WITH STANDARDS – UNLOCK THE POWER OF DATA

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2022
CHINA
INTERCHANGE
29-30 JULY | VIRTUAL EVENT

State of the CDISC Standards

Amy Palmer, Head of Standards Development

Meet the Speaker

Amy Palmer

Title: Head of Standards Development

Organization: CDISC

Amy Palmer is the Head of Standards Development at CDISC. Amy has been with CDISC since 2013. She is a member of the CDISC Technical Leadership Team and leads the Global Governance Group. Amy has over 26 years' experience working in clinical research. She has been involved in the development of multiple therapeutic area user guides as well the foundational standards and has been working with CDISC standards since 2010.

Amy has a BS from Mary Washington College and an MPH from the University of Montana.

Agenda

1. CDISC 2021 Development Highlights
2. New and Ongoing Standards Development Activities

CDISC Standards Development in 2021

2021 Foundational Standards Publications

SENDIG v3.3.1	Published 30 March 2021
SEND Conformance Rules v4.0	Published 29 July 2021
Define-XML v2.1Conformance Rules	Published 30 March 2021
CDASH SAE Supplement v2.0	Published 21 April 2021
CDASH v1.2	Published 28 September 2021
CDASHIG v2.2	
SDTM v2.0 and Conformance Rules	Published 29 November 2021
SDTMIG v3.4 and Conformance Rules	
ADaMIG v1.3 and Conformance Rules	
ADaMIG OCCDS v1.1 and Conformance Rules	
ADaMIG Medical Devices v1.0 and Conformance Rules	
ADaMIG Non-compartmental Analysis v1.0 and Conformance Rules	

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2021 Therapeutic Area User Guides Publications

- Type 1 Diabetes
- COVID-19
- Crohn's Disease
- Pancreatic Cancer

2021 Other Standards Publications

- Vaccination Administration v1.0
- Quarterly Controlled Terminology Releases
- SDTM Metadata Submission Guidelines v2.0
- QRS Supplements
- HL7 FHIR to CDISC Mapping
- CDISC Glossary v16.0

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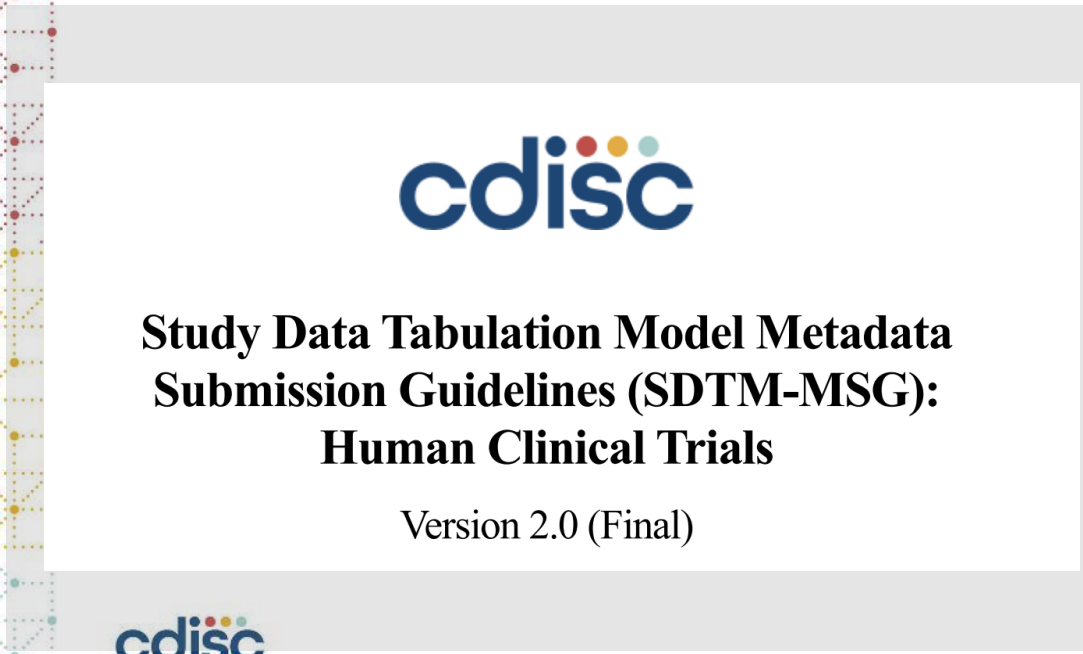
Vaccination Administration v1.0

- Goal to create a global core data standard that will enable the success of various vaccine credentialing and vaccine ‘passport’ applications to foster rapid and comprehensible sharing of essential information for uses such as safe international travel
- Developed in Collaboration with the Learning Health Community
- Consolidating key data element recommendations from the European eHealth Network, the World Health Organization and US Centers for Disease Control
- Relevant standards developed through ISO, HL7, and CDISC have been applied and harmonized

