
# Making the Electronic Protocol a Reality
# The TransCelerate/CDISC Digital Data Flow Project, ICH M11 Protocol, and How They Work Together

Presented by Chris Decker, CEO and President, CDISC

# 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?

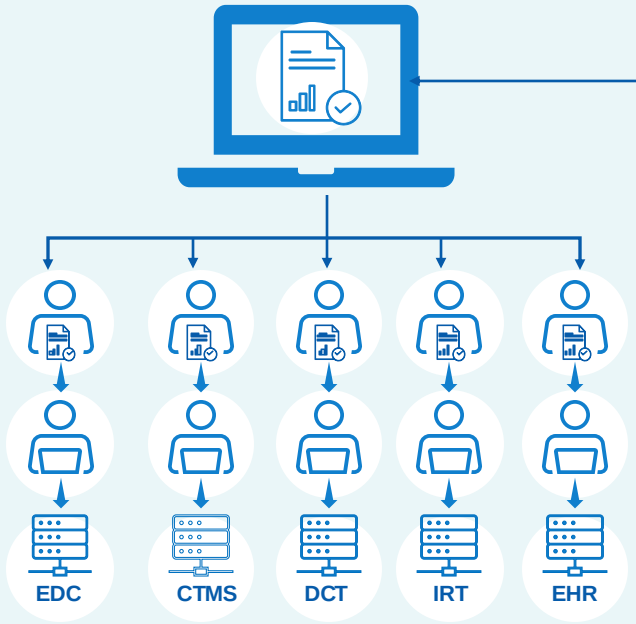
# Introduction to the Digital Data Flow Project and Unified Study Data Model (USDM)

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

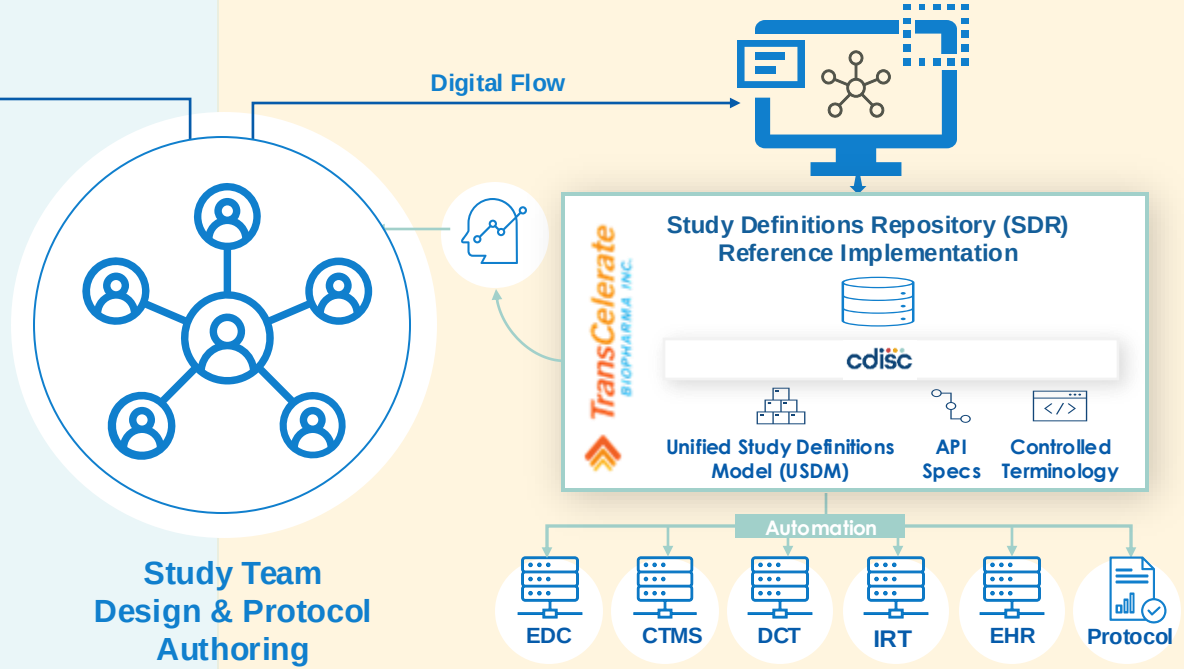
# TransCelerate Digital Data Flow (DDF) Ambition

*Write Once, Read Many*

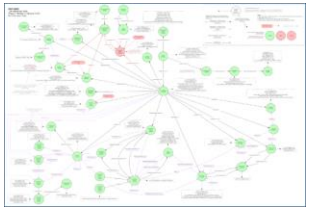
**TODAY:** Document-based paradigm for protocol creation, interpretation, and transcription into consuming systems




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



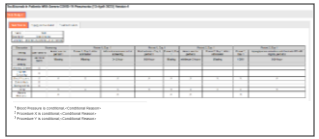
# DDF Initiative encompasses technical delivery, change management, and industry engagement



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**

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

**Growing Solution Collaboration Forum (SCF)***

trials.ai · ZS · InteliNotion · formedix · PHARMASEAL · nurocor · merative · TriNetX · castor · ORACLE · Sycamore Informatics · medidata · TRYAL · 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.*

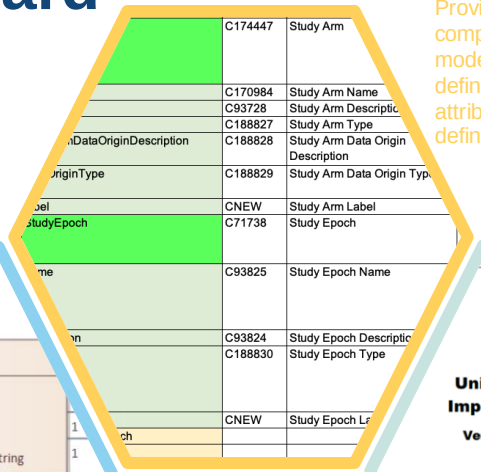


TransCelerate BIOPHARMA INC.

