



# 2023

## EUROPE INTERCHANGE

### COPENHAGEN | 26-27 APRIL



CDISCs Activities on DDF, Benefits for the Community and Looking Ahead  
Version 3

Presented by D Iberson-Hurst  
Partner d4k & CDISC DDF Product Owner



# Meet the Speaker

## Dave Iberson-Hurst

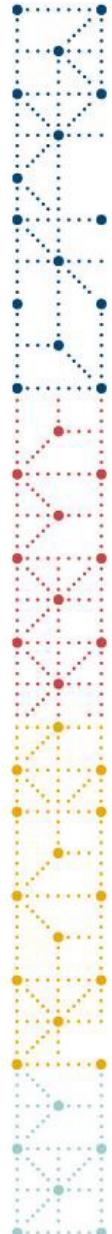
**Title:** Partner

**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.*

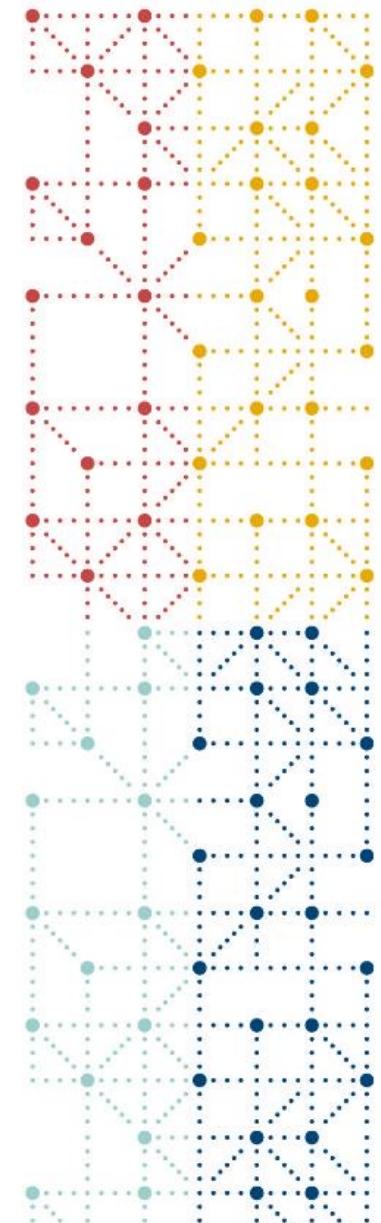
*During this time, he has worked on, and led, several CDISC teams, co-led CDISC's eSource initiative (eSDI) and presented in many forums in Europe, the US, and elsewhere across the globe. He has worked closely with the FDA, EMA, HL7, ISO, and other standards organizations and was a member of CDISC's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

*He is a partner at data4knowledge in Copenhagen and is focused on getting greater value and utility from clinical trial data.*



## Disclaimer and Disclosures

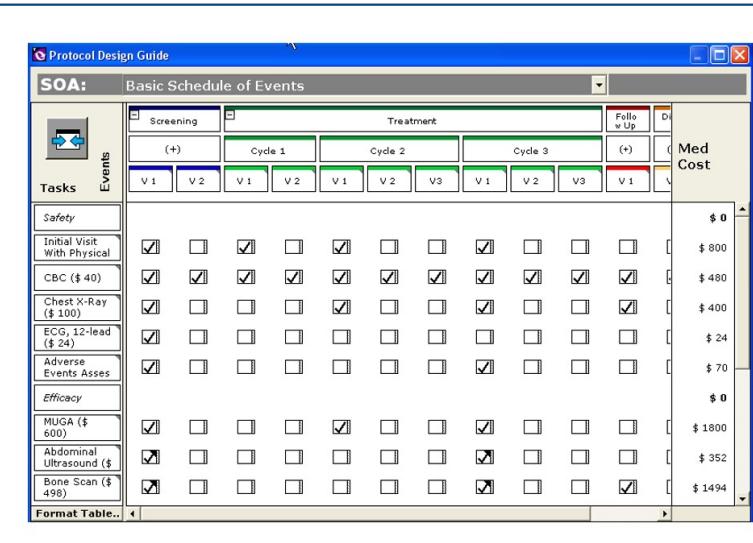
- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.*
- *On contract to CDISC for the DDF work*



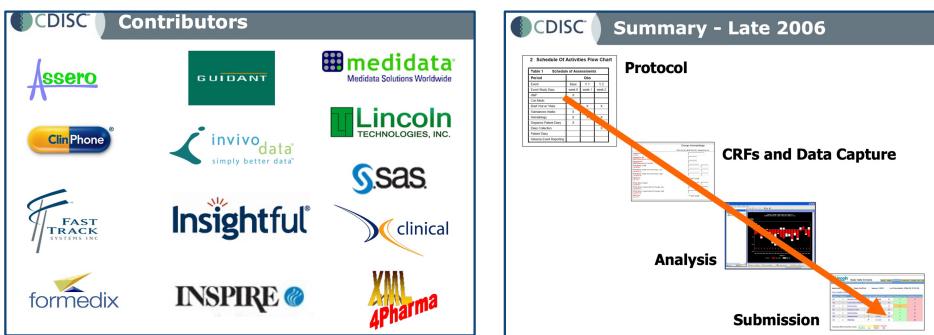
# Agenda

1. Introduction
2. DDF - The Project
3. The Challenges
4. Benefits and Use Cases
5. Looking Forward
6. Summary

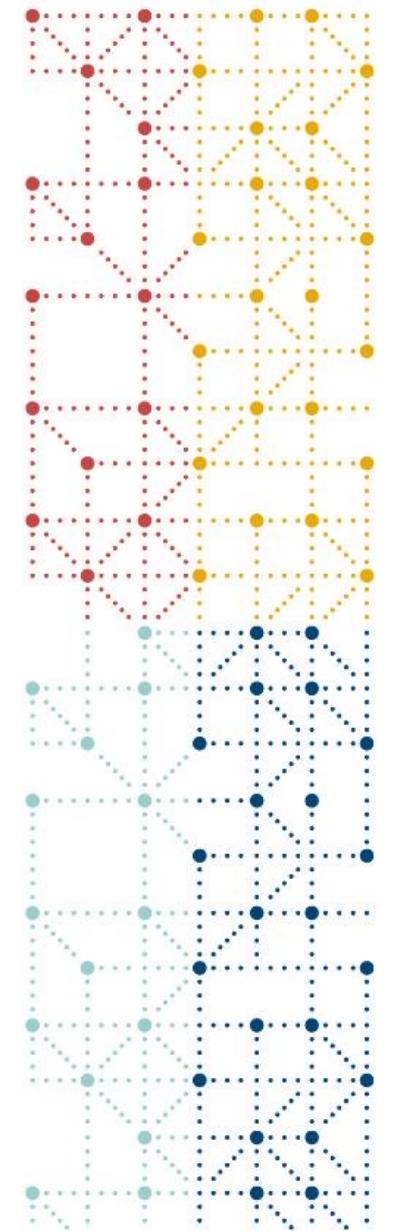
# Montreux, 2007



Generating the Schedule of Activities and study schema in TSD generates data reusable by clinical trial execution systems. For example: the structure and timing of periods, sub-periods, and visits.



