Paper PH06

Is It Time to Upgrade CDISC SDTM from v1.1/v3.1.1 to v1.2/v3.1.2?

Susan M. Fehrer, BioClin, Inc., Emporia, KS

ABSTRACT

The FDA is now accepting submissions in CDISC SDTM v1.2/v3.1.2. However, many studies are in v1.1/v3.1.1 format. Should these studies be converted again, this time to v1.2/v3.1.2? If not, what will happen with a common CRF variable, RACEOTH, that is, in v1.1/v3.1.1, in SC.SCTESTCD and is in v1.2/v3.1.2 in SUPPDM.QNAM? The author will give practical examples and offer assistance to those facing this common situation.

INTRODUCTION

Is it time to upgrade to CDISC SDTM v1.2/IG v3.1.2? When does it make the most sense to spend the time to upgrade? Who is affected by these changes? What changes are to be made?

According to the FDA, all studies initiated after 2011-06-13 must use the new SDTM version[1]. That is the easy part. However, most studies have been initiated prior to 2011-06-13 and are in the v1.1/v3.1.1 format. What if some pre-June 13 studies are to be pooled with studies initiated after June 13? How will the differences in the domain variables be handled? Will the clinical and statistical SAS® programmers have to jump through hoops to pool data?

DEFINITIONS

Clinical Data Interchange Standards Consortium (CDISC) documentation has been evolving based on feedback from the US Food and Drug Administration (FDA) and industry users.

The Study Data Tabulation Model (SDTM) has been in use since 2004 as version 1.0 and since 2008-11-12 as version 1.2. The Implementation Guide (IG) has been in use since 2004 as version 3.1 and since 2008-11-12 as version 3.1.2. The SDTM gives the structure of the clinical data standards, whereas the IG gives instruction on how to implement the data standards.

DETAILS

In a published FDA document, all studies initiated after 2011-06-13 must use the new SDTM version. There is also an amendment to the SDTM v1.2 / IG v3.1.2 effective 2011-04-15 which has been released for comment and is for "trial use in advance of the next formal release of the SDTM and SDTM IG." Therefore, the amendment is to be included in creating the SDTM domains for submission and publication to the FDA.

SDTM v1.2 / IG v3.1.2 Change Highlights

New "Multiple" Rule:
When multiple responses are given for topic or qualifier variables (not including DS), the value in the domain is 'MULTIPLE', and the distinct values are found in the SUPP domain, with QNAM = *variable name in domain* || *value number,* QVAL = *response value.* For example, in DM, when a study subject is of multiple races, DM.RACE = 'MULTIPLE', SUPPDM.QNAM = 'RACE1', QVAL = 'ASIAN', SUPPDM.QNAM = 'RACE2', QVAL = 'WHITE'.

New Timing Variables:
In v1.1/v3.1.1, --STRF and --ENRF were used to signify timing information such as 'BEFORE' and 'AFTER' based on RFSTDTC. In v1.2/v3.1.2, new timing variables were added to convey similar meaning at any point in time, not tethered to the study reference start or end dates. These variables are –STRTPT, --STTPT, --ENRTPT, --ENTPT.

DM domain:
Race, Other (RACEOTH): v1.1/v3.1.1, SC.SCTESTCD = 'RACEOTH', SC.SCORRES = *value*; v1.2/v3.1.2, DM.RACE = 'OTHER', SUPPDM.QNAM = 'RACEOTH', SUPPDM.QVAL = *value.*

[1] FDA Study Data Standards Catalog (Ver 1.0; Effective 2011-06-13), www.fda.gov

The label for ARMCD and ARM is now 'Planned Arm Code' and 'Planned Arm'. New DM variables from the SDTM Amendment are ACTARMCD / ACTARM with the labels 'Actual Arm Code' and 'Actual Arm'. These are Required variables and the length of ACTARMCD is also 20.

New Expected variables now include DTHDTC, Date of Death, DTHFL, Subject Death Flag, along with new timing variables: RFXSTDTC, Date/Time of First Study Treatment Exposure, RFXENDTC, Date/Time of Last Study Treatment Exposure, RFICDTC, Date/Time of Informed Consent, RFPENDTC, Date/Time of End of Participation. In this new version, RFSTDTC, the Reference Start Date, only one meaning is allowed, and it will be used to calculate study day variables.

