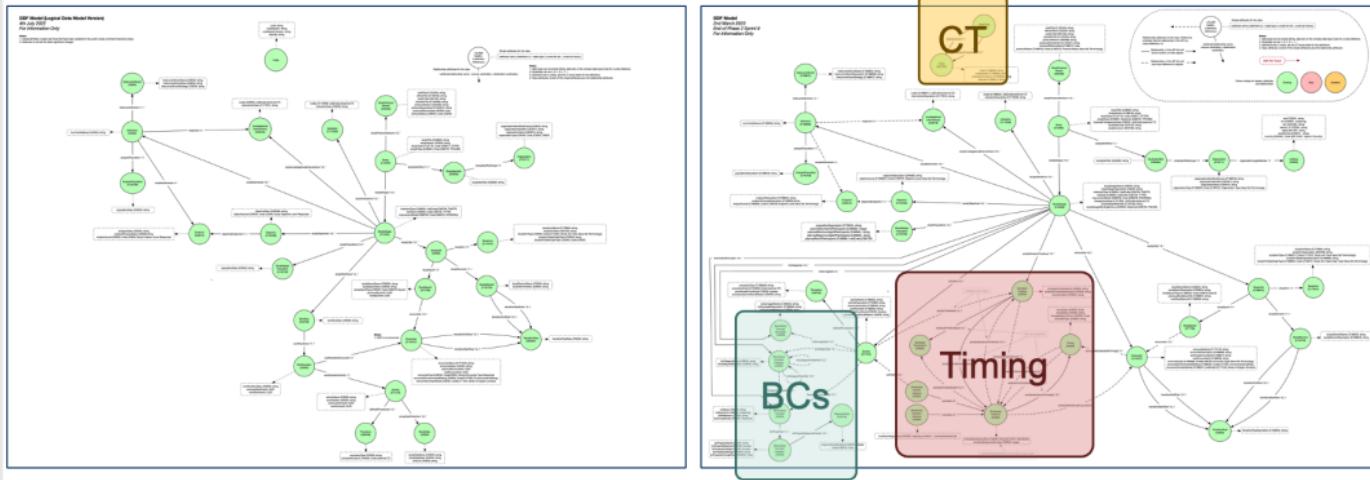
- Phase 1 -> USDM V1
- Phase 2 -> USDM V2
- **At GGG Apporval Stage**
- **To Be Published July 2023**

MIRO Board Status

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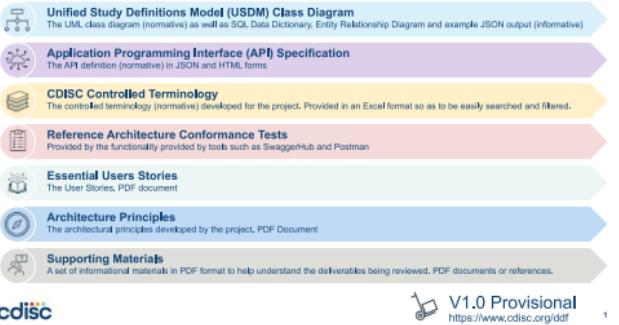
Phase One and Two

CDISC DDF Phase One v Two

CDISC DDF Phase One

July, 2021 – July 2022

Unified Study Definitions Model (USDM) Class Diagram
The UML class diagram (normative) as well as SQL Data Dictionary, Entity Relationship Diagram and example JSON output (informative)

Application Programming Interface (API) Specification
The API definition (normative) in JSON and HTML forms

CDISC Controlled Terminology
The controlled terminology (normative) developed for the project. Provided in an Excel format so as to be easily searched and filtered.

Reference Architecture Conformance Tests
Provided by the functionality provided by tools such as SwaggerHub and Postman

Essential Users Stories
The User Stories. PDF document

Architecture Principles
The architectural principles developed by the project. PDF Document

Supporting Materials
A set of informational materials in PDF format to help understand the deliverables being reviewed. PDF documents or references.

cdisc

V1.0 Provisional
https://www.cdisc.org/ddf

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

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

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	C93490	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	StudyProtocolVersion	Attribute	briefTitle	C132345	Brief Protocol Title	Abbreviated Protocol Title	The short descriptive name for the protocol.	N
14	StudyProtocolVersion	Attribute	officialTitle	C132346	Official Protocol Title		The formal descriptive name for the protocol.	N
15	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
16	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
17	StudyProtocolVersion	Attribute	protocolVersion	C93490	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
18	StudyProtocolVersion	Attribute	protocolAmendment	C132347	Study Protocol Amendment		A written description of a change(s) to, or formal clarification of, a protocol. (ICH E6)	N
19	StudyProtocolVersion	Attribute	protocolEffectiveDate	C188817	Study Protocol Amendment Effective Date		The date and time specifying when the protocol amendment takes effect or becomes operative.	N
20	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

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

**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
2023-03-08	2.0 Draft for Internal Review
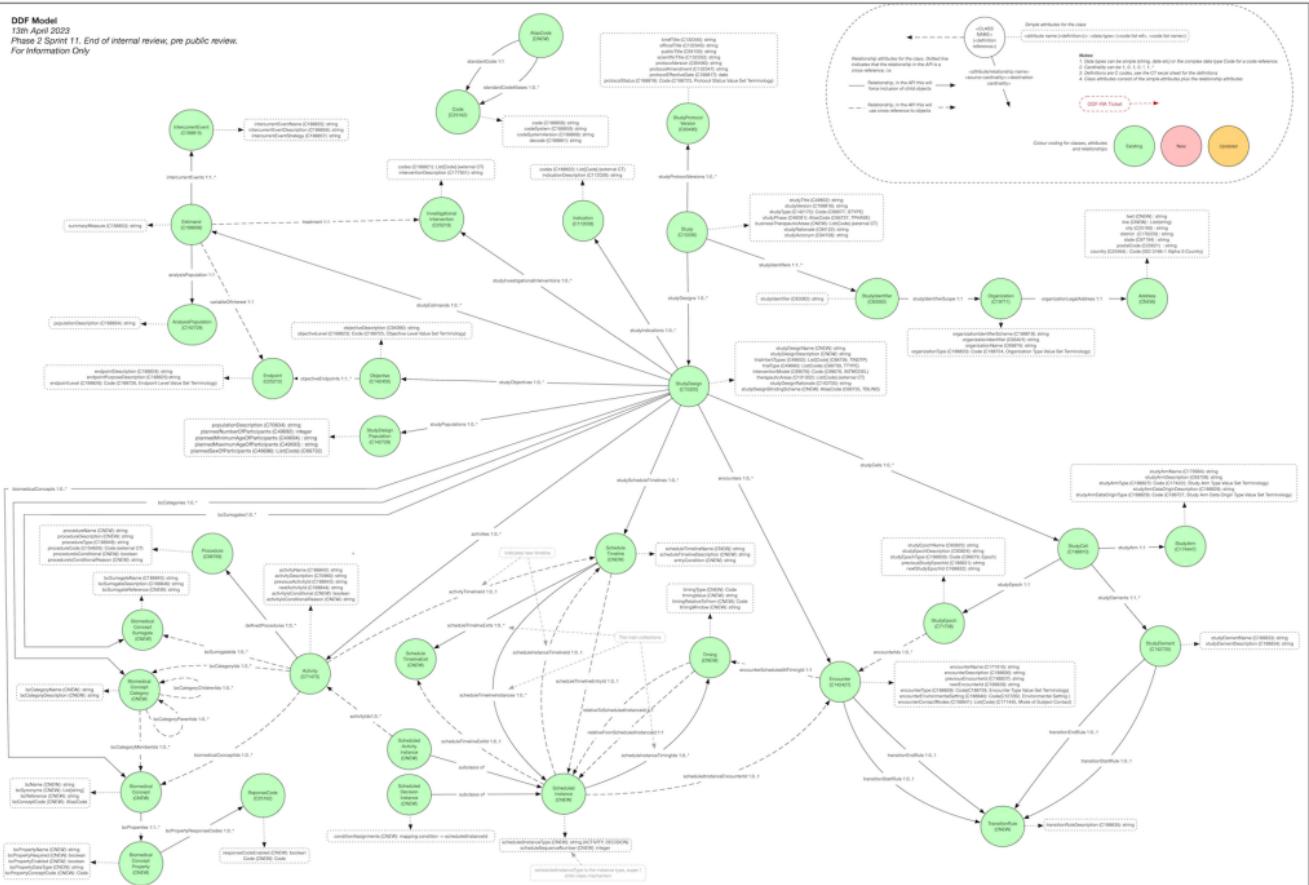
Overview
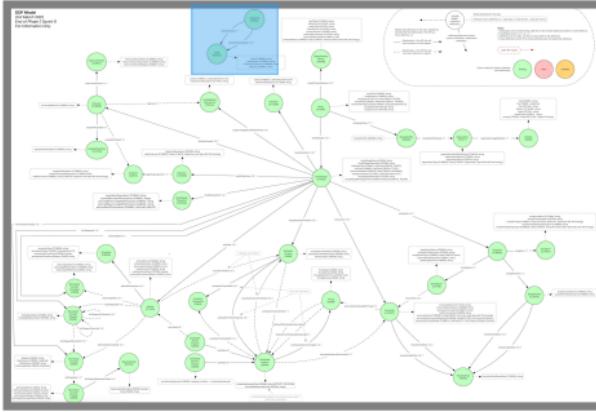
- Study
  - Protocol Version
  - Study Identifiers
- Study Design
  - Arms, Epochs ...
  - Study Timing
  - Biomedical Concepts
  - Study Populations
  - Study Objectives & Endpoints
  - Study Estimands
  - Interventions
  - Indications
- Utility
  - CT References

