



2023

KOREA

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SEOUL | 11-14 DECEMBER



RWD Activities Update

Rhonda Facile MS
VP, Partnerships and Development



Meet the Speaker

Rhonda Facile, MS

Title: VP, Partnerships and Development

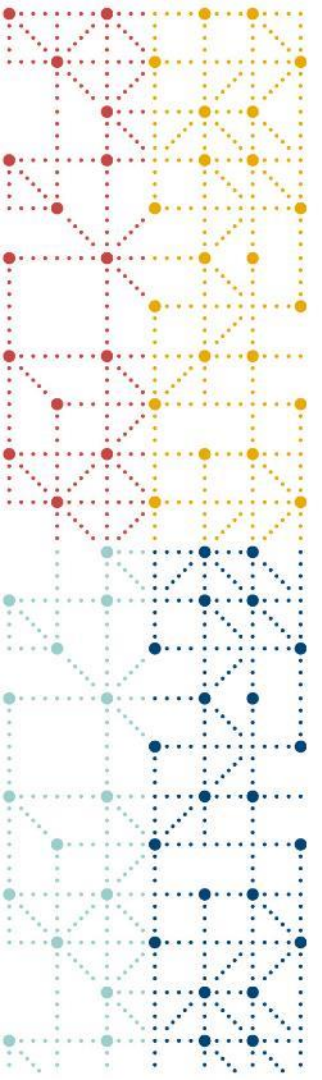
Organization: CDISC

Rhonda Facile is Vice President, Partnerships and Development at CDISC where she oversees business development and new project development. She brings together, key and diverse stakeholder communities to establish effective collaboration structures to ensure project success. At CDISC Rhonda has led numerous standards development projects and initiatives including CDASH, therapeutic area guides and more recently CDISC RWD Connect. Prior to joining CDISC, Rhonda worked in clinical operations and regulatory affairs in Pharmaceutical, Biotechnology, and Contract Research Organizations in the US and Europe.



Agenda

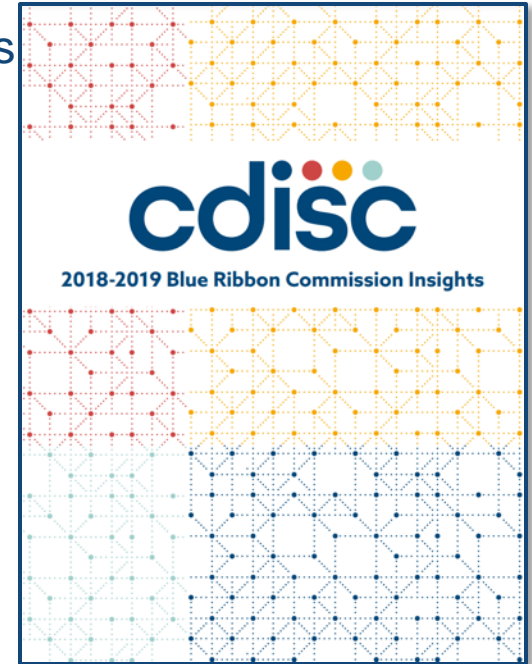
1. CDISC RWD Background
2. CDISC RWD Strategy
3. CDISC RWD Activities and Resources



CDISC RWD Background

Blue Ribbon Commission Recommendations

- CDISC standards are **growing in use-cases** beyond the original regulatory approvals use case
- The most **important use case** for CDISC to support is standardization of:
 - **Academic research**
 - **Observational research**
 - **Patient-reported outcomes**
 - **EHR data – the largest source of clinical data**
- **Areas of Focus:**
 - User specific education
 - Visual, web-based, natural-language search
 - Success stories and case studies publication
 - Accessible training
 - Expand membership to new groups
 - Leverage the data sharing movement



https://www.cdisc.org/system/files/about/brc/2018-2019_Blue_Ribbon_Commission_Insights.pdf

CDISC RWD Connect Delphi

Recommendations:

- Standardization of RWD is **necessary**. The primary focus should be on **improving data sharing and quality**.

