PharmaSUG China 2024 – Paper 10091

Introduction of Ophthalmic Examinations and the Preparation of SDTM OE Using SDTM IG 3.3

Shuang Qiu, Everest Clinical Research Corporation

ABSTRACT

CDISC SDTM Implementation Guide 3.3 was finalized on November 20th, 2018. FDA started to accept submissions following SDTM IG 3.3 on July 7th, 2020. Several domains for physiology and morphology findings across different body systems have been added in SDTM IG 3.3, including the Ophthalmic Examinations (OE) domain. The OE domain contains assessments that measure a person's ocular health and visual status to detect abnormalities in the components of the visual system and determine how well the person can see. As a new dataset in SDTM IG 3.3, there are few relevant references about it. This paper will primarily focus on introducing the structure of OE domain and the assessments performed for an ophthalmic study. It will demonstrate how to map each CRF (Case Report Form) question to the datasets and list considerations before the mapping process. Detailed explanations will be provided on how key variables are derived during dataset mapping. Additionally, the process of implementing SDTM OE will be introduced with sample codes. Finally, common Pinnacle 21 issues and challenges encountered when programming OE will be discussed.

INTRODUCTION

The number of clinical trials in ophthalmology has increased in recent years. SDTM OE is the most important dataset in ophthalmic studies. Therefore, standardizing the implementation of SDTM OE for more efficient analysis in ophthalmic studies is certainly of essence. The guidelines for SDTM OE development have been regulated in SDTM IG 3.3. SDTM OE follows the structure of one record per ophthalmic finding per method per location, per time point per visit per subject. The following table is a typical example of SDTM OE.

DOMAIN	USUBJID	FOCID	OESEQ	OETEST	OECAT	OEORRES	OESTRESC	OELOC	OELAT	OEMETHOD	VISITNUM	VISIT	OEDTC
OE	XXXXXX-20001	OD	1	Number of Letters Correct	BEST CORRECTED VISUAL ACUITY	52	52	EYE	RIGHT	ETDRS EYE CHART	2	Enrollment	2023-12-28
OE	XXXXXX-20002	OS	2	Constant Number of Letters Correct	BEST CORRECTED VISUAL ACUITY	30	30	EYE	LEFT	ETDRS EYE CHART	2	Enrollment	2023-12-28
OE	XXXXXX-20003	OS	3	Visual Acuity Score	BEST CORRECTED VISUAL ACUITY	80	80	EYE	LEFT	ETDRS EYE CHART	2	Enrollment	2023-12-28

Table 1 SDTM OE

The OE domain is a findings domain that stores results from ophthalmologic evaluations. Typically, the following assessments are conducted in an ophthalmic study.

Best corrected Visual Acuity (BCVA)

BCVA is the most commonly used endpoint in ophthalmic clinical trials for diseases such as age-related macular degeneration, Diabetic macular edema and other retinal diseases that can cause vision loss. This endpoint is recognized by the EMA (European Medicines Agency) and the FDA (Federal and Drug Administration). BCVA measures the best visual acuity a patient can achieve with glasses or contact lenses at specific distances. In ophthalmic clinical trials, the ETDRS (Early Treatment Diabetic Retinopathy) chart is commonly used to perform BCVA measurements.

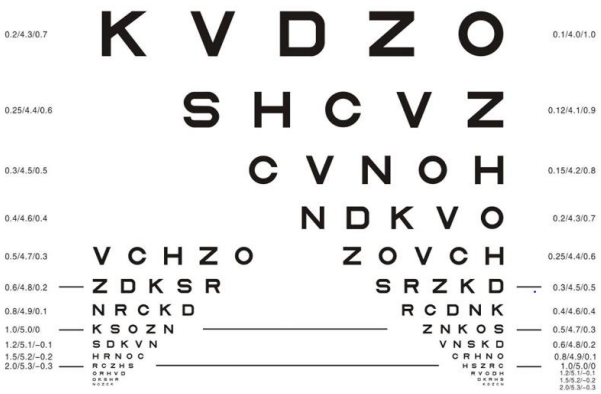

Figure 1 ETDRS Chart

The most common primary endpoint in ophthalmic clinical trails is the change in BCVA from baseline between the investigational drug and the comparator. One of the key efficacy endpoints is the percentage of subjects who achieve a 15-letter improvement in BCVA from baseline.

Intraocular Pressure (IOP)

IOP is the pressure of the fluid inside the eyes. High IOP can stress the eyes and damage the optic nerve. It is an important endpoint in ophthalmic clinical trials for efficacy analysis. Changes in IOP should be monitored before and after the application of investigational drugs. The common method for measuring IOP measure is applanation tonometry.

Overall Slit Lamp Findings

A slit lamp is a microscope with a bright light used to examine overall eye health. It is also a critical endpoint in ophthalmic clinical trials for efficacy analysis. The slit-lamp examination typically consists of the following categories:

- **Slit lamp eye structure**
  This involves detecting the abnormality in eye structure using such as conjunctiva, cornea, sclera, anterior chamber, lens and anterior vitreous using the slit lamp.
- **Slit lamp findings**
  The number and percentage of patients with each grade for each assessment are summarized for all visits. Parameters assessed and summarized may include anterior chamber cells, anterior chamber flare, vitreous cell, vitreous hemorrhage, cataract, etc.
- **Slit lamp lens information**
  This assesses the lens status before and after the application of investigational drugs.