"Green Blob" Diagram

- **Not Normative**
- Informative view of the model
- Used to discuss ideas before putting into normative UML
- Used as a cross-check of normative deliverables at end of sprints
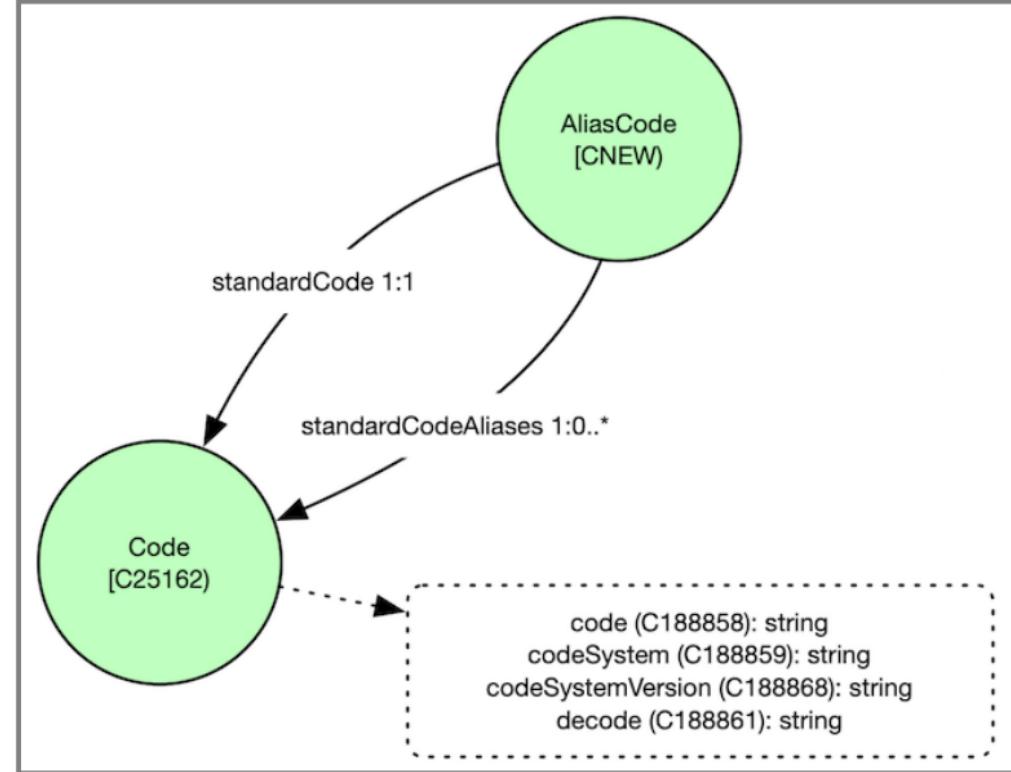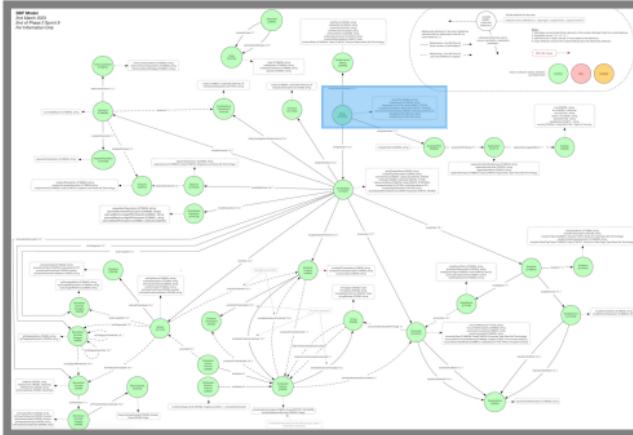
AliasCode and Code

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

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

AliasCode [CNEW]

standardCode 1:1

standardCodeAliases 1:0..*

Code [C25162]

code (C188858): string
codeSystem (C188859): string
codeSystemVersion (C188868): string
decode (C188861): string

Study

```json
{
  "studyId": "<UUID HERE>",
  "studyTitle": "Small Simple Test Study (SSTS)",
  "studyVersion": "1",
  "studyType": {
    "codeId": "code_11",
    "code": "C98388",
    "codeSystem": "http://www.cdisc.org",
    "codeSystemVersion": "2022-03-25",
    "decode": "Interventional Study"
  },
  "studyPhase": {
    "codeId": "code_10",
    "code": "C49686",
    "codeSystem": "http://www.cdisc.org",
    "codeSystemVersion": "2022-03-25",
    "decode": "Phase IIa Trial"
  },
  "businessTherapeuticAreas": [
    {
      "codeId": "code_34",
      "code": "12345",
      "codeSystem": "Sponsor",
      "codeSystemVersion": "2022",
      "decode": "Business Unit A"
    }
  ],
  "studyIdentifiers": [],
  "studyProtocolVersions": [],
  "studyDesigns": [],
  "studyRationale": "Demonstration"
  "studyAcronym": "SSTS"
}
```


Study

- Root of the whole model
- One study links to many study designs
- Study also links to
  - identifiers
  - protocol versions
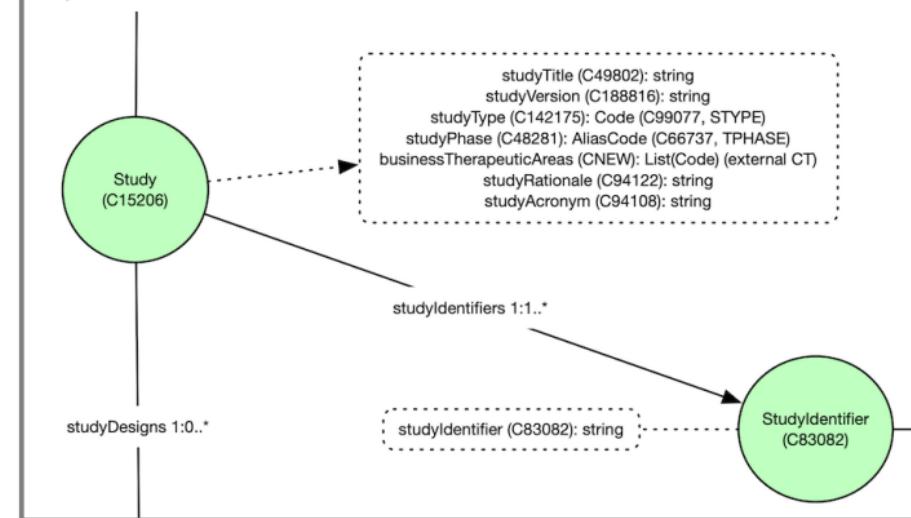
Instance Identifiers

- Study has a UUID (allocated by the SDR)
- All other objects have internal ids that should be unique across the study, used for cross-references
- See **red** in example
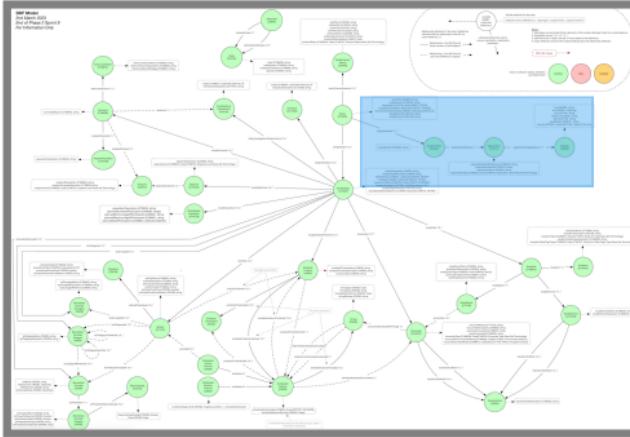
Business Therapeutic Area

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

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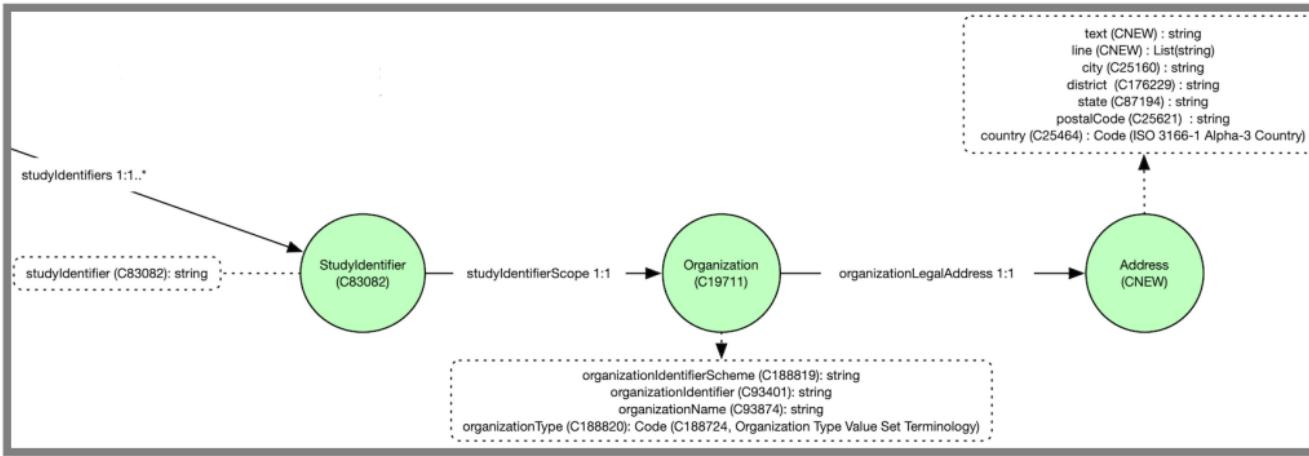
- USDM allows for many study designs within a single study
- This accommodates master, umbrella studies etc.

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)
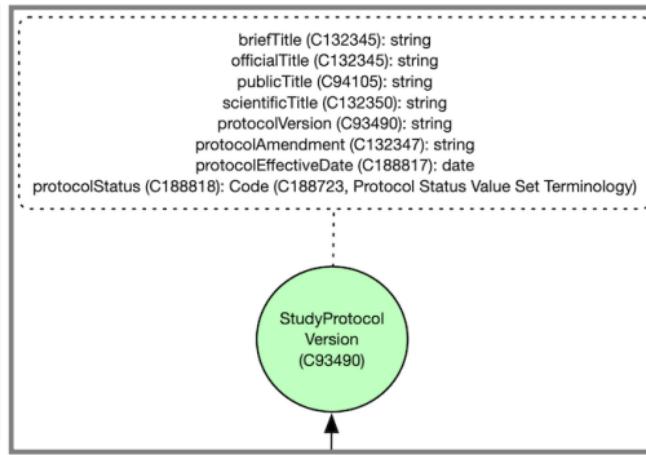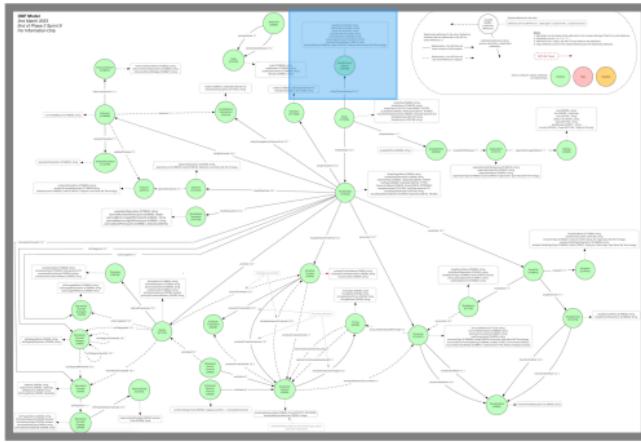
```
{
  "studyIdentifierId": "study_identifier_id_3",
  "studyIdentifier": "ACME-5678",
  "studyIdentifierScope": {
    "organizationId": "organization_1",
    "organisationIdentifierScheme": "DUNS",
    "organisationIdentifier": "123456789",
    "organisationName": "ACME Pharma",
    "organisationType": {
      "codeId": "code_13",
      "code": "C70793",
      "codeSystem": "http://www.cdisc.org",
      "codeSystemVersion": "2022-03-25",
      "decode": "Clinical Study Sponsor"
    },
    "organizationLegalAddress": {
      "text": "123",
      "line": "fake street",
      "city": "some town",
      "district": "district 19",
      "state": "TX",
      "postalCode": "12345",
      "country": {
        "codeId": "code_15",
        "code": "USA",
        "codeSystem": "ISO 3166 1 alpha3",
        "codeSystemVersion": "2020-08",
        "decode": "United States of America"
      }
    }
  }
}
```
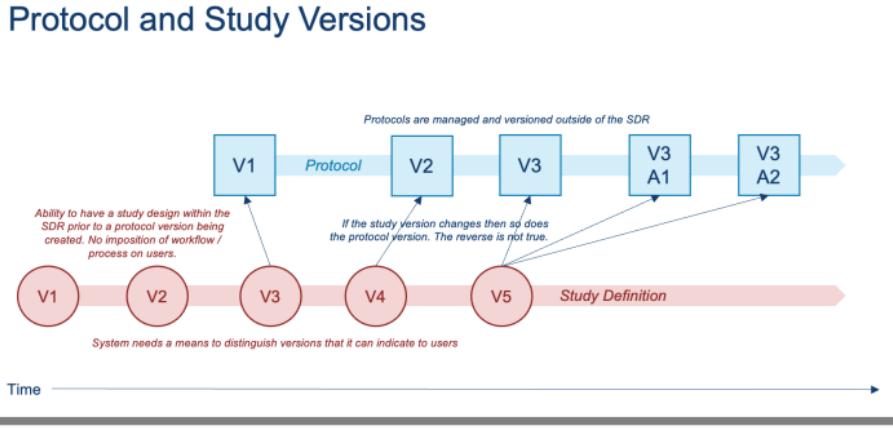
Protocol Version

