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Single Day Event

Latest Developments in CDISC Standards

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Disclaimer

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Agenda

- CDISC: Introduction & Evolution
- Standards Updates
  - Foundational, Data Exchange, TA
  - Standards <in progress>
  - SDTM IG v3.4
- CDISC Library
- CDISC Open-Source Alliance (COSA)
  - CORE
  - OAK
- Regulatory Agencies Updates
- Discussions

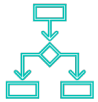
CDISC: Introduction

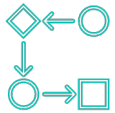
CDISC: Evolution

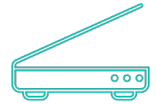
SDTM

SDTM
ADaM
CDASH
ODM

SDTM, ADaM
CDASH, TA
Validation Rules
Metadata, TMF



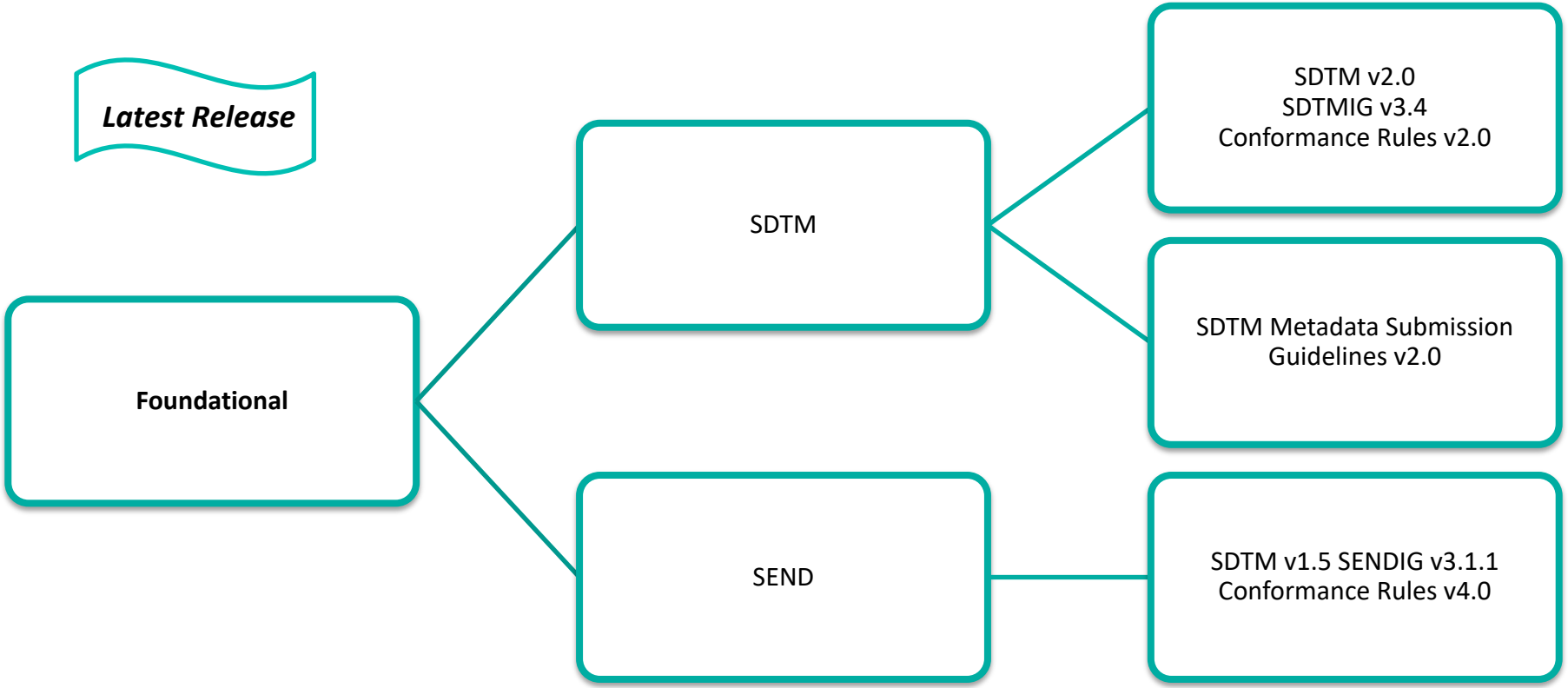




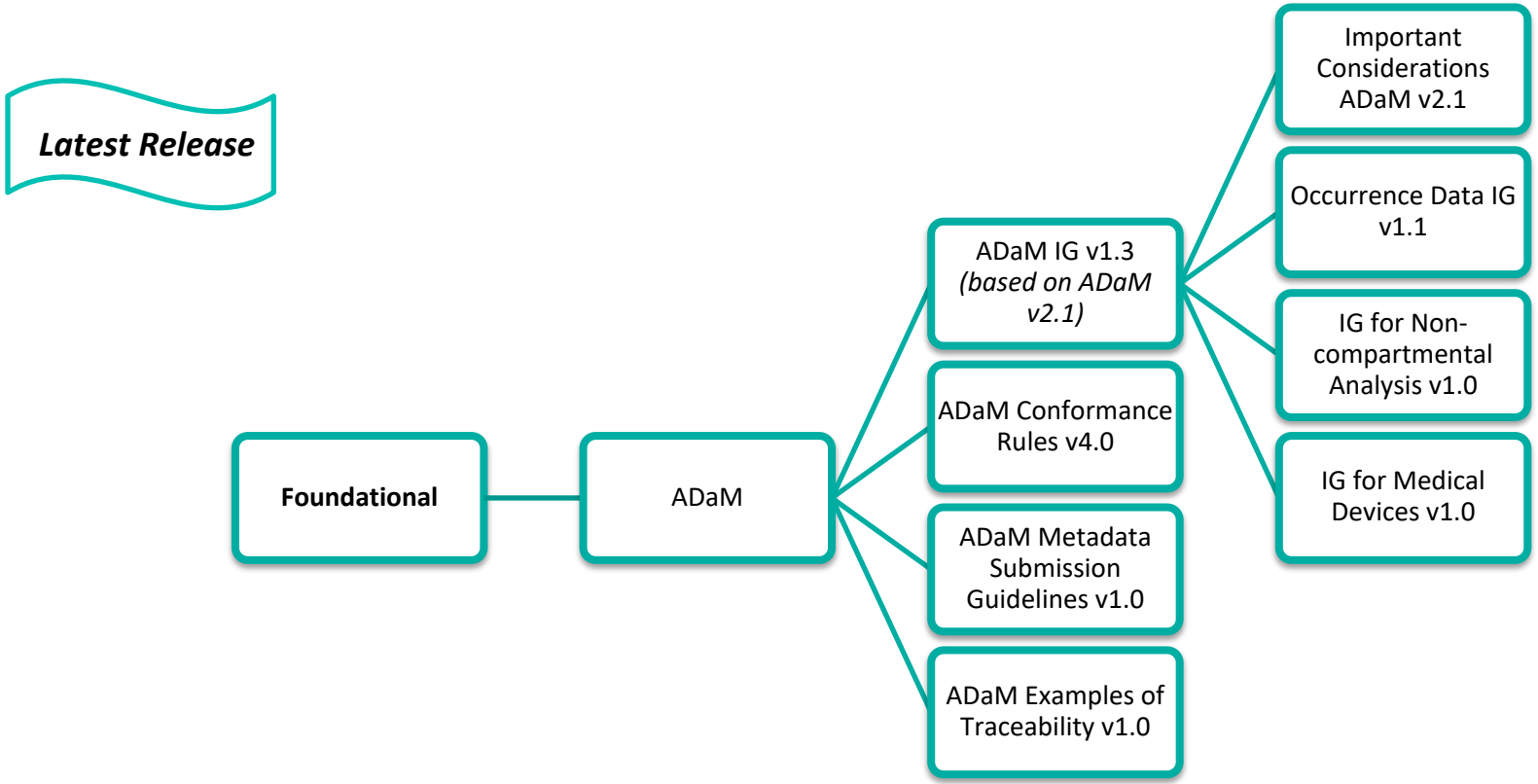
2004 US FDA Recommendation → **2014** US FDA & Japan PMDA Requirement Published* → **2019** China NMPA Requirement → **2021** US FDA Technical Rejection Criteria → **2022** CDISC COSA

