Digital Data Flow (DDF) Project – Phase 3 Public Review Webinar

Presented by

Bill Illis, Novartis, DDF Workstream Lead

John Owen, Head PMO, CDISC

Dave Iberson-Hurst, DDF Technical Product Owner, CDISC

Berber Snoeijer, DDF Technical Lead, CDISC

1st February 2024

Today's Speakers

Bill Illis

DDF Workstream Lead
Novartis

Dave Iberson-Hurst

CDISC DDF Product Owner
CDISC

Berber Snoeijer

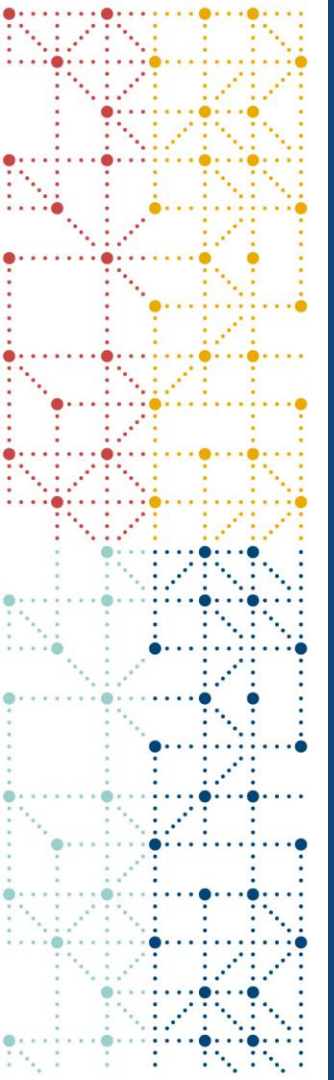
DDF Technical Lead
CDISC

John Owen

DDF Project Manager
CDISC

Agenda

1. TransCelerate Introduction to DDF (Bill Illis)
2. CDISC Project Introduction and Status (John Owen)
3. Overview of the USDM v3.0 (Dave Iberson-Hurst/Berber Snoeijer)
4. Public Review Information (John Owen)
5. Upcoming Events Related to DDF (John Owen)



TransCelerate Introduction to DDF

Bill Illis

Digital Data Flow Initiative Introduction

CDISC USDM Phase 3 Public Review Webinar

February 1, 2024

William Illis

Global Head, Collaboration & Technology Strategy, Clinical Development & Analytics, Novartis

Digital Data Flow, Workstream Initiative Lead

Content

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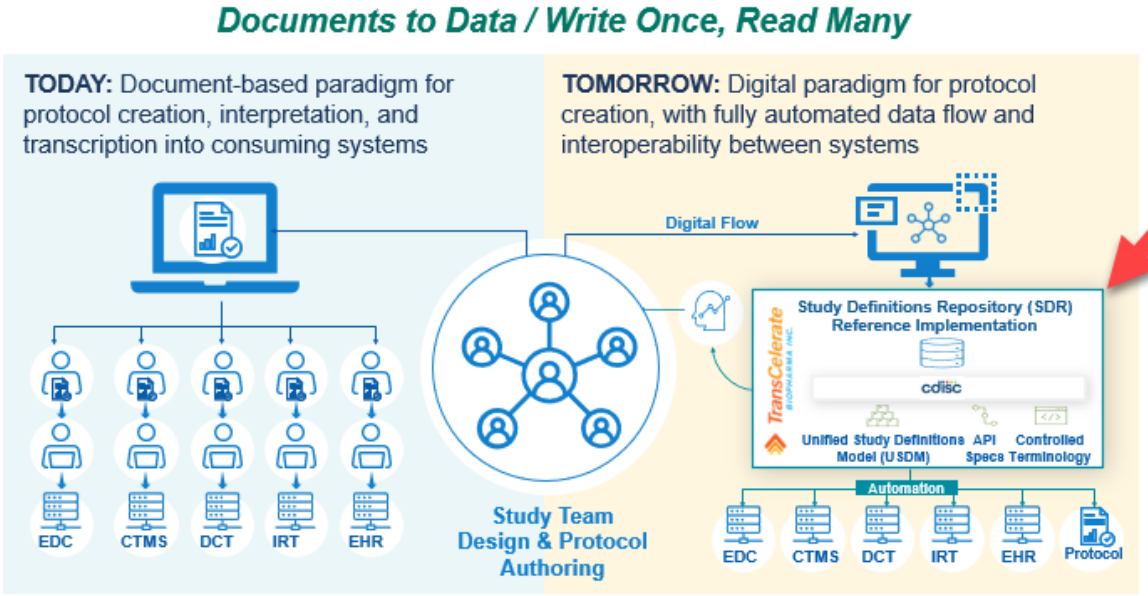
Digital Data Flow Ambition: Breaking the Document Paradigm

Digital - standard representation of study protocol
- ✓ structured
- ✓ machine readable
- ✓ executable

Data Flow – industry-wide interoperability
- ✓ exchange of data
- ✓ non-cooperating organizations
- ✓ minimal effort



Eliminate non-value added activities
Enable automation of downstream study startup and conduct processes
Create foundation for study design analytics insights

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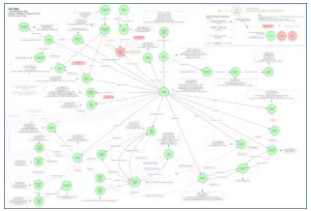
DDF Initiative encompasses technical delivery, change management, and industry engagement



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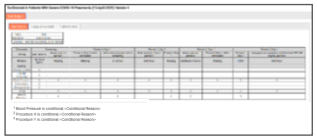
Unified Study Definitions Model (USDM) Reference Architecture

TransCelerate's Study Definitions Repository (SDR)



Digital Data Flow Initiative

Suite of DDF Adoption Resources, Videos & Change Management Tools

Continued Industry Collaboration between TransCelerate, CDISC ICH, and HL7

VULCAN HL7 FHIR · cdisc · TransCelerate BIOPHARMA INC. · HL7 International · ICH harmonisation for better health

Growing Solution Collaboration Forum (SCF)*

trials.ai · ZS · IntelliNotion · formedix · PHARMASEAL · nurocor · merative · TriNetX · Sycamore Informatics · castor · ORACLE · medidata · TRIAL · REDCAP CLOUD · indegene · Medable · saama · THREAD · Target Health · Taimei Technology

**Company logos illustrate current involvement and are not used to imply endorsement of specific vendors for DDF or to identify a comprehensive list of all actual or potential future participants in DDF.*

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CDISC Project Introduction and Status

John Owen

Digital Data Flow

- **Phase 1**
  - Base model design
    - UML
    - API
    - Controlled Terminology
  - Topics
    - Objectives and endpoints
    - High Level Study Design
    - Eligibility criteria
    - Activities and assessments
    - Basic schedule of activities and assessments
    - Basic data collection configuration related to activities and assessments

- **Phase 2**
  - Extended model
    - UML
    - API
    - Controlled Terminology
    - USDMIG
    - Example Data
  - Topics
    - Enable greater population of study set-up elements
    - Represent structured study design information for more complex trials
      - Handling of complex study timing
    - Support electronic data capture (EDC) automation
      - Expand model to include Biomedical Concepts
    - Demonstrate population of the TransCelerate Common Protocol Template (CPT)
    - Demonstrate population of SDTM Trial Design Domains

2021 **2022** **2023**

https://www.cdisc.org/ddf

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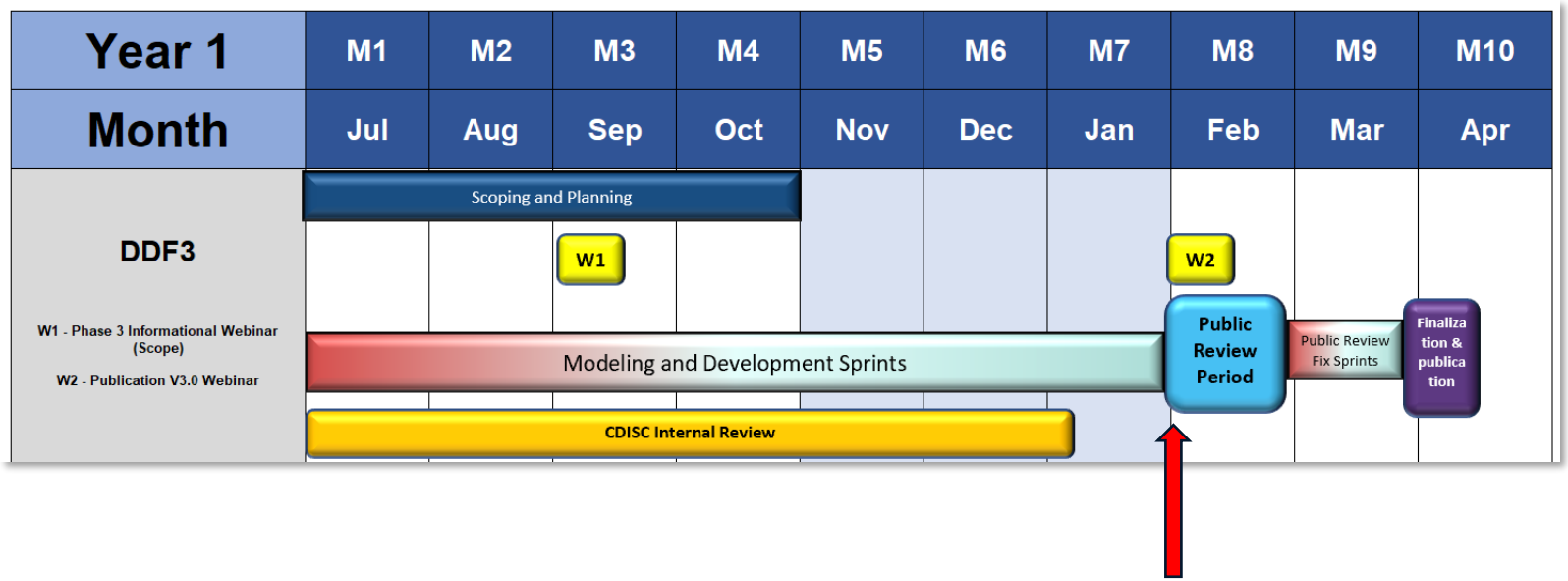
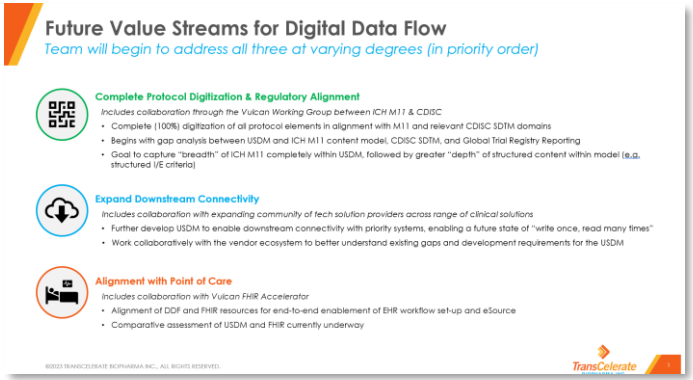
DDF Phase 3 Timelines



