



2024 CDISC + TMF
EUROPE INTERCHANGE

The background of this section is a photograph of the Berlin skyline during sunset or sunrise, featuring the TV tower and various buildings.

BERLIN

24-25 APRIL: CONFERENCE & EXPO | 22, 23, 26 APRIL: TRAININGS

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

Dave Iberson-Hurst, CDISC DDF / USDM product Owner
Version 3



Meet the Speaker

Dave Iberson-Hurst

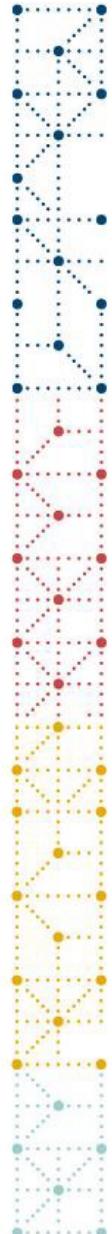
Title: Partner

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.

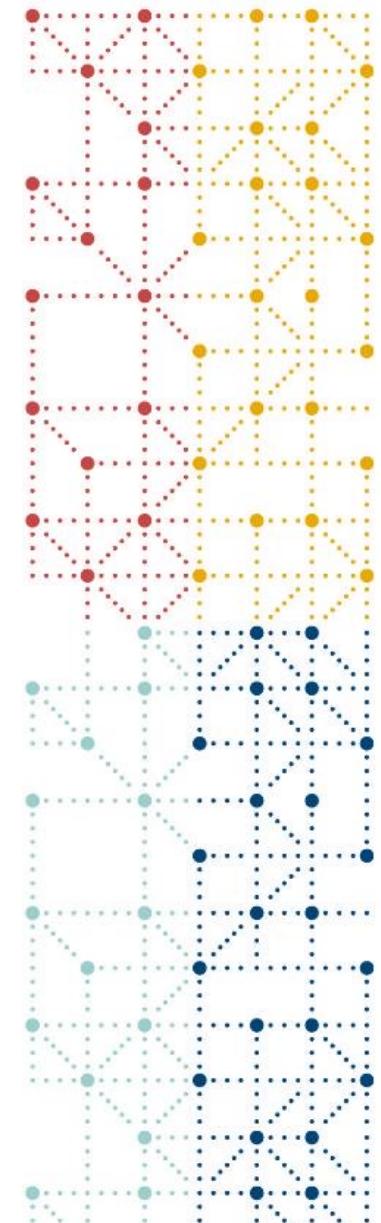
During this time, he has served as the CDISC CTO, worked on, and led, several CDISC teams, presented in many forums in Europe, the US, and elsewhere across the globe. He has worked closely with the FDA, EMA, HL7, ISO, and other standards organizations and was a member of CDISC's Blue Ribbon commission. 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*



