PharmaSUG China 2021 - Paper DS-036

SDTM Annotated CRF Digitalization

Chunpeng Zhao, Mijun Hu, Jiapeng He and Aide Zhou, BeiGene

ABSTRACT

We human can read SDTM aCRF to know which fields are mapped into which SDTM variables/values. The challenge is how to make computer to read SDTM aCRF and know this mapping information. The paper will introduce how to digitalize SDTM aCRF so that computer can utilize SDTM mapping information to do CRF data SDTM annotation and transformation automatically.

Through SAS® Procedure Groovy, we run Java code in PrintTextLocations.java from Apache® PDFBox to extract each letter and its coordinate in its page in Unique Annotated CRF. With SAS®, we concatenate letters into words, then into sentences. Field Label and Field OID are linked with the same sequence number in circle, if CRF is exported from Rave electronic data capture (EDC) system. Field Label and its Field options are much closer than other Field Labels and their Field options vertically. Based on each letter and its coordinate in a CRF page, we extract Form name, Field OID, Field Label, Field Options, and their coordinates from CRF. We digitalize a CRF file into SAS dataset.

We export SDTM annotations from SDTM aCRF into FDF file. With SAS®, we extract SDTM annotation contents, their attributes (e.g., font size, background color…), and their coordinates in their CRF pages from FDF file. We digitalize a CRF file's SDTM annotations into SAS dataset.

Based on Fields' coordinates and SDTM annotations' coordinates in their CRF pages, we classify SDTM annotations into each field, since SDTM annotations are closer to its field vertically than other fields. With SAS®, we digitalize the mapping from Field to SDTM annotation, i.e., which SDTM annotations are mapped into which field, and calculating SDTM annotations' relative coordinates to its field. We name the digitalization as 1st digitalization. With 1st digitalization, we realize SDTM annotation automation, if fields in new trial CRF are same as reference 1st digitalization library.

We further digitalize SDTM annotation based on 1st digitalization. We derive each field's corresponding domain name according to background color of SDTM annotation and extract each field's corresponding SDTM variable names/values from SDTM annotations. We digitalize which field is mapped into which SDTM variables/values. We name the digitalization as 2nd digitalization. With 2nd digitalization, we convert SDTM mapping rules into SAS code logics to create SDTM datasets. CRF data SDTM automation comes true.

INTRODUCTION

Most of CRF fields (about 80%, even more) in a clinical trial are copied directly from other trials. Their SDTM annotations and SDTM transformations are the same with reference trials. The paper will introduce an approach to recycle each field's SDTM annotations and SDTM transformation through SDTM Annotated CRF Digitalization, making a road to cheaper SDTM transformation.

The sole purpose of life has been to pass on what was learned (Professor Norman, 2014). Let us see how to pass on what was learned on SDTM transformation of a CRF field from one trial to another, automatically and dynamically, just like passing on DNA in organism from one generation to next.

SDTM ANNOTATED CRF DIGITALIZATION FOR SDTM ANNOTATION

SDTM annotated CRF digitalization is that the process of converting SDTM annotated CRF to digital form (i.e., SAS dataset), to make machine (i.e., SAS® Software) understand a CRF field's SDTM annotations and SDTM transformation like human.

CRF FIELDS DIGITALIZATION

Through Apache® PDFBox Java code in SAS® Procedure Groovy and SAS code, read each CRF field's field name, field label, field options and their locations from a CRF file (i.e., form name, page number, coordinates in a page). See Yin-Jhen Yan etc., 2018 for details.