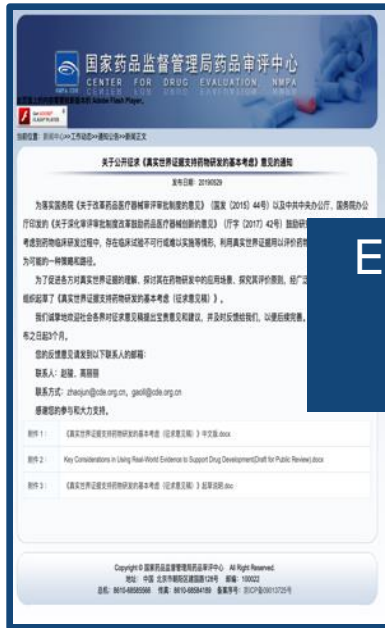
Priorities:

- Electronic health records**, such as data shared using HL7-FHIR and data stemming from observational studies, wearables and patient-reported outcomes.
- With different standardization efforts already underway in these areas a gap analysis should be performed to **identify the areas where synergies and efficiencies are possible**, e.g., extension of SDTM for RWD
- Collaborate with stakeholders to **create or extend existing mappings between CDISC and other standards**, controlled terminologies, and models to represent data originating across different sources
- JMIR Med Inform 2021;9(11):e30363) doi: 10.2196/30363



RWD Regulatory Environment

China's NMPA



国家药品监督管理局药品审评中心
CENTER FOR DRUG EVALUATION, NMPA
CHINA

关于公开征求《真实世界证据支持药物研发的基本考量》意见的通知

发布日期: 20190229

为贯彻落实《关于改革药品医疗器械审评审批制度的意见》(国发〔2015〕44号)以及中共中央办公厅、国务院办公厅印发的《关于深化审评审批制度改革鼓励药品医疗器械创新的意见》(厅字〔2017〕42号)精神,考虑药物临床试验过程中,存在临床试验不可行或以实施等情形,利用真实世界证据用以评价药物为可的一种策略和途径。

为了促进各方对真实世界证据的理解,探讨其在药物研发中的应用场景,探究其评价的原则,经广泛征求意见,《真实世界证据支持药物研发的基本考量(征求意见稿)》,我们诚挚地邀请社会各界对征求意见稿提出宝贵意见和建议,并及时反馈给我们,以便后续完善,希之关注3个月。

您的反馈意见和建议到以下联系人的邮箱:
联系人: 赵超、高研
联系方式: zhaoc@cdisc.org.cn, gaoy@cdisc.org.cn
贵单位的参与和大力支持。

附件:
附件1: 《真实世界证据支持药物研发的基本考量(征求意见稿)》中文意见.docx
附件2: Key Considerations in Using Real-World Evidence to Support Drug Development(Draft for Public Review).docx
附件3: 《真实世界证据支持药物研发的基本考量(征求意见稿)》征求意见表.doc

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December 2018
www.fda.gov

<http://www.cde.org.cn/news.do?method=argelInfo&id=23a2b4cbe0807fe2>

US FDA



FDA U.S. FOOD & DRUG ADMINISTRATION

FRAMEWORK FOR FDA'S
REAL-WORLD

December 2018
www.fda.gov

<https://www.fda.gov/media/120060/download>

EU EMA



EUROPEAN MEDICINES AGENCY
SCIENCE · MEDICINES · HEALTH

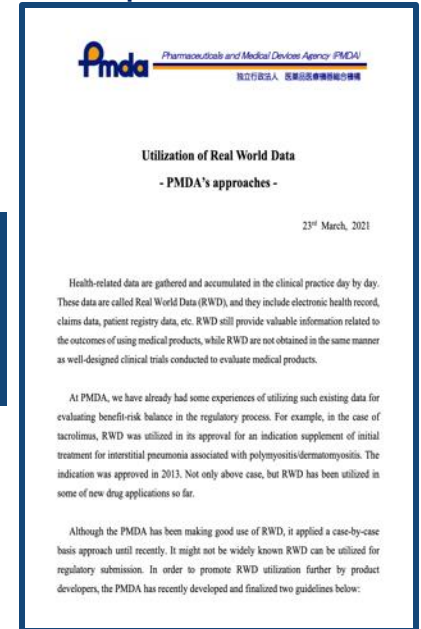
Regulatory Procedural Guideline on
Real-World Evidence