**US FDA – Study Starting 17-Dec-2016*
Japan PMDA – Study submitted post 01-Oct-2016

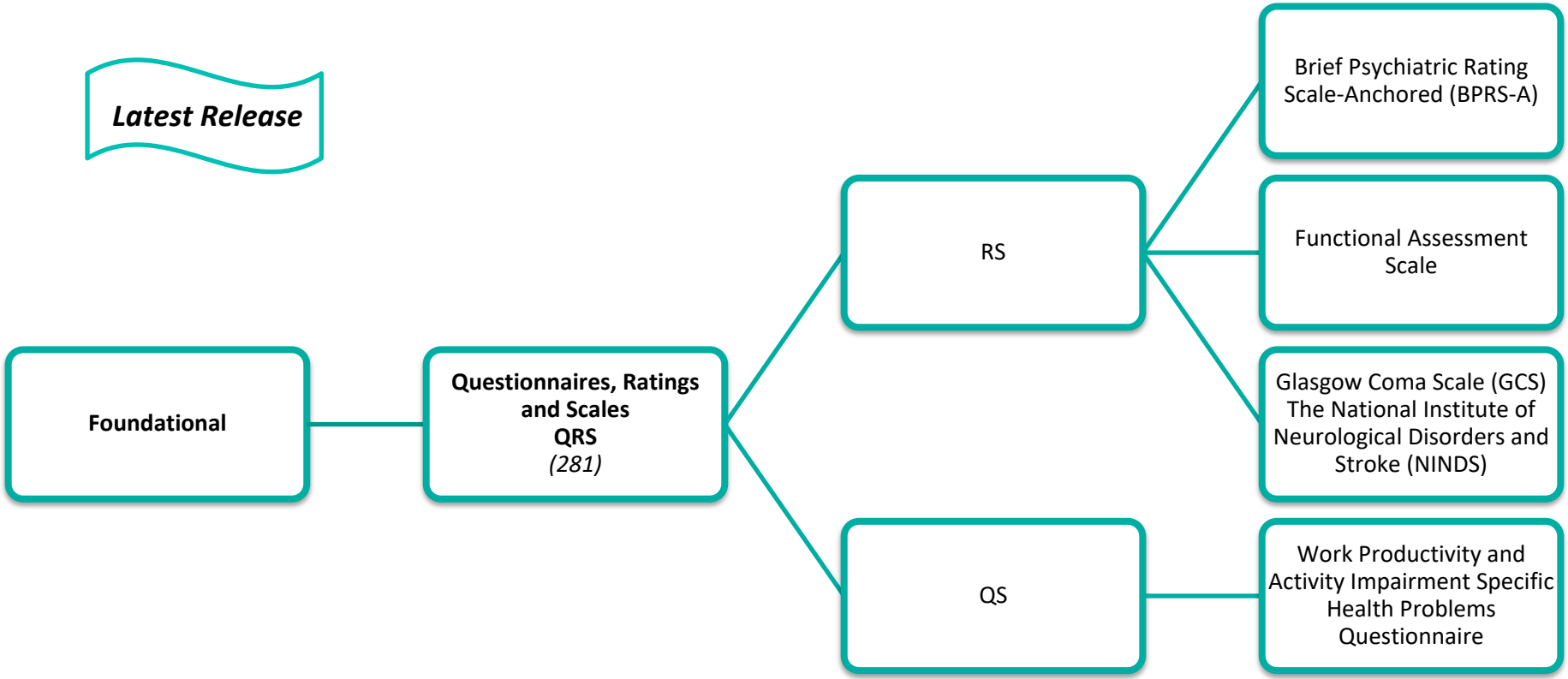
CDISC Standards: Updates



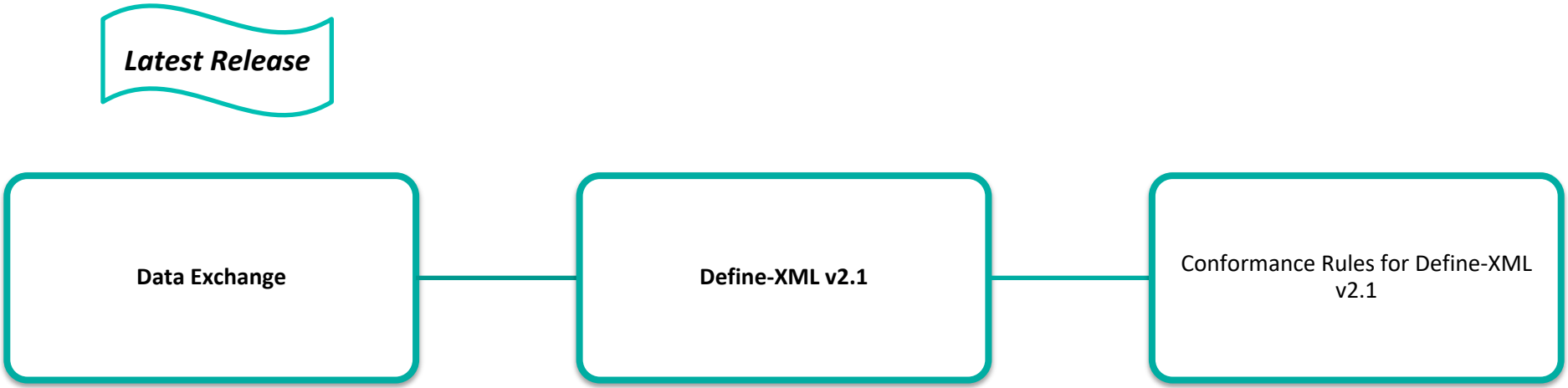
CDISC Standards: Updates



CDISC Standards: Updates



CDISC Standards: Updates



CDISC Standards: Updates

Therapeutic Area

~47

