



2024 CDISC + TMF
US INTERCHANGE

PHOENIX/SCOTTSDALE

23-24 OCTOBER: CONFERENCE & EXPO | 21, 22, 25 OCTOBER: TRAININGS

ICH M11, TransCelerate, CDISC & HL7 Vulcan: Driving the Adoption of Digital Protocol

Presented by Peter Van Reusel, Chief Standards Officer, CDISC

Meet the Speaker

Peter Van Reusel

Title: Chief Standards Officer

Organization: CDISC



Peter Van Reusel provides executive leadership to the development and implementation of clinical standards in line with CDISC's strategy and operational plans, working closely with the President and CEO, as well as CDISC staff and stakeholders. He has over 20 years' experience in senior roles in pharma and at CROs, providing standards expertise and carrying out other standards work in various organizational settings. A long-time, CDISC-authorized instructor, Peter has helped significantly in developing CDISC training courses.

He previously served as CDISC's European Liaison, fostering relationships with key European regulatory, academic, and biopharma stakeholders. Peter is also an active PHUSE collaborator.



Agenda

1. Introduction to the Digital Data Flow Project and USDM
2. Overview of M11 and the CDISC/ICH Partnership
3. USDM, M11, and the HL7 UDP – how do they come together?



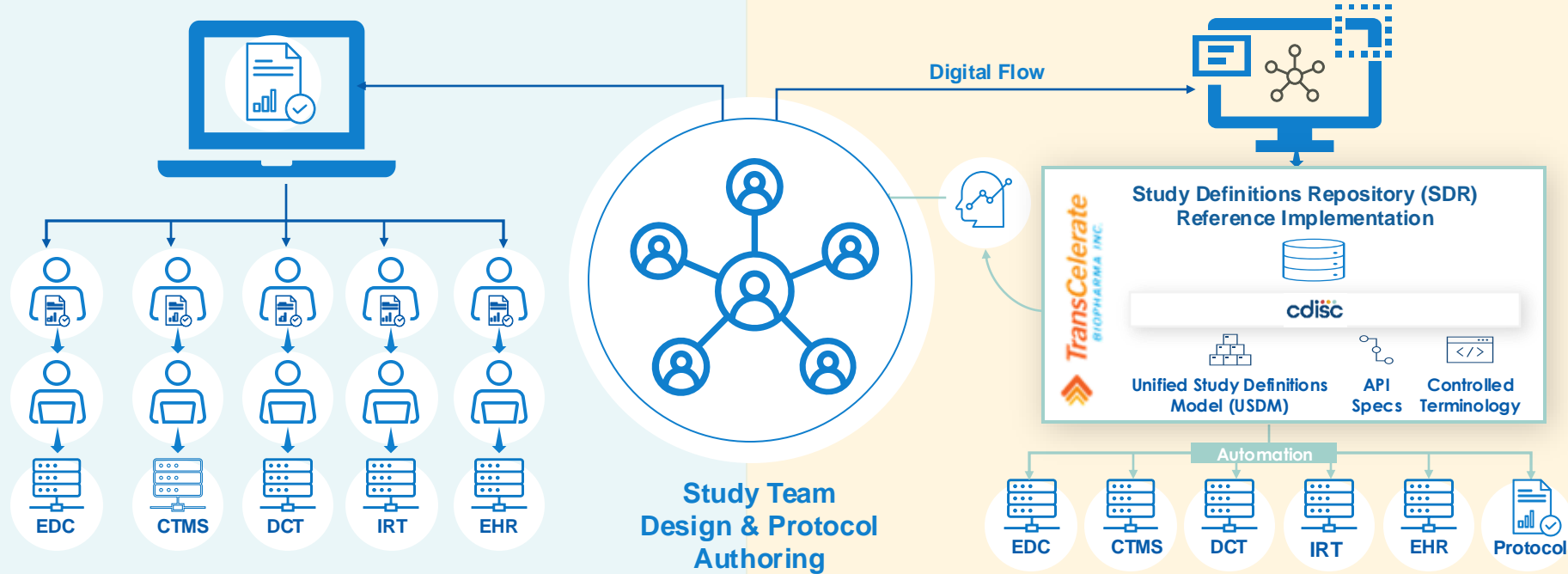
Introduction to the Digital Data Flow Project (DDF) and the Unified Study Definition Model (USDM)

