PHUSE SDE UTRECHT, SEP 2023

Insights into the TransCelerate DDF Initiative and the corresponding CDISC USDM data model

TransCelerate BIOPHARMA INC.

cdisc Clear Data. Clear Impact.

Clin Line

Content

- Introduction
- TransCelerate DDF
- CDISC DDF / USDM / M11
- Q&A

Background

- ClinLine
- TransCelerate
- CDISC

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TransCelerate is a Not-for-Profit Entity Created to Foster Collaboration

Our mission is to collaborate across the global biopharmaceutical R&D community to identify, prioritize, design, and facilitate the implementation of solutions designed to drive the efficient, effective, and high-quality delivery of new medicines.

A Member-Driven Mission

Experts from across our participating Member Companies dedicate their time to TransCelerate.

TransCelerate **identifies the issues and challenges** facing our industry.

TransCelerate **designs and delivers practical solutions** for global adoption by any stakeholder.

Who are our Members?

View a full list of our members

Membership* is available to biopharmaceutical research and development organizations that engage in innovative discovery, development and manufacturing of new medicines

* to be eligible for membership, companies must meet specified eligibility criteria.

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Our Collaboration is Worldwide

Since inception, TransCelerate has prioritized robust collaboration with key stakeholders across the R&D ecosystem.

View select translated solutions here.

Patient Advocacy Community

CROs, Technology & Data Providers

Global Health Authorities

Clinical Research Sites and Academic Research

Industry Consortia

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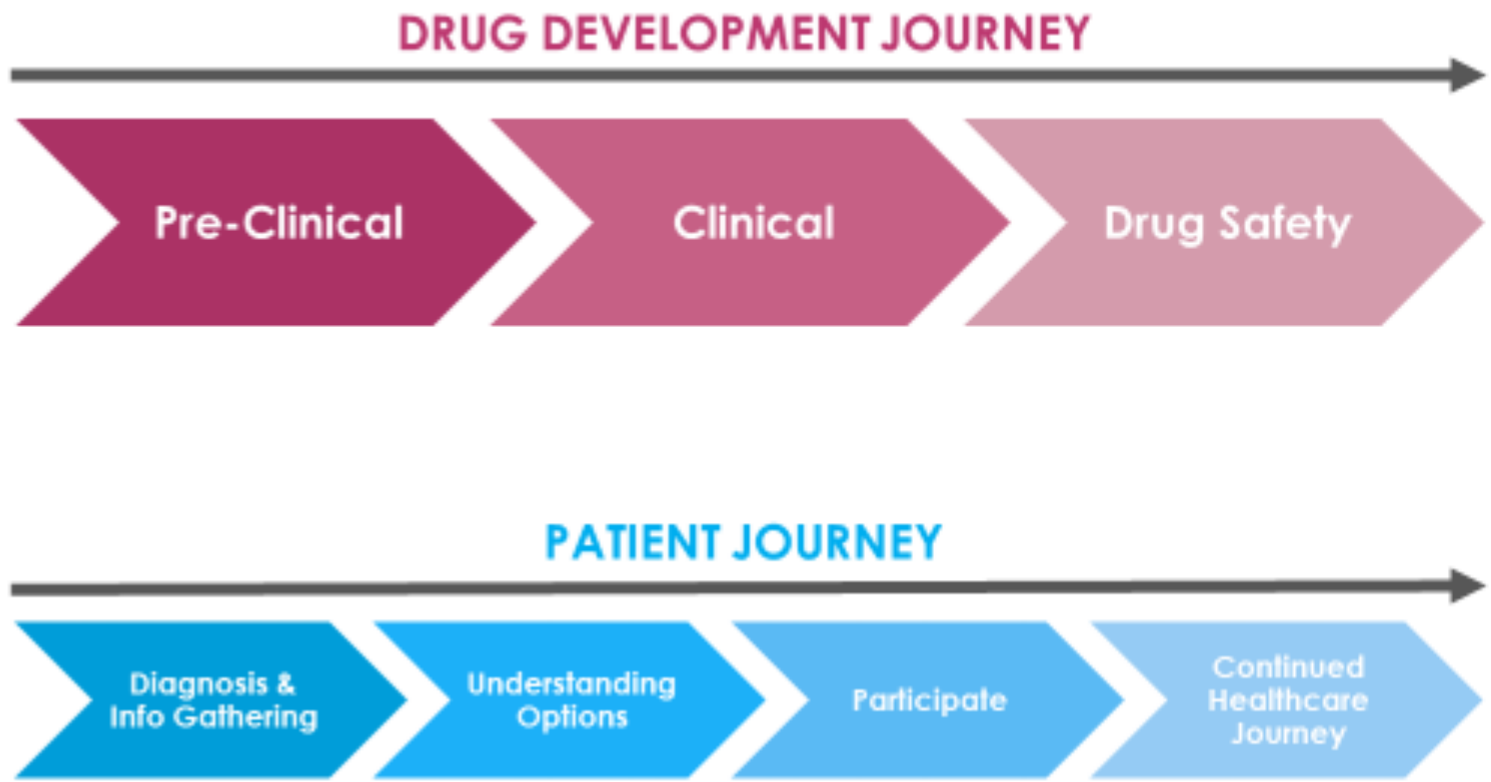
Our approach is pragmatic. Our solutions are transformative.
Our aim is to modernize drug development and improve patients' lives.