Agenda

1. Introduction
2. Drivers for Adoption
3. Current Adoption
4. Resources
5. What's Next
6. Summary

2006



2018



2006

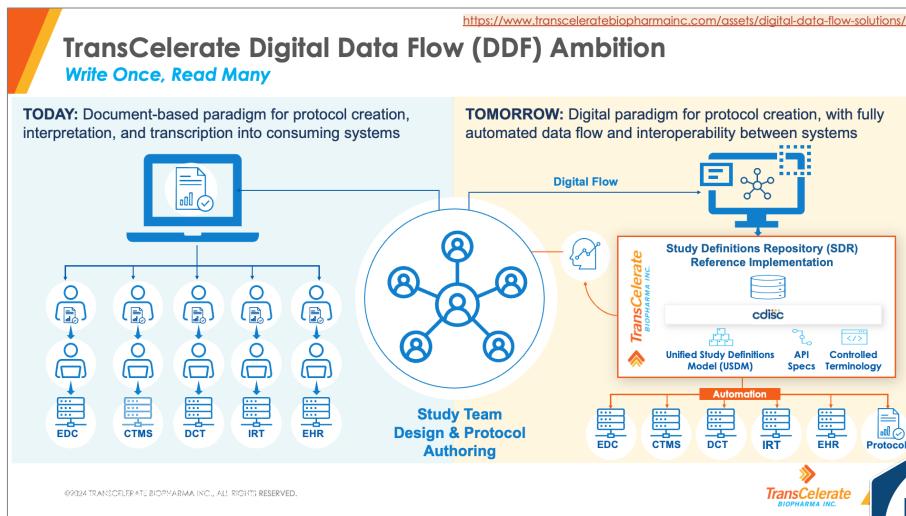


2007 E3C Meeting



2024

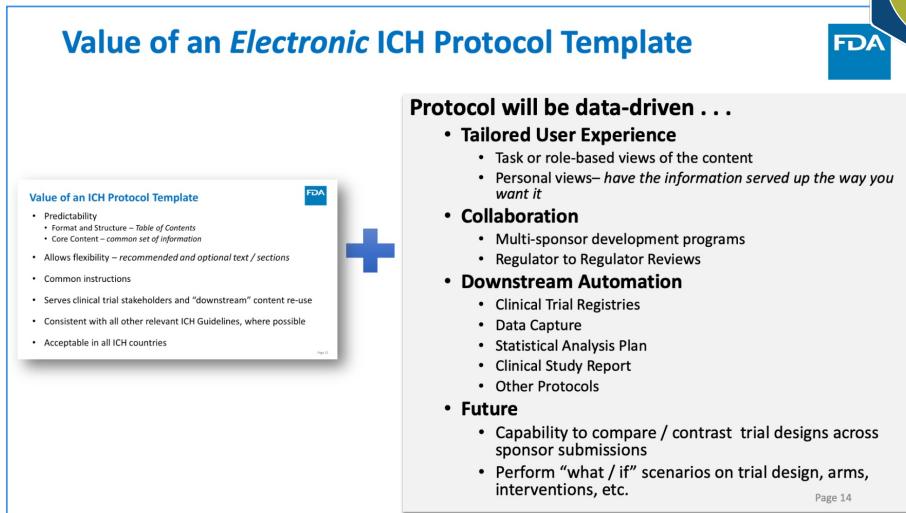
- 2003 Dublin (*not an interchange*)
- 2004 Brussels
- 2005 Paris
- 2006 Berlin**
- 2007 Montreux
- 2008 Copenhagen
- 2009 Budapest
- 2010 London
- 2011 Brussels
- 2012 Stockholm
- 2013 Bad Nauheim (Frankfurt)
- 2014 Paris
- 2015 Basel
- 2016 Vienna
- 2017 London
- 2018 Berlin**
- 2019 Amsterdam
- 2020 Virtual
- 2021 Virtual
- 2022 Virtual
- 2023 Copenhagen
- 2024 Berlin**



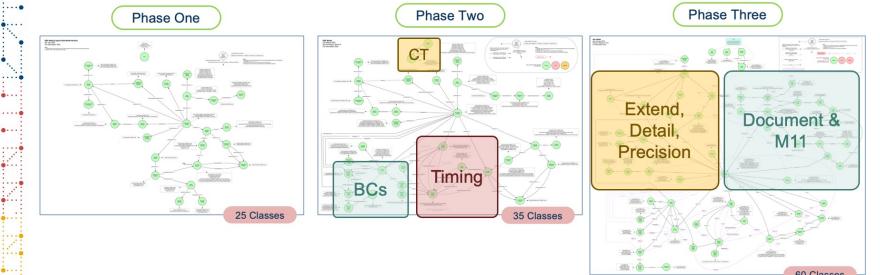
The USDM Standard

Logical Model

6



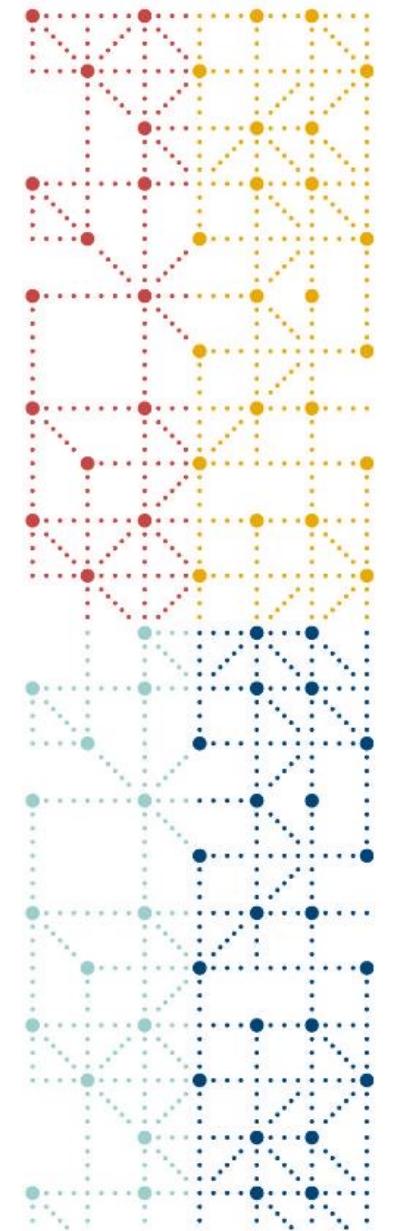
CDISC DDF / USDM: Phases One, Two and Three



- 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) & BCs
- The protocol document still an external entity

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Drivers for Adoption

ICH CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL (CeSharP)



Founding Regulatory Members	Founding Industry Members	Standing Regulatory Members	Regulatory Members	Industry Members
<ul style="list-style-type: none">EC, Europe (EMA)FDA, United StatesMHLW / PMDA, Japan	<ul style="list-style-type: none">EFPIAJPMAPhRMA	<ul style="list-style-type: none">Health Canada, CanadaSwissmedic, Switzerland	<ul style="list-style-type: none">ANVISA, BrazilCOFEPRIS, MexicoEDA, EgyptHSA, SingaporeMFDS, Republic of KoreaMHRA, UKNMPA, ChinaSFDA, Saudi ArabiaTFDA, Chinese TaipeiTITCK, Türkiye	<ul style="list-style-type: none">BIOGlobal Self-Care FederationIGBA



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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.