Protocol
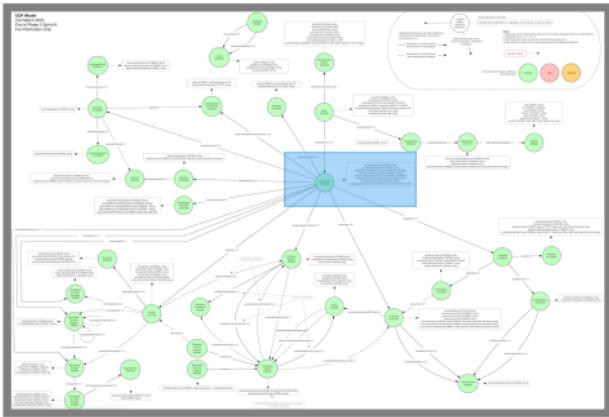
- Links the Study to the protocol version
- With DDF the existing protocol "document", e.g. MS Word, has been split into
    - a document
    - an electronic design (DDF USDM)
- Need to link which design is valid with which version of the document

The StudyProtocolVersion diagram shows:

```
briefTitle (C132345): string
officialTitle (C132345): string
publicTitle (C94105): string
scientificTitle (C132350): string
protocolVersion (C93490): string
protocolAmendment (C132347): string
protocolEffectiveDate (C188817): date
protocolStatus (C188818): Code (C188723, Protocol Status Value Set Terminology)
```

StudyProtocolVersion (C93490)

Protocol and Study Versions

Protocols are managed and versioned outside of the SDR

V1 | Protocol | V2 | V3 | V3 A1 | V3 A2

Ability to have a study design within the SDR prior to a protocol version being created. No imposition of workflow / process on users.

If the study version changes then so does the protocol version. The reverse is not true.

V1 | V2 | V3 | V4 | V5 | Study Definition

System needs a means to distinguish versions that it can indicate to users

Time

```
"studyProtocolVersions": [
  {
    "briefTitle": "COVACTA",
    "officialTitle": "A Study to Evaluate the Safety and
Efficacy of Tocilizumab in Patients With Severe COVID-19
Pneumonia",
    "publicTitle": "",
    "scientificTitle": "",
    "protocolVersion": "3",
    "protocolAmendment": null,
    "protocolEffectiveDate": "2020-06-11",
    "protocolStatus": {
      "code": "C85255",
      "codeSystem": "http://www.cdisc.org",
      "codeSystemVersion": "2022-03-25",
      "decode": "Draft"
    }
  }
]
```
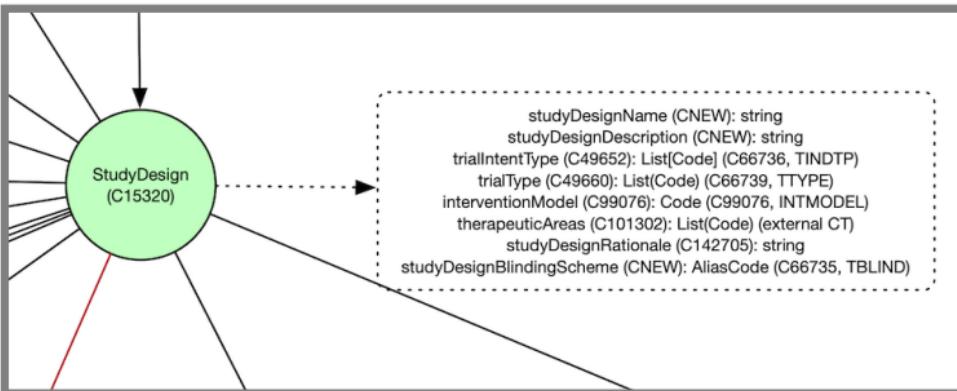
Study Design

Study Design
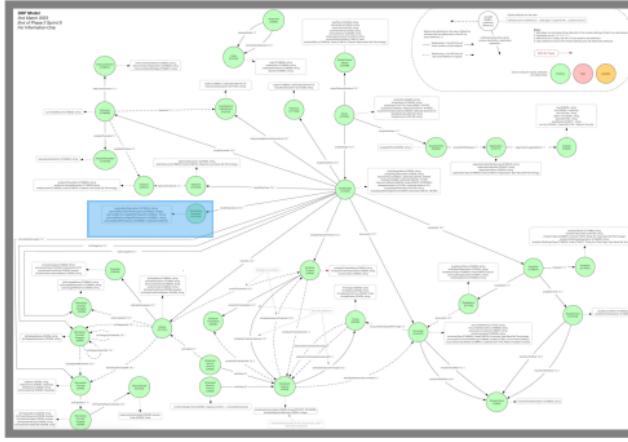
- Root of a single design
- Links all the pieces

Therapeutic Areas

Dictionary / Terminology Name	URL
EUDRACT	https://eudract.ema.europa.eu/docs/technical/EUDRACT_Eutct_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.nlm.nih.gov/healthit/snomedct/index.html
US FDA	https://www.fda.gov/drugs/development-resources/spectrum-diseasesconditions

StudyDesign (C15320)

studyDesignName (CNEW): string
studyDesignDescription (CNEW): string
trialIntentType (C49652): List[Code] (C66736, TINDTP)
trialType (C49660): List(Code) (C66739, TTYPE)
interventionModel (C99076): Code (C99076, INTMODEL)
therapeuticAreas (C101302): List(Code) (external CT)
studyDesignRationale (C142705): string
studyDesignBlindingScheme (CNEW): AliasCode (C66735, TBLIND)

```
{
    "studyDesignId": "study_design_1",
    "studyDesignName": "Study Design",
    "studyDesignDescription": "foobar",
    "trialIntentTypes": [
        {
            "codeId": "code_24",
            "code": "C15714",
            "codeSystem": "http://www.cdisc.org",
            "codeSystemVersion": "2022-03-25",
            "decode": "Basic Research"
        }
    ],
    "trialType": [
        {
            "codeId": "code_25",
            "code": "C158288",
            "codeSystem": "http://www.cdisc.org",
            "codeSystemVersion": "2022-03-25",
            "decode": "Biosimilarity Study"
        },
        {
            "codeId": "code_26",
            "code": "C49666",
            "codeSystem": "http://www.cdisc.org",
            "codeSystemVersion": "2022-03-25",
            "decode": "Efficacy Study"
        }
    ],
    "interventionModel": {
        "codeId": "code_27",
        "code": "C82639",
        "codeSystem": "http://www.cdisc.org",
        "codeSystemVersion": "2022-03-25",
        "decode": "Parallel Study"
    },
    ... >>>
}
```

```
<<< ...
    "studyCells": [],
    "studyIndications": [],
    "studyInvestigationalInterventions": [],
    "studyStudyDesignPopulations": [],
    "studyObjectives": [],
    "studyWorkflows": [],
    "therapeuticAreas:": [
        {
            "codeId": "code_28",
            "code": "123456789",
            "codeSystem": "SNOMED",
            "codeSystemVersion": "2022",
            "decode": "Something"
        }
    ],
    "studyEstimands": [],
    "encounters": [],
    "activities": [],
    "studyDesignRationale": "",
    "studyDesignBlindingScheme": null,
    "biomedicalConcepts": [],
    "bcCategories": [],
    "bcSurrogates": []
}
```

Study Populations

populationDescription (C70834): string
plannedNumberOfParticipants (C49692): integer
plannedMinimumAgeOfParticipants (C49694) : string
plannedMaximumAgeOfParticipants (C49693) : string
plannedSexOfParticipants (C49696): List(Code) (C66732)

StudyDesign
Population
(C142728)

```
"studyStudyDesignPopulations": [
  {
    "studyDesignPopulationId": "population_1",
    "populationDescription": "Population 1",
    "plannedNumberOfParticipants": 100,
    "plannedMaximumAgeOfParticipants": "80 years",
    "plannedMinimumAgeOfParticipants": "18 years",
    "plannedSexOfParticipants": []
  }
]
```
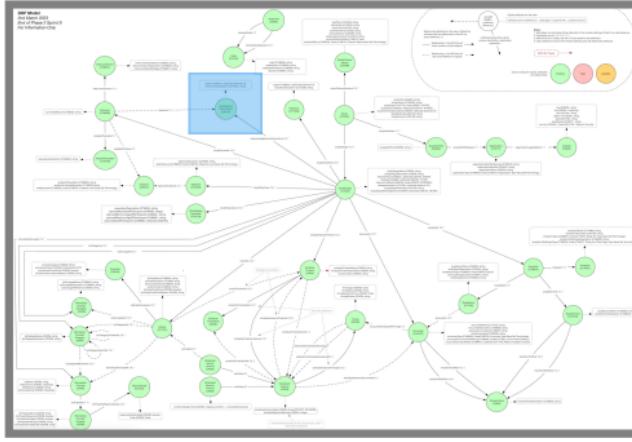
Study Objectives and Endpoints

objectiveDescription (C94090): string
objectiveLevel (C188823): Code (C188725, Objective Level Value Set Terminology)

endpointDescription (C188824): string
endpointPurposeDescription (C188825):string
endpointLevel (C188826): Code (C188726, Endpoint Level Value Set Terminology)

Endpoint (C25212) — objectiveEndpoints 1:1..* — Objective (C142450)
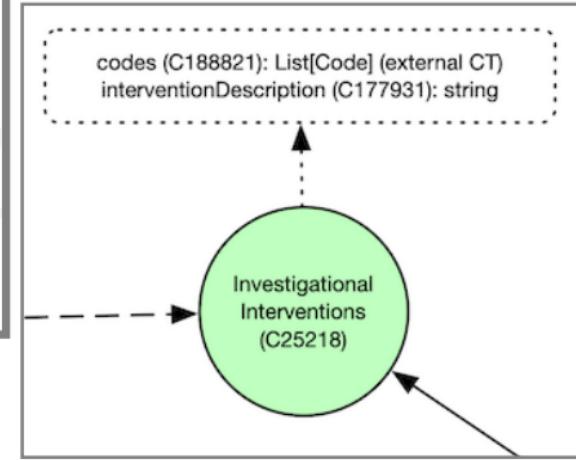
```
"studyObjectives": [
  {
    "objectiveDesc": "Evaluate sensitivity index from baseline to end of study (16 weeks)",
    "objectiveLevel": {
      "code": "C85826",
      "codeSystem": "http://www.cdisc.org",
      "codeSystemVersion": "2022-03-25",
      "decode": "Trial Primary Objective"
    },
    "objectiveEndpoints": [
      {
        "endpointDesc": "Survival rate after cycle 8 of treatment",
        "endpointPurposeDesc": "EFFICACY",
        "endpointLevel": {
          "code": "C94496",
          "codeSystem": "http://www.cdisc.org",
          "codeSystemVersion": "2022-03-25",
          "decode": "Primary Endpoint"
        }
      }
    ]
  }
]
```