-  **What is TrialSpace Designer?**
- A collaborative environment for study design and clinical protocol authoring environment
    - Word based environment that collects Deep Structured Trial Design Information in XML
  - Most relevant to this discussion...
    - Planned Interventions and Procedures
    - Clinical variables mapped to Procedures
    - Schedule of Activities
      - What activities at which events
      - Events built into superstructure of elements and arms
      - Formal Designs: Crossover, Titration, Adaptive
      - Conditionality: go here if..., do this if...
      - Iterations: cycles...
      - Continuous events... diary, concomitant meds
      - Unplanned events... SAE

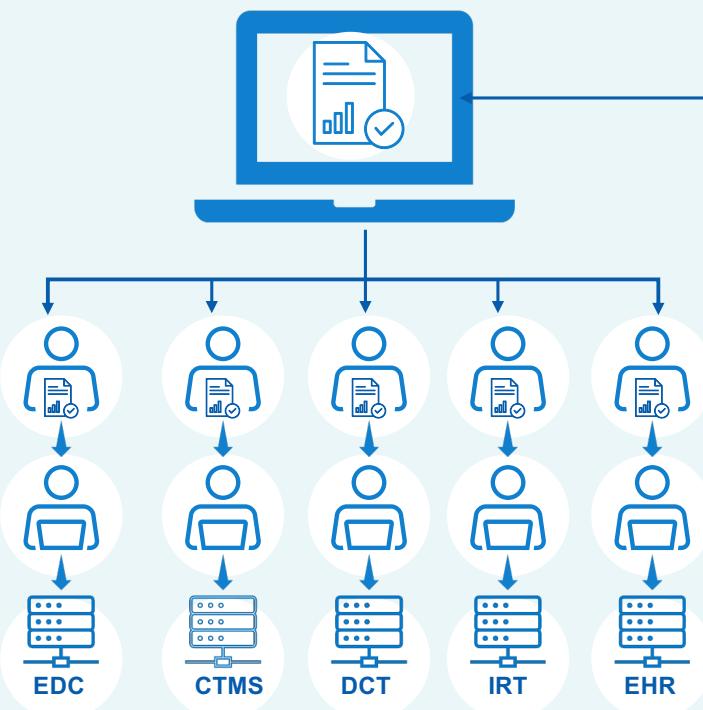


# Digital Data Flow - The Project

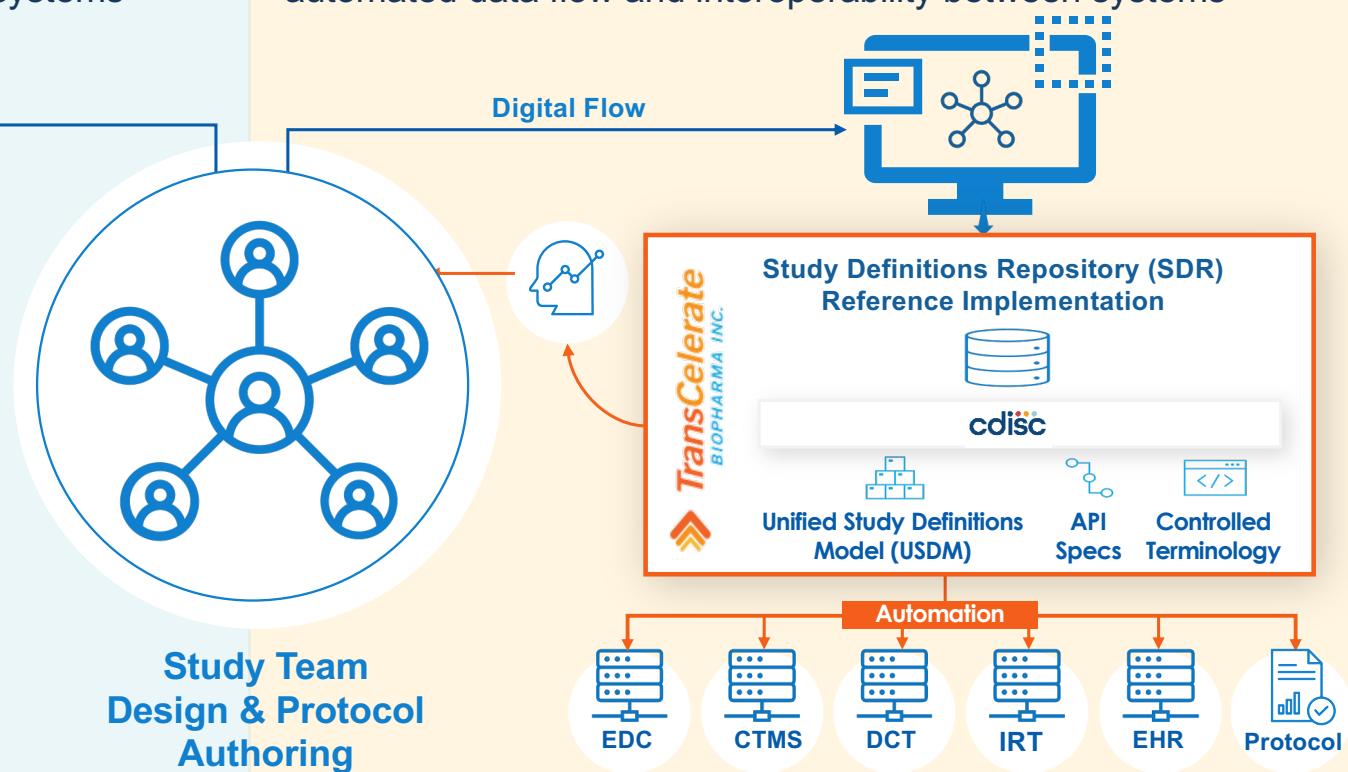
# TransCelerate Digital Data Flow (DDF) Ambition

*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



# CDISC DDF Phase One



July, 2021 – July 2022



## Unified Study Definitions Model (USDM) Class Diagram

The UML class diagram (normative) as well as SQL Data Dictionary, Entity Relationship Diagram and example JSON output (informative)



## Application Programming Interface (API) Specification

The API definition (normative) in JSON and HTML forms



## CDISC Controlled Terminology

The controlled terminology (normative) developed for the project. Provided in an Excel format so as to be easily searched and filtered.



## Reference Architecture Conformance Tests

Provided by the functionality provided by tools such as SwaggerHub and Postman



## Essential Users Stories

The User Stories. PDF document



## Architecture Principles

The architectural principles developed by the project. PDF Document



## Supporting Materials

A set of informational materials in PDF format to help understand the deliverables being reviewed. PDF documents or references.