The Therapeutic Area User Guides (TAUGs) build upon the Foundational Standards and provide a comprehensive framework for capturing data related to specific disease areas.

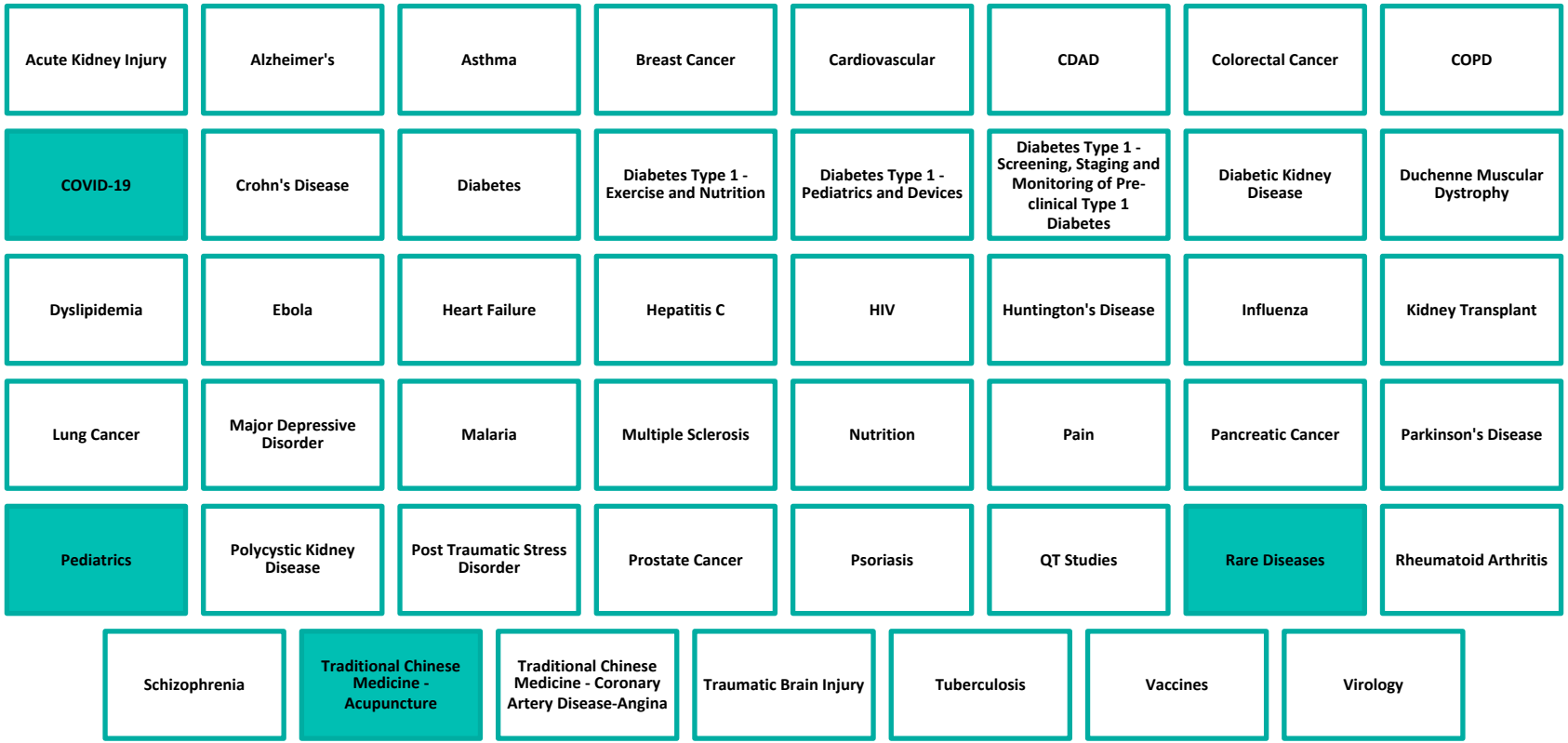
These guides consist of disease-specific metadata, practical examples, and guidance for implementing CDISC standards across various applications, including global regulatory submissions.