HL7 FHIR to CDISC Mapping

- Fast Healthcare Interoperability Resources (FHIR) is a new standard published by HL7 for exchanging healthcare information electronically
- Goal of mapping is to achieve greater interoperability and exchange of data from Electronic Health Records (EHRs) **to** clinical research submission-ready datasets
- Scope: Adverse Events, Medications, Concomitant Medications, Demographics, Medical History, Procedures, Vital Signs, Laboratory Test Results
- Mappings jointly balloted by CDISC and HL7 using their respective governance processes

Metadata Submission Guidelines



- The Guidelines and the Sample Submission Package illustrate the components recommended for the submission of SDTM data
- The Sample Submission Package consists of new or revised datasets, annotated CRF, submission components and a study data reviewer's guide
- ADaM MSG Internal Review Planned for Q2 2022

New and Ongoing Standards Development Activities

Foundational Standards and Therapeutic Areas Planned to be Published in 2022

ADaM Examples of Traceability	ADaM Oncology Examples	ADaM popPK Implementation Guide	SDTMIG-Medical Devices Conformance Rules
ODM v2.0	Pediatrics User Guide v1.0	Rare Diseases TAUG v1.0	TCM – Acupuncture TAUG v1.0

https://www.cdisc.org/standards/in-development

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Rare Diseases User Guide

- Collaboration with National Organization for Rare Disorders (NORD)
- Document scope includes cross-cutting concepts, endpoints, questionnaires, terminology
- Public review anticipated Fall 2022

Rare Diseases User Guide Scope

- Diagnosis
  - Newborn Screening Tests
  - Genetic Testing
  - Biochemical Tests
  - Special Lab Tests
  - Clinical Criteria
- Study Conduct
  - Inclusion/Exclusion Criteria
  - Withdrawals/Discontinuations
- Demography
  - Date of Birth and Age
  - Sex
  - Ethnicity and Race
  - Date of Death
- Family History
- Prior/Concomitant Medications & Procedures
- Study Treatment
- Endpoints
- Safety Assessments
  - Adverse Events

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Pediatrics User Guide

conect 4children
COLLABORATIVE NETWORK FOR EUROPEAN CLINICAL TRIALS FOR CHILDREN

imi innovative medicines initiative

efpia

Areas of Focus

- Information about the subject (e.g., demography, vital signs, diet and nutrition, body system assessments
- Information about the subject's family (e.g., medical conditions, medications, substance use)
- Pregnancy and Birth
- Study Conduct
- QRS

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DRAGON: An IMI-Funded Project

Develop AI-enhanced tools for evaluating COVID patients' *CT scans* and *clinical data* to provide accurate diagnoses and predict patient outcome.

cdisc's Role

- EHR data harmonization design and mapping support to feed data to AI
- COVID-19 User Guide v2.0 Imaging Guide
- Considerations for using CDISC standards for observational research
- CDISC Basic: abridged CDASH & SDTM for non-submission research

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Tobacco Implementation Guide (TIG) v1.0

Non-proprietary, consensus-based, freely available standards for use in studies of tobacco products

An overview of standards and general implementation

With guidance by topics and use cases; e.g.

- OMB Forms
- Nonclinical
- Clinical Studies

Key scientific concepts and maps

Data Collection (*CDASH eCRFs*, *ODM-XML*)

Data Tabulation (*SEND*, *SDTM Human Clinical*, *Define-XML*)

Analysis (*ADaM, Analysis Results*, *Define-XML*)

Common Language (*Controlled Terminology*)

Measures of Adherence (*Conformance Rules*)

Accessible in platforms which optimize use (including *CDISC website*, *CDISC Library*)

Education and Outreach (including *webinars*, *formal training*)