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



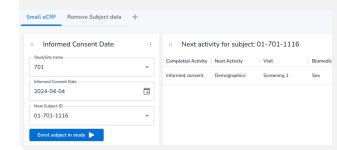
Regulatory

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



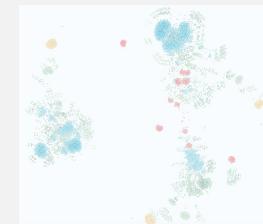
Data Capture

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

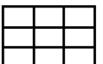


Subject Impact

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

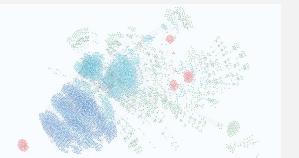
There are many use cases, these are just a few examples

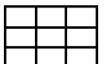
Example Use Cases 2



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

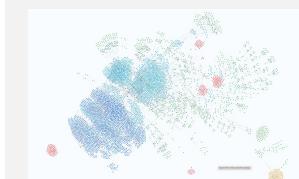
Use of the detailed study design information available within USDM to provide a solid foundation for the automated generation of SDTM data domains





aCRF

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





<ODM> Define.xml

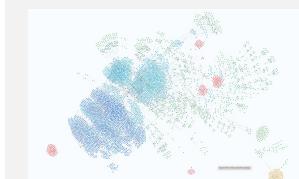
Use of the detailed study design to create a define.xml for the study



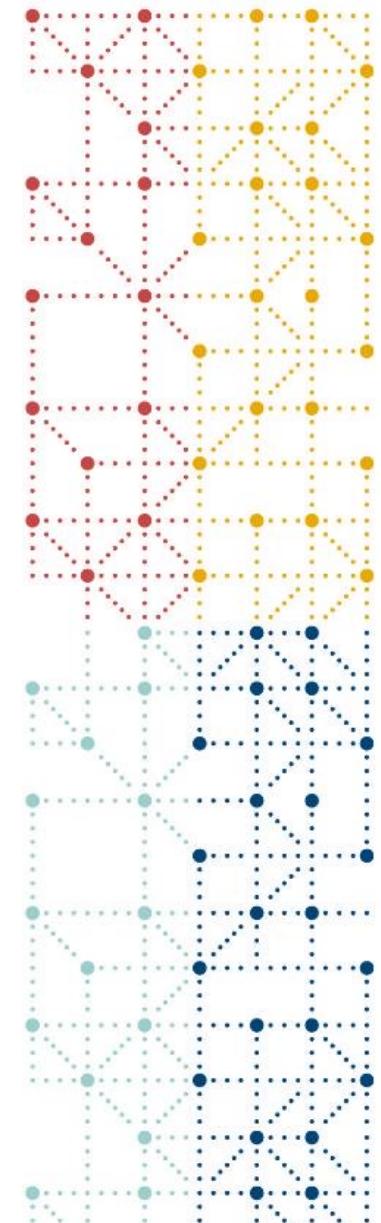


Data Decay

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



Current Adoption

Discovery Day (September 2023)