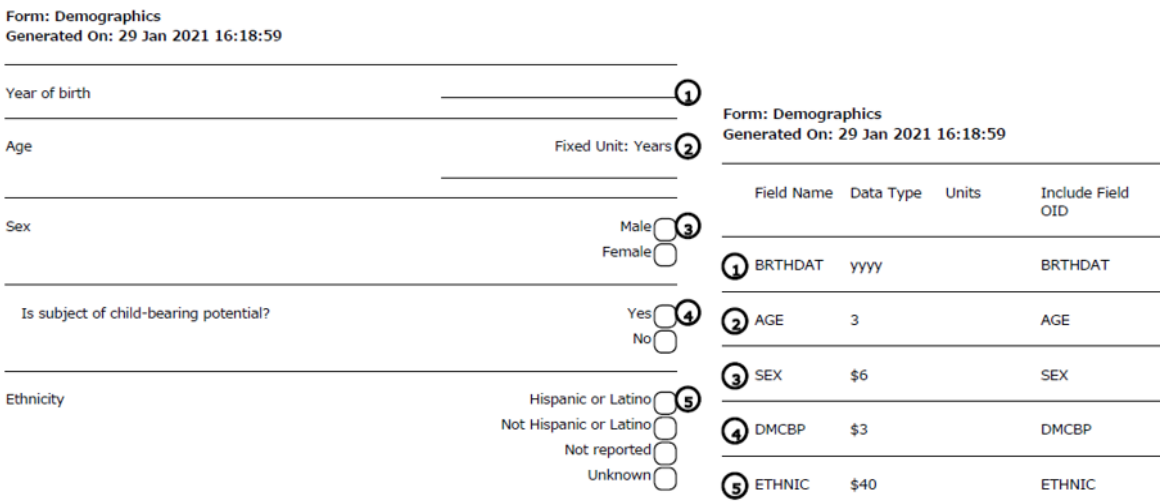

Figure 1. Sample of CRF Fields

Table 1 Sample of CRF Fields's Digitalization

Page	CRFForm	Field SEQ	FieldName	FieldLabel	FieldOption	FieldLabel STX	Fieldlabel ENX	FieldOptio nSTX	FieldOptio nENX
11	Demographics	0	Form	Demographics		90			
11	Demographics	1	BRTHDAT	Year of birth		90	144.6839 751		
11	Demographics	2	AGE	Age	Fixed Unit: Years	90	106.7400 057	443.877	518.999985 1
11	Demographics	3	SEX	Sex	Male	90	105.8940 05	485.84	506.000003
11	Demographics	3	SEX	Sex	Female	90	105.8940 05	474.347	506.000014 6
11	Demographics	4	DMCBP	Is subject of child-bearing potential?	Yes	100	260.1819 146	490.655	506.000001
11	Demographics	4	DMCBP	Is subject of child-bearing potential?	No	100	260.1819 146	493.994	506.000011 9
11	Demographics	5	ETHNIC	Ethnicity	Hispanic or Latino	90	127.6739 96	427.511	506.000043 8
11	Demographics	5	ETHNIC	Ethnicity	Not Hispanic or Latino	90	127.6739 96	409.052	506.000058 6
11	Demographics	5	ETHNIC	Ethnicity	Not reported	90	127.6739 96	450.038	506.000005 4
11	Demographics	5	ETHNIC	Ethnicity	Unknown	90	127.6739 96	464.96	506.000069 6

Page	CRFForm	Field SEQ	FieldName	FieldLabel	FieldOption	Y	YEnd	OptionYST	OptionY
11	Demographics	0	Form	Demographics		0	146.4329 992		
11	Demographics	1	BRTHDAT	Year of birth		172.893	174.893	172.893	174.893
11	Demographics	2	AGE	Age	Fixed Unit: Years	206.893	208.893	206.893	208.893
11	Demographics	3	SEX	Sex	Male	257.393	273.393	257.393	259.393
11	Demographics	3	SEX	Sex	Female	257.393	273.393	273.393	273.393
11	Demographics	4	DMCBP	Is subject of child-bearing potential?	Yes	312.393	328.393	312.393	314.393

11	Demographics	4	DMCBP	Is subject of child-bearing potential?	No	312.393	328.393	328.393	328.393
11	Demographics	5	ETHNIC	Ethnicity	Hispanic or Latino	367.393	415.393	367.393	369.393
11	Demographics	5	ETHNIC	Ethnicity	Not Hispanic or Latino	367.393	415.393	383.393	383.393
11	Demographics	5	ETHNIC	Ethnicity	Not reported	367.393	415.393	399.393	399.393
11	Demographics	5	ETHNIC	Ethnicity	Unknown	367.393	415.393	415.393	415.393

For example, from Table 1, SAS® will know Field SEX its field name or field OID is SEX, which is its variable name in raw dataset extracted from EDC system. Field SEX its label is sex. It has two options, Male and Female. Its field sequence number is 3. It is in Form Demographics at Page 11. Each CRF page's origin of coordinate (0, 0) is at the left top conner in CRF Fields's Digitalization. Field label rectangular box coordinates are (90, 257, 106, 259), i.e., (Field label start X (FieldLabelSTX), Field label start Y (OptionYST), Field label end X (FieldlabelENX), Field label end Y (OptionY)). In practice, field label and its first option share the same Y coordinates. Each option's rectangular box coordinates are (Field option start X (FieldOptionSTX), Field option start Y (OptionYST), Field option end X (FieldOptionENX), Field option end Y (OptionY)). And the whole field's rectangular box coordinates are (Field label start X (FieldLabelSTX), Field label start Y (Y), Field option end X (FieldOptionENX), the last Field option end Y (YEnd)). We also create a dummy Field Form, whose SDTM annotation will be applied to all fields of the same domain in a form, e.g., domain labels.