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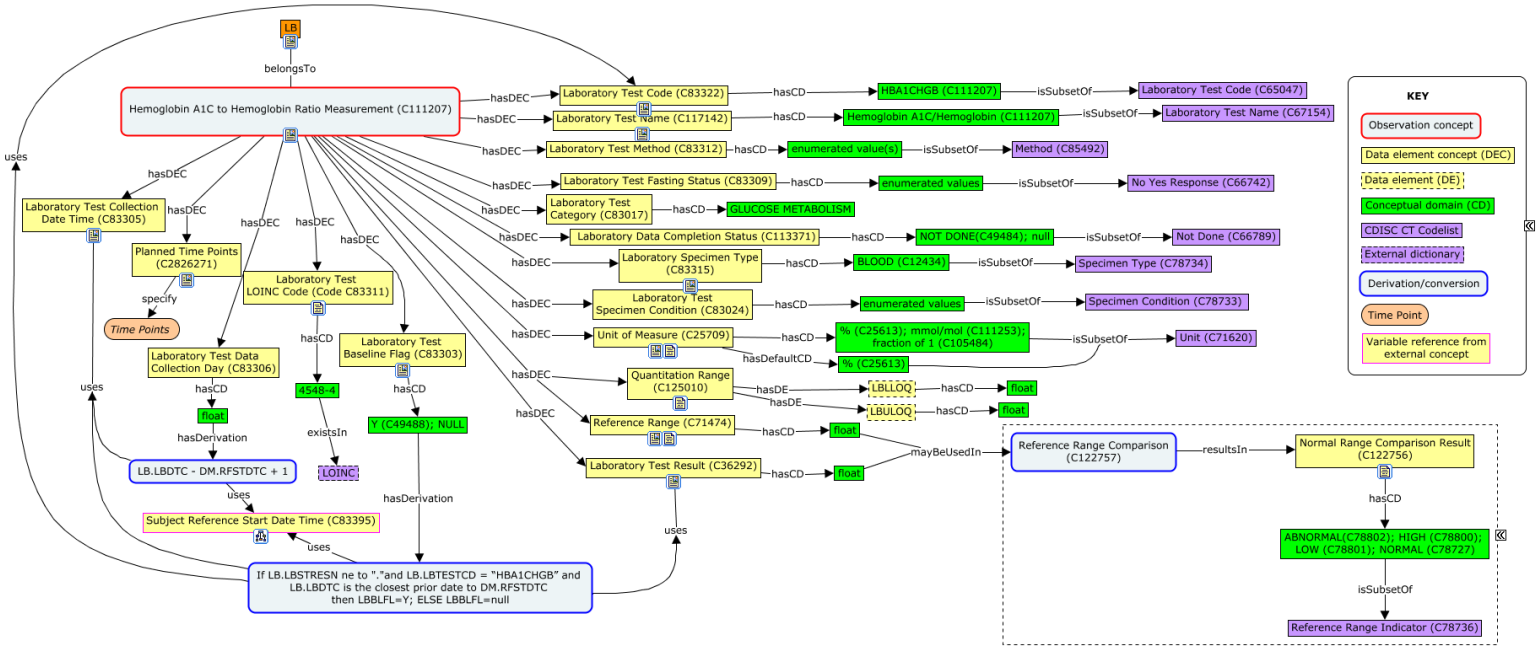
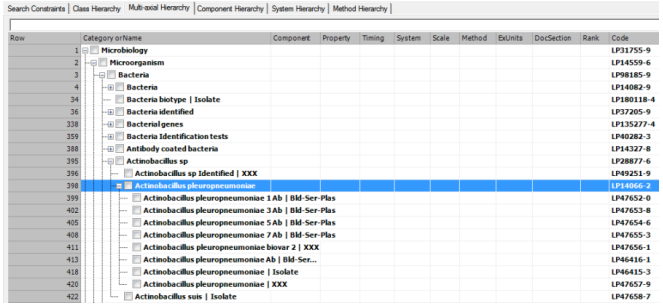
Biomedical Concept Update



Biomedical Concepts: Approach that Separates the Concepts and Data Models

Concept Model

- Create hierarchical concept model
- Create semantics
- Create concept codes
- Add synonymous concepts



Data Model

- Add relationships
- Add operational metadata
- Add specializations
- Add concept code

vs.xpt, Vital Signs — Findings, Version 3.2. One record per vital sign measurement per time point per visit per subject, Tabulation

Variable Name	Variable Label	Type	Controlled Terms, Codelist or Format	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		Identifier	Unique identifier for a study.	Req
DOMAIN	Domain Abbreviation	Char	VS	Identifier	Two-character abbreviation for the domain.	Req
USUBJID	Unique Subject Identifier	Char		Identifier	Identifier used to uniquely identify a subject across all studies for all applications or submissions involving the product.	Req
VSSEQ	Sequence Number	Num		Identifier	Sequence Number given to ensure uniqueness of subject records within a domain. May be any valid number.	Req
VSGRPID	Group ID	Char		Identifier	Used to tie together a block of related records in a single domain for a subject.	Perm
VSSPID	Sponsor-Defined Identifier	Char		Identifier	Sponsor-defined reference number. Perhaps pre-printed on the CRF as an explicit line identifier or defined in the sponsor's operational database.	Perm
VSTESTCD	Vital Signs Test Short Name	Char	(VSTESTCD)	Topic	Short name of the measurement, test, or examination described in VSTEST. It can be used as a column name when converting a dataset from a vertical to a horizontal format. The value in VSTESTCD cannot be longer than 8 characters, nor can it start with a number (e.g."1TEST"). VSTESTCD cannot contain characters other than letters, numbers, or underscores. Examples: SYSBP, DIABP, BMI.	Req