# The USDM Standard

## CDISC Controlled Terminology

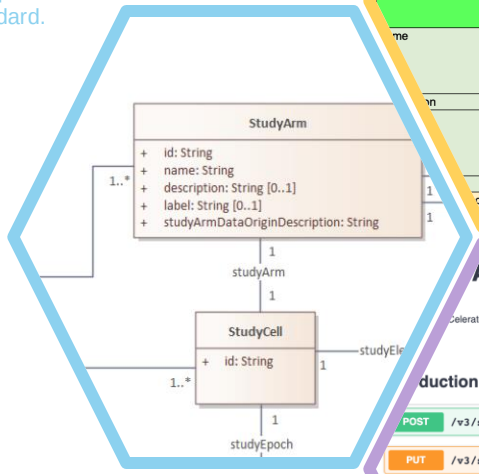
Provides further semantics, complementing the UML model. Includes the definition of classes and attributes along with the definition of value sets



| | | |
|---|---|---|
| | 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.



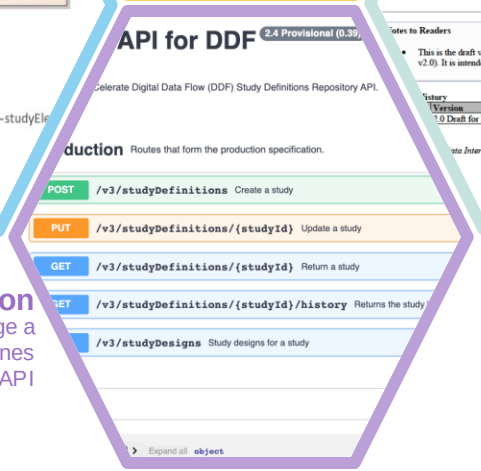

## Examples

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-
```

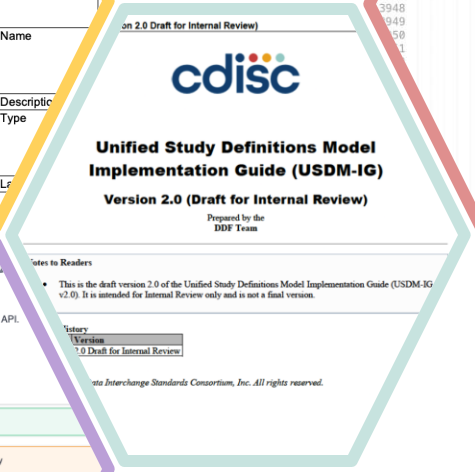
## API Specification

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



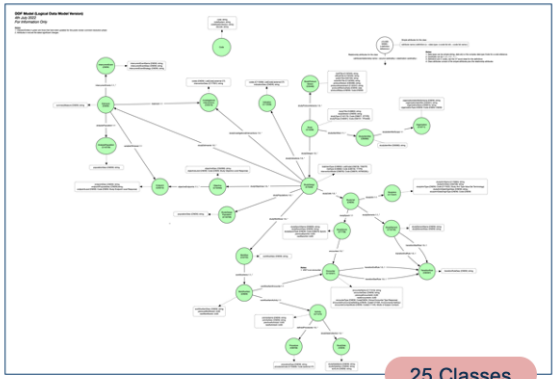

## Implementation Guide

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



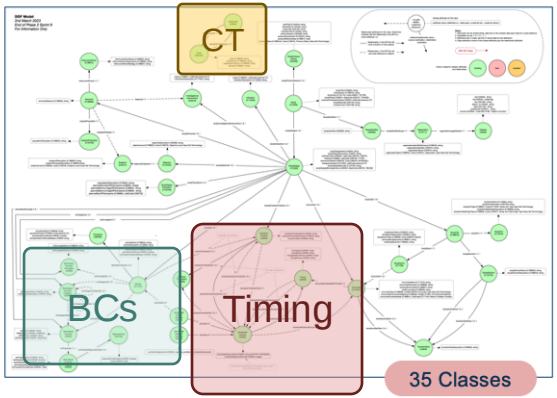
# CDISC DDF / USDM: Phases One, Two and Three

## Phase One



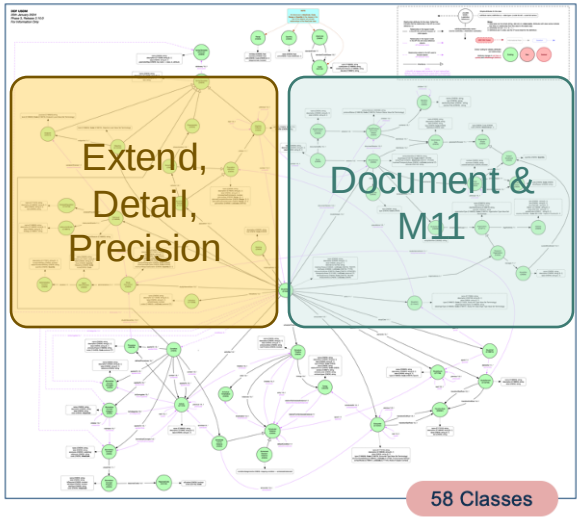

- Solid foundation
- The protocol document was an external entity into which the structured content could be exported

## Phase Two



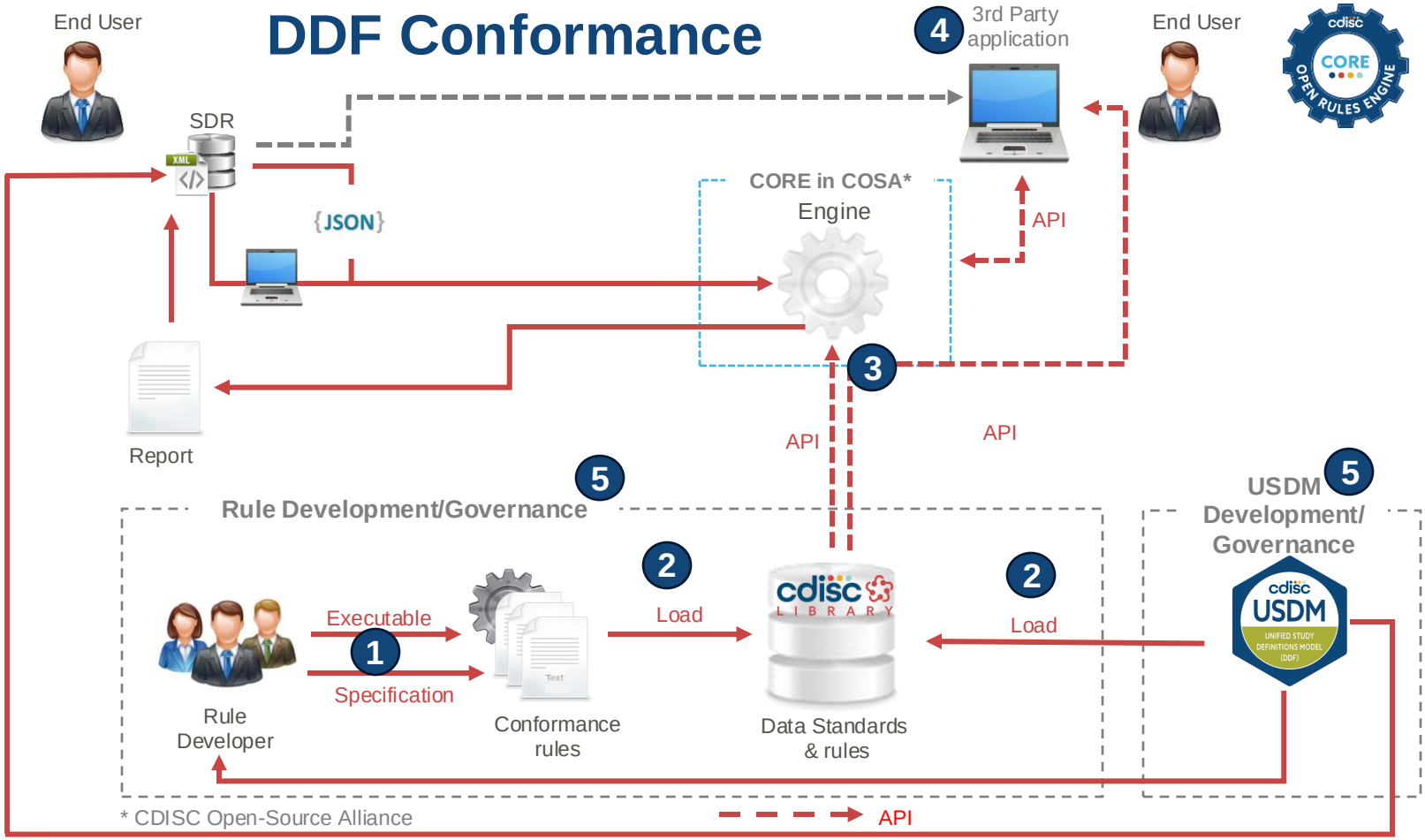

- Focused on the structured elements of the protocol, e.g. the Schedule of Activities (SoA) & Biomedical Concepts (BCs)
- The protocol document still an external entity

## Phase Three



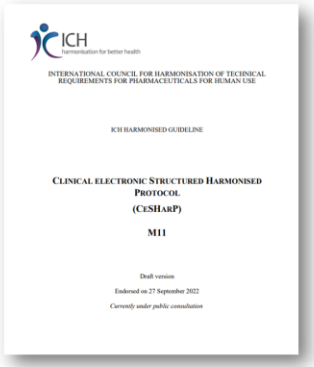

- Now contains structured and unstructured elements
- The entire protocol document can be held within the USDM
- Allows for the protocol document to be generated from the model

# DDF Conformance



# USDM generates various formats

Guideline & Template → Tech Spec


ICH harmonisation for better health

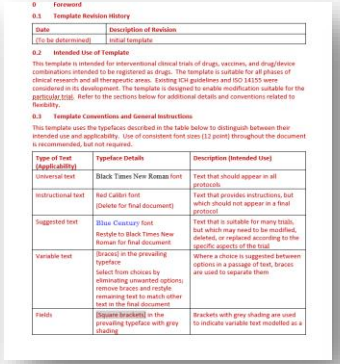
INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL
(CESHARP)

M11

Draft version
Endorsed on 27 September 2022
*Currently under public consultation*