Interventions

codes (C188821): List[Code] (external CT)
interventionDescription (C177931): string

Investigational
Interventions
(C25218)
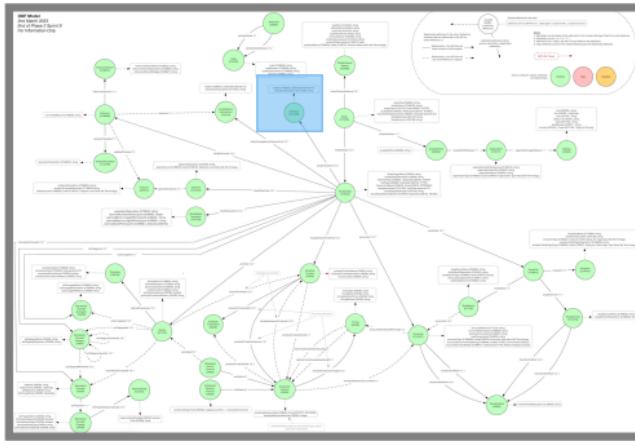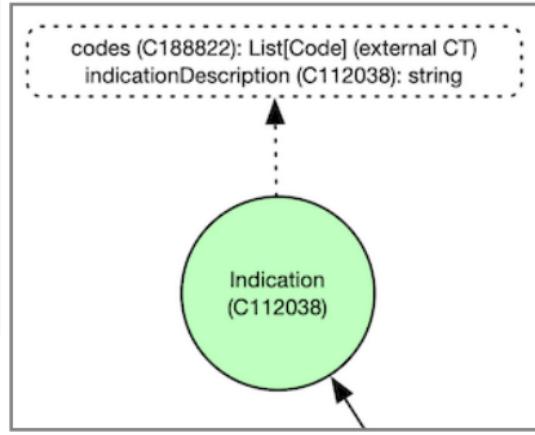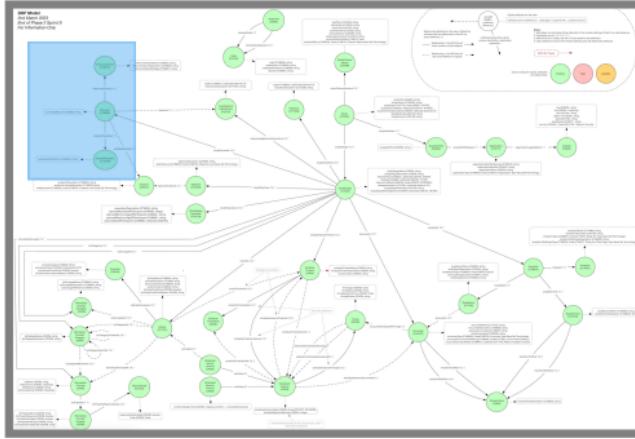
```
"studyInvestigationalInterventions": [
  {
    "codes": [
      {
        "code": "XX031ZA",
        "codeSystem": "ATC",
        "codeSystemVersion": "2021",
        "decode": "SubstX"
      }
    ],
    "interventionDesc": "Treatment with substX"
  }
]
```

Indications

codes (C188822): List[Code] (external CT)
indicationDescription (C112038): string
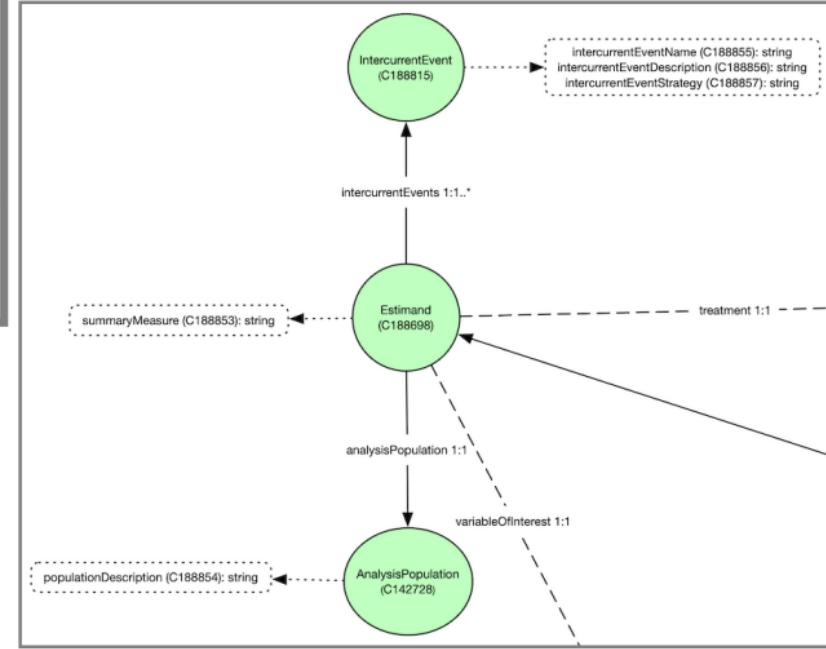
Indication
(C112038)

```
"studyIndications": [
  {
    "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)"
      }
    ],
    "indicationDesc": "Diabetes Type II"
  },
  {
    "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)"
      }
    ],
    "indicationDesc": "Diabetes Type I"
  }
]
```
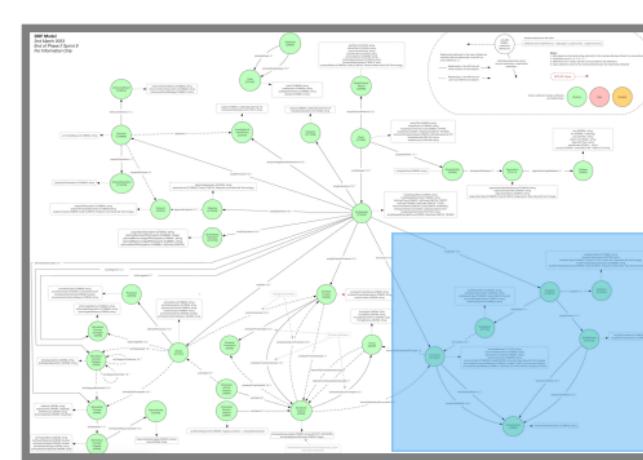
Study Estimands
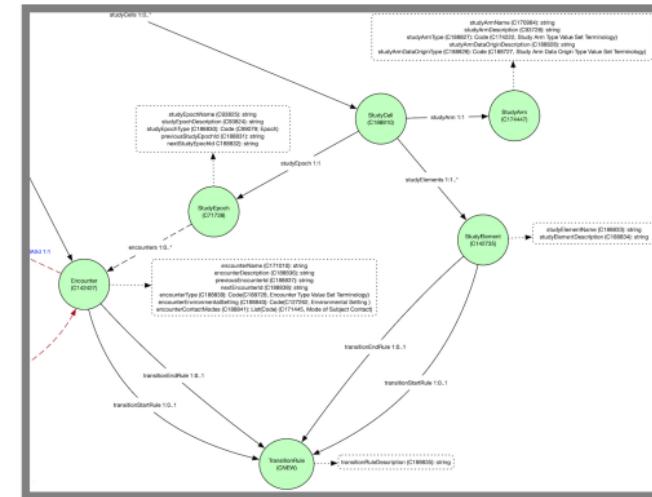
```
"studyEstimands": [
    {
        "estimandId": "Estimand_1",
        "summaryMeasure": "Survival of all patients",
        "analysisPopulation": {
            "analysisPopulationId": "AnalysisPopulation_1",
            "populationDescription": "ITT"
        },
        "treatment": "InvestigationalIntervention_2",
        "variableOfInterest": "Endpoint_1",
        "intercurrentEvents": [
            {
                "intercurrentEventId": "IntercurrentEvent_1",
                "intercurrentEventName": "termination",
                "intercurrentEventDescription": "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"