Supplemental Reasons Variables:
Sometimes, the reason why something was collected may be collected. For Findings domains, the reason should be put into a SUPP domain, with QNAM = --REAS. (Intervention domains allow the use of –INDC and –ADJ for the reason for the intervention or dose adjustment).

Pre-specified Interventions and Events:
Data may be collected in these domain types as free text or as pre-specified terms. When a term is pre-specified on the CRF and selected, then --PRESP = 'Y'; if not selected, then --PRESP = (null).

Updated Values:
V1.1/v3.1.1, DSDECOD = 'WITHDRAWAL OF CONSENT'; v1.2/v3.1.2, DSDECOD = 'WITHDRAWAL BY SUBJECT'. V1.1/V3.1.1, VSTEST = 'Frame Size'; v1.2/v3.1.2, VSTEST = 'Body Frame Size'. V1.1/v3.1.1, VSORRESU = 'BEATS PER MINUTE'; v1.2/v3.1.2, VSORRESU = 'BEATS/MINUTE'

MedDRA Variables and Codes:
With the Amendment, MedDRA variables and codes are now Expected variables in Adverse Events and may be included in other Events domains, such as Medical History. Now, --LLT, --LLTCD, --PTCD, --HLT, --HLTCD, are among the MedDRA variables now to be in the AE domain.

Treatment Emergent Flag:
The AE domain now has a new Expected variable, AETRTEM, Treatment Emergent Flag. The definition of 'treatment emergent' should be defined in the metadata and in the protocol. Valid values are 'Y' and '(null)'.

There are many more updates between the two versions of the SDTM and the SDTM IG. The Implementation Guide has increased from 183 pages to 298 pages. I have only highlighted some of the major changes. Please read the manuals to keep abreast of changes.

FEDERAL REGULATIONS

The FDA has not legislated when ALL submissions must be in CDISC SDTM format. That day is coming and we all must be aware and prepare.

The new SDTM and SDTM IG must be used for all studies initiated after 2011-06-13. The Amendment must be used for all studies using v1.2/v3.1.2.

CONCLUSION

For all submissions with some studies in the older version and some studies in the newer version, plan the updates for the domains sooner rather than later. The database updates may take longer than you think, and many of your standard TLF programs will need to be updated, with another set of validation before going into production. All of this takes time. Nothing is difficult, it just takes time.

When timelines were created when initially planning your submission, time for rework of the database and TLFs was not included. And, as we all know, it is doubtful that extra time will be added for this rework.

Thoroughly document all changes affecting your studies, plan your method of implementing these changes, and program carefully.

Good luck!

REFERENCES

CDISC Submission Data Standards Team, Study Data Tabulation Model, v1.1 Final, 2005-04-28

CDISC Submission Data Standards Team, Study Data Tabulation Model Implementation Guide: Human Clinical Trials, v3.1.1 Final, 2005-08-26

CDISC Submission Data Standards Team, Study Data Tabulation Model, v1.2 Final, 2008-11-12

CDISC Submission Data Standards Team, Study Data Tabulation Model Implementation Guide: Human Clinical Trials, v3.1.2 Final, 2008-11-12

CDISC Submission Data Standards Team, Amendment 1 to the Study Data Tabulation Model (SDTM) v1.2 and the SDTM Implementation Guide: Human Clinical Trials V3.1.2, 2011-04-05

www.fda.gov

ACKNOWLEDGEMENTS

The author would like to thank Adrienne Boyance, Thomas Guinter, Janet Reich, Victoria Bold, and Sophia Paterakis for their sharing of CDISC SDTM knowledge.

CONTACT INFORMATION

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

Susan M. Fehrer
BioClin, Inc.
1001 Woodland Street
Emporia, KS
Work Phone: 609-351-3302

e-mail: susanfehrer@yahoo.com

[i] SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc. in the USA and other countries. ® indicates USA registration.