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V1.0 Provisional  
<https://www.cdisc.org/ddf>

# CDISC DDF Phase Two



Oct, 2022 – June 2023

## Unified Study Definitions Model (USDM) Class Diagram



The UML class diagram (normative) as well as SQL Data Dictionary, Entity Relationship Diagram and example JSON output (informative)

## Application Programming Interface (API) Specification



The API definition (normative) in JSON and HTML forms

## CDISC Controlled Terminology



The controlled terminology (normative) developed for the project. Provided in an Excel format so as to be easily searched and filtered.

## Test Files



Examples of USDM JSON files

## Implementation Guide



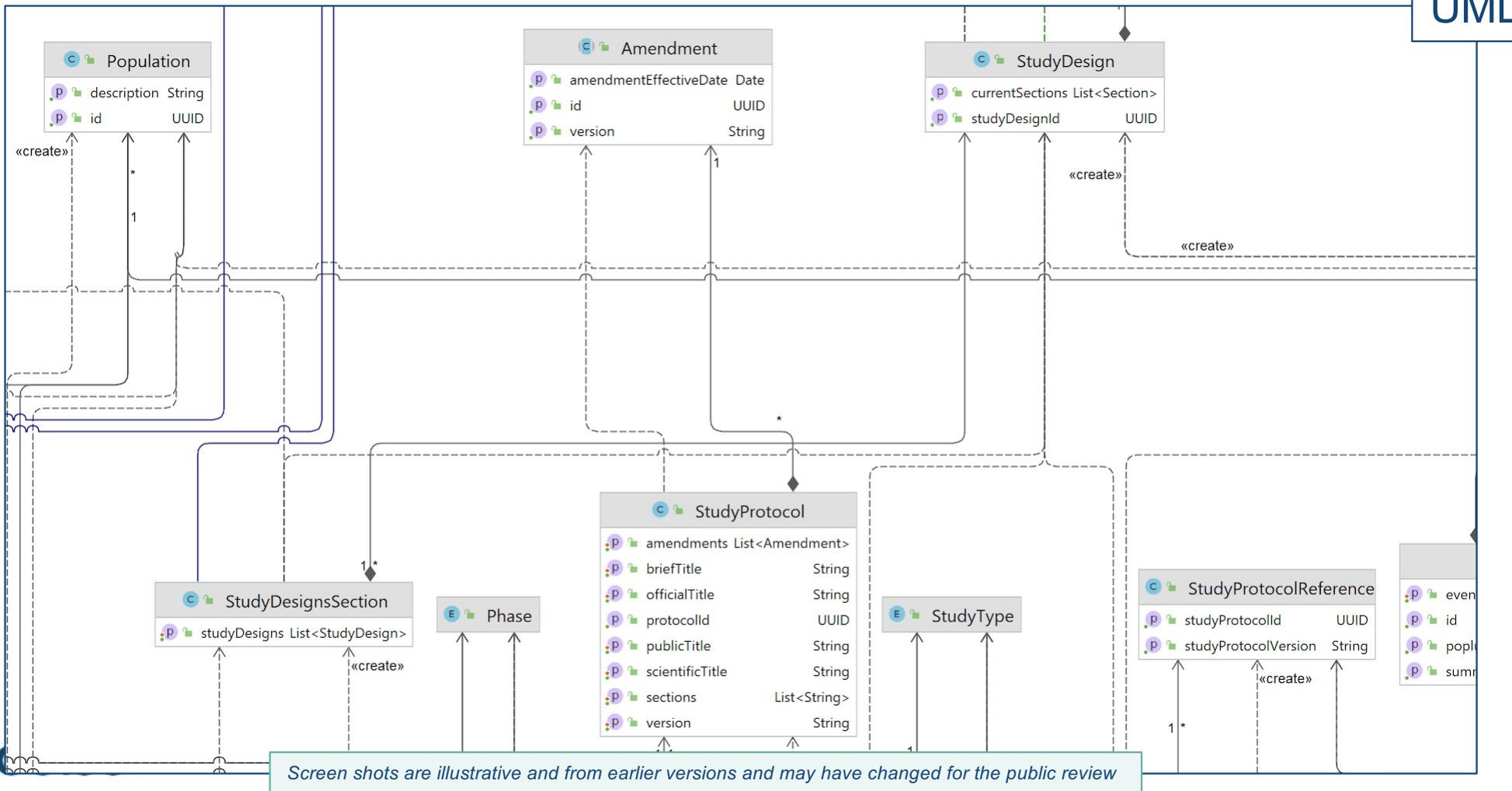
Improved explanation of the model and its use, examples etc



## Unified Study Definitions Model (USDM) Class Diagram

The UML class diagram (normative) as well as SQL Data Dictionary, Entity Relationship Diagram and example JSON output (informative)

UML





## Application Programming Interface (API) Specification

The API definition (normative) in JSON and HTML forms

### Simple API for DDF 1.1 Provisional (0.23) OAS3

/openapi.json

A simple TransCelerate Digital Data Flow (DDF) Study Definitions Repository API.

**Production** Routes that form the production specification.

**POST** /v1/studyDefinitions Create a study

**GET** /v1/studyDefinitions/{uuid} Return a study

**GET** /v1/studyDefinitions/{uuid}/history Returns the study history

**GET** /v1/studyDesigns Study designs for a study

Web: OAS3

```
{  
  "openapi": "3.0.0",  
  "info": {  
    "title": "Simple API for DDF",  
    "description": "This is a sample API for the DDF project – including sectioning (Accordions), security, and more.",  
    "license": {  
      "name": "MIT",  
      "url": "https://opensource.org/licenses/MIT"  
    },  
    "version": "1.2.6"  
  },  
  "servers": [  
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      "url": "https://virtserver.swaggerhub.com/CDISC1/DDF/1.2.6",  
      "description": "SwaggerHub API Auto Mocking"  
    }  
  ],  
  "paths": {  
    "/studydefinitionrepository/v1/{study)": {  
      "get": {  
        "tags": [  
          "default"  
        ],  
        "summary": "Get study build sections",  
        "description": "Get Study Build Sections",  
        "operationId": "get.studydesignrepository.sections",  
        "parameters": [  
          {  
            "name": "study",  
            "in": "path",  
            "description": "Study Builder Study",  
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            "style": "simple",  
            "explode": false,  
            "schema": {  
              "type": "string",  
              "example": "ACME001"  
            }  
          }  
        ]  
      }  
    }  
  }  
}
```





## CDISC Controlled Terminology

The controlled terminology (normative) developed for the project. Provided in an Excel format so as to be easily searched and filtered.

