Automation of SDTM Programming in Oncology Disease Response Domain

Yiwen Wang, Yu Cheng, Ju Chen
Eli Lilly and Company, China

ABSTRACT

Study Data Tabulation Model (SDTM) is an evolving global standard which is widely used for regulatory submissions. The automation of SDTM programming is essential to maximize the programming efficiency and improve the data quality. This paper intends to present some core programming logics to automatically create the Disease Response (RS) domain which is stated in CDISC SDTM IG v3.2 to represent the collected tumor data either quantitative measured or qualitative assessed in most of the clinical trials in oncology therapeutic area. The automation is realized by using SAS® macro facilities which include 1) the environment setting; 2) meta-data automation; 3) functionality oriented macros; 4) SUPPQUAL dataset automation; 5) structured end-to-end automation; 6) log check. The SAS® macros presented in this paper could also be applied to the automation of other SDTM oncology domains (i.e. TU, TR) or be extended to the domains in the SDTM Findings Observation Class.

Automation of SDTM Programming in Oncology Disease Response Domain

Yiwen Wang, Yu Cheng, Ju Chen
Eli Lilly and Company, China

BACKGROUND

Raw Data (EDS)

CRF data
Non-CRF data e.g. PK, Central Lab, IWRS
Other source data
Dictionary

SDTM Specification

Data set attributes
Data set structure
Variable attributes
Variable mapping rules
Variable code list/control terminology
Scheduled time points
Trial design

SDTM domains are generated based on the multiple source datasets (raw data from INFORM) and SDTM specifications, which will involve complicated programming work.

To streamline the SDTM programming process, SAS macro facilities were developed to automatically map Raw Data to SDTM and help to write SAS codes, e.g.:

- read the attributes from specs
- write the attributes by itself
- convert data structure

AUTOMATION'S GOAL

Readability → Flexibility → Feasibility

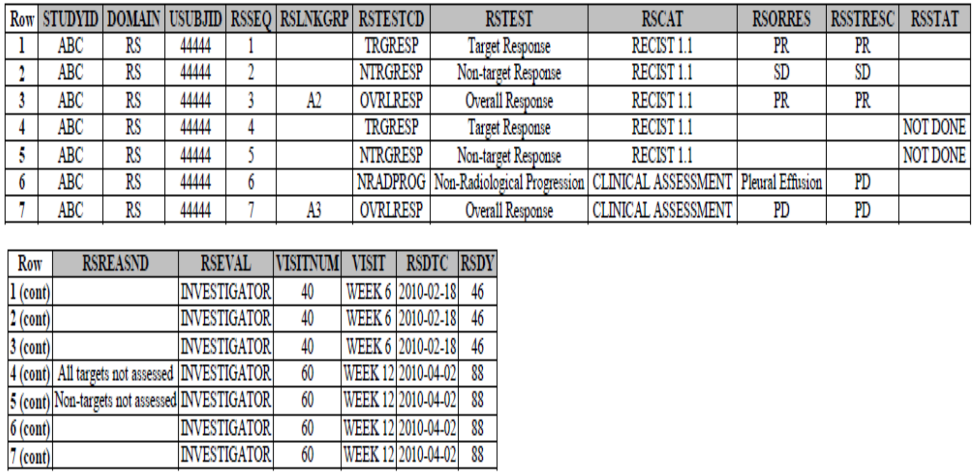
Automation of SDTM Programming in Oncology Disease Response Domain

Yiwen Wang, Yu Cheng, Ju Chen
Eli Lilly and Company, China

DISEASE RESPONSE (RS) - GENERAL DESCRIPTION

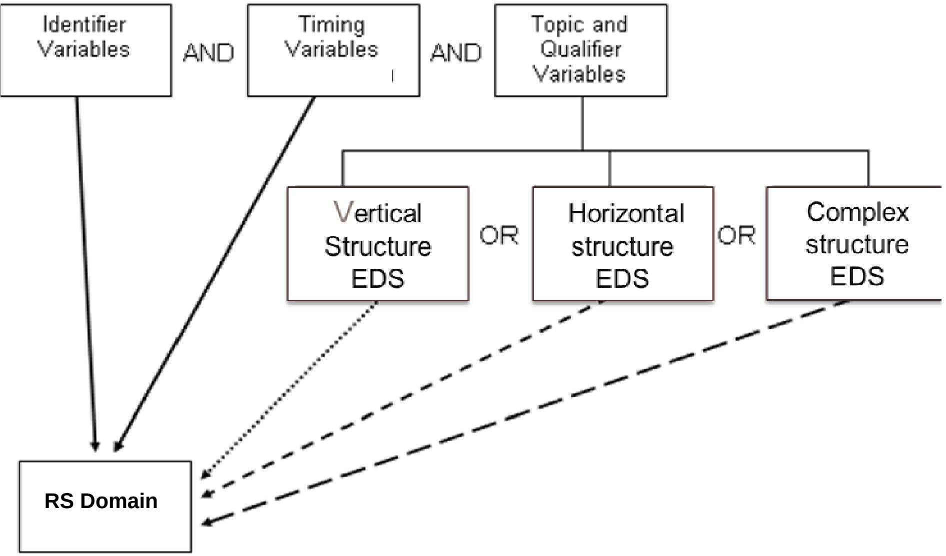
Represent the collected tumor data either quantitative measured or qualitative assessed, the response evaluation(s) determined from the data in Tumor Results (TR)