Indirect ophthalmoscopy

Indirect ophthalmoscopy was used to obtain a wider view of fundus. The BIO device consists of a headband, binocular lens with mirrors, and a light source.

Figure 2 binocular indirect ophthalmoscope and a condensing lens

For indirect ophthalmoscopy, the number and percentage of patients with a retina break or detachment will be provided for each visit.

Snellen Visual Acuity

The Snellen visual chart measures visual acuity and is a more traditional approach compared to the ETDRS chart.

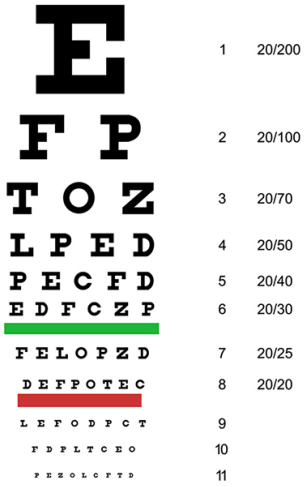

Figure 3 Snellen Visual Acuity Chart

Snellen VA should be scored using pinhole, refraction, or spectacle correction according to standard clinical practice at the site. Snellen VA will be assessed after obtaining ETDRS BCVA and before instilling dilating drop.

The corresponding results from the above assessments will be mapped to OE domain.

SDTM IMPLEMENTATION

Procedure

Converting incoming ophthalmic assessment data to a submission-ready format typically involves the following procedures:

- **Preparing**: Annotating the CRF to determine how to name each OETEST/TESTCD and how to report the test result values in standard format.
  -Structuring the OE domain by deciding what variables to keep in the dataset. The following macro could be used.
    - %attrib to attributing the labels.
    - %keepvar to define the variable keep list.
- **Programming-**Aggregating the source dataset and mapping each variable one-to-one with the OE variables.
  -Converting the OETEST/TESTCD and OEORRES/STRESC/STRESN/STRESU to standard format.
  -Deriving the Last Observation Before Exposure Flag to define the last non-missing value on or before the first treatment date.
  -Adding any supplementary variables to SUPPOE.
- **Checking against CDISC standards-**Generating Pinnacle 21 reports.

Assumptions

The following assumptions were stated in SDTM IG 3.3.

- To identify the side of the treatment. FOCID was introduced in SDTM IG 3.3 to identify the eyes. It's recommended to use the following values for FOCID: OD stands for oculus dexter (Right Eye); OS stands for oculus sinister (Left Eye); OU stands for oculus uterque (Both Eyes). The terms are included in non-extensible "Ophthalmic Focus of Study Specific Interest" (OEFOCUS) CDISC codelist.

Code	Codelist Code	Codelist Extensible (Yes/No)	Codelist Name	CDISC Submission Value	CDISC Synonym(s)	CDISC Definition	NCI Preferred Term
C119013		No	Ophthalmic Focus of Study Specific Interest	OEFOCUS	Ophthalmic Focus of Study Specific Interest	Terminology relevant to the identification of a focus of ophthalmic observations.	CDISC SDTM Ophthalmic Focus of Study Specific Interest Terminology
C119333	C119013		Ophthalmic Focus of Study Specific Interest	OD		The eye positioned in the right orbit, Oculus Dexter.	Right Eye
C119334	C119013		Ophthalmic Focus of Study Specific Interest	OS		The eye positioned in the left orbit, Oculus Sinister.	Left Eye
C119335	C119013		Ophthalmic Focus of Study Specific Interest	OU		Of or pertaining to both the left and right eyes, Oculus Uterque.	Both Eyes

Table 2 SDTM Controlled Terminology

- FOCID should be included in any subject level domains (findings, interventions, or events) for studies using it. If FOCID is not used for a study. --LOC and --LAT should be mapped for records related to eyes. FOCID, --LOC and --LAT are very useful in ophthalmic studies since it's helpful to connect information in OE domain with other domains.
- Identifiers, Timing variables, or Findings general observation class qualifiers were generally added to OE domain. However, the following were not generally added: --MODIFY, --NSPCES, --POS, --BODSYS, --ORREF, --STREFC, --STREFN, --CHRON, --DISTR, --ANTREG, --LEAD, --FAST, --TOX, --TOXGR, --LLOQ, --ULOQ.

CRF Mapping

To describe the procedure of CRF mapping, a sample for intraocular pressure will be used.

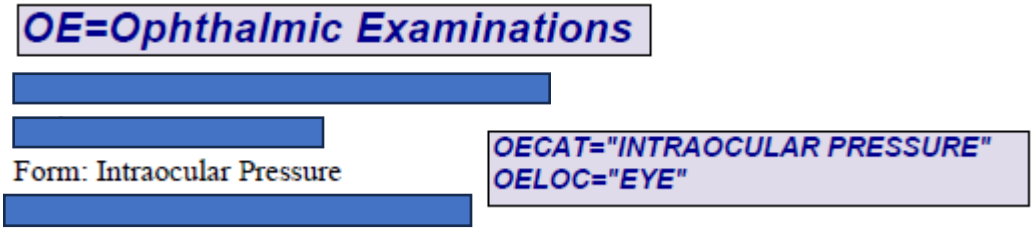

Figure 4 Header of sample CRF of intraocular pressure

Above is the header of intraocular pressure form. As we can see from the form name, we can assign OECAT = 'INTRAOCULAR PRESSURE'. As we can see from IG 3.3, OECAT is used to define a category of topic-variable values. In principle, we will map the variable following the controlled terminology. For OECAT, we will assign the value using form name since OECAT cannot be find in controlled terminology list. OESCAT is used to define a further categorization of OECAT values. For example, the intraocular pressure will be collected for both eyes. Study eye is the eye for study specific interest. The data will be collected specifically for studyeyes. Then we can assign the OESCAT to be 'STUDY EYE' to differentiate the OECAT values for both eyes.

