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FDA CDER Common Data Standards Issues
Evolution of SDTM Submission Standards

Peter Van Reusel, Business & Decision Life Sciences, Brussels, Belgium
Tina Apers, Business & Decision Life Sciences, Brussels, Belgium
Davy Baele, Business & Decision Life Sciences, Brussels, Belgium

INTRODUCTION

The Study Data Tabulation Model (SDTM) V1.2 and its Implementation Guide (SDTMIG) V3.1.2 have been put in production since March 2009. Except for the development of new therapeutic area domains, no major changes have been made to this standard.

An Amendment to the SDTM Implementation Guide V3.1.2 has been posted on the CDISC website. Additionally FDA CDER has published its Common Data Standards Issues document on their website, providing additional guidelines for submission datasets.

CDER DATA STANDARDS ISSUES

Due to differences in sponsor implementation of the standard CDER has observed significant variability in past submissions.

The Common Data Standards Issues document lists a number of expectations to increase reviewability. These guidelines are expected to be incorporated in the submission datasets.

It is stated that sponsors should always use the latest version of the SDTM standard and that they should refer to the Amendment to the SDTM Implementation Guide V3.1.2. Furthermore a number of expectations are listed with regards to terminology, SDTM datasets and SDTM variables.

The request to include Epoch and Trial Element variables for every subject-level data observation will probably have the largest impact on the creation of SDTM datasets.

SDTM AMENDMENT

New variables have been introduced to the SDTM model to accommodate the reviewers' needs.

The Demographics (DM) model has been expanded with additional variables to better support the difference between what was planned for and what has actually happened to a subject during the course of a clinical trial. A set of additional Date/Time variables has been developed to better represent crucial time points during the course of a study. Table 1 provides the metadata for these new variables.

Table 1: Additional variables for the Demographics (DM) domain

Variable Name	Variable Label	Type	Controlled Terms, Codelist or Format	Role	Core
ACTARMCD	Actual Arm Code	Char		Record Qualifier	Req

Variable Name	Variable Label	Type	Controlled Terms, Codelist or Format	Role	Core
ACTARM	Description of Actual Arm	Char		Synonym Qualifier	Req
RFXSTDTC	Date/Time of First Study Drug Exposure	Char	ISO 8601	Record Qualifier	Exp
RFXENDTC	Date/Time of Last Study Drug Exposure	Char	ISO 8601	Record Qualifier	Exp
RFPSTDTC	Date/Time of First Subject Contact	Char	ISO 8601	Record Qualifier	Req
RFPENDTC	Date/Time of End of Subject Participation	Char	ISO 8601	Record Qualifier	Exp
DTHDTC	Date of Death	Char	ISO 8601	Record Qualifier	Exp
DTHFL	Subject Died Flag	Char	(NY)	Record Qualifier	Exp

The newly added variables in the Events General Observation Class are included to more accurately model external dictionary data (MedDRA) in the Adverse Events (AE) domain. Most of these variables used to exist in Supplemental Qualifiers datasets. Now these have been promoted to the parent domain. The metadata for the new variables in the Adverse Events domain is listed in Table 2. It is important that any other Events domain used by the sponsor that contains MedDRA codings should make use of these new Events General Observation Class variables instead of storing this information in the obsolete Supplemental Qualifiers as stated in the appendix of the SDTMIG V3.1.2.

Table 2: Additional variables for the Adverse Events (AE) domain

Variable Name	Variable Label	Type	Controlled Terms, Codelist or Format	Role	Core
AETRTEM	Treatment Emergent Flag	Char	(NY)	Record Qualifier	Exp
AELLT	Lowest Level Term	Char	MedDRA	Variable Qualifier	Exp
AELLTCD	Lowest Level Term Code	Num	MedDRA	Variable Qualifier	Exp
AEPTCD	Preferred Term Code	Num	MedDRA	Variable Qualifier	Exp
AEHLT	High Level Term	Char	MedDRA	Variable Qualifier	Exp
AEHLTCD	High Level Term Code	Num	MedDRA	Variable Qualifier	Exp
AEHLGT	High Level Group Term	Char	MedDRA	Variable Qualifier	Exp
AEHLGTCD	High Level Group Term Code	Num	MedDRA	Variable Qualifier	Exp
AESOC	Primary System Organ Class	Char	MedDRA	Variable Qualifier	Exp
AESOCCD	System Organ Class Code	Num	MedDRA	Variable Qualifier	Exp
AEBDSYCD	System Organ Class Code		MedDRA	Variable Qualifier	Exp

IMPACT

This evolution of SDTM submission standards inherently has consequences on the underlying processes used by the sponsor and subcontracted Contract Research Organizations (CRO) to create SDTM datasets, to ensure SDTM compliance, and to create analysis datasets (ADaM). Sponsors should be very careful in their documentation and communication that their SDTM datasets are SDTMIG V3.1.2 compliant with or without respect to the amendment.

To implement Amendment to the SDTMIG V3.1.2 sponsors should create a new version of their SDTM library that contains the metadata definitions for these new variables. The mappings used by the tools to generate SDTM from the underlying clinical database (CDASH) should be carefully revised and adjusted.
Additionally the procedures used to check the compliance of the resulting SDTM datasets should be adjusted, and additional (electronic) checks will need to be performed in relation to this new version of the standard.
The tools to create the resulting analysis datasets (ADaM) from the SDTM will need an update to be able to handle this new variables and attributes, while still accommodating for full traceability throughout the process chain.

The request from CDER to include Epoch and Trial Element variables for every subject-level observation to serve as Timing variables will have a significant impact on the process used to create SDTM datasets.
For most clinical trials these variables are not included in the clinical database. The most common seen timing variables are a study visit identifier, the start date of this visit, and the date of entry or collection date of the data item.
Due to lack of database variables to populate these SDTM variables, their values will need to be calculated based upon predefined algorithms to create the SDTM datasets. These derivations can become very complex and time consuming with respects to their added value for tabulation purposes.
A possible way of overcoming this problem is to include Epoch and Trial Element variables during clinical database setup. This approach enforces sponsors to define the SDTM Data, Metadata and Trial Design structures upfront, thereby significantly reducing turnover costs.

CONCLUSION

SDTMIG V3.1.2 together with Amendment 1 is becoming a more mature version of the de-facto standard for new submissions. Sponsors should be aware of the additional CDER guidelines and should carefully incorporate these to consistently adhere to the requirements as much as possible.

CONTACT INFORMATION (HEADER 1)

Your comments and questions are valued and encouraged. Contact the author at:

P. Van Reusel, T. Apers, D. Baele
Business & Decision Life Sciences
Rue Saint-Lambert, 141
Brussels / 1000
Work Phone: +32 (0) 2 774 11 00
Fax: +32 (0) 2 774 11 99
Email: info.ls-be@businessdecision.com
Web: www.businessdecision-lifesciences.com