CDISC Standards: Updates

Acute Kidney Injury	Alzheimer's	Asthma	Breast Cancer	Cardiovascular	CDAD	Colorectal Cancer	COPD
COVID-19	Crohn's Disease	Diabetes	Diabetes Type 1 - Exercise and Nutrition	Diabetes Type 1 - Pediatrics and Devices	Diabetes Type 1 - Screening, Staging and Monitoring of Pre-clinical Type 1 Diabetes	Diabetic Kidney Disease	Duchenne Muscular Dystrophy
Dyslipidemia	Ebola	Heart Failure	Hepatitis C	HIV	Huntington's Disease	Influenza	Kidney Transplant
Lung Cancer	Major Depressive Disorder	Malaria	Multiple Sclerosis	Nutrition	Pain	Pancreatic Cancer	Parkinson's Disease
Pediatrics	Polycystic Kidney Disease	Post Traumatic Stress Disorder	Prostate Cancer	Psoriasis	QT Studies	Rare Diseases	Rheumatoid Arthritis

Schizophrenia	Traditional Chinese Medicine - Acupuncture	Traditional Chinese Medicine - Coronary Artery Disease-Angina	Traumatic Brain Injury	Tuberculosis	Vaccines	Virology

CDISC Standards: Updates



CDISC Standards: <in progress>

2023-2024

Development

> Analysis Results Metadata (ARM) Conformance Rules

> Analysis Results Standard v1.0

> Safety User Guide v1.0

> SDTM for Observational Studies v1.0

> SDTM v2.1

> SENDIG v4.0

> Tobacco Implementation Guide v1.0

Preparing - Public Review

> CDASH v1.3

> CDASHIG v2.3

Public Review Comments

> ADaM Oncology Examples

> ADaM popPK Implementation Guide v1.0

> SEND Tumor Combinations v1.0

> SENDIG-DART (Developmental and Reproductive Toxicology) v1.2

> SENDIG-Genotoxicity v1.0

> ODM v2.0

ADaM – Planning for a consolidated ADaM IG
SDTM – Multiple Subject Participations – DM and DC domains

CDISC Standards: SDTMIG v3.4

Class (Domains)

- Interventions (7)
- Events (7)
- Findings (30)
- Findings About (2)
- Special-Purpose (5)
- Trial Design (7)
- **Study Reference (1)**
- Relationship (4)