SDTM ANNOTATION DIGITALIZATION AND CONNECTION TO CRF FIELDS

There are two ways to digitalize SDTM annotations.

1. SDTM annotations can be exported into FDF file from SDTM annotated CRF, in which SDTM annotations are manually annotated. With SAS®, extract each SDTM annotation's attributes (e.g., Annotation content, rectangular box coordinates, background color…) from FDF file. See Walter Hufford, 2014 for details. Based on CRF fields' coordinates and SDTM annotations' coordinates, we can link them together, if they are close enough with each in CRF pages.
2. Assign SDTM annotations' contents and box background color to each CRF field in excel file. With SAS®, calculate annotation box's size according to annotation's contents. See Steven Black, 2016 for details. Each annotation box's coordinates can also be calculated since we already know each annotation's corresponding field's coordinates and the field's options' coordinates in a CRF page. We can put each annotation box close to its field without covering its field label or field options through annotation box's coordinate calculation.

In practice, above two ways are complementary to each other on CRF SDTM annotation digitalization and connection to CRF fields. Each CRF page's origin of coordinate (0, 0) is at the left bottom conner in SDTM Annotation Digitalization, which is different from CRF Fields' Digitalization. We can do coordinate transformation between Fields' Digitalization and SDTM Annotation Digitalization with PDF page height = 792 points. Y in Field Digitalization = 792 - Y in SDTM Annotation Digitalization. See PDF Page Coordinates for details.