TransCelerate Digital Data Flow (DDF) Ambition

Write Once, Read Many

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

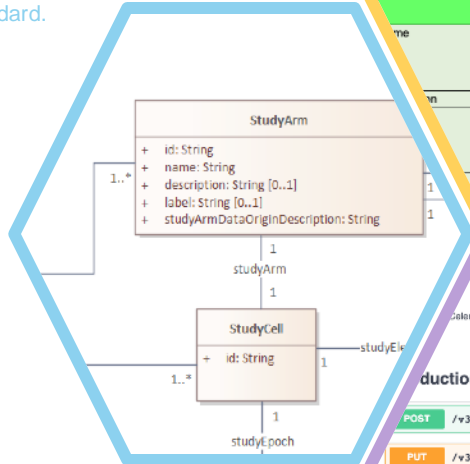
TOMORROW: Digital paradigm for protocol creation, with fully automated data flow and interoperability between systems



The USDM Standard

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
C168827	Study Arm Type
C188826	Study Arm Data Origin Description
C188829	Study Arm Data Origin Type
CNEW	Study Arm Label
C71738	Study Epoch
C93825	Study Epoch Name
C93824	Study Epoch Description
C188830	Study Epoch Type
CNEW	Study Epoch Label

CDISC Controlled Terminology

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

CDISC
Unified Study Definitions Model Implementation Guide (USDM-IG)
Version 2.0 (Draft for Internal Review)
 Prepared by the DDF Team

API for DDF

2.4 Provisional (0.32)

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

```

"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"
    }
  }
]

```

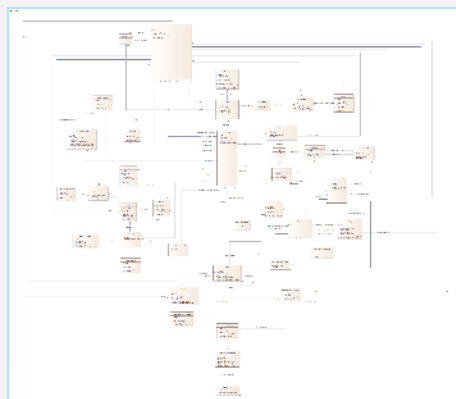
Examples

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

Implementation Guide

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

USDM Content



Controlled
Terms

Study, Identifiers,
Amendments

Estimands

Unstructured Content

Populations

Inclusion &
Exclusion

Study Designs,
Arms, Epochs

Interventions &
Indications

Objectives &
Endpoints

Detailed Study Logic,
Encounters

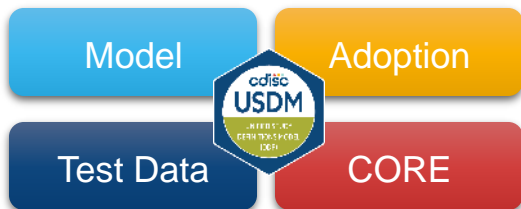
Procedures, Biomedical Concepts

DDF Evolution: Phases One to Four

		PHASE ONE July 2021 – July 2022	PHASE TWO Oct 2022 – Sep 2023	PHASE THREE July 2023– May 2024	PHASE FOUR Apr 2024– 1Q 2025
CDISC's USDM Reference Architecture	USDM Data Model	✓	✓	✓	□
	API Specification	✓	✓	✓	□
	CDISC Controlled Terminology	✓	✓	✓	□
	Implementation Guide		✓	✓	□
	Test Files		✓	✓	□
	Conformance CORE Rules – POC			✓	TBD
TransCelerate's SDR & Implementation Support	Study Definitions Repository (SDR)	✓	✓	✓	□
	Common Protocol Template (CPT) Interface Tool – POC		✓		
	Implementation Architecture Scenarios Toolkit		✓	◆	◆
	Persona Toolkits (MW, DM, IT)		✓	◆	◆
	Cloud Agnostic SDR – POC			✓	

