GUF 2025-06-24 : Digital Protocol

Digital Data Flow : Etat des lieux en Juin 2025

Presented by

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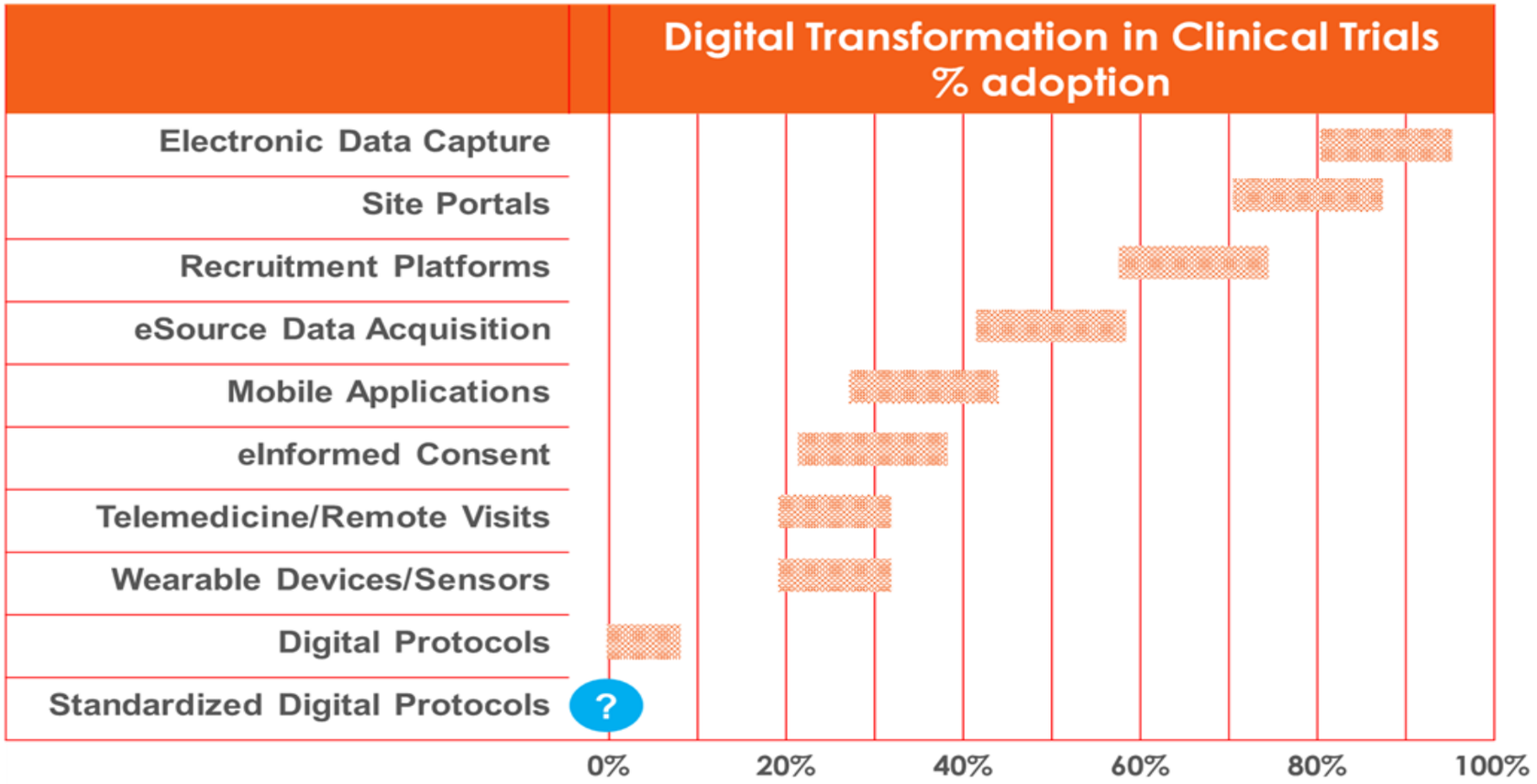
Why Digital Data Flow?

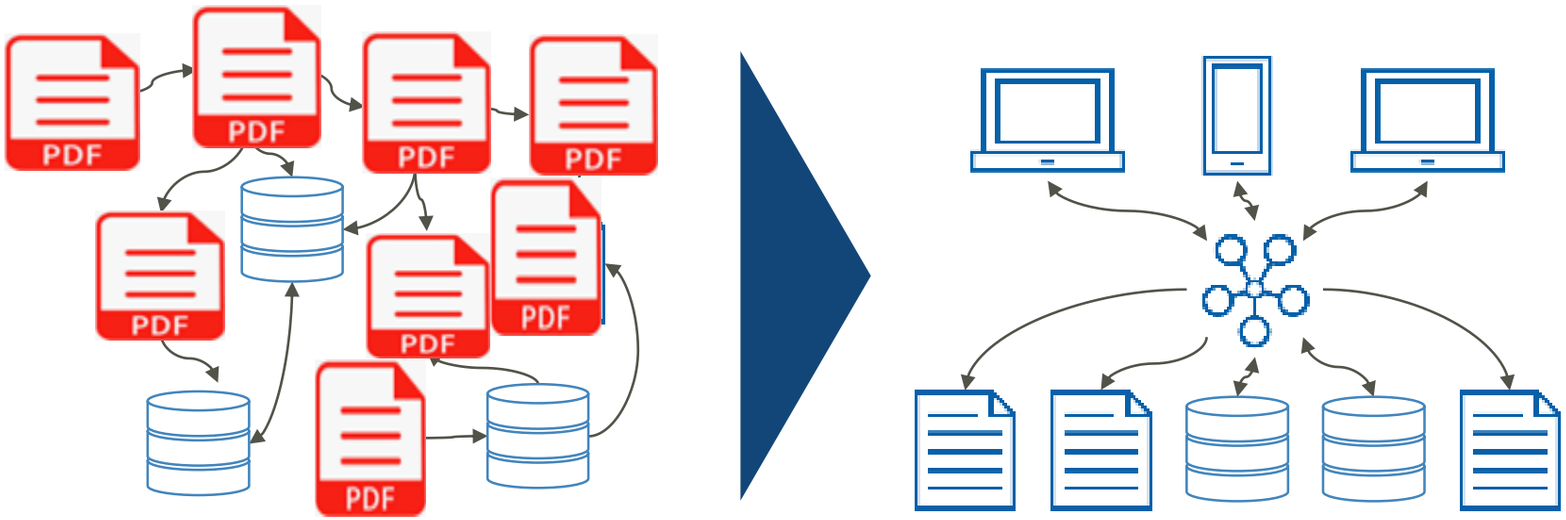
The industry has not kept pace with the complexity of clinical study data or the systems used to manage it. There is opportunity to modernize the manual, slow processes and improve reliability.