OECAT	Category for Ophthalmic Test or Exam	Char	*	Grouping Qualifier	Used to define a category of topic-variable values. Examples: "VISUAL ACUITY", "CONTRAST SENSITIVIY", "OCULAR COMFORT".	Perm

Figure 5 OECAT in SDTM IG 3.3

OELOC	Location Used for the Measurement	Char	(LOC)	Record Qualifier	Anatomical location of the subject relevant to the collection of the measurement. Examples: "EYE" for a finding record relative to the complete eye, "RETINA" for a measurement or assessment of only the retina.	Exp

Figure 6 OELOC in SDTM IG 3.3

OELOC has been mapped to 'EYE' since the location of the measurement for intraocular pressure is to the compete eye, and the mapping followings LOC CT list.

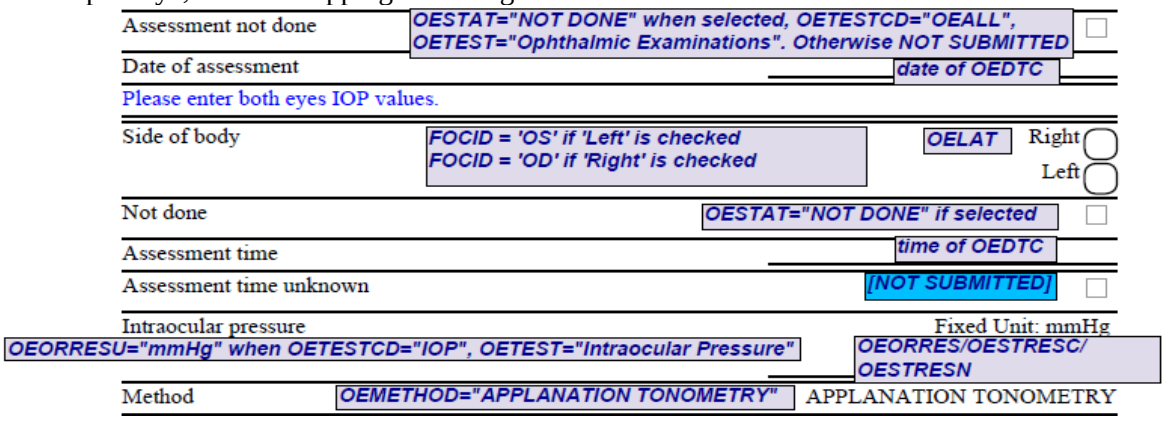

Figure 7 Sample CRF of intraocular pressure

The above is the CRF mapping for intraocular pressure. If the data on the CRF was missing and assessment not done was not explicitly captured, a record should not be created to indicate the data was not collected. If a group of tests for intraocular pressure were not done. The TESTCD should be 'OEALL'.

OETESTCD	Short Name of Ophthalmic Test or Exam	Char	(OETESTCD)	Topic	Short character value for OETEST used as a column name when converting a dataset from a vertical format to a horizontal format. It can be used as a column name when converting a dataset from a vertical to a horizontal format. The value in OETESTCD cannot be longer than 8 characters, nor can it start with a number (e.g., "1TEST" is not valid). OETESTCD cannot contain characters other than letters, numbers, or underscores. Example: "NUMLCOR".	Req
OETEST	Name of Ophthalmic Test or Exam	Char	(OETEST)	Synonym Qualifier	Long name for the test or examination used to obtain the measurement or finding. The value in OETEST cannot be longer than 40 characters. Example: Number of Letters Correct for OETESTCD = "NUMLCOR".	Req

Figure 8 OETESTCD/TEST in SDTM IG 3.3

For findings domain, it's critical to map TEST/TESTCD with ORRES/STRESC/STRESN. When programming SDTM OE, two variables are utilized to describe the ophthalmic test information: OETESTCD and OETEST. OETEST is the long name for the test or examination performed. OETESTCD is the short character value of OETEST and must be eight characters long. The mapping must follow CDISC controlled terminology. If the test is IOP, it should OETESTCD = "IOP", OETEST = "Intraocular Pressure", OEORRES is numeric value. If standard CT value cannot be found in the list, the value of TEST/TESTCD can be assigned to be consistent with the name of the examination. For example, in the best corrected visual acuity form, the OETEST of visual acuity score will be assigned to 'Score' and OETESTCD will be assigned to be 'SCORE'.