DDF 3 USDM Scope

- Represent ICH M11 in USDM
- SDTM Trial Design Population
- Clinical Trial Registry Population
- Complex Studies/Cohorts
- Model Enhancements



Future Value Streams for Digital Data Flow

Team will begin to address all three at varying degrees (in priority order)

Complete Protocol Digitization & Regulatory Alignment

Includes collaboration through the Vulcan Working Group between ICH M11 & CDISC

- Complete (100%) digitization of all protocol elements in alignment with M11 and relevant CDISC SDTM domains
- Begins with gap analysis between USDM and ICH M11 content model, CDISC SDTM, and Global Trial Registry Reporting
- Goal to capture "breadth" of ICH M11 completely within USDM, followed by greater "depth" of structured content within model (e.g. structured I/E criteria)

Expand Downstream Connectivity

Includes collaboration with expanding community of tech solution providers across range of clinical solutions

- Further develop USDM to enable downstream connectivity with priority systems, enabling a future state of "write once, read many times"
- Work collaboratively with the vendor ecosystem to better understand existing gaps and development requirements for the USDM

Alignment with Point of Care

Includes collaboration with Vulcan FHIR Accelerator

- Alignment of DDF and FHIR resources for end-to-end enablement of EHR workflow set-up and eSource
- Comparative assessment of USDM and FHIR currently underway

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Other Areas of Development for DDF Phase 3

- **USDM Test Data Tool**
  - Continued development to create USDM JSON test data from Protocols using an Excel and Python tool
- **Biomedical Concepts**
  - Create Biomedical Concepts that would fully cover the LZZT (CDISC Test Protocol)
  - Allow ability to represent majority of LZZT BCs in the LZZT Test data
- **DDF 3A**
  - USDM Conformance Rule Development POC using CORE
  - Demonstrating that USDM JSON files are USDM compliant,
    - e.g., Transfer of USDM JSON file from one organization to another (e.g., Vendor to Sponsor)
  - Scope
    - Develop a representative set of conformance rule specifications (up to 100)
    - Cover a wide breadth of the different types of rules required to demonstrate DDF conformance
    - Enhance the CORE open-source engine to run these Conformance Rules against a USDM JSON file
    - Scope CDISC Library modifications (to store DDF conformance rules and the USDM model)

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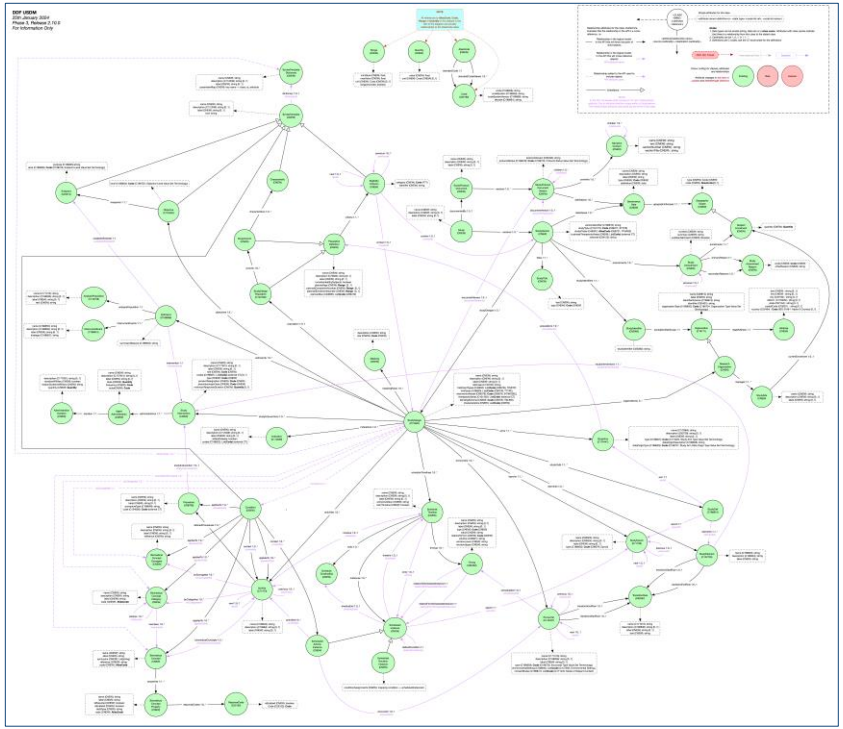
Overview of the USDM v3.0

Dave Iberson-Hurst and Berber Snoeijer

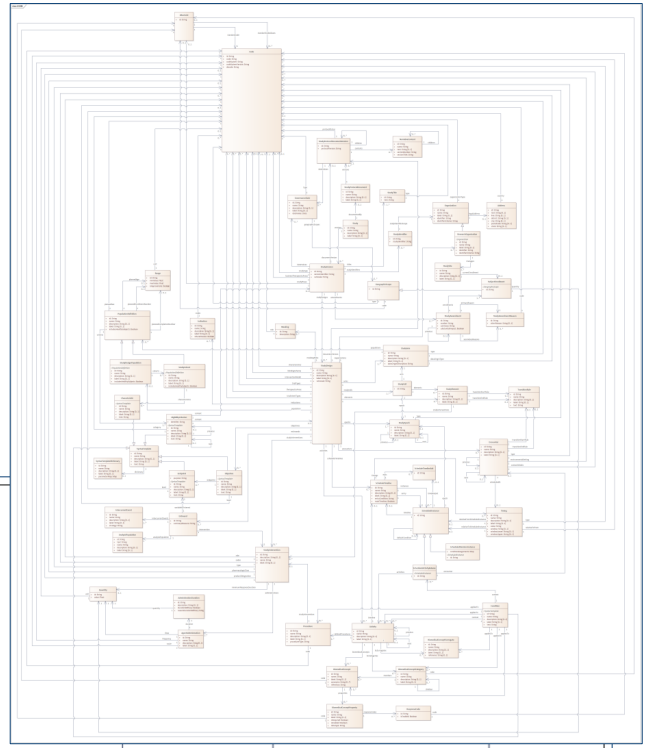
Shift of Focus

- 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



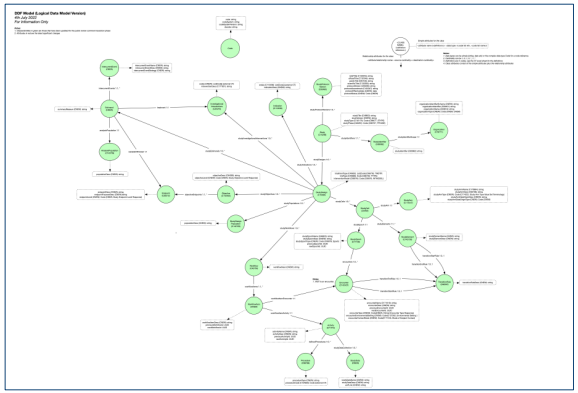
The Model and UML

- During Phase 3 we changed the way in which the UML is managed
- Moved from a tool that produced the diagram to Enterprise Architect
- Results in improved deliverables and ability to control the diagram layout
- Also allows for sub-views



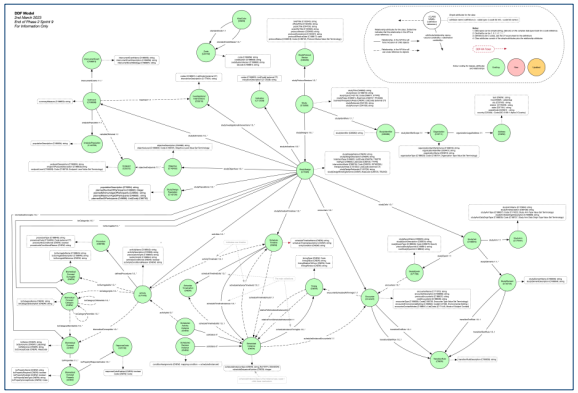
CDISC DDF / USDM, Phases One, Two and Three