RS Example 1



Row	STUDYID	DOMAIN	USUBJID	RSSEQ	RSLNKGRP	RSTESTCD	RSTEST	RSCAT	RSORRES	RSSTRESC	RSSTAT
1	ABC	RS	44444	1		TRGRESP	Target Response	RECIST 1.1	PR	PR	
2	ABC	RS	44444	2		NTRGRESP	Non-target Response	RECIST 1.1	SD	SD	
3	ABC	RS	44444	3	A2	OVRLRESP	Overall Response	RECIST 1.1	PR	PR	
4	ABC	RS	44444	4		TRGRESP	Target Response	RECIST 1.1			NOT DONE
5	ABC	RS	44444	5		NTRGRESP	Non-target Response	RECIST 1.1			NOT DONE
6	ABC	RS	44444	6		NRADPROG	Non-Radiological Progression	CLINICAL ASSESSMENT	Pleural Effusion	PD	
7	ABC	RS	44444	7	A3	OVRLRESP	Overall Response	CLINICAL ASSESSMENT	PD	PD	

Row	RSREASND	RSEVAL	VISITNUM	VISIT	RSDTC	RSDY
1 (cont)		INVESTIGATOR	40	WEEK 6	2010-02-18	46
2 (cont)		INVESTIGATOR	40	WEEK 6	2010-02-18	46
3 (cont)		INVESTIGATOR	40	WEEK 6	2010-02-18	46
4 (cont)	All targets not assessed	INVESTIGATOR	60	WEEK 12	2010-04-02	88
5 (cont)	Non-targets not assessed	INVESTIGATOR	60	WEEK 12	2010-04-02	88
6 (cont)		INVESTIGATOR	60	WEEK 12	2010-04-02	88
7 (cont)		INVESTIGATOR	60	WEEK 12	2010-04-02	88



Automation of SDTM Programming in Oncology Disease Response Domain

Yiwen Wang, Yu Cheng, Ju Chen
Eli Lilly and Company, China

PRE-PROCESSING

Step 1: Environment & Domain Metadata Setting

```
/*********************************************/
/*             Environment setting           */
/*********************************************/
%setexecpath;


/*********************************************/
/*          Domain metadata setting          */
/*********************************************/
%let _sdtm=rs;
%sdtm_metadata(domain=&_sdtm);
%sdtm_shell(input_meta=&_sdtm._meta, domain=&_sdtm);
```

%setexecpath: automatically identify current working folder, initialize and set programming environment

%sdtm_metadata: read the attributes(order, length, type); parameter values and controlled terminology from sdtm specs, and SAS format generation

%sdtm_shell: convert the metadata attributes to a data step to create a shell dataset

Automation of SDTM Programming in Oncology Disease Response Domain

Yiwen Wang, Yu Cheng, Ju Chen
Eli Lilly and Company, China

PRE-PROCESSING

Step 2: Source Datasets Initialization
Map with Domain Shell

```
/*********************************************/
/*      Source Datasets Initialization       */
/*********************************************/
%sdtm_varchg(inds=eds.rs1001,metads=meta_rs,outds=rs1001a);

/*********************************************/
/*        set RS with shell                  */
/*********************************************/
data rs1001b;
  set rs_shell rs1001a;
run;
```

%sdtm_varchg: change the input dataset attributes either by the spec or by user definition, considering multiple input datasets may contain different attributes for the same variable, this macro allow user to be more flexible on dealing with attributes

