WHITEPAPER

CDISC standards for BA/BE studies

an FDA perspective

The FDA Safety and Innovation Act of 2012. Statute on authorized electronic submissions states that-Beginning not earlier than 24 months after final guidance issued after public notice submissions shall be submitted in such electronic format as specified by the secretary in such guidance. The final guidance was published in December 2014. Thus, all studies that start in the year 2017 or later will be required to submit their data to the FDA in an electronic format i.e. CDISC.

The CDISC mission is to develop and support global, platform-independent data standards that enable information system interoperability to improve medical research and related areas of healthcare. CDISC standards are vendor-neutral, platform-independent and freely available via the CDISC website. CDISC standards are to support the acquisition, exchange, submission and archive of clinical research data and metadata.

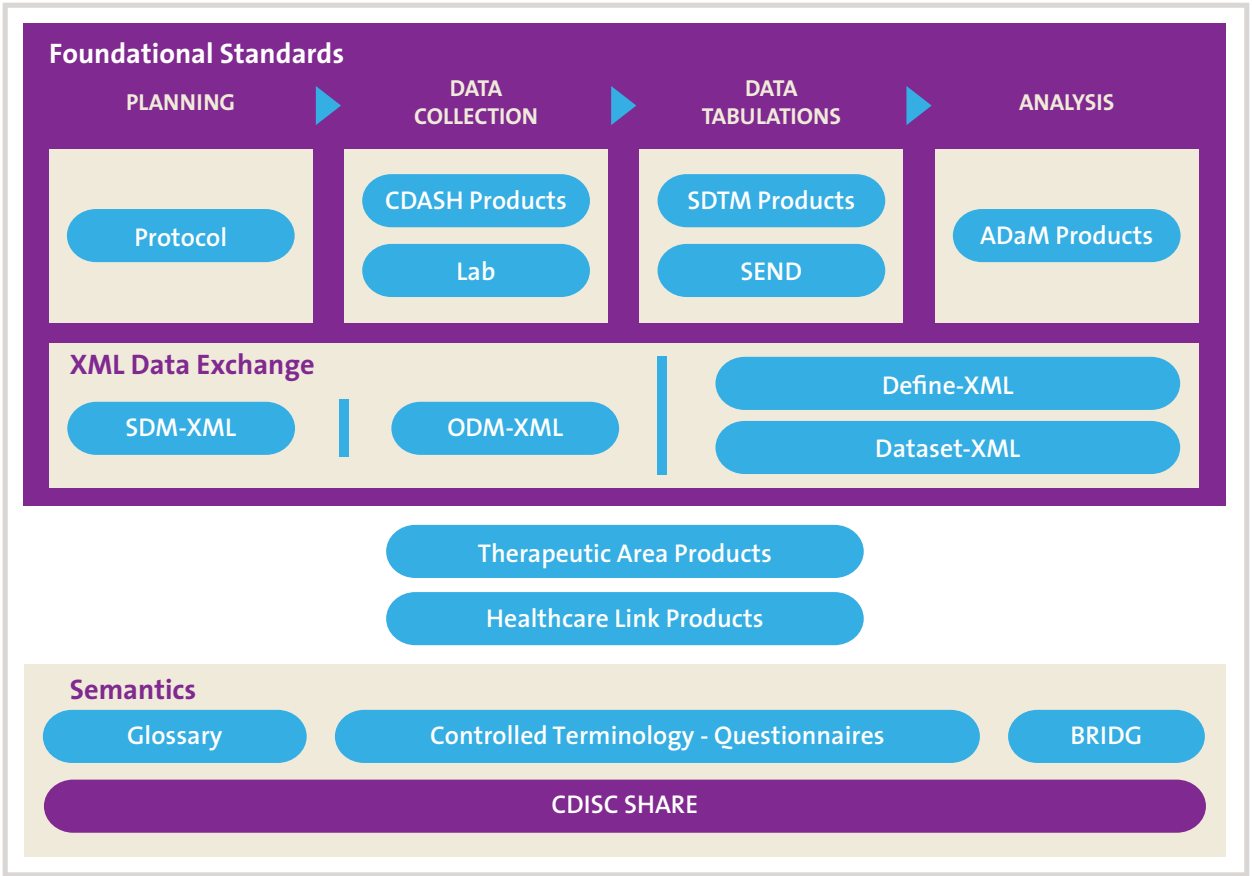
Process for data standards

Purpose of the creating the document is to identify the CDISC requirements for standardizing the BA/BE studies based on the specifications/data provided by the clients.

The goal of CDISC is to help the drug development process become more efficient. Efficiencies are gained by improving the data flow process within a company, allowing sharing/combining of data across companies, and potentially reducing questions from a reviewer.