**The statistics shared on this slide are crowdsourced, obtained from multiple sources via various personal communications with the presenter.*

Protocol Digitalization Vision

Shift from "**document-first**" to "**data-first**" paradigm for clinical study setup, unlocking value through seamless integration, process automation and data-based insights



Digital - standard representation of study protocol
- ✓ structured
- ✓ machine readable
- ✓ executable

Data Flow – industry-wide interoperability
- ✓ exchange of data
- ✓ non-cooperating organizations
- ✓ minimal effort

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

Example DDF Use Cases across Clinical Study Data Flow (1/2)

Study Design → **Study Start-up**

Subject Impact

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

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

Define.xml

<ODM>

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

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

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

Example DDF Use Cases across Clinical Study Data Flow (2/2)

Study Execution / Data Acquisition → **Analysis & Reporting** → **Regulatory Submission Enablement**

Data Decay

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

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

Regulatory

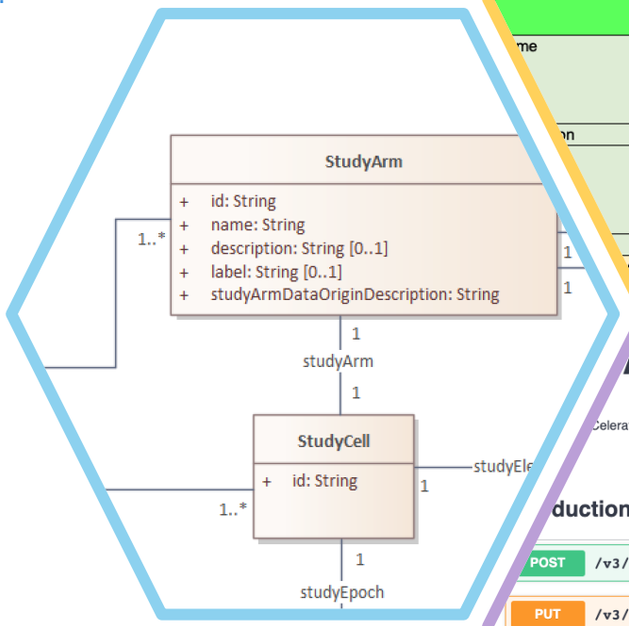
Automate or ease the process of providing protocols and protocol information to regulators and clinical trial registries

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

The USDM Standard

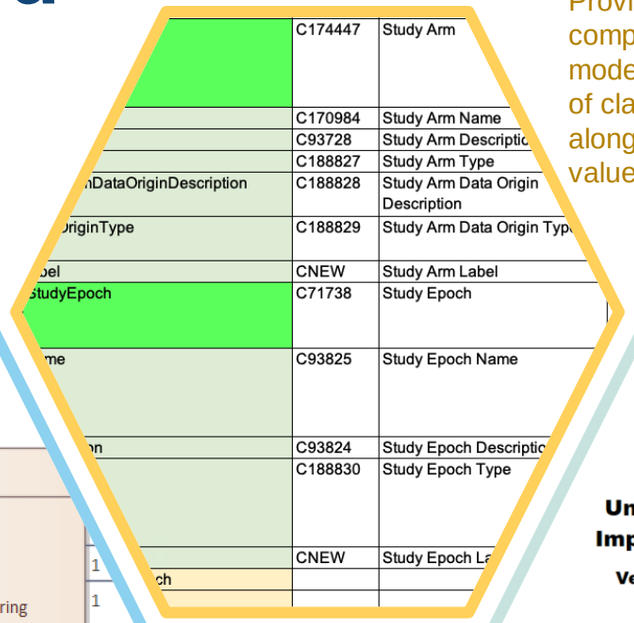
Logical Model

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



CDISC Controlled Terminology

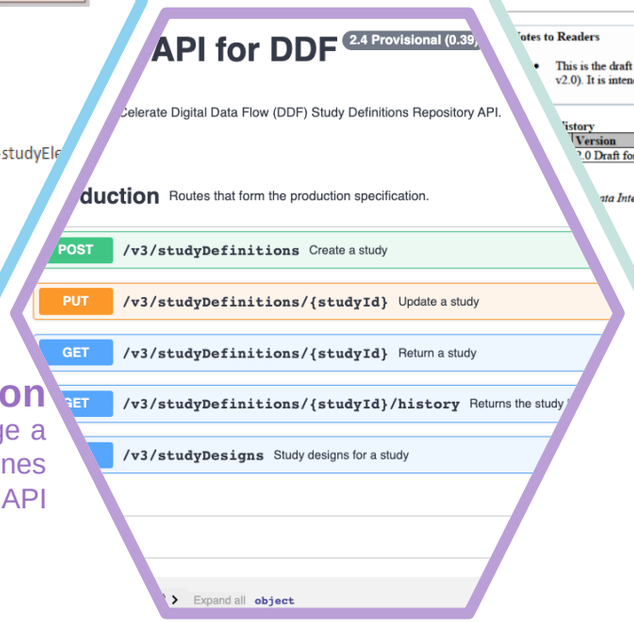
Provides further semantics, complementing the UML model. Includes the definition of classes and attributes along with the definition of value sets