Phase One



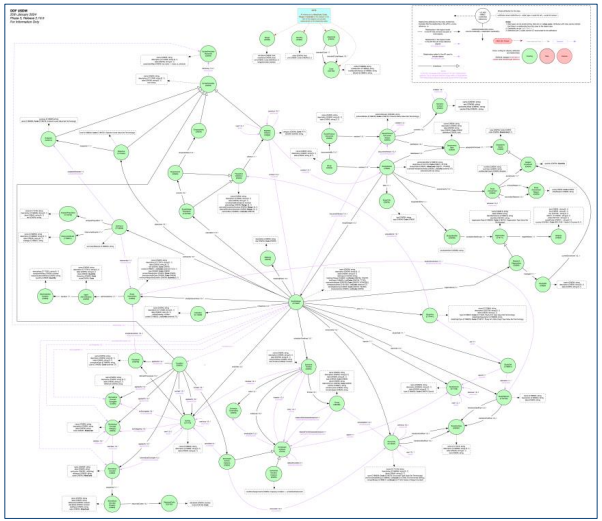
25 Classes

Phase Two



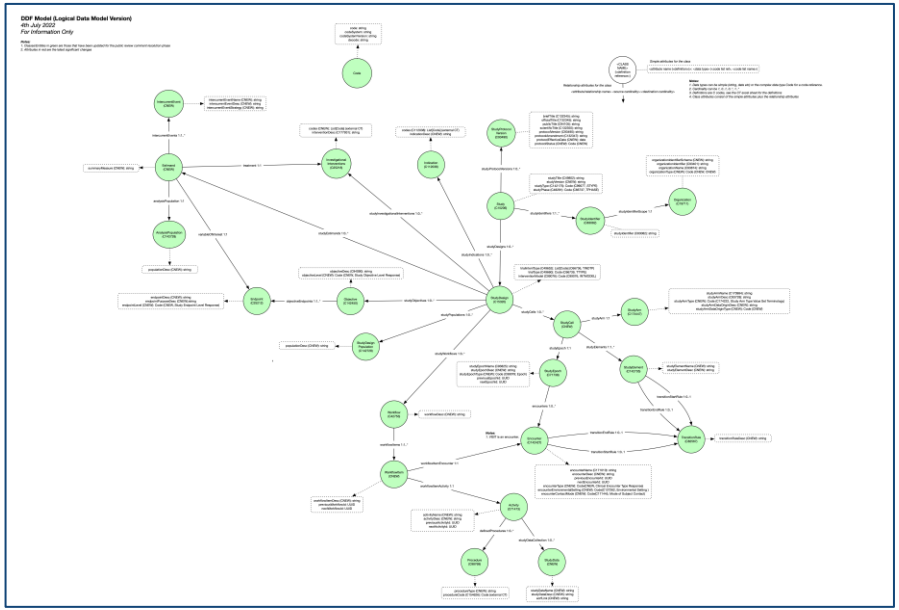
35 Classes

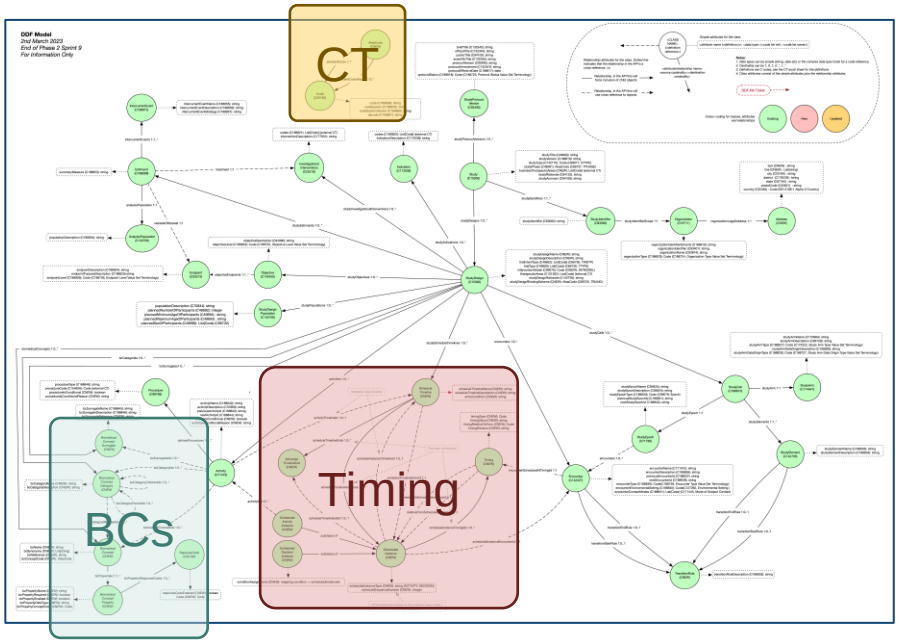
Phase Three



58 Classes

CDISC DDF / USDM, Phase One v Two





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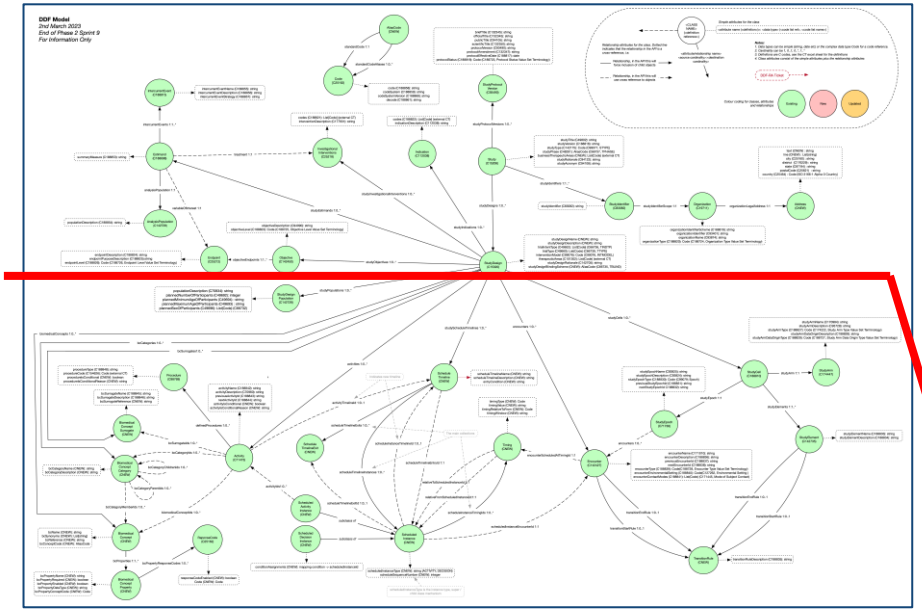
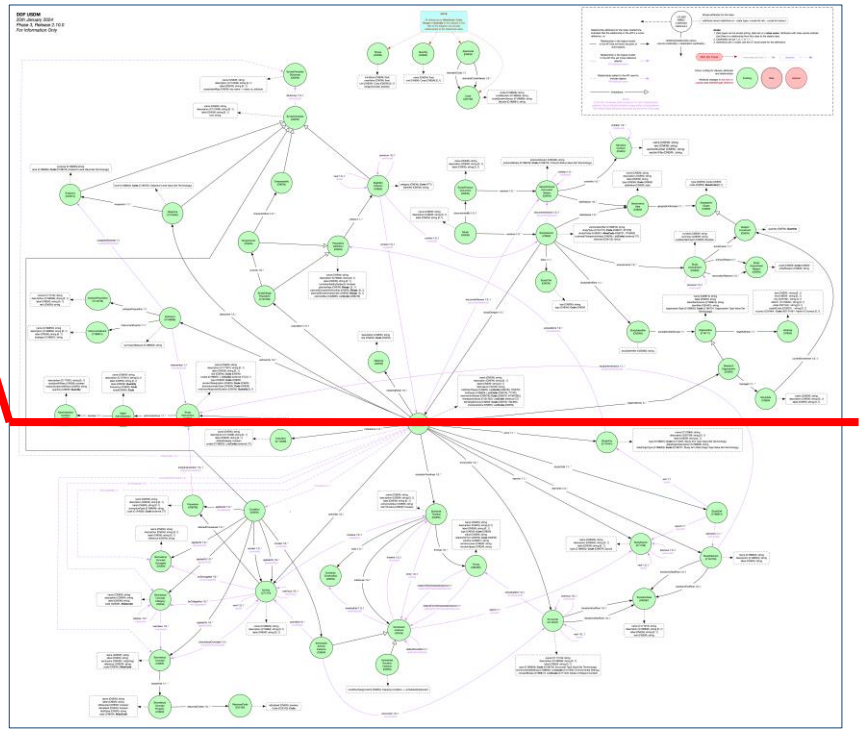
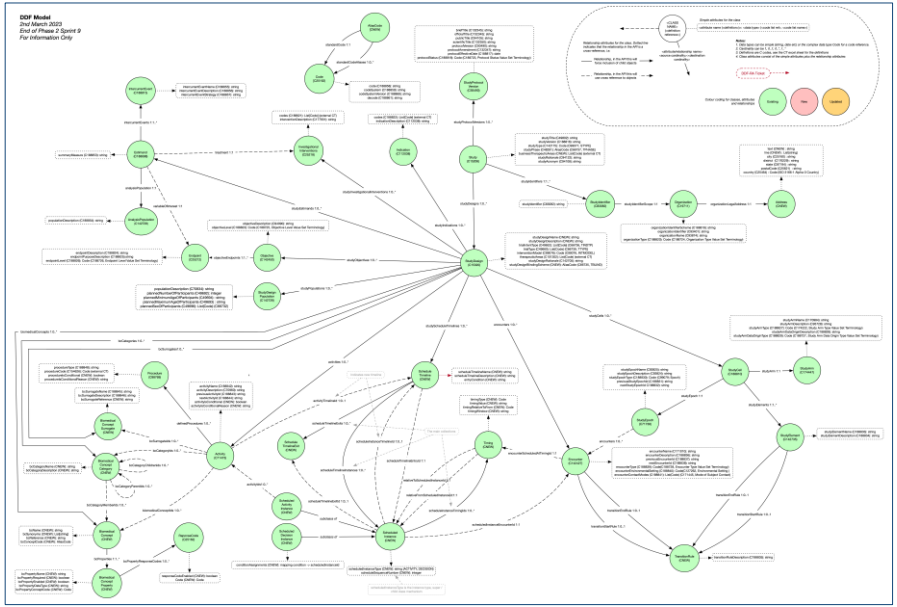
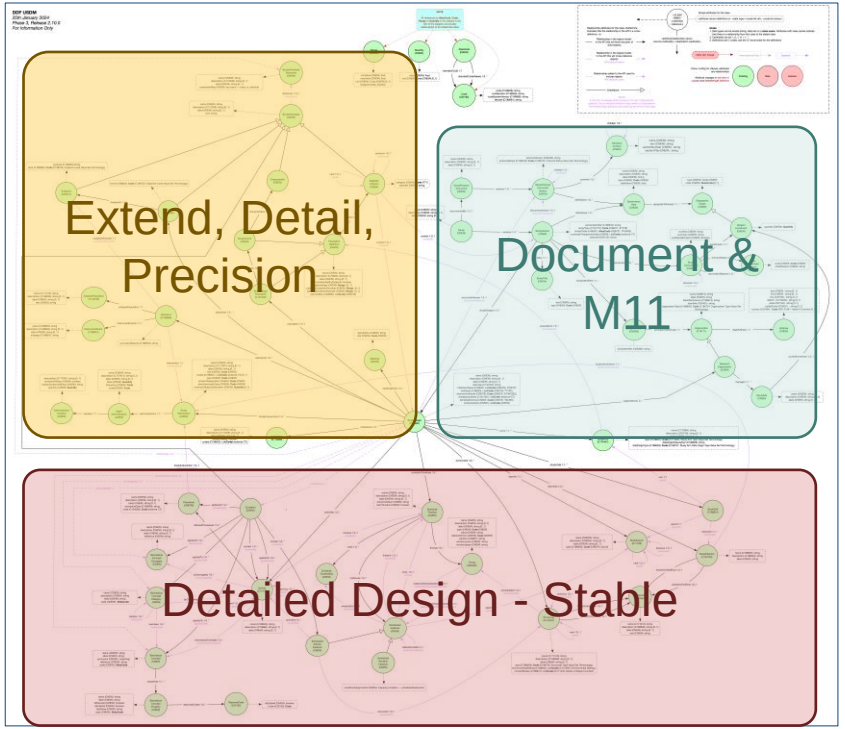
CDISC DDF / USDM, Phase Two v Three





