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

PHUSE US Connect 2024 (DS02)

Dave Iberson-Hurst, CDISC Product Owner

26th February 2024

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 served as the CDISC CTO, worked on, and led, several CDISC teams, 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 currently the CDISC Product Owner for the Digital Data Flow project.

He is a partner at data4knowledge 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*

Abstract

Over the last two years CDISC, in collaboration with Transcelerate, have been working on the Digital Data Flow (DDF) initiative. This initiative aims to *"modernize clinical trials by enabling a digital workflow to allow for the automated creation of study assets and configuration of study systems to support clinical trial execution."*. The work is focused on the protocol and associated study designs and manifests itself in a new CDISC standard, the Unified Study Definitions Model (USDM), and an open-source implementation of the USDM known as the Study Definitions Repository (SDR).

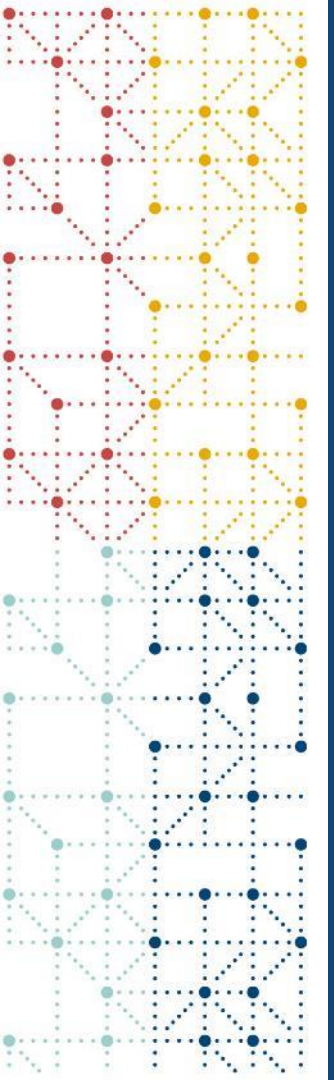
Now coming to the end of the second phase, with the third phase about to commence, the DDF project delivers a new standard that allows for the digitization of study designs and the foundation of the digital protocol.

This presentation will detail:

- The work performed in phases one and two.
- The work planned as part of phase three.
- The use cases supported by the model.
- How the model/standard can enable protocol creation, automated data flow and interoperability between systems.
- How the model/standard can be deployed and implemented today.

Agenda

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



Introduction

TransCelerate Digital Data Flow (DDF)

DISCOVERY DAY 2023

ALOFT Hotel Boston Seaport District

Summer Ballroom

September 19th, 2023

8:30 AM – 5:00 PM

** Invite-only, face-to-face event **

Envision a Future with a Digitized Clinical Study Protocol with Automated Data Flow and Streamlined Analytics Insights

From Documents to Data: Write Once, Read Many Times

Digitized Protocols

abling the use of technologies that
ntify and assemble study elements
sing a common, industry-standard
digital language allows industry to
move to digital protocols

Advanced Analytics

tter enabling the use of advanced
lytics, such as Artificial Intelligence
and Machine Learning to improve
study designs

Connectivity of Data and Processes

Enabling traceability, automated flow of content to key clinical documents, and automation to clinical & operational systems (e.g. EDC, CTMS)

Open & Flexible Solution

A functioning, example solution to enable exchange of protocol info between systems that is vendor agnostic, flexible, and provided in open source