EMA

December 2018

https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/ema-regulatory-science-2025-strategic-reflection_en.pdf

Japan PMDA



Pmda Pharmaceuticals and Medical Devices Agency (PMDA)
独立行政法人 医薬品医療機器総合機構

Utilization of Real World Data
- PMDA's approaches -

23rd March, 2021

Health-related data are gathered and accumulated in the clinical practice day by day. These data are called Real World Data (RWD), and they include electronic health record, claims data, patient registry data, etc. RWD still provide valuable information related to the outcomes of using medical products, while RWD are not obtained in the same manner as well-designed clinical trials conducted to evaluate medical products.

At PMDA, we have already had some experiences of utilizing such existing data for evaluating benefit-risk balance in the regulatory process. For example, in the case of tacrolimus, RWD was utilized in its approval for an indication supplement of initial treatment for interstitial pneumonia associated with polymyositis/dermatomyositis. The indication was approved in 2013. Not only above case, but RWD has been utilized in some of new drug applications so far.

Although the PMDA has been making good use of RWD, it applied a case-by-case basis approach until recently. It might not be widely known RWD can be utilized for regulatory submission. In order to promote RWD utilization further by product developers, the PMDA has recently developed and finalized two guidelines below:

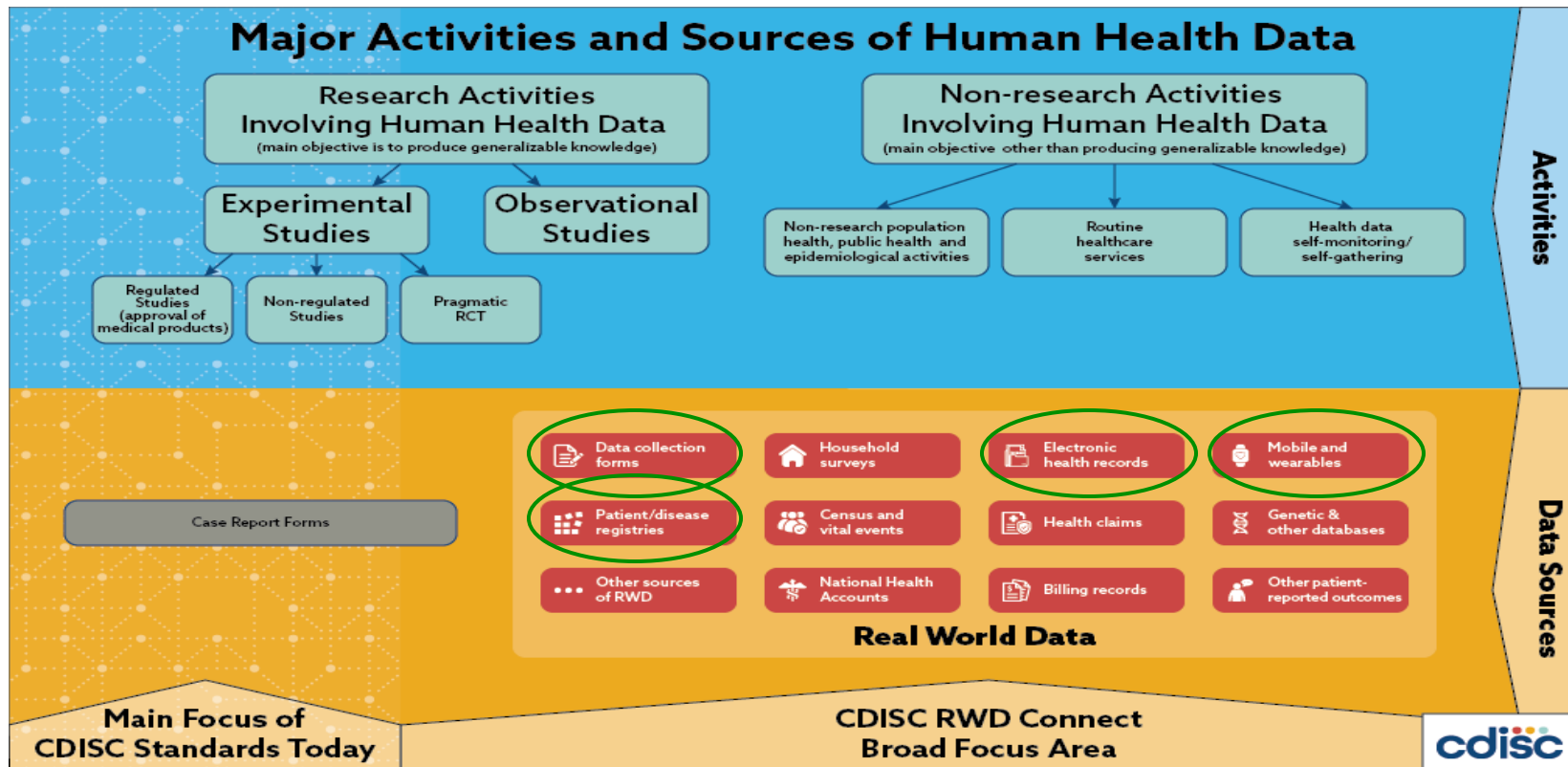
<https://www.pmda.go.jp/english/about-pmda/0004.pdf>