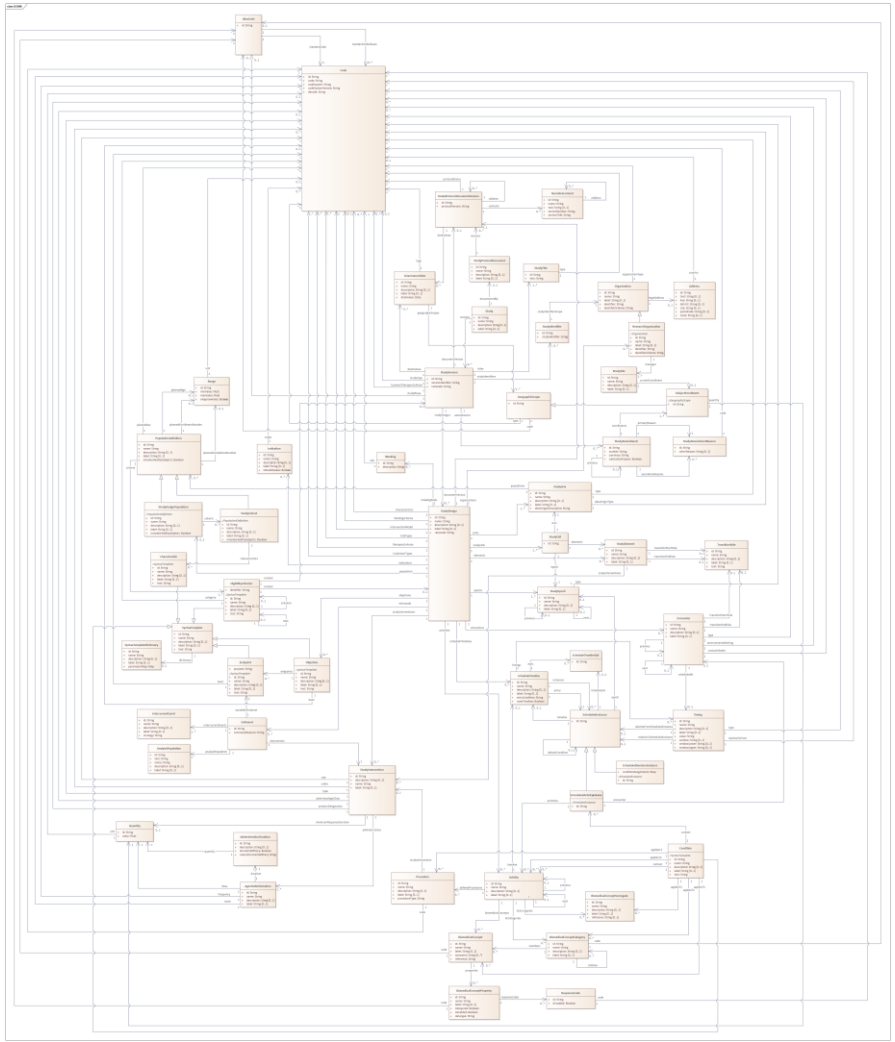
CDISC DDF / USDM, Phase Two v Three





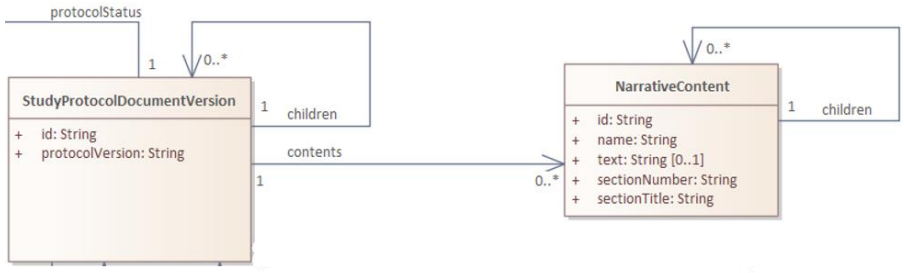
Changes for USDM v3.0

- Major model changes
  - Narrative Content
  - Syntax Templates
  - Eligibility criteria
  - Versioning, Study documents and Amendments
  - Intervention and administration
  - Study population and cohorts
  - Research Organization and Study sites
  - Conditionality
- Other
  - UML formatting
  - API and model improvements
  - Test data tool
  - IG updates and improvements
    - New paragraphs
    - Mapping
    - Handling footnotes
  - Mapping and alignment to
    - M11
    - Clintrials.gov
    - SDTM trial summary domains



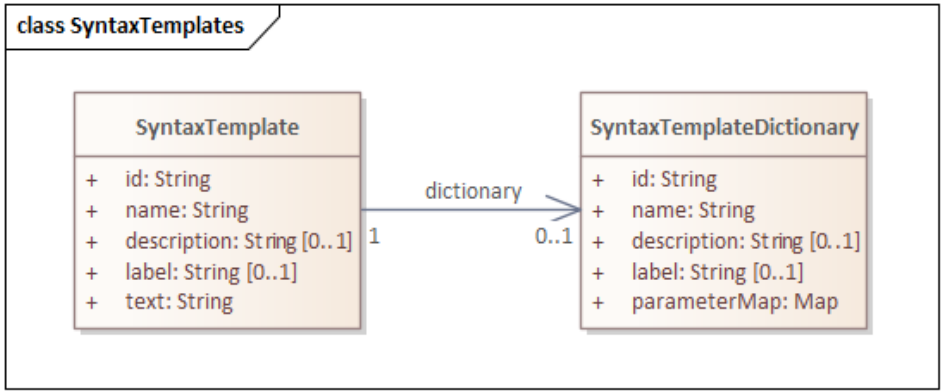
Narrative content

- Storage of protocol content in a specific format like:
  - M11
  - CPT
  - Sponsor defined formats
- Content of a specific protocol document version:
  - Section number
  - Section title
  - Formatted section content
- Nesting of subsections
  - Children
- Can refer to items stored elsewhere in the USDM data model using HTML cross-referencing



Syntax templates

- HTML formatted Text including parameterized elements
- Parameters stored in dictionary enabling reuse
  - optionally mapped to elements stored elsewhere in the data model.
- Syntax template class elements inherited by classes using this capability, in version 3.0 used for:
  - Eligibility criteria
  - Cohort characteristics
  - Objectives
  - Endpoints
  - Activity Conditions