0 Foreword

0.1 Template Revision History

| Date | Description of Revision |
|---|---|
| (To be determined) | Initial template |

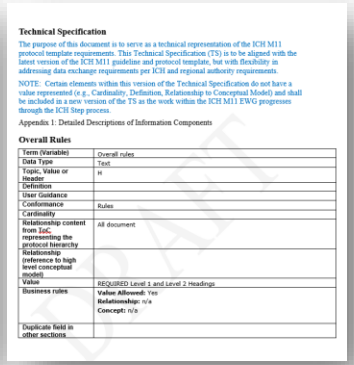
0.2 Intended Use of Template

This template is intended for interventional clinical trials of drugs, vaccines, and drug/device combinations intended to be registered as drugs. The template is suitable for all phases of clinical research and all therapeutic areas. Existing ICH guidelines and ISO 14155 were considered in its development. The template is designed to enable modification suitable for the particular trial. Refer to the sections below for additional details and conventions related to flexibility.

0.3 Template Conventions and General Instructions

This template uses the typefaces described in the table below to distinguish between their intended use and applicability. Use of consistent font sizes (12 point) throughout the document is recommended, but not required.

| Type of Text (Applicability) | Typeface Details | Description (Intended Use) |
|---|---|---|
| Universal text | Black Times New Roman font | Text that should appear in all protocols |
| Instructional text | Red Calibri font (Delete for final document) | Text that provides instructions, but which should not appear in a final protocol |
| Suggested text | Blue Century font Restyle to Black Times New Roman for final document | Text that is suitable for many trials, but which may need to be modified, deleted, or replaced according to the specific aspects of the trial |
| Variable text | [Braces] in the prevailing typeface Select from choices by eliminating unwanted options; remove braces and restyle remaining text to match other text in the final document | Where a choice is suggested between options in a passage of text, braces are used to separate them |