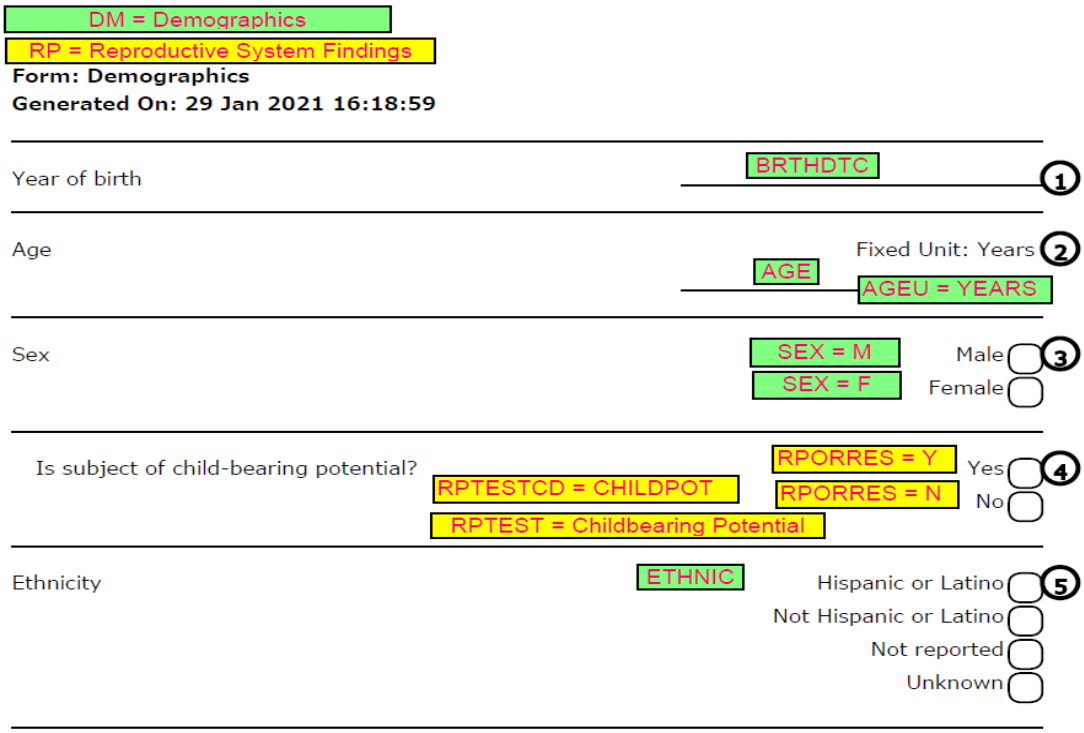

Figure 2 Sample of SDTM annotated CRF

Table 2 Sample of SDTM Annotation Digitalization

AnnoColor	AnnoContent	AnnoFont	AnnoRect	AnnoPage
0.501953 1.0 0.501953	AGE	/DA(0 0 0 rg /F1 10 Tf)/DS(font: Helvetica,sans-serif 10.0pt; text-align:center; color:#FF006E)	400.842 570.936 428.842 583.936	11
0.501953 1.0 0.501953	AGEU = YEARS	/DA(0 G 0 0 0 rg 0 Tc 0 Tw 100 Tz 0 TL 0 Ts 0 Tr /Helv 10 Tf)/DS(font: Helvetica,sans-serif 10.0pt; text-align:left; color:#FF006D)	444.463 561.941 526.361 575.652	11
0.501953 1.0 0.501953	BRTHDTC	/DA(0 0 0 rg /F1 10 Tf)/DS(font: Helvetica,sans-serif 10.0pt; text-align:center; color:#FF006E)	397.629 622.03 453.629 635.03	11
0.501953 1.0 0.501953	DM = Demographics	/DA(0 0 0 rg /F1 10 Tf)/DS(font: Helvetica,sans-serif 10.0pt; text-align:center; color:#FF006E)	84.8627 724.183 189.862 737.183	11
0.501953 1.0 0.501953	ETHNIC	/DA(0 0 0 rg /F1 10 Tf)/DS(font: Helvetica,sans-serif 10.0pt; text-align:center; color:#FF006D)	352.07 424.169 397.07 437.169	11
0.501953 1.0 0.501953	RACE = AMERICAN INDIAN OR ALASKA NATIVE	/DA(0 0 0 rg /Helv 10 Tf)/DS(font: Helvetica 10.0pt; text-align:center; color:#FF006B)	289.589 295.213 521.347 307.219	11
0.501953 1.0 0.501953	RACE = ASIAN	/DA(0 0 0 rg /Helv 10 Tf)/DS(font: Helvetica 10.0pt; text-align:center; color:#FF006B)	128.237 266.114 208.61 280.124	11
1.0 1.0 0.0	RP = Reproductive System Findings	/DA(0 0 0 rg /F1 10 Tf)/DS(font: Helvetica,sans-serif 10.0pt; text-align:center; color:#FF006E)	84.8627 719.183 265.862 732.183	11
1.0 1.0 0.0	RPORRES = N	/DA(0 0 0 rg /Helv 10 Tf)/DS(font: Helvetica,sans-serif 10.0pt; text-align:left; color:#FF0069)	409.886 463.199 487.233 477.209	11
1.0 1.0 0.0	RPORRES = Y	/DA(0 G 0 0 0 rg 0 Tc 0 Tw 100 Tz 0 TL 0 Ts 0 Tr /Helv 10 Tf)/DS(font: Helvetica,sans-serif 10.0pt; text-align:left; color:#FF006C)	408.756 480.207 486.104 494.217	11
1.0 1.0 0.0	RPTEST = Childbearing Potential	/DA(0 0 0 rg /F1 10 Tf)/DS(font: Helvetica,sans-serif 10.0pt; text-align:center; color:#FF006D)	265.199 448.844 431.199 461.844	11

1.0 1.0 0.0	RPTESTCD = CHILDPOT	/DA(0 0 0 rg /Helv 10 Tf)/DS(font: Helvetica,sans-serif 10.0pt; text-align:left; color:#FF006B)	266.284 466.021 395.207 480.031	11
0.501953 1.0 0.501953	SEX = F	/DA(0 0 0 rg /Helv 10 Tf)/DS(font: Helvetica 10.0pt; text-align:center; color:#FF006B)	400.165 515.872 463.197 529.882	11
0.501953 1.0 0.501953	SEX = M	/DA(0 0 0 rg /Helv 10 Tf)/DS(font: Helvetica 10.0pt; text-align:center; color:#FF006D)	399.315 531.53 462.346 545.54	11

Each SDTM annotation box's relative coordinates to its field can be calculated since both their coordinates in a CRF page are known already. We can create Table 3 with Each SDTM annotation box's relative coordinates to its field, i.e., (Relative left X (RefAnnoRectR1), Relative bottom Y (RefAnnoRectR2), Relative right X (RefAnnoRectR3), Relative top Y (RefAnnoRectR4)).