	C174447	Study Arm
	C170984	Study Arm Name
	C93728	Study Arm Descriptio
	C188827	Study Arm Type
nDataOriginDescription	C188828	Study Arm Data Origin Description
riginType	C188829	Study Arm Data Origin Typ
el	CNEW	Study Arm Label
tudyEpoch	C71738	Study Epoch
me	C93825	Study Epoch Name
n	C93824	Study Epoch Descriptio
	C188830	Study Epoch Type
	CNEW	Study Epoch La
ch		

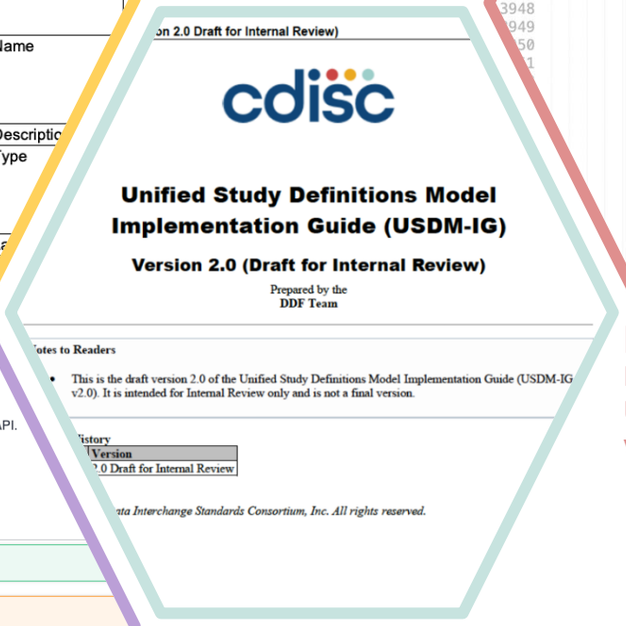
Examples

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



API Specification

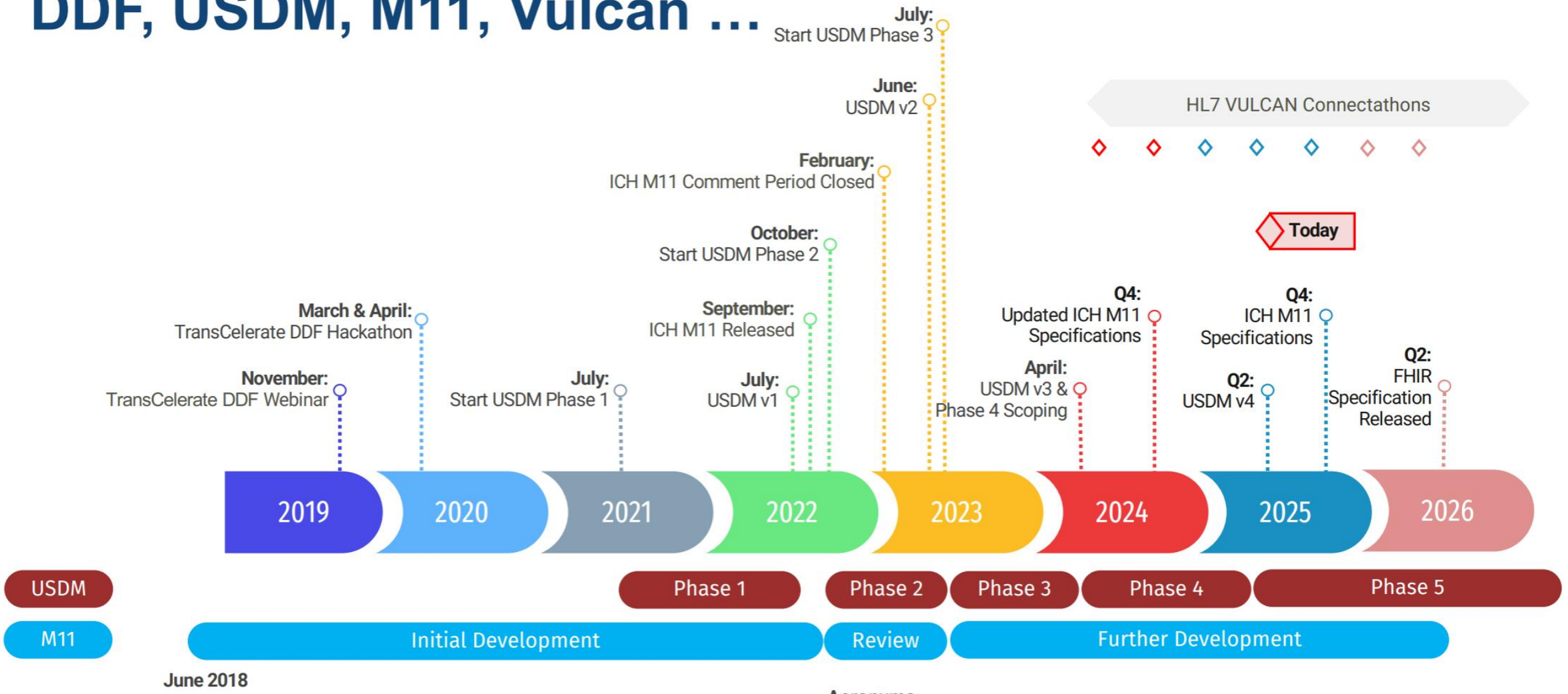
Provides the means to exchange a single study between machines using a JSON API