Our Strategic Programs

- Enhance Drug Safety
- Enhance Sponsor Efficiencies
- Harmonize Process
- Improve the Patient Experience
- Improve the Site Experience
- Share Information



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The Challenge

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.

Custom collections of systems used to power a study, often varying by research partner or individual study team

Expanding systems & data landscape used in clinical studies (EHR & eSource, mHealth)

Manual transcription from documents (e.g., protocol) to multiple systems

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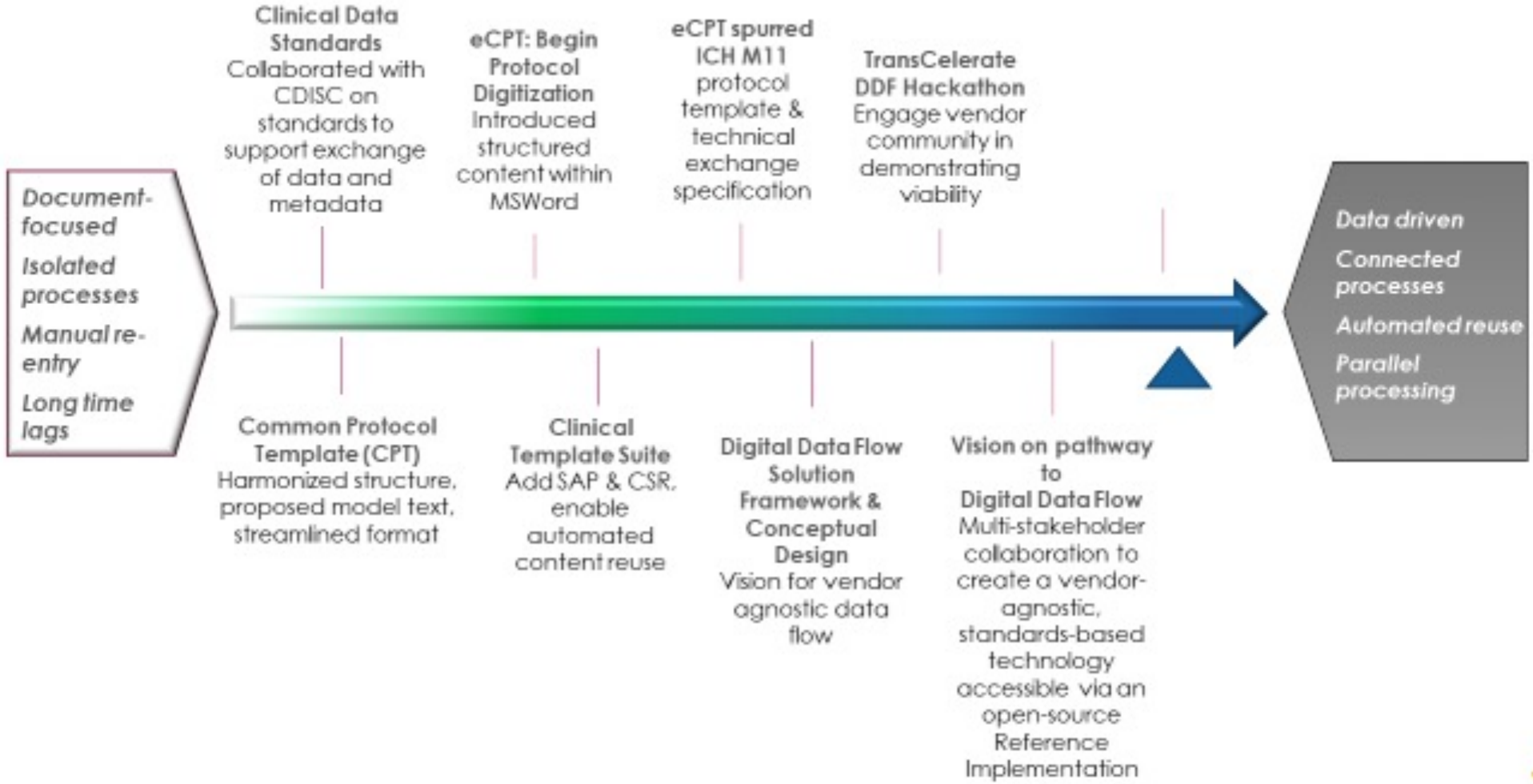
TransCelerate is part of a journey to break down barriers to industry transformation