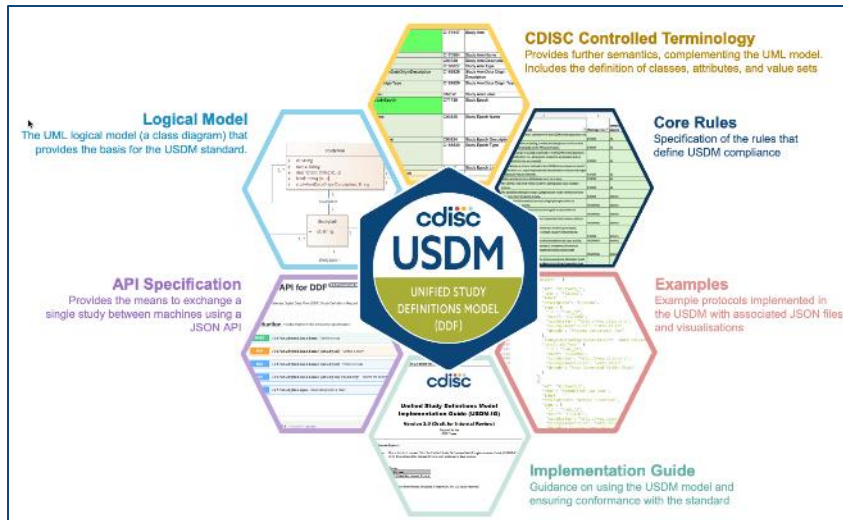
Phase 4 Overview

- More focus on refinement rather than new content
- Need to pay attention to backward compatibility
- Maximum alignment with ICH M11
- Conformance Rules now part of the standard



Phase Four Focus

- 1 **USDM Enhancements** Further IDMP Alignment, M11 amendments and versions, complex studies designs such as multiphase seamless designs, additional trial registration mappings, and statistical / estimands enhancements
- 2 Continued alignment of USDM with ICH M11
- 3 Participation in the Utilizing the Digital Protocol (UDP) project with TransCelerate, ICH and HL7 Vulcan
- 4 Continue development of USDM Conformance Rules to support USDM v3.0 and v4.0
- 5 Continue support and development of test data and test tools
- 6 Development of training and, education materials in conjunction with TransCelerate's Change and Engagement team to foster adoption of DDF



DDF Reference Architecture & Github

- The source of DDF Reference Architecture deliverables

- Unified Study Definitions Model (USDM) Class Diagram**
The UML class diagram (normative) as well as SDI, 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**
Explanation of the model and its use, exemplar etc
- Conformance Rules**
Specification of the CDISC CORE rules required for USDM conformance

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

cdisc-org / DDF-RA

Code Issues 49 Pull requests Zenhub Discussions Actions Projects Wiki Security Insights

DDF-RA Public
generated from [cdisc-org/COSMAckathonTemplate](#)

main 4 Branches 34 Tags

github-actions Generate Diff and Data Dict 6 months ago 631 Commits

Deliverables Generate Diff and Data Dict 2 weeks ago

Documents Update informative diagram for criteria tweak 3 weeks ago

HowTos Initial commit 2 years ago

images Initial commit 2 years ago

.gitignore Updated Objective and Endpoint class 10 months ago

CODE_OF_CONDUCT.md Updated the enforcement contact 2 years ago

CONTRIBUTING.md Initial commit 2 years ago

LICENSE

README.md

README Code of co

DDF-RA

About

This is the repository for all code and documentation for the DDF-RA project.