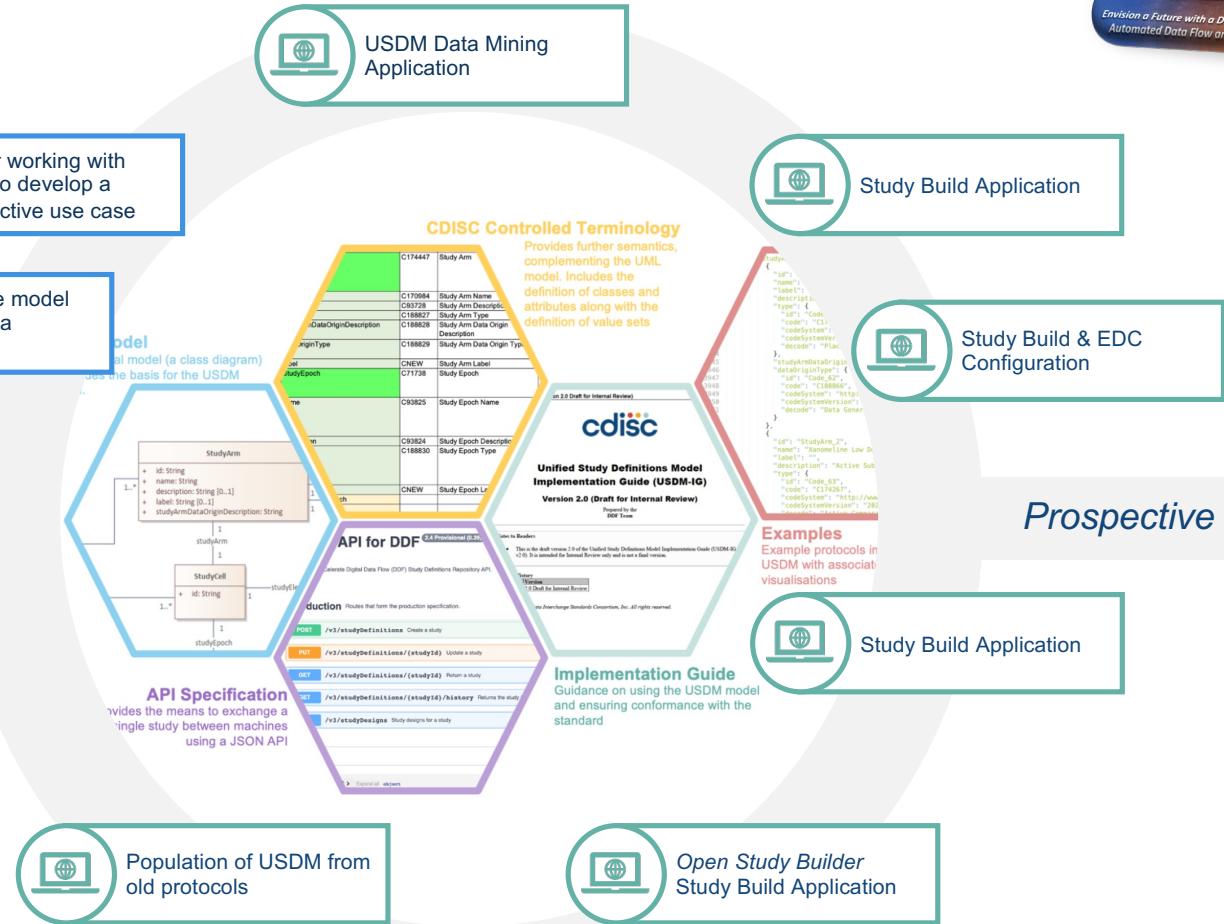


Retrospective has a lower risk as a first point of entry into using USDM

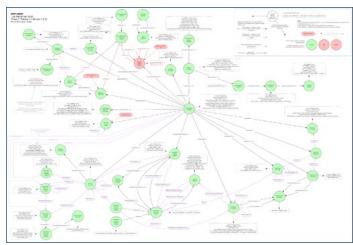
Retrospective Studies

The “footnote conundrum”

- Retrospective study re-creation brings a few challenges
- We are not constrained by the “2D” paper world. USDM enables an “improved” reconstruction
- Sponsors need to consider their “philosophy”, their approach to “reconstruction” of protocols

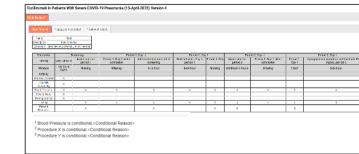


DDF Initiative encompasses technical delivery, change management, and industry engagement

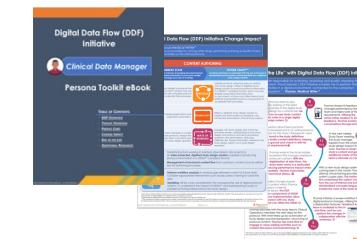


cdisc
Unified Study
Definitions Model
(USDM) Reference
Architecture

TransCelerate's
Study Definitions
Repository (SDR)



Suite of DDF Adoption
Resources, Videos &
Change Management Tools



Continued Industry Collaboration
between TransCelerate, CDISC
ICH, and HL7



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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.

Team Testing

- Three full protocols have been “converted” into USDM
- Another protocol is ready to be upgraded from an earlier USDM version
- Another complex protocol has been provided by a Transcelerate member company
- Also have LZZT in M11 format which could be placed into USDM format
- Add aim to get 7-10 protocols “converted”
- Each takes approximately three days to “convert”

The screenshot shows a web-based utility titled "USDM Excel to JSON Utility". At the top right are navigation icons for a menu, search, and refresh. Below the title is a section titled "Excel File List" with a sub-section "File List.". It displays a single item: "CDISC_Pilot_Study.xlsx, loaded at 2024-04-20, 07:52:42Z". To the right of the file name are several small icons: a red folder, a trash can, a green document, a blue document, an orange bug, a white document with a 'W', a gear, and an alarm clock. Below this section is another titled "Upload New Excel File" with a "CLICK TO UPLOAD NEW FILE" button.