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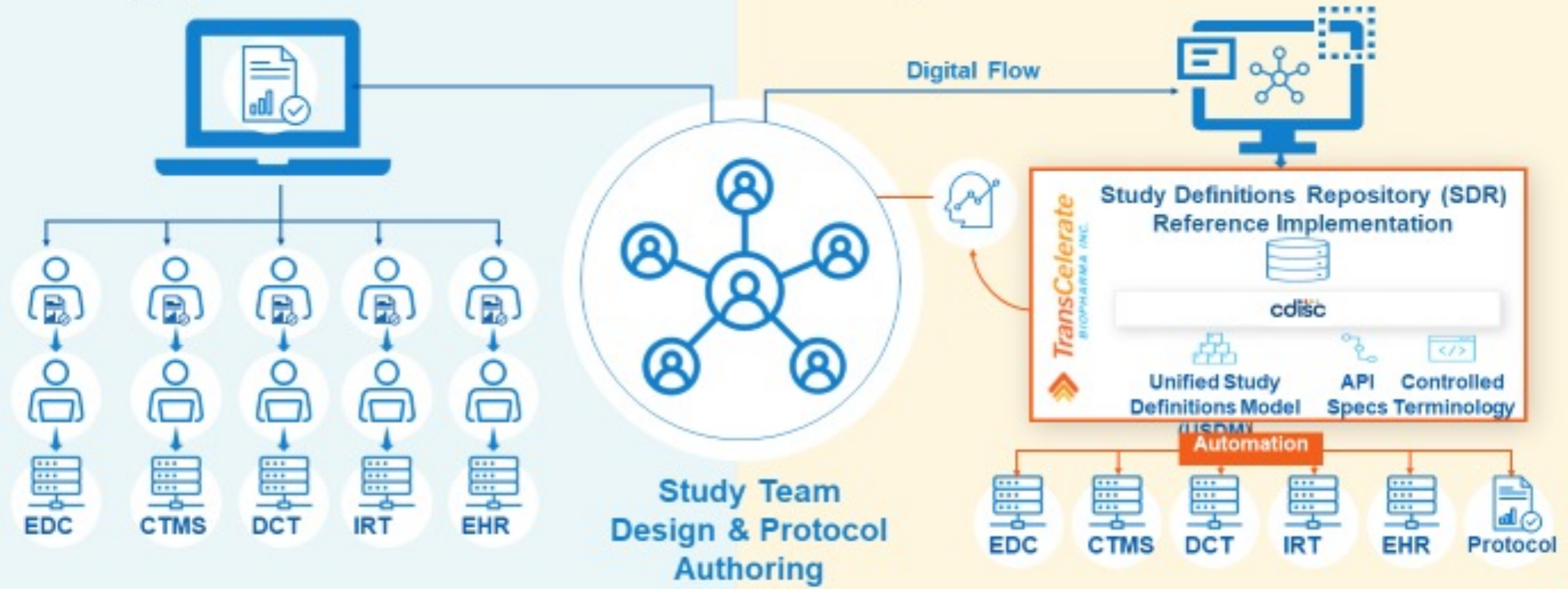
TransCelerate Digital Data Flow (DDF) Initiative Ambition

Documents to Data / 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



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The Digital Data Flow Initiative (DDF) aims to break the document paradigm to enable seamless flow of the data within

Digitized Protocols

Enabling the use of technologies that identify and assemble study elements allows industry to move to digital protocols

Connectivity of Data and Processes

Enabling traceability, automated flow of content to key clinical documents, and automation to clinical & operational systems (e.g.. EDC, CTMS)

Advanced Analytics

Better enabling the use of advanced analytics such as Artificial Intelligence and Machine Learning to improve study designs

Open and Flexible Solution

Developing a dynamic, fully automated solution that is vendor agnostic, open and flexible

Development principles to enable broad collaboration, stakeholder input, and sustainability

- Open Source
- Vendor Agnostic
- Agile Development
- Dynamic Alignment to Standards

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Where are we going next?

Key Focus Areas on the Digital Data Flow Roadmap

Digitization of Study Elements and Downstream EDC Automation (Completed July 2023)

Accomplished in the MVP Phase and Phase II (recently completed)

- Support electronically populating and configuring EDC/CRFs based on the digital protocol specification
- Use digital protocol specification to demonstrate (as a proof of concept) the population of elements in a human readable protocol document

Complete Protocol Digitization & Regulatory Alignment (In Progress for 2024)

Includes collaboration through the Vulcan Working Group between ICH M11 & CDISC

- Complete (100%) digitization of all protocol elements in alignment with M11 and relevant CDISC SDTM domains
- Begins with gap analysis between USDM and ICH M11 content model, CDISC SDTM, and Global Trial Registry Reporting
- Goal to capture "breadth" of ICH M11 completely within USDM, followed by greater "depth" of structured content within model (e.g., structured I/E criteria)

Expand Downstream Connectivity (In Progress for 2024)

Includes collaboration with expanding community of tech solution providers across range of clinical solutions