CDISC's RWD Strategy

- Expansion of CDISC Standards to **address multiple modalities of data capture**, exchange, processing, analysis and reporting
- Collaborate, **partner and harmonize with other industry standards** to enable an efficient pathway for RWD to be transformed for ultimate use cases, such as data sharing; regulatory submissions; exploratory analysis and incorporation into clinical research trials
- Enable the **development and use of open-source solutions** that utilize standards to collect, exchange, process, transform and analyze clinical data
- Partner with technology providers to **embed CDISC standards within the most commonly-used formats and platforms** to provide machine-ready forms of the standards for use
- **Develop, release and govern standards validation rules and an open-source conformance engine** for verification of the integrity and completeness of data for use
- **Provide the industry with training and education** on the use and importance of standards in the RWD ecosystem
- Support and **Facilitate the use of RWD by Regulatory Agencies** and the development of the tools necessary for proper, efficient data transformations and metadata-rich data exchange

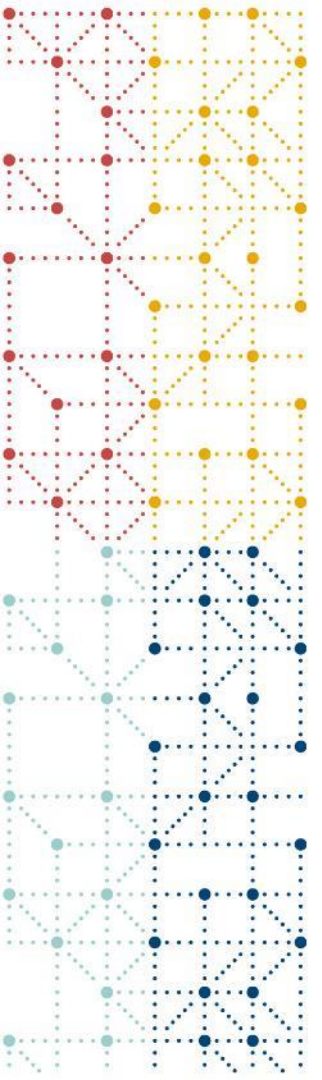
Real World Data





Note!

