2023 US INTERCHANGE

FALLS CHURCH, VA | 18-19 OCTOBER

Digital Data Flow, Phase 3: The USDM meets M11

Dave Iberson-Hurst, CDISC Product Owner

18 Oct 2023, Version 3

Meet the Speaker

Dave Iberson-Hurst

Title: **Partner**

Organization: **d4k, Copenhagen**

Dave has over 40 years' experience across several industries with the last 20 years spent in the pharmaceutical industry combining his technology and software development experience with clinical data standards.

During this time, he has worked on, and led, several CDISC teams, co-led CDISC's eSource initiative (eSDI) and presented in many forums in Europe, the US, and elsewhere across the globe. He has worked closely with the FDA, EMA, HL7, ISO, and other standards organizations and was was a member of CDISC's Blue Ribbon commission.

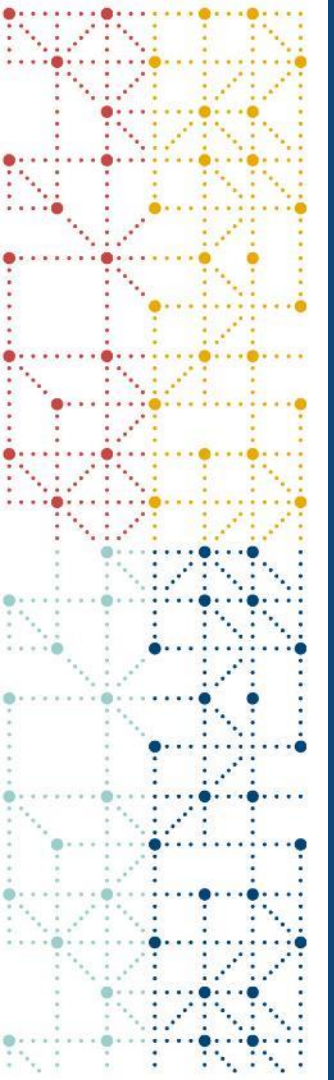
He is a partner at data4knoweldge in Copenhagen and is focused on getting greater value and utility from clinical trial data.

Disclaimer and Disclosures

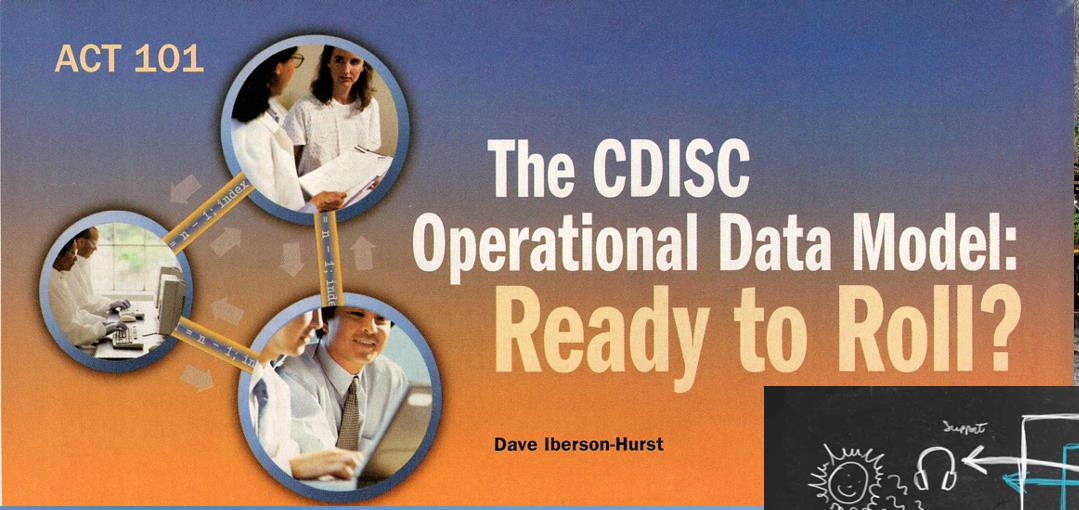
- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.*
- *On contract to CDISC for the DDF work*

