

The Evolution of SDTM – What's new

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ABSTRACT

In July 2012 CDISC released the final version of SDTM V1.3 and SDTMIG V3.1.3. This version incorporates all the changes published in "Amendment 1 to SDTMIG V3.1.2". Changes were made to the trial design datasets, namely to the trial summary codes and the oncology therapeutic area is now included. Shortly after this release, CDISC published the first batches of SDTMIG V3.1.4 for public review and this new SDTM version was announced to be published soon. CDISC is also actively collaborating with other partners on the development of Therapeutic Area Data Standards. We have to notice that not only for SDTM, but also for other CDISC models, the release of new standards has been accelerated. The Technical Plan Project Schedule provides a detailed overview of the upcoming CDISC planned project deliverables. More and more CDISC model releases are coming our way and the pharmaceutical industry has to be prepared to deal with these continuous changes in industry standards. This results in the set-up of Data Standard Governance Boards in companies to maintain their Data Standard Libraries.

INTRODUCTION

In July 2012 CDISC released the final version of SDTM V1.3 and SDTMIG V3.1.3.

In the mean time, CDISC has published 3 batches of SDTM V1.4 and SDTMIG V3.1.4 for public review.

CDISC is also actively collaborating with other partners on the development of Therapeutic Area Data Standards.

We have to notice that not only for SDTM, but also for other CDISC models, the release of new standards has been accelerated.

THE EVOLUTION OF THE CDISC STANDARD

The Technical Plan Project Schedule provides a detailed overview of the upcoming CDISC planned project deliverables (see figure 1).

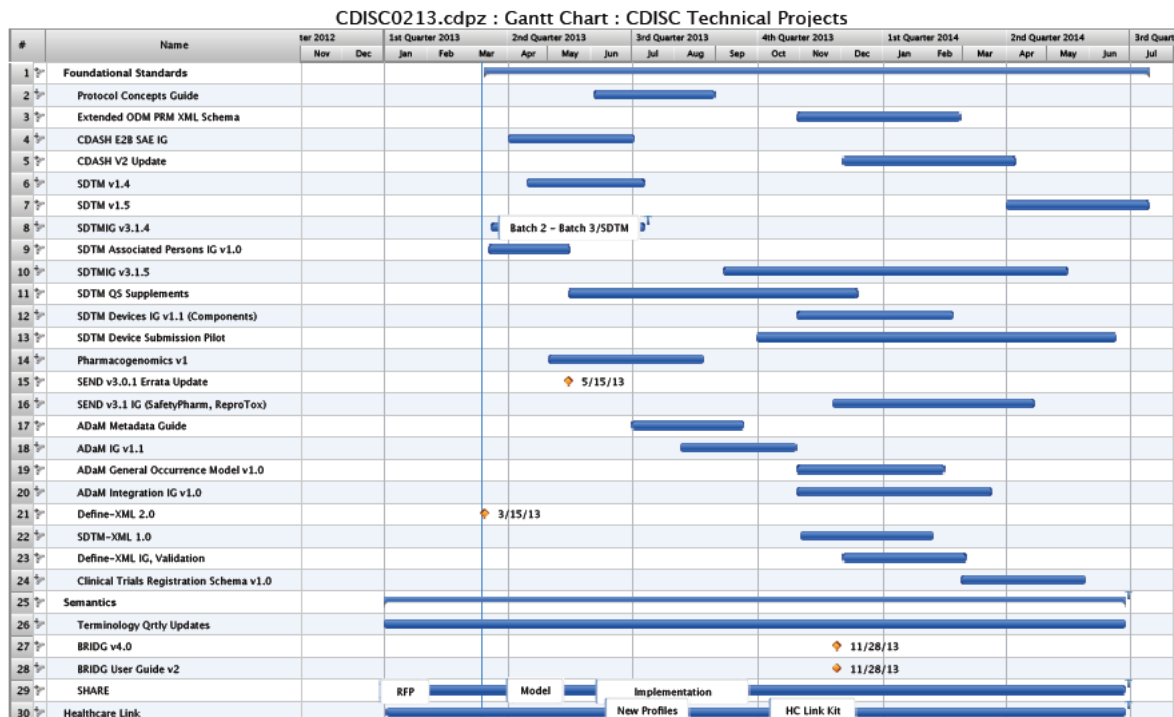


Figure 1

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More and more CDISC model releases are coming our way and the pharmaceutical industry has to deal with these continuous changes in data standards. This results in the set-up of Data Standard Governance Boards in companies to maintain their Data Standard Libraries (see figure 2)