```
{
  "studyCellId": "study_cell_1",
  "studyArm": {
    "studyArmId": "study_arm_id_1",
    "studyArmName": "Placebo",
    "studyArmDescription": "The Placebo Arm",
    "studyArmType": {
      "codeId": "code_20",
      "code": "C174268",
      "codeSystem": "http://www.cdisc.org",
      "codeSystemVersion": "2022-03-25",
      "decode": "Placebo Control Arm"
    },
    "studyArmDataOriginDescription": "Captured subject data",
    "studyArmDataOriginType": {
      "codeId": "code_18",
      "code": "C6574y",
      "codeSystem": "http://www.cdisc.org",
      "codeSystemVersion": "1",
      "decode": "SUBJECT DATA"
    }
  },
  "studyEpoch": {
    "studyEpochId": "study_epoch_data_id_1",
    "studyEpochName": "Run In",
    "studyEpochDescription": "The run in",
    "studyEpochType": {
      "codeId": "code_21",
      "code": "C98779",
      "codeSystem": "http://www.cdisc.org",
      "codeSystemVersion": "2022-03-25",
      "decode": "Run-in Period"
    }
    ...
  }
  ...
}
```
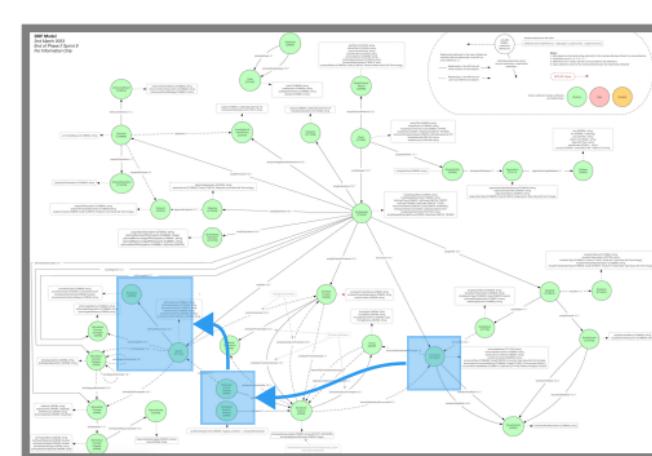
Trial Summary Domain

Trial Summary (TS) Domain

- Initial mapping
- In the IG
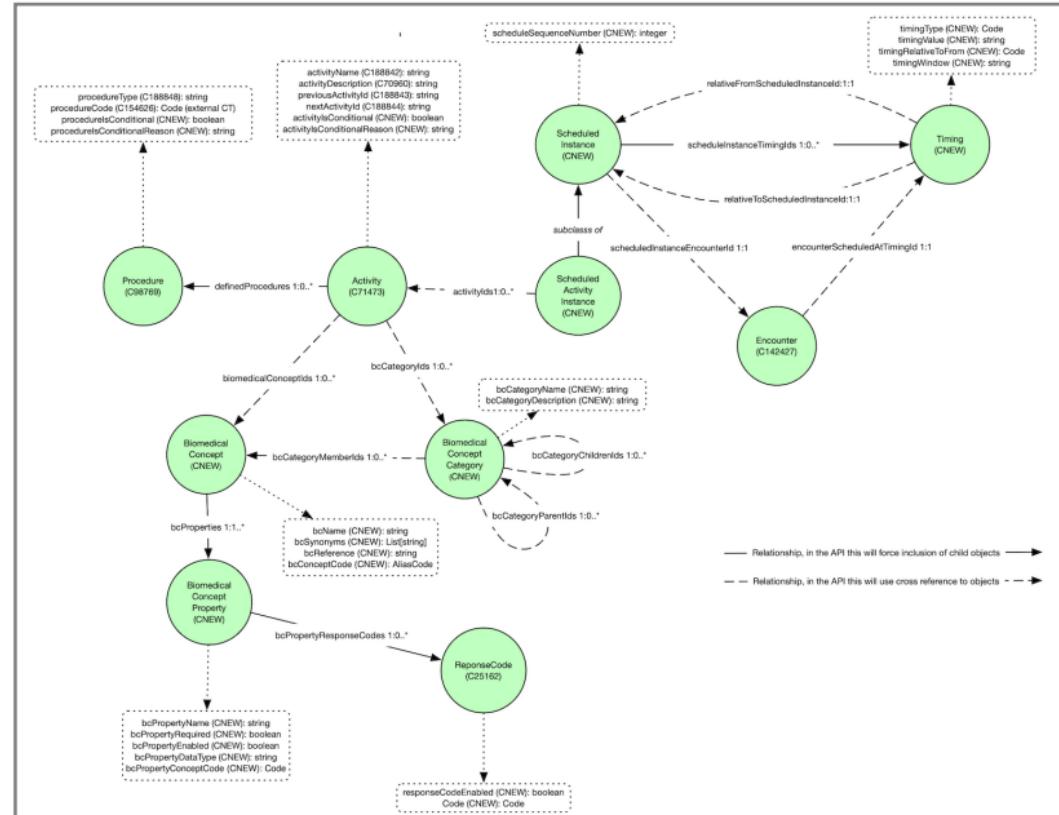
| Code	CDISC Submission Value	CDISC Synonym(s)	CDISC Definition	NCI Preferred Term	USDM Entity Name	USDM Role	USDM Item Name
C101302	THERAREA	Therapeutic Area	A knowledge field that focuses on research and development of specific treatments for diseases and pathologic findings, as well as prevention of conditions that negatively impact the health of an individual. (NCI)	Therapeutic Area	StudyDesign	Attribute	therapeuticAreas
C112038	INDIC	Trial Disease/Condition Indication; Trial Disease/Condition Indication Description	The textual representation of the condition, disease or disorder that the clinical trial is intended to investigate or address.	Trial Indication	Indication	Entity	Indication
C112038	INDIC	Trial Disease/Condition Indication; Trial Disease/Condition Indication Description	The textual representation of the condition, disease or disorder that the clinical trial is intended to investigate or address.	Trial Indication	Indication	Attribute	indicationDescription
C142175	STYPE	Study Type; Study Type Classification	The nature of the investigation for which study information is being collected. (After clinicaltrials.gov)	Study Type	Study	Attribute	studyType
C48281	TPHASE	Trial Phase; Trial Phase Classification	A step in the clinical research and development of a therapy from initial clinical trials to post-approval studies. NOTE: Clinical trials are generally categorized into four (sometimes five) phases. A therapeutic intervention may be evaluated in two or more phases simultaneously in different trials, and some trials may overlap two different phases. [21 CFR section 312.21; After ICH Topic E8 NOTE FOR GUIDANCE ON GENERAL CONSIDERATIONS FOR CLINICAL TRIALS, CPMP/ICH/291/95 March 1998]	Trial Phase	Study	Attribute	studyPhase
C49652	TINDTP	Trial Intent Type	The planned purpose of the therapy, device, or agent under study in the clinical trial.	Clinical Study by Intent	StudyDesign	Attribute	trialIntentType
C49658	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 describe 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
C49660	TTYPE	Trial Scope; Trial Type	The nature of the interventional study for which information is being collected.	Trial Type	StudyDesign	Attribute	trialType
C49692	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
C49693	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
C49694	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
C49696	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 AttributeobjectiveLevel
C85827	OBJSEC	Study Secondary Objective; Trial Secondary Objective	An auxiliary objective of the study.	Trial Secondary Objective	Objective	Valid Value	Valid Value Set for AttributeobjectiveLevel
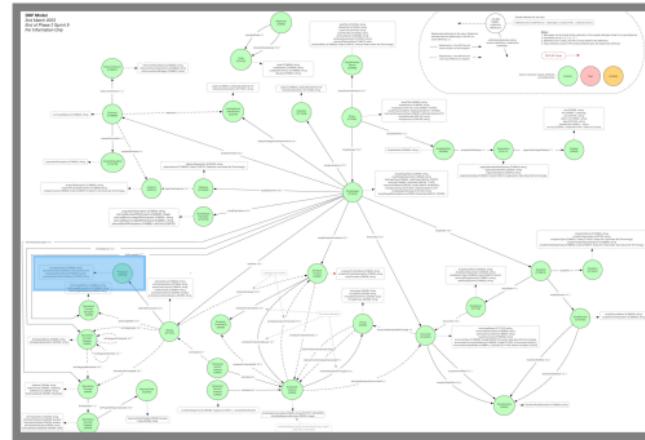
Activities, Encounters & "Glue"

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
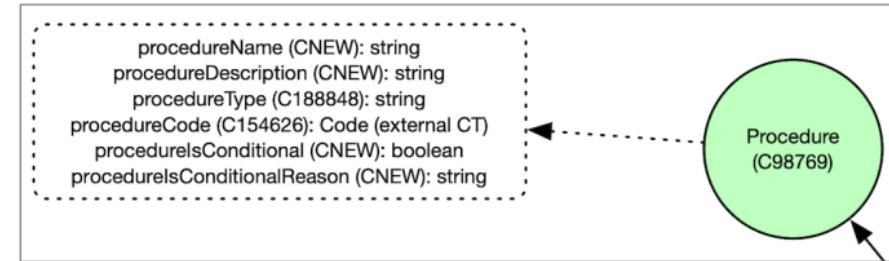
Procedures
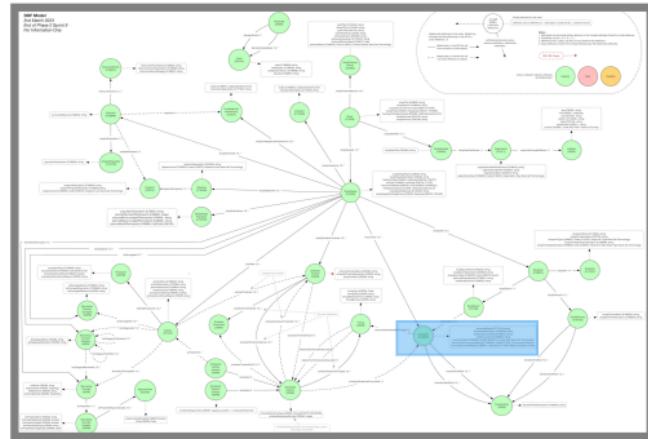
Procedures

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

```
{
  "procedureId": "Procedure_2",
  "procedureType": "XXX",
  "procedureName": "Test9",
  "procedureDescription": "Test Nine",
  "procedureCode": {
    "codeId": "Code_7",
    "code": "12345679",
    "codeSystem": "SNOMED",
    "codeSystemVersion": "January 31, 2018",
    "decode": "Test"
  },
  "procedureIsConditional": true,
  "procedureIsConditionalReason": "Only do it they have man flu"
}
```

procedureName (CNEW): string
procedureDescription (CNEW): string
procedureType (C188848): string
procedureCode (C154626): Code (external CT)
procedureIsConditional (CNEW): boolean
procedureIsConditionalReason (CNEW): string

Procedure (C98769)
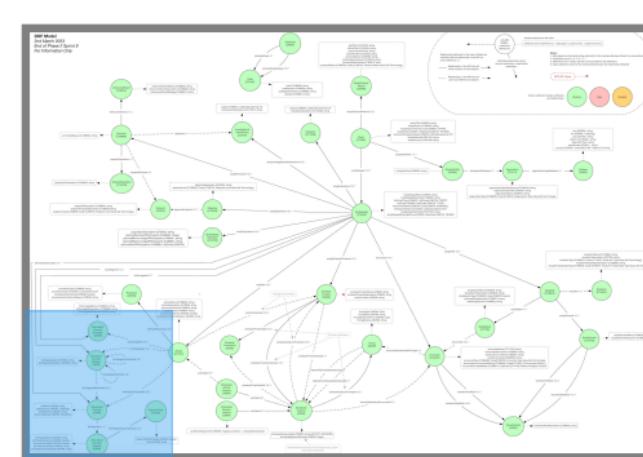
Encounters

Encounters

- Definition of an encounter
- Cross referenced from Epochs
- References timing to detail the encounter window
- Note encounter type, currently only value is "Visit"
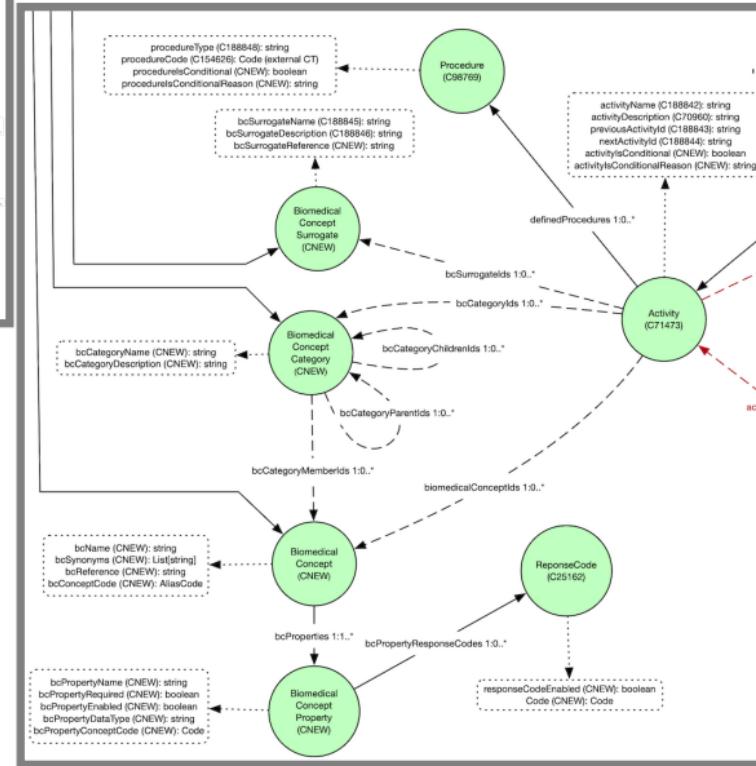
```
{
  "encounterId": "Encounter_1",
  "encounterName": "Screening",
  "encounterDescription": "Screening encounter",
  "previousEncounterId": null,
  "nextEncounterId": "Encounter_2",
  "encounterType": {
    "codeId": "Code_13",
    "code": "C25716",
    "codeSystem": "http://www.cdisc.org",
    "codeSystemVersion": "2022-12-16",
    "decode": "Visit"
  },
  "encounterEnvironmentalSetting": {
    "codeId": "Code_14",
    "code": "C51282",
    "codeSystem": "http://www.cdisc.org",
    "codeSystemVersion": "2022-12-16",
    "decode": "Clinic"
  },
  "encounterContactModes": [],
  "transitionStartRule": {
    "transitionRuleId": "TransitionRule_1",
    "transitionRuleDescription": "Subject identified"
  },
  "transitionEndRule": {
    "transitionRuleId": "TransitionRule_2",
    "transitionRuleDescription": "IEs passed"
  },
  "encounterScheduledAtTimingId": null
}
```

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

DDF, USDM and Biomedical Concepts

Dave Iberson-Hurst
15th December 2022
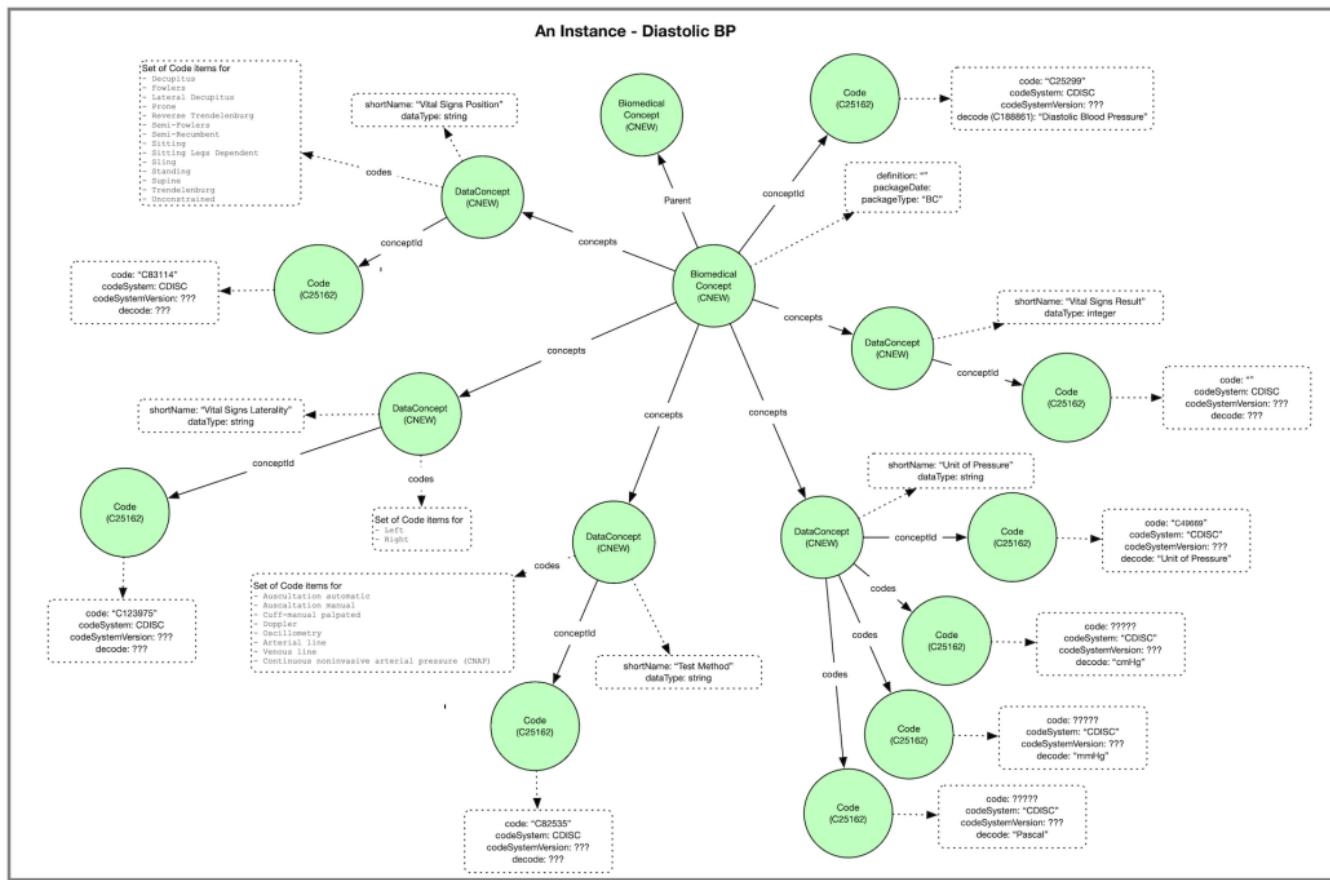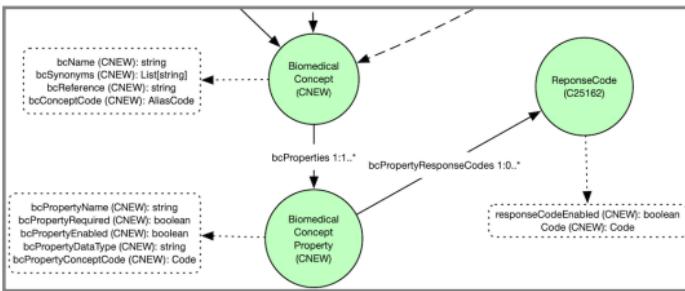
cdisc

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

