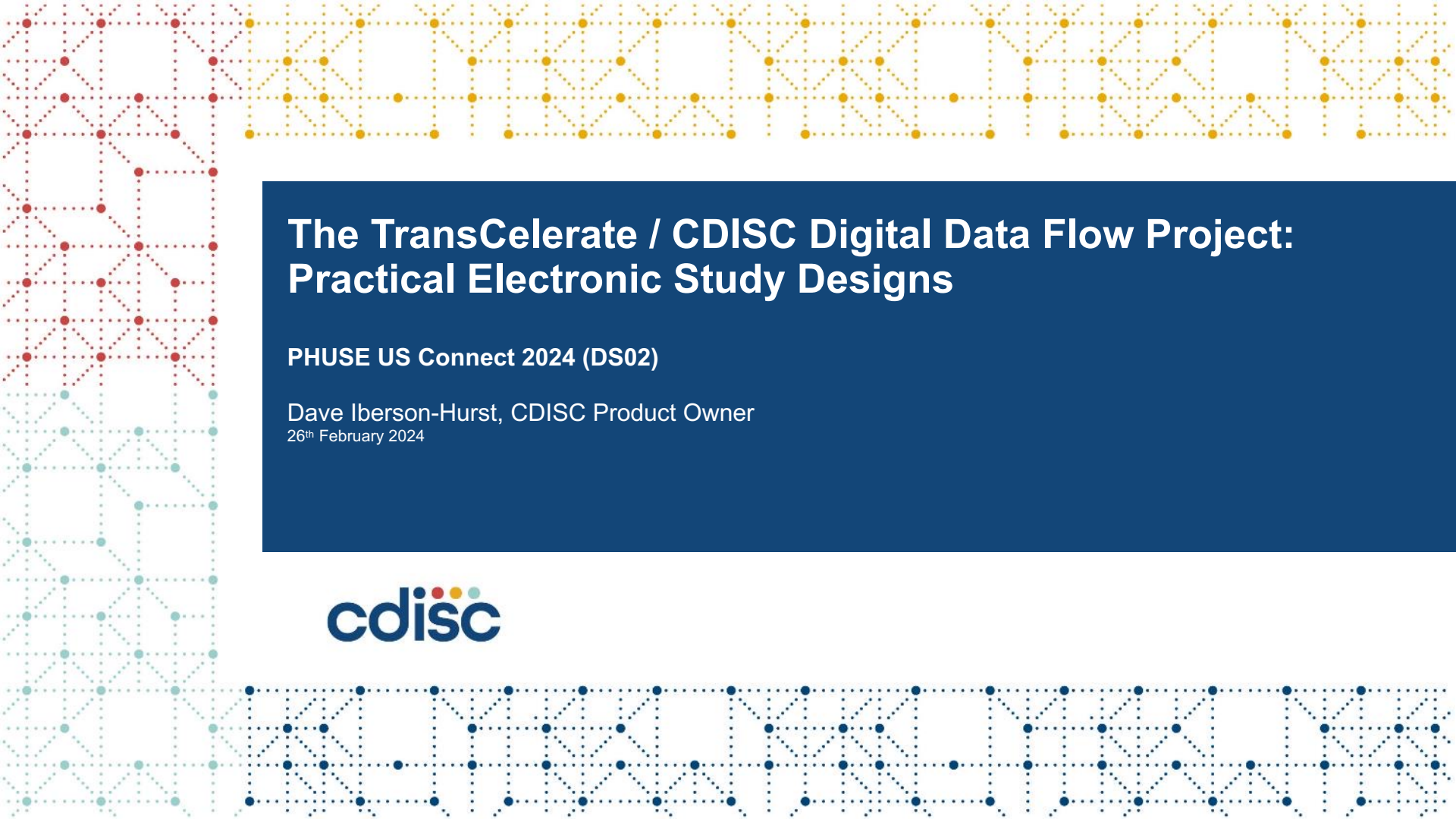




The TransCelerate / CDISC Digital Data Flow Project: Practical Electronic Study Designs

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 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*



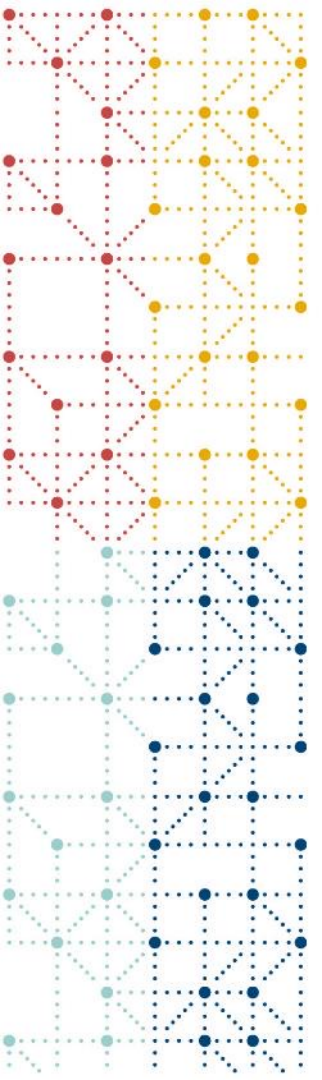
Abstract

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.