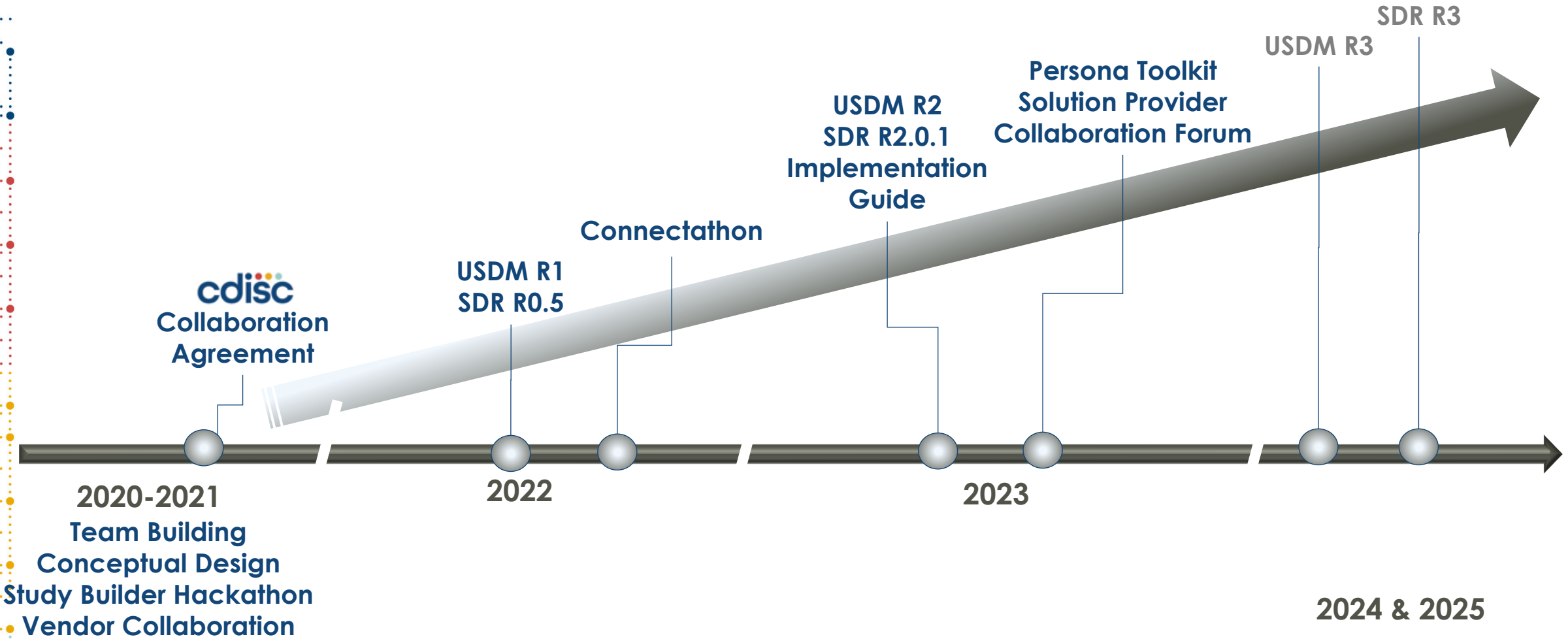
- Further develop USDM to enable downstream connectivity with priority systems, enabling a future state of "write once, read many times"
- Work collaboratively with the vendor ecosystem to better understand existing gaps and development requirements for the USDM

Alignment with Point of Care (In Progress for 2024)

Includes collaboration with Vulcan FHIR Accelerator

- Comparative assessment of USDM and FHIR
- Alignment of DDF and FHIR resources for end-to-end enablement of EHR workflow set-up and eSource

DDF Timeline



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Digital Data Flow

- **Phase 1**
  - Base model design
    - UML
    - API
    - Controlled Terminology
  - Topics
    - Objectives and endpoints
    - High Level Study Design
    - Eligibility criteria
    - Activities and assessments
    - Basic schedule of activities and assessments
    - Basic data collection configuration related to activities and assessments

- **Phase 2**
  - Extended model
    - UML
    - API
    - Controlled Terminology
    - USDMIG
    - Example Data
  - Topics
    - Enable greater population of study set-up elements
    - Represent structured study design information for more complex trials
      - Handling of complex study timing
    - Support electronic data capture (EDC) automation
      - Expand model to include Biomedical Concepts
    - Demonstrate population of the TransCelerate Common Protocol Template (CPT)
    - Demonstrate population of SDTM Trial Design Domains

https://www.cdisc.org/ddf

CDISC Study Definition Repository RA Deliverables

Unified Study Definitions Model (USDM) Class Diagram

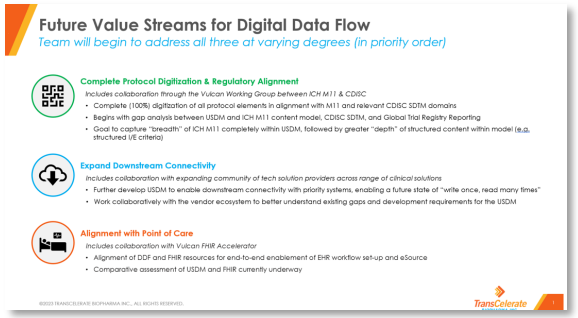
Application Programming Interface (API) Specification