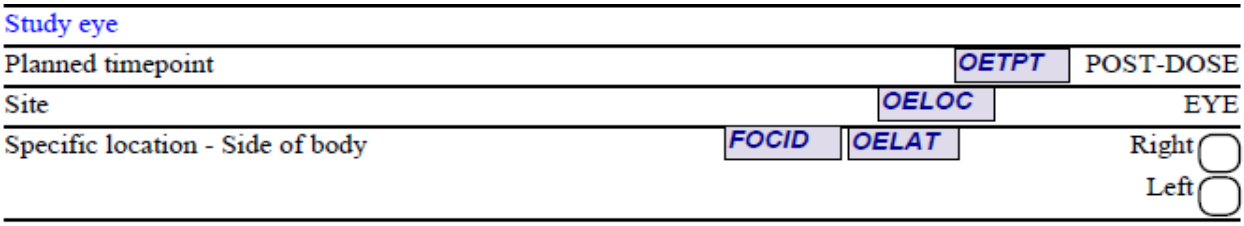

Figure 9 Sample CRF of intraocular pressure

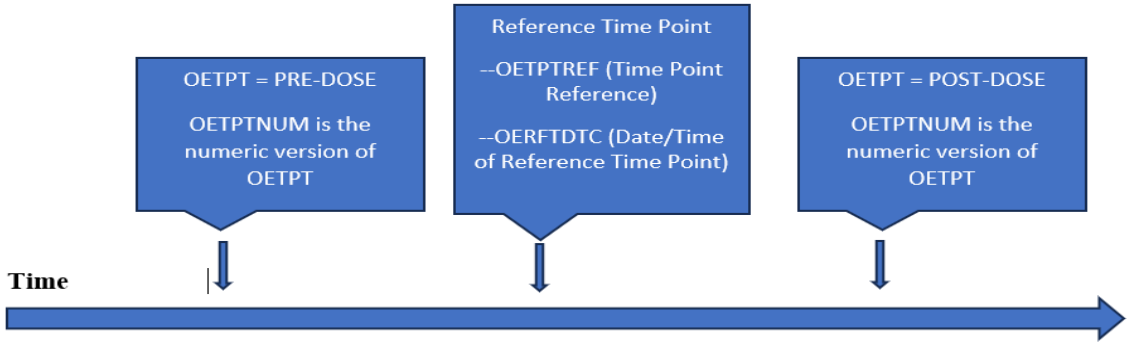

Figure 10 Diagram of OETPT/TPTNUM assignment

In general, intraocular pressure will be measured for study eye at visits prior to and after the application

of the investigational drugs. OETPT/TPTNUM was used to describe the time when a measurement or observation should be taken as defined in the protocol. Figure 10 shows how to assign OETPT and OETPTNUM.

In some cases, OETESTCD/TEST will be the same for results in different categories. Therefore, further description of OETESTCD/TEST would be necessary. OETSTDTL was introduced to further explain the OETESTCD/TEST.

OETSTDTL	Ophthalmic Test or Exam Detail	Char	*	Variable Qualifier	Further description of OETESTCD and OETEST.	Perm

Figure 11 OETSTDTL in SDTM IG 3.3

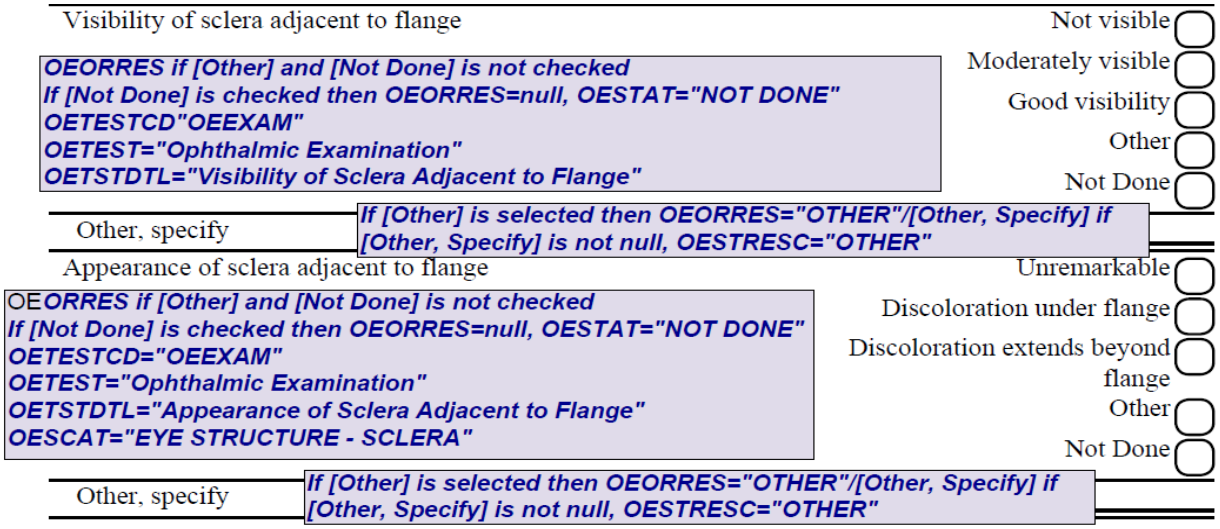

Figure 12 Sample CRF of slit lamp implant related findings

Above is the CRF for slit lamp related findings. As we can see from the CRF, OETESTCD is the same for 'Visibility of sclera adjacent to flange' and 'Appearance of sclera adjacent to flange'. Therefore, the best option is to use OETSTDTL to further describe OETEST. Please see Figure 12.

SDTM Programming

We have already explained how to annotate the CRF for an ophthalmic test form. Then we will start to program the dataset.

Normally, we will get a high volume of data from various sources. Preprocessing each incoming dataset is necessary. Using macros to map each OE variables one-to-one from the source will save time and avoid tedious programming codes.