```yaml
---
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:
  -
    ...
```
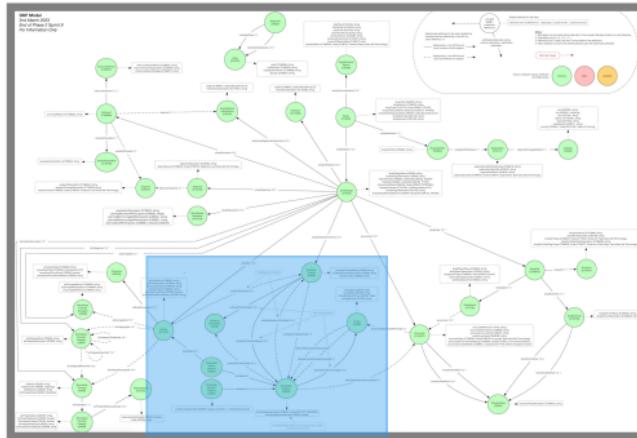
```yaml
  bcProperties:
  -
    bcPropertyname: Vital Signs Result
    bcPropertyEnabled: true
    bcPropertyRequired: true
    bcPropertyDataType: integer
    bcPropertyConceptId:
      code: C173522
      codeSystem: http://www.cdisc.org
      codeSystemVersion: "2022-03-25"
      decode: Vital Signs 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
```
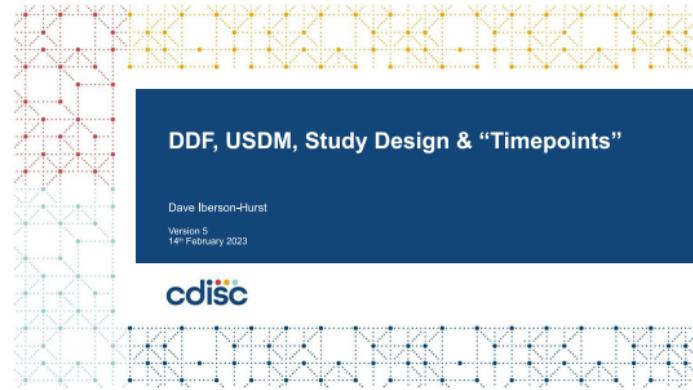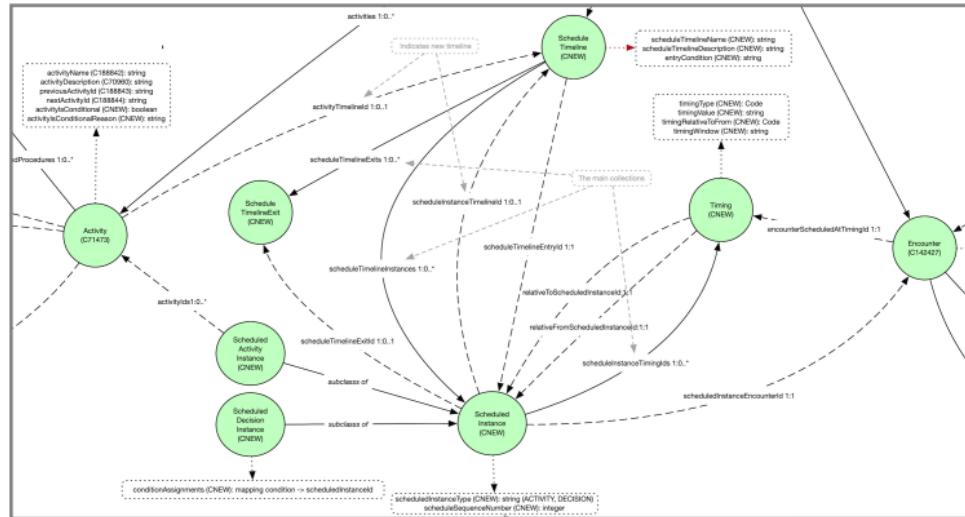
Study Design and Timing
"Timepoints"

- "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

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

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
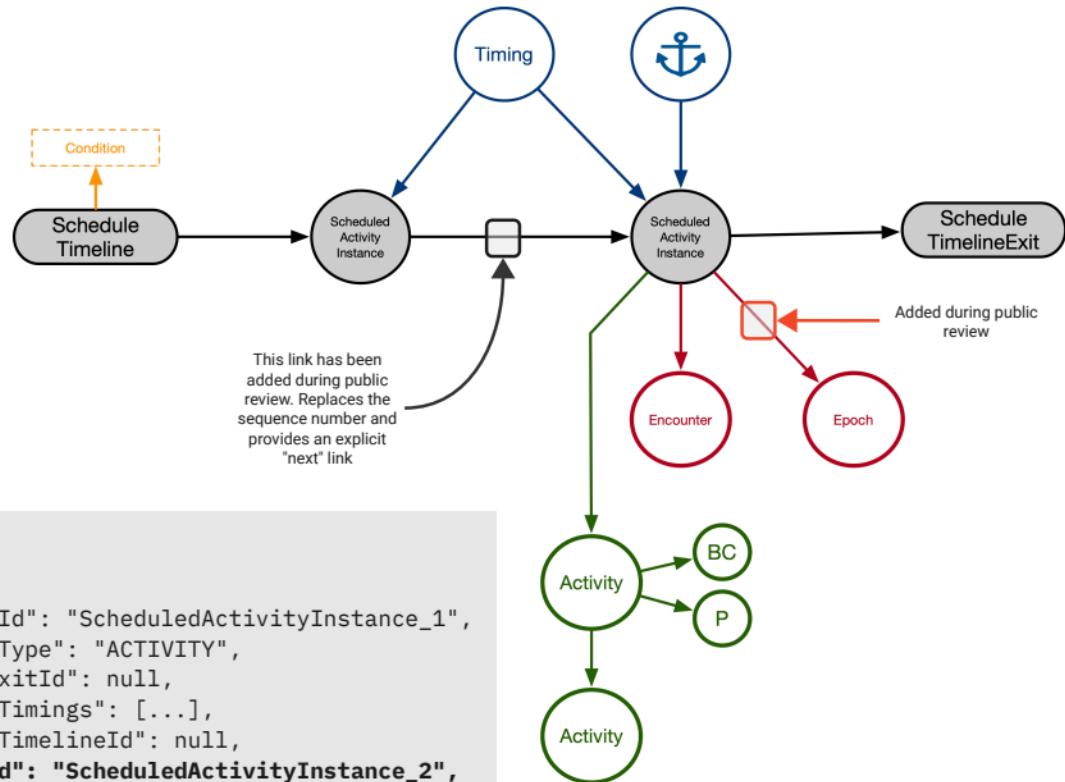
v14.2 Branch is "work in progress", fixing issues

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

A S**cheduledActivityInstance** Example. Colour coding to match diagram

This link has been added during public review. Replaces the sequence number and provides an explicit "next" link

Added during public review
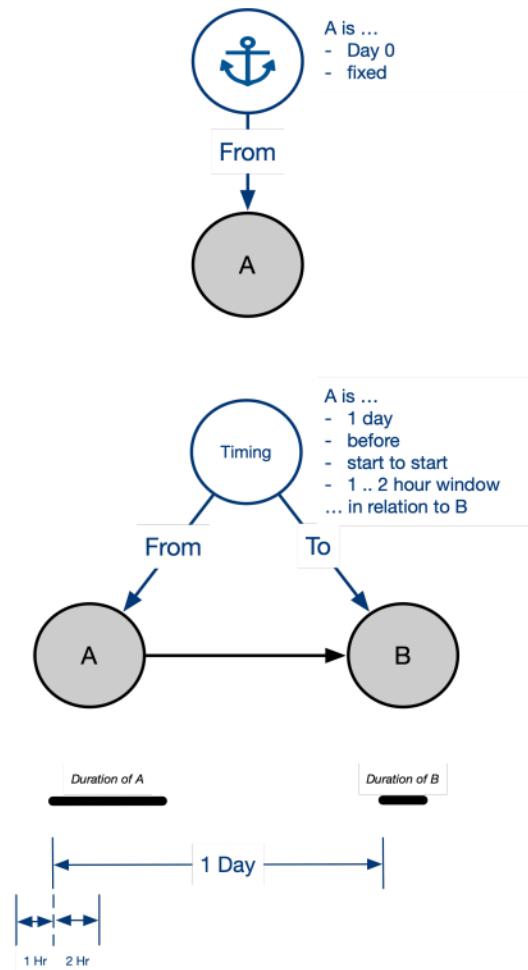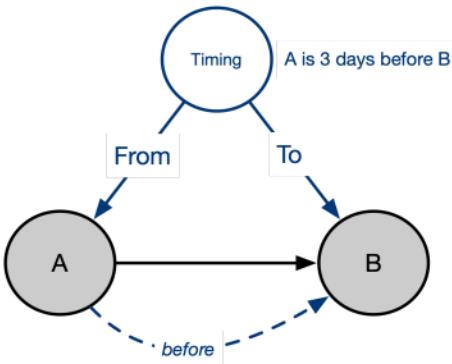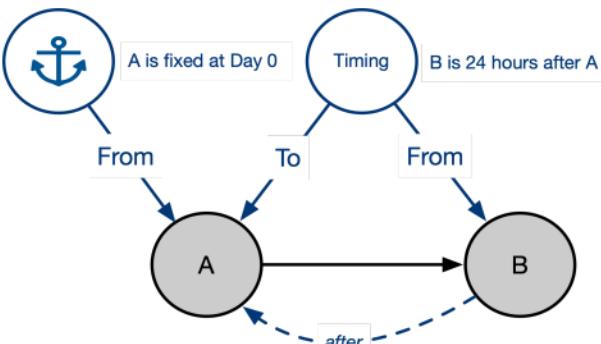
Timing

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