Team Testing – Use Cases

- What do I wish to structure?
 - SoA
 - Inclusion & Exclusion Criteria
 - Objectives & Endpoints
 - Amendments
 - Interventions
 - Populations
 - ... and more
- What are the use case(s) for the resulting structured protocols?
 - Use in new protocols
 - Learning from mistakes (e.g. amendments)
 - Searching old studies
 - ...etc
- Doing a few protocols manually teaches you a lot, allows you to think about the mechanics and aims of any automated process



USDM Training, Berlin, April 2024

	Screening 1	Screening 2	Baseline	Week 2	Week 4	Week 6	Week 8	Week 12	Week 16	Week 20	Week 24	Follow Up	Week 26	Week 28	Week 30
Study drug record , Medications dispensed, Medications returned	X	X	X	X	X		X		X		X	X			
TTS Acceptability Survey													X		
ADAS-Cog	X ¹		X			X			X			X			
CIBIC+	X ³		X			X			X			X			
DAD	X ⁴		X			X			X			X			
NPI-X	X ⁵		X	X	X	X	X	X	X	X	X	X	X	X	X

1 Performed if patient is an insulin-dependent diabetic

2 Practice only - It is recommended that a sampling of the CIBIC+, ADAS-Cog, DAD, and NPI-X be administered at Visit 1. Data from this sampling would not be considered as study data and would not be collected.

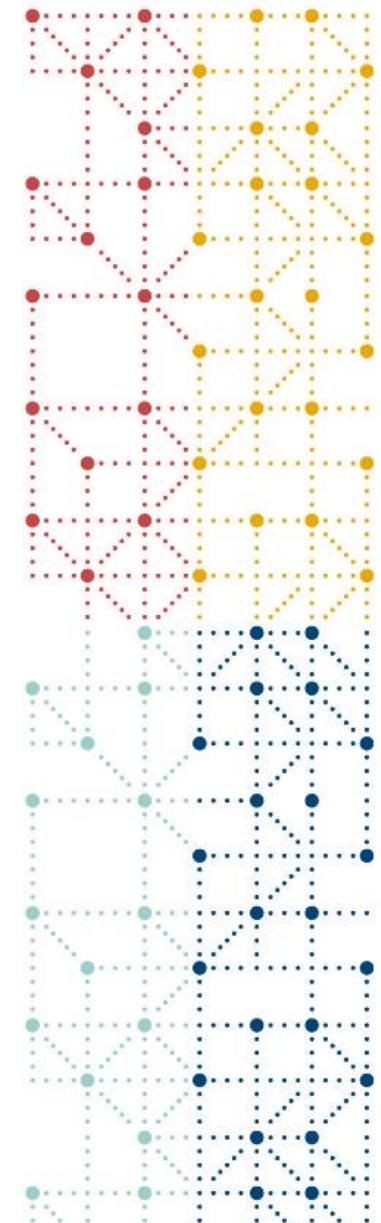
3 Practice only - It is recommended that a sampling of the CIBIC+, ADAS-Cog, DAD, and NPI-X be administered at Visit 1. Data from this sampling would not be considered as study data and would not be collected.

4 Practice only - It is recommended that a sampling of the CIBIC+, ADAS-Cog, DAD, and NPI-X be administered at Visit 1. Data from this sampling would not be considered as study data and would not be collected.

5 Practice only - It is recommended that a sampling of the CIBIC+, ADAS-Cog, DAD, and NPI-X be administered at Visit 1. Data from this sampling would not be considered as study data and would not be collected.



This relates to existing protocols being digitized (retrospective use case) not the authoring of new protocols



Resources

Example Resources – CDISC

Digital Data Flow

<https://www.cdisc.org/ddf>

Overview What is the USDM Participate Webinar Versions FAQ Contact Us

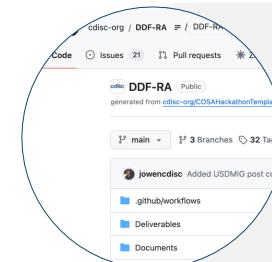


Welcome to Digital Data Flow (DDF) for Clinical Trial Protocols

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.

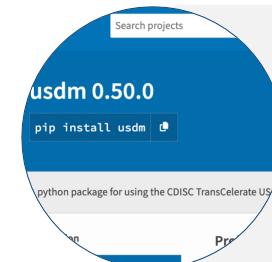
Below are a list of the different websites sourcing specific content and resources. Depending on where you are in the journey, please feel free to explore the different websites and their information.