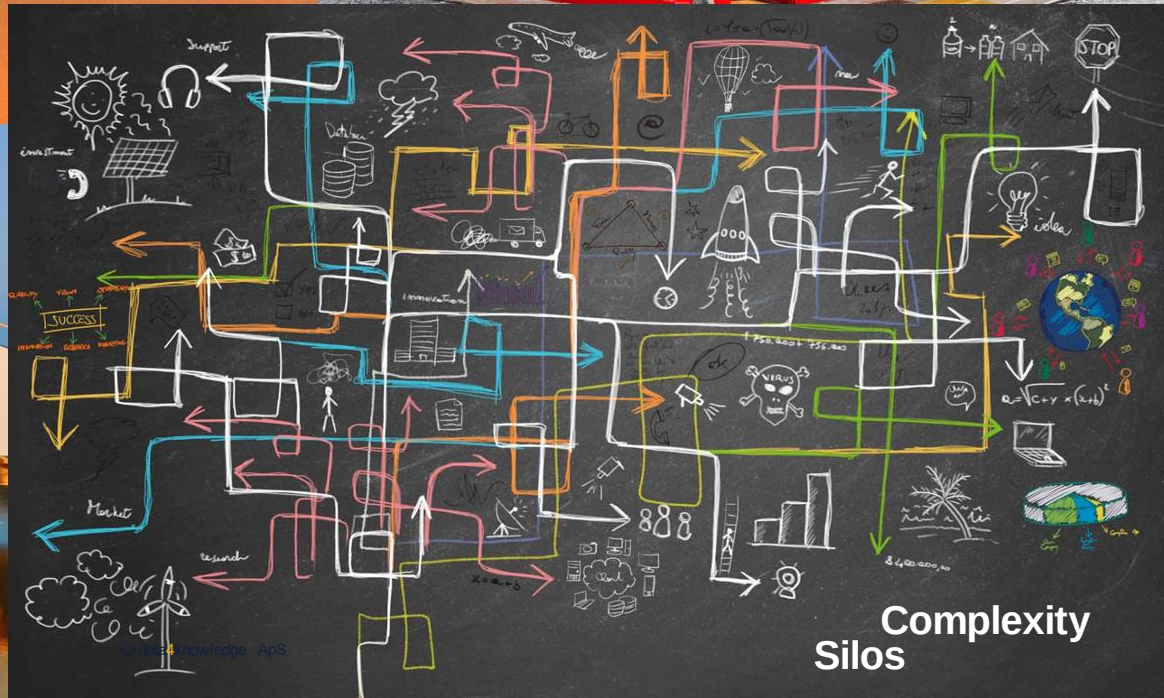
Agenda

1. Introduction
2. Digital Data Flow – The Project
3. Use Cases
4. Phase Three: USDM Meets M11
5. Summary



Introduction





Complexity
Silos

Digital Data Flow - The Project

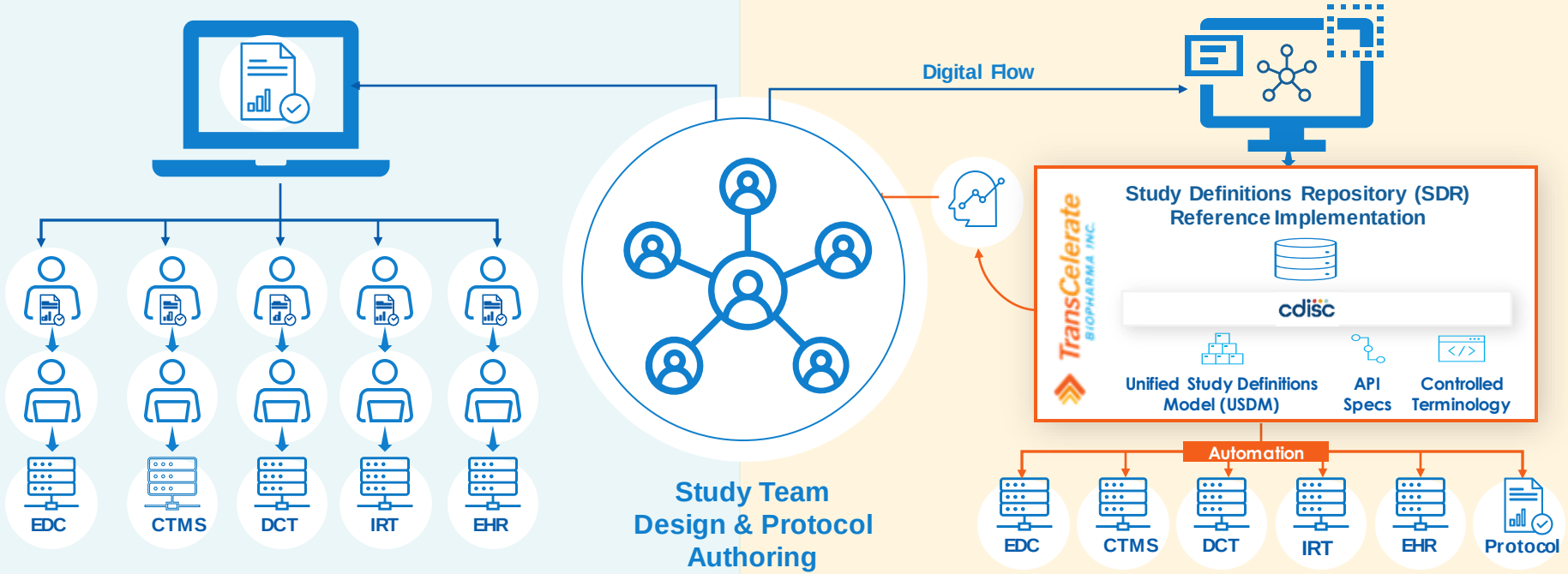
https://www.transceleratebiopharmainc.com/assets/digital-data-flow-solutions/

TransCelerate Digital Data Flow (DDF) Ambition

Write Once, Read Many

TODAY: Document-based paradigm for protocol creation, interpretation, and transcription into consuming systems

TOMORROW: Digital paradigm for protocol creation, with fully automated data flow and interoperability between systems



TransCelerate BIOPHARMA INC.

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.

V1.0.0

https://github.com/cdisc-org/DDF-RA

CDISC DDF Phase Two

Oct 2022 – June 2023

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.