Step 1 – For those variables can be directly retrieved from the source dataset, using macro to preprocess them. Note that the OEDTC should be in ISO 8601 format.

```
%Macro oe(dsn=,form=,whr=,oetestcd=,oetest=,oetstdtl=,oecat=,
oescat=,oeorres=,oeorresu=,oestresc=,oestresn=,oestresu=,oestat=,oeloc=,
oelat=,oemethod=,cont=,datevar=,timepts=,dsnout=);
      data &dsnout;
         set &dsn;
          where &whr;
            %Attrib(vars = STUDYID DOMAIN USUBJID OESPID OETESTCD
            OETEST OETSTDTL OECAT OESCAT OEORRES OEORRESU OESTRESC OESTRESN
            OESTRESU OELOC OELAT OEMETHOD OEORRES OEDTC);
```

```
            studyid = strip(project);
            domain = 'OE';
            %usubjid(subject);
            oespid = "xxxxxxxxxxx";
            oetestcd = &oetestcd.;
            oetest = &oetest.;
            oetstdtl = &oetstdtl.;
            oecat = &oecat.;
            oescat = &oescat.;
            oeorres = &oeorres.;
            oeorresu = &oeorresu.;
            oestresc = &oestresc.;
            oestresn = &oestresn.;
            oestresu = &oestresu.;
            if &cont. then do;
                 oestat = 'NOT DONE';
            end;
            oeloc = &oeloc.;
            oelat = &oelat.;
            if upcase(OELAT) = 'RIGHT' then focid = 'OD';
             else if upcase(OELAT) = 'LEFT' then focid = 'OS';
            oemethod = &oemethod.;
            if not missing(&datevar.) and not missing(&timepts.) then
            oedtc= catx("T",strip(put(datepart(&datevar.),e8601da.)),
            catx(":",put(input(scan(&timepts.,1,""),best.),z2.),put(input(sca
            n(&timepts.,2," "),best.),z2.)));
            if not missing(&datevar.) and missing(&timepts.) then oedtc =
            strip(put(datepart(&datevar.),e8601da.));
      run;
%mend oe;
%oe(dsn=raw.iop,whr= %str(notdn=1),oetestcd='OEALL',oetest='Ophthalmic
Examination',oetstdtl=' ',oecat='INTRAOCULAR
PRESSURE',oescat='',oeorres='' ,oeorresu='',oestresc=oeorres, oestresn=.,oest
resu='',cont=missing(oeorres), oeloc=' ',oelat='',oemethod=' ',
datevar=date,timepts=time,dsnout=IOP1);
%oe(dsn=raw.iop,whr=%str(notdn = 0),oetestcd = 'IOP',oetest='Intraocular
Pressure',oetstdtl=' ',oecat='INTRAOCULAR PRESSURE',oescat=' ',oeorres =
strip(put(iop,best12.)),oeorresu='mmHg',oestresc=oeorres,oestresn=iop,oestres
u='mmHg',cont=missing(oeorres),oeloc='EYE',oelat=strip(lat),oemethod=strip(me
thod),datevar=date,timepts=time,dsnout=IOP2);
```

Step 2 – After using macro to map each variable according to the CRF annotation, set all the datasets together.

```
data oe_all;
     set work.dsn;
run;
```

Step 3 – Mapping with SV by the date to get the visit information.

```
data oe_all_1;
      merge oe_all(in=a) sv;
      by usubjid svstdtc;
      if a;
run;
```

Step 4 – Standardizing the test result and test units. The units should be dictionary preferred. For qualitative results, the abbreviation should be expanded, and spelling should be correct.

Step 5 – Deriving OEDY.

```
*------------------------------
 Derive study day
*------------------------------;
%macro dy(datin=, var1=, var2=);
proc sort data=&datin;
   by usubjid;
run;
proc sort data=sdtm.dm (keep=usubjid rfstdtc) out=dm;
  by usubjid;
run;
data &datin;
  merge &datin(in=in1) dm (in=in2);
  by usubjid;
  %if  &datin=ds_a %then %do;
  if in1;
  %end;
  %else %do;
  if in1 and in2;
  %end;
  if rfstdtc ne '' and length(scan(&var1.dtc, 1, 'T')) eq 10 then do;
            if
input(substr(&var1.dtc,1,10),yymmdd10.)>=input(substr(rfstdtc,1,10),yymmdd10.
) then
            &var1.dy=input(substr(&var1.dtc,1,10),yymmdd10.) -
input(substr(rfstdtc,1,10),yymmdd10.)+1;
       else &var1.dy=input(substr(&var1.dtc,1,10),yymmdd10.) -
input(substr(rfstdtc,1,10),yymmdd10.);
  end;
  %if &varn=2 %then %do;
   if rfstdtc ne '' and length(scan(&var2.dtc, 1, 'T')) eq 10 then do;
if
input(substr(&var2.dtc,1,10),yymmdd10.)>=input(substr(rfstdtc,1,10),yymmdd10.
) then
            &var2.dy=input(substr(&var2.dtc,1,10),yymmdd10.) -
input(substr(rfstdtc,1,10),yymmdd10.)+1;
       else &var2.dy=input(substr(&var2.dtc,1,10),yymmdd10.) -
input(substr(rfstdtc,1,10),yymmdd10.);
   end;
  %end;
  drop rfstdtc;
run;
%mend dy;
%dy(datin=oe_all_1, var1=oe_all_2, var2=);
```