 CDISC DDF Website You are here!	 DDF Website	 DDF GitHub	 Transcelerate DDF Initiative Solutions
Learn about the Unified Study Definitions Model (USDM) Reference Architecture supporting Protocol Standards	As the main website for DDF, learn and access all resources supporting DDF	Learn about and access the Study Definitions Repository Reference Implementation	Learn about DDF background and initiative roadmap
Target Audience: Those interested in data standards	Target Audience: All those interested in implementing DDF Solutions	Target Audience: Those interested in SDR development	Target Audience: All those generally interested



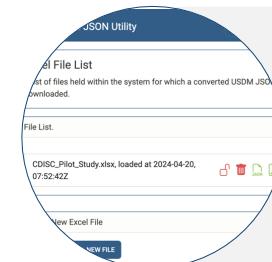
CDISC Github housing the USDM deliverables (model, CT, API etc) along with examples of protocols placed into USDM.

<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

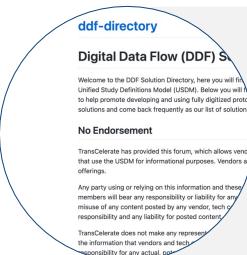
The screenshot shows the TransCelerate Digital Data Flow initiative page. At the top, there's a back-to-solutions button and a main title "Digital Data Flow". Below the title, a paragraph describes the initiative's goal: moving from manual study start-up asset creation to a fully automated dynamic, study start-up readiness solution. There are four main navigation links: "INITIATIVE SOLUTIONS" (highlighted in orange), "KEY RESOURCES", "INITIATIVE OVERVIEW", and "NEWS ARTICLE: DEVELOPMENT OF DIGITAL DATA FLOW". To the right, there's a "DIGITAL DATA FLOW OVERVIEW VIDEO" button with a play icon.

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



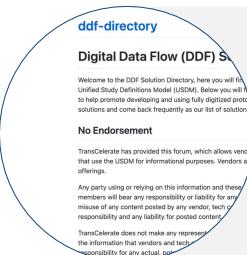
TransCelerate web page holding a significant number of DDF and USDM resources including the persona guides

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



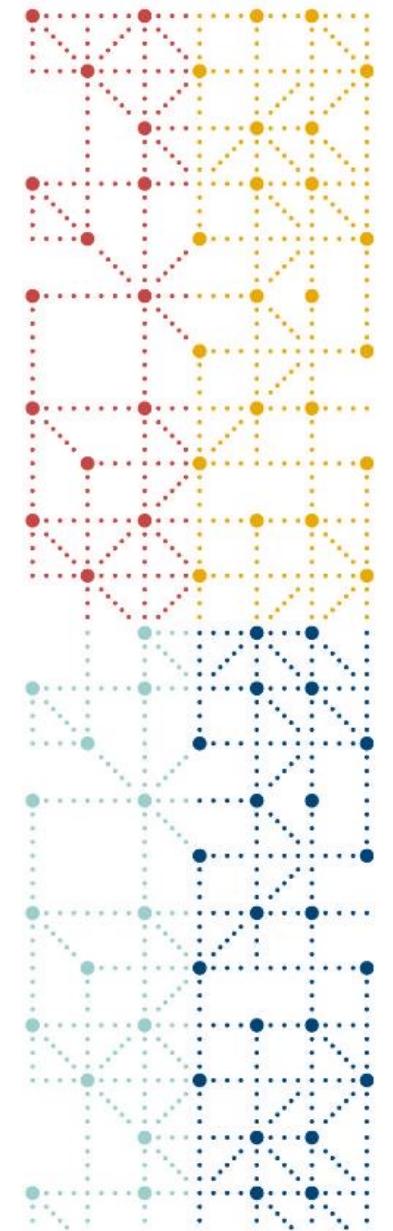
Github housing the source for the Study Definition Repository (SDR) Reference Implementation of the USDM