Implementation Guide

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

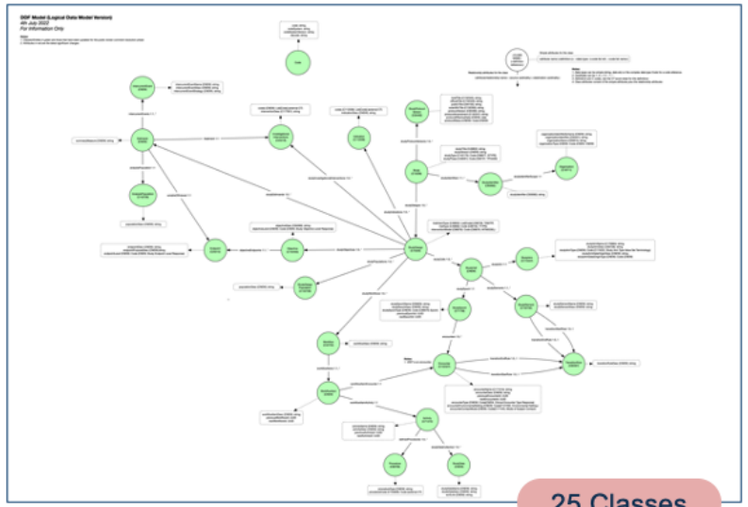
DDF, USDM, M11, Vulcan …



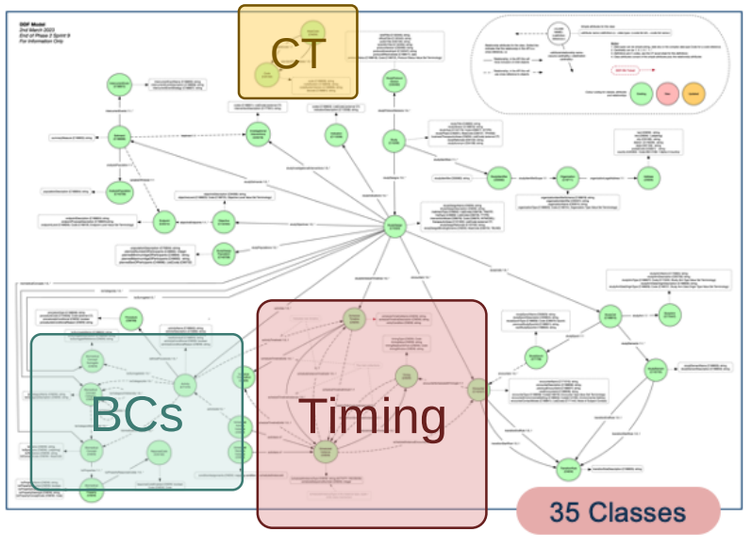
Acronyms
DDF: Digital Data Flow
USDM: Unified Study Definitions Model
ICH: International Council for Harmonisation
M11: Clinical electronic Structured Harmonised Protocol (CeSHarP)