- Readme
- MIT license
- Code of conduct
- Activity
- Custom properties
- 16 stars
- 11 watching
- 1 fork
- Report repository

Releases 34

cdisc-org / DDF-RA

Code Issues 44 Pull requests Discussions Actions Projects Wiki Security Insights

Files

main + Q

Go to file

.github

Deliverables

- API
- CT
- IG
- RULES
- UML
- Documents
- HowTos
- images

DDF-RA / Deliverables /

Dave Ibersen-Hurst Pushed to wrong branch, reverting

Name	Last commit message
..	
API	API updates
CT	Update USDM_CT.xlsx
IG	Added USDMIG post copy editing
RULES	Set of USDM v3.0 rules
UML	Pushed to wrong branch, reverting

Example Resources – CDISC

Digital Data Flow <https://www.cdisc.org/ddf>



Overview | What is the USDM | Participate | Webinar | Versions | FAQ | Contact Us



Welcome to Digital Data Flow (DDF) for Clinical Trials Protocols

Digital Data Flow Initiative will help modernize clinical trials by enabling a digital workflow with protocol digitization. This initiative establishes a foundation for a future state of automated & dynamic readiness that can transform the drug development process.

Below are a list of the different websites sourcing specific content and resources. Depending on where you are in the journey, please feel free to explore the different websites and their information.

 CDISC DDF Website <i>You are here!</i> Learn about the Unified Study Definitions Model (USDM) Reference Architecture supporting Protocol Standards Target Audience: Those interested in data standards	 DDF Website As the main website for DDF, learn and access all resources supporting DDF Target Audience: All those interested in implementing DDF Solutions	 DDF GitHub Learn about and access the Study Definitions Repository Reference implementation Target Audience: Those interested in SDR development	 Transcelerate DDF Initiative Solutions Learn about DDF background and initiative roadmap Target Audience: All those generally interested
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CDISC Github housing the USDM deliverables (model, CT, API etc) along with examples of protocols placed into USDM.

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



Open-source python package that implements USDM V3. Can be used by anyone to build test data

<https://pypi.org/project/usdm/>



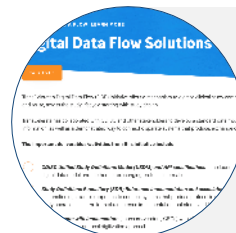
Web-based version of the USDM test tooling.

<https://usdm-service.fly.dev/>

Example Resources – TransCelerate



<https://www.transceleratebiopharmainc.com/initiatives/digital-data-flow/>



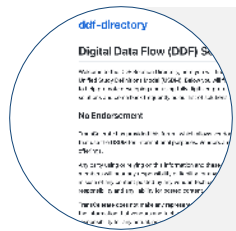
TransCelerate web page holding a significant number of DDF and USDM resources including the persona guides

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



Github housing the source for the Study Definition Repository (SDR) Reference Implementation of the USDM

<https://github.com/transcelerate/ddf-sdr-platform>



DDF solutions directory. A growing list of self-reported solutions which utilize and follow the DDF Unified Study Definitions Model (USDM)