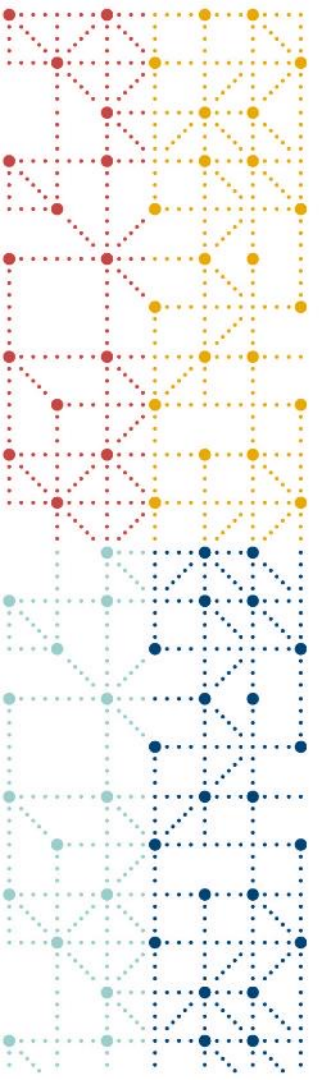
This presentation will detail:

- 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

Enabling the use of technologies that identify and assemble study elements using a common, industry-standard digital language allows industry to move to digital protocols

Advanced Analytics

After enabling the use of advanced analytics, 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)

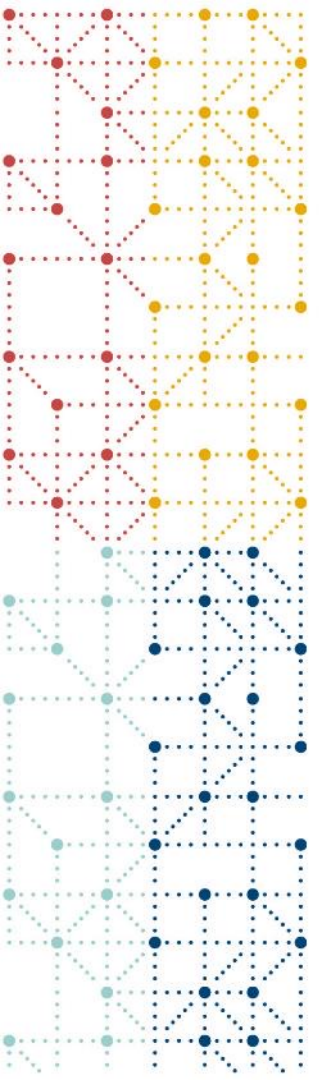
Open & Flexible Solution

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



“Art of the Possible”



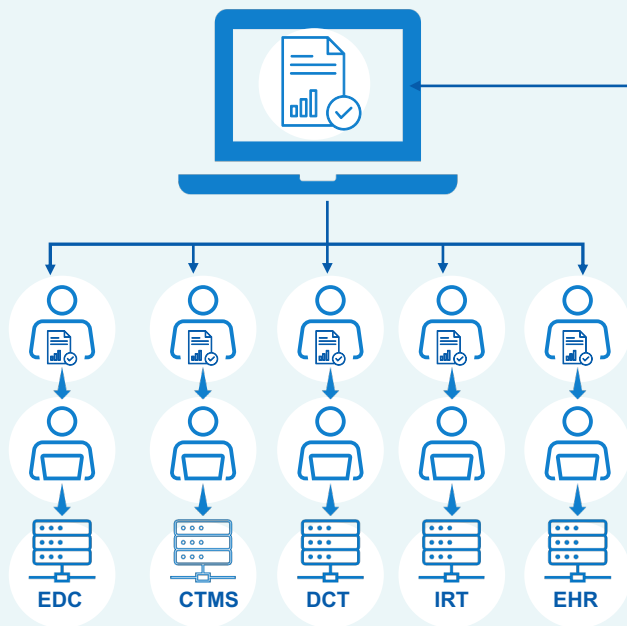


Digital Data Flow - The Project

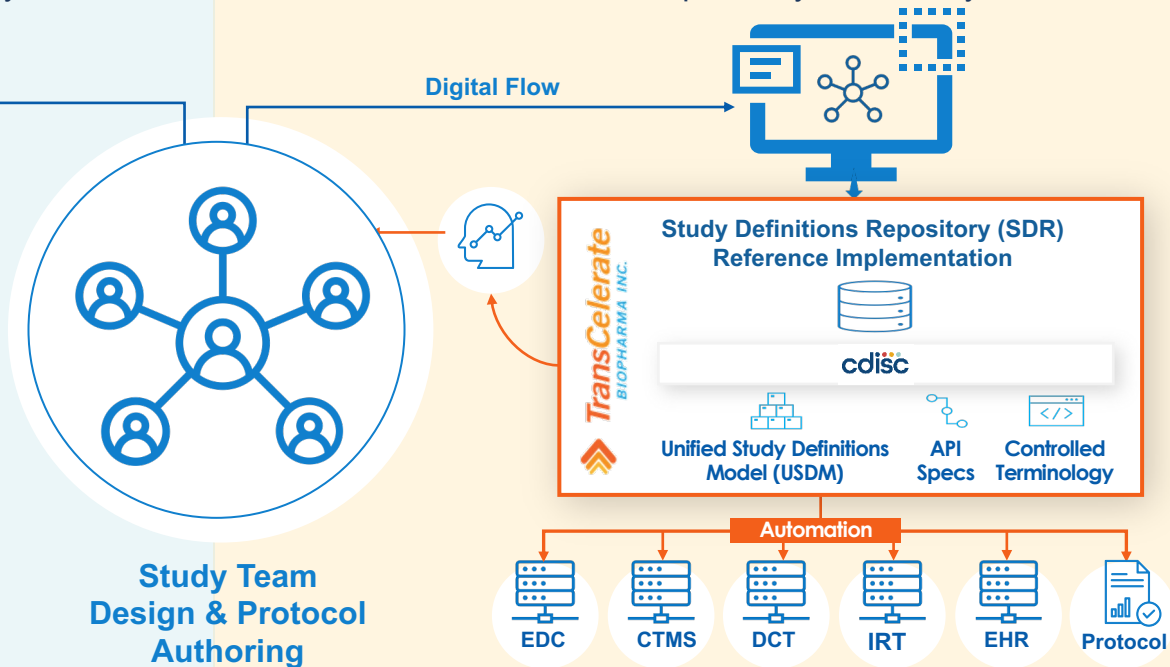
TransCelerate Digital Data Flow (DDF) Ambition