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



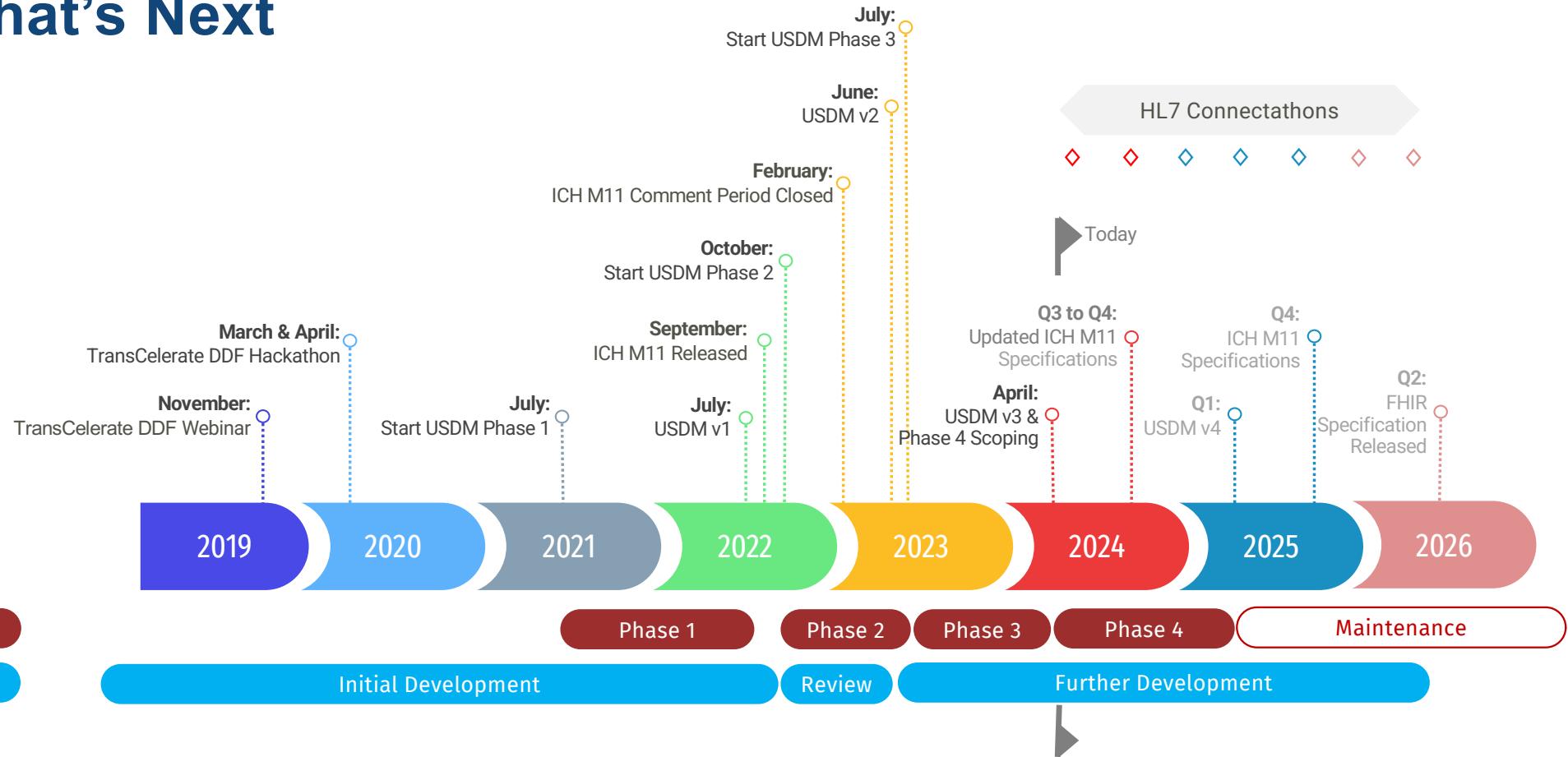
DDF solutions directory. A growing list of self-reported solutions which utilize and follow the DDF Unified Study Definitions Model (USDM)

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



What's Next

What's Next



DDF: Digital Data Flow

USDM: Unified Study Definitions Model

ICH: International Council for Harmonisation

M11: Clinical electronic Structured Harmonised Protocol (ceSHarP)

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

CDISC and ICH Technical Development

ICH M11 Specifications

The image shows three ICH M11 specification documents side-by-side. Each document has a blue header with the ICH logo and 'INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE'. The first document is titled 'CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL (CESharp) M11'. The second is 'CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL (CESharp) M11 TEMPLATE'. The third is 'CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL (CESharp) M11 TECHNICAL SPECIFICATION'. All three documents mention 'Draft version' and 'Endorsed on 27 September 2022'.

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

USDM

Existing Formats (e.g. CTRs)

DDF/USDM

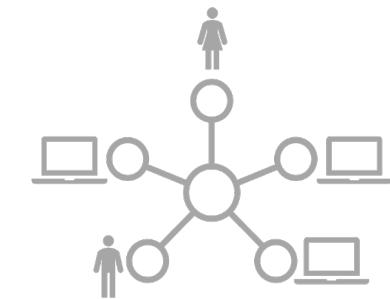
HL7 FHIR

PDF

DOCX

XML, JSON

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Exchange

Protocol information exchanged seamlessly between humans and machines allowing for ease of creation and consumption.