Analysis Results Current State

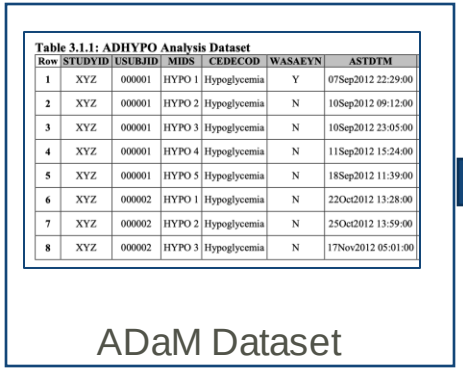
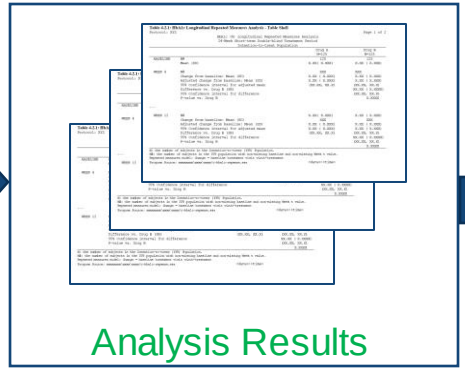


Table 3.1.1: ADHYPO Analysis Dataset

Row	STUDYID	USUBJID	MIDS	CEDECOD	WASAEYN	ASTDTM
1	XYZ	000001	HYPO 1	Hypoglycemia	Y	07Sep2012 22:29:00
2	XYZ	000001	HYPO 2	Hypoglycemia	N	10Sep2012 09:12:00
3	XYZ	000001	HYPO 3	Hypoglycemia	N	10Sep2012 23:05:00
4	XYZ	000001	HYPO 4	Hypoglycemia	N	11Sep2012 15:24:00
5	XYZ	000001	HYPO 5	Hypoglycemia	N	18Sep2012 11:39:00
6	XYZ	000002	HYPO 1	Hypoglycemia	N	22Oct2012 13:28:00
7	XYZ	000002	HYPO 2	Hypoglycemia	N	25Oct2012 13:59:00
8	XYZ	000002	HYPO 3	Hypoglycemia	N	17Nov2012 05:01:00