```
{
  "timingId": "Timing_3",
  "timingType": {
    "codeId": "Code_41",
    "code": "C99901x1",
    "codeSystem": "http://www.cdisc.org",
    "codeSystemVersion": "2022-12-16",
    "decode": "After"
  },
  "timingValue": "P3D",
  "timingDescription": "3 Days",
  "timingRelativeToFrom": {
    "codeId": "Code_44",
    "code": "C99900x1",
    "codeSystem": "http://www.cdisc.org",
    "codeSystemVersion": "2022-12-16",
    "decode": "Start to Start"
  },
  "relativeFromScheduledInstanceId": "ScheduledActivityInstance_3",
  "relativeToScheduledInstanceId": "ScheduledActivityInstance_2",
  "timingWindowLower": "PT12H",
  "timingWindowUpper": "PT12H",
  "timingWindow": "12..12 Hours"
}
```

Note that the C codes yet to be allocated so "C99901xN" are example codes. Will be allocated for September 2023 CT Release

A is fixed at Day 0

B is 24 hours after A

From   To   From

A ——→ B

after

A is ...
- Day 0
- fixed

From

A

A is 3 days before B

From   To

A ——→ B

before

A is ...
- 1 day
- before
- start to start
- 1 .. 2 hour window
... in relation to B

From   To

A ——→ B

Duration of A   Duration of B

1 Day

1 Hr   2 Hr
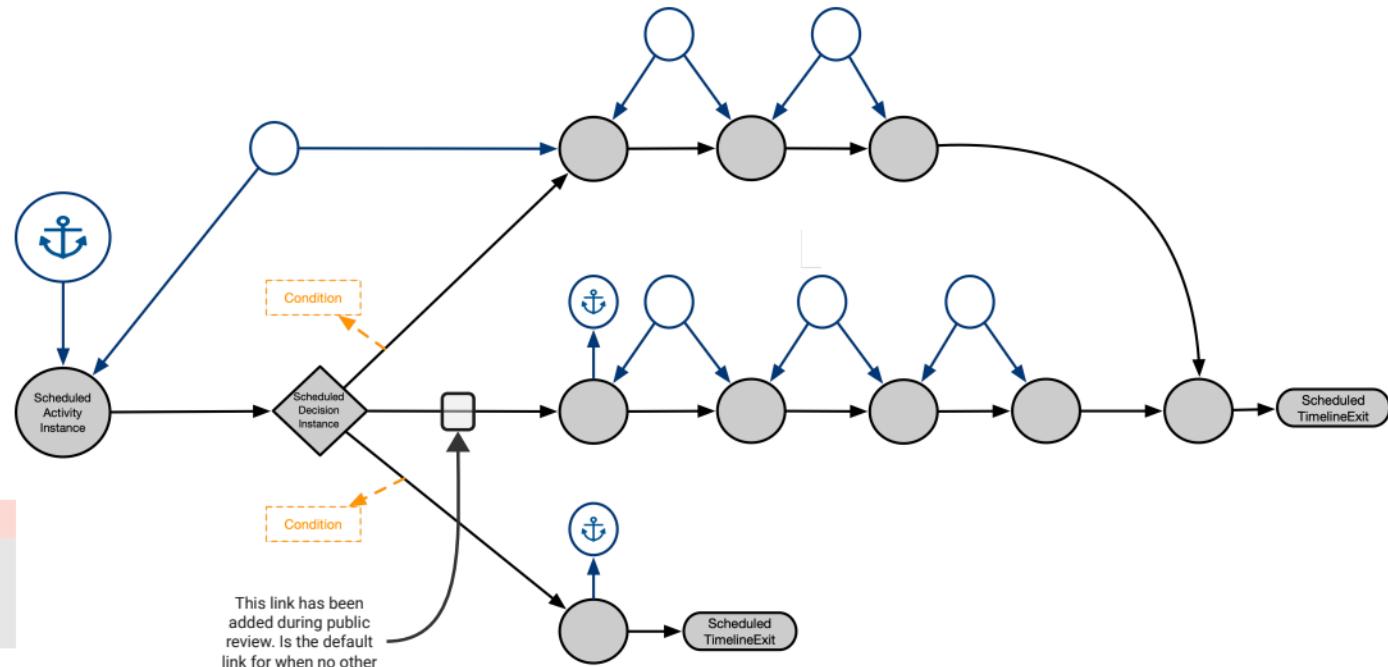
Branching

Basics

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

Scheduled
Activity
Instance

Scheduled
Decision
Instance

Condition

Condition

Scheduled
TimelineExit

Scheduled
TimelineExit

This link has been
added during public
review. Is the default
link for when no other
condition is met
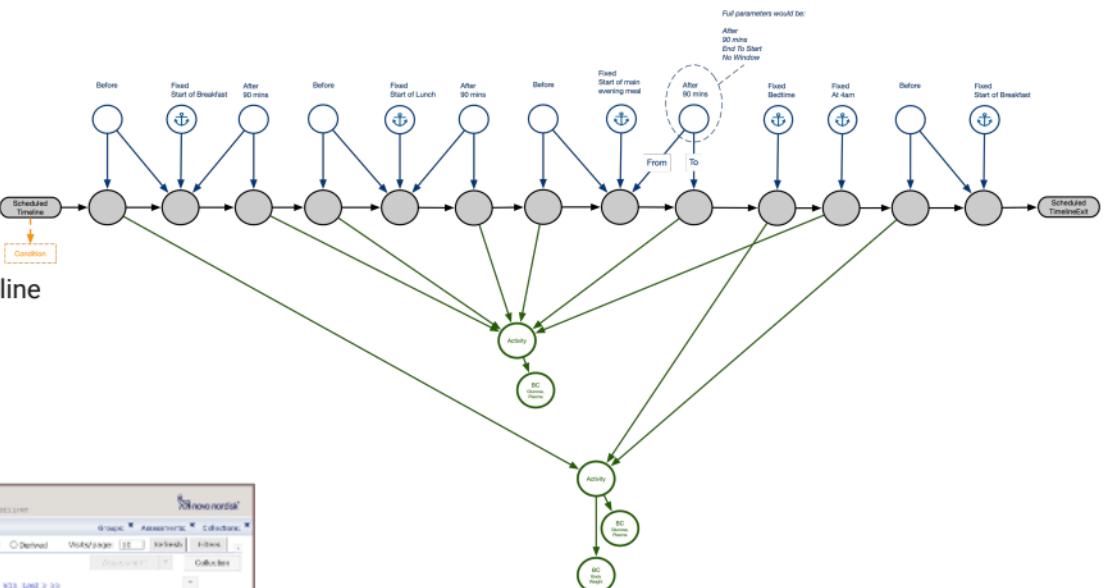
Profile

Basics

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

Profile linked from timeline

Profile linked from activity

Trial ID:	CDISC360-2
Trial Definition ID:	CTR
Trial Metadata	
Version:	4
Trial Definition	
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

Add Time Point   Delete Time Point   Sav

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
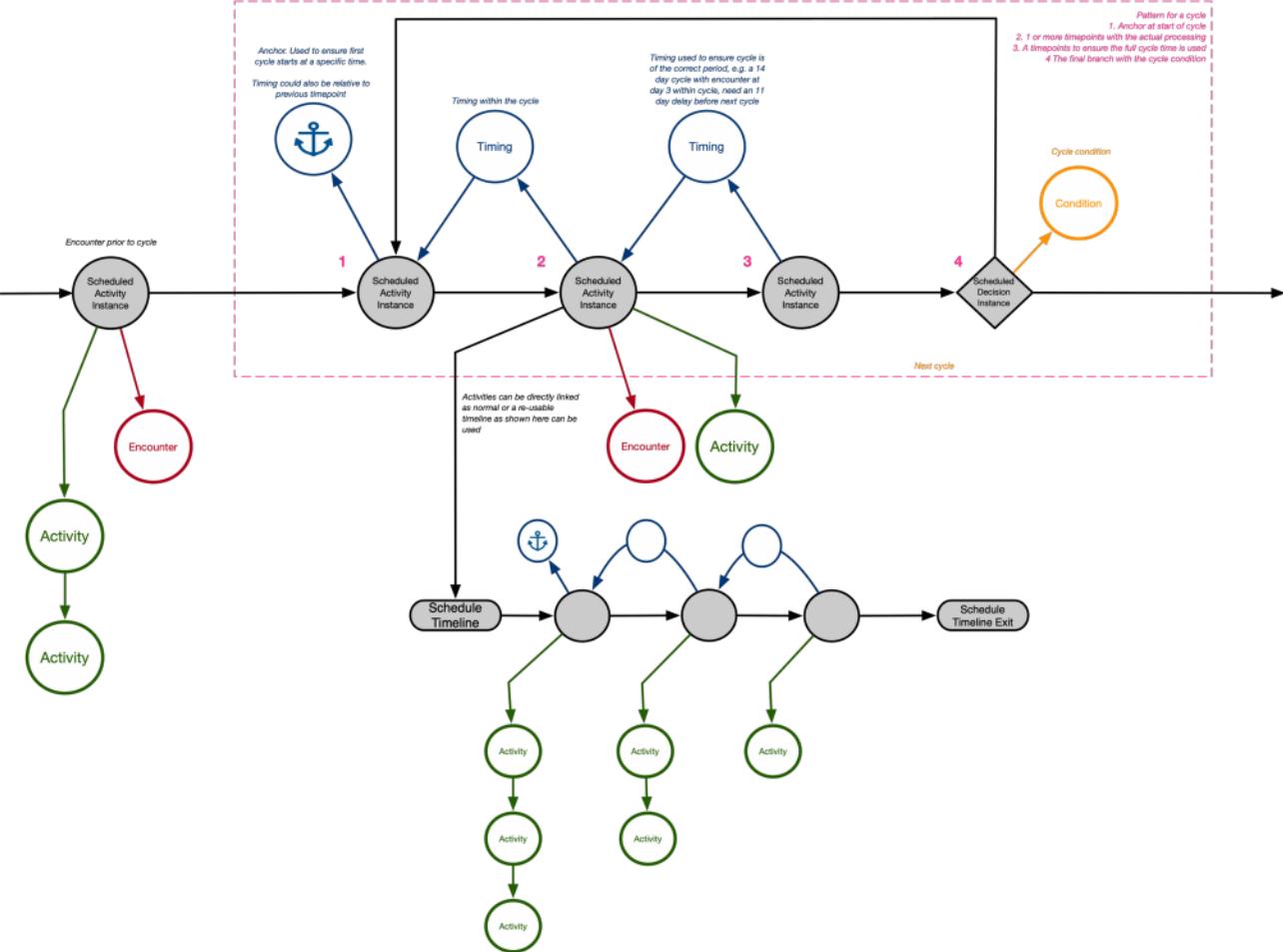
Cycles

Basics

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

Anchor. Used to ensure first cycle starts at a specific time.

Timing could also be relative to previous timepoint

Timing within the cycle

Timing used to ensure cycle is of the correct period, e.g. a 14 day cycle with encounter at day 3 within cycle, need an 11 day delay before next cycle

Pattern for a cycle
1. Anchor at start of cycle
2. 1 or more timepoints with the actual processing
3. A timepoints to ensure the full cycle time is used
4 The final branch with the cycle condition

Cycle condition

Condition

Encounter prior to cycle

1 Scheduled Activity Instance

2 Scheduled Activity Instance

3 Scheduled Activity Instance

4 Scheduled Decision Instance

Next cycle

Activities can be directly linked as normal or a re-usable timeline as shown here can be used

Encounter

Activity

Encounter

Activity

Activity

Schedule Timeline

Schedule Timeline Exit

Activity

Activity

Activity

Activity

Activity

Activity

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
v14.2 branch

Note
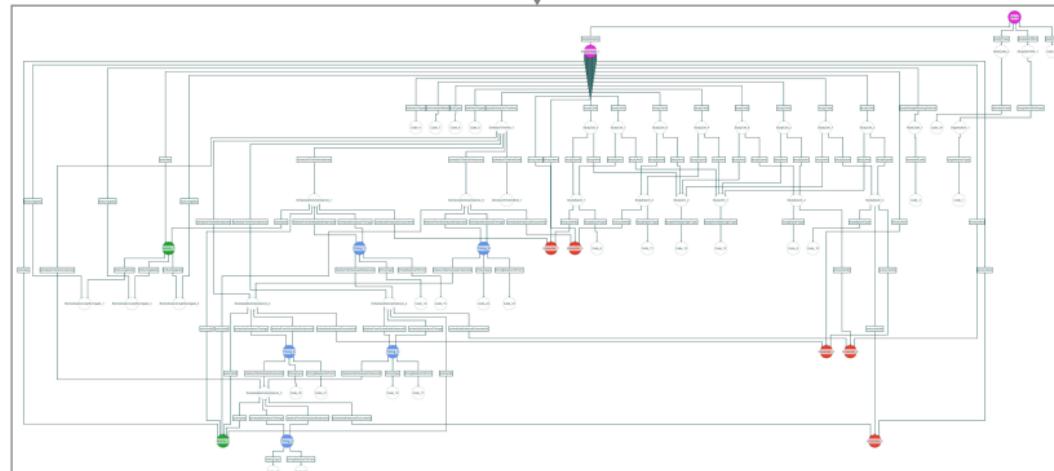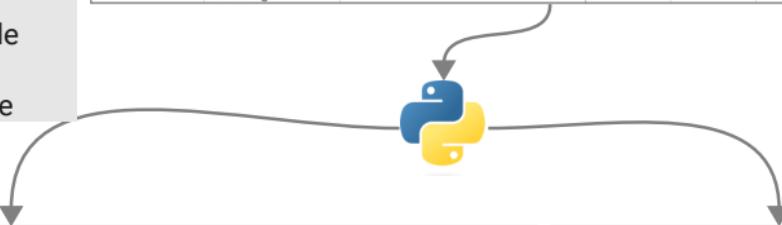
- No BC category example as yet

Current Examples

- A Roche Study
- CDISC Pilot Study
- Eli Lilly Study
- Others
  - Simple example
  - Cycle example
  - Profile example
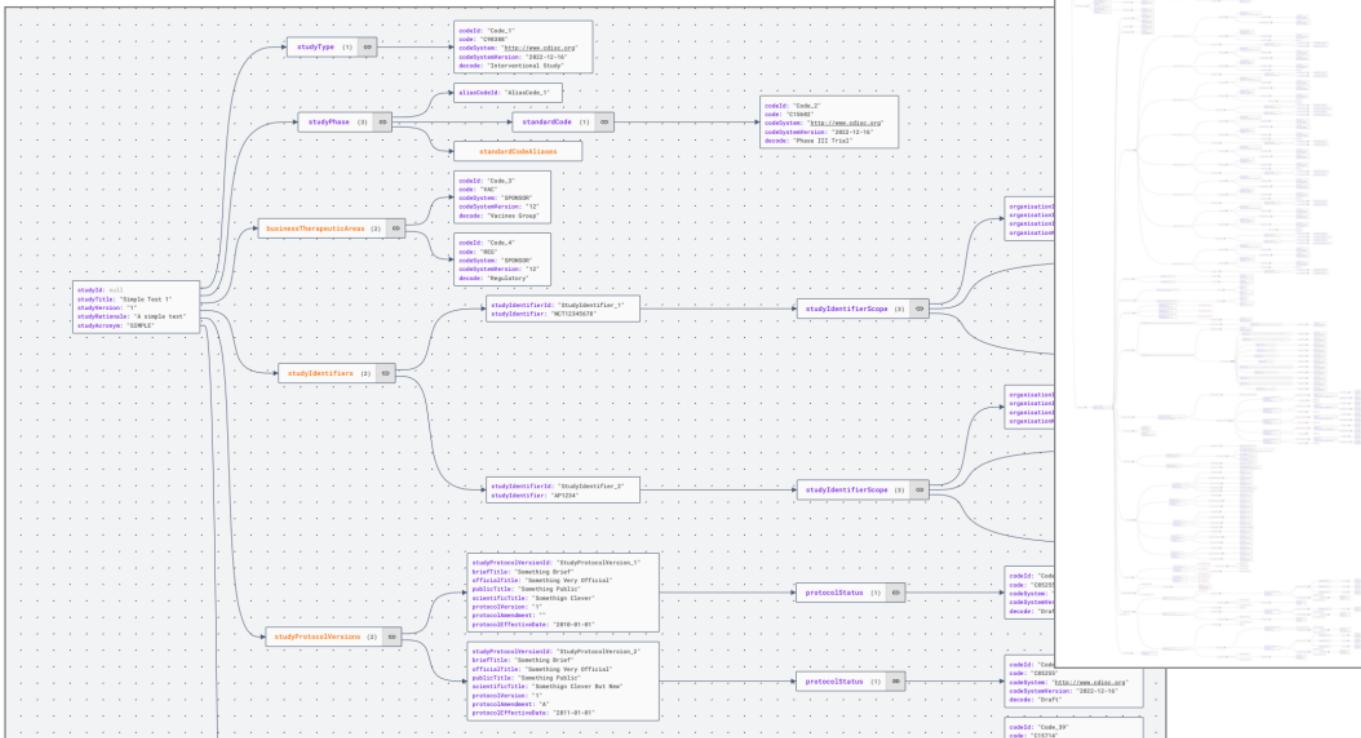
Epoch	Screening	Baseline	Treatment		Follow-Up
Cycle	-	-	-		-
First Cycle Start	-	-	-		-
Cycle Period	-	-	-		-
Cycle End Rule	-	-	-		-
Timing	N: 0..2 Days	N: Pre Dose	A:	P: +24 Hours	P: +7 Days
Visit Label	Screening	Baseline	15 min	Day 24	Day 35
Visit Window			0..4 Hours	0..1 Hours	-3..3 Days

Parent Activity	Child Activity	BC/Profile				
-	Demographics	BC:Age, BC:Sex, BC:Race	X			
-	Something Else	-	X	X	X	X	X