| Fields | [Square brackets] in the prevailing typeface with grey shading | Brackets with grey shading are used to indicate variable text modelled as a |


**Technical Specification**

The purpose of this document is to serve as a technical representation of the ICH M11 protocol template requirements. This Technical Specification (TS) is to be aligned with the latest version of the ICH M11 guideline and protocol template, but with flexibility in addressing data exchange requirements per ICH and regional authority requirements.

NOTE: Certain elements within this version of the Technical Specification do not have a value represented (e.g., Cardinality, Definition, Relationship to Conceptual Model) and shall be included in a new version of the TS as the work within the ICH M11 EWG progresses through the ICH Step process.

Appendix 1: Detailed Descriptions of Information Components

**Overall Rules**

| Term (Variable) | Overall rules |
|---|---|
| Data Type | Text |
| Topic, Value or Header | H |
| Definition | |
| User Guidance | |
| Conformance | Rules |
| Cardinality | |
| Relationship content from ToC, representing the protocol hierarchy | All document |
| Relationship (reference to high level conceptual model) | |
| Value | REQUIRED Level 1 and Level 2 Headings |
| Business rules | **Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a |
| Duplicate field in other sections | |

DRAFT

**Electronic Document**
**Human Readable Form**

cdisc USDM
UNIFIED STUDY DEFINITIONS MODEL (DDF)

**Machine-Readable Form**





VULCAN HL7 FHIR

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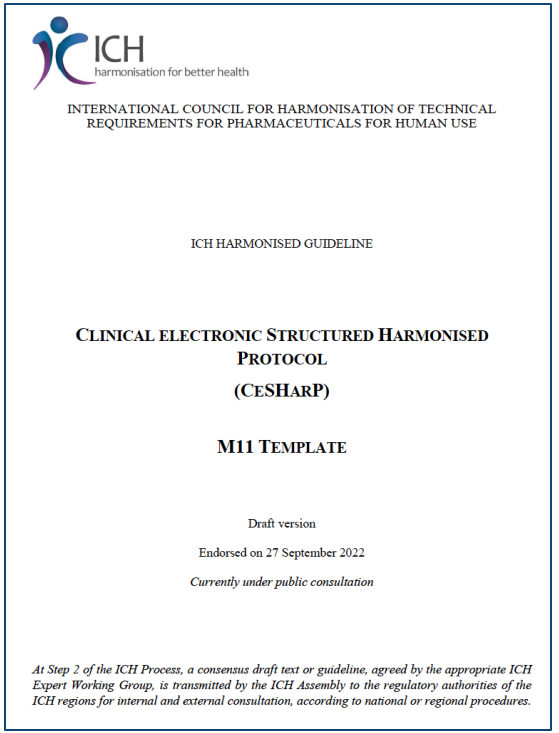