Digital Data Flow - The Project

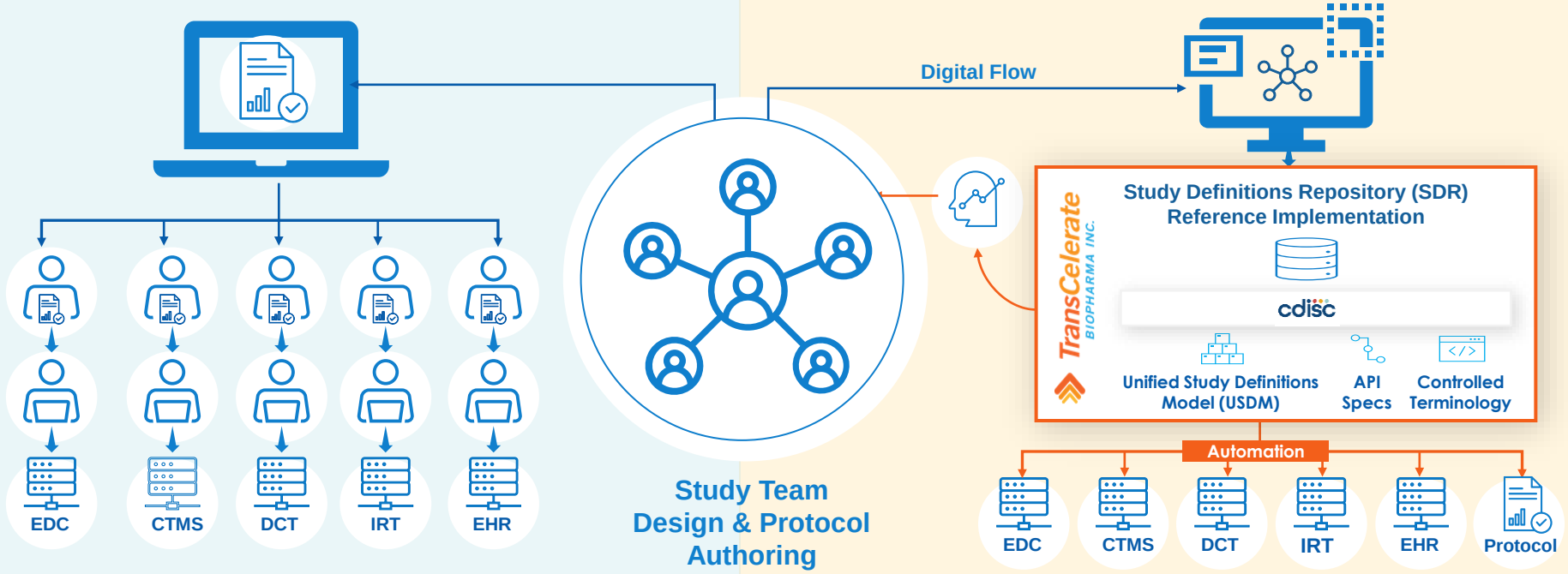
https://www.transceleratebiopharmainc.com/assets/digital-data-flow-solutions/

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



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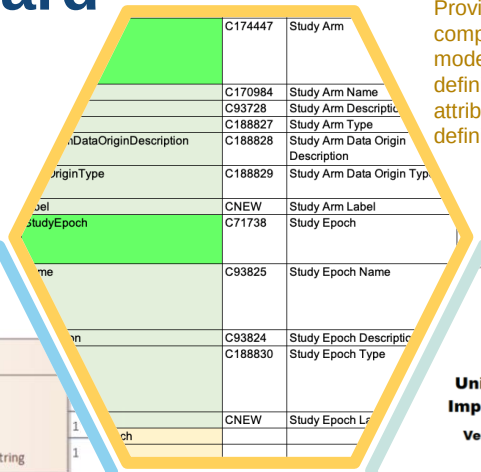
The USDM Standard

CDISC Controlled Terminology

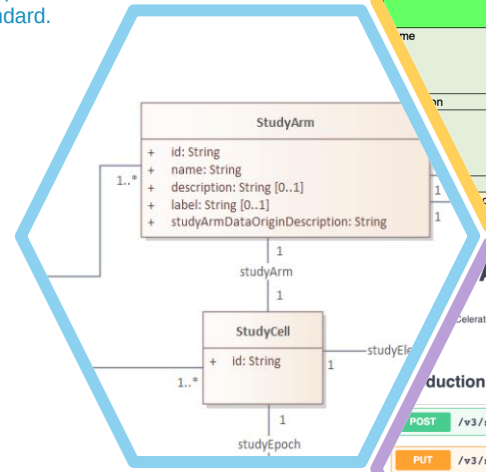
Provides further semantics, complementing the UML model. Includes the definition of classes and attributes along with the definition of value sets



	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.



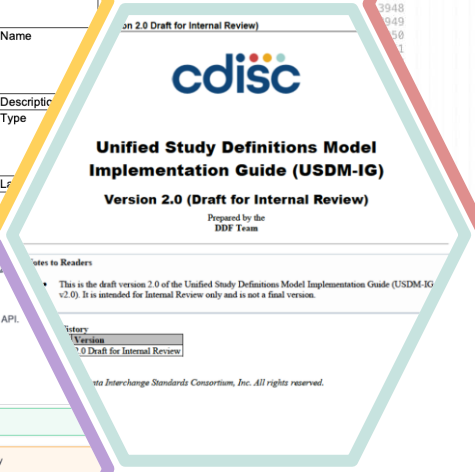
Examples

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

```
tudyArms": [
{
  "id": "StudyArm_1",
  "name": "Placebo",
  "label": "",
  "description": "Placebo",
  "type": {
    "id": "Code_61",
    "code": "C174268",
    "codeSystem": "http://www.cdisc.org",
    "codeSystemVersion": "2022-12-16",
    "decode": "Placebo Comparator Arm"
  },
  "studyArmDataOriginDescription": "Data collec
  "dataOriginType": {
    "id": "Code_62",
    "code": "C188866",
    "codeSystem": "http://www.cdisc.org",
    "codeSystemVersion": "2022-12-16",
    "decode": "Data Generated Within Study"
  }
},
{
  "id": "StudyArm_2",
  "name": "Xanomeline Low Dose",
  "label": "",
  "description": "Active Substance",
  "type": {
    "id": "Code_63",
    "code": "C174267",
    "codeSystem": "http://www.cdisc
    "codeSystemVersion": "2022-12-
```