CDISC DDF / USDM: Phases One, Two and Three

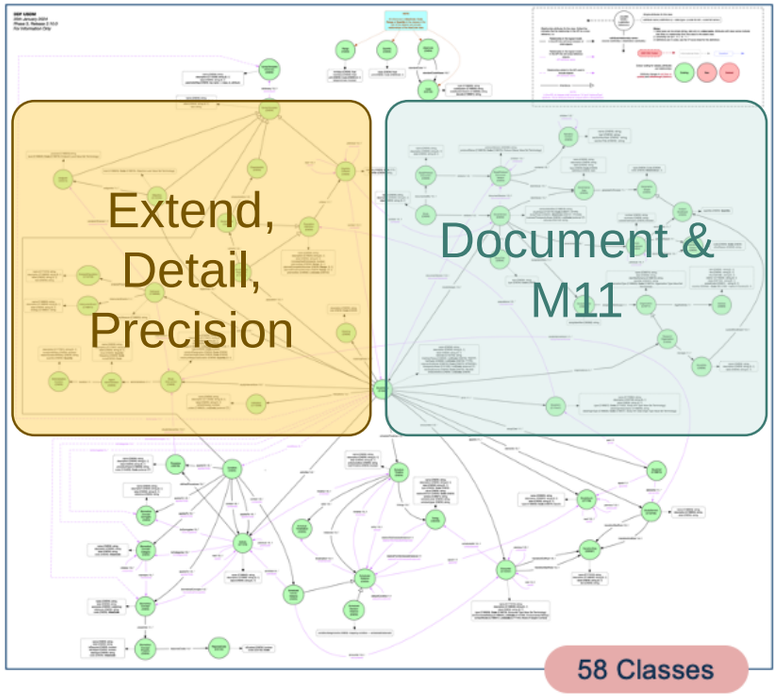
Phase One



Phase Two



Phase Three



Solid foundation

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

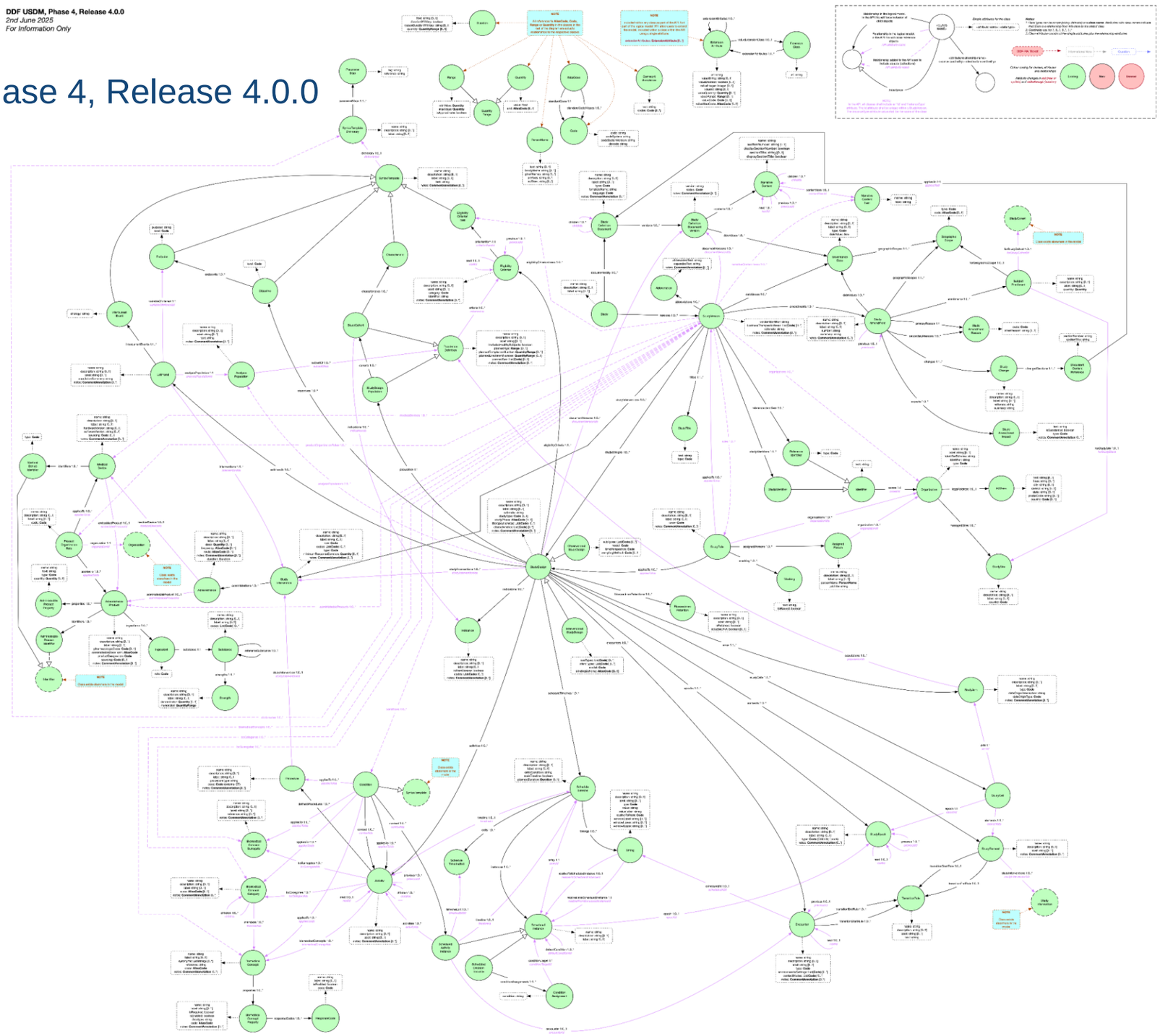
- Focused on the structured elements of the protocol, e.g. the Schedule of Activities (SoA) & Biomedical Concepts (BCs)
- The protocol document still an external entity

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

DDF USDM, Phase 4, Release 4.0.0
2nd June 2025



[DDF-RA/Documents/DDF USDM Model Informative.png at main · cdisc-org/DDF-RA · GitHub]

Additional Opportunities to Stay Involved with DDF

You can stay involved and learn more about the Digital Data Flow initiative by visiting the following websites:

DDF Website

As the main website for DDF, learn and access all resources supporting DDF

Scan QR Code to explore DDF Website

CDISC DDF Website

Learn about and access the Unified Study Definitions Model (USDM) Reference Architecture supporting Protocol Standards

TransCelerate DDF Initiative Solutions

Learn about DDF initiative background and roadmap

DDF GitHub Repos

Learn about and access the Study Definitions Repository Reference Implementation and supporting codebase