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



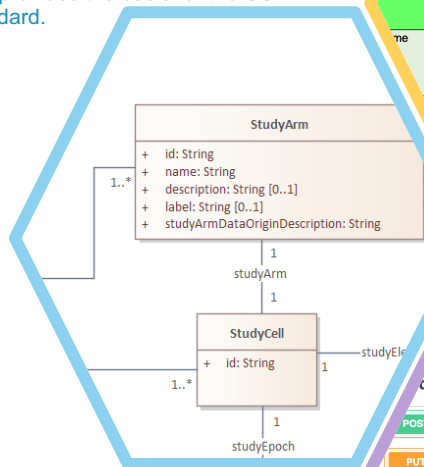
The USDM Standard

CDISC Controlled Terminology

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

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

	C174447	Study Arm
	C170984	Study Arm Name
	C93728	Study Arm Description
	C188827	Study Arm Type
DataOriginDescription	C188828	Study Arm Data Origin Description
OriginType	C188829	Study Arm Data Origin Type
Label	CNEW	Study Arm Label
StudyEpoch	C71738	Study Epoch
Name	C93825	Study Epoch Name
Description	C93824	Study Epoch Description
Type	C188830	Study Epoch Type
Label	CNEW	Study Epoch Label

API for DDF

2.4 Provisional (0.39)
Accelerate Digital Data Flow (DDF) Study Definitions Repository API.

Introduction Routes that form the production specification.

POST	/v3/studyDefinitions	Create a study
PUT	/v3/studyDefinitions/{studyId}	Update a study
GET	/v3/studyDefinitions/{studyId}	Return a study
GET	/v3/studyDefinitions/{studyId}/history	Returns the study history
GET	/v3/studyDesigns	Study designs for a study

> Expand all object

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.

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Implementation Guide

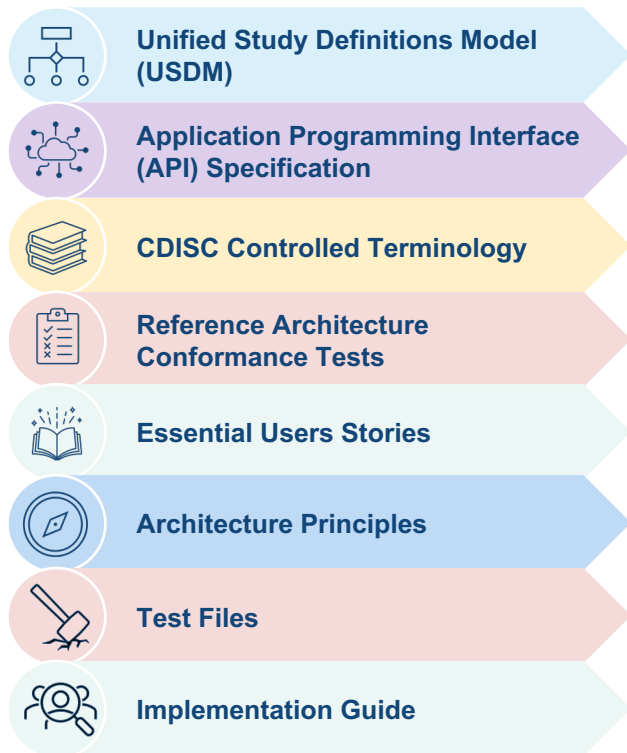
Guidance on using the USDM model and ensuring conformance with the standard

```
studyArms": [
  {
    "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 collected from external source",
    "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.org",
      "codeSystemVersion": "2022-12-16",
      "decode": "Active Comparator"
    }
  }
]
```