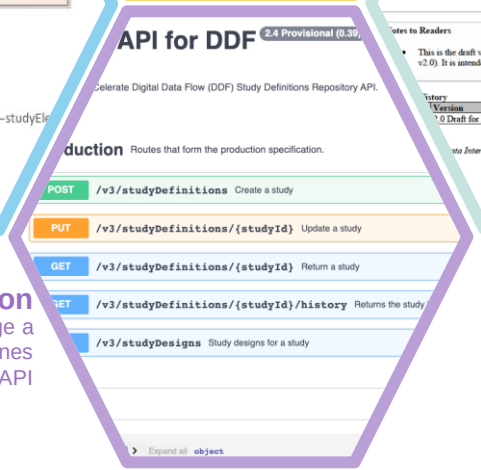
Implementation Guide

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



API Specification

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



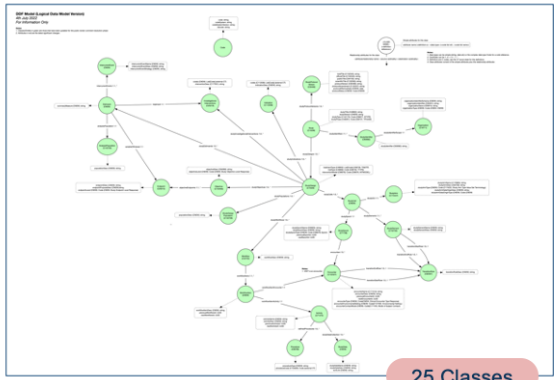
PUBLIC REVIEW

USDM Status

	PHASE ONE *July 2021 – July 2022*	PHASE TWO *Oct 2022 – June 2023*	PHASE THREE *July 2023 – Apr 2024*
Unified Study Definitions Model (USDM)	✓	✓	✓
Application Programming Interface (API) Specification	✓	✓	✓
CDISC Controlled Terminology	✓	✓	✓
Reference Architecture Conformance Tests	✓		*Being replaced by CDISC CORE rules*
Essential Users Stories	✓		
Architecture Principles	✓	*Still applicable*	*Still applicable*
Test Files		✓	✓
Implementation Guide		✓	✓

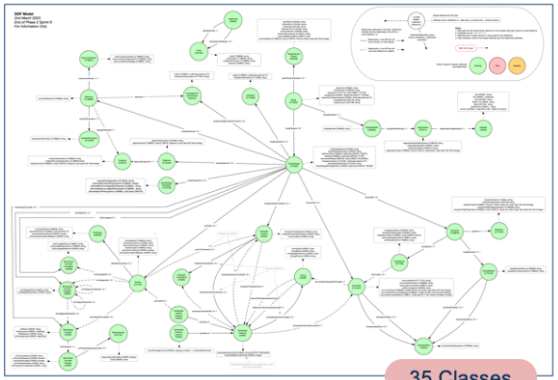
CDISC DDF / USDM: Phases One, Two and Three

Phase One



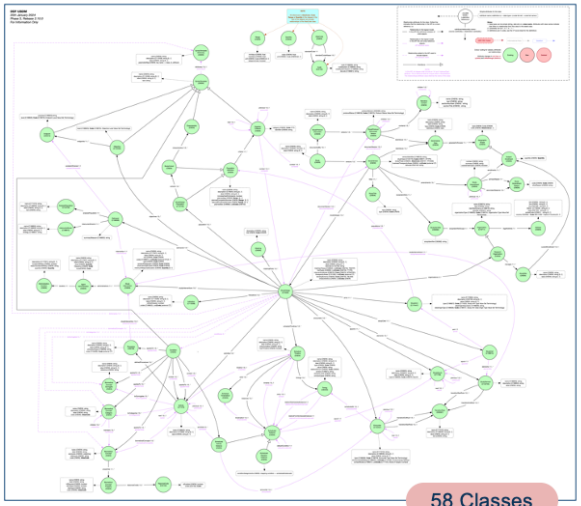
- Solid foundation
- The protocol document was an external entity into which the structured content could be exported