Test Files
Examples of USDM JSON files

Implementation Guide
Improved explanation of the model and its use, examples etc

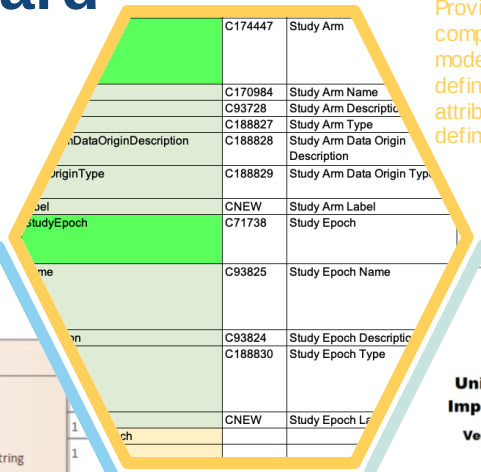
V2.0.0

https://github.com/cdisc-org/DDF-RA

The USDM Standard

CDISC Controlled Terminology

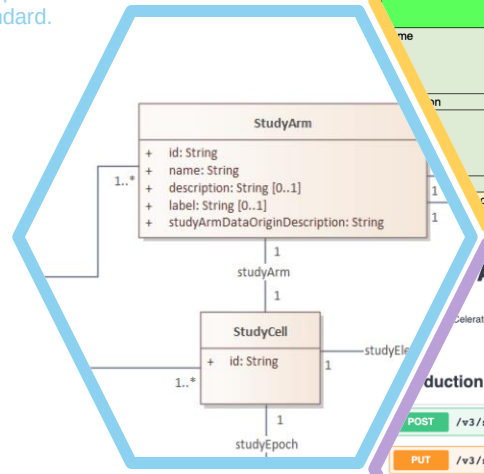
Provides further semantics, complementing the UML model. Includes the definition of classes and attributes along with the definition of value sets

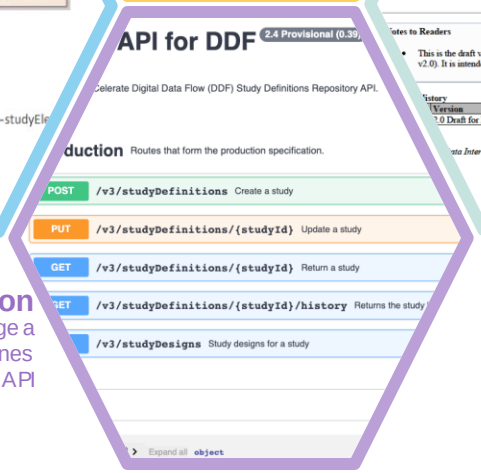


	C174447	Study Arm
	C170984	Study Arm Name
	C93728	Study Arm Descriptio
	C188827	Study Arm Type
DataOriginDescription	C188828	Study Arm Data Origin Description
OriginType	C188829	Study Arm Data Origin Typ
bel	CNEW	Study Arm Label
StudyEpoch	C71738	Study Epoch
me	C93825	Study Epoch Name
on	C93824	Study Epoch Descriptio
	C188830	Study Epoch Type
	CNEW	Study Epoch La
ch		

Logical Model

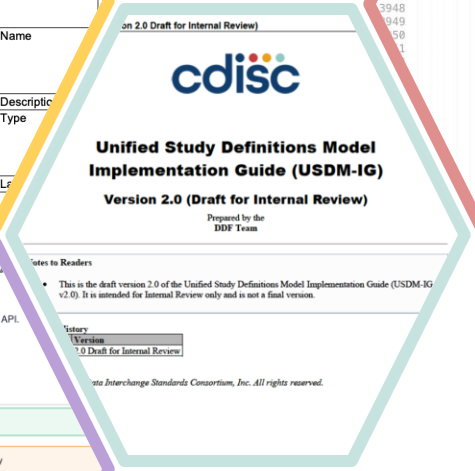
The UML logical model (a class diagram) that provides the basis for the USDM standard.





API Specification

Provides the means to exchange a single study between machines using a JSON API



Implementation Guide

Guidance on using the USDM model and ensuring conformance with the standard

Examples

Example protocols implemented in the USDM with associated JSON files and visualisations

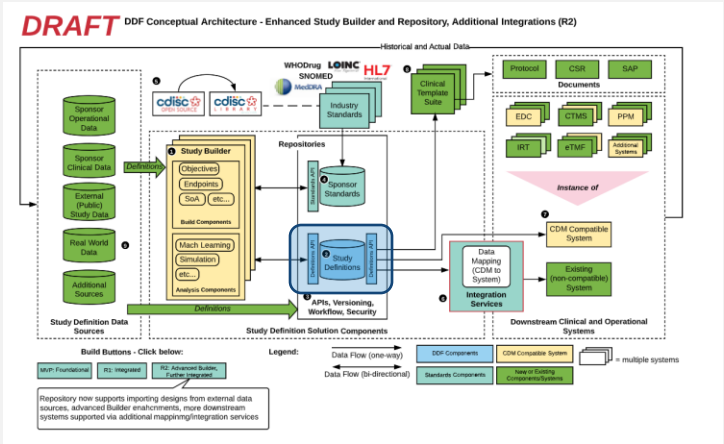
Choices …

- Recreate the current world or look for something better?
- How radical do we wish to be?
- Don’t just want to recreate the “paper world”
- Align with existing CDISC standards but not be constrained by them
- Don’t reinvent the wheel
- Don’t constrain implementations
- The project exposes the complexity of our world