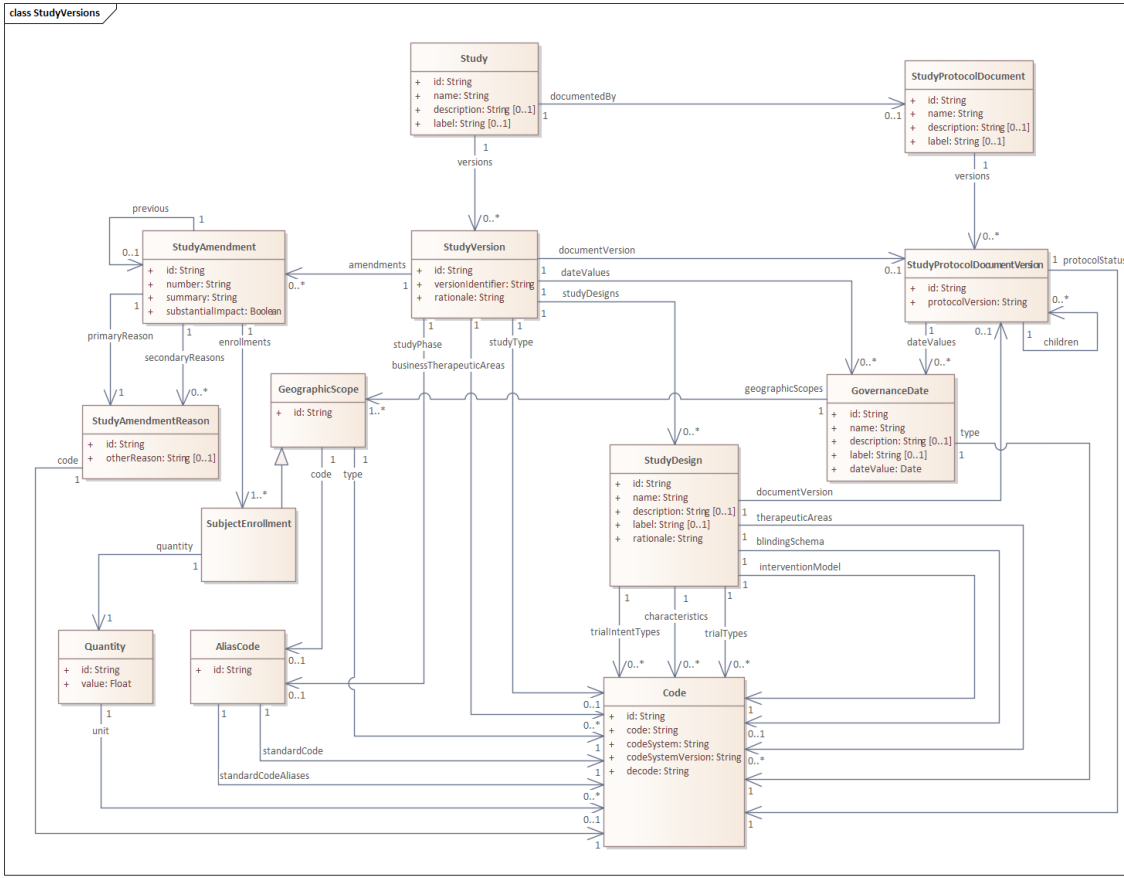


Eligibility Criteria

- Inherits syntax Template attributes
- Ordered by previous/next attributes
- Includes a category and identifier attribute to align with SDTM TI domain
- Are directly referenced from out of the study population or a specific cohort
- Are put in context of the whole study or a specific study design

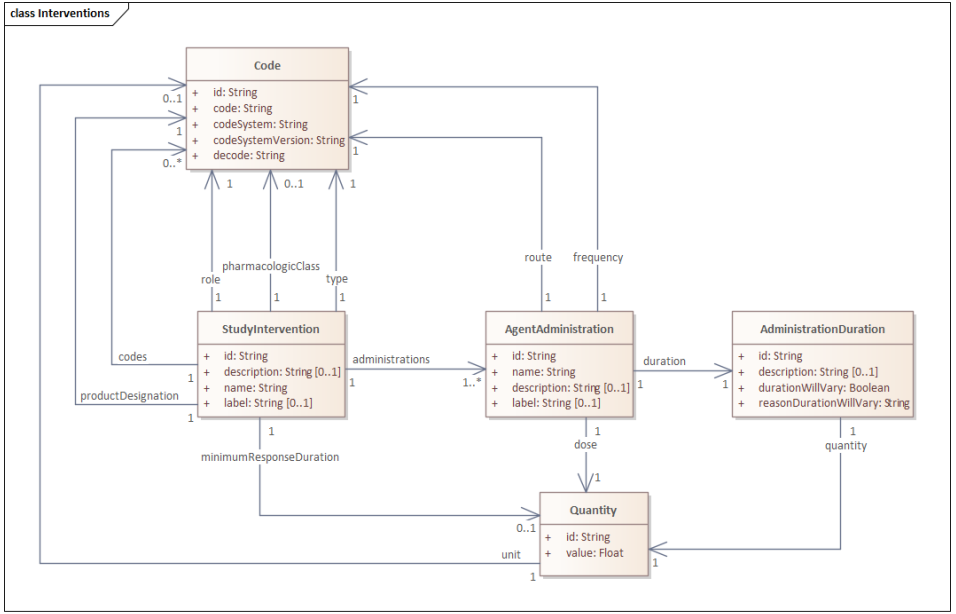
Versioning, study documents and amendments

- Study -> StudyVersion
  - Only 1 to be submitted
- StudyProtocolDocument -> StudyProtocolDocument Version
- Amendments
  - Reason
  - No or % of patients enrolled per geographic area
- Dates
  - Type
  - Geographic scope



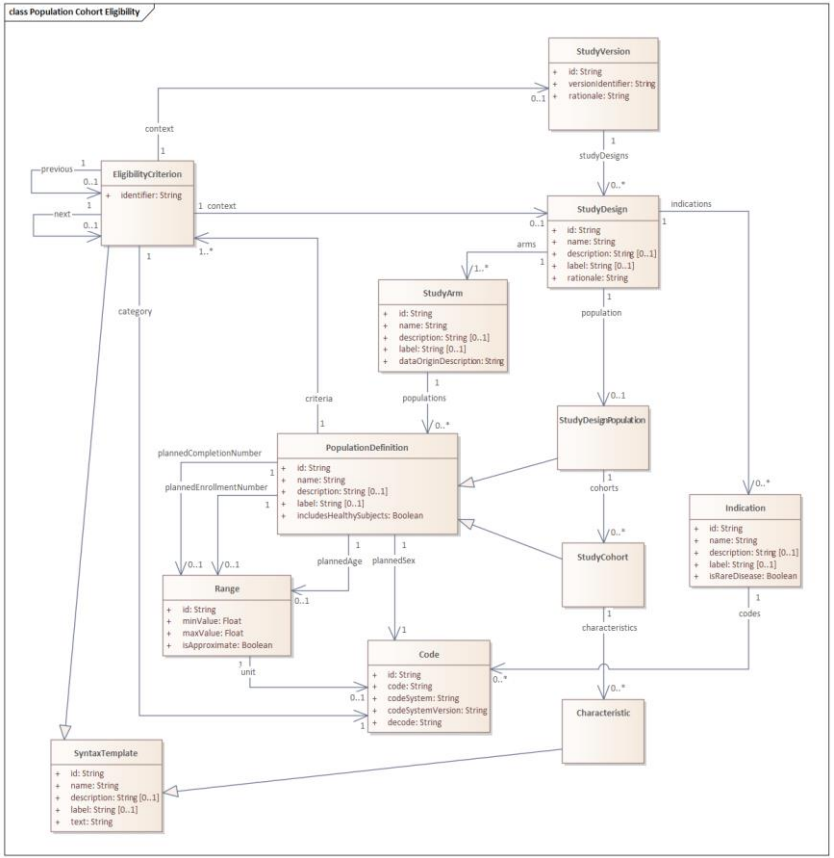
Intervention and administration

- Generalized to Study Intervention
  - Before: Investigational Intervention
- Added attributes to characterize the intervention
  - role, type and productDesignation
- Agent administration
  - Route, frequency, duration
- M11 and standards alignment
  - MinimumResponseDuration
  - AdministrationDuration



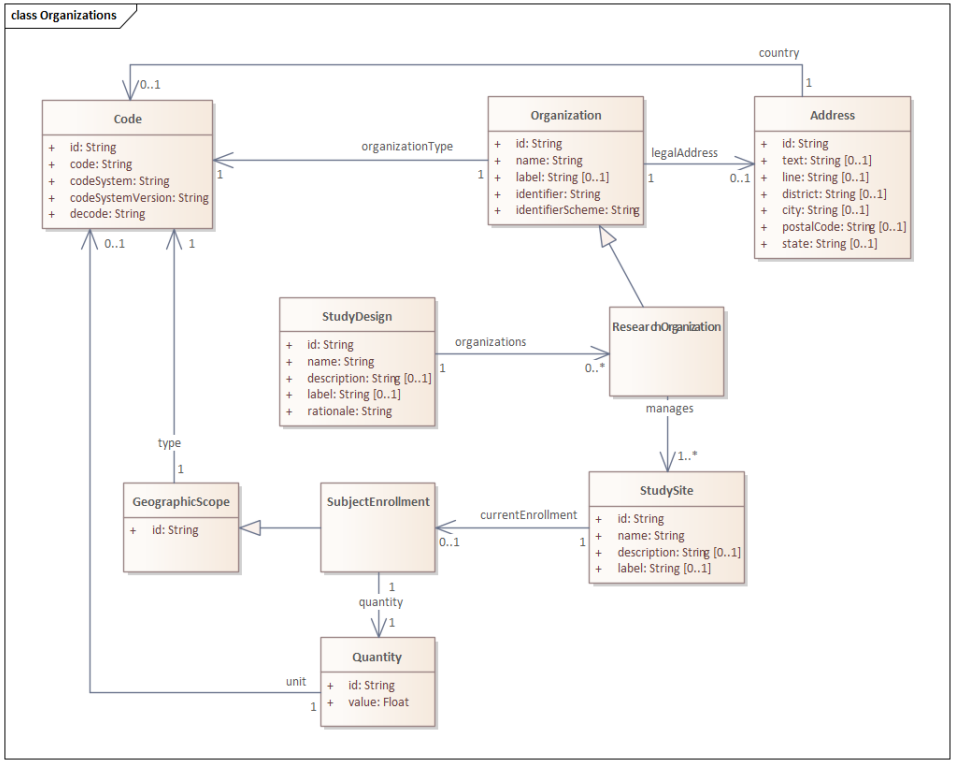
Study Population and cohorts

- 1 Study Population
- Optional cohorts
- Inheriting Population Definition attributes
  - Criteria
  - Age range
  - Planned enrollment number
  - Planned completion number
  - Planned sex
- Additional characteristics can be defined for cohorts
  - Referencing to other attributes in USDM using syntax template feature