CDISC Controlled Terminology

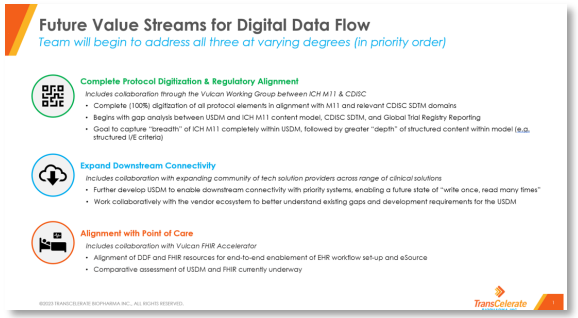
USDM Implementation Guide

DDF 3 USDM Scope

- Represent ICH M11 in USDM
- SDTM Trial Design Population
- Clinical Trial Registry Population
- Complex Studies/Cohorts
- Model Enhancements

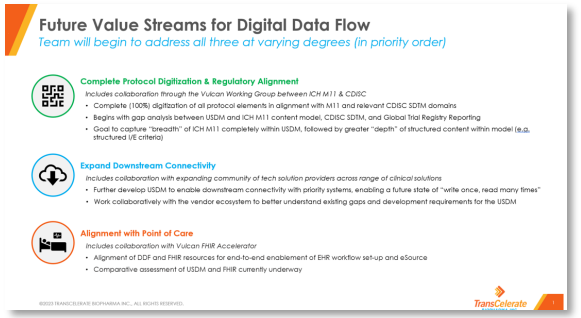


DDF 3 USDM Scope



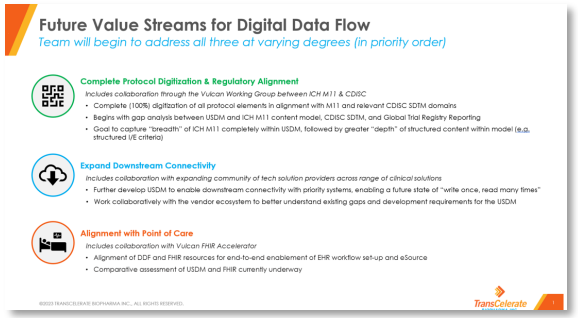
- Include breadth of ICH M11 into the USDM
  - Narrative Content
    - Covers free text parts of the M11 specification (i.e., without data elements)
  - Structured content
    - Using data elements to build sections of text
    - Individual structured elements (e.g., Study acronym, phase)
- SDTM Trial Design Population
  - Population of the planning parts of the SDTM trial design information
  - Some mapping performed in DDF 2
  - Additional mapping to allow population of existing SDTM trail design information (particularly the FDA required parameters)
  - Identification of new alignments between ICH M11 and SDTM trial design artefacts
    - What other trail design elements from the ICH M11 protocol could we represent in SDTM T domains
- Clinical Trial Registry Population
  - Expand on existing CTR.xml standard
  - POC to show population of structured fields from USDM for registering and updating studies in clinical Trial registries

DDF 3 USDM Scope

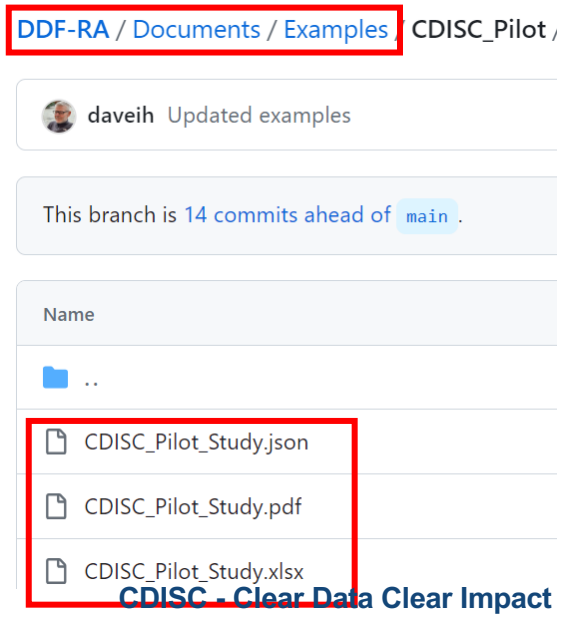


- Complex Studies, Complex Cohorts
  - Enhancements to ensure the model can hold complex study designs with complex cohorts
  - Allow for more modern protocol designs (e.g., basket trials, adaptive trials)
  - Include feedback from users of USDM v2.0
- Model Enhancements
  - Create a true logical data model with logical relationships that are visible and understandable with a separate document that details the API step to enable serialization to produce the required JSON
  - Improve element naming for consistency and standardize some elements within each class (e.g., name, description fields)
  - Improve general readability of the UML model