Use Cases

Use Cases: USDM with BCs allows for …

Data Capture	*Automate the setup of data capture systems , incl. RWE, and capture the data.*
SoA	*Use the study design to build the FHIR SoA message.*
Data Import	*Import data from a variety of sources . Can be re-exported thus allowing for conversion across versions.*
Common Protocol Template (CPT)	*Generation of the CPT from a study design.*
Data Decay	*Re-import data using the USDM as a framework to rebuild a study design & data using the SDTM Trial Design Domains.*
Scoring	*The "scoring" of a study for such purposes as site impact, subject impact, environmental impact etc.*
Feasibility	*The use of the design to determine study feasibility including subject recruitment. A study data template.*
CT Registry	*The provision of study information to a CT registry.*
FAIR Data	*The use of the design to aid Findability, Accessibility, Interoperability, and Reusability.*
CTMS, TMF …	*The provision of protocol information to down stream systems needing "study" information.*
Query	*Having multiple studies that have a common structure allows for data export and query across the set of studies*
SDTM	*Automate the generation of SDTM datasets using the study design and BCs, including the "T" Domains*



Plus many more …

USDM Adoption

USDM Data Mining Application

Sponsor working with CDISC to develop a retrospective use case

Sponsor is using the model for retrospective data ingestion

Retrospective has a lower risk as a first point of entry into using USDM

Study Build Application

Study Build & EDC Configuration

Study Build Application

Open Study Builder Study Build Application

Population of USDM from old protocols

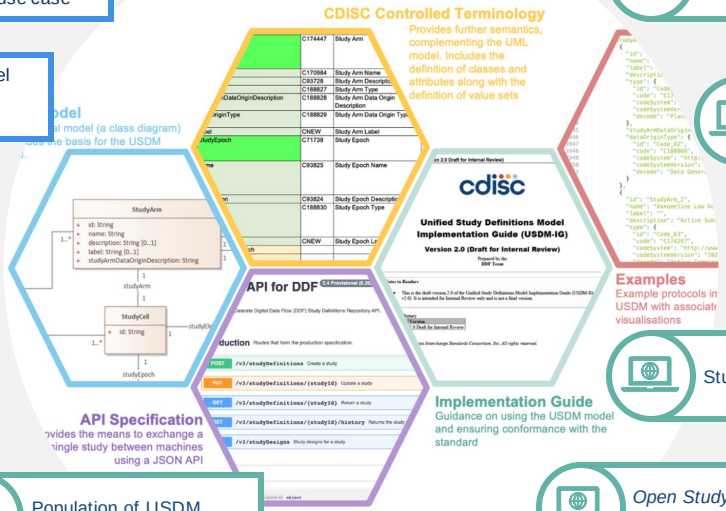
Academic institution using the model as a component of a data import application

Retrospective Studies

Prospective Studies

The "footnote conundrum"

- *Retrospective study re-creation brings a few challenges*
- *We are not constrained by the "2D" paper world. USDM enables an "improved" reconstruction.*
- *Sponsors need to consider their "philosophy", their approach to "reconstruction" of protocols*



Phase Three: USDM Meets M11

Next Steps – Phase Three

Slide from May 2023

USDM

SDR

1

- Baseline model for specifying a study in digital format
- Model supports use of a CRF link to specify which forms to use in EDC.
- Handles simple study designs

- Consume digitized study specification from an upstream source e.g., study builder)
- Store, view and search study concepts
- Downstream EDC systems may pull study specification to aid in set-up

2

- Improved support for complex study designs with a fully specified digitized Schedule of Activities (SoA)
- Model supports the identification of the appropriate CRFs for data collection to enable automated, faster configuration via use of Biomedical Concepts
- Improved CPT alignment
- Initial 'T' Domain support

- Downstream vendors can readily consume the SoA from the SDR
- Sponsor system admins can perform a visual check that SoA data received from an upstream system displays an accurate, human-readable SoA table
- Opportunity to aggregate robust historical protocol information to support analytics to drive smart design and assess risk

3

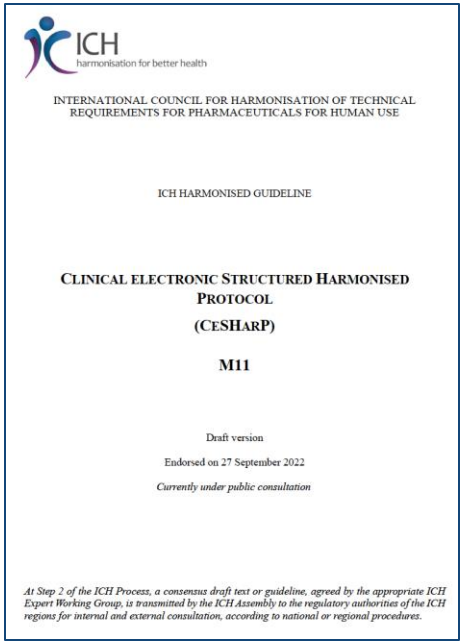
Focus for Phase 3 is currently being determined. Current expectations are:

- Expand ability to handle increasingly complex studies
- ICH M11 & CPT alignment

M11 Is …

ICH CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL (CeSHarP)

https://www.ich.org/page/multidisciplinary-guidelines



ICH harmonisation for better health

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL

(CESHARP)