Phase Two



- Focused on the structured elements of the protocol, e.g. the Schedule of Activities (SoA) & Biomedical Concepts (BCs)
- The protocol document still an external entity

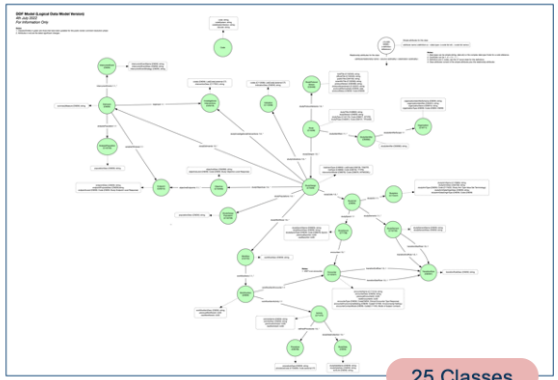
Phase Three



- Now contains structured and unstructured elements
- The entire protocol document can be held within the USDM
- Allows for the protocol document to be generated from the model

CDISC DDF / USDM: Phases One, Two and Three

Phase One



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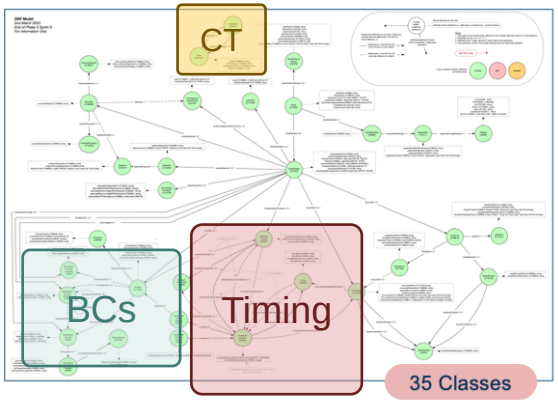

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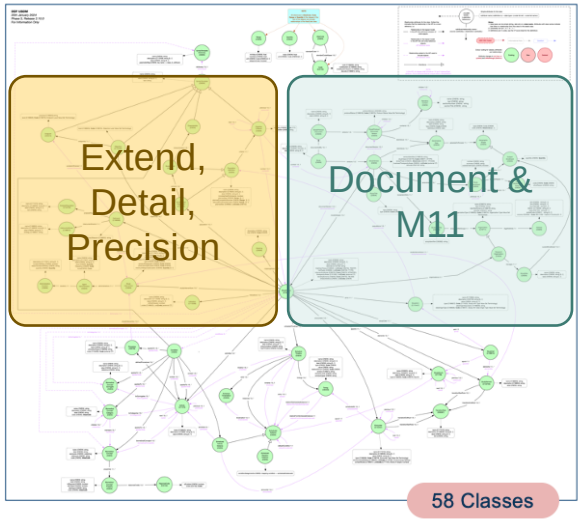

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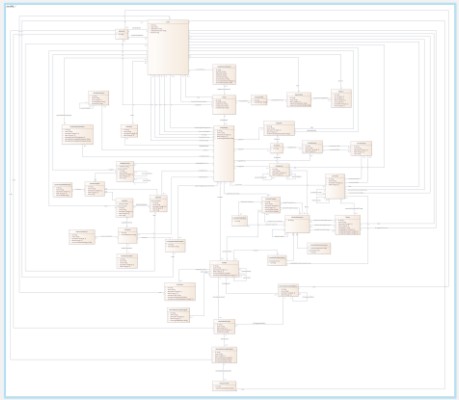
USDM Content