The foundational standards provide the basis for the complete CDISC suite of standards, supporting the clinical research process from protocol through data collection, data management, data analysis and reporting. These standards focus on the core principles for defining research data standards, and generally represent interest areas that are common across all research studies such as demographics, medical history, medication history and concomitant medications, adverse events and other common domains.

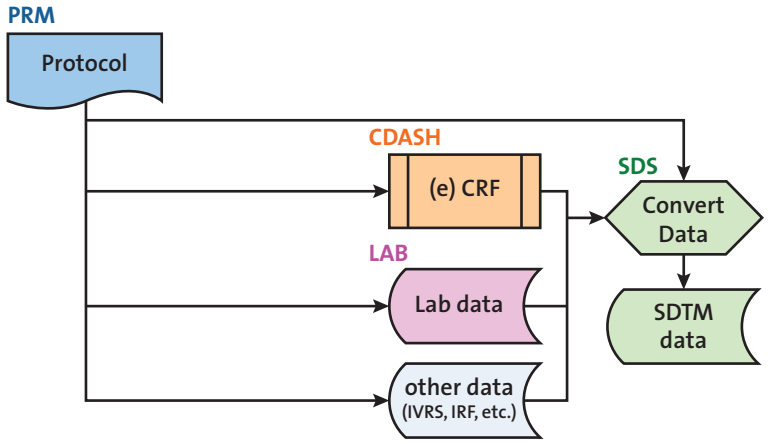
The standards shown in the diagram below includes those at the data content level, plus additional standards that help us exchange/share data, further clarify data, and make implementation choices that are appropriate for specific therapeutic areas. This diagram serves as a visual guide for all of the standards in the CDISC arena.



CDISC Foundational Standards shows all the models used to standardize data content throughout the clinical process, from planning, through data collection and data tabulation, and into statistical analysis.

SDTM is probably the most familiar of all the CDISC models. It was created by the CDISC Submission Data Standards (SDS) team to provide a model for the submission of tabulation data in a study. Clinical data can be captured via several means. An example of data flow into SDTM, from both the CDISC standards described thus far and other possible non-CDISC sources, such as an Interactive Voice Randomization System (IVRS) or an Independent Review Facility (IRF), is shown here:

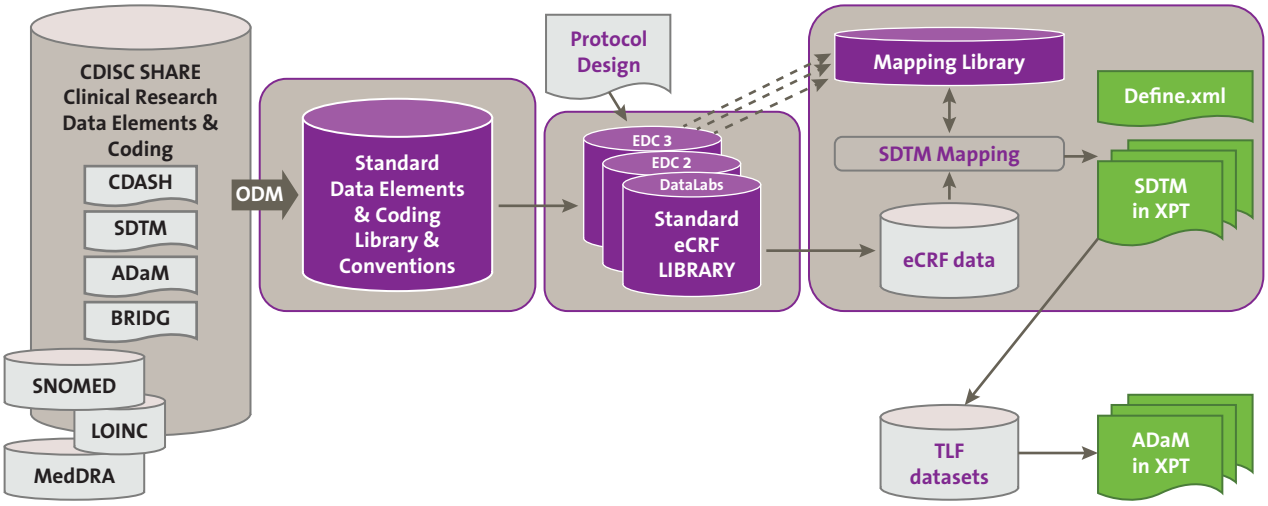
Data Flow into the SDTM Standard



SDTM has three basic structures, called General Observation Classes, based on the type of data that was collected. These classes are events, interventions, and findings. The SDTM document describes these observation classes and includes naming conventions for their variables. It also includes an overview of some data that doesn't fit into the general observation classes, such as demographics, comments, and trial design.

Implementing data standards diagram will explain about the process flow for data standards.