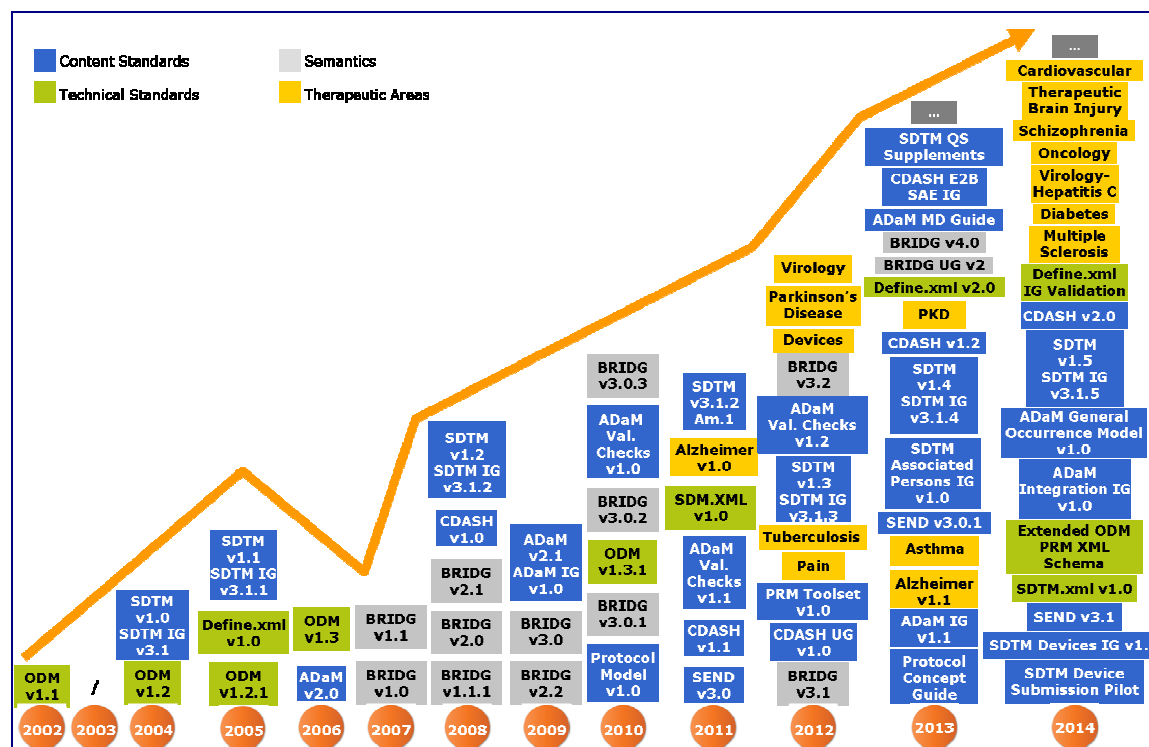


Figure 2

THE DEVELOPMENT OF THERAPEUTIC AREAS

The Coalition for the Advancement of Standards and Therapies (CAST) is a joint initiative of CDISC & C-Path responsible for the development of therapeutic area standards along with FDA and TransCelerate Biopharma, Inc.

The development of new Therapeutic Area standards has been defined in a “Therapeutic Area Data standards Roadmap”.

CDISC had an existing development process that worked well and has gained experience in developing TA standards over the past years. With CAST in place the development process will be enhanced to facilitate scale-up and ensure quality (see figure 3).