Controlled Terms

Study, Identifiers, Amendments

Estimands

Populations

Inclusion & Exclusion

Interventions & Indications

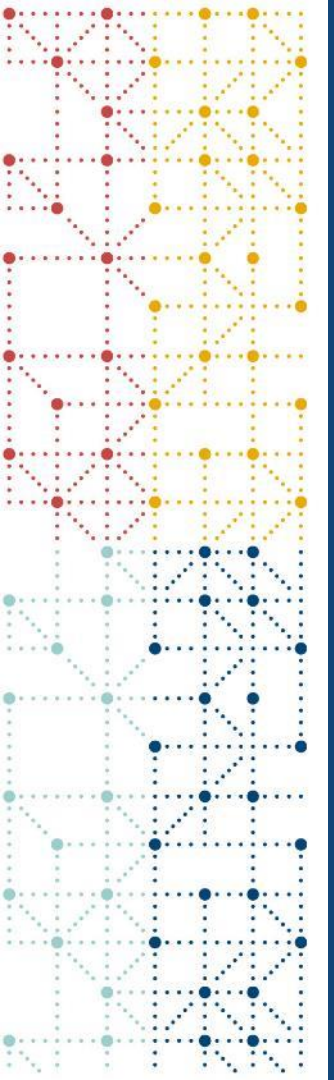
Objectives & Endpoints

Unstructured Content

Study Designs, Arms, Epochs

Detailed Study Logic, Encounters

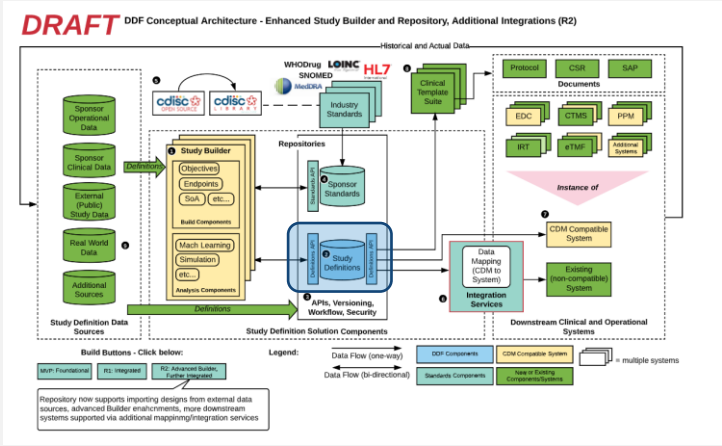
Procedures, Biomedical Concepts



Use Cases and Adoption

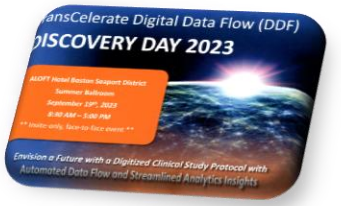
Use Cases

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 downstream 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.*



Any time we read some portion of a protocol … is a use case

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

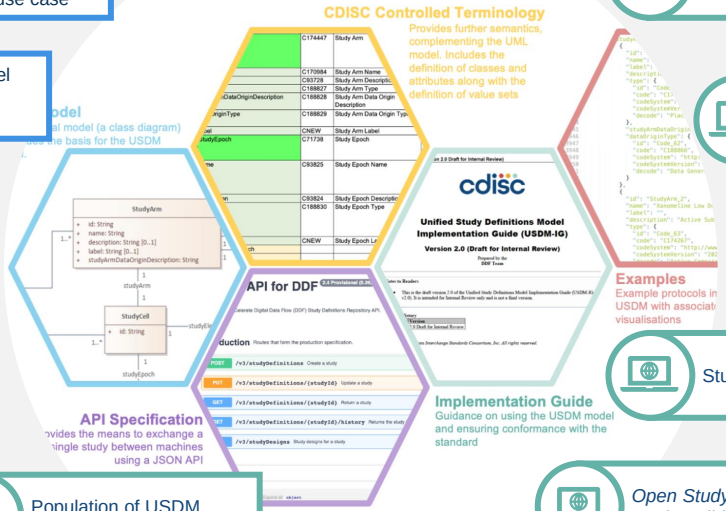
Study Build Application

Study Build & EDC Configuration

Retrospective 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*



Prospective Studies

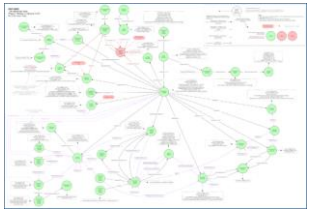
Study Build Application

Population of USDM from old protocols

Open Study Builder
Study Build Application

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

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



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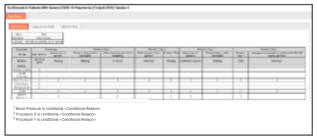
Unified Study Definitions Model (USDM) Reference Architecture

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 · medegene · 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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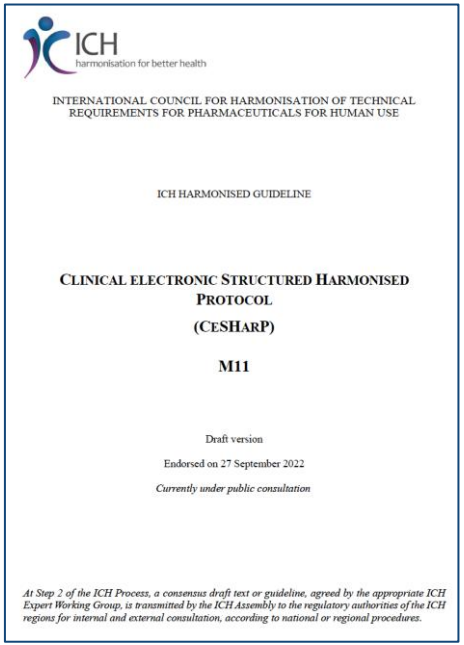
Phase Three: USDM Meets M11