Table 3 Sample of SDTM Annotation Connection to CRF Fields

CRFForm	FieldName	FieldLabel	RefTriggeredAnnotation	RefAnnoAnchor	RefAnnoRectR1	RefAnnoRectR2	RefAnnoRectR3	RefAnnoRectR4	Other Attributes (e.g., color ...)
Demographics	Form	Demographics	DM = Demographics	Form	-5.1373	-67.817	165.862	-54.817	
Demographics	BRTHDAT	Year of birth	BRTHDTC		307.629	2.923	363.629	15.923	
Demographics	AGE	Age	AGE		310.842	-14.171	338.842	-1.171	
Demographics	AGE	Age	AGEU = YEARS		354.463	-23.166	436.361	-9.455	
Demographics	SEX	Sex	SEX = M		309.315	-3.077	372.346	10.933	
Demographics	SEX	Sex	SEX = F		310.165	-18.735	373.197	-4.725	
Demographics	DMCBP	Is subject of child-bearing potential?	RP = Reproductive System Findings	Form	-5.1373	-87.576	165.862	-74.576	
Demographics	DMCBP	Is subject of child-bearing potential?	RPORRES = Y		308.756	0.6	386.104	14.61	
Demographics	DMCBP	Is subject of child-bearing potential?	RPTESTCD = CHILDPOT		166.284	-13.586	295.207	0.424	
Demographics	DMCBP	Is subject of child-bearing potential?	RPORRES = N		309.886	-16.408	387.233	-2.398	
Demographics	DMCBP	Is subject of child-bearing potential?	RPTEST = Childbearing Potential		165.199	-30.763	331.199	-17.763	
Demographics	ETHNIC	Ethnicity	ETHNIC		262.07	-0.438	307.07	12.562	

TRIGGER AND ANCHOR OF SDTM ANNOTATIONS

To make SDTM annotation automaton more dynamic, we introduce two concepts Trigger and Anchor of SDTM annotations.

1. Trigger determines whether a SDTM annotation should be annotated in a CRF page. Each Field is a trigger, which always triggers at least one SDTM annotations.
2. Anchor determines a SDTM annotation's location in a CRF page. In most cases, Anchor is the same field as Trigger.
3. Trigger and Anchor of a SDTM annotation can be different Fields.
4. Form Name is taken as a dummy Field.
5. A SDTM annotation should be anchored at Form Name if all following 2 criteria are met.
    a. The SDTM annotation is triggered by every Field of a Domain.
    b. Variable value in the SDTM annotation is assigned.
6. A SDTM annotation can be taken to be triggered by Form Name, if all following 2 criteria are met.
    a. The SDTM annotation is anchored at Form Name.
    b. Every page of the Form has at least one field of the domain.

In Table 3, Field "Is subject of child-bearing potential?" triggers SDTM annotation "RP = Reproductive System Findings", which is anchor at dummy field Form. With Table 3, CRF SDTM annotation automation comes true. In a new CRF file, if Field "Is subject of child-bearing potential?" appears in Demographics form, it always triggers following 5 SDTM annotations.

1. RP = Reproductive System Findings, which is anchored at dummy Field Form. Domain label annotation is always anchored at the top of a CRF page.
2. The rest 4 ones, RPTESTCD = CHILDPOT, RPTEST = Childbearing Potential, RPORRES = Y, and RPORRES = N, they are anchored at the field-self based on their annotation boxes' relative coordinates to the field. It means they will move up and down in new CRF, even into another page along with the field's new location.

When we use Table 3 to create SDTM annotation FDF file for new CRF file, we should programmatically check whether their field labels and field options are consistent to make sure the same field name in two CRF files has the same clinical meanings.

PARSING SDTM ANNOTATIONS FOR SDTM TRANSFORMATION

We can create Table 4, through parsing SDTM annotations in Table 3 and merging ALS by Form name and Field OID or Field Name. ALS (Architect Loader Specification) is an MS Excel-based format supported by RAVE which allows the exporting and importing of the complete study design information required to build studies in RAVE).