M11

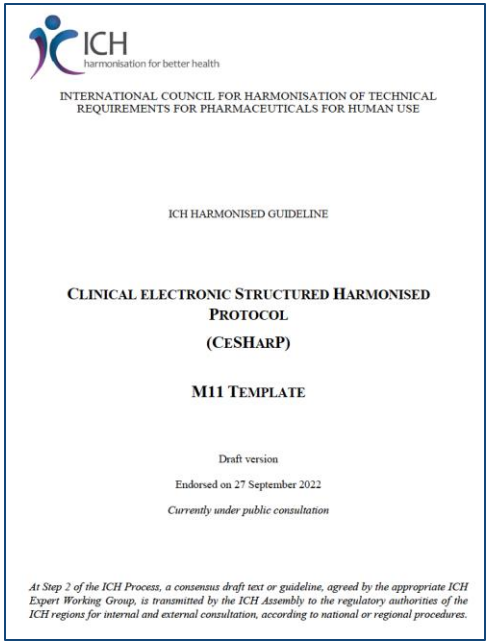
Draft version

Endorsed on 27 September 2022

Currently under public consultation

At Step 2 of the ICH Process, a consensus draft text or guideline, agreed by the appropriate ICH Expert Working Group, is transmitted by the ICH Assembly to the regulatory authorities of the ICH regions for internal and external consultation, according to national or regional procedures.

Provides background, purpose, and scope as a guideline



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CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL

(CESHARP)

M11 TEMPLATE

Draft version

Endorsed on 27 September 2022

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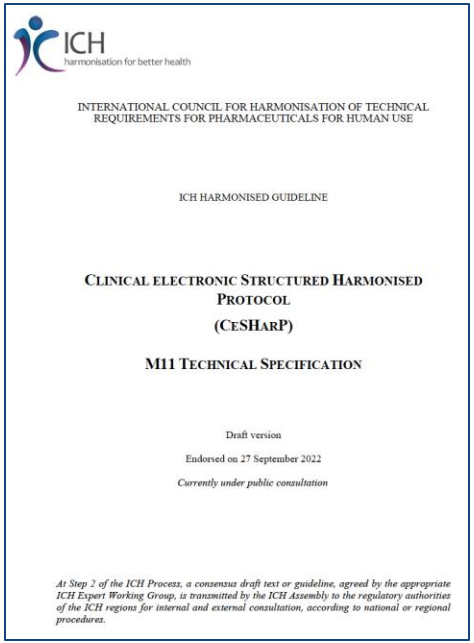
Provides the written format for the Interventional Clinical Trial Protocol Template



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(CESHARP)

M11 TECHNICAL SPECIFICATION

Draft version

Endorsed on 27 September 2022

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Provides the technical representation aligned with the guideline and protocol template

cdisc

Idea for slide layout shamelessly stolen from Rebecca Baker

M11 Simple Example

Template Specification

Protocol Full Title:	[Protocol Full Title] The protocol should have a descriptive title that identifies the scientific aspects of the trial sufficiently to ensure it is immediately evident what the trial is investigating and on whom, and to allow retrieval from literature or internet searches.
Sponsor Confidentiality Statement:	[Sponsor Confidentiality Statement] Insert the Sponsor's confidentiality statement, if applicable, otherwise delete.
Protocol Number:	[Protocol Number] A unique alphanumeric identifier for the trial, designated by the Sponsor, is a standard part of trial data, and should be included for most trials.
Version:	[Version] An optional field for use by the Sponsor at their discretion.
Amendment Number:	[Amendment Number] Enter the amendment number. If this is the original instance of
Compound Number(s):	[Compound Number] Enter the Sponsor's unique identifier for investigational compound(s) in the trial. Add or delete additional fields as needed.
Compound Name(s):	[Nonproprietary Name]. [Proprietary Name]. [Additional Proprietary Name] Delete this line from the table if a nonproprietary name has not yet been assigned. Omit proprietary name fields if not yet established.
Trial Phase:	[Trial Phase] [Description of Trial Phase Other] Acceptable entries are: "Early Phase 1", "Phase 1", "Phase 1/Phase 2", "Phase 2", "Phase 2/Phase 3", "Phase 3", "Phase 4",

Trial Phase: [Trial Phase] [Description of Trial Phase Other]
Acceptable entries are: "Early Phase 1", "Phase 1", "Phase 1/Phase 2", "Phase 2", "Phase 2/Phase 3", "Phase 3", "Phase 4",

Technical Specification

Term (Variable)	Trial Phase
Data Type	Pick list
Topic, Value or Header	D
Definition	
User Guidance	For trials combining investigational drugs or vaccines with devices, classify according to the phase of drug development.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Title Page
Relationship (reference to high level conceptual model)	
Value	Early Phase 1 Phase 1 Phase 1/Phase 2 Phase 2 Phase 2/Phase 3 Phase 3 Phase 4 Other
Business rules	**Value Allowed:** yes **Relationship:** n/a **Concept:** Protocol short title
Duplicate field in other sections	

Controlled Terms

Template Specification

Protocol Full Title:	[Protocol Full Title] The protocol should have a descriptive title that identifies the scientific aspects of the trial sufficiently to ensure it is immediately evident what the trial is investigating and on whom, and to allow retrieval from literature or internet searches.
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Business rules	**Value Allowed:** yes **Relationship:** n/a **Concept:** Protocol short title
Duplicate field in other sections	