Domains

BE Biospecimen Events
BS Biospecimen Findings
CP Cell Phenotyping Findings
GF Genomics Findings
RELSPEC Related Specimens

MO Morphology

Key Updates

- 10 new variables in LB
- Scope expansion DA, IS, SC
- Guidance updates FA, TU, TR
- More variables under Controlled Terminology
- Appendix C1 Trial Summary Codes dropped
- ISO formats now more granular
- Structural updates SV, SUPPQUAL

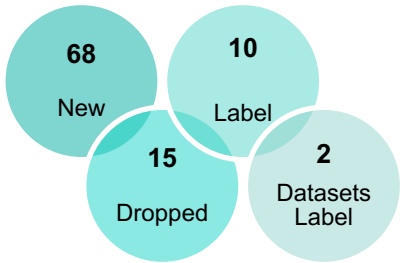
Conformance Rules

455

Changes

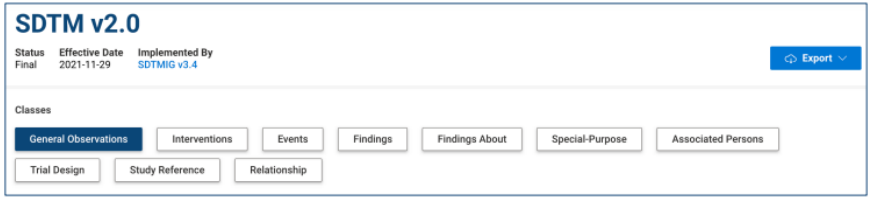
13384 – Total		
12426 Major	199 Minor	759 New

Variables



CDISC Library

- CDISC Library is for everyone
- Data Standards Browser
- API (Application Programming Interface)



Application

- Authoritative source of CDISC standards metadata
- Access and easily browse multiple versions of standards and CT
- Export standards metadata in various formats
- Create machine-readable diff reports
- Test upcoming standards' releases

Content

- CDASH/CDASHIG
- SDTM/SDTMIG
- SENDIG
- ADaM/ADaMIG
- QRS
- Controlled Terminology

CDISC Open-Source Alliance

COSA supports, promotes, and sometimes sponsors open source and free software development projects related to CDISC standards

COSA Repository Directory : 17 Tools

COSA collaborates with other open-source initiatives with similar missions

CDISC Open-Source Alliance

Admiral
ADaM in R Asset Library.

CDISC Rules Engine (CORE)
Deliver and execute a governed set of executable Conformance Rules for each Foundational Standard

CDISC-ODM-XML-CRF-SDTM-Annotations
An XMLMAP for ODM-XML and for Define-XML along with a small set of SAS macros for each, converting the XML documents to SAS datasets following familiar data models shared by MDR and validation tools.

CORE - Rule Editor
Creating additional Conformance Rules in a common specification for CORE

Define-XML XSL Stylesheets
This projects provides a Define-XML v2.0 and v2.1 XSL stylesheet

defineR
An open-source R package capable of generating the Define-XML.

Source: cosa.cdisc.org

CDISC Open-Source Alliance

Digital Data Flow
The DDF initiative aims to modernize clinical trials by enabling a digital workflow that allows for automated creation of study content and configuration of study systems to support clinical trial execution.

odmlib
odmlib is a Python library that simplifies creating and processing ODM and its extensions, such as Define-XML.

Open CST
The SAS Open Clinical Standards Toolkit (OpenCST) is a framework for the validation of CDISC data, especially SDTM, and the generation of define.xml.

Open Study Builder
The OpenStudyBuilder is a new approach to working with studies that once fully implemented will drive end-to-end consistency and more efficient processes.

R4DSXML
R4DSXML is R package for import both CDISC Dataset-XML and Define-XML as R data frame.

Smart Submission Dataset Viewer
Dataset viewer allowing to inspect CDISC SDTM, SEND and ADaM submission files.

TFL Designer
An open-source TFL designer to create study-specific analysis output display and in parallel generate machine-readable metadata.