USDM

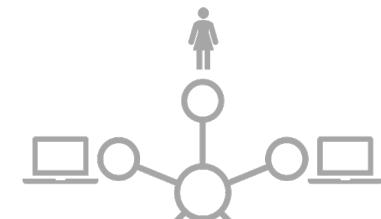
A logical view of a protocol and study design information for use across the pharmaceutical enterprise

Transport

Transported between machines using existing and new formats such as DDF/USDM and FHIR (serialised as JSON or XML) with the ability to render the entire document into a human-readable form.



CDISC and ICH Technical Development



ICH M11 Specifications



April 30th, 5-6pm CET



Utilizing the Digital Protocol Webinar Series



Apr
30

11:00 – 12:00 pm EDT
08.00 – 09.00 am PDT
17.00 – 18.00 pm CET

UDP Webinar 1: Collaborating to Digitize Exchange of Clinical Research Protocol

The Vulcan FHIR® Accelerator Project Utilizing the Digital Protocol (UDP) is a collaborative effort among Vulcan, CDISC, ICH M11, and TransCelerate, to enable an electronic exchange standard for the ICH M11 Clinical electronic Structured Harmonised Protocol (CeSHarp).

The webinar will provide an introduction to all aspects of the project and future webinars will do deeper dives into the project.



<https://www.linkedin.com/events/7186665509034110976/>



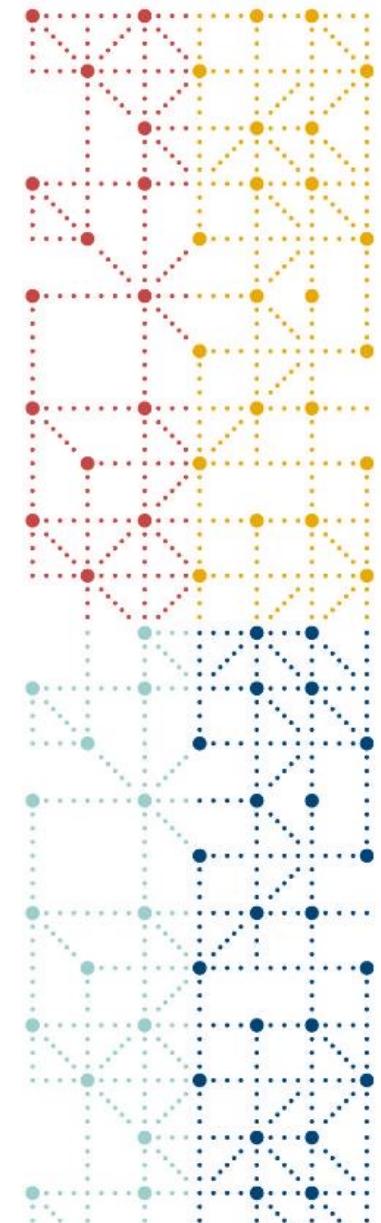
Formats
(e.g. CTRs)

XML, JSON

or XML) with the ability to render the entire document into a human-readable form.



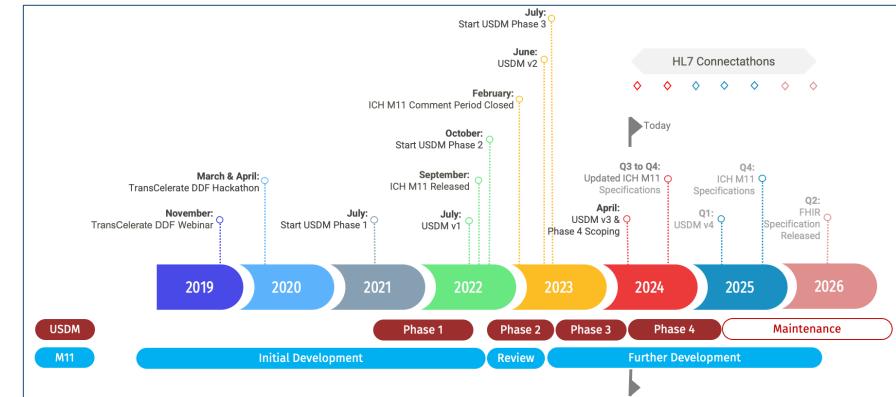
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Summary

Summary

- A demonstrable & implementable logical model capable of structuring and holding an entire protocol
- The model supports any protocol format, in particular:
 - Sponsor template(s)
 - TCB CPT template
 - ICH M11 template
- Initial proof-of-concept of CORE rules validating USDM content
- Collaboration with ICH M11, EMA and FDA working together on the HL7 Vulcan FHIR Utilizing the Digital Protocol (UDP) project
- Sponsors and vendors have started to pilot and implement
- Phase 4 commencing



Contacts:

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CDISC Team:

- | | |
|---|--|
| <ul style="list-style-type: none">• Gerry Campion• Drew Mills• Erin Muhlbradt | <ul style="list-style-type: none">• John Owen• Berber Snoeijer• Craig Zwickl |
|---|--|