FAST Program Overview – July 2013

Therapeutic Area Standards Under Development

		Coordinating Organization(s)	Stage 0	Stage 1	Stage 2	Stage 3a	Stage 3b	Stage 3c	Issues
		Project Manager	Scoping & Input	Concept Modeling	Standards Development	Internal Review	Public Review	Publication	
Alzheimer's V1.1		CPATH/CDISC Jon Neville	Jan	Mar	Jun	Jul	Sep	Q313	
Asthma V1		CDISC Rhonda Facile	Jan	Mar	Jun	Jul	Sep	Q413	
Cardiovascular Endpoints V1		CDISC/DCRI Amy Palmer	Jun	Jul	Aug			Q114	
Multiple Sclerosis V1		CPATH/CDISC Bess Leroy	May	Aug	Jul			Q114	Concept modeling done prior to standards development step.
Diabetes V1		TCR/CDISC Rachael Zride	Mar	Jun	Aug			Q214	
QT Studies V1		TCR/CDISC John Owen	Jul	Sep				Q214	
Traumatic Brain Injury V1		CDISC TBD	Aug					Q214	
Hepatitis C V1		TBD	Sep					Q314	
Schizophrenia V1		CDISC/DCRI Amy Palmer	Oct					Q314	
Oncology		TBD	Oct						SAC working to define scope and deliverables.
Project Status:  On track  At risk  Critical issues  Stage ongoing  Stage completed <i>Italics = Projected</i>									



Figure 3

WHAT IS NEW IN SDTMIG V3.1.3 AND SDTMIG V3.1.4

SDTMIG V3.1.3 is presented as an annotated version of SDTMIG V3.1.2. Sticky notes are used to indicate what has changed or what has been inserted. In addition, document attachments are pinned to the document and obsolete sections have been blanked out.

SDTMIG V3.1.3 incorporates all the changes published in “Amendment 1 to SDTMIG V3.1.2”, as well as some other additional updates. Changes were made to the trial design datasets, namely to the trial summary codes and the oncology therapeutic area is now included.

SDTMIG V3.1.3: THE USE OF THE NULL FLAVOR VARIABLE IN THE TS DOMAIN

The null flavor variable is included to supplement the TSVAL variable in the Trial Summary (TS) dataset.

It was realized that the Trial Summary model did not have a good way to represent the fact that a protocol placed no upper limit on the age of study subjects.

SDTMIG V3.1.3: THE ONCOLOGY DOMAINS

The tumor package consists of 3 SDTM Findings domains linked by the RELREC domain (see figure 4). The three domains are related but each has a distinct purpose. When creating an analysis dataset, data from the three SDTM domains can be combined. The three domains are introduced below:

- TU (Tumor Identification)

The TU domain represents data that uniquely identifies tumors. The tumors are identified by an investigator and/or independent assessor and classified according to the disease assessment criteria. In RECIST terms this equates to the identification of Target, Non-Target or New tumors. A record in the TU domain contains the following information: a unique tumor ID value; anatomical location of the tumor; method used to identify the tumor; role of the individual identifying the tumor; and timing information.

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- TR (Tumor Results)

The TR domain represents quantitative measurements and/or qualitative assessments of the tumors identified in the TU domain. These measurements are usually taken at baseline and then at each subsequent assessment to support response evaluations. A record in the TR domain contains the following information: a unique tumor ID value; test and result; method used; role of the individual assessing the tumor; and timing information.

Clinically accepted evaluation criteria expect that a tumor identified by the tumor ID is the same tumor at each subsequent assessment. The TR domain does not include anatomical location information on each measurement record because this would be a duplication of information already represented in TU. This duplication of data was a deciding factor in multi-domain approach to representing this data.

- RS (Disease Response)

The RS domain represents the response evaluation(s) determined from the data in TR. Data from other sources (in other SDTM domains) might also be used in an assessment of response.