<https://transcelerate.github.io/ddf-directory/directory/directory.html>

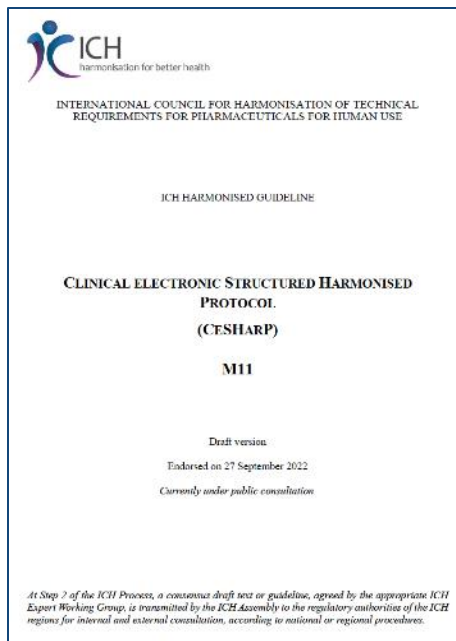


Overview of M11 and the ICH/CDISC Partnership

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

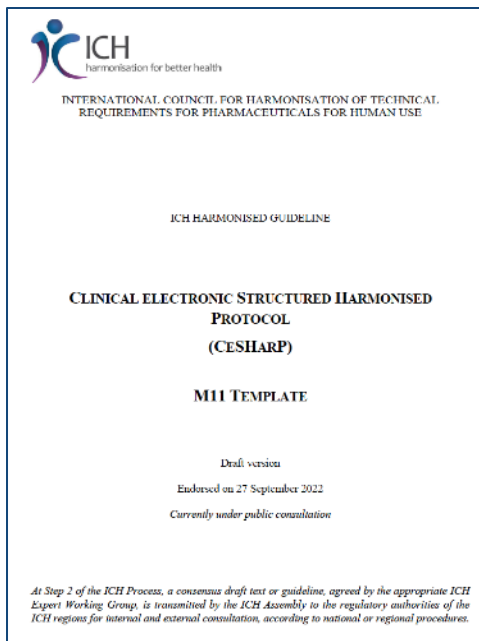
CLINICAL ELECTRONIC STRUCTURED HARMONISED
PROTOCOL
(CESHARP)

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



ICH
harmonisation for better health

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

ICH HARMONISED GUIDELINE

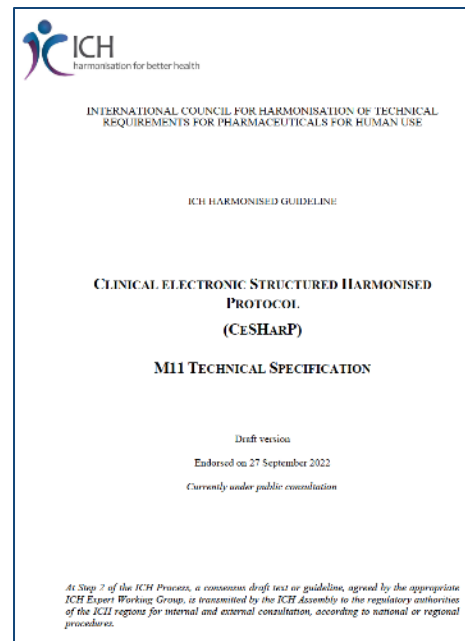
CLINICAL ELECTRONIC STRUCTURED HARMONISED
PROTOCOL
(CESHARP)

M11 TEMPLATE

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 the written format for the
Interventional Clinical Trial Protocol
Template



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 TECHNICAL SPECIFICATION

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 the technical representation
aligned with the guideline and protocol
template

M11 Controlled Terms

Technical Specification

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

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	

CDISC CT

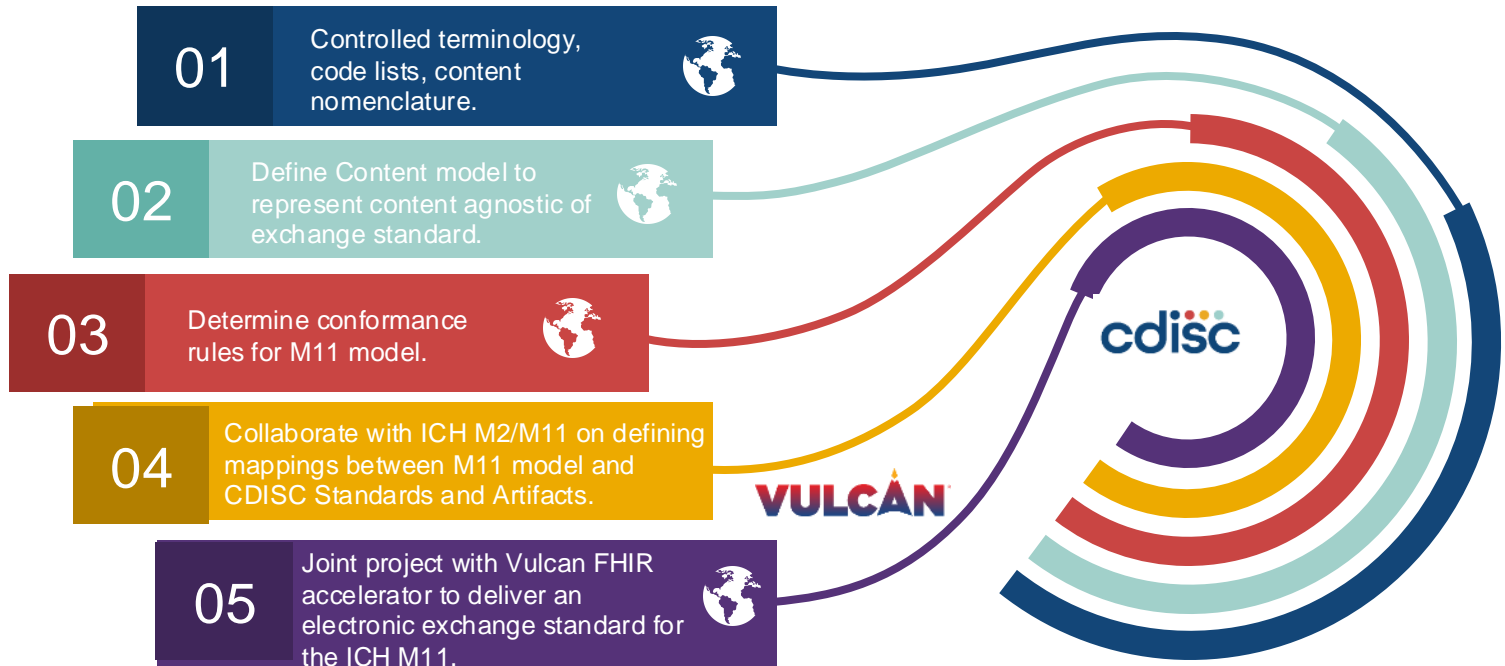
Trial Phase Response (C66737)