Row #	UML Class Name	UML Item Name	Role	NCI C-code	CT Item Preferred Name	Synonym(s)	Definition	Has Value List
1	STUDY	STUDY	Entity	C15206	Clinical Study		A clinical study involves research using human volunteers (also called participants) that is intended to add to medical knowledge. There are two main types of clinical studies: clinical trials (also called interventional studies) and observational studies. ( <a href="http://ClinicalTrials.gov/(CDISC Glossary">http://ClinicalTrials.gov/(CDISC Glossary</a> )	N
2	STUDY	study_title	Attribute	C49802	Study Title	Trial Title; Official Study Title; Study Title	The sponsor-defined name of the clinical study.	N
3	STUDY	study_version	Attribute	C93490	Study Protocol Version		A plan at a particular point in time for a formal investigation to assess the utility, impact, pharmacological, physiological, and/or psychological effects of a particular treatment, procedure, drug, device, biologic, food product, cosmetic, care plan, or subject characteristic. (BRIDG)	N
4	STUDY	study_status	Attribute	CNEW	Protocol Status		A condition of the protocol at a point in time with respect to its state of readiness for implementation.	Y (CNEW Protocol Status Response)
5	STUDY	study_protocol_version	Attribute	C93490	Study Protocol Version		A plan at a particular point in time for a formal investigation to assess the utility, impact, pharmacological, physiological, and/or psychological effects of a particular treatment, procedure, drug, device, biologic, food product, cosmetic, care plan, or subject characteristic. (BRIDG)	N
6	STUDY_TYPE	STUDY_TYPE	Entity	C142175	Study Type	Study Type; Study Type Classification	The nature of the investigation for which study information is being collected. (After clinicaltrials.gov)	N
7	STUDY_TYPE	study_type_desc	Attribute	C142175	Study Type Classification	Study Type; Study Type Classification	The nature of the investigation for which study information is being collected. (After clinicaltrials.gov)	Y (C99077 STYPE)
8	STUDY_PHASE	STUDY_PHASE	Entity	C48281	Trial Phase	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 four (sometimes five) phases. A therapeutic intervention may be evaluated in two or more phases simultaneously in different trials, and some trials may overlap two different phases. [21 CFR section 312.21; After ICH Topic E8 NOTE FOR GUIDANCE ON GENERAL CONSIDERATIONS FOR CLINICAL TRIALS, CPMP/ICH/291/95 March 1998]	N
9	STUDY_PHASE	study_phase_desc	Attribute	C48281	Trial Phase Classification	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 four (sometimes five) phases. A therapeutic intervention may be evaluated in two or more phases simultaneously in different trials, and some trials may overlap two different phases. [21 CFR section 312.21; After ICH Topic E8 NOTE FOR GUIDANCE ON GENERAL CONSIDERATIONS FOR CLINICAL TRIALS, CPMP/ICH/291/95 March 1998]	Y (C66737 TPHASE)
10	STUDY_IDENTIFIER	STUDY_IDENTIFIER	Entity	C83082	Study Identifier		A sequence of characters used to identify, name, or characterize the study.	N
11	STUDY_IDENTIFIER	org_code	Attribute	CNEW	Study Identifier Organization Code		A coded value specifying the organization that creates and/or assigns the study identifier.	N
12	STUDY_IDENTIFIER	name	Attribute	CNEW	Study Identifier Name		The literal identifier (i.e., distinctive designation) of the sequence	



## Implementation Guide

Improved explanation of the model and its use, examples etc

CDISC USDM-IG (Version 2.0 Draft for Internal Review)

**cdisc**

**Unified Study Definitions Model Implementation Guide (USDM-IG)**

**Version 2.0 (Draft for Internal Review)**

Prepared by the DDF Team

**Notes to Readers**

- This is the draft version 2.0 of the Unified Study Definitions Model Implementation Guide (USDM-IG v2.0). It is intended for Internal Review only and is not a final version.

**Revision History**

Date	Version
2023-03-08	2.0 Draft for Internal Review

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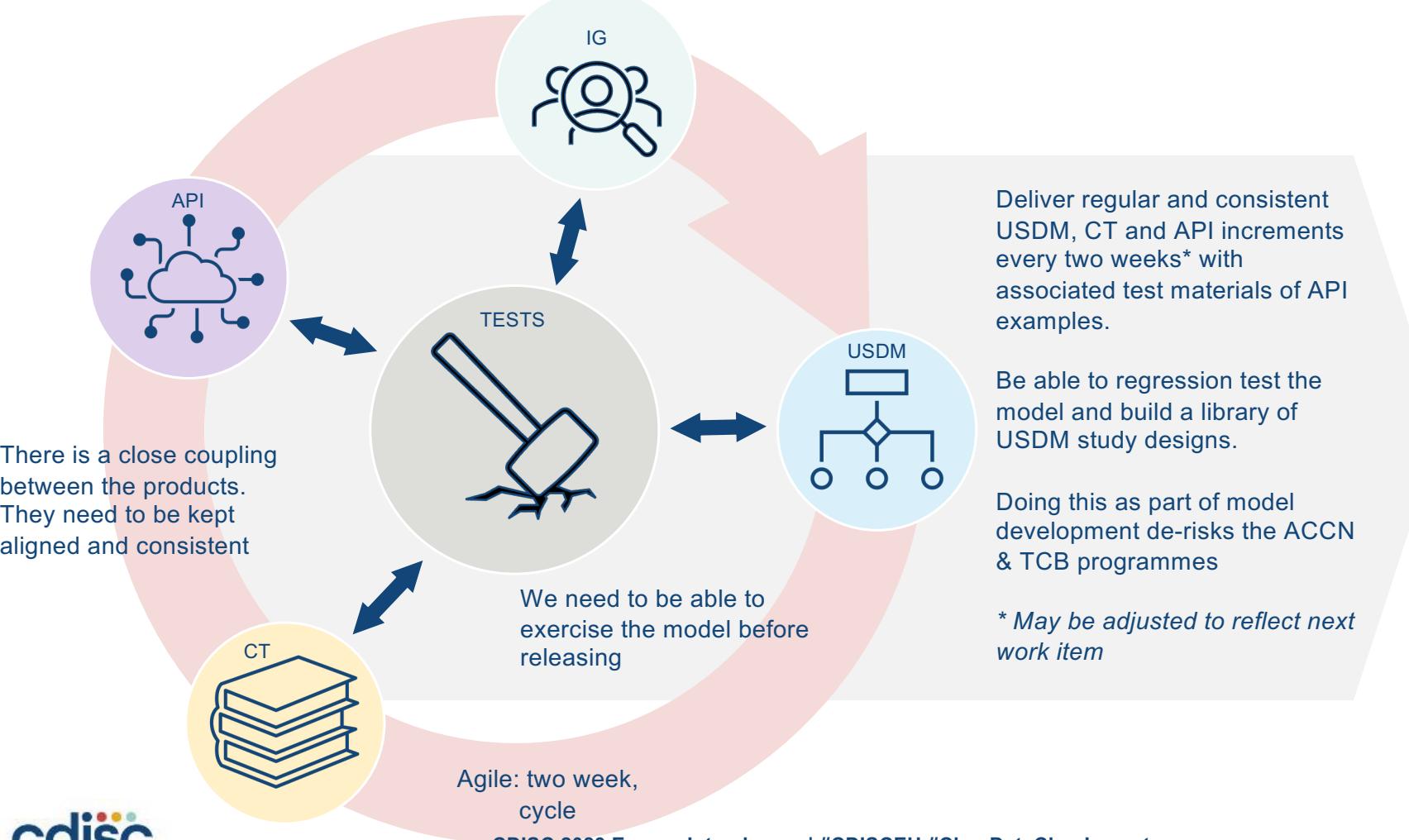
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Draft for Internal Review