Examples

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

USDM Status



PHASE ONE

July 2021 – July 2022



PHASE TWO

Oct 2022 – June 2023



Still applicable



PHASE THREE

July 2023 – Apr 2024



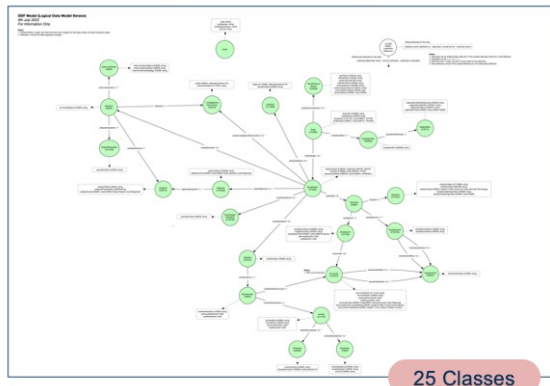
*Being replaced by
CDISC CORE rules*

Still applicable

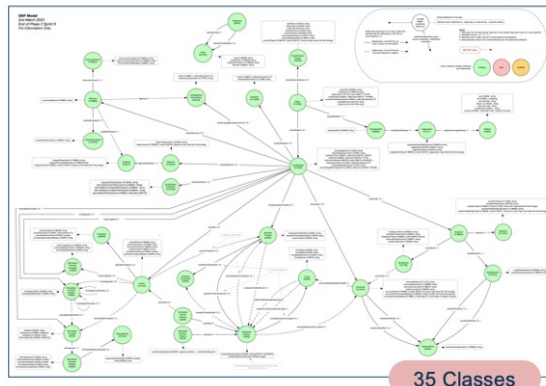


CDISC DDF / USDM: Phases One, Two and Three

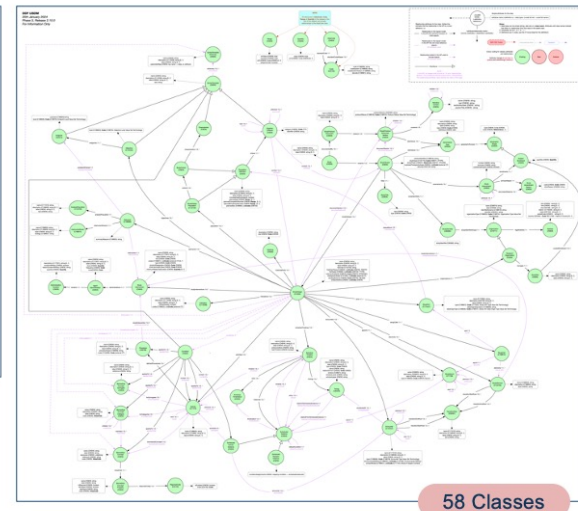
Phase One



Phase Two



Phase Three

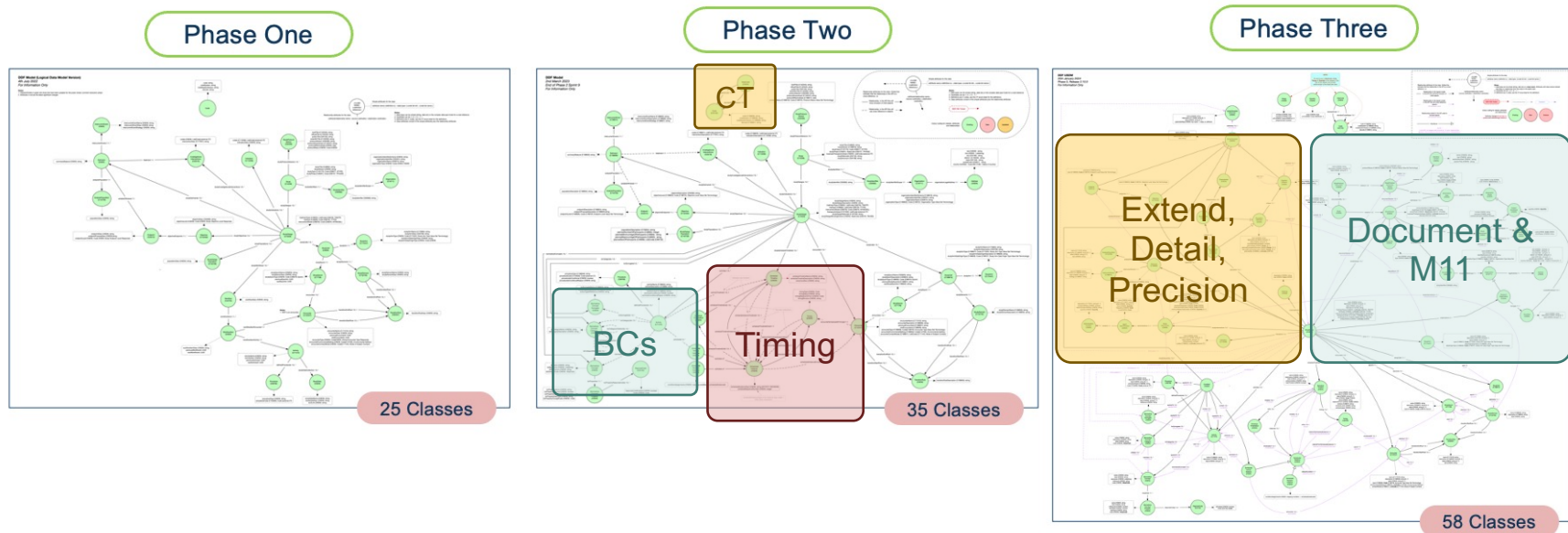


- Solid foundation
- The protocol document was an external entity into which the structured content could be exported