Questions? Feedback? Please email us at DDF@transceleratebiopharmainc.com

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			☑	

Legend ◆ *Still Applicable*

Golden Nuggets – How You can Get Started

1. Use USDM Control Terminology (CT) if you start building interfaces or databases to store study data

	C174447	Study Arm
	C170984	Study Arm Name
	C93728	Study Arm Descriptic
	C188827	Study Arm Type
nDataOriginDescription	C188828	Study Arm Da Description
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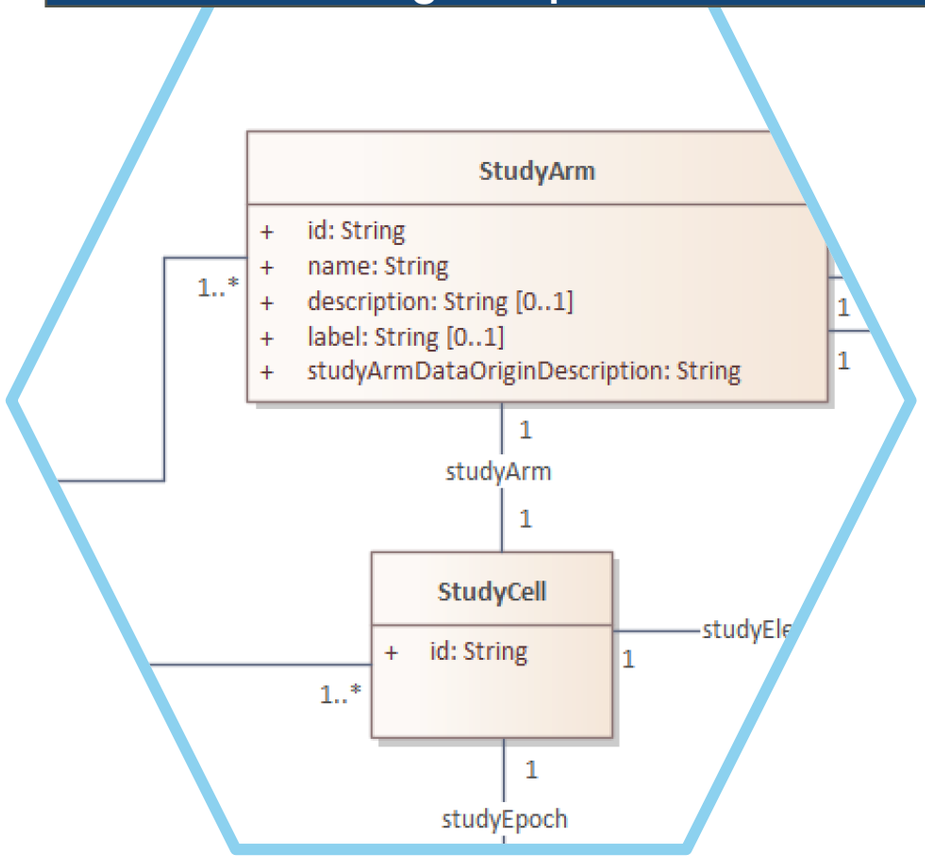
me	C93825	Study Epoch Name
n	C93824	Study Epoch Descriptic
	C188830	Study Epoch Type
	CNEW	Study Epoch La
ch		

Control Terminology not only for content but also for variable names

2. Look at the USDM Class structure to see what the global picture is.



USDM

QR Code for Image

USDM in Action
Use Cases Supporting the DDF Vision

TransCelerate BIOPHARMA INC.

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Use Cases

Retrospective

Prospective

Protocol 'Store'

Past Protocols
The storage of past sponsor protocols in to support a variety of use cases such as:

- Therapeutic area specific content
- Standard inclusion and exclusion criteria.
- Libraries of objectives, endpoints and estimands.
- Asses the past to prevent protocol amendments.
- General search across the library

Study Design

Protocol Authoring
Support the authoring of new protocols including complex studies such as Master, Umbrella etc.

This would include analyzing previous protocol information to inform design choices (see Protocol Store).

Writing associated SAP, Informed Consent, Monitoring Plan, Drug Plan etc via content reuse.

Study Build
Build of the study based on the protocol I including all detailed procedures and assessments to allow for immediate deployment.

Feasibility & Cost
Support study feasibility and complexity evaluations.

Determine the cost of the study including such items as vendor and CRO costs and support the laboratory RFP process

Regulatory Authority
Approval for the execution of the study including IND, CTA etc and discussions with regulatory authorities

Stakeholder Views
Tailored views for stakeholders such as IRB and ethic committees.

Study Start-up

Deployment
Deployment of the study across the enterprise using the USDM to support electronic configuration rather than manual data entry including Data collection systems (incl. EDC), CTMS, IRT, Data transmission specifications and more

TMF
Linking the protocol to the specification of milestones and essential documents

Data Collection Strategy
Ensure all data that is needed for analysis is collected. Remove unnecessary procedures & data collection to reduce trial cost and patient burden.

Trial Registries
Registration of the study with registries such as CT.gov, CTIS etc.

Training
Provision of training materials to those involved in the study including sites

Site Support
Provision of tailored information to sites regarding study execution.

Study Execution

Amendments
Support the amendment process with the ability to indicate the precise changes to the user community.

Ensure fewer amendments (see Protocol Store).

Subject Information
Provision of improved information to subjects regarding study execution, improve expectation management.

Drug & Study Materials
Assist in the planning and provision of study drug, materials and supplies

Subject Recruitment
Support the identification of subjects to help improve subject recruitment to the study. Help support EHR participation identification.

Analysis & Reporting

Automation
Provide a solid foundation for the automation of analysis and reporting outputs such as TLFs and CSRs.

SDTM
Creation of 'T' domains. Auto generation of data domains

ADaM
Use the protocol statistical metadata to assist in the derivation of analysis datasets

Statistical Analysis Plan
Use the protocol as the initial source of the SAP to ensure consistency with objectives, endpoints, estimands

Regulatory Submission

Submission
Preparation of the submission by the sponsor

Regulatory Review
Review of the submission by the regulatory authority and discussions / questions with the sponsor

Statistical and Safety Review
Support the comparison of data by arm or study design.

Allow for the verification of planned (protocol) data versus actual (study data) captured data

Indication of the areas of the model that would be used to satisfy a given use case. Informative

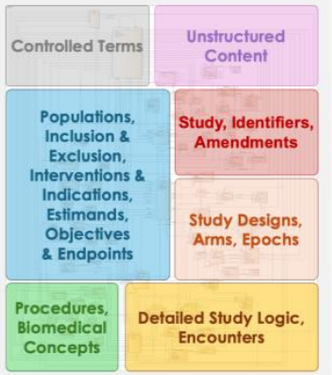
Across The Lifecycle

Dashboards
The display of protocol related information sourced from one or more protocols in ways which have not been achievable before

Comparison
Compare and verify differences across versions and similar protocols

NOTE: The use cases presented are illustrative and the list is not intended to be exhaustive.

Unified Study Definitions Model (USDM)



Study Details
The overall study, its various versions, identifiers and associated governance. Also includes the amendments made to the study

Study High Level Design
The single or set of study designs making up the study detailing the epochs, arms etc.