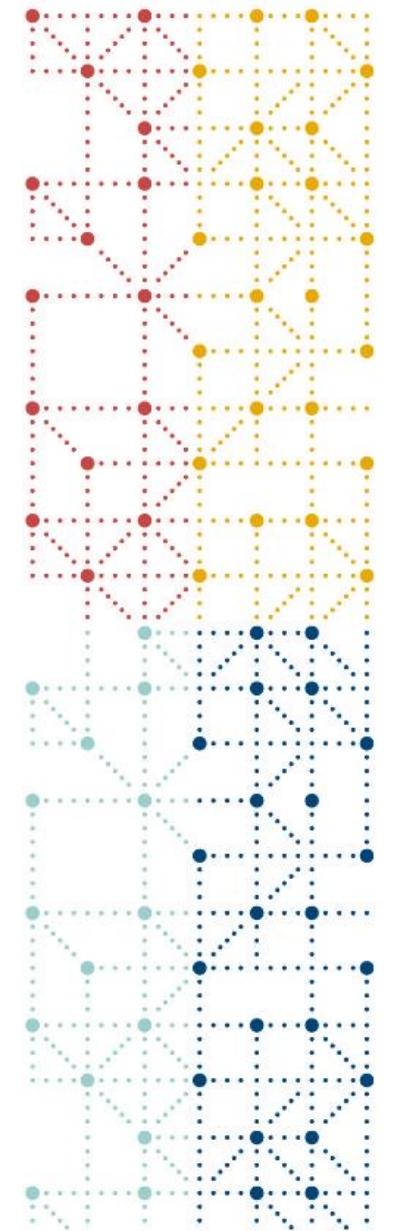
Page 1  
[Publish Date]

- Note that the Implementation Guide is version 2
- There was no Implementation Guide with version 1 of the USDM



# Improved Process





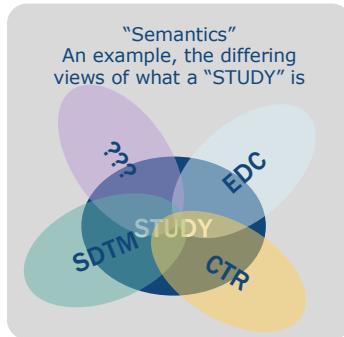
# The Challenges

## Challenges and Choices ...

- Choices
  - Recreate the current world or look for something better?
  - How radical do we wish to be?
  - Don't just want to recreate the "paper world"
- DDF is not a "normal" CDISC project, it has technical and content aspects
- Scope and perspective of the participants
- The project exposes the complexity of our world



# Challenges and Standards



XML standards are about getting information from A to B, from system to system. But, they define content, semantics, definitions etc.

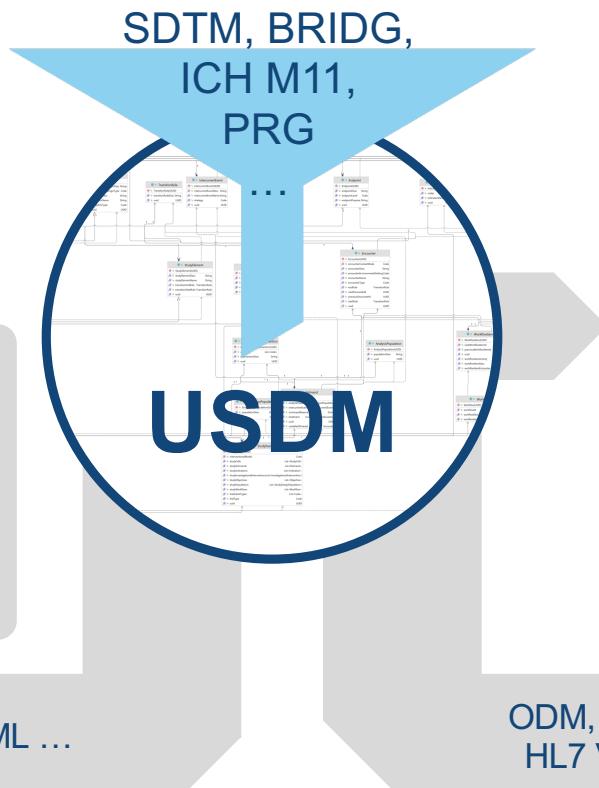
Other standards define models and content, controlled terms etc.

But these overlap.

BRIDG has Inclusion / Exclusion criteria models. So does CTR, so does SDTM, all subtly different.

CT standards may also inform the process.  
SNOMED, MedDRA, LOINC all have  
"models" behind their content

Every standard  
has something  
to say about  
some USDM  
related  
information



CPT XML, Rest API, CTR XML ...

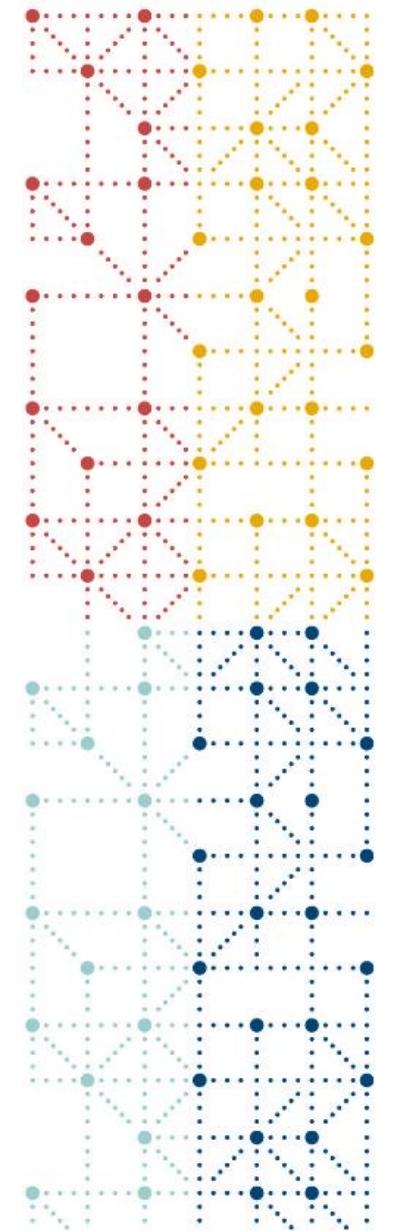
ODM, Rest API, ALS, CTR XML,  
HL7 Vulcan SoA, CPT XML ...

A Full eProtocol  
The DDF Vision

The important "human readable" form.

Key question: Should USDM support the whole eProtocol ... AND / OR ... Should SDR being able to generate the complete protocol?





## Benefits and Use Cases

# Overview and Benefit



Phase 2 Use Case

Imports

Protocol Authoring /  
Study Builders

Common Protocol  
Template (CPT)

Others?

