A guide to CDISC standards used in the clinical research process

The Clinical Data Interchange Standards Consortium is an organization dedicated to helping to improve medical research by driving communication through data standardization. This data standardization enables the rapid design, build, analysis, and submission of clinical trials.

CDISC and the FDA have worked closely to allow regulatory reviewers to process and review clinical trials more effectively. The FDA now requires studies to be submitted using "standardized data". These standards make it easier for a regulator to understand and process clinical trial data.

Implementing CDISC standards gives the following benefits:

- Greater efficiency.
- Full traceability in the clinical research process from start to end.
- Allows for greater innovation.
- Better data quality.
- Allows the sharing of data.
- Reduction of costs.
- Processes are streamlined.

Now that the industry is working together using these same standards, clinical trials are optimized. There's an increase in data quality and a reduction in design and execution time. Ultimately that means getting more quality products to the market faster, for less cost.

What CDISC standards are required for submission?

The FDA and the Japan PMDA require the following:

- SEND
- SDTM
- ADAM
- Define-XML
- Controlled Terminology

Additionally, CDISC standards are the preferred standards for electronic submissions to the China NMPA.

How are CDISC standards grouped?

CDISC has produced a suite of standards for the clinical research process. They standardize content from planning and data collection through to data analysis and reporting.

CDISC standards can be grouped into 2 different areas.

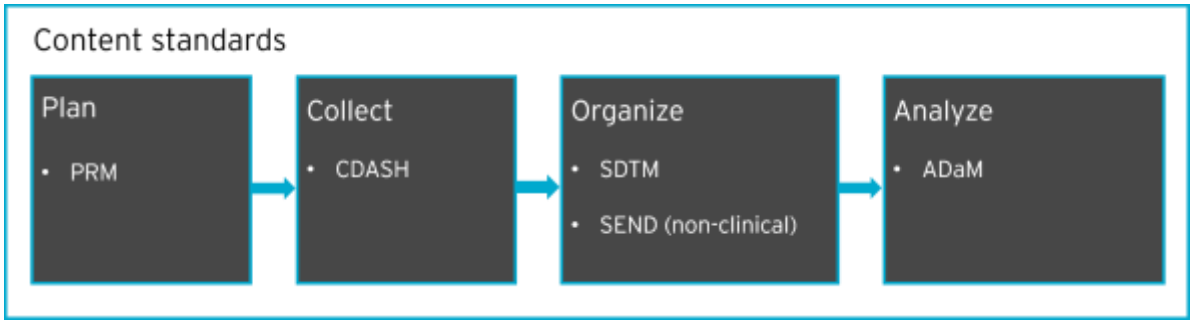
1. Content standards.
2. Data exchange standards.

Both of these areas consist of individual standards and are discussed in this article.

What are content standards in the clinical research process?

The content standards define what objects are allowed. For example, an Adverse Events dataset and the variables it contains.

Content standards described in this article include those in the diagram below.



The Protocol Representation Model (PRM)

PRM is the very first stage in the end to end clinical trial planning process. It's a conceptual model that's used to organize the protocol. It identifies items in the protocol and organizes them into a machine-readable structure.

CDISC describes it as "the Protocol Representation Model (PRM) provides a standard for planning and designing a research protocol with focus on study characteristics such as study design, eligibility criteria, and requirements from the ClinicalTrials.gov, World Health Organization (WHO) registries, and EudraCT

registries. PRM assists in automating CRF creation and EHR configuration to support clinical research and data sharing."

PRM is not a deliverable and it's not as commonly used as other CDISC standards such as SDTM and ADaM.

Clinical Data Acquisition Standards Harmonization (CDASH)

CDASH provides guidance and defines the best way to structure your CRFs to make sure you gather all the data you need for commonly used domains.

CDASH standards help to improve data quality, reduce data queries, and make it easier and more efficient to do the SDTM mappings required for regulatory submission.

Study Data Tabulation Model (SDTM)

SDTM was developed to organize data collected in human and animal clinical trials. SDTM gives the FDA a clear description of the structure, attributes, and content of each dataset, as well as the variables submitted as part of a clinical trial. SDTM metadata is submitted to regulators using the Define-XML data exchange standard.

It was developed because clinical trial submissions were all over the place. They differed vastly from each other, for example, there were differences between domain names, variables used, and variable names. The review process was overly complex and time-consuming. The end result was that it took far longer to get a drug to the market.