**Standard Message Exchange Formats**

# Overview of M11 and the ICH/CDISC Partnership

# ICH CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL (CeSHarP)

| Founding Regulatory Members | Founding Industry Members | Standing Regulatory Members | Regulatory Members | Industry Members |
|---|---|---|---|---|
| • EC, Europe (EMA)<br>• FDA, United States<br>• MHLW / PMDA, Japan | • EFPIA<br>• JPMA<br>• PhRMA | • Health Canada, Canada<br>• Swissmedic, Switzerland | • ANVISA, Brazil<br>• COFEPRIS, Mexico<br>• EDA, Egypt<br>• HSA, Singapore<br>• MFDS, Republic of Korea<br>• MHRA, UK<br>• NMPA, China<br>• SFDA, Saudi Arabia<br>• TFDA, Chinese Taipei | • BIO<br>• Global Self-Care Federation<br>• IGBA |



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.*

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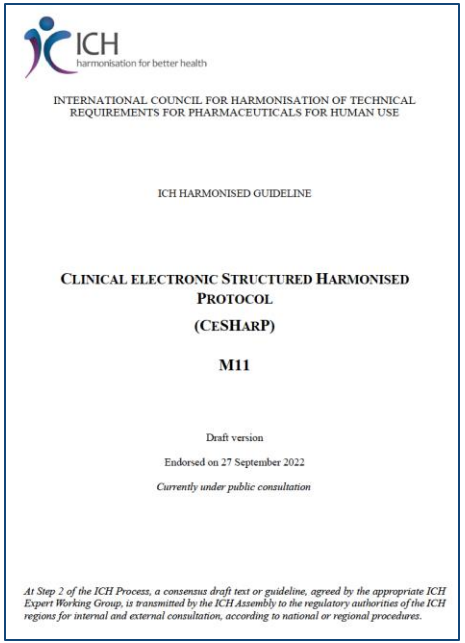
# M11 Is …

*ICH CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL (CeSHarP)*

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



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ICH HARMONISED GUIDELINE

**CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL**

**(CESHARP)**

**M11**

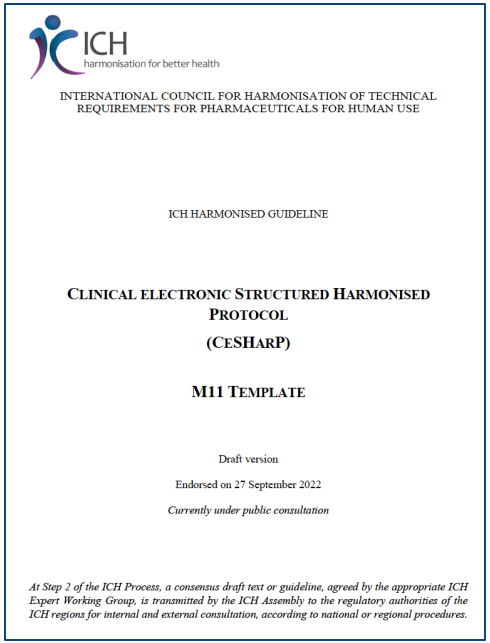
Draft version

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

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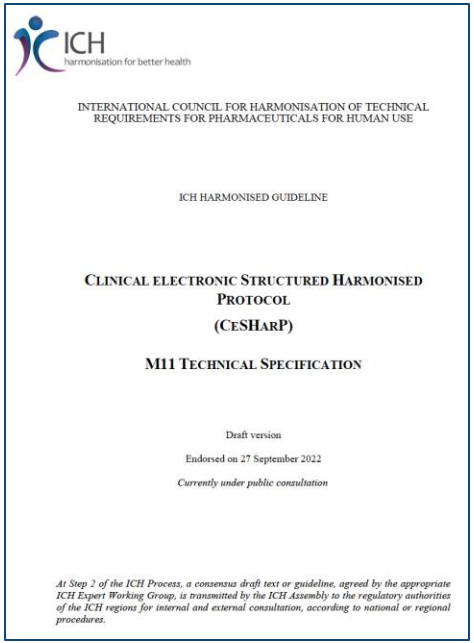
*At Step 2 of the ICH Process, a consensus draft text or guideline, agreed by the appropriate ICH Expert Working Group, is transmitted by the ICH Assembly to the regulatory authorities of the ICH regions for internal and external consultation, according to national or regional procedures.*

Provides the written format for the Interventional Clinical Trial Protocol Template