ADaM Dataset



Analysis Results

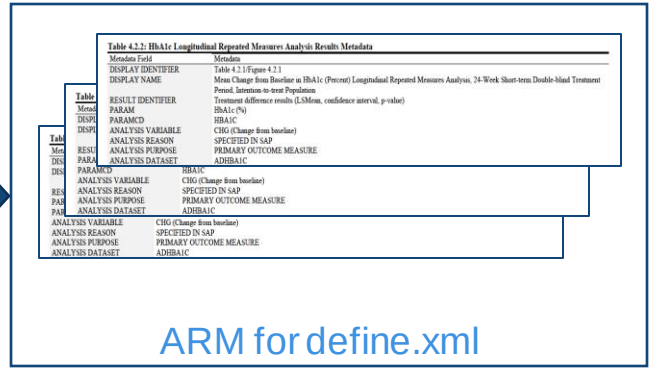


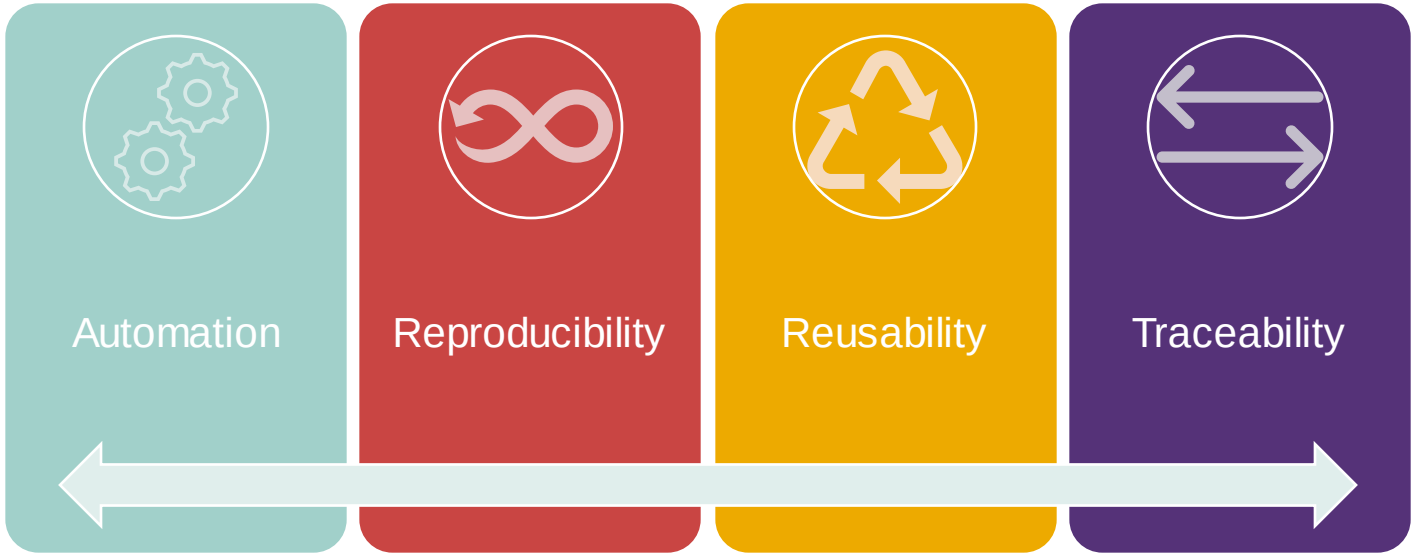
Table 4.2.2: HbA1c Longitudinal Repeated Measures Analysis Results Metadata

Metadata Field	Metadata
DISPLAY IDENTIFIER	Table 4.2.1/Figure 4.2.1
DISPLAY NAME	Mean Change from Baseline in HbA1c (Percent) Longitudinal Repeated Measures Analysis, 24-Week Short-term Double-blind Treatment Period, Intention-to-treat Population
RESULT IDENTIFIER	Treatment difference results (LSMeans, confidence interval, p-value)
PARAM	HbA1c (%)
PARAMCD	HBA1C
ANALYSIS VARIABLE	CHG (Change from baseline)
ANALYSIS REASON	SPECIFIED IN SAP
ANALYSIS PURPOSE	PRIMARY OUTCOME MEASURE
ANALYSIS DATASET	ADHBA1C

ARM for define.xml

- Static results created for Clinical Study Report
- Expensive to generate and only used once, no or limited reusability
- ARM v1.0 describes *metadata* about displays (PDF) and results (at high level), no formal analysis and results model or results data
- Limited traceability

Analysis Results Future State



Why is CDISC doing CORE?

- Ensure each standard has a set of unambiguous, executable Conformance Rules
- Ensure consistency across Conformance Rule implementations
- Expedite the availability of executable Conformance Rules for new Foundational Standards
- Create executable Conformance Rules vetted by the CDISC standards development teams
- Develop an open-source engine that serves as a Reference Implementation
- Publish the Rules in the CDISC Library and the engine under the CDISC Open Source Alliance (COSA)

https://www.cdisc.org/core

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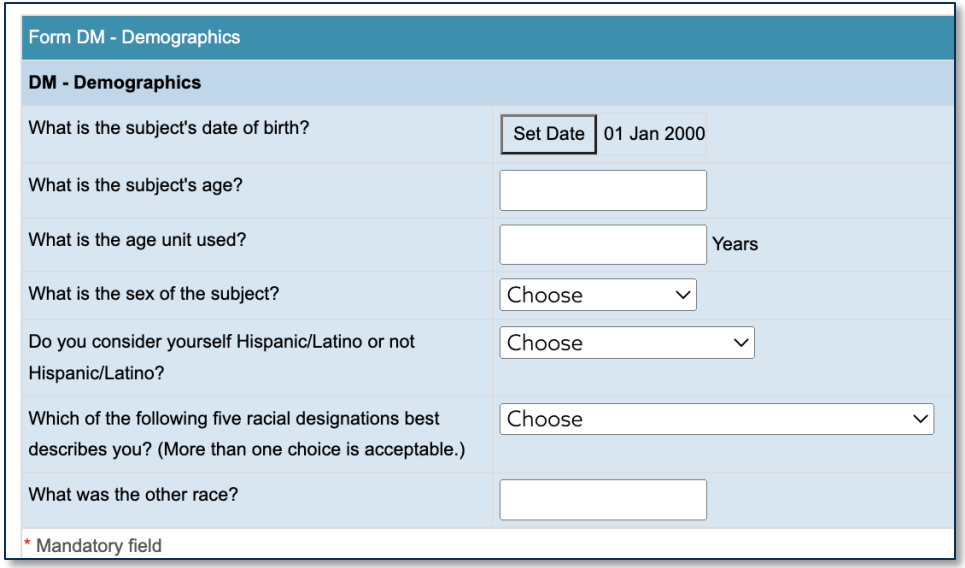
CDASH eCRF Portal