Source: cosa.cdisc.org

CDISC Open-Source Alliance

tfrmt

The {tfrmt} R package is a table formatting framework that provides the means to flexibly design and build mock results summaries.

tidyCDISC

tidyCDISC is a shiny app to easily create custom tables and figures from ADaM-ish data sets.

Tplyr

Tplyr is a grammar of data format and summary, designed to simplify the creation of clinical safety summaries.

Visual Define-XML Editor

Visual Editor for Define-XML 2.0 and ARM standards.

Source: cosa.cdisc.org

CDISC COSA: CORE

CDISC Conformance Rules are an essential component of the Foundational Standards

The CORE Project aims to establish a definitive, controlled set of unambiguous, and operational Conformance Rules for each Foundational Standard

CDISC has partnered with Microsoft and other organizations to develop the CDISC Open Rules Engine (CORE), an open source software

The software uses the machine readable CDISC conformance rules from CDISC Library

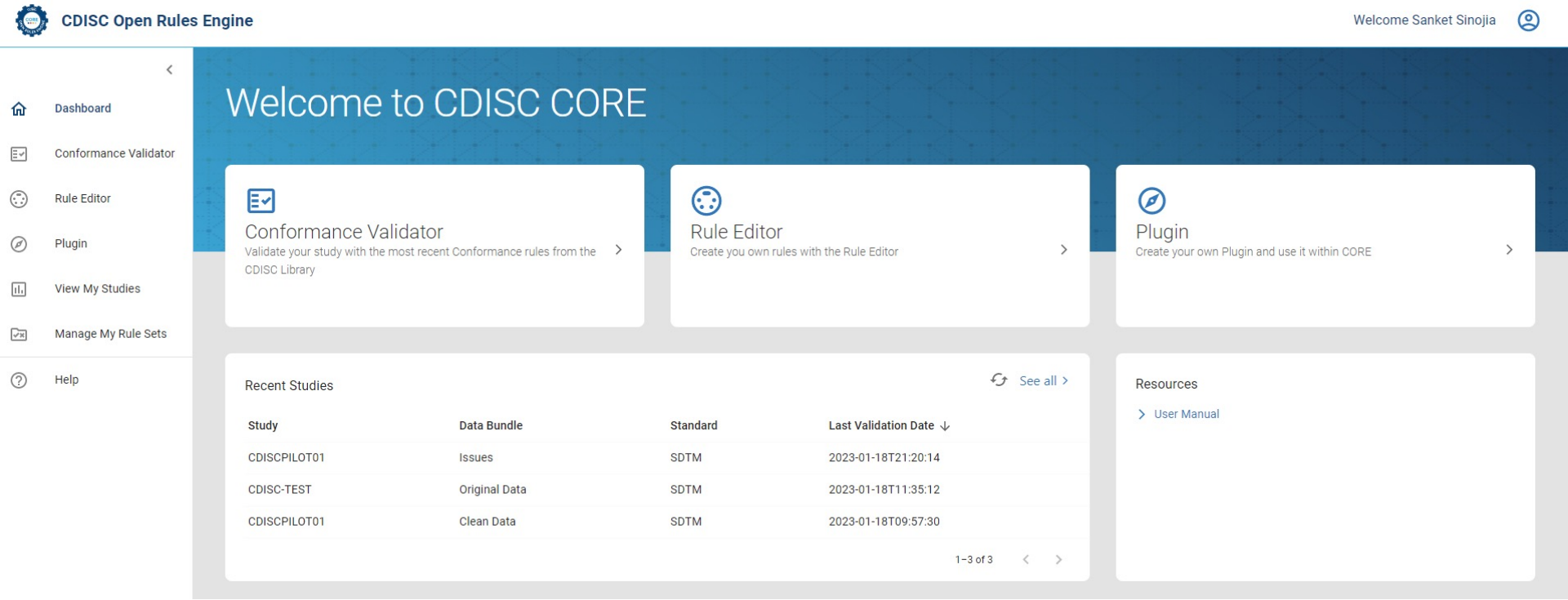
CDISC has release initial release of software, can be accessed on CDISC website