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

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.
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",

CDISC M2/M11 Engagement



ICH and CDISC MOU (Memorandum of Understanding)

As a collaboration between ICH and CDISC, the goals of the agreement are to:

- Use a unified governance process and terminology services for the long-term support of ICH controlled terminologies
- Curate and maintain ICH controlled terminologies
- Follow a robust process for the public review and publication of ICH terminologies
- Ensure the terminologies are freely available to the public following public review

Scope

For ICH members to adopt and implement a clinical information standard it is critical that all terminology components, including but not limited to definitions described in the technical specification, are part of a greater international controlled terminology resource managed by an internationally recognized standards development organization (SDO). CDISC has been identified by ICH as a reputable SDO with the qualifications and capabilities to support the maintenance and facilitation of the governance process for ICH controlled terminology.

This Memorandum of Understanding (MOU) sets forth the roles and responsibilities of each party as they relate to the governance of the ICH terms and definitions developed in collaboration with CDISC. This MOU is intended to describe the goals, the high-level governance process, and how each party will collaborate. Specific projects (e.g., M11 controlled terminology) will be defined in detail as part of an annex to this MOU mutually agreed upon by CDISC and ICH.

Goals

As a collaboration between ICH and CDISC, the goals of the agreement are to:

1. Use a unified governance process and terminology services for the long-term support of ICH controlled terminologies.
2. Curate and maintain ICH controlled terminologies.
3. Follow a robust process for the public review and publication of ICH terminologies
4. Ensure the terminologies are freely available to the public following public review.



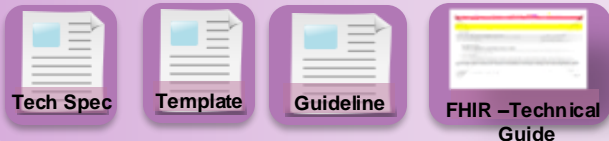


USDM, M11, and the HL7 UDP – how do they come together?

ICH M11 and Vulcan Utilizing Digital Protocol (UDP)



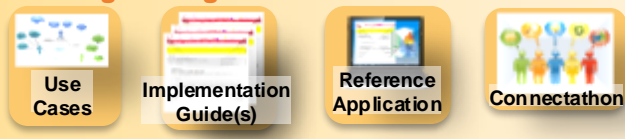
CeSHarP



USDM and Terminology



Utilizing the Digital Protocol – UDP



Inputs:

ICH M11 template

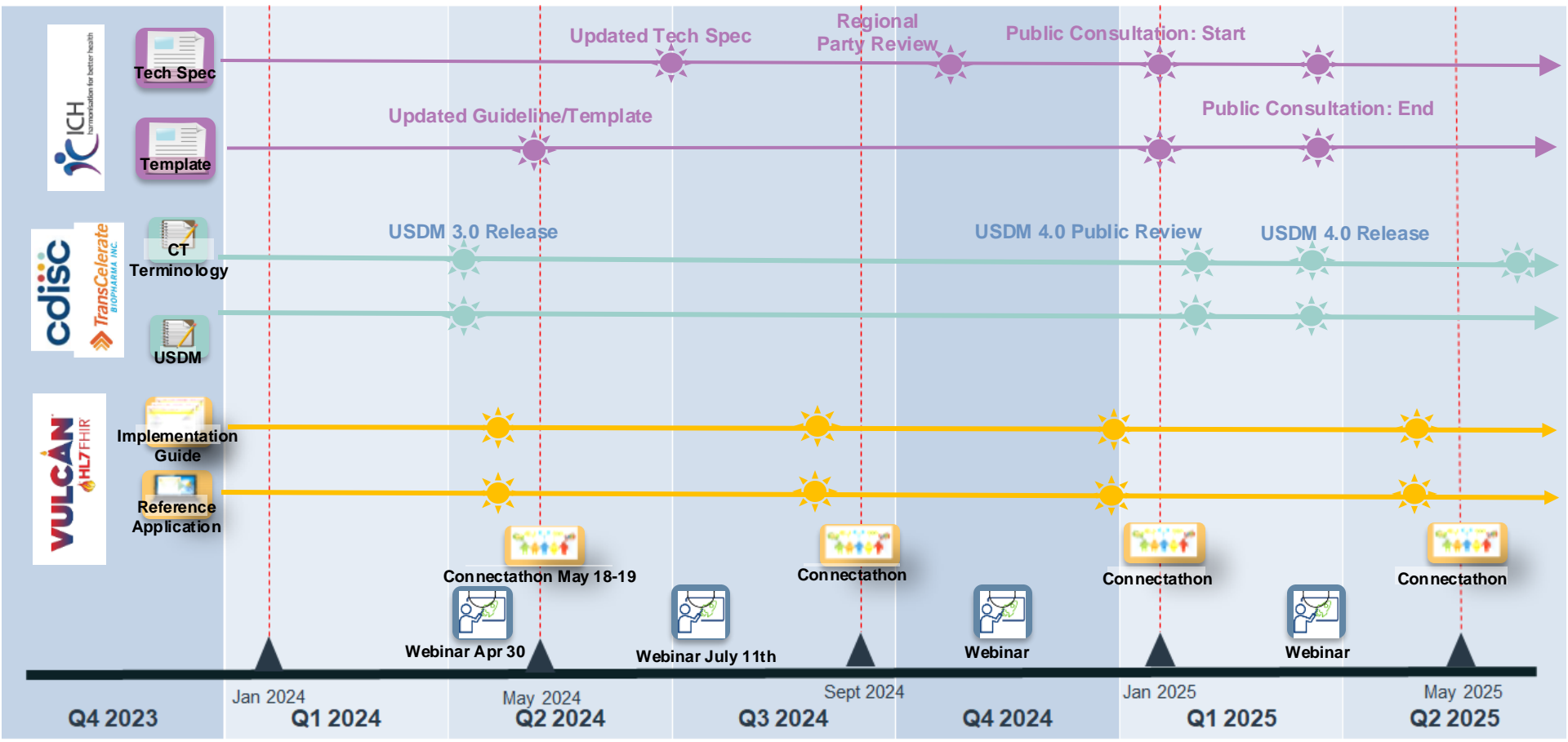
ICH M11 technical specification

Models, definitions

FHIR will carry CDISC CT and USDM content

The technical specification can be used to develop other Implementation Guides

Timelines



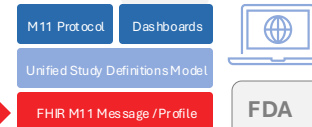
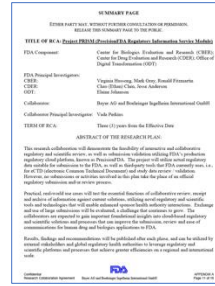
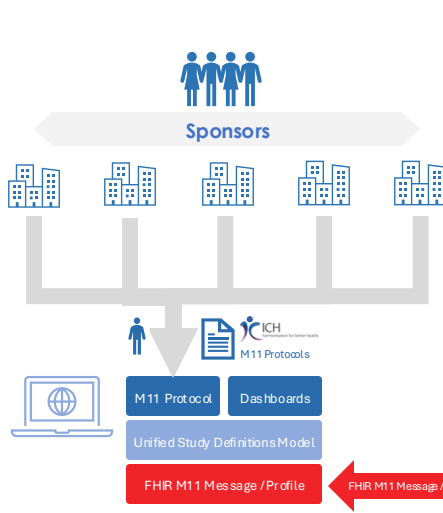
PROJECT PRISM



A Regulatory Cloud Collaborative Initiative

precisionFDA Regulatory Information Service Module
FDA-Industry Research Collaboration Agreement
(Public-Private Partnership)

PRISM USE CASE



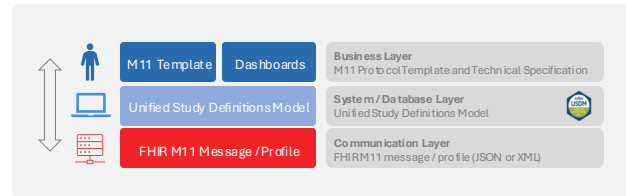
FDA

- FHIR → USDM → M11 Presentation
- Dashboards, what is possible?

Sponsor

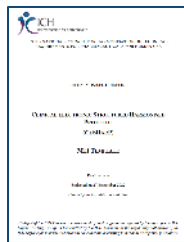
1

- M11 '.docx' → USDM → FHIR
- Try and make it easy, "a few clicks"



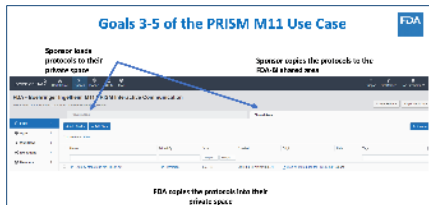
Status

ICH & M11 Specifications
 USDM being kept aligned with the ICH M11 work via close communication and development of M11 CT



- Phase Four Focus**
- 1 USDM E-Pharmaco is the only digital platform for pharmaceuticals and biotech sponsors and regulatory agencies. It is the only platform for regulatory agencies to interact with sponsors.