- 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

- 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

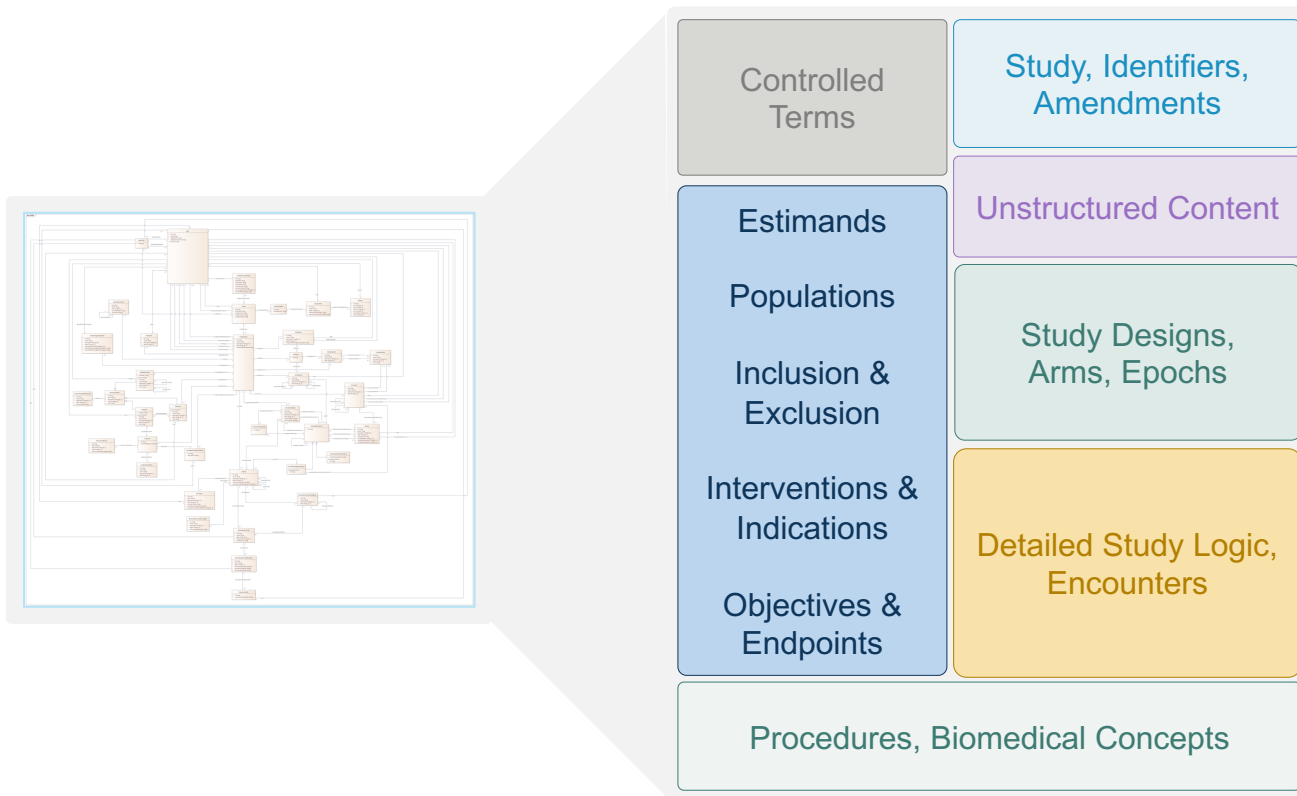


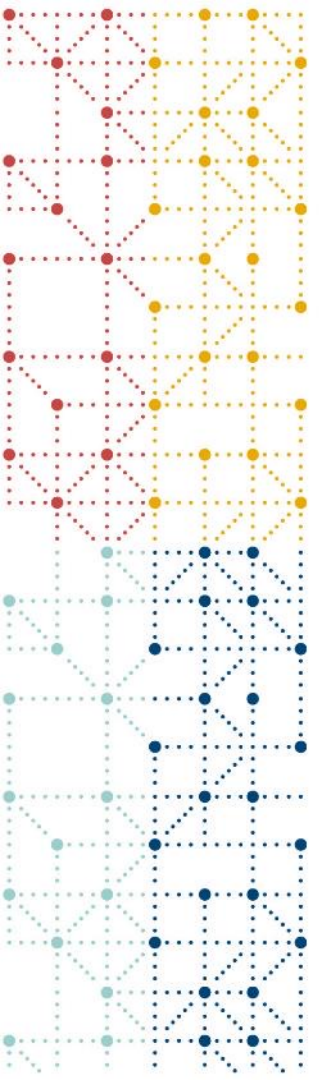
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USDM Content





Use Cases and Adoption

Use Cases

Data Capture

Automate the setup of data capture systems, incl. RWE, and capture the data.

CTMS, TMF ...

The provision of protocol information to downstream systems needing "study" information.

SoA

Use the study design to build the FHIR SoA message.

Query

Having multiple studies that have a common structure allows for data export and query across the set of studies.

Data Import

Import data from a variety of sources. Can be re-exported thus allowing for conversion across versions.

SDTM

Automate the generation of SDTM datasets using the study design and BCs, including the "T" Domains.

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.

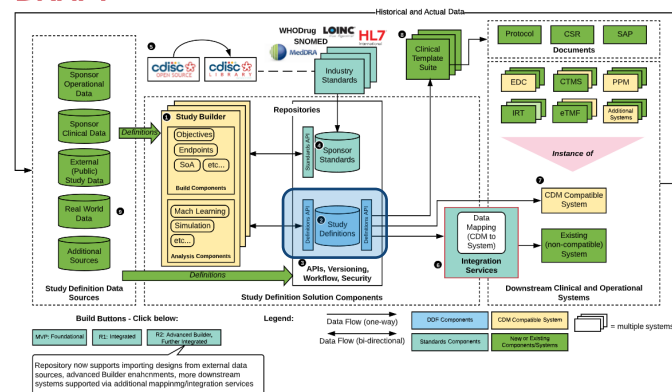
CT Registry

The provision of study information to a CT registry.