User can customize existing rules or create new rules

The UI is very simple, easy to navigate and comprehensive

The report can be viewed within software and exported as well

CDISC COSA: CORE



Source: core.cdisc.org

CDISC COSA: OAK

OAK is an open-source community project by CDISC COSA

To generate SDTM datasets based on CDASH mapping

To generate synthetic raw datasets

OAK is an R-based and metadata-driven solution that Roche successfully developed to automate SDTM Domains

Automate ~80% of SDTM domains based on ~22 Reusable Algorithms

Project kick started in early 2023

Regulatory Agencies Updates

U.S. FOOD & DRUG ADMINISTRATION

Study Data Technical Conformance Guide v5.1 (March 2023)

This Guide provides technical recommendations to sponsors for the submission of animal and human study data and related information in a standardized electronic format in INDs, NDAs, ANDAs, and BLAs.

Key Updates

- Section updated for Transport file XPT – Naming convention, Custom SAS files clarity
- Addition of Immunogenicity Domain (IS)
- Addition of Immunogenicity Analysis under Key Efficacy/Safety Data
- Clarification on SEND requirements
- Details added for SDTM-SEND-ADaM define.xml - eCTD study tagging file (STF)
- Details added for Medication Reference Terminology (MED-RT) for Pharmacological Class

Source: US FDA

Regulatory Agencies Updates

Data Standards Catalog April 2023

Data Standard	Version(s)	Designated Implementation Guide Version(s)	Date Support Begins (MM/DD/YYYY)	Date Support Ends (MM/DD/YYYY)	Date Requirement Begins (MM/DD/YYYY)	Date Requirement Ends (MM/DD/YYYY)
ADaM	ADaM v 2.1	1	Ongoing	03/15/2019 [1] 03/15/2020 [2]	12/17/2016 [1] 12/17/2017 [2]	03/15/2019 [1] 03/15/2020 [2]
ADaM	ADaM v 2.1	1.1	03/15/2018		03/15/2019 [1] 03/15/2020 [2]	
ADaM	ADaM v 2.1	1.2, 1.3	07/18/2022		03/15/2024	
SDTM	SDTM v 1.3	3.1.3	12/01/2012	3/15/2021	12/17/2016 [1] 12/17/2017 [2]	3/15/2021
SDTM	SDTM v 1.4	3.2	08/17/2015		03/15/2018 [1] 03/15/2019 [2]	
SDTM	SDTM v 1.7	3.3	03/15/2021		03/15/2023	
Define	2.1	N/A	03/15/2021		03/15/2023	

[1] For NDAs, ANDAs, and certain BLAs.
[2] For certain INDs.

Source: US FDA

Regulatory Agencies Updates

Technical Conformance Guide(June 2022)

This guide provides detailed matters and precautions regarding the submission of electronic study data, electronic files, including eCTD.

Key Pointers

- Guidance on SDTM & ADaM datasets in Japanese language
- Requirement of validation rules
- File formats requirements – xpt, .sas or software extension, ASCII, Phoenix Projects (*.phxproj), WinNonlin Files (*.pmo, *.pwo)
- ARM for ADaM Define.xml is strongly recommended
- SI Units required for Finding domains
- Either version of Define.xml 1.0/2.0 are acceptable, Define.pdf not required

Source: Japan PMDA

Regulatory Agencies Updates

PMDA Data Standards Catalog (2023-02-28)

Data Exchange Standard	Supported Version(s)	Implementation Guide Version	Date Support Begins (YYYY-MM-DD)	Date Support Ends (YYYY-MM-DD)
SDTM	1.7	3.3	2023-04-01	
SDTM	1.4	3.2	2016-10-01	
SDTM	1.3	3.1.3	2016-10-01	
SDTM	1.2	3.1.2 Amendment1	2016-10-01	
SDTM	1.2	3.1.2	2016-10-01	
ADaM	2.1	1.1	2022-01-01	
ADaM	2.1	1.0	2016-10-01	
Define	2.0	-	2016-10-01	
Define	1.0	-	2016-10-01	2025-03-31

Source: Japan PMDA

Time for Discussion

References

CDISC

US FDA

JAPAN PMDA

Thank You

The Global Healthcare Data Science Community

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