Implementing Data Standards



ADaM provides another representation of clinical data. Where SDTM contains all clinical data collected about every subject in the study, ADaM reconfigures the data as needed for analysis. ADaM structures are based on SDTM data as input, but are also dependent on analysis needs.

ADaM has three defined structures: the Subject Level Analysis Dataset (ADSL), the Basic Data Structure (BDS) and the Adverse Events Analysis Dataset (ADAE). Most analysis results can be quickly derived using data in these structures. The ADaM document contains some basic information about the structures, but similar to SDTM.

- ADaM Examples in Commonly Used Statistical Analysis Methods (Examples)
- ADaM Basic Data Structure for Time-to-Event (TTE) Analyses
- The Adverse Event Analysis Document (ADAE)

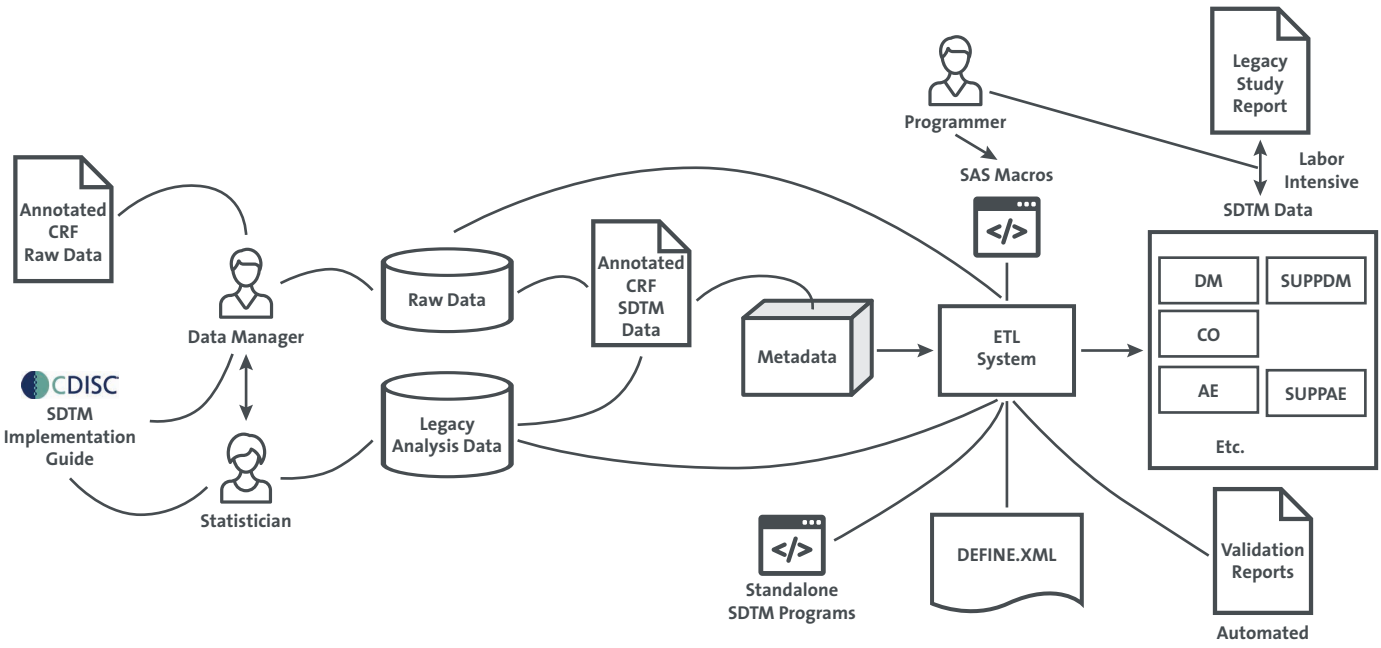
Process flow for standardizing BA/BE studies

For any human interventional trail, CDISC (SDTM) is going to be the preferred data format. CDISC (SDTM) data are organized into different datasets called domains. Even for simple BA/BE studies where data collection is very limited, we can generate required SDTM domains for regulatory submission. Some of the common relevant domains for BA/BE analysis are:

- Demographic Information-DM
- Exposure Information-EX
- Vital Signs-VS
- Pharmacokinetic Concentration-PC
- Pharmacokinetic parameters-PP

The following diagram explains about the pre-requisites and the process flow about standardizing the BA/BE studies.

Data flow and the process for standardizing the BA/BE studies



Conclusion

The CDISC data standards give us a common way across the industry to represent information collected when running a clinical study and producing results about the study. This includes information about study design, such as seen in the PRM and Study Design standards and the SDTM trial design domains. It also includes information about the subject and/or device under study, as captured in CDASH, Lab, SDTM, SEND, and ADaM.