FAIR Data

The use of the design to aid Findability, Accessibility, Interoperability, and Reusability.

DRAFT DDF Conceptual Architecture - Enhanced Study Builder and Repository, Additional Integrations (R2)



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

Accelerate Digital Data Flow (DDF)

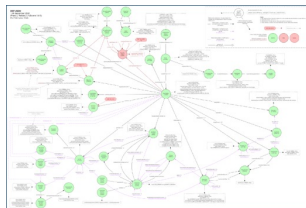
DISCOVERY DAY 2023

ALDOT Hotel Bonaventure Tangent District
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*Envision a Future with a Digitized Clinical Study Protocol with
 Automated Data Flow and Streamlined Analytics Insights*



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



cdisc
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

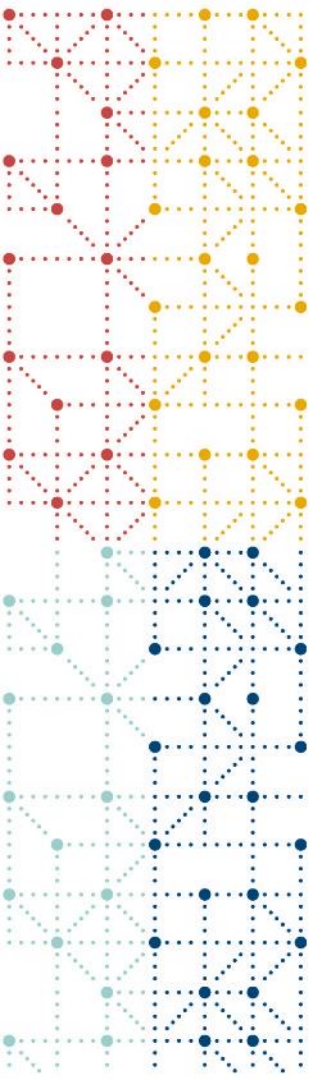
Continued Industry Collaboration
between TransCelerate, CDISC
ICH, and HL7



Growing Solution
Collaboration Forum (SCF)*



**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.*



Phase Three: USDM Meets M11

M11 Is ...

ICH CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL (CeSHaRP)

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



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



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

ICH HARMONISED GUIDELINE

**CLINICAL ELECTRONIC STRUCTURED HARMONISED
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M11 TEMPLATE

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



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

ICH HARMONISED GUIDELINE

**CLINICAL ELECTRONIC STRUCTURED HARMONISED
PROTOCOL
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M11 TECHNICAL SPECIFICATION

Draft version
Endorsed on 27 September 2022
Currently under public consultation

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Provides the technical representation aligned with the guideline and protocol template

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

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",

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.
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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

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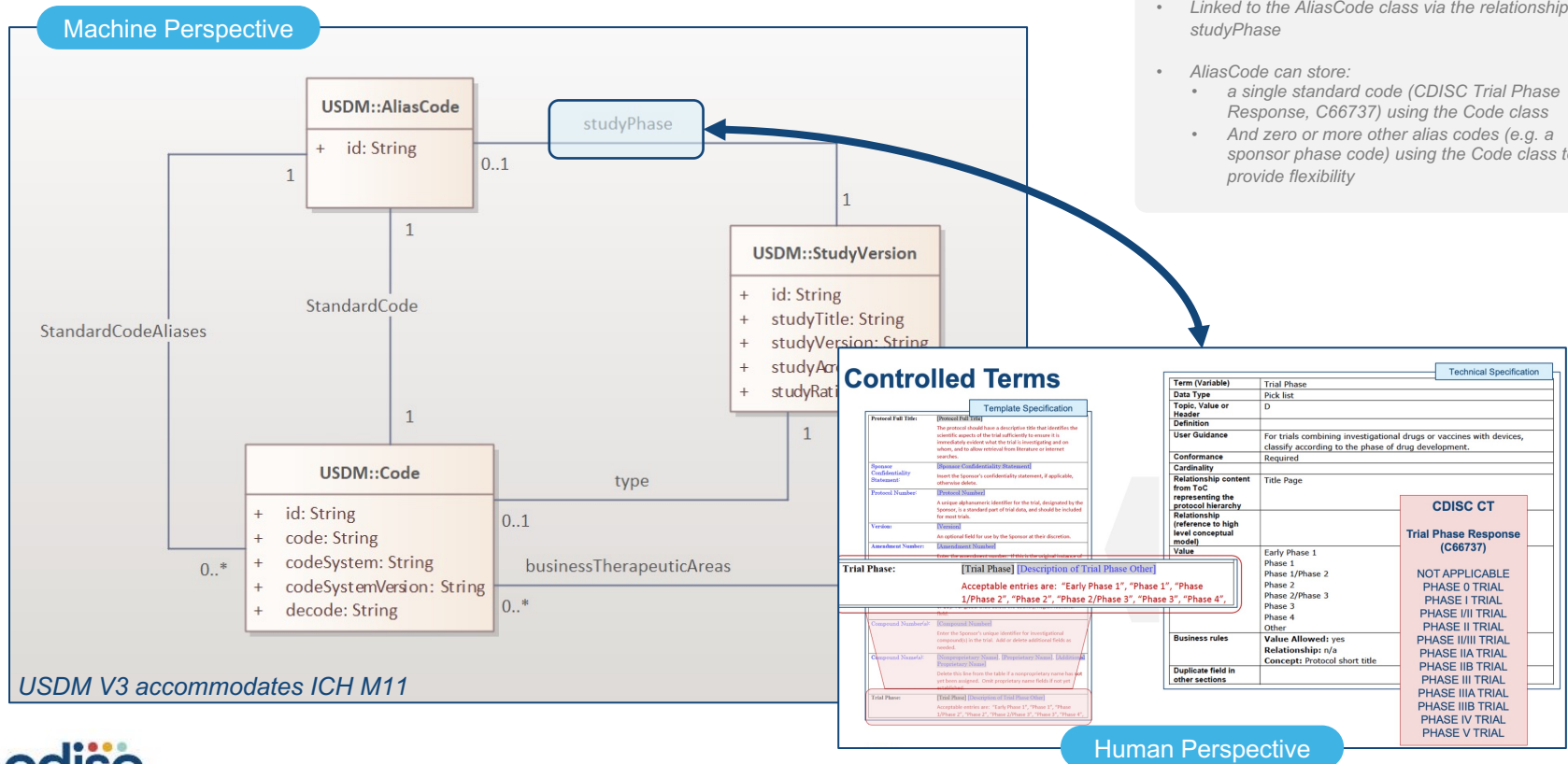
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CDISC CT