```json
{
    "studyId": null,
    "studyTitle": "Simple Test 1",
    "studyVersion": "1",
    "studyType": {
        "codeId": "Code_1",
        "code": "C98388",
        "codeSystem": "http://www.cdisc.org",
        "codeSystemVersion": "2022-12-16",
        "decode": "Interventional Study"
    },
    "studyPhase": {
        "aliasCodeId": "AliasCode_1",
        "standardCode": {
            "codeId": "Code_2",
            "code": "C15602",
            "codeSystem": "http://www.cdisc.org",
            "codeSystemVersion": "2022-12-16",
            "decode": "Phase III Trial"
        },
        "standardCodeAliases": []
    },
    "businessTherapeuticAreas": [ ▬ ],
    "studyIdentifiers": [ ▬ ],
    "studyProtocolVersions": [ ▬ ],
    "studyDesigns": [ ▬ ],
    "studyRationale": "A simple test",
    "studyAcronym": "SIMPLE"
}
```

USDM Examples II

Online conversion tool here.

USDM Excel to JSON Utility   STATUS

Excel File List

A list of files held within the system for which a converted USDM JSON file can be downloaded.

File List.

Roche Phase 3 NCT04320615.xlsx, dated 2023-04-14

cycles_1.xlsx, dated 2023-04-14

simple_3.xlsx, dated 2023-04-14

Upload New Excel File

CLICK TO UPLOAD NEW FILE

Online Utility

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

Visualise Examples

Useful JSON tool, JSON Crack Editor

Online Utility

- Useful visualisation
- Does NOT do cross references

USDM Examples III

Conformance & Rules

Class	Attributes (Generic names)	Rules
StudyDesign, StudyEpoch, Encounter, ScheduleTimeline, Activity, Procedure, BiomedicalConceptSurrogate, BiomedicalConceptCategory	Name and Description attributes	Name should always be present but Description is optional
Activity, Procedure	Conditional and ConditionalReason	If Conditional is true then Reason must be present. If false then reason should be ignored
Timing	timingWindow, timingWindowLower, timingWindowUpper	If timing window present then Lower and Upper should be present
	From To	For anchor then To does not need to be set or could be set the same as From
ScheduledInstance	defaultConditionId, scheduleTImelineExitId	Only one should be set. Generally default is set, but if Exit is set then no default.