DDF 3 USDM Supporting Documentation

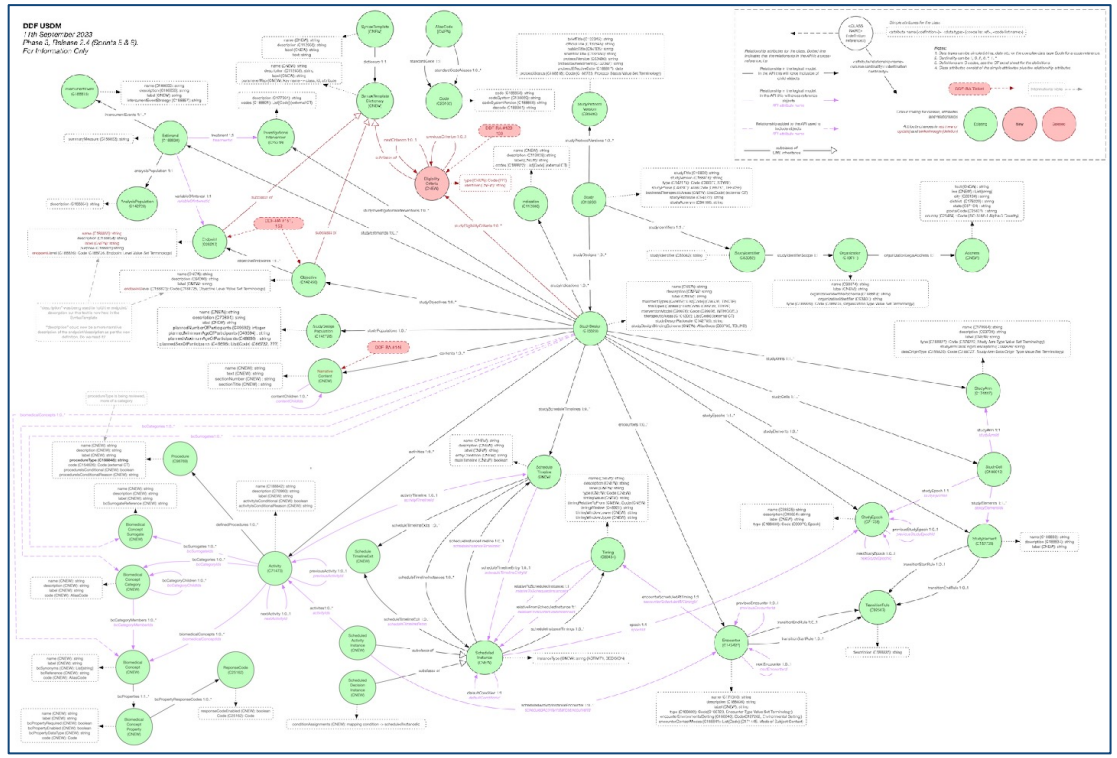


- USDMIG
  - Improve USDMIG content based on user feedback
  - Add additional Guidance for new elements added to the model
- USDM Test Data
  - Maintain test data developed during DDF2 to include new elements added to the model
  - Develop new test data for more complex study designs



Shift of Focus

- Phases One & Two
  - Focused on the structured elements of the protocol, e.g. the Schedule of Activities (SoA)
  - The protocol document was an external entity into which the structured content could be exported
- Phase Three
  - Now contains structured and unstructured elements
  - The entire protocol document is held within the USDM
  - Allows for the protocol document to be generated from the model



ICH M11, CDISC & HL7

- "FHIR-based exchange standard for ICH's Clinical electronic Structured Harmonised Protocol (CeSHarP), aligned to CDISC standards"
- The USDM and CDISC CT will be used in the project
- Initial project discussions have been underway for a few months

For Immediate Release

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Vulcan FHIR® Accelerator Connects CDISC, HL7, and ICH M11 in a Project to Digitize Exchange of Clinical Research Protocols

HL7 Vulcan and CDISC are announcing a project that will deliver an electronic exchange standard for the ICH M11 Clinical electronic Structured Harmonised Protocol (CeSHarP)

Ann Arbor, MI. and Austin, TX — June 6, 2023 — A structured, harmonized, digitized protocol accessible to the biopharmaceutical industry and to researchers in the care setting will enable transformations to improve clinical research. The project announced by HL7 Vulcan and CDISC will build on work products of ICH M11 to accelerate this vison. Vulcan is an HL7® FHIR Accelerator dedicated to connecting clinical and translational research to clinical care through Fast Healthcare Interoperability Resources (FHIR®). CDISC is a non-profit standards development organization that develops standards that support acquisition, exchange, submission, and archive of biopharmaceutical data. CDISC is also a member of Vulcan. ICH M11 is the topic of the International Council for Harmonization to create a Clinical electronic Structured Harmonised Protocol (CeSHarP).

"The project marks an important milestone in the long journey towards a digital protocol." said Vulcan Co-Chair, Amy Cramer. "Over the years, various organizations have contributed key building blocks. Vulcan is pleased to serve as a convener where contributors across the global research community can collaborate towards this shared and important goal."

"We are looking forward to partnering with ICH M11 and HL7 on this important project that aims to enable the digital transformation of protocols in support of automation," said David Evans, President and CEO, CDISC. "This project represents another step in CDISC's strategic evolution to embrace governance of clinical research information standards, not just clinical data standards."