- CDISC Standards **Do Not** specify what data should be collected or how to conduct clinical trial protocols, assessments or endpoints.
- CDISC Standards specify **how** to structure data to support efficient data sharing for regulated clinical trials
- **You can't standardize everything**
 - Focus on commonalities, cross-cutting concepts, data collected repeatedly



RWD Activities and Resources



CDISC Real World Data Resources

HL7-FHIR to CDISC Mapping – Extracting eHR data to SDTM

Considerations - Using SDTM for Observational Studies

CDISC eCRF Portal, REDCap & OpenClinica - CDASH eCRFs

Digital Health Technologies

Knowledge Base

eCRFs

Peer-reviewed Articles



HL7–FHIR to CDISC Mapping

- Aim: provide a pathway for going from extracted EHR data to SDTM format
- Joint effort between CDISC and HL7
 - Balloted by both SDOs
- Domains mapped:
 - Events: AE, MH
 - Interventions: PR, CM
 - Findings: LB, VS, Lab Model
 - Special Purpose: DM
- Published 1 Sep 2021

Title: Concomitant Medications

Concomitant Medication Category CMCAT <i>Hidden/pre-populated</i>	GENERAL
Were any concomitant medications taken? CMYN Not Submitted	<input checked="" type="radio"/> Yes <input type="radio"/> No <NY codelist>
CM Number CMSPID	<input type="text" value="1"/>
What was the medication? CMTRT	<input type="text" value="CAPTOPR"/>
For what indication was the medication taken? CMINDC	<input type="text" value="HYPERTENSION"/>
Dose CMDSTXT CMDOSTXT/CMDOSE	<input type="text" value="25"/>
Unit CMDOSU	<input type="text" value="mg"/> <UNIT codelist>
Dose Form CMDOSFRM	<input type="text" value="TABLET"/> <FRM codelist>
Frequency CMDOSFRQ	<input type="text" value="BID"/> <FREQ codelist>
Route CMROUTE	

Indicate if the subject took any concomitant medications/treatments. If Yes, include the appropriate details where indicated on the CRF.

If collected on the CRF, sponsor may insert instructions to ensure each record has a unique identifier.

Record only one treatment per line. Provide the full trade or proprietary name of the medication/treatment; otherwise, record the generic name .

Record the reason the medication was taken based on clinical investigator's evaluation. If taken to treat a condition, and a diagnosis was made, the indication should be the diagnosis. If taken to treat a condition, and no diagnosis was made, the indication should be the signs and symptoms. If taken as prophylaxis, report as "Prophylaxis for " and include a description of the condition(s).

Record the dose of medication/treatment per administration (e.g., 200).

Record the dose unit of the dose of concomitant medication/treatment taken (e.g., mg).

Record the pharmaceutical dosage form (e.g., TABLET CAPSULE, SYRUP) of delivery for the concomitant [medication/treatment/therapy] taken.

Record how often the medication was taken (e.g., BID, PRN).

Provide the route of administration for the medication.

MedicationStatement.category

Not submitted - What constitutes a 'concomitant' drug is study-specific and would need to be evaluated on a study level. FHIR would not normally store that information.

MedicationStatement.identifier

MedicationStatement.medicationCodeableConcept

SNOMED-CT =318821008

MedicationStatement.reasonCode

SNOMED-CT =59621000 OR ICD-10=I10

MedicationStatement.medicationReference.resolve().form

MedicationStatement.dosage.doseAndRate.doseQuantity

FHIR to CDISC Joint Mapping Implementation Guide v1.0

View

Edit

Delete

Clone

Release Date: 01 September 2021

Version 1.0 of the FHIR to CDISC Joint Mapping Implementation Guide defines mappings between [FHIR release 4.0](#), HL7's standard for exchanging healthcare information electronically and three CDISC Standards: [CDASHIG v2.1](#), [SDTMIG v3.2](#), and [LAB v1.0.1](#) to streamline the flow of data from electronic health records (EHRs) to CDISC submission-ready datasets.