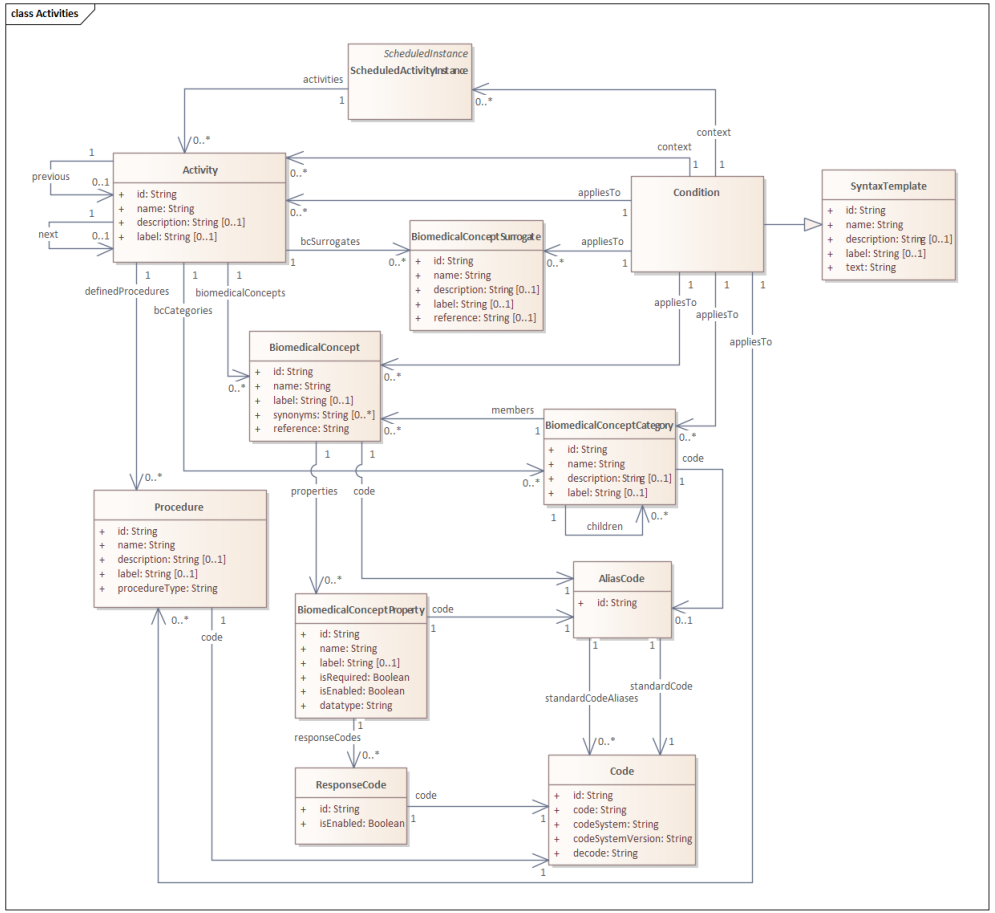
Research organization and study sites

- Can be defined per study design
- New Research Organization class
  - Inherits from the organization class
  - Manages study sites
- New Study Site class
  - Can define geographic scope
  - Can define current enrollment per site at time of design (0 at start of study, 0 or more in case of an amendment).



Conditionality

- Account for conditionality of activities at the following levels
  - Activity,
  - Assessment (BC or surrogate BC),
  - Procedure, or
  - Category of assessments (BC category
- A condition relates to
  - An overall activity defined in the SoA, or
  - a specific timepoint in the SoA timeline.
- Handling of footnotes



API and model improvements

- Set of standard attributes
  - Name, Label, Description
- Standardization of attribute naming
  - Remove class name from attribute name if redundant
- Avoid repeats of information
  - Disconnected UML model from API in case of cross references, like:
    - InterventionId (API) instead of intervention (UML)
    - BiomedicalConcept**Ids** instead of biomedicalConcept**s**
    - ChildIds instead of Children
- Include class name in the API
  - InstanceType

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Mapping and alignment to other standards

- Uniform reference style
- All design parameters included for
  - SDTM trial design
  - CT.gov

TSPARM	TSPARMCD	Code	Codelist Code	TSVAL USDM Path and Attribute	Selection / Derivations	TSSEQ	TSGRPID
Adaptive Design	ADAPT	C146995	C66738	Study/@versions /StudyVersion/@studyDesigns /StudyDesign/@characteristics /code/@decode	If characteristics include "ADAPTIVE" then TSVAL="Y" and TSVALCD="C49488" Otherwise TSVAL="N" and TSVALCD="C49487"		
Planned Minimum Age of Subjects	AGEMIN	C49693	C66738	Study/@versions /StudyVersion/@studyDesigns /StudyDesign/@population (/StudyDesignPopulation/@cohorts) /StudyDesignPopulation |StudyCohort/@plannedAge /Range/@minValue + @unit	Use minimum of minimum age values of all populations included (studyDesignPopulations and Cohorts). Transform according to ISO 8601 standards. If one ore more populations have a null minValue then TSVAL should be set to null and TSVALNF should be filled instead according to ISO 21090.		

The mapping to **Study Identification** is presented below. See Section 4.7, Study Identifiers and Titles, for a description of the related features in the USDM.

CT.gov Path	CT.gov Variable	CT.gov Requirement	USDM path and attribute	Selection/Derivation
Study Identification	Brief Title	Required	Study/@versions /StudyVersion/@titles /StudyTitle/@Text	..StudyTitle/@Type/Code/@decode="Brief Study Title" limit to 300 characters
Study Identification. Brief Title	Acronym	Required, If available	Study/@versions /StudyVersion/@titles /StudyTitle/@Text	..StudyTitle/@Type/Code/@decode="Study Acronym" limit to 14 characters