CDISC M2/M11 engagement

01 Controlled terminology, code lists, content nomenclature.

02 Define Content model to represent content agnostic of exchange standard.

03 Determine conformance rules for M11 model.

04 Collaborate with ICH M2/M11 on defining mappings between M11 model and CDISC Standards and Artifacts.

05 Joint project with Vulcan FHIR accelerator to deliver an electronic exchange standard for the ICH M11.

* CDISC Europe Interchange, 26-27 April, Panagiotis Telonis, EMA

PUBLIC

DDF USDM Model Information Graphic

DDF-RA / Documents /

daveih Updates after review

Name
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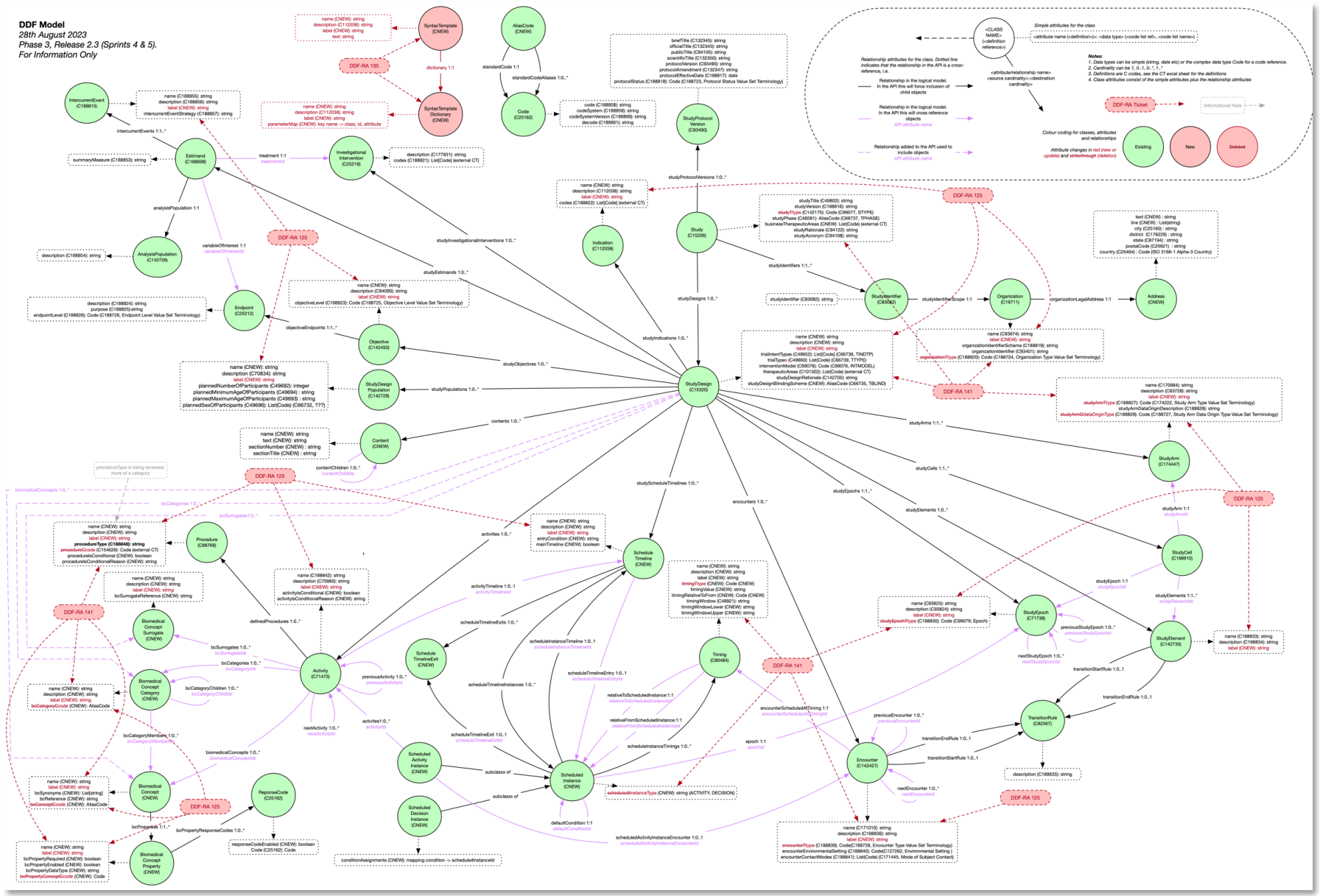
Examples
DDF USDM Model Informative.graffle
DDF USDM Model Informative.png
DDF USDM Model Walkthrough.pdf
README.md