Trial Phase Response (C66737)

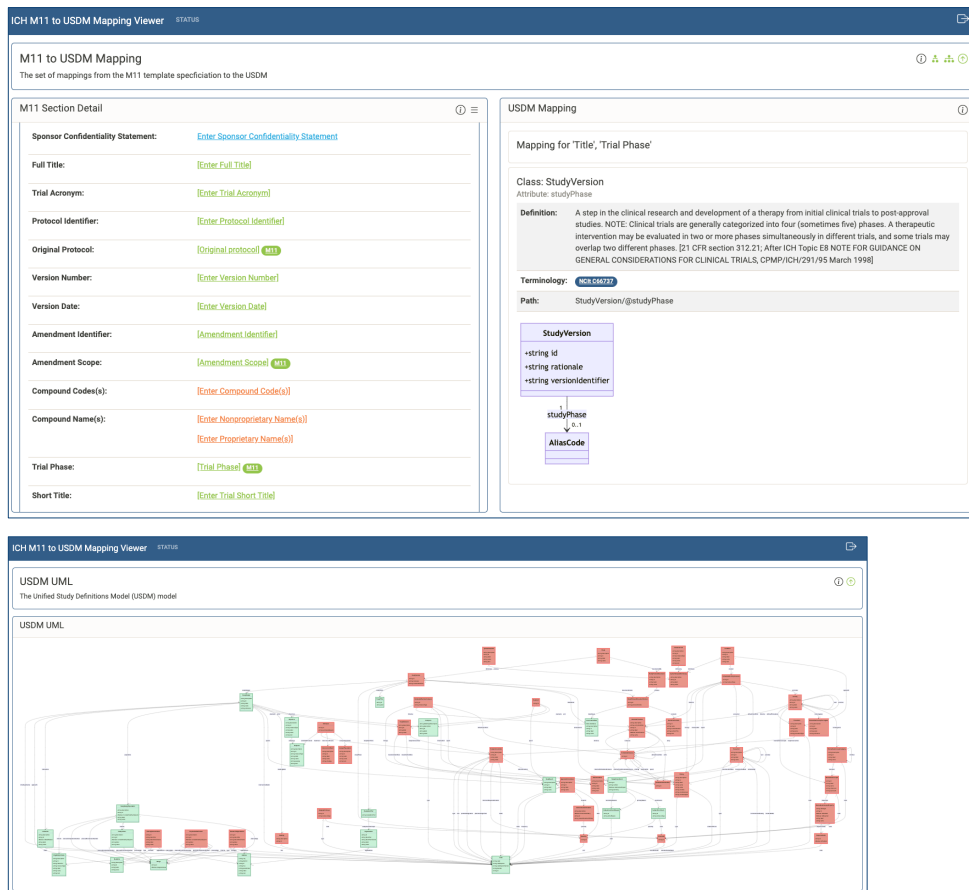
NOT APPLICABLE
 PHASE 0 TRIAL
 PHASE I TRIAL
 PHASE I/II TRIAL
 PHASE II TRIAL
 PHASE II/III TRIAL
 PHASE IIA TRIAL
 PHASE IIB TRIAL
 PHASE III TRIAL
 PHASE IIIA TRIAL
 PHASE IIIB TRIAL
 PHASE IV TRIAL
 PHASE V TRIAL