- Out-of-the-box" solution for new users
- Meets the basic needs for many users, but also customizable
- Increase use of CDASH



https://www.cdisc.org/kb/ecrf

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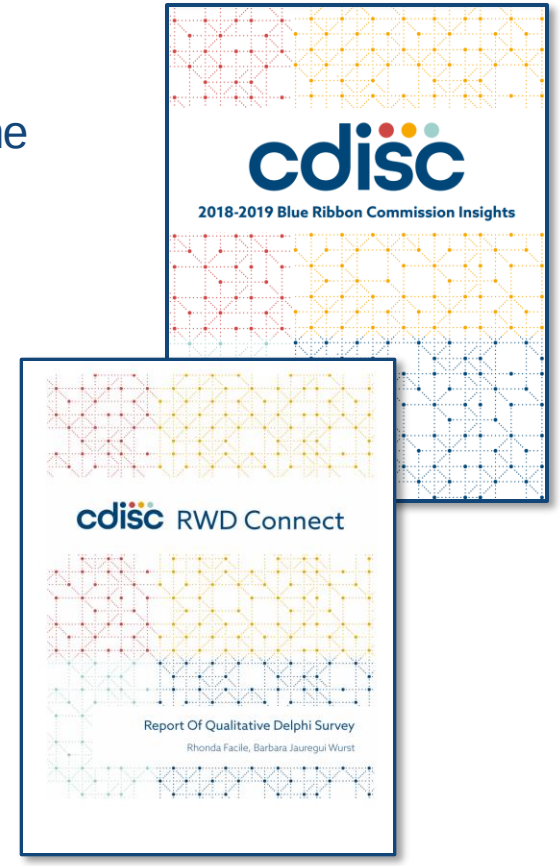
- The eCRF Portal adds functionality to the CDASH model.
  - Visual representation of CRF layout with CDASH annotations
  - Machine-readable ODM format
- Includes CRFs from:
  - CDASH Implementation Guide v2.1
  - Crohn's Disease Therapeutic Area User Guide
  - Upcoming – COVID-19 Therapeutic Area User Guide
- Formedix offered the CDISC community MDR use at no cost

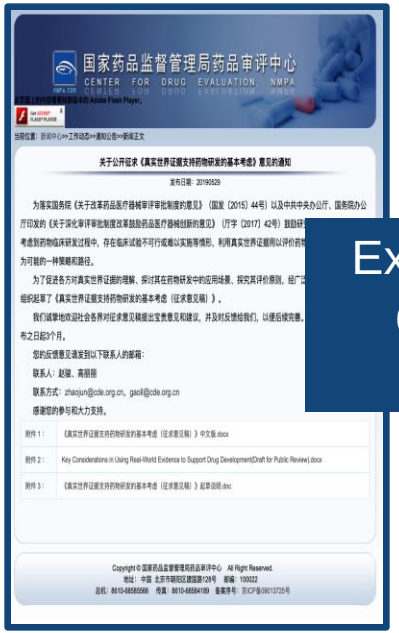
CDISC, Beyond Regulated Research

- 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



RWD and the Regulatory Environment

China's NMPA



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

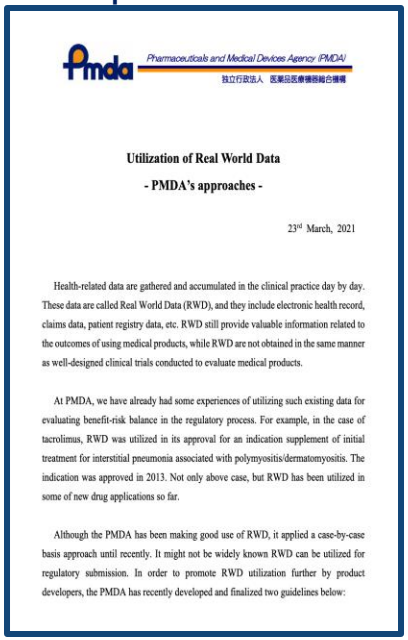
US FDA

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

EU EMA

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

Japan's PMDA



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

Exploring and promoting the use of high-quality RWD in decision-making as a strategic goal