CDISC CT

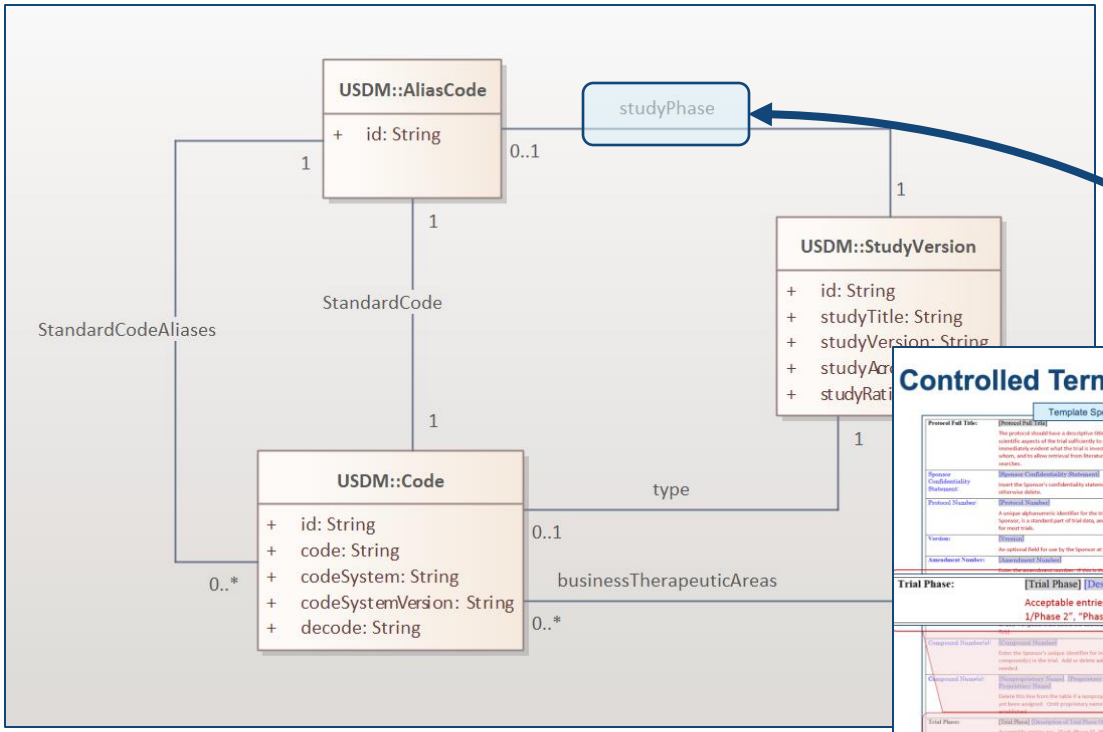
Trial Phase Response (C66737)

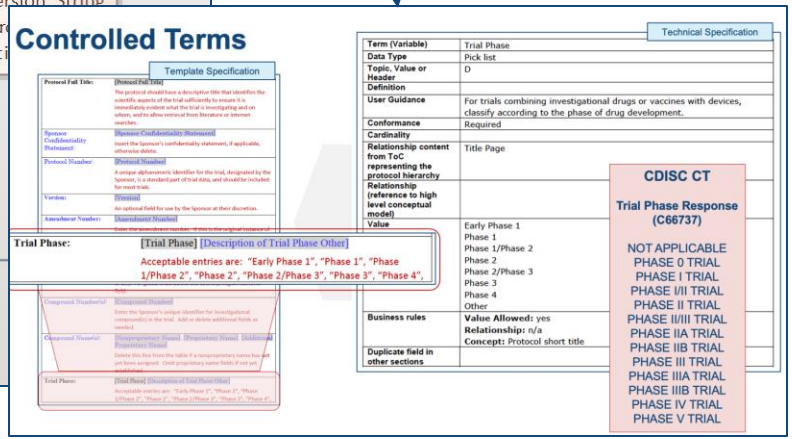
NOT APPLICABLE
PHASE 0 TRIAL
PHASE I TRIAL
PHASE I/II TRIAL
PHASE II TRIAL
PHASE II/III TRIAL
PHASE IIA TRIAL
PHASE IIB TRIAL
PHASE III TRIAL
PHASE IIIA TRIAL
PHASE IIIB TRIAL
PHASE IV TRIAL
PHASE V TRIAL