- [FHIR to CDISC Mapping Implementation Guide](#) - A spreadsheet of the FHIR to CDISC mappings with domain tabs and details from FHIR to CDASH to SDTM.
- [FHIR to CDISC Mapping Implementation Guide Public Review Comments*](#)
- [FHIR to CDISC Mapping Implementation Guide in XML Format](#)

Additional RWD Resources

- [LOINC to LB Mapping File](#) is an additional resource for capturing real-world data. [Logical Observation Identifiers Names and Codes \(LOINC®\)](#) terminology includes laboratory and clinical observations used in healthcare systems around the globe.
- [Unit-UCUM Codetable](#) provides mapping to toggle between UCUM and CDISC Units. Unified Code for Units of Measure (UCUM) contains a blueprint for the creation of compliant units of measure from more than 300 terminal unit symbols. UCUM is used in healthcare to populate electronic health records, such as laboratory records in LOINC, and in the [ISO IDMP](#) standard.

By making it easier to convert data between HL7 FHIR (commonly used in clinical systems to collect and share healthcare data) and CDISC standards, both organizations aim to reduce the barriers to using clinical information to support research.

HL7 FHIR Resources

In FHIR, implementation guides are a set of rules of how a particular interoperability or standards problem is solved through the use of FHIR resources. The [FHIR to CDISC Joint Mapping Implementation Guide \(IG\) v1.0](#) is also posted to the [HL7 website](#) and provides the same content in a format similar to other FHIR implementation guides.

* CDISC posts Public Review comments and resolutions to ensure transparency and show implementers how comments were addressed in the standard development process.

This page is part of the CDISC Mapping FHIR IG (v1.0.0: [STU 1](#)) based on [FHIR R4](#). This is the current published version in its permanent home (it will always be available at this URL). For a full list of available versions, see the [Directory of published versions](#).

1 IG Home Page

1.0.1 Introduction

[CDISC](#) defines a number of standards that support the capture and sharing of information related to research and clinical trials. [FHIR](#) is an [HL7](#) standard for the capturing and sharing of healthcare information for a wide variety of purposes. This implementation guide, a joint effort of CDISC and HL7 defines mappings between [FHIR release 4.0](#) and three specific CDISC standards:

- [Study Data Tabulation Model Implementation Guide \(SDTMIG\) 3.2](#)
- [Clinical Data Acquisition Standards Harmonization Implementation Guide \(CDASH\) 2.1](#)
- [LAB 1.0.1](#)

By making it easier to convert data between HL7 FHIR (commonly used in clinical systems to collect and share healthcare data) and CDISC standards (commonly used to submit clinical trial data for analysis and regulatory approval), both organizations aim to reduce the barriers to using clinical information to support research. Possible uses include:

- Capturing 'real world evidence' (RWE) where clinical data not directly captured for clinical trial purposes can be used to support regulatory applications.
- Allowing trial-driven data capture to occur directly inside clinical systems rather than separate clinical trial management solutions, leveraging technologies like [SMART on FHIR](#). This is sometimes referred to as e-sourced data.
- Making it easier to leverage clinical data in retrospective studies.
- Supporting the creation of case report forms (CRFs) that link to data elements defined using FHIR resources and profiles.
- Enabling experts from both standards communities to understand each others terms and better align both sets of specifications as they continue to evolve.

As indicated by the use-cases, this guide will principally be used to support conversion of FHIR data into CDISC standards. The focus is on identifying which FHIR locations are most likely to have data needed to populate the in-scope CDISC specifications. However, the mapping information provided could also be used to generate FHIR instances from existing collections of CDISC data if there was a desire to do that.