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

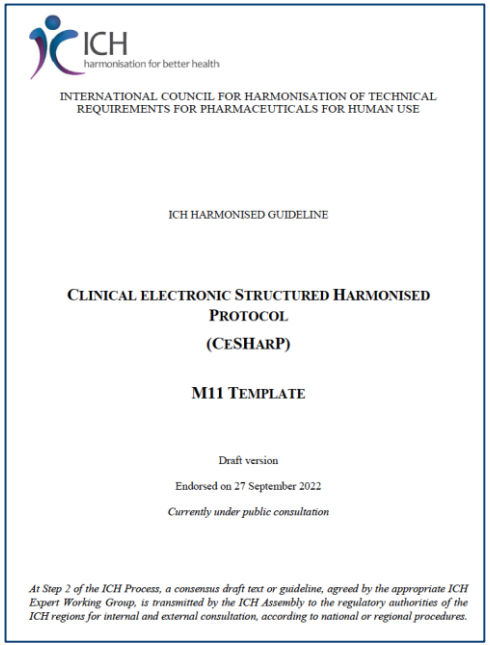
Draft version

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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(CESHARP)

M11 TEMPLATE

Draft version

Endorsed on 27 September 2022

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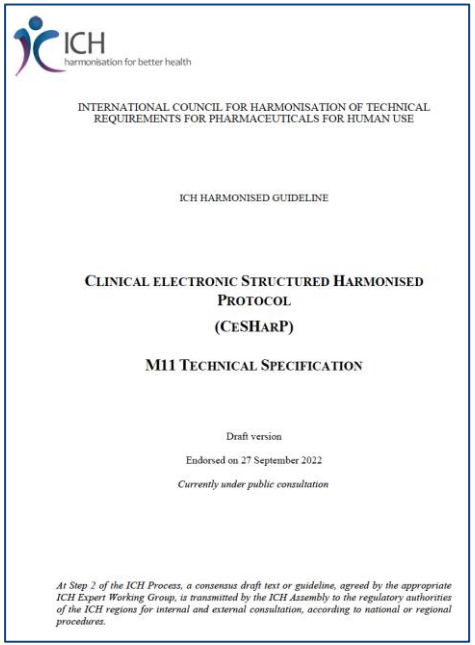
Provides the written format for the 'Interventional Clinical Trial Protocol Template'



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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 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

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Duplicate field in other sections	

CDISC CT

Trial Phase Response (C66737)

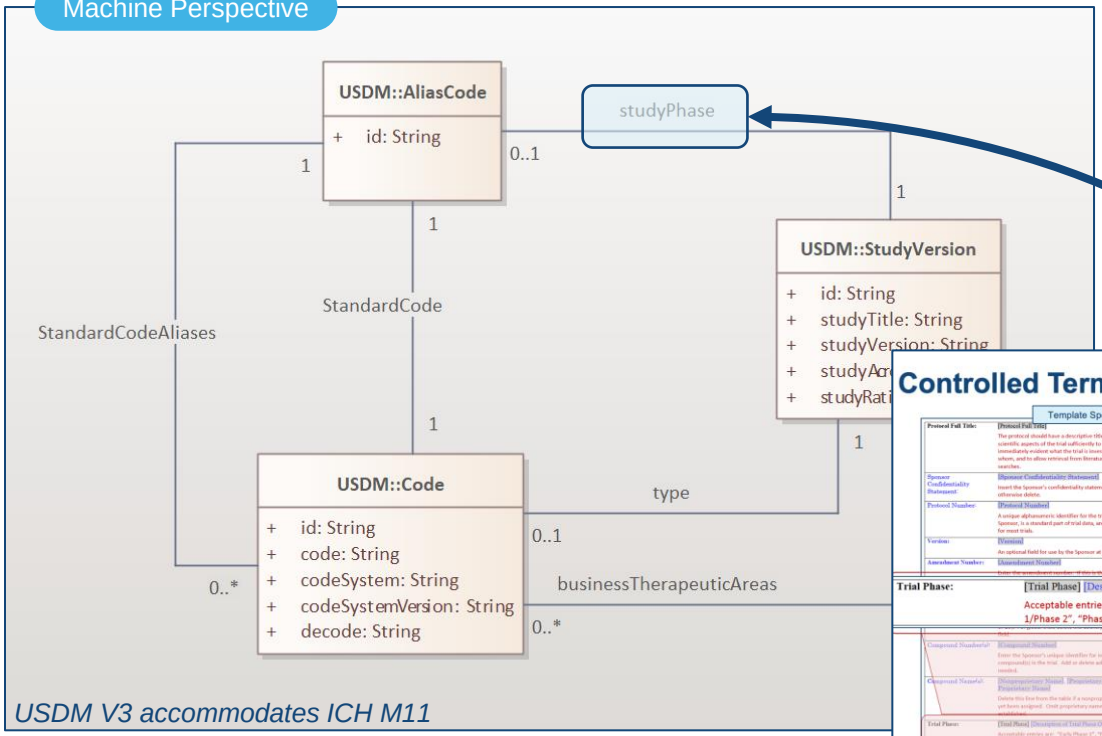
NOT APPLICABLE
PHASE 0 TRIAL
PHASE I TRIAL
PHASE I/II TRIAL
PHASE II TRIAL
PHASE II/III TRIAL
PHASE IIA TRIAL
PHASE IIB TRIAL
PHASE III TRIAL
PHASE IIIA TRIAL
PHASE IIIB TRIAL
PHASE IV TRIAL
PHASE V TRIAL