- Updated mapping of CPT to new style and USDM v3.0
  - No new mapping

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Examples

- Will be updating and improving the examples as we go through public review, adding more detail
- Public workshops will also provide further information to implementors and more example materials
- Updated BC Library combined with improved CDISC library interface will allow CDISC Pilot example to be updated


```
"id": "StudyVersion_1",
"versionIdentifier": "2",
"rationale": "The discontinuation rate associated with th
"studyType": {
"id": "Code_1",
"code": "C98388",
"codeSystem": "http://www.cdisc.org",
"codeSystemVersion": "2023-09-29",
"decode": "Interventional Study",
"instanceType": "Code"
},
"studyPhase": {
"id": "AliasCode_1",
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"id": "Code_2",
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"codeSystemVersion": "2023-09-29",
"decode": "Phase II Trial",
"instanceType": "Code"
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"documentVersionId": "StudyProtocolDocumentVersion_1",
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{
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```
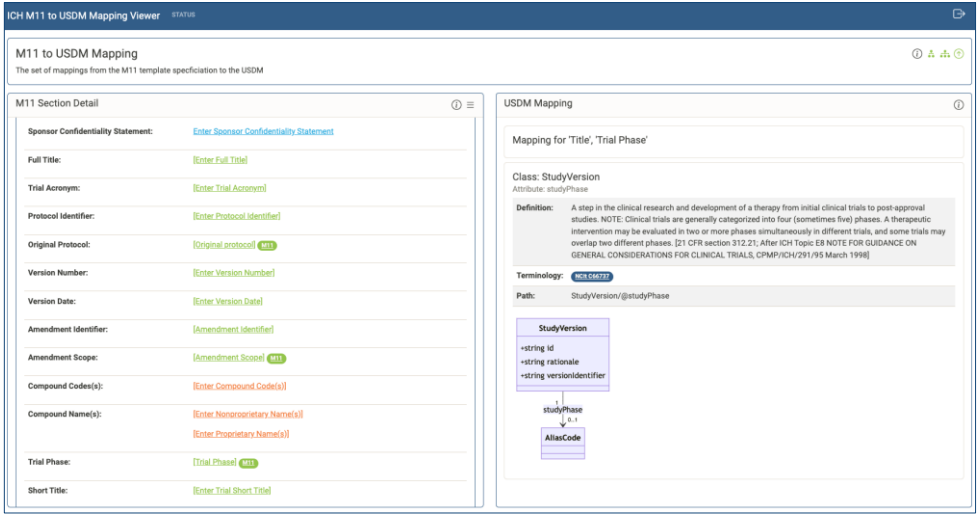
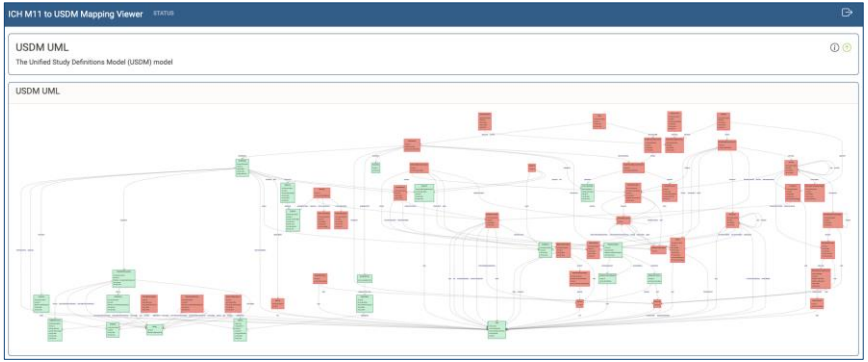

ICH M11 Protocol Specifications

- Original plan was to release USDM V3 at a similar time to the first issue of the ICH M11 specification
- ICH M11 Delivery timelines are currently being amended
- USDM V3 accommodates the latest available ICH M11 information
- ICH, HL7 Vulcan and CDISC now working together on the ICH Technical Implementation Guide (TIG) that will be part of the ICH release

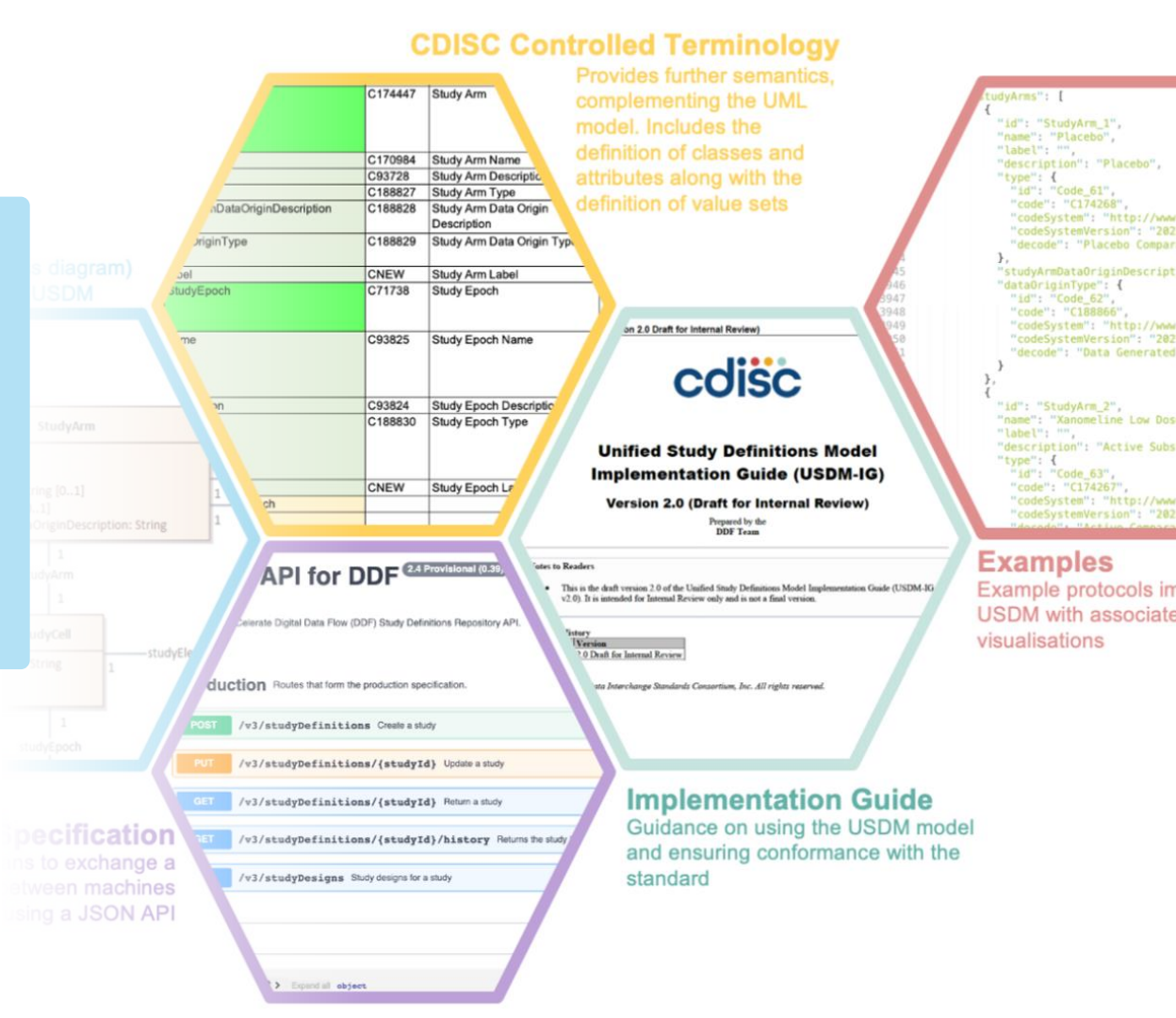




Thank You

CDISC DDF Team:

- Gerry Campion
- Drew Mills
- Erin Muhlbradt
- John Owen
- Berber Snoeijer
- Craig Zwickl



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Public Review Information

John Owen

DDF Phase 3 Public Review Dashboard

CDISC, in continued collaboration with TransCelerate's Digital Data Flow Project, has updated the USDM reference architecture, which will serve as a standard model for the development of a Study Definitions Repository. The Repository is a novel central component aimed at facilitating the exchange of structured study definitions across clinical systems using technical and data standards. CDISC invites you to submit comments on the draft v3.0 of the Unified Study Definitions Model (USDM) during the 30-day Public Review period.

The focus of Phase 3 is:

- Representation of draft ICH M11 CeSHarP (Clinical electronic Structured Harmonised Protocol) elements in USDM
- Addition of elements to the USDM to demonstrate automated population of selected SDTM Trial Design datasets
- Addition of elements to the USDM to demonstrate automated population of selected Clinical Trial Registry fields
- Updates to the USDM to cater for more Complex Studies/Cohort Studies
- USDM Model Enhancements

Deliverables include a logical data model, supporting Controlled Terminology, API specifications, and an associated Implementation Guide.

Public review is a key quality step in our Standards Development Process. CDISC relies on your input to ensure neutral, consensus-based data standards are developed and adopted by a diverse global community interested in improving research processes and quality for the benefit of all.

Thank you for contributing your time and expertise.

Public Review Dates

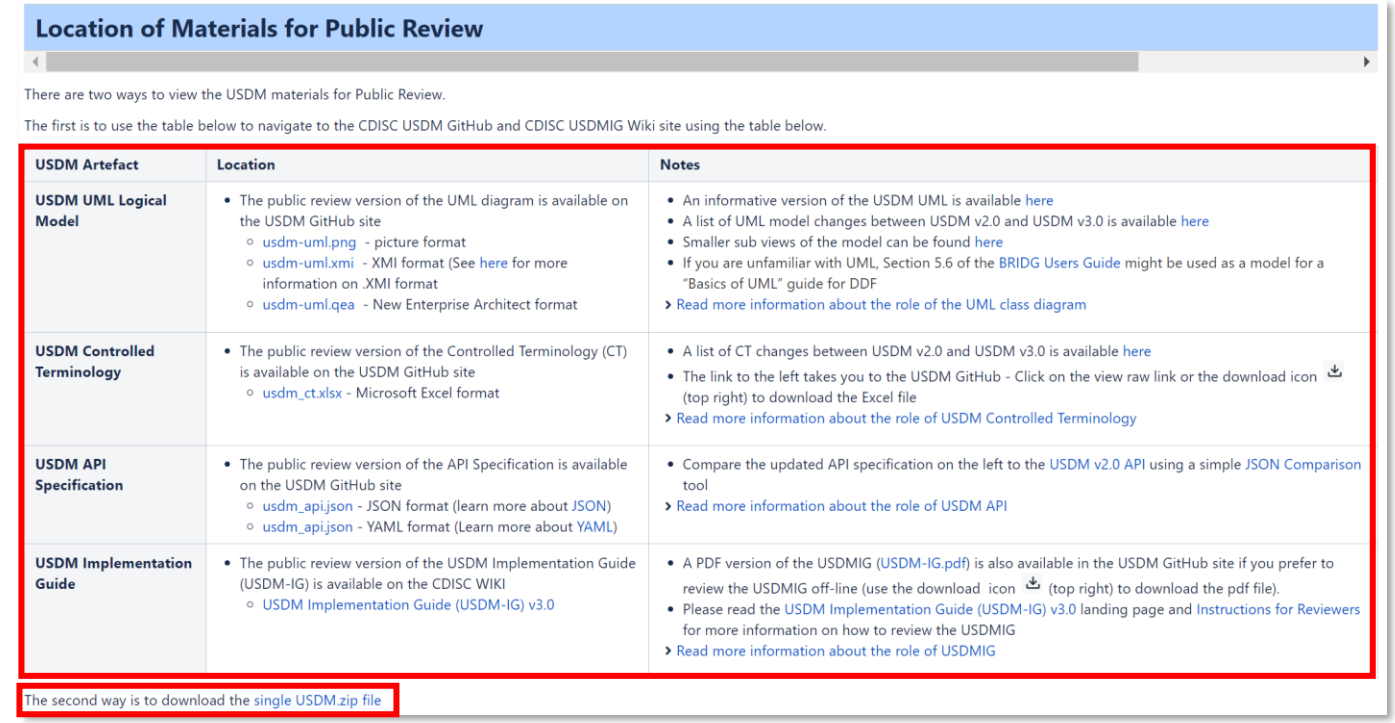
Public Review Comment Period Start: Tuesday 30 Jan 2024

Public Review Comment Period End: Thursday 22 Feb 2024

Comments received after 22 Feb 2024 may not be addressed during the public review period but will be deferred to the next version of the USDM.

https://wiki.cdisc.org/display/PUB/DDF+Phase+3+Public+Review+Dashboard

DDF Phase 3 Public Review Dashboard



Location of Materials for Public Review

There are two ways to view the USDM materials for Public Review.

The first is to use the table below to navigate to the CDISC USDM GitHub and CDISC USDMIG Wiki site using the table below.

USDM Artefact	Location	Notes
USDM UML Logical Model	• The public review version of the UML diagram is available on the USDM GitHub site ◦ usdm-uml.png - picture format ◦ usdm-uml.xmi - XMI format (See here for more information on .XMI format ◦ usdm-uml.qea - New Enterprise Architect format	• An informative version of the USDM UML is available here • A list of UML model changes between USDM v2.0 and USDM v3.0 is available here • Smaller sub views of the model can be found here • If you are unfamiliar with UML, Section 5.6 of the BRIDG Users Guide might be used as a model for a "Basics of UML" guide for DDF › Read more information about the role of the UML class diagram
USDM Controlled Terminology	• The public review version of the Controlled Terminology (CT) is available on the USDM GitHub site ◦ usdm_ct.xlsx - Microsoft Excel format	• A list of CT changes between USDM v2.0 and USDM v3.0 is available here • The link to the left takes you to the USDM GitHub - Click on the view raw link or the download icon (top right) to download the Excel file › Read more information about the role of USDM Controlled Terminology
USDM API Specification	• The public review version of the API Specification is available on the USDM GitHub site ◦ usdm_api.json - JSON format (learn more about JSON) ◦ usdm_api.json - YAML format (Learn more about YAML)	• Compare the updated API specification on the left to the USDM v2.0 API using a simple JSON Comparison tool › Read more information about the role of USDM API
USDM Implementation Guide	• The public review version of the USDM Implementation Guide (USDM-IG) is available on the CDISC WIKI ◦ USDM Implementation Guide (USDM-IG) v3.0	• A PDF version of the USDMIG (USDM-IG.pdf) is also available in the USDM GitHub site if you prefer to review the USDMIG off-line (use the download icon (top right) to download the pdf file). • Please read the USDM Implementation Guide (USDM-IG) v3.0 landing page and Instructions for Reviewers for more information on how to review the USDMIG › Read more information about the role of USDMIG