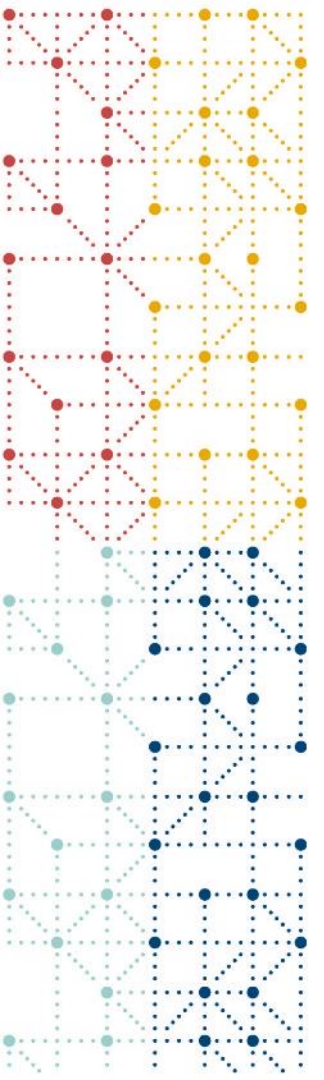
Put Into Context ... the USDM



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

Value of an ICH Protocol Template

- Predictability
 - Format and Structure – Table of Contents
 - Core Content – common set of information
- Allows flexibility – recommended and optional text / sections
- Common instructions
- Serves clinical trial stakeholders and “downstream” content re-use
- Consistent with all other relevant ICH Guidelines, where possible
- Acceptable in all ICH countries



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 sponsor submissions

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

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in 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

Technologies that enable study elements to be captured in a standard, machine-readable format allows industry to capture digital protocols

Advanced Analytics

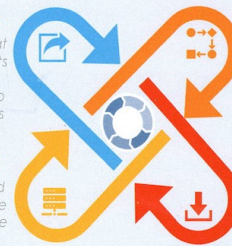
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Open & Flexible Solution

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



Summary

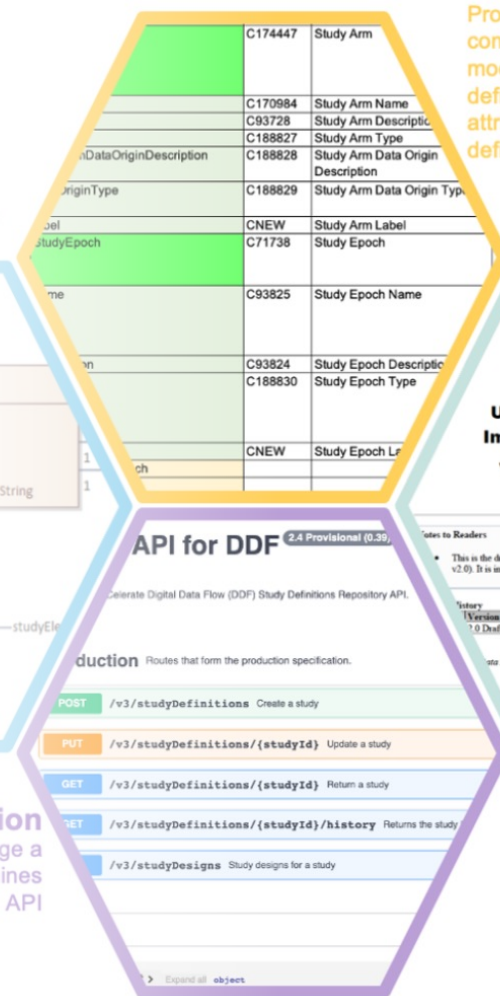
- Digital Data Flow / Unified Study Definitions Model (DDF/USDM) fills an important gap
- USDM is but one building block, but an important one
- USDM accommodation of ICH M11 will be an important step forward
- Can support various use cases, the prospective versus the retrospective
- We are only limited by our imagination, the art of the possible

Provides further s
complementing th
model. Includes th
definition of classe
attributes along w
definition of value

class diagram)
for the USDM



API Specification
the means to exchange a
study between machines
using a JSON API



on 2.0 Draft for Internal Review

cdi

Unified Study Definitions Model Implementation

Version 2.0 (Draft for Internal Review)

Prepared by
DDF Team

Notes to Readers

- This is the draft version 2.0 of the Unified Study Definitions Model (USDM) v2.0. It is intended for Internal Review only and is not for external use.

History

Version 2.0 Draft for Internal Review

Interchange Standards Consortium, Inc.

Implement
Guidance on
and ensuring
standard

Thank You

Contacts:

Dave IH: diberson-hurst.external@cdisc.org

John Owen: jowen@cdisc.org

Links:

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

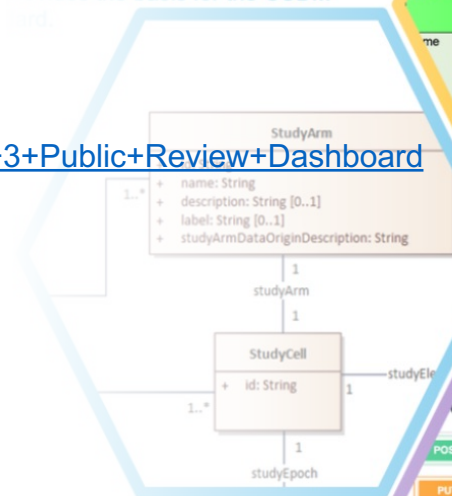
Github: <https://github.com/cdisc-org/DDF-RA>

CDISC Team:

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

Logical Model

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	C188829	Study Arm Data Origin Type
	CNEW	Study Arm Label
	C71738	Study Epoch
	C93825	Study Epoch Name
	C93824	Study Epoch Description
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API for DDF 2.4 Provisional (0.39)

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	/v3/studyDesigns	Study designs for a study

API Specification

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