Step 6 – Deriving Last Observation Before Exposure Flag.

```
*------------------------------
 Derive last observation before exposure flag
*------------------------------;
%macro lobxfl(domain=, ds=, outds=, key=, vardtc=, refdtc=rfxstdtc);
      ** Change visit number for unscheduled visits, so that unscheduled
visits are not flagged if done on same day as regular visits;
      data datain;
            set &ds;
            if visitnum eq . then visitnum_=visitnum;
            else if visitnum ne floor(visitnum) then visitnum_=0;
            else visitnum_=visitnum;
      run;
```

```
      proc sort data=datain (where=(&vardtc<=&refdtc and &domain.orres ne
'')) out=bas;
                  by &key.;

      run;
      data bas;
            set bas;
              by &key.;
               %if &domain=OE%then %do;
                  if last.&domain.lat;
                %end;
                 %else %do;
               if last.&domain.testcd;
                    %end;
               &domain.LOBXFL='Y';

      run;

      proc sort data=&ds;
            by usubjid &domain.seq;
      run;
      proc sort data=bas;
            by usubjid &domain.seq;
      run;

      data &outds;
            merge &ds bas(keep=usubjid &domain.seq &domain.BLFL);
            by usubjid &domain.seq;
      run;
%mend lobxfl;
%lobxfl(domain=OE, ds=oe_all_2, outds= oe_all_3, key=%str(STUDYID USUBJID
OECAT OESCAT OETESTCD OETSTDTL OERESCAT OELOC OELOCDTL OELAT OEDTC),
vardtc=oedtc, refdtc=rfxstdtc);
```

Last Observation Before Exposure Flags should have only a single record for the same test for subject. The keys to derive the flag must be unique to differentiate the records. The following macro is useful to check multiple keys to generate the flag.

```
%macro chkkey(din=, key=);
proc sql;
  select &key
     from &din
      group by &key
       having count(*)>1;
quit;
%mend chkkey;
%chkkey(din=oe_all_2,key=%str(STUDYID, USUBJID, OECAT, OESCAT, OETESTCD,
OETSTDTL, OERESCAT, OELOC, OELOCDTL, OELAT, OEDTC));
```

Step 7 – Deriving OESEQ.

```
%macro seq(_in=,_key=, _seqvar=);
proc sort data=&_in.;
      by &_key.;
run;
data &_in.;
      set &_in.;
      by &_key.;
```

```
        length _SEQ &_seqvar 8;
        if first.USUBJID then _SEQ = 0;
        _SEQ + 1;
        &_seqvar = _SEQ;

        drop _SEQ;
run;
%mend seq;
%seq(_in=oe_all_3,key=%str(STUDYID USUBJID OESPID OECAT OESCAT OETESTCD
OETSTDTL OERESCAT OELOC OELOCDTL OELAT OEDTC),_seqvar=OESEQ);
```

Step 8 – Add any supplementary variables to SUPPOE.

Generating Pinnacle 21 reports

Both Pinnacle 21 community and Pinnacle 21 Enterprise can be used for generating validation reports. This is based on Sponsor's preference.

Validation Issues

Manage Issues in Enterprise

Dataset	Rule ID	Message	Affected	Changed	Impact	Type	Status	Assignee	Sources	Explanation	Comments
OE	SD0029	Missing value for OESTRESU when OESTRESC is provided	3,077	0	High	Warning	Closed		Data, Mapping	The units were not collected for these records.	
OE	SD0058	Variable appears in dataset, but is not in SDTM model	1	0	High	Error	Closed		Mapping	OELOCDTL were added in to OE.	
OE	CT2002	OEEVAL value not found in 'Evaluator' extensible codelist	110,263	0	Medium	Warning	Closed		Design, Mapping	"CLINICAL INVESTIGATOR" was defined for the evaluator of Ophthalmic Examinations.	
OE	CT2002	OELOC value not found in 'Anatomical Location' extensible codelist	8,910	0	Medium	Warning	Closed		Design, Mapping	Data collected as it is.	
OE	CT2002	OEMETHOD value not found in 'Method' extensible codelist	33,108	0	Medium	Warning	Closed		Design, Mapping	Data collected as it is. 'DIGITAL PHOTO' was defined in the aCRF.	
OE	SD0026	Missing value for OEORRESU when OEORRES is provided	3,077	0	Medium	Warning	Closed		Data	Data collected as it is.	
OE	SD0045	Missing value for OESTRESC when OERESCAT is populated	7,461	0	Medium	Warning	Closed		Data, Mapping	Data collected as it is. The original value was not collected.	
OE	SD1117	Duplicate records	43,751	0	Medium	Warning	Closed		Data, Mapping, Metadata	The records were differed in OERESCAT.	
OE	SD1122	Missing value for OESTRESN	35	0	Medium	Warning	Closed		Data, Mapping	OESTRESN cannot be derived from OESTRESC.	
OE	SD1203	OEDTC date is after RFPENDTC	34	0	Medium	Error	Fix Later		Mapping	DM issues	
OE	SD1229	OEORRES value is null when (OETESTCD == 'OEALL')	463	0	Medium	Error	Closed		Metadata	Data collected as it is.	
OE	SD2239	Inconsistent value for OETPT	1,706	0	Low	Error	Closed		Mapping	Data collected as it is.	