 - 2 Continued alignment of USDM with ICH M11
 - 3 Participation in the Utilizing the Digital Protocol (UDP) project with TransCelerate, IQVIA and HL7 Vulcan
 - 4 Continue development of USDM Performance Rules to support USDM v3.0 and v4.0
 - 5 Continue support and development of test cells and test tools
 - 6 Development of training and education materials in partnership with TransCelerate's Change and Engagement team to foster adoption of USDM

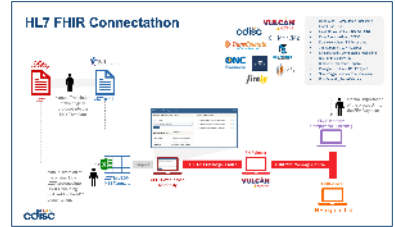
USDM Phase 4
 Refine, improve, adopt



FDA & PRISM
 Working with FDA to pilot first electronic transfer of an M11 protocol as well as tooling to support



HL7 Vulcan & UDP
 Working with HL7 Vulcan to build FHIR message to support exchange of USDM / M11 content. Next connection is Atlanta, Sept 2024



EMA & CTIS
 Working with EMA to align USDM with CTIS to facilitate work such as dashboards



ABSTRACT SUBMISSIONS ARE NOW OPEN!

Abstracts are due on July 19. Learn more about the submission process [here](#).

DDF VENDOR SHOWCASE
 26 September

DDF IN ACTION DAY
 10 October

TransCelerate & Adoption
 Several sponsors and vendors working with USDM. Latest adoption will be visible at the TransCelerate 'DDF in Action' day





Thank You!

cdisc