1.0.2 Content

This implementation guide is purely a 'descriptive' guide. It does not (currently) define any FHIR profiles, value sets or other artifacts. Instead, it provides mapping tables that show the mappings between elements in portions of selected CDISC specifications map to FHIR. This content is organized as follows:

- **Mapping Overview:** Provides an explanation of the approach to the mappings, a description of how the mapping tables are organized, and other information relevant to reading and interpreting this specification.
- **Mapping Caveats & Considerations:** Additional background on aspects of CDISC standards that provide additional challenges when mapping from FHIR and guidance on how to address those challenges.
- **Mapping domains:** Separate pages that describe the mappings for different areas of clinical research information
 - [Adverse Events](#)
 - [Concomitant Medications](#)

Contents:

- [Introduction](#)
- [Content](#)
- [Credits](#)

Considerations for Using CDISC Standards for Observational Studies

Goal

- Publish a CDISC-endorsed approach to working with observational research data
- Provide a “stake in the ground” for future expansion

Scope of Use Cases

- **Observational Research Studies**
 - Cross-sectional studies
 - Cohort studies
- **Clinical trials:** external control arm using RWD

Development Scope

- SDTM
- CDASH, ADaM could come in subsequent version

Considerations for Using CDISC Standards for Observational Studies - Overview

Discussion on common issues encountered when implementing SDTM for observational studies / RWD for External Control Arm studies

Implementation strategies or guidance to address these issues.

Examples illustrating these strategies (where applicable)

- Reuse existing standards; create new domains and variables only if necessary

Examples illustrating any new concepts/strategies that may be identified

Discussion on adjusting conformance rules to better fit these data

- New conformance rules as needed
- Note irrelevant conformance rules for validation checks of observational studies.

Lessons learned so far...

There aren't many truly show-stopping conformance rules

Existing SDTM domains cover what we need for the use cases we've examined.

Existing variables can also be used as-is or repurposed

SDTM Examples are less informative than discussions of considerations

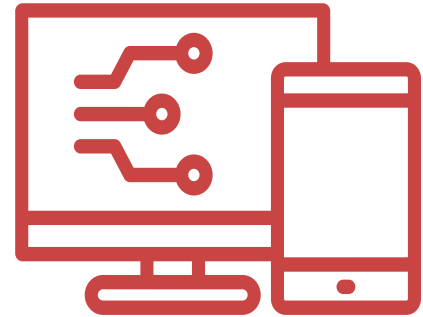
- Examples look like normal SDTM examples
- Discussing how we arrived at the modeling, and how to explain that to reviewers is more impactful

**Now Available in
the CDISC
Knowledge Base**

<https://www.cdisc.org/kb/articles/considerations-using-cdisc-standards-observational-studies>

Digital Health Technologies (DHT)

- An electronic method, system, product, or process that generates, stores, displays, processes and/or uses data within a healthcare setting.
- Examples include mobile health (mHealth), health information technology (IT), wearable devices, telehealth and telemedicine, and personalized medicine.





CDISC Digital Health Technologies (DHT) Team

The purpose of this team is to explore and enhance standardization of digital health technologies data.

Our aims are to:

- Increase our collective knowledge of digital health technologies and related data;
- In collaboration with a diverse group of stakeholders;
- To determine how CDISC standards can further support use of DHTs; and to
- Develop and publish new supporting standards.

CDISC Standards Are Robust Enough to Represent DHT Data

ECG Test Results Domain



Identifier Variable Connects Device Information with Results

Device Domains

Example





Deliverables

Initial areas of focus include standards for data:

- Collected using DHTs which contribute to endpoints
- About attributes of devices used

Under consideration are:

- Enhancements to the SDTM and other foundational standards
- Controlled Terminologies and Codetable Mapping Files for digital endpoints
- TBD

CDISC Digital Health Technologies (DHT) Team

- **Team** of ~ thirty members with diverse experience with DHTs (DEEP, Droice Labs, DiME, C-Path and regulatory agencies)
- **Research areas** include cardiovascular, central nervous system, dermatology, infectious diseases, respiratory, oncology



CDISC Knowledge Base

eCRF Portal – 65 eCRFs available

CDISC eCRFs

- The eCRF Portal contains machine readable eCRFs
 - Visual representation of CRF layout with CDASH annotations
 - Machine-readable in ODM format
- Includes CRFs from:
 - CDASH Implementation Guide v2.1
 - Crohn's Disease Therapeutic Area UG
 - COVID-19 Therapeutic Area UG
 - 65 customizable eCRFs are available
 - Freely downloadable from:

Demographics

Overview eCRF Considerations eCRF Preview **Download**

Form DM - Demographics

DM - Demographics

What is the subject's date of birth? 01 Jan 2000

What is the subject's age?