Figure 13 P21 issue summary for OE

Next, I would like to list the common issues and suggest the resolution of fixing them.

Message	Solutions
Variables appears in dataset but is not in SDTM model.	If it's not a SDTM variable, then we should drop the variable and move it to the SUPP dataset
XXX not found in XXX extensible codelist	Firstly, we need to check the SDTM controlled terminology list. If the value cannot be found in CT list. Then we need to replace the value with the best match from the code list.

Multiple BASELINE or -LOBXFL records for the same test	Check if it's the data issue
	If it's not a data issue. Then use the following macro to check if the keys to generate the flags are not enough to differentiate the records.
	`%macro chkkey(din=, key=);`
	`proc sql;`
	`  select &key`
	`  from &din`
	`  group by &key`
	`  having count(*)>1;`
	`quit;`

	`%mend chkkey;` `%chkkey(din=oe_all_2,key=%str(STUDYID, USUBJID, OECAT, OESCAT, OETESTCD, OETSTDTL, OERESCAT, OELOC, OELOCDTL, OELAT, OEDTC));`
Permissible variable with missing value for all records	When permissible variables were all missing values. Then we can drop it from the dataset. Permissible variables were only kept in the dataset when there were data collected.
OEDTC is after RFPENDTC	Check the assessment date and last disposition date. If the assessment date is after DSSTDTC then this should be a data issue. We should query the issue to DM.
Missing value for OEORRESU when OEORRES is provided	Check the source data of the original results unit. If the result is not missing and unit is missing. We should send the query to DM.
Duplicated records	Check the source data. If the records were collected duplicated for the same test on the same date. Then we should send the query to DM. Check if it's the programming issue. Check if we can add another variable to differentiate the records.

Table 3 Common issues and resolutions of OE generation

Pinnacle 21 is a useful tool to validate dataset. It can improve the overall quality of submissions.

Programming Challenge and Resolutions

Due to the high volume and complexity of the ophthalmic assessments data, programming OE is always challenging.
Firstly, many tests will be performed in an ophthalmic clinical. The data source may come from a different database i.e. CRF or EDC. We should annotate the CRF properly and create the specifications clearly. To reduce lengthy programs, creation of the look-up tables is always helpful to map the raw data to OE.

STUDYID	USUBJID	CRF Form Name	OECAT	OESCAT	OETESTCD	OETEST	OETSTDTL
XXXXX	XXXXX-XXXXX	BCVA 4m Test	BEST CORRECTED VISUAL ACUITY		OEALL	Ophthalmic Examinations	
XXXXX	XXXXX-XXXXX	BCVA 1m Test	BEST CORRECTED VISUAL ACUITY		NUMLCOR	Number of Letters Correct	TESTING DISTANCE: 4M
XXXXX	XXXXX-XXXXX	BCVA 1m Test - Right Eye	BEST CORRECTED VISUAL ACUITY		OEALL	Ophthalmic Examinations	
XXXXX	XXXXX-XXXXX	BCVA 1m Test - Right Eye	BEST CORRECTED VISUAL ACUITY		NUMLCOR	Number of Letters Correct	TESTING DISTANCE: 1M
XXXXX	XXXXX-XXXXX	BCVA 1m Test - Left Eye	BEST CORRECTED VISUAL ACUITY		OEALL	Ophthalmic Examinations	
XXXXX	XXXXX-XXXXX	BCVA 1m Test - Left Eye	BEST CORRECTED VISUAL ACUITY		NUMLCOR	Number of Letters Correct	TESTING DISTANCE: 1M
XXXXX	XXXXX-XXXXX	BCVA Low Vision Test	BEST CORRECTED VISUAL ACUITY	LOW VISION	OEALL	Ophthalmic Examinations	
XXXXX	XXXXX-XXXXX	BCVA Low Vision Test	BEST CORRECTED VISUAL ACUITY	LOW VISION	CFDIST	Count Fingers Distance	

Table 4 OETEST look up table

The standard macro mentioned in the previous section was also efficient to reduce lengthy code.
Using arrays and formats is also helpful to shorten the code. Please see the following code.

```
data val1;
      set raw.val;
```

```
        %Attrib(vars = STUDYID DOMAIN USUBJID OESPID OETESTCD
         OETEST OETSTDTL OECAT OESCAT OEORRES OEORRESU OESTRESC
         OESTRESN OESTRESU OELOC OELAT OEMETHOD OEORRES OEDTC);
         domain='OE';
         studyid=strip(project);
         %usubjid(subject);
         oespid="xxxxxxxxx";
         oecat = "VISUAL ACUITY";
         oescat = "OVERALL EVALUATION";
         oemethod = "SNELLEN EYE CHART";
         if not missing(asmdt) then oedtc = put(datepart(asmdt),e8601da.);
         oelat = strip(latdv);
         oeloc = "EYE";
         if oelat = "RIGHT" then focid = "OD";
          else if oelat = "LEFT" then focid = "OS";
         if notdone = 1 then do;
            oetestcd = "OEALL";
            oestat = "NOT DONE";
            oeorres = '';
            oestresc = oeorres;
         output;
         end;
         else if not missing(snlmf) then do;
            array oetest[5] $200. dataname notdone snlmf snlmfv snfmethod;
              do I=1 to 5;
                oetestcd=strip(put(vname(oetest(I)),$testcd.));
                oestat = strip(put(vname(oetest(I)),notdone.));
                oeorres = strip(upcase(vname(oetest(I))));
                oestresc = strip(upcase(vname(oetest(I))));
                oemethod = strip(put(vname(oetest(I)),$method.));
              output;
              end;
         end;
run;
```

In addition, in some cases, we will have the source data with empty value but there is an indicator to indicate that this record has no change from last visit. Please see table 5.