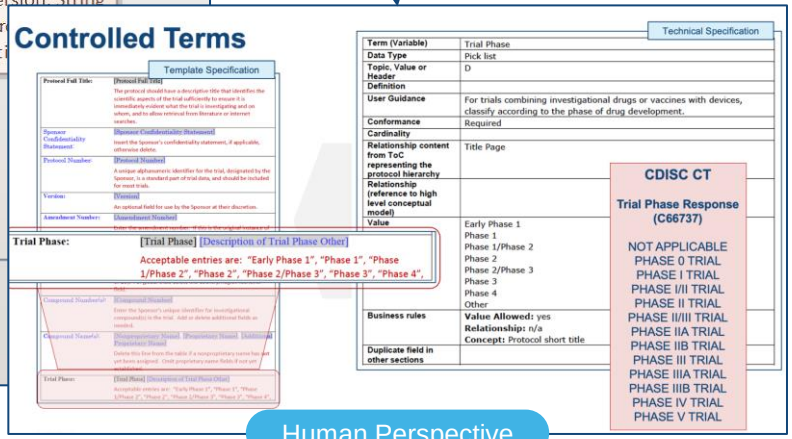
Put Into Context … the USDM

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*

Machine Perspective

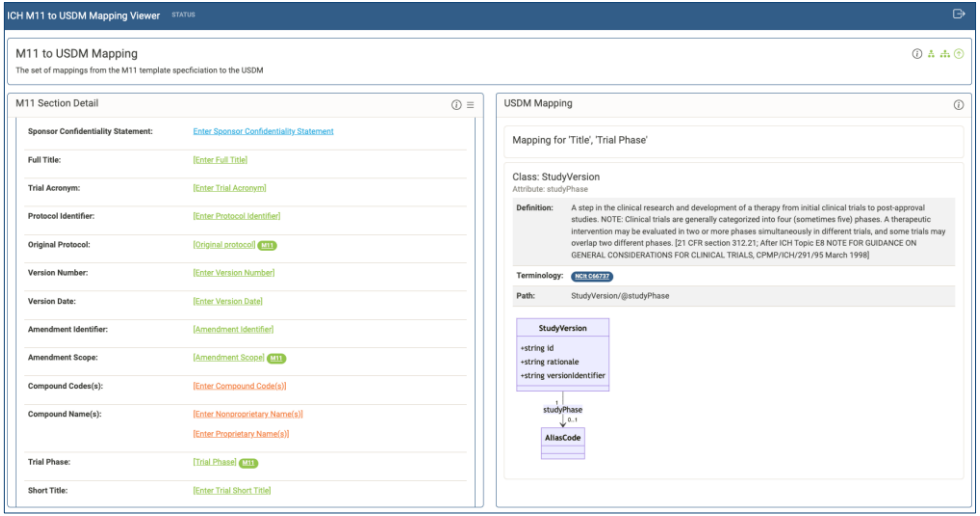


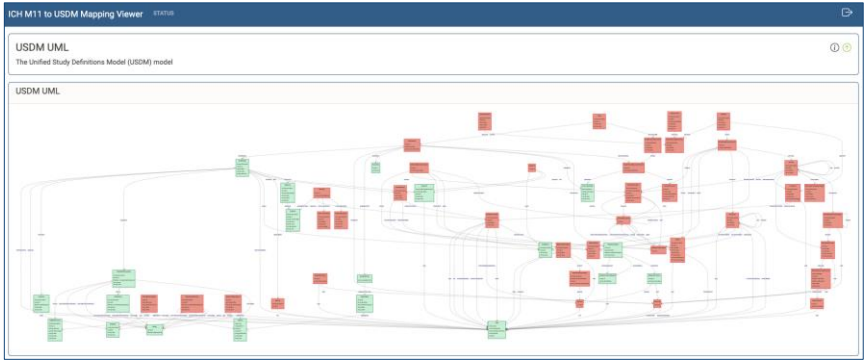


Human Perspective

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





Summary

The Art Of The Possible

Tailored User Experience

Value of an *Electronic* ICH Protocol Template

FDA

Protocol will be data-driven . . .