Automation of SDTM Programming in Oncology Disease Response Domain

Yiwen Wang, Yu Cheng, Ju Chen
Eli Lilly and Company, China

TEMPLATE PROGRAM

Step 3: Handling Identifier and Timing Variables
Vertical Structure Transformation

```
data rs1;
  set rs1001b;
  if missing(rsdatdd) then rsdatdd=dd;
  if missing(rsdatmo) then rsdatmo=mo;
  if missing(rsdatyy) then rsdatyy=yy;
  %sdtm_isodate(yy=rsdatyy,mo=rsdatmo,dd=rsdatdd,hr='',mi='',dtc=RSDTC);
  ……
run;
/*********************************************************/
/*   Merge with DM to get studyid, rfstdtc, usubjid etc  */
/*********************************************************/
%sdtm_relday(inds=rs1, dmsubset=%nrstr(if first.%scan(&mergeby,-1,%str(|
,)) and last.%scan(&mergeby,-1,%str(| ,)) or input(scan(usubjid,-
1,''),??best.)=input(subjid,??best.)), mergeby=usubjid, addvar=studyid,
rfstdtc=rfstdtc, outds=rs2_1);

/*********************************************************/
/*   Vertical structure transformation                   */
/*********************************************************/
%sdtm_tran(domain=&_sdtm, inds=rs2_1, outds=rs2_2, debug=Y);
%sdtm_visitnum(in=rs2_2,out=rs3_1,datec=rsdtc);
```

%sdtm_isodate: covert date to ISO8601 date by using open SAS codes

%sdtm_relday: extract Identifier variables and essential Timing variables from DM domain, and calculate study days of response assessment (RSDY)

%sdtm_tran: transform the data structure from horizontal to vertical, matching with metadata from SDTM spec

Key variables:
RSCAT RSTESTCD
Corresponding variables:
RSEVAL RSGRPID RSORRES RSREASND RSTEST …

%sdtm_visitnum: map timing variables: visitnum, visit, epoch

Automation of SDTM Programming in Oncology Disease Response Domain

Yiwen Wang, Yu Cheng, Ju Chen
Eli Lilly and Company, China

POST-PROCESSING

Step 4: Data Cut-Off if Needed
Sort Observations & Variables Order
Remove Format/Informat
Add Domain Label

```
%sdtm_cutoff(in=rs3_1,out=rs3_2,datec=rsdtc); /*data cut-off based on needs*/

%sdtm_sortorder(domain=&_sdtm, inds=rs3_2, seqvar=&_sdtm.seq, outds=&_sdtm.1);

%sdtm_finalds(domain=&_sdtm, inds=&_sdtm.1, outds= sdtm.&_sdtm);
```

%sdtm_cutoff: data cut-off may be applied based on needs (e.g. safety review)

%sdtm_sortorder: add SEQID and sort the dataset either by the spec or by user definition (e.g. for debugging purpose)

%sdtm_finalds: final handling to generate final domain

- Sort Variables Order
- Remove Format / Informat
- Add Dataset Label

Automation of SDTM Programming in Oncology Disease Response Domain

Yiwen Wang, Yu Cheng, Ju Chen
Eli Lilly and Company, China

SUPPRS

Step 5: SUPPQUAL (All Vertical Structure)

```
%sdtm_metadata(domain=supp&_sdtm);
%sdtm_shell(input_meta=supp&_sdtm._meta, domain=supp&_sdtm);

proc sort data=supp&_sdtm; by usubjid &_sdtm.seq; run;

%sdtm_supp(domain=supp&_sdtm, inds=supp&_sdtm, meta_values=supp&_sdtm._meta_values, outds=supp&_sdtm.1);

%sdtm_sortorder(domain=supp&_sdtm,
                inds=supp&_sdtm.1(rename=(&_sdtm.seq=idvarvalx)),
                numpar=idvarvalx,
                outds=supp&_sdtm.2,
                debug=Y);

%sdtm_finalds(domain=supp&_sdtm, inds=supp&_sdtm.2,outds=sdtm.supp&_sdtm);
```

```
%thePostProc;
```

→ **LOG CHECK**

Automation of SDTM Programming in Oncology Disease Response Domain

Yiwen Wang, Yu Cheng, Ju Chen
Eli Lilly and Company, China

SUMMARY

Enable data mapping automation: the macro-based tools (SDTM utility macros) allow data to be mapped automatically according to the required specifications. This automation tool works like a reader and automatically generates program codes as long as the specification is written in a machine-readable manner. The tools can apply to different SDTM domains including SUPPQUAL and RELREC.

Standardize programming style: streamlined the SDTM programming logic and standardized the coding style. The standardized templates for the key safety domains and Oncology efficacy domains were created which can be re-used and as a result reduces the variability of quality among programmers.

Engage a broader range of applications: The developed macros could be used across different studies, therapeutic areas and for different delivery needs.

Automation of SDTM Programming in Oncology Disease Response Domain

Yiwen Wang, Yu Cheng, Ju Chen
Eli Lilly and Company, China

ACKNOWLEDGMENTS

The authors would like to thank all of my colleagues who reviewed this paper and provided insight comments.

CONTACT INFORMATION

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

Yiwen Wang, E-mail: wang_yi_wen_even@lilly.com

Yu Cheng, E-mail: cheng_yu_ella@lilly.com

Ju Chen, E-mail: chen_ju@lilly.com