USUBJID	OEDTC	OETESTCD	VISIT	OEORRES	CHANGE FROM LAST VISIT
xxxxxx	2023-10-18	INTP	SCREENING	ABNORMAL	
xxxxxx	2023-12-28	INTP	BASELINE/DAY 1		NO
xxxxxx	2023-12-29	INTP	WEEK 4		NO
xxxxxx	2023-12-27	INTP	WEEK 8		NO
xxxxxx	2024-01-24	INTP	WEEK 12		NO
xxxxxx	2024-03-28	INTP	WEEK 20		NO
xxxxxx	2024-05-19	INTP	WEEK 28		NO
xxxxxx	2024-06-30	INTP	WEEK 36		NO
xxxxxx	2024-06-23	INTP	WEEK 52		NO

Table 5 source data has empty value but not change from last visit

We would like to retain the value from the last visit and add the indicator variable to the supplementary dataset. See table 6.

USUBJID	OEDTC	OETESTCD	VISIT	OEORRES	CHANGE FROM LAST VISIT
xxxxxx	2023-10-18	INTP	SCREENING	ABNORMAL	
xxxxxx	2023-12-28	INTP	BASELINE/DAY 1	ABNORMAL	NO
xxxxxx	2023-12-29	INTP	WEEK 4	ABNORMAL	NO
xxxxxx	2023-12-27	INTP	WEEK 8	ABNORMAL	NO
xxxxxx	2024-01-24	INTP	WEEK 12	ABNORMAL	NO
xxxxxx	2024-03-28	INTP	WEEK 20	ABNORMAL	NO
xxxxxx	2024-05-19	INTP	WEEK 28	ABNORMAL	NO
xxxxxx	2024-06-30	INTP	WEEK 36	ABNORMAL	NO
xxxxxx	2024-06-23	INTP	WEEK 52	ABNORMAL	NO

Table 6 source data has empty value but not change from last visit

We will use retain statement to carry out the last observation.

```
data cflvtest1;
      set cflvtest;
                by studyid usubjid oecat oetestcd oetstdtl oelat
                 oeloc visitnum oedtc oeloc oescat;
                    retain preorres preorresu;
                              length preorres preorresu $200;
               if missing(change) or change = 'Y' then  preorres = oeorres;
               if missing(change) or change = 'Y' then preorresu = oeorresu;
               if oeorres=. and change='N' then oeorres=preorres;
               if oeorresu='' and change='N' then oeorresu=preorresu;

run;
```

Another method to deal with this is to use the indicator saved in supplementary dataset to carry the last observation in ADOE. Under these circumstances, the OESTAT will be 'NOT DONE' in OE for those records. Otherwise, the P21 will report the issue.

DISCUSSION

SDTM OE is a newly added domain in IG 3.3. Due to the complexity of the CRF design, the volume of the data usually is very large. Therefore, it's critical to standardize the process for the creation of the SDTM OE. Identifying those hidden issues is helpful to improve the overall submission quality. Programmers can use this paper as a reference when creating SDTM OE.

REFERENCES

Study Data Tabulation Model Implementation Guide: Human Clinical Trials Version 3.3
https://www.cdisc.org/standards/foundational/sdtmig/sdtmig-v3-3/html
Best Corrected Visual Acuity (BCVA)- Eye know Clinical
https://eyeknow.co.uk/best-corrected-visual-acuity/
Leopold Schmetterer, Hendrik Scholl, Gerhard Garhöfer, Lucas Janeschitz-Kriegl, Federico Corvi, SriniVas R. Sadda, Felipe A. Medeiros,Endpoints for clinical trials in ophthalmology,Progress in Retinal and Eye Research,Volume 97,2023,101160,ISSN 13509462,

Endpoints for clinical trials in ophthalmology - ScienceDirect
Eye(Intraocular) Pressure
Eye (Intraocular) Pressure: What It Is & How It's Measured (clevelandclinic.org)
Daniel Porter, What is a Slit Lmap?
What is a Slit Lamp? - American Academy of Ophthalmology (aao.org)
Peter A.Karth, MD, Vedant Sathye,Binocular Indirect Ophthalmoscopy
Binocular Indirect Ophthalmoscopy - EyeWiki (aao.org)
Vinita Dora, Shivam Kumar, PHUSE US Connect 2021, Challenges and Solutions in SDTM Implementation and Programming of the Ophthalmic Examinations (OE) Domain
PRE_SI05.pdf (lexjansen.com)
Lyma Faroz, Seattle Genetics, Inc., Bothell WA Sruthi Kola, Seattle Genetics, Inc., Bothell WA, 2021, Demystifying SDTM OE, MI, and PR Domains
PharmaSUG-2020-DS-110.pdf (lexjansen.com)

CONTACT INFORMATION

Your comments and questions are valued and encouraged.

Contact the author at:

Shuang Qiu

Everest Clinical Research Clinical Corporation

+86 15621762998

Miya.Qiu@ecrscorp.com