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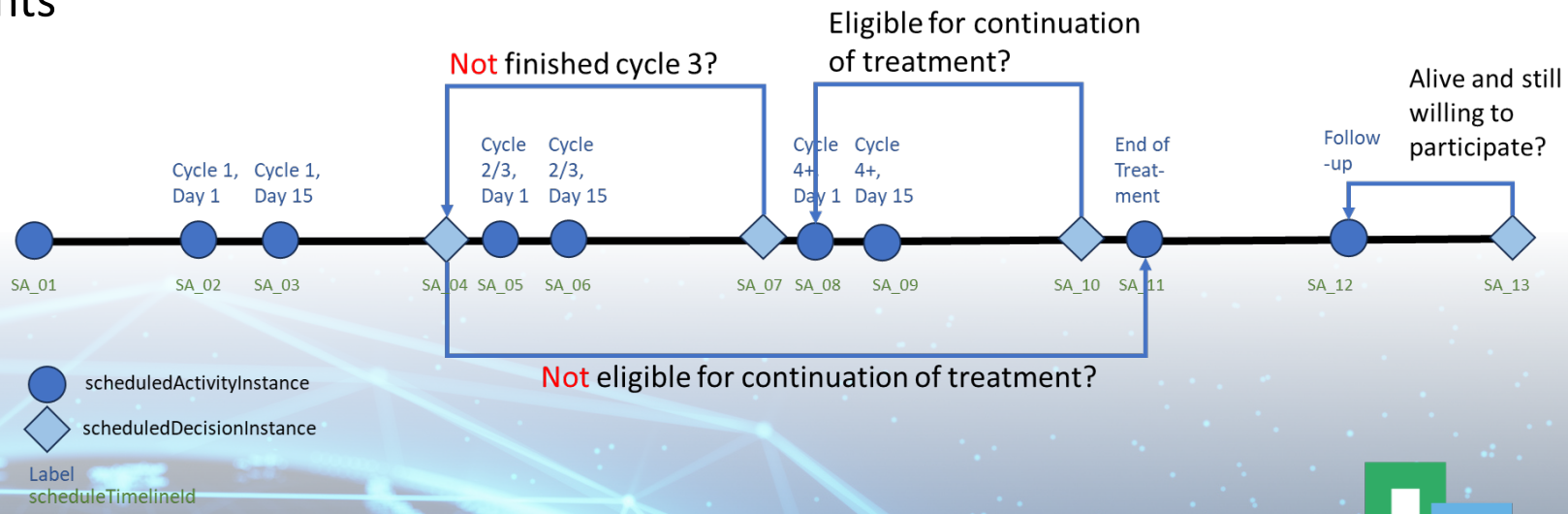
Insights: translate SoA to timelines

- Logical representation
- Account for most footnotes
  - Timing within an encounter
  - Conditional assessments
- Allowing for
  - sub-timelines
  - Cycles
  - Unscheduled / provisional visits



Insights: map to SDTM TS

- Variable mapping
- Grouping + Sequencing
  - Medications
  - Objectives/endpoints
  - …
- Coding
  - Indications
  - Identifiers
  - …

Code	Codelist Code	Codelist Extensible (Yes/No)	Codelist Name	CDISC Submission Value	CDISC Synonym(s)	CDISC Definition	NCI Preferred Term	USDM Entity Name	USDM Role	USDM Item Name
C101302	C66738		Trial Summary Parameter Test Code	THERAREA	Therapeutic Area	A knowledge field that focuses on research and development of specific treatments for diseases and pathologic findings, as well as prevention of conditions that negatively impact the health of an individual. (NCI)	Therapeutic Area	StudyDesign	Attribute	therapeuticAreas
C112038	C66738		Trial Summary Parameter Test Code	INDIC	Trial Disease/Condition Indication; Trial Disease/Condition Indication Description	The textual representation of the condition, disease or disorder that the clinical trial is intended to investigate or address.	Trial Indication	Indication	Entity	Indication
C112038	C66738		Trial Summary Parameter Test Code	INDIC	Trial Disease/Condition Indication; Trial Disease/Condition Indication Description	The textual representation of the condition, disease or disorder that the clinical trial is intended to investigate or address.	Trial Indication	Indication	Attribute	indicationDescription
C142175	C66738		Trial Summary Parameter Test Code	STYPE	Study Type; Study Type Classification	The nature of the investigation for which study information is being collected. (clinicaltrials.gov)	Study Type	Study	Attribute	studyType
C48281	C66738		Trial Summary Parameter Test Code	TPHASE	Trial Phase; Trial Phase Classification	A step in the clinical research and development of a therapy from initial clinical trials to post-approval studies. **Note:** Clinical trials are generally categorized into 4 (sometimes 5) phases. A therapeutic intervention may be evaluated in two or more phases	Trial Phase	Study	Attribute	studyPhase

Summary/Conclusions

- DDF and corresponding USDM RA are game-changing especially with the introduction of M11
- Although still improving and in development, USDM can already be used for covering most of the study design.
- Implementation guide and education on how to implement USDM is in progress.
- Most importantly: USDM is the basis for end-to-end automation!

More information

- Contact
  - B.Snoeijer@clinline.eu
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  - WWW.ClinLine.eu
- Presentations / webinars
  - CDISC DDF webinar 14 September
  - PHUSE SDE Copenhagen 10 October
  - CDISC US Interchange 18-19 October
  - PHUSE EU Connect 5-8 November
    - Hands-on Workshop 05 November
    - Dedicated session 07 November
  - ClinLine 30-minute Break&Learn webinar
    - 06 December: breaking down the silos using the digital data flow