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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

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# M11 Simple Example

Template Specification

| | |
|---|---|
| **Protocol Full Title:** | [Protocol Full Title]<br>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]<br>Insert the Sponsor's confidentiality statement, if applicable, otherwise delete. |
| Protocol Number: | [Protocol Number]<br>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]<br>An optional field for use by the Sponsor at their discretion. |
| **Amendment Number:** | [Amendment Number]<br>Enter the amendment number. If this is the original instance of |
| **Trial Phase:** | [Trial Phase] [Description of Trial Phase Other]<br>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]<br>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]<br>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]<br>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<br>Phase 1<br>Phase 1/Phase 2<br>Phase 2<br>Phase 2/Phase 3<br>Phase 3<br>Phase 4<br>Other |
| **Business rules** | **Value Allowed:** yes<br>**Relationship:** n/a<br>**Concept:** Protocol short title |
| **Duplicate field in other sections** | |

# Controlled Terms

Template Specification

| | |
|---|---|
| **Protocol Full Title:** | [Protocol Full Title]<br>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]<br>Insert the Sponsor's confidentiality statement, if applicable, otherwise delete. |
| Protocol Number: | [Protocol Number]<br>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]<br>An optional field for use by the Sponsor at their discretion. |
| **Amendment Number:** | [Amendment Number]<br>Enter the amendment number. If this is the original instance of |
| Compound Number(s): | [Compound Number]<br>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]<br>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]<br>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

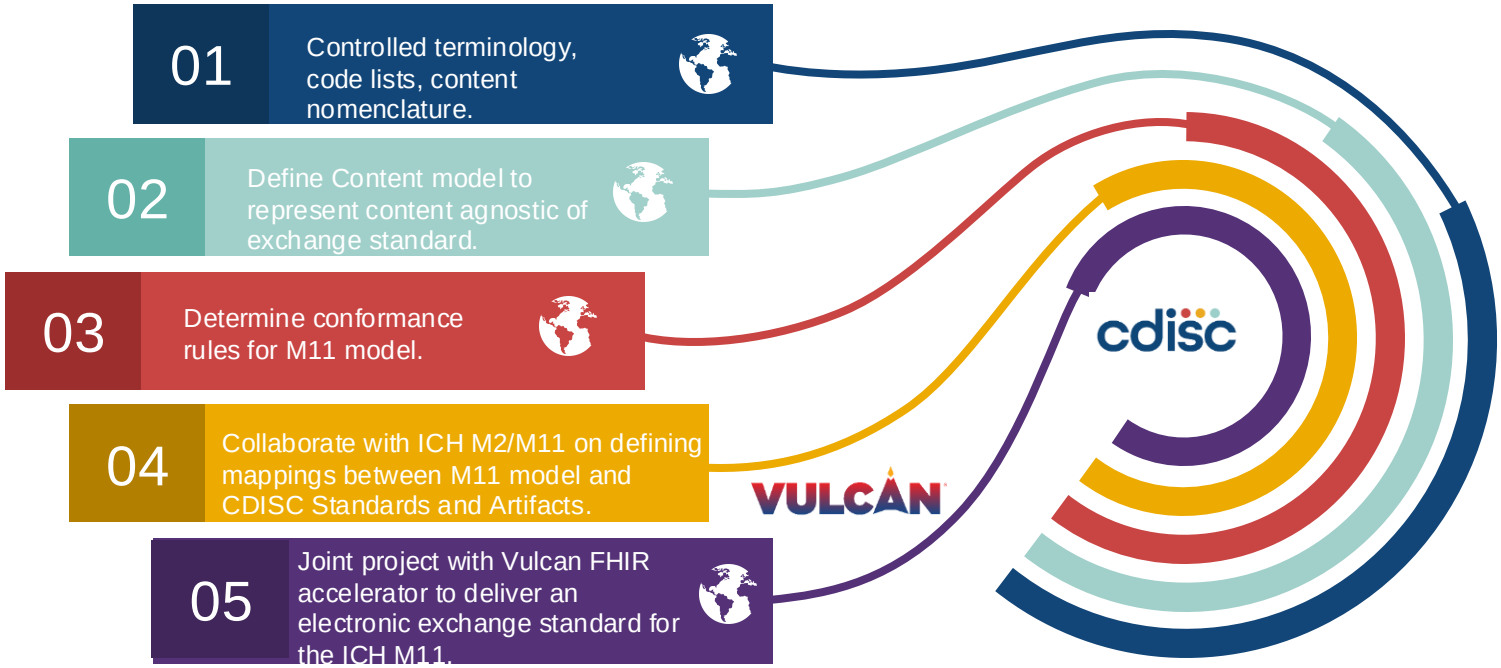
| | |
|---|---|
| **Term (Variable)** | Trial Phase |
| **Data Type** | Pick list |
| **Topic, Value or Header** | D |
| **Definition** | |
| **User Guidance** | For trials combining investigational drugs or vaccines with devices, classify according to the phase of drug development. |
| **Conformance**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

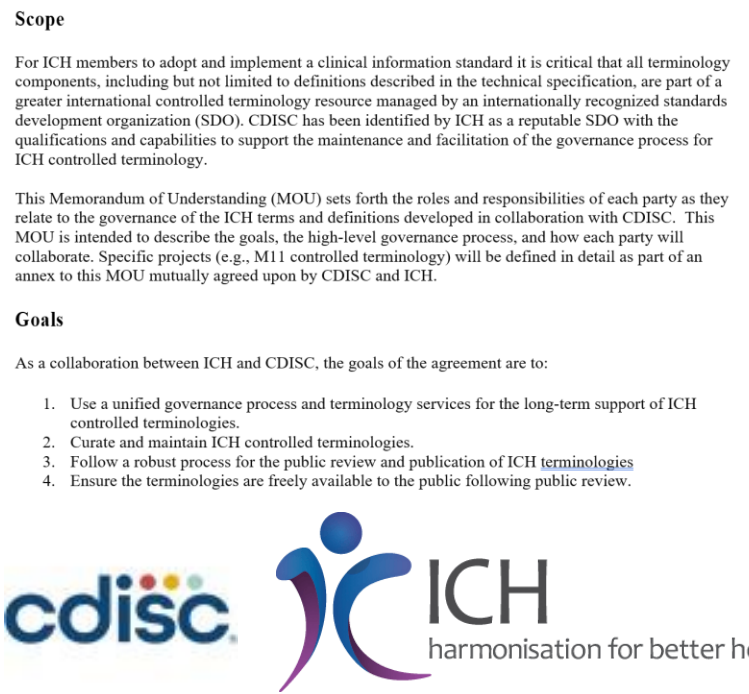
# CDISC M2/M11 Engagement



# 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.

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ICH harmonisation for better health

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

# Example Use Cases I

## Authoring

Protocol authoring and sharing including the providing a **tailored user experience.**

Provide a solid foundation for study execution

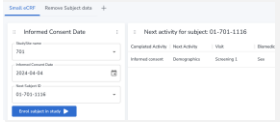
A standard for protocol information re-use during and after study execution

## Regulatory

Automate or ease the process of providing protocols and protocol information to regulators and clinical trial registries

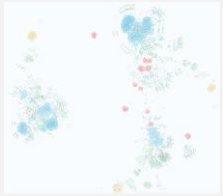
## Data Capture

The use of detailed study design information to ease the configuration data capture systems



## Insights

Use of protocol information to gain insights into past performance to improve future outputs and processes



## Subject Impact

Use of protocol information to assess impact on subjects such as subject burden, time and risk