Study Science
The detailed description of the study science: the populations and the associated inclusion and exclusion criteria, the indications being studied, the interventions being used and the objectives, endpoints and the associated estimands.

Detailed Study Logic
A precise definition of the study logic including support for the Schedule of Activities.

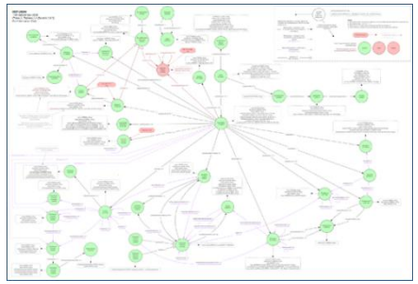
Unstructured Content
The ability to support one or more document presentations of the USDM content including the ICH M11 protocol template, sponsor templates and other documents.

Procedures and Biomedical Concepts
The detail around the procedures and observations to be performed as part of the detailed study designs.

Controlled Terms
The controlled terminology needed to define the semantics within the model. Managed in the same manner as all CDISC CT and aligned with the M11 template standard.

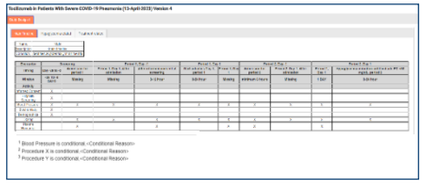
Version 6, 16th April 2025. Prepared by D Iberson-Hurst for the TransCelerate 'DDF in Action' day.
With thanks to Rob Ferendo (TransCelerate), Bill Illis (Novartos), Jasmine Kestemont (Argenx), Kirsten Langendorf (d4k), Mary Lynn Mercado (Novartis), Lissa Morgan (Amgen), Johannes Ullander (d4k) and Peter Van Reusel (CDISC)

DDF Initiative encompasses Technical Standards & Solutions, Change Management, and Industry Engagement



Unified Study Definitions Model (USDM) Reference Architecture

TransCelerate's Study Definitions Repository (SDR) Reference Implementation



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.*

Digital Protocol Multi-Stakeholder Collaboration

M11 / Regulatory-driven Implementation of Harmonized Protocol Guideline

Regulator Receipt of Digitized Protocol (USDM + FHIR)

Operational & EHR-related Uses of Digitized Protocols

From USDM to ICH M11

Alignment with ICH M11

Support for complex studies, interventional & observational studies, and medical devices

Maximise content re-use and support for multiple document templates

Model Extension mechanism to provide flexibility

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M11 is not just *one* document

Guideline

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

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.

Template

Provides 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 TEMPLATE

Draft version

Endorsed on 27 September 2022

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Technical Specifications

Provides technical representation aligned with the guideline and 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

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Guideline

- Explains the need, outlines development

Template

- Specifies headers, common text, instructions, data fields, and terminologies.

Technical Specification

- open, nonproprietary standard to enable electronic exchange of clinical protocol information

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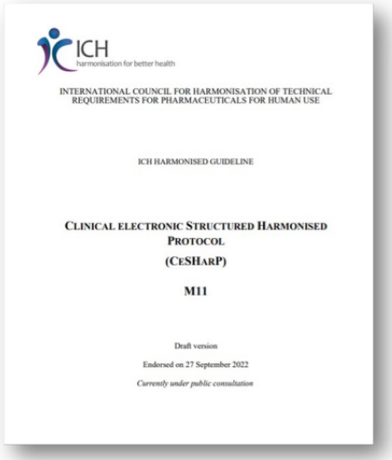
M11 Template can be exchanged using many formats

Guideline & **Template** → **Tech Spec** → **Technical Implementation Guide** → **FHIR Profiles**



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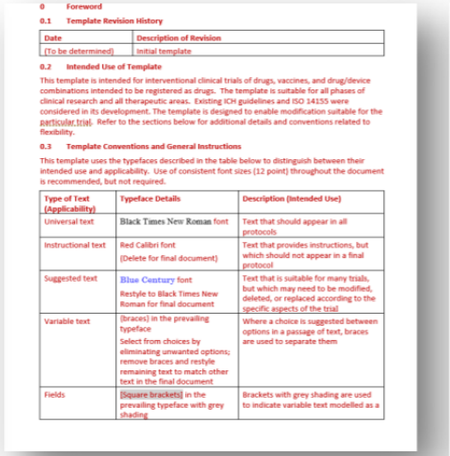


0 Foreword

0.1 Template Revision History

Date	Description of Revision
(To be determined)	Initial template

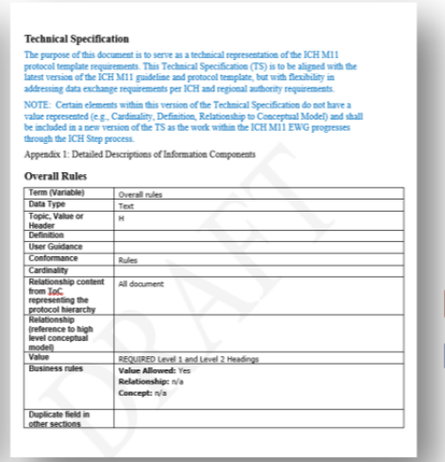
0.2 Intended Use of Template

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	

Electronic Document

Human Readable Form

Machine - Readable Form

Per ICH Regional Requirements

Standard Message Exchange Formats*

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* Technical Implementation Guides may be needed for various use cases