Upstream

*Study Builders is a confusing term.  
Prefer Protocol Authoring to include  
study design*

**USDM**  
(Unified Study Definitions Model)  
**SDR**  
(Study Definitions Repository)

USDM provides context to downstream  
systems providing a machine readable  
definition of the study

Exports

EDC

CTMS

CT Registry

eCPT

Others?

Downstream



The all important  
human-readable  
protocol document

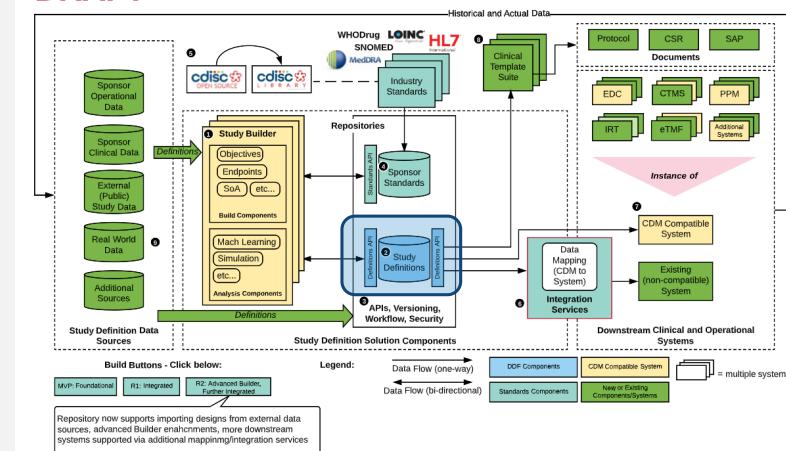
- Speed of execution, stems from the automation which comes from a common understanding
- Data Quality resulting from better context and consistency
- Data Utility, the ability to reuse data when the context is available
- APIs will facilitate building of systems and eco systems
- A single source [of truth] for the protocol



# Use Cases: USDM with BCs allows for ...

Data Capture	Automate the setup of data capture systems ,incl. RWE, and capture the data.	CTMS, TMF ...	The provision of protocol information to down stream systems needing "study" information.
SoA	Use the study design to build the FHIR SoA message.	Query	Having multiple studies that have a common structure allows for data export and query across the set of studies
Data Import	Import data from a variety of sources . Can be re-exported thus allowing for conversion across versions.	SDTM	Automate the generation of SDTM datasets using the study design and BCs
Common Protocol Template (CPT)	Generation of the CPT from a study design. 		
Data Decay	Re-import data using the USDM as a framework to rebuild a study design & data using the SDTM Trial Design Domains.		
Scoring	The "scoring" of a study for such purposes as site impact, subject impact, environmental impact etc.		
Feasibility	The use of the design to determine study feasibility including subject recruitment. A study data template.		
CT Registry	The provision of study information to a CT registry.		
FAIR Data	The use of the design to aid Findability, Accessibility, Interoperability, and Reusability.		

**DRAFT** DDF Conceptual Architecture - Enhanced Study Builder and Repository, Additional Integrations (R2)



Plus many more ...



# The Data Capture Use Case (EDC)

**NIH U.S. National Library of Medicine**  
**ClinicalTrials.gov**

Find Studies ▾ About Studies ▾ Submit Studies ▾ Resources ▾ About Site ▾ PRS Login

Home > Search Results > Study Record Detail  Save this study

A Study to Evaluate the Safety and Efficacy of Tocilizumab in Patients With Severe COVID-19 Pneumonia (COVACTA)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our [disclaimer](#) for details.

ClinicalTrials.gov Identifier: NCT04329132

Recruitment Status: Completed  
First Posted: March 25, 2020  
Results First Posted: June 30, 2020  
Last Update Posted: June 30, 2020

Sponsor: Hoffmann-La Roche Ltd  
Information provided by Hoffmann-La Roche Ltd

**PROTOCOL**

**TITLE:** A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTICENTER STUDY TO EVALUATE THE SAFETY AND EFFICACY OF TOCILIZUMAB IN PATIENTS WITH SEVERE COVID-19 PNEUMONIA

**PROTOCOL NUMBER:** WA42380  
**VERSION NUMBER:** 3  
**EUDRACT NUMBER:** 2020-001154-22  
**IND NUMBER:** 148225  
**NCT NUMBER:** NCT04320615  
**TEST PRODUCT:** Tocilizumab (RO4877533)  
**MEDICAL MONITOR:** [REDACTED], M.D.  
**SPONSOR:** F. Hoffmann-La Roche Ltd  
**APPROVAL DATE:** See electronic date stamp below

**PROTOCOL AMENDMENT APPROVAL**

## Increasing Detail

Provide precision on the data to be captured to the capture systems in a generic manner to facilitate automation. The data precision has not, typically, been in the “paper” protocol. It is SoA “plus”, SoA+

## Data & Procedures



## Visits & Activities

### Arms & Epochs



Study Design



## Current “Limit”

SoA is where we are today with associated footnotes and free text. Activities sit at a CRF form “level”

## Technology Independent

Definition should be independent of any capture technology

# Increasing Detail – SoA

Appendix 1 Schedule of Activities: Days 1 and 2					
	Screening <sup>a, b</sup>	Baseline			
Study Day	-2 to 0		1	2	
Time Post Initial Treatment (Assessment Window)		0 Pre-dose (-4 hrs)	15 min After end of infusion (+1 hr)	24 hrs (±4 hrs)	36 hrs (±4 hrs)
Informed consent	x				
Demographic data	x	x			
Medical history		x			

Study Tocilizumab in Patients With Severe COVID-19 Pneumonia - WA42380								
Owner: , Version: 0.1.0								
Screening	Treatment							
Screening	Baseline	Day 1	Day 2A	Day 2B	Day 3	Day 4	Day 5	
Informed consent	◇ X							
Inclusion/exclusion criteria	◇ X	X						
Demographics	◇ X							

# Increasing Detail – Observations

Appendix 1 Schedule of Activities: Days 1 and 2					
	Screening <sup>a, b</sup>	Baseline			
Study Day	-2 to 0	1	2		
Time Post Initial Treatment (Assessment Window)		0 Pre-dose (-4 hrs)	15 min After end of infusion (+1 hr)	24 hrs (±4 hrs)	36 hrs (±4 hrs)
Informed consent	x				
Demographic data	x	x			
Medical history		x			

## 4.5.2 Medical History, Baseline Conditions, Concomitant Medication, and Demographic Data

Medical history, including clinically significant diseases, surgeries, cancer history (including prior cancer therapies and procedures), reproductive status, smoking history, home oxygen use, will be recorded at baseline. In addition, all medications (e.g., prescription drugs, over-the-counter drugs, vaccines, herbal or homeopathic remedies, nutritional supplements) used by the patient within 7 days prior to first dose of study drug will be recorded. At the time of each follow-up physical examination, an interval medical history should be obtained and any changes in medications and allergies should be recorded.

Demographic data will include age, sex, and self-reported race/ethnicity.