There are many use cases, these are just a few examples

# Example Use Cases 2

## SDTM T Domains

Use of protocol information to generate SDTM trial design domains

Can also read trial design domains to assist in rebuilding studies

## SDTM Data

Use of the detailed study design information available within USDM to provide a solid foundation for the automated generation of SDTM data domains

## aCRF

Use of the detailed study design to create an annotated Case Report Form for the study

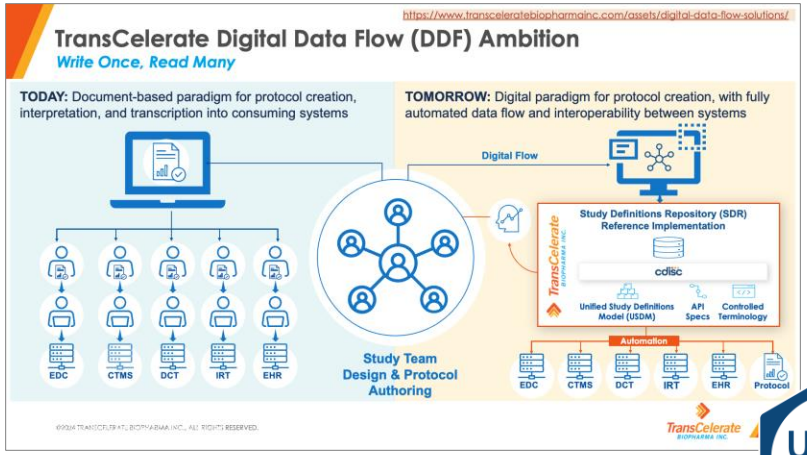
## Define.xml

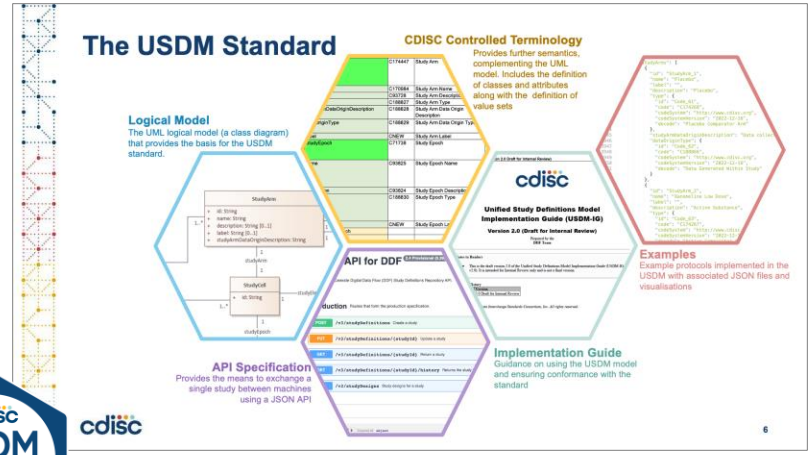
Use of the detailed study design to create a define.xml for the study

## Data Decay

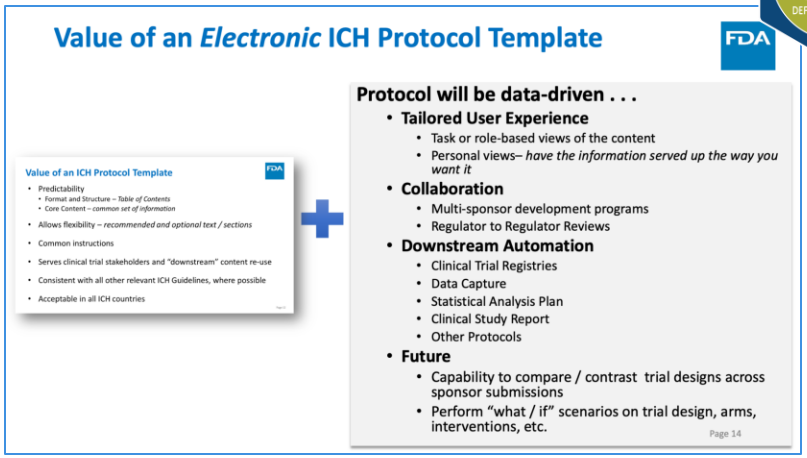
Use of the detailed study design information available within USDM to provide a framework for ingesting old study data

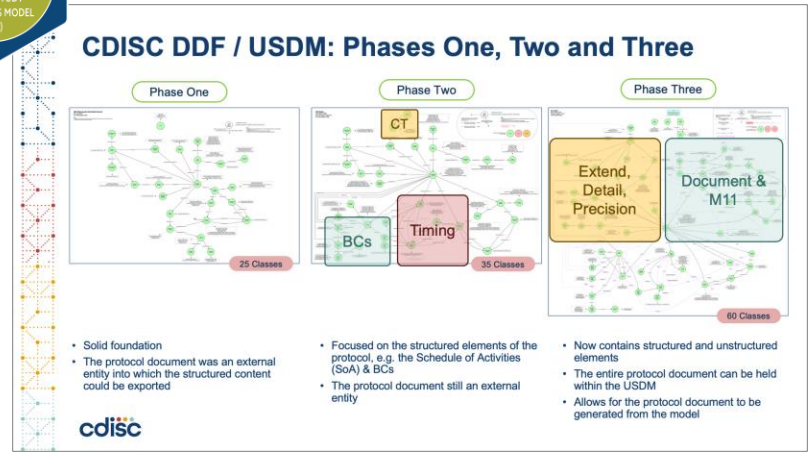
There are many use cases, these are just a few examples



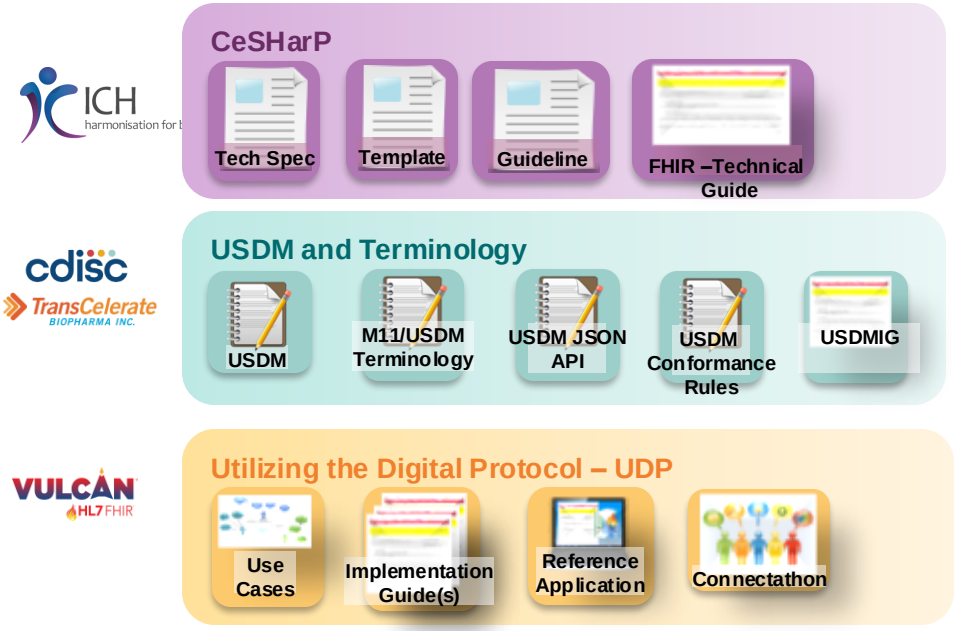




cdisc USDM
UNIFIED STUDY DEFINITIONS MODEL (DDF)



# ICH M11 and Vulcan Utilizing Digital Protocol (UDP)



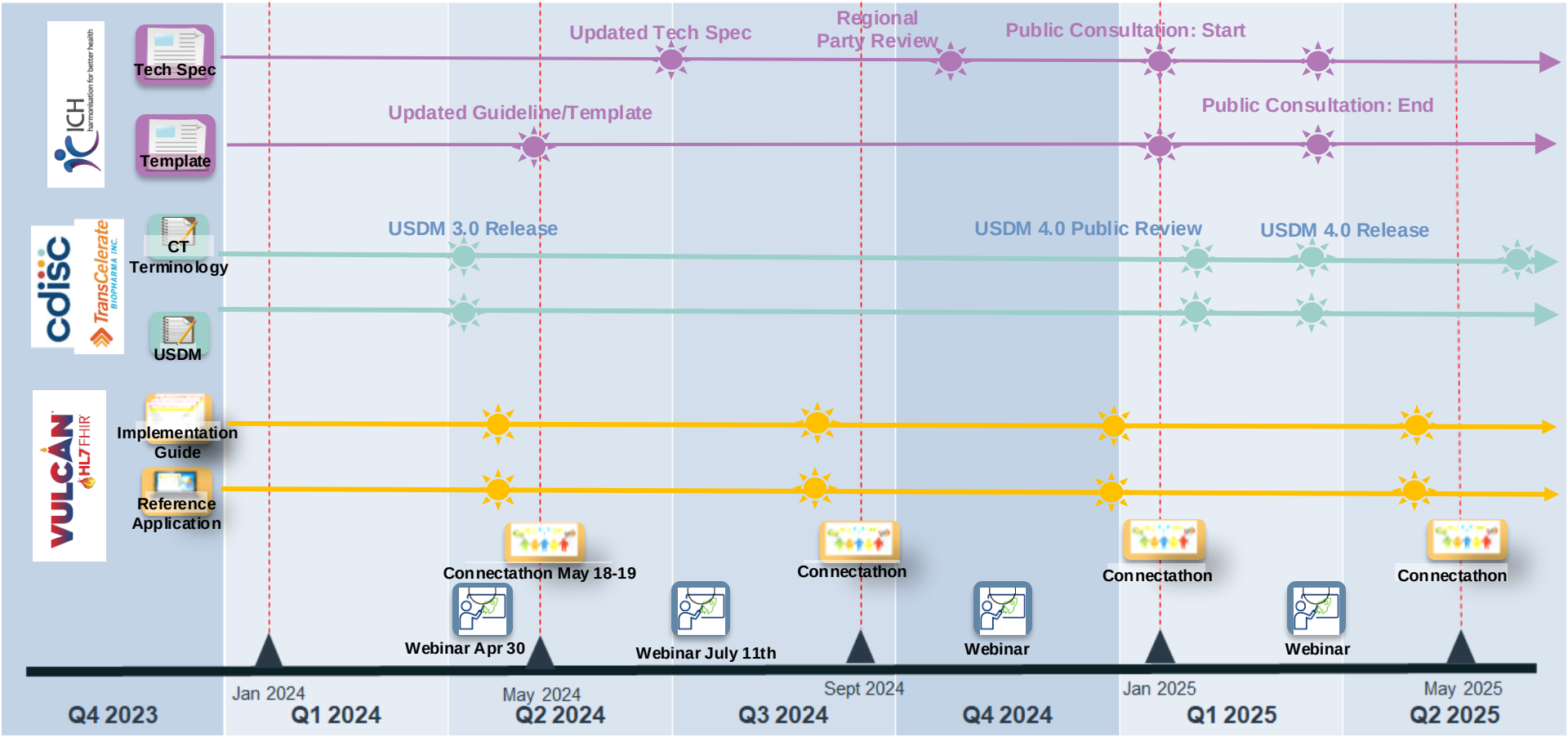

## Inputs:

- 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


Tech Spec
Template
CT Terminology
USDM
Implementation Guide
Reference Application
Updated Tech Spec
Regional Party Review
Public Consultation: Start
Updated Guideline/Template
Public Consultation: End
USDM 3.0 Release
USDM 4.0 Public Review
USDM 4.0 Release
Connectathon May 18-19
Connectathon
Connectathon
Connectathon
Webinar Apr 30
Webinar July 11th
Webinar
Webinar
Jan 2024
May 2024
Sept 2024
Jan 2025
May 2025
Q4 2023
Q1 2024
Q2 2024
Q3 2024
Q4 2024
Q1 2025
Q2 2025

# Thank You!