

Macro to manage the PCSA

Claude Guyot, Sanofi-Aventis, Chilly-Mazarin, France

ABSTRACT

The Potentially Clinically Significant Abnormalities (PCSA) definitions can be interpreted and/or labeled in various ways depending on the person, which can lead to differences in the counting of the PCSA.

In Sanofi-Aventis, to avoid this “freedom” in the interpretation and in the labeling of the PCSA, a standard SAS® macro has been developed. This macro centralizes all the PCSA definitions of the laboratory data, the vital signs and the electro-cardiogram (ECG) provided by the Pharmacovigilance (PV) department.

When a consensus is found in the interpretation and in the labeling of the PCSA, the SAS® condition is developed and included in the macro. By using this macro, all the biostatisticians and programmers use the same condition and the same label for each PCSA which allows the standardization of the reporting.

INTRODUCTION

This presentation will show briefly how the PCSA are standardized. Then, the macro and its components will be presented. Finally, we will see that this standard macro is not so rigid.

THE STANDARDIZATION OF THE PCSA DEFINITION

PCSA DEFINED BY THE PV DEPARTMENT

The PV department defines the PCSA and provides two lists to the Biostatistics & Programming (B&P) department: one list for Phase1 studies and one list for Phases 2/3 studies. The updates of these lists occur once or twice by year.

B&P DEPARTMENT HOMOGENIZES BOTH LISTS INTO ONLY ONE LIST

In B&P department, the team of the standards creates only one list from both of PV department by clarifying the PCSA criteria and by homogenizing the labeling between all the study phases.

Some rules of derivation are also defined or explained in standard documents as the statistical rules of derivations and the safety guideline.

MACRO OF THE PCSA DERIVATIONS

The macro to derive the PCSA is