Study Tocilizumab in Patients With Severe COVID-19 Pneumonia - WA42380								
Owner: , Version: 0.1.0								
Screening	Treatment							
Screening	Baseline	Day 1	Day 2A	Day 2B	Day 3	Day 4	Day 5	
Informed consent	◊ X							
Inclusion/exclusion criteria	◊ X	X						
Demographics	◊ X							

Demographics	X	X
Race		
Sex		
Age		

# Increasing Detail – Observation Detail

**Appendix 1**  
**Schedule of Activities: Days 1 and 2**

	Screening <sup>a, b</sup>	Baseline			
Study Day	-2 to 0	1	2		
Time Post Initial Treatment (Assessment Window)		0 Pre-dose (-4 hrs)	15 min After end of infusion (+1 hr)	24 hrs (±4 hrs)	36 hrs (±4 hrs)
Informed consent	x				
Demographic data	x	x			
Medical history	x				

## 4.5.2 Medical History, Baseline Conditions, Concomitant Medication, and Demographic Data

Medical history, including clinically significant diseases, surgeries, cancer history (including prior cancer therapies and procedures), reproductive status, smoking history, home oxygen use, will be recorded at baseline. In addition, all medications (e.g., prescription drugs, over-the-counter drugs, vaccines, herbal or homeopathic remedies, nutritional supplements) used by the patient within 7 days prior to first dose of study drug will be recorded. At the time of each follow-up physical examination, an interval medical history should be obtained and any changes in medications and allergies should be recorded.

Demographic data will include age, sex, and self-reported race/ethnicity.

## Study Tocilizumab in Patients With Severe COVID-19 Pneumonia - WA42380

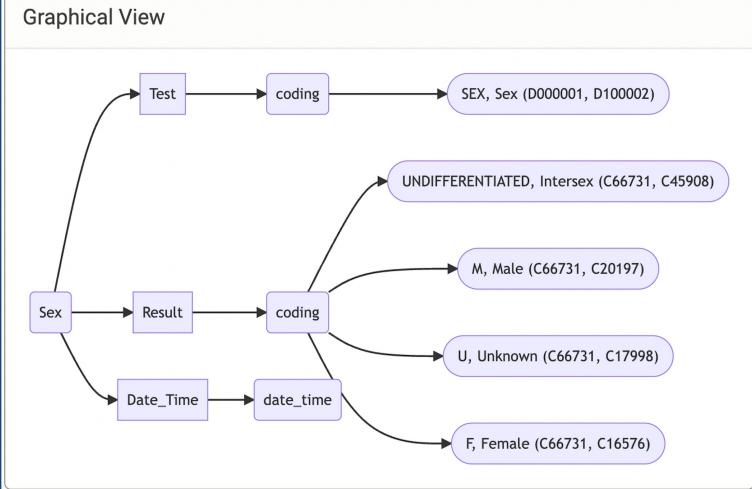
Owner: , Version: 0.1.0

Screening	Treatment						
Screening	Baseline	Day 1	Day 2A	Day 2B	Day 3	Day 4	Day 5

Informed consent X

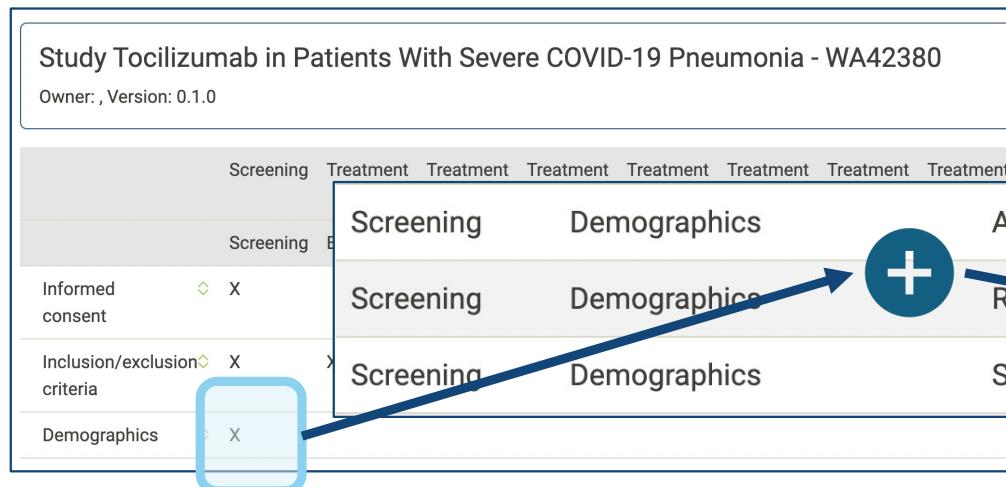
Inclusion/exclusion criteria X X

Demogr



X

# Increasing Detail – Data Contract



## Form Recommendation

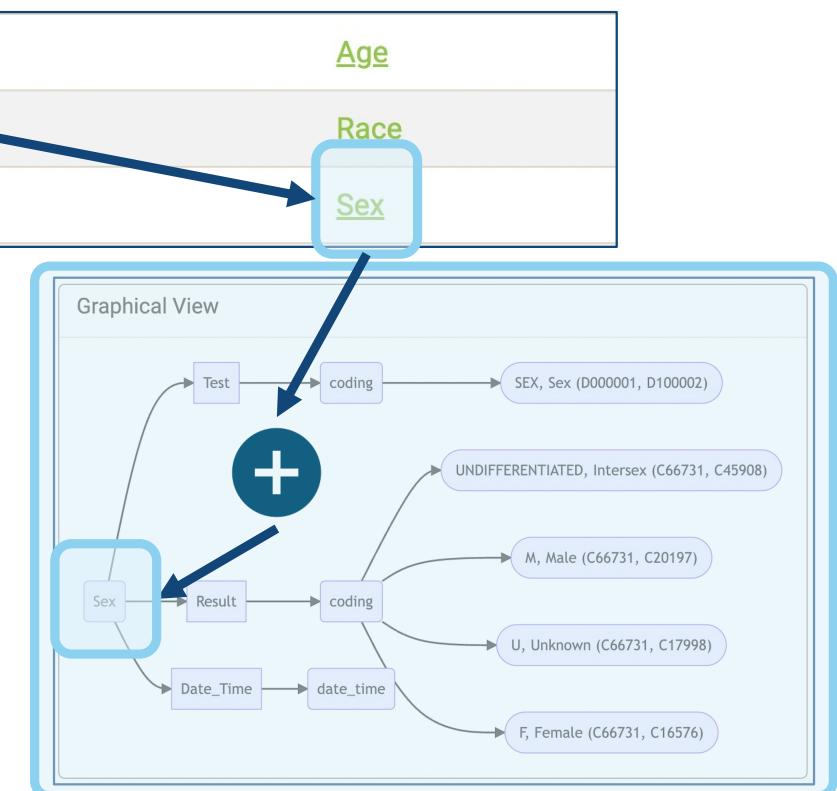
Systems can use the richness of definition to suggest forms for data capture builds