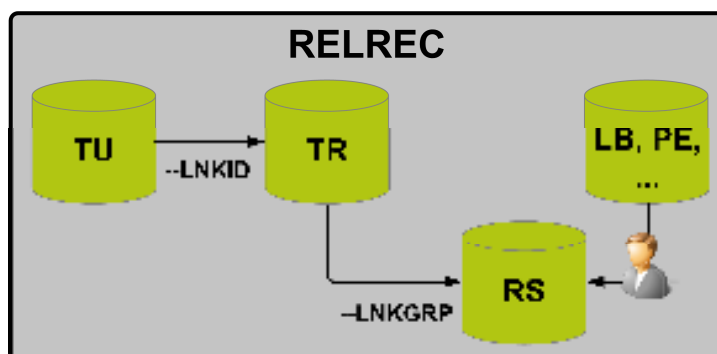


Figure 4

WHAT IS NEW IN SDTM 3.1.4

CDISC published the first batches of SDTMIG V3.1.4 for public review and this new SDTM version was announced to be published soon.

The Batch 1 package includes:

- **Exposure Domains Supplement:** the new domain "Exposure as Collected (EC)" has been included. In addition, variables have been clarified and some variables have been proposed for deprecation.
- Two new **Immunogenicity Domains** have been defined: "Immunogenicity Specimen Assessments (IS)", which is a findings domain that contains assessments determining whether a therapy provoked/caused/induced an immune response and "Skin Response (SR)" which is a findings about intervention domain reporting dermal responses to antigens.
- The **Reproductive Details Domain** captures all Reproduction details related to the subject in a Findings domain

The Batch 2 package includes specifications for representing morphology, histopathology and physiology data.

- **Morphology (MO)** domain captures macroscopic results (e.g. size, shape, color, and abnormalities of body parts or specimens) in a findings domain
- **Microscopic Findings (MI)** reports a record for each microscopic finding observed in a FINDINGS domain
- **Cardiovascular Physiology (CV)** domain captures findings of a cardiovascular diagnostic procedure including information relating to the heart, blood vessels and circulation, such as ischemic myocardium percentage, stenosis, and New York Heart Association Class. Data describing structural measurements of the heart would rather be captured in the Morphology Domain (MO). Information about the conduct of the procedure(s) will be reported in the Procedure Domain (PR)
- **Procedures (PR)** describes a subject's therapeutic and diagnostic procedures in an interventions domain
- **Trial Disease Assessments (TD)** captures information on the protocol-specified disease assessment schedule; it is used for comparison with the actual occurrence of the efficacy assessments in order to determine whether there was good compliance with the schedule.
- **Death (DD)** domain details domain captures information pertaining to the death of a subject, including the cause of death.
- **Subject Status (SS)** captures data relating to general subject characteristics that are evaluated periodically to

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determine if they have changed. This is linked to related domains by the RELREC domain

This batch also contains a proposal for **alternative handling of Supplemental Qualifiers**.

The SDTM Supplemental Qualifiers structure is a method for representing non-standard variables (NSVs) in a standard way within the SDTM. The current format for representing NSVs (those variables not found in SDTM Tables) is as separate SUPP-- datasets that are associated with the corresponding "parent" general-observation-class and Demographics datasets. This document presents a proposal for updating the SDTM to allow NSVs to be represented in the parent datasets, and the conditions under which this practice would be permitted.

The Batch 3 package includes proposed changes to the Study Data Tabulation Model V1.4 and the new Study Data Tabulation Model Associated Persons Implementation Guide (SDTMIG-AP). Associated Persons (AP) are persons who can be associated with a study, a particular study subject or a device used in the study. AP may or may not have a familial relationship to a study subject. AP domains are created using SDTM variables, with the application of specific AP rules

In addition it includes 1 new domain: **The Healthcare Resource Utilization (HO)** domain generally includes a description of hospitalizations and events such as nursing home stays, rehabilitation facility stays or visits, and emergency department visits. This may include information such as start and end of the stay or the duration of the stay.

CONCLUSION

With the release of SDTMIG V3.1.3, we have an enhanced, richer version of the industry data standards. Even though SDTM 3.1.2 submissions will still be accepted for a certain period of time, departments involved in the preparation of an SDTM submission should be aware of the changes and can begin to take advantage of the improved functionality of the new published standards. In addition, the pharmaceutical industry needs to be prepared to deal with these continuous changes in industry standards.

REFERENCES

<http://www.cdisc.org/>

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