Each CRF form's corresponding raw dataset name is from ALS. Each field' Control Type is also from ALS. Each field's values or options could be from CRF or ALS either.

In a CRF form, SDTM annotation boxes' background colors are consistent per domain. According to a domain label's SDTM annotation background colors at the top of a CRF page, we know which color is for which domain. Each CRF field could be dispatched into its corresponding domain according to its SDTM annotation color. For example, in Figure 2, we know DM domain color is green, RP domain color yellow.

And we can also know whether a CRF field is dispatched into a SUPP dataset from its SDTM annotation, e.g., "**SUPP**DM.QVAL where QNAM = RACEOTH".

Each field with topic variable SDTM annotation (i.e., including SDTM variables –TEST, --TRT, --TERM) triggers a SDTM record, which is indicated with SDTMRecordID. In Table 4, Field "Is subject of child-bearing potential?" has a SDTM annotation "RPTEST = Childbearing Potential", which triggers a SDTM record, indicating with SDTMRecordID= DMCBP. If there is another CRF field annotated with another RPTEST, it will also trigger another SDTM record with another SDTMRecordID value. If SDTMRecordID

is missing, corresponding SDTM variable's value will be applied into all SDTM records. For example, SDTM variable DOMAIN=RP will be applied into all records in RP domain.

Assigned SDTM variable's values are also extracted from SDTM annotations. We define several algorithms to map each CRF field value to its corresponding SDTM variable value. For example, Field Sex, its values Male and Female are converted into SDTM controlled terminology values M and F respectively. The algorithm "IfAssigned" can be auto-populated according to CRF field values Male and Female and their corresponding SDTM annotations SEX=M and SEX=F. To make Table 4 standalone to transform CRF data into SDTM-like data successfully, Controlled Terminology Values or assigned Values should be specified in SDTM Annotations.

Based on Table 4, there are two ways to transform CRF collected data into SDTM-like datasets.

1. Develop one macro to transform all CRF data into SDTM-like datasets, since all CRF forms' SDTM transformation metadata, i.e., Table 4, share the same data structure.
2. Auto-create traditional by-domain SAS programs first. These auto-created SAS programs are just like that those human programmers manually write, with intents, line break and comments. Then run each domain SAS program to create each domain SDTM-like dataset.

In practice, we use both ways to create SDTM datasets to QC each other.

Table 4 Sample of Parsing SDTM Annotation

CRFForm	FieldName	FieldLabel	RefTriggeredAnnotation	SourceDataset	ControlType	FieldValue	Domain	Dataset
Demographics	Form	Demographics	DM = DemograpShics	DM			DM	DM
Demographics	BRTHDAT	Year of birth	BRTHDTC	DM	DateTime		DM	DM
Demographics	AGE	Age	AGEU = YEARS	DM	Text		DM	DM
Demographics	AGE	Age	AGE	DM	Text		DM	DM
Demographics	SEX	Sex	SEX = F	DM	DropDownList	Female	DM	DM
Demographics	SEX	Sex	SEX = M	DM	DropDownList	Male	DM	DM
Demographics	DMCBP	Is subject of child-bearing potential?	RPTEST = Childbearing Potential	DM	DropDownList		RP	RP
Demographics	DMCBP	Is subject of child-bearing potential?	RPORRES = N	DM	DropDownList	No	RP	RP
Demographics	DMCBP	Is subject of child-bearing potential?	RPTESTCD = CHILDPOT	DM	DropDownList		RP	RP
Demographics	DMCBP	Is subject of child-bearing potential?	RPORRES = Y	DM	DropDownList	Yes	RP	RP
Demographics	DMCBP	Is subject of child-bearing potential?	RP = Reproductive System Findings	DM	DropDownList		RP	RP
Demographics	RACEOTH	Other, specify	SUPPDM.QVAL where QNAM = RACEOTH	DM	LongText		DM	SUPPDM

CRFForm	FieldName	FieldLabel	RefTriggeredAnnotation	SDTMRecordID	VariableName	VariableValue	Algorithm
Demographics	Form	Demographics	DM = Demographics		DOMAIN	DM	Assigned
Demographics	BRTHDAT	Year of birth	BRTHDTC		BRTHDTC		DT2DTC
Demographics	AGE	Age	AGEU = YEARS		AGEU	YEARS	Assigned
Demographics	AGE	Age	AGE		AGE		CopyUpcase
Demographics	SEX	Sex	SEX = F		SEX	F	IfAssigned