The second way is to download the single USDM.zip file

https://wiki.cdisc.org/display/PUB/DDF+Phase+3+Public+Review+Dashboard

DDF Phase 3 Public Review Dashboard

Public Review Webinar

- We invite you to register and attend the DDF Public Review Webinar on Thursday 01 Feb 2024 11:00am-12:30pm US Eastern Time, where representatives from the TransCelerate Biopharma and CDISC DDF teams will present on the updates made to the USDM during this phase of development, as well as providing information on how to provide public review comments.
- A recoding of the webinar will be posted here

Other USDM Resources

The list below contains useful information if you are new to Digital Data Flow and the Unified Study Definitions Model (USDM) including:

- How to find introductory information on DDF
- Overview of the USDM
- Biomedical Concepts in the USDM
- Current developed test data
- Using your own study using the test data tools

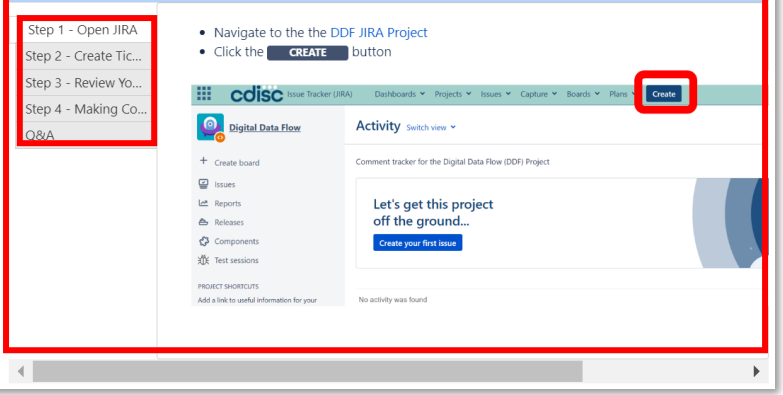
› Click here to find more USDM orientation informaion

Instructions to create a JIRA comment for the USDM Implementation Guide

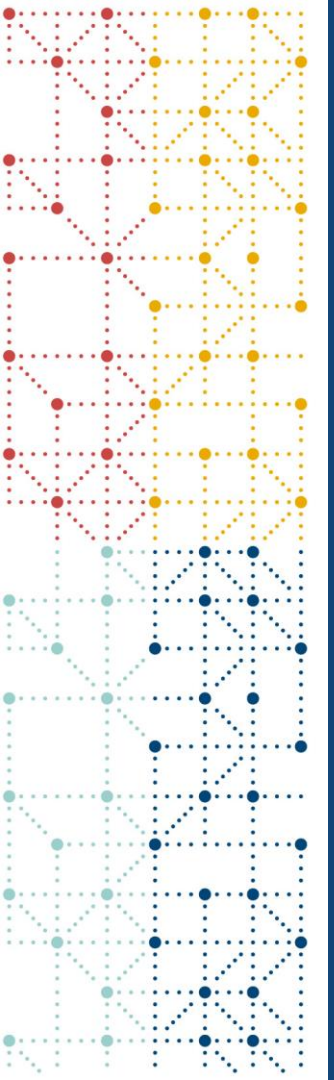
Note that the USDM Implementation Guide has been developed in the CDISC WIKI and therefore JIRA comments can be made direct in the WIKI

Please see the USDM Implementation Guide (USDM-IG) v3.0 landing page and the Instructions for Reviewers section of the USDM IG

Instructions to create a JIRA comment for the UML, CT and API Deliverables



https://wiki.cdisc.org/display/PUB/DDF+Phase+3+Public+Review+Dashboard



Upcoming events related to DDF

John Owen

Upcoming Events

Mark your calendars!

Major/ Interactive Event | General Awareness | Virtual option available

Upcoming Events of 2024	Date
SCOPE Summit 2024 Digital Data Flow: Digitalizing Clinical Protocol Information to Accelerate Clinical Research and Pharma to Healthcare Interoperability SCOPE Summit 2024 | February 11-14, 2024 | Orlando, FL	11-14 February 2024
27th DIA Japan Annual Workshop for Clinical Data Management Workshop Event Page - Tokyo, Japan	19-20 February 2024
PHUSE US Connect 2024, Bethesda, MD (Register Here) • [2/25] DDF Workshop: Mastering USDM Standards with an Interactive Demo and Hands-on Workshop • [2/26 morning] DS: Digital Data Flow Track • [2/26 afternoon] SM12: Embracing the Future of Digitization: Uninterrupted Data Flows from Protocol Design to Electronic Data Capture	25-28 February 2024
Data Driven, Hybrid and Full Decentralized Clinical Trials 2024 Event Page - Philadelphia, PA	16-17 April 2024
2024 CDISC + TMF Europe Interchange, Berlin, Germany Digital Data Flow Workshop – Tuesday, April 23, 2024; 9:00 AM – 3:00 PM CET 2024 CDISC + TMF Europe Interchange | CDISC	22-26 April 2024

* Please note, related industry events are not formally endorsed by TransCelerate and are listed for awareness only

TransCelerate BIOPHARMA INC.

phuse·connect connect·share·advance | US Connect 2024

Sunday February 25

Time (EST)	Salon F/G	Salon H	Time (EST)
From 2:00pm	**Registration –** Main Level Foyer		From 2:00pm
2:30pm–4:00pm	**Hands-on Workshop** Step 1 to Becoming Multi-Lingual *Instem*	**Hands-on Workshop** Mastering USDM Standards with an Interactive Demo and Hands-on Workshop *CDISC & TransCelerate*	2:00-4:00 pm

Monday February 26

Time (EST)	Salon A	Salon B	Salo
9:00am–10:30am	**Keynote Speaker** – Peter Ronco, *Emmes* 'The Clinical Trial Process is Still Fundamentally Broken' | Salon D		
10:30am–11:00am	**Morning Break** – Sponsored by Pinnacle 21 by Certara		
11:00am–11:30am	**DH01: How to Monitor SDTM Data Health** *Bioforum The Data Masters*	**Connect Theme Presentations (DS)** Digital Data Flow – From Vision to Reality **DS01: ICH M11 Clinical Electronic Structured Harmonised Protocol (CeSHarP) and CDISC: Making the Electronic Protocol a Reality** *CDISC*	**ETO** **Artif** *IBM*
11:30am–12:00pm	**DH02: Eliminating SDTM Double Programming by Using a Validation Tool and Dummy Data** *SGS Health Science*	**DS02: The TransCelerate/CDISC Digital Data Flow Project: Practical Electronic Study Designs** *CDISC*	**ETO** **Gene** *Syne*
12:00pm–12:30pm	**DH03: Addressing Challenges in Structuring CDISC SDTM and ADaM Datasets to Report Adverse Events Spanning Two Treatment Periods** *MSD*	**DS03: Digital Protocol Vision ... How Digital Information Can Transform and Automate Our Processes** *Instem*	**ETO** **Web** *Symb*

PHUSE US Connect

CDISC EU Interchange 2024

Tuesday 23rd April

CDISC Workshops

Digital Data Flow Workshop

9:00 AM-3:00 PM CET

- Deep dive into all aspects of the model and how study protocols and designs can be represented using the USDM
- Focused sessions covering the theory on an individual aspect of the model combined with hands-on exercises and discussion
- Timing, biomedical concepts, interventions, versioning, links with other standards such as SDTM, ICH M11, Trial Registries

Day 2
25 April 2024

11:00 - 12:30
Session 6A: Digital Data Flow

Stijn Rogers, argenx
Europa 5

11:00 - 11:30
ICH M11 Presentation
Peter Van Reusel, CDISC

11:30 - 12:00
DDF Presentation
Dave Iberson-Hurst, CDISC

12:00 - 12:30
DDF: The Art of the Possible Becomes a Reality
Bron Kisler, Nurocor

13:30 - 15:30
Session 7A: Digital Data Flow

Sujit Khune, Novo Nordisk A/S
Europa 5

13:30 - 13:50
Development of Unified Studies Definition Model (USDM) Through Translation of the Human-Readable Protocols
Jasmine Kestemont, Innovion

13:50 - 14:10
Ripping up the Protocol: Pairing up USDM and ICH M11 to Inform Real-Time Study Builds
Zaid Al-Jubouri, Lindus Health

14:10 - 14:40
Demonstrating e2e Study Data Automation Using Extended USDM Model
Kirsten Walther Langendorf, data4knowledge ApS

14:40 - 15:00
From OpenStudyBuilder to the Digital Data Flow- USDM Format
Maurizio Mazzei, Neo4J

15:00 - 15:30
Panel Discussion

https://www.cdisc.org/events/interchange/2024-cdisc-tmf-europe-interchange

Thank You