Put Into Context … the USDM

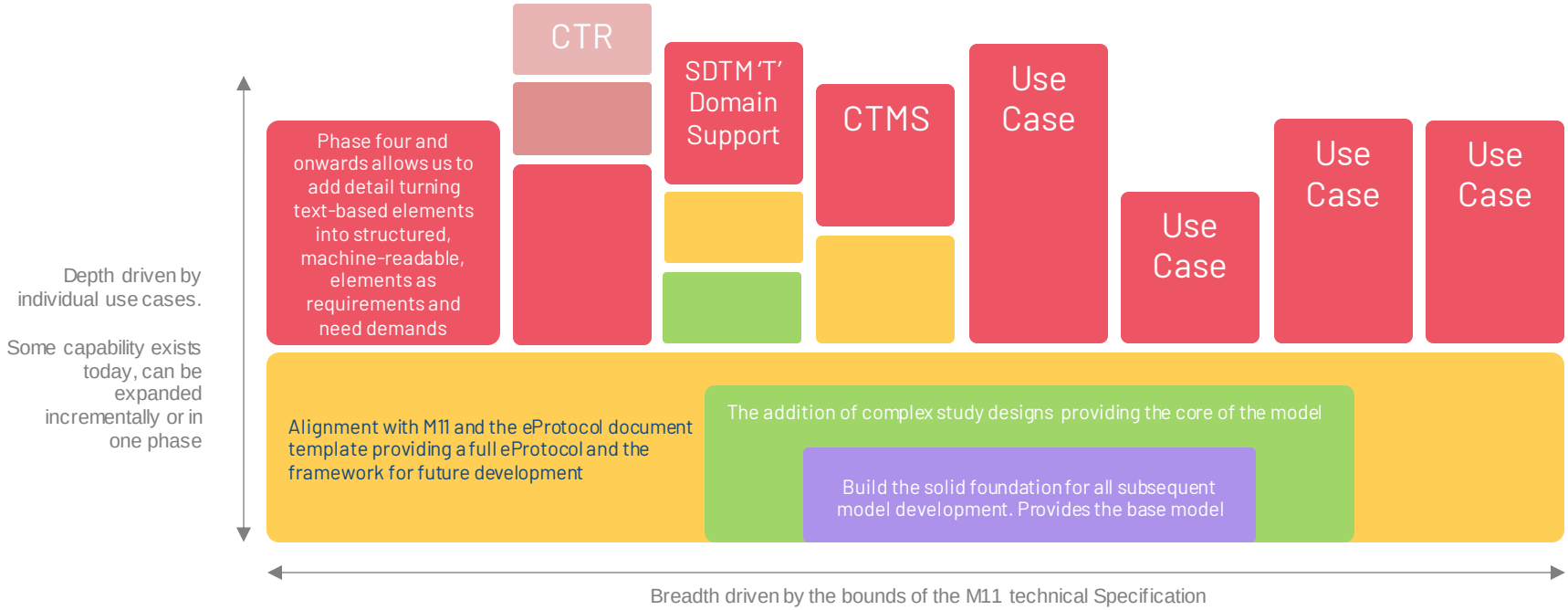
Walkthrough

- *A StudyVersion has a studyPhase*
- *Linked to the AliasCode class via the relationship studyPhase*
- *AliasCode can store:*
  - *a single standard code (CDISC Trial Phase Response, C66737) using the Code class*
  - *And zero or more other alias codes (e.g. a sponsor phase code) using the Code class to provide flexibility*