What is the age unit used? Years

What is the sex of the subject?

Do you consider yourself Hispanic/Latino or not Hispanic/Latino?

Which of the following five racial designations best describes you? (More than one choice is acceptable.)

What was the other race?

* Mandatory field



cdisc eCRF Portal



Funding provided by





Special Issue:
Innovative
Implementation
of CDISC Standards

cdisc
Clear Data. Clear Impact.

Current Issue
Volume 2 • Issue 3 • Fall 2022 • Innovative Implementation of CDISC Standards

- Papers focused on CDISC implementation use cases (all data sources)
- 8 articles published
- 9 articles near completion

<https://www.js.cdm.org/issue/9/info/>



Standardizing Paediatric Clinical Data: The Development of the conect4children (c4c) Cross Cutting Paediatric Data Dictionary

Anando Sen , Victoria Hedley , John Owen , Ronald Cornet , Dipak Kalra , Corinna Engel , Avril Palmeri , Joanne Lee , Jean-Christophe Roze , Joseph F Standing , Adilia Warris , Claudia Pansieri , Rebecca Leary , Mark Turner and Volker Straub

📅 2023-02-13 📖 Volume 2 • Issue 3 • 2022 • Fall 2022 - Innovative Implementation of CDISC Standards



Electronic Submission and Utilization of CDISC Standardized Clinical Study Data in Japan

Yuki Ando

📅 2023-01-13 📖 Volume 2 • Issue 3 • 2022 • Fall 2022 - Innovative Implementation of CDISC Standards



Implementation of COVID-19 Pandemic Impact Standards

Miho Hashio , Sarah Huggett , Stephen Hamburg , Robyn Eichenbaum and Nadeem Gul

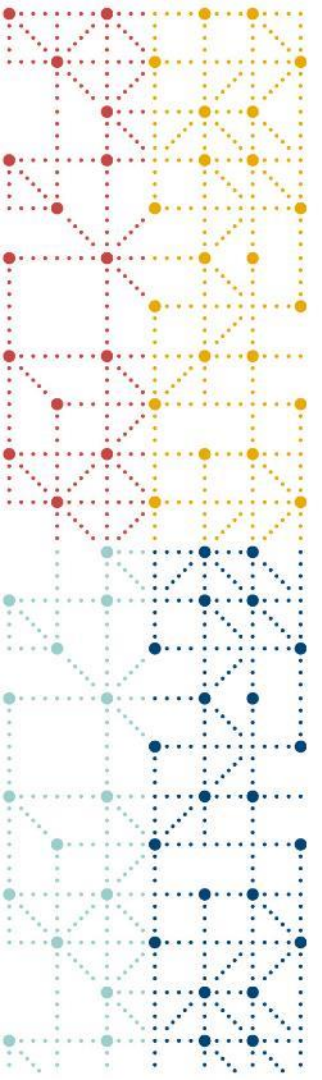
📅 2023-01-05 📖 Volume 2 • Issue 3 • 2022 • Fall 2022 - Innovative Implementation of CDISC Standards



Developing Technical Specifications for Submitting Clinical Trial Data Sets for Treatment of Noncirrhotic Nonalcoholic Steatohepatitis (NASH) Liver Fibrosis

Y. Veronica Pei , Vaishali Popat , Aaron Belowich and Chenoa Conley

📅 2023-01-05 📖 Volume 2 • Issue 3 • 2022 • Fall 2022 - Innovative Implementation of CDISC Standards



Thank you!

cdisc

Clear data. Clear impact.