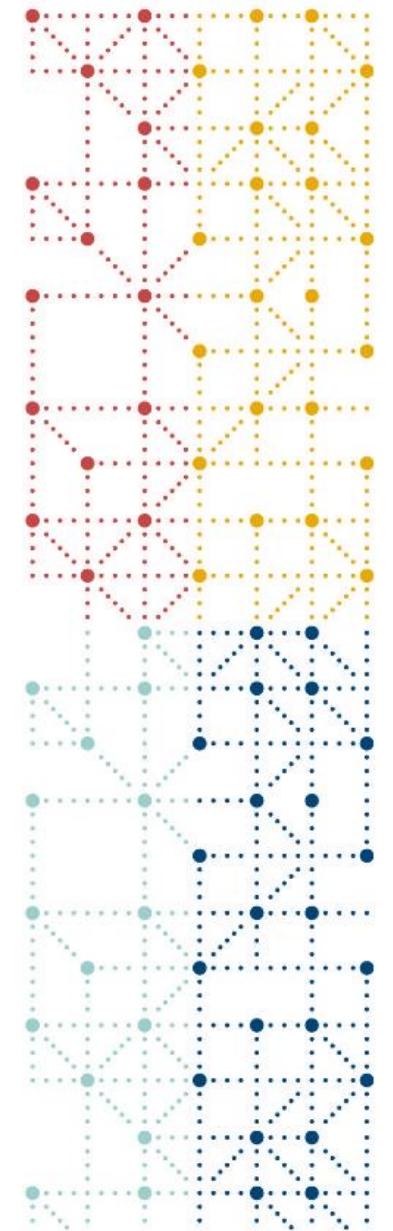
Demographics Age, Race, Sex

Demographics\_2: Enrollment, Ethnicity, Sex, Age [0.6666666666666666]  
Demographics: Enrollment, Sex, Age [0.6666666666666666]

## Increasing Detail

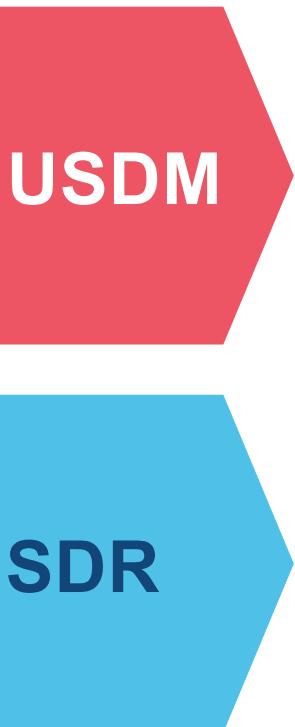
The SoA to SoA+ expansion of detail. Detailing every data need results in a “data contract”. Capture technology independent.





**Looking Forward**

# Next Steps – Phase Three



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1

- Baseline model for specifying a study in digital format
- Model supports use of a CRF link to specify which forms to use in EDC.
- Handles simple study designs

2

- Improved support for complex study designs with a fully specified digitized Schedule of Activities (SoA)
- Model supports the identification of the appropriate CRFs for data collection to enable automated, faster configuration via use of Biomedical Concepts
- Improved CPT alignment
- Initial 'T' Domain support

3

Focus for phase 3 is currently being determined. Current expectations are:

- Expand ability to handle increasingly complex studies
- ICH M11 & CPT alignment

# Adoption ...



cdisc

1

- Baseline model for specifying a study in digital format
- Model supports use of a CRF link to specify which forms to use in EDC.
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- Improved support for complex study designs with a fully specified digitized Schedule of Activities (SoA)
- Model supports the identification of the appropriate CRFs for collection to enable auto configuration via use of Concepts
- Improved CPT alignment
- Initial 'T' Domain support

3



- Potential use cases
  - Transcelerate Focus: CPT & EDC
  - But what else ...
- Prospective & retrospective
- Lower risk use cases

# Summary

- Digital Data Flow / Unified Study Definitions Model (DDF/USDM) fills an important gap
- A single source of truth
- [First] Use of Biomedical Concepts brings precision
- It is complex and that complexity becomes visible
- Can be deployed to support various use cases



1

- Baseline model for specifying a study in digital format
- Model supports use of a CRF link to specify which forms to use in EDC.
- Handles simple study designs

- Consume digitized study specification from an upstream source e.g., study builder)
- Store, view and search study concepts
- Downstream EDC systems may pull study specification to aid in set-up

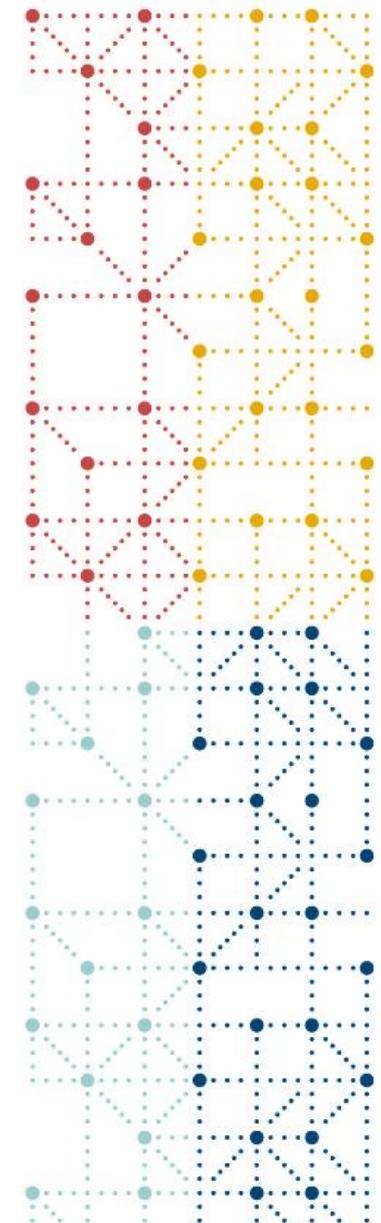
2

- Improved support for complex study designs with a fully specified digitized Schedule of Activities (SoA)
  - Model supports the identification of the appropriate CRFs for data collection to enable automated, faster configuration via use of Biomedical Concepts
  - Improved CPT alignment
  - Initial 'T' Domain support
- 
- Downstream vendors can readily consume the SoA from the SDR
  - Sponsor system admins can perform a visual check that SoA data received from an upstream system displays an accurate, human-readable SoA table
  - Opportunity to aggregate robust historical protocol information to support analytics to drive smart design and assess risk

3

Focus for phase 3 is currently being determined. Current expectations are:

- Expand ability to handle increasingly complex studies
- ICH M11 & CPT alignment



# Thank You

Dave Iberson-Hurst

[diberson-hurst.external@cdisc.org](mailto:diberson-hurst.external@cdisc.org)

John Owen

[jowen@cdisc.org](mailto:jowen@cdisc.org)

Phase 2 Public Review:

<https://wiki.cdisc.org/display/PUB/DDF+Phase+II+Public+Review+Review+Dashboard>

Phase 2 Public Review Webinar:

<https://www.cdisc.org/events/webinar/digital-data-flow-project-phase-2-public-review>