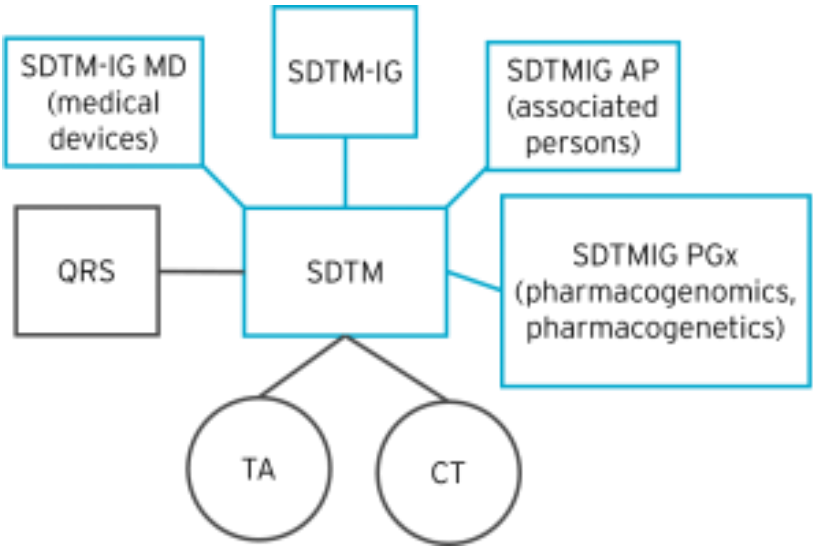
CDISC SDTM consists of 2 parts, the underlying Study Data Tabulation Model and Implementation Guides (SDTM-IGs) that define how the SDTM should be used to represent some common data domains in human clinical trials.

The core model provides a standardized set of variables, which are grouped into "classes". These are refined and built into domains, for example, Vital Signs. The implementation guides serve as a guide for implementing the CDISC SDTM standard.

The latest versions are:

- SDTM v1.7 for SDTM-IG v3.3
- SDTMIG-MD (Medical Devices) v1.1.
- SDTMIG-PGx (Pharmacogenomics, Pharmacogenetics) v1.0
- SDTMIG-AP (Associated Persons) v1.0

The diagram below shows an example of the different types of CDISC SDTM-related content that contribute to a final SDTM submission.



QRS, TA, and CT in the diagram above are covered later in this article.

Standard for Exchange of Non-Clinical Data (SEND)

SEND standardizes the exchange of non-clinical data between systems in a consistent format. SEND metadata is submitted to regulators using the Define-XML data exchange standard. It's required by the FDA for submissions. It's an implementation of the SDTM standard that's used for animal studies. In other words, data that is collected for animal studies can differ from data that is collected for humans, and the SEND standard attempts to fill this gap.

The Analysis Dataset Model (ADaM)

The ADaM standard was developed to standardize analysis data. It ties in very closely with SDTM. While SDTM is for collected data, ADaM is for presenting analysis data. Adam datasets must always be derived from SDTM datasets. ADaM metadata is submitted to regulators using the Define-XML data exchange standard, and also the related Analysis Results Metadata standard.

The characteristics of the ADaM standard are as follows:

- It's submitted using Define-XML.

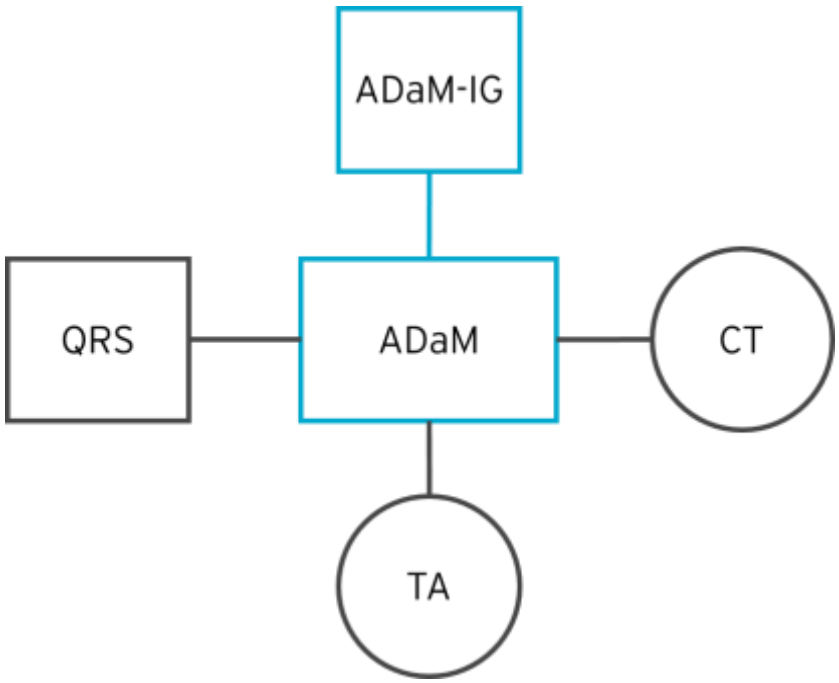
- It's more flexible than SDTM.
- Traceability is built-in among analysis results, analysis data, and data represented in the SDTM.
- It fulfills most data analysis requirements.

Like SDTM, the ADaM standard also has an implementation guide.

The latest versions are:

- ADaM v1.2
- ADaM-IG v1.2

The diagram below shows an example of the different types of CDISC ADaM-related content that contribute to a final ADaM submission.



What are Questions, Ratings, and Scales (QRS)?