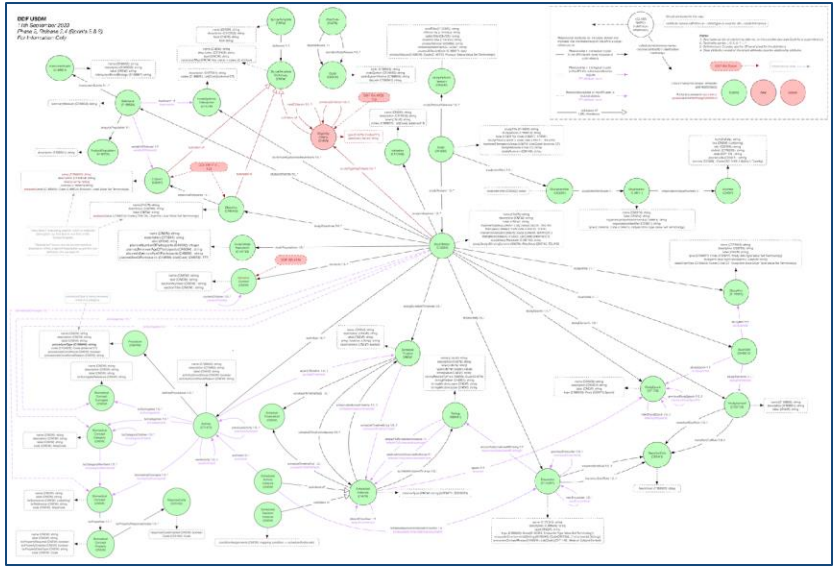


Breadth versus Depth



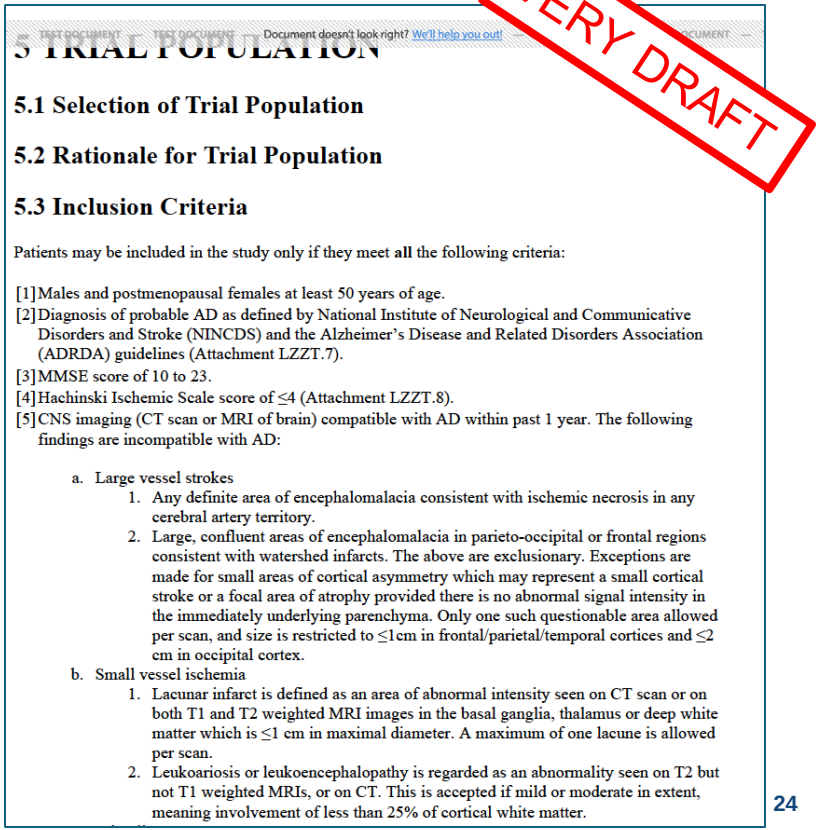
Shift of Focus

- 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



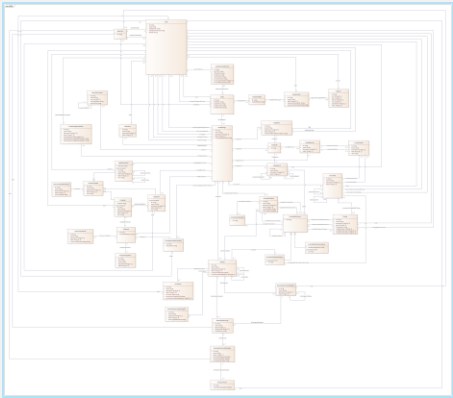
M11 Template Example Document

- First attempt to create a protocol document from the USDM, both structured [non-narrative] and unstructured [narrative text] content.
- Functionality has been added to the Excel test data tool
- More work is needed, this is very much a first draft



USDM Summary

- Structured content along with the ability to hold unstructured content



Controlled Terms

Study, Identifiers, Amendments

Estimands

Populations

Inclusion & Exclusion

Interventions & Indications

Objectives & Endpoints

Unstructured Content

Study Designs, Arms, Epochs

Detailed Study Logic, Encounters

Procedures, Biomedical Concepts

Summary

M11 & The CDISC Project

Phase Three Timeline

- January 2024
  - Phase 3 development sprints complete
- February 2024
  - Phase 3 public review
- April 2024
  - Version 3 USDM published

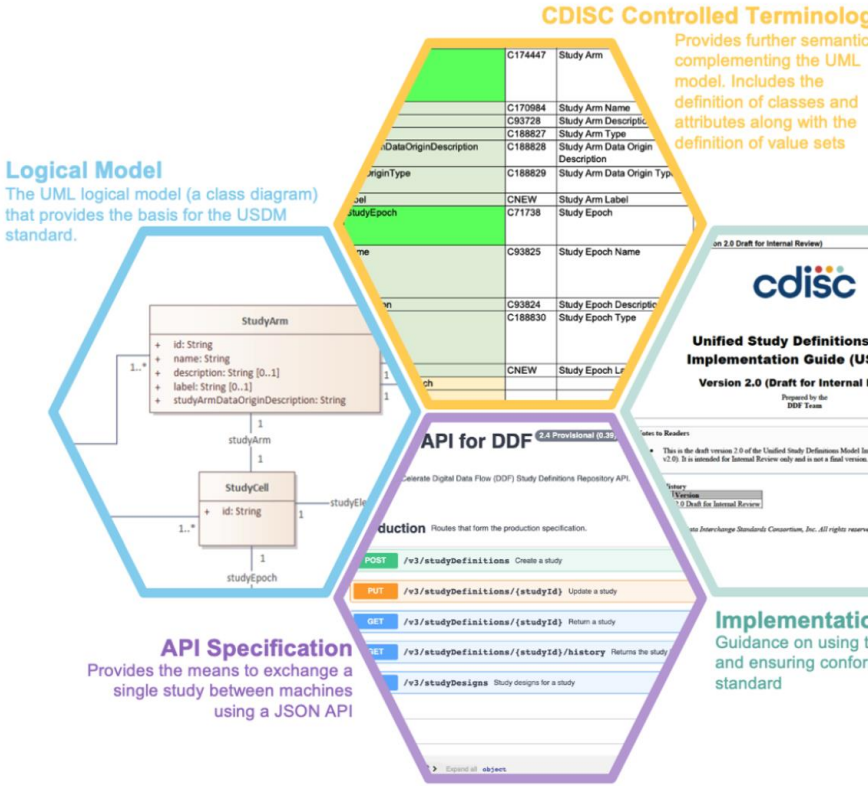
Dates may be adjusted to align with ICH M11 publication dates.

M11 next version expected early in 2024 with formal release towards the end of 2024

Photo courtesy of Stijn Rogiers, argenx & CDISC E3C

Summary

- We are “understanding” the complexity
- We can start to remove the silos and join the dots
- Digital Data Flow / Unified Study Definitions Model (DDF/USDM) fills an important gap
- USDM is but one building block, but an important one
- USDM alignment with ICH M11 will be an important step forward
- Can support various use cases, the prospective versus the retrospective
- We are only limited by our imagination



Thank You

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John Owen: jowen@cdisc.org

Link:

Github: https://github.com/cdisc-org/DDF-RA

Team:

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

PHUSE EU Connect, Sunday 5th November

Hands-on Workshop
Mastering USDM Standards with an Interactive Demo and Hands-on Workshop

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