Demographics	SEX	Sex	SEX = M		SEX	M	IfAssigned
Demographics	DMCBP	Is subject of child-bearing potential?	RPTEST = Childbearing Potential	DMCBP	RPTEST	Childbearing Potential	Assigned
Demographics	DMCBP	Is subject of child-bearing potential?	RPORRES = N	DMCBP	RPORRES	N	IfAssigned
Demographics	DMCBP	Is subject of child-bearing potential?	RPTESTCD = CHILDPOT	DMCBP	RPTESTCD	CHILDPOT	Assigned
Demographics	DMCBP	Is subject of child-bearing potential?	RPORRES = Y	DMCBP	RPORRES	Y	IfAssigned
Demographics	DMCBP	Is subject of child-bearing potential?	RP = Reproductive System Findings		DOMAIN	RP	Assigned
Demographics	RACEOTH	Other, specify	SUPPDM.QVAL where QNAM = RACEOTH		RACEOTH		CopyUpcase

INTEGRATED REFERENCE LIBRARY

We create an integrated reference library to store each CRF file specific fields' CRF SDTM annotation and transformation metadata, i.e., Table 3 and Table 4. If a CRF field's SDTM annotation and transformation was done in a previous trial, its SDTM annotation and transformation rules can be copied into new trial dynamically and automatically. Users can only focus on new study specific fields' SDTM annotation and transformation.

When users go through CRF SDTM annotation and transformation process in their trials, their manual work on new study specific fields' SDTM annotation and transformation, i.e., their Table 3 and Table 4 will be uploaded into and integrated reference library automatically for other trials to reference. It means one CRF field only need SDTM annotation and transformation once, when it appears at first time in a trial. If the same CRF field is reused in new trial, its SDTM annotation and transformation metadata will be copied into new trial automatically.

Based on our practice, even there are only several trials' CRF SDTM annotation and transformation metadata in integrated reference library, and even CRF design does not follow CDASH process completely (i.e., CRFs should not be developed on a trial-by-trial basis within the implementer organization, but rather be brought into a study from a library of approved CRFs based on the CDASH Model and Implementation Guide, see Section 3.1 in CDASH IG Version 2.1 for details), integrated reference library can cover 70%-90% fields in a new trial. Users can focus on the rest 10%-30% new fields' SDTM annotation and transformation. It means 70%-90% CRF SDTM annotation and transformation work can be saved in new trials!

CONCLUSION

Through SDTM annotated CRF digitalization, together with CRF design CDASH process, in a new trial, estimated more than 80% CRF fields' SDTM annotations and transformations can be directly copied from previous trials. The more trials' SDTM annotated CRF digitalization implements, the more SDTM transformation work will be saved in new trials.

Since SDTM annotated CRF digitalization could be done once CRF is available, SDTM annotations and transformations metadata can be ready before the first patient the first visit. CRF collected data can be synchronized into SDTM data once CRF collected data is available. Data cleaning and data monitoring can be based on SDTM data instead of EDC data.

REFERENCES

Professor Norman, 2014. "Lucy Quotes" https://www.magicalquote.com/moviequotes/the-sole-purpose-of-life/

Yin-Jhen Yan etc., 2018 “No Solution to Auto-generating acrf.pdf? Try to Use GROOVY Procedure!” https://www.pharmasug.org/proceedings/china2018/AD/Pharmasug-China-2018-AD71.pdf

Walter Hufford, 2014 “Automating Production of the blankcrf.pdf” Automating Production of the blankcrf.pdf (pharmasug.org)

Steven Black, 2016 “Have SAS® Annotate Your Blank CRF for You! Plus Dynamically Add Color and Style to Your Annotations” https://support.sas.com/resources/papers/proceedings16/8480-2016.pdf

PDF Page Coordinates, https://www.pdfscripting.com/public/PDF-Page-Coordinates.cfm

Section 3.1 in CDASH IG Version 2.1
https://www.cdisc.org/system/files/members/standard/foundational/CDASHIG%20v2.1-Final_Rev.pdf

CONTACT INFORMATION

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

Chunpeng Zhao
BeiGene
Chunpeng.zhao@beigene.com
Mijun Hu
BeiGene
mijun.hu@beigene.com
Jiapeng He
BeiGene
jiapeng.he@beigene.com
Aide Zhou
BeiGene
aide.zhou@beigene.com