QRS instruments are questions, tasks, or assessments for qualitative and quantitative assessment for clinical trials. A questionnaire is a series of related questions that produce 1 or more scores. Ratings are a ranking of quality, standard,

or performance. Scales are defined based on criteria that result in a single measurement.

The QRS team develops Controlled Terminology and SDTM supplements, while the ADQRS team develops ADaM supplements. CDISC creates supplements for questionnaires, functional tests, and clinical classifications. These supplements provide standards for collecting and storing responses from QRS.

Some examples of published supplements include the 6 minute walking scale, Hamilton anxiety rating scale, and the Neuropathic pain scale.

What is Controlled Terminology (CT)?

CDISC partnered up with the National Cancer Institute (NCI) to publish an evolving set of terminology standards. These are used along with content standards like SDTM to help ensure that the content of the data is easy to understand and is consistent.

Controlled terminology is a set of codelists and valid values that are used for items in datasets. In a nutshell, it tells you how you should submit collected data for a data item in a dataset. For example, if a question on the CRF is to record sex, the allowed values are F (female), M (male), U (unknown), or UNDIFFERENTIATED.

Controlled terminology is used for PRM, CDASH, SDTM, SEND, and ADaM standards.

What are Therapeutic Area Standards (TA)?

Therapeutic area standards are an extension of the foundational standards. They serve to represent data for specific therapeutic areas such as asthma, diabetes, multiple sclerosis, and many more.

Therapeutic Area User Guides (TAUGs) are implementation guides for each specific area. The CDISC foundational standards define in general how each different type of data should be submitted, and the TAUGs provide more specific information about how to interpret the foundational standards within a particular therapeutic area. For example, they might define how a variable should be interpreted in the context of a specific TA.

What are data exchange standards in the clinical research process?

Data exchange standards are ways of representing metadata and data in a standardized way in order to make it easier to exchange data between different parties. They define how you describe an object.

Data exchange standards described in this article include those in the diagram below.

ODM-XML

The CDISC Operational Data Model (ODM) is an XML-based model for standardizing the transfer of metadata for clinical trials and the associated data. It can be used for defining the data collected in a trial, such as CRFs and patient diaries, to provide an upfront specification for the trial. This can then be used to help automate the build of the data collection systems. It can also be used for transferring the data itself once collected.

The latest version is ODM-XML v1.3.2.

Some other models such as Define-XML, Dataset-XML, and Analysis Results Metadata are implemented as extensions to ODM-XML.

By using ODM and CDASH together, you can rapidly define the data you need to collect in your clinical trials. This ultimately helps to reduce the time it takes to get a drug to the market.

Dataset-XML

Dataset-XML supports the exchange of tabular data using ODM based XML technologies. It allows communication of study datasets for regulatory submissions.

Define-XML

Define-XML is a data model that allows a standardized description of tabular dataset structures, helping to drive process efficiencies throughout the clinical lifecycle. Simply put, it describes the structure and content of data collected or submitted during the clinical trial process. This includes system-specific dataset structures that are exported from an EDC system and standardized CDISC domains such as SDTM.

It's an extension of the CDISC ODM standard and is a key requirement for describing datasets that are to be electronically submitted to the FDA and PDMA.

Define-XML 2.1 is the current version of the standard.

Analysis Results Metadata (ARM)

CDISC standardized the description of ARM for describing tables, listings, and figures. This references the data in standardized ADaM datasets, making it easier to re-use analysis results metadata across different studies.

Laboratory Data Model (LAB)

Lab was established to standardize the transfer of data between clinical laboratories and sponsor companies. The CDISC LAB model is widely used in pharmaceutical and biotechnology companies today.

It was developed because of the many variations between data acquired in laboratories, such as lab test names and units. So by using the LAB model, laboratory data is standardized allowing seamless transfer between laboratories and CROs, which saves time and costs.

CDISC Library

CDISC library is a central repository for developing, integrating, and accessing CDISC metadata standards. In other words, it's an online electronic source for the CDISC content standards, allowing them to be viewed in a machine-readable way. It makes it easier for users to implement CDISC standards via clinical trial software such as a CTMS (clinical trial management system). CDISC library's standards help to gather, aggregate, and analyze standardized data from early design through to end analysis.

It provides an API that helps to automate the implementation of CDISC standards. Users can access standards in real-time in a number of different formats. For example, RDF, XML, JSON, and CSV.

And, did you know that CDISC uses the Formedix clinical metadata repository to design and store their eCRF standards? Keep reading to find out a bit more about Formedix.

Formedix can help

Formedix has been strong advocates for the use of CDISC data standards in clinical and non-clinical research and has become industry leaders in CDISC software, professional services, and training.

In fact, we're on the CDISC XML technical team! We were involved in creating the CDISC ODM and Define models. So we know a fair bit about CDISC standards. Learn more about how we help you with CDISC Compliance.

Our clinical metadata repository and clinical trial automation software supports all versions of CDISC standards and SDTM automation. Our platform is kept updated with the latest CDISC and NCI standards. So you'll always be regulatory compliant.