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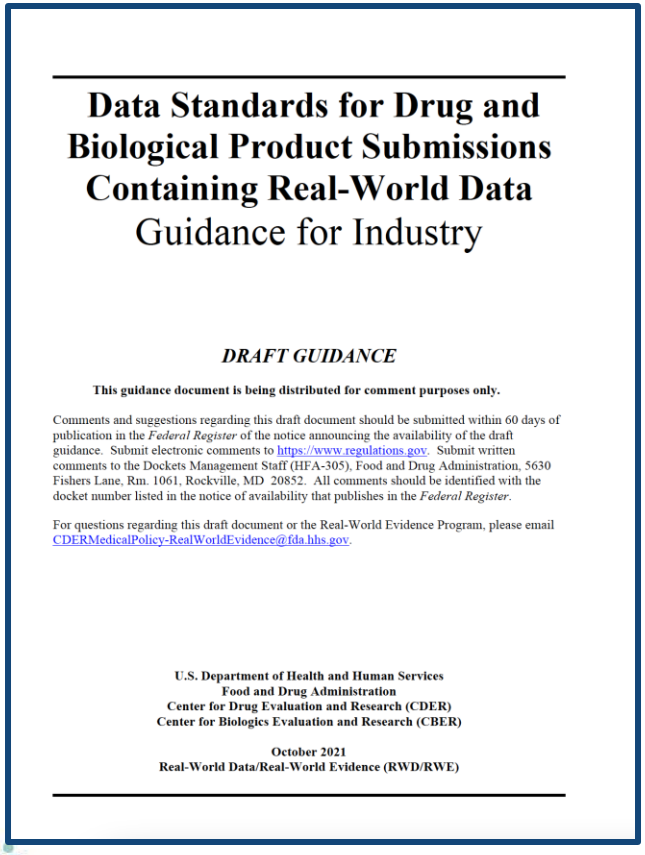
Draft FDA RWD and Registry Guidance



Data Standards for Drug and Biological Product Submissions Containing Real-World Data

Guidance for Industry

DRAFT GUIDANCE

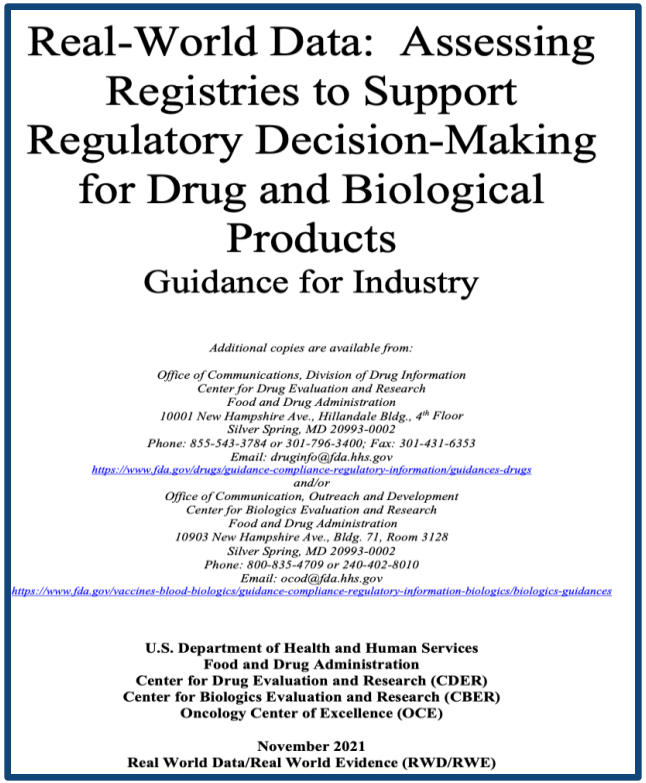
This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document or the Real-World Evidence Program, please email CDERMedicalPolicy-RealWorldEvidence@fda.hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

October 2021
Real-World Data/Real-World Evidence (RWD/RWE)



Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products

Guidance for Industry

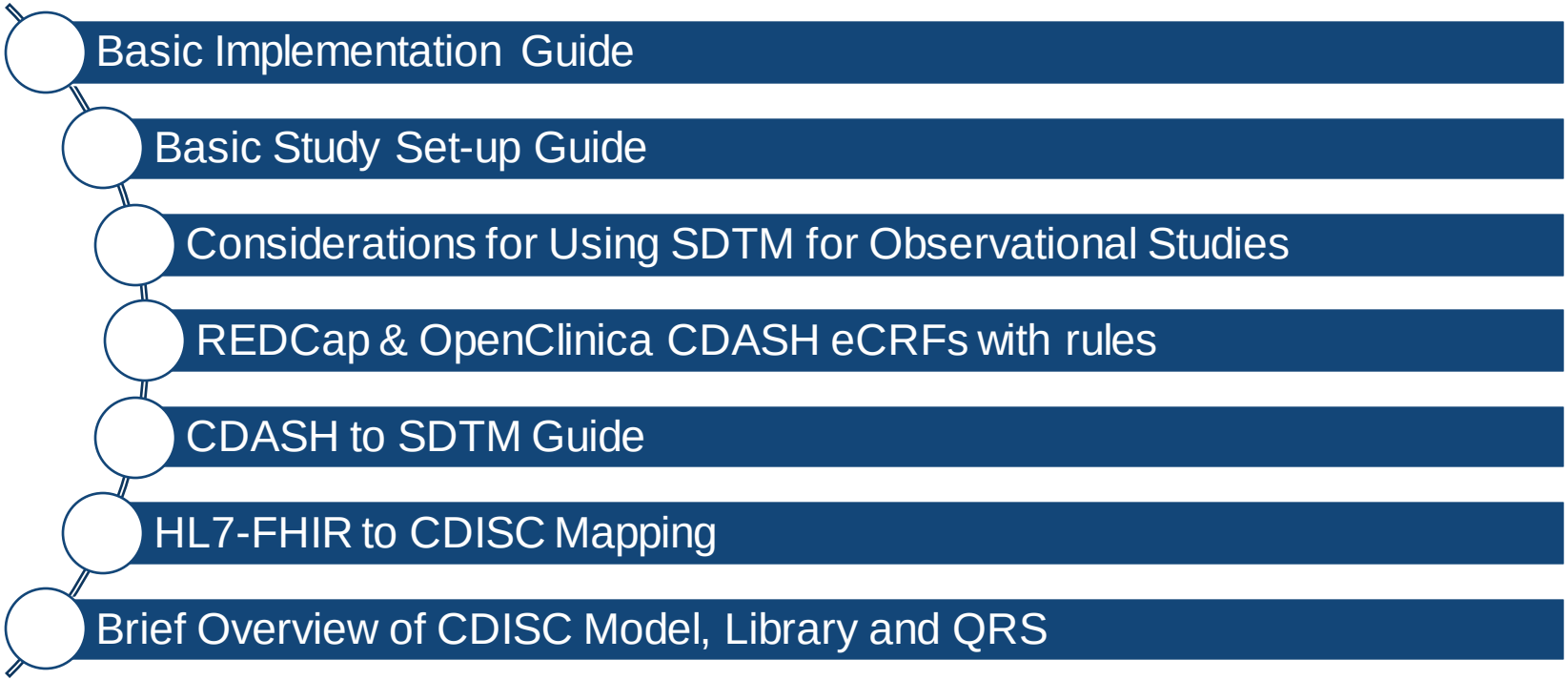
Additional copies are available from:

Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10001 New Hampshire Ave., Hillandale Bldg., 4th Floor
Silver Spring, MD 20993-0002
Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353
Email: druginfo@fda.hhs.gov
https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs
and/or
Office of Communication, Outreach and Development
Center for Biologics Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., Bldg. 71, Room 3128
Silver Spring, MD 20993-0002
Phone: 800-835-4709 or 240-402-8010
Email: ocod@fda.hhs.gov
https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Oncology Center of Excellence (OCE)

November 2021
Real World Data/Real World Evidence (RWD/RWE)

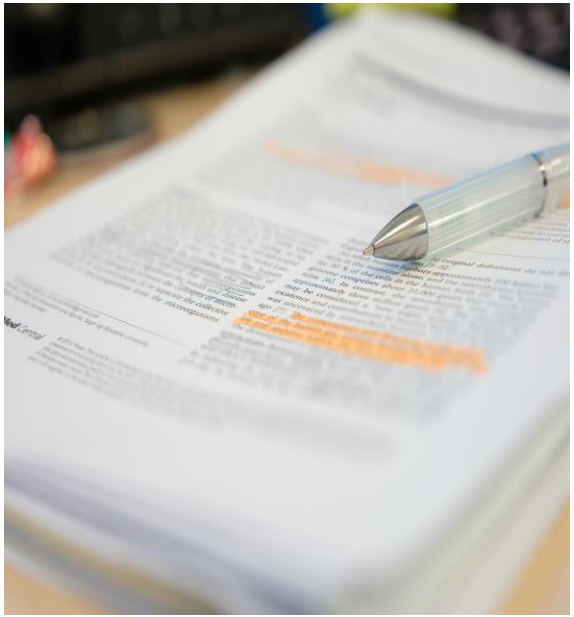
RWD Guides and Resources



CDISC Focused Special Edition of JSCDM

Papers focused on CDISC implementation use cases in submissions.

- 24 Abstracts accepted
- Publication Q4 2022



Certification Program Highlights

Validate Skills

Assess Potential Hires

Provide Clients With Proven Expertise

Visit the CDISC website for more information
www.cdisc.org/education/cdisc-standardscertification

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Thank You!