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M11 - Next steps

1.c. Future anticipated key milestones

Expected future completion date	Milestone
Feb. 2025	*Step 2 approval of the draft updated Technical Specification*
Apr. 2025	*Regional Public Consultation on the draft updated Technical Specification*
Jul. 2025	*Adjudication of Public Comments on the Technical Specification*
Oct. 2025	*Updated Guideline, Template and Technical Specification*
Nov. 2025	*Step 3 Sign-off & Step 4 adoption of the Guideline, Template and Technical Specification*
Jan. 2026	*Final versioned training materials*
Feb. 2026	*Step 2 (Testing) of the ICH Technical Implementation Guide for Fast Healthcare Interoperability Resources (FHIR)*
May 2026	*Step 4 adoption of ICH Technical Implementation Guide for FHIR*

ICH_M11_EWG_WorkPlan_2025_0214.pdf

EMA

Vendors Implementing DDF Solutions

1 Solution Collaboration Forum

30+ vendors are part of the Solution Collaboration Forum:

- Applying collective technology. solution provider engagement and enthusiasm in DDF to further solution development

2 DDF Solution Directory

The Solution Directory is a TransCelerate Github page (link here) that hosts a growing list of self-reported solutions which utilize and follow the DDF Unified Study Definitions Model (USDM).

This directory may help companies find DDF solutions and is a constantly growing list!
**TransCelerate does not endorse vendors

3 DDF Solution Showcase Webinar Series

TransCelerate and CDISC are partnering to co-host the DDF Solution Showcase webinar series involving sponsor companies, clinical solution providers, and key industry stakeholders. **The Showcase is an opportunity for qualifying solution providers to share a 30-minute presentation of protocol digitalization solutions followed by a 10-minute Q&A.**

Look out for more information (including registration) in the coming weeks **on the second "DDF Solution Showcase" webinar scheduled for Dec.5, 2024.**

First showcase in this series - conducted on Sept. 26 - showcased two organizations – NNIT and EQTY Life Sciences and ClinLine. Access the webinar recording here

NNIT demonstrated how USDM can be mapped to FHIR standards to enable automated EDC set-up

EQTY/ClinLine showcased the use of USDM standards to facilitate the use and creation of synthetic RWE and RWD arms

*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.

October 10, 2024

DDF in Action Day

Transforming Clinical Trials with Standards and Digitalization

"Continuing the Journey, Charting the Future"

First full day in-person public event with biopharma, solution providers and others held across two locations - J&J, New Jersey and Novo Nordisk, Copenhagen

DDF in Action Day Highlights

- **DDF in Action Day aimed to explore pathways and proofs of concept** to implement DDF solutions in the near- or mid-term
- **Agenda topics included** a keynote and plenary discussion covering various use cases, a solution provider poster session and panel discussion, as well as networking opportunities.
- **Two common themes** surfaced through the day:
  - Leadership engagement and organizational change management (OCM) are critical to success
  - Change is coming. Don't wait to get started

Organizations Represented*

- Amgen
- Ascendis Pharma
- AstraZeneca
- Bayer
- Bristol Myers Squibb
- Eli Lilly
- GlaxoSmithKline
- Johnson&Johnson
- Merck
- Novartis
- Novo Nordisk
- Pfizer
- Recursion
- Regeneron
- Roche
- Sanofi
- Shionogi
- UCB
- CDISC
- ClinLine
- Content Rules
- CTDN
- Data4Knowledge
- EQTY Lifesciences
- EZ Research Solutions
- Faro Health
- Futurpostif Consulting
- NNIT
- Nurocor
- OpenStudyBuilder
- PFMD
- Sycamore Informatics
- TATA Consultancy Services
- Veeva

Scan to register

Registration closes August 15

DDF: Mission Possible! Practical Approaches for Protocol Digitalization - TransCelerate

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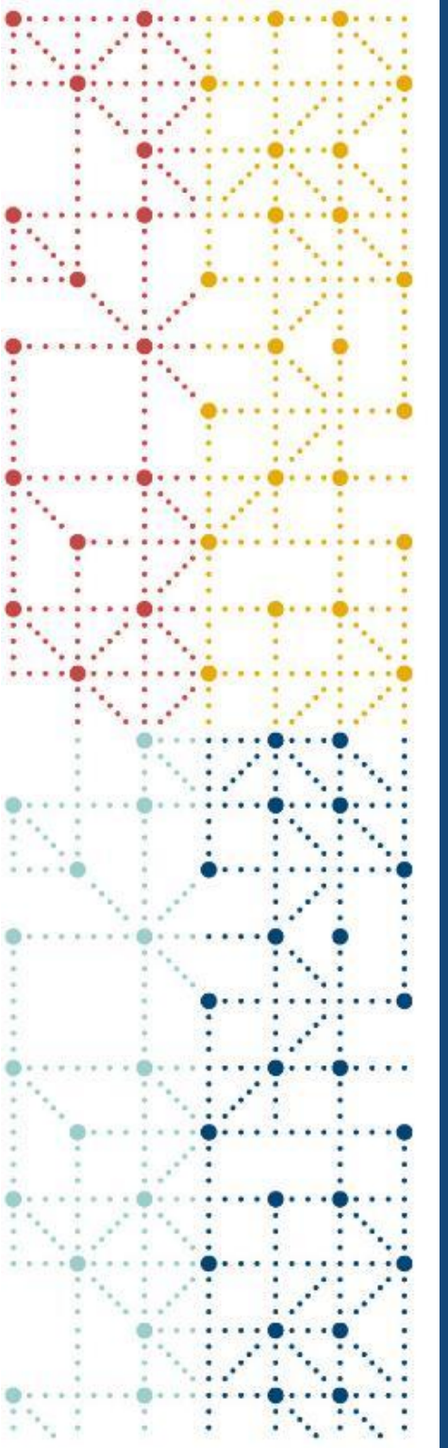

Demo time with the OpenStudyBuilder

Thank You!