- **Tailored User Experience**
  - Task or role-based views of the content
  - Personal views– *have the information served up the way you want it*
- **Collaboration**
  - Multi-sponsor development programs
  - Regulator to Regulator Reviews
- **Downstream Automation**
  - Clinical Trial Registries
  - Data Capture
  - Statistical Analysis Plan
  - Clinical Study Report
  - Other Protocols
- **Future**
  - Capability to compare / contrast trial designs across
  - ions

if" scenarios on trial design, arms,
c.

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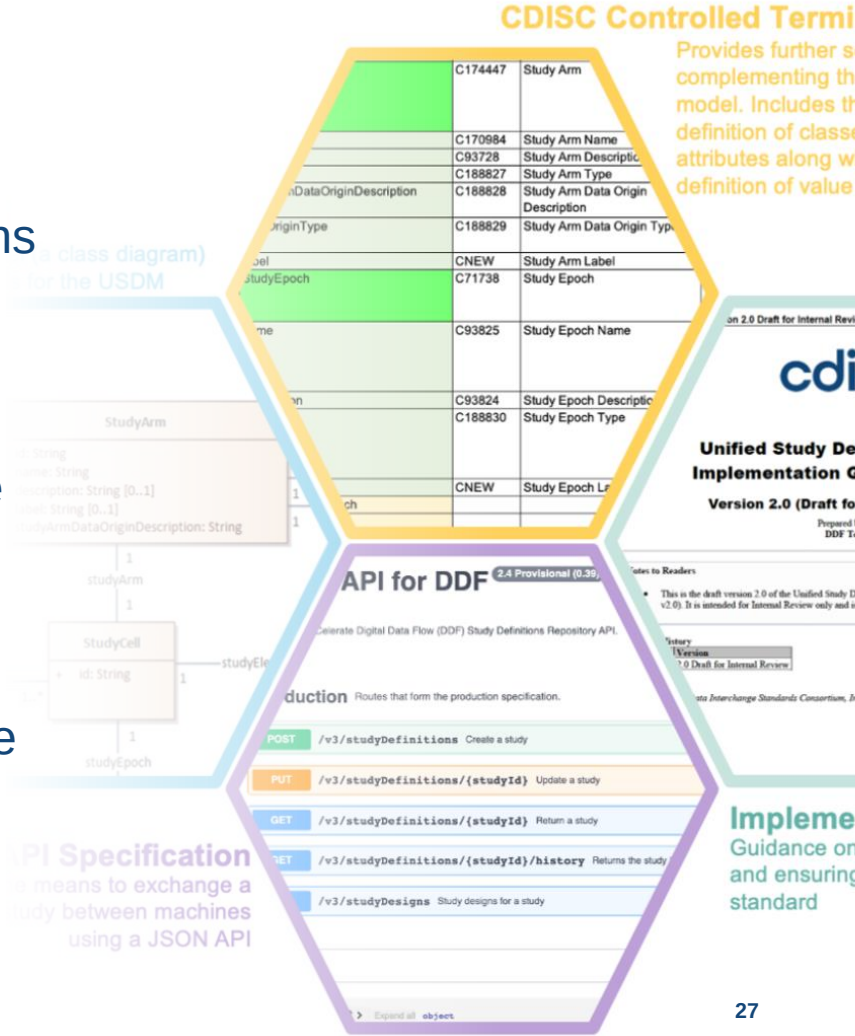
Slide taken from CDISC US Interchange 2023 Presentation

"ICH M11 Clinical Electronic Structured Harmonized Protocol"

Ron Fitzmartin, PhD, MBA
Center for Biologics Evaluation and Research
Food and Drug Administration

Summary

- Digital Data Flow / Unified Study Definitions Model (DDF/USDM) fills an important gap
- USDM is but one building block, but an important one
- USDM accommodation of 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, the art of the possible



Thank You

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Links:

Public Review: https://wiki.cdisc.org/display/PUB/DDF+Phase+3+Public+Review+Dashboard
Github: https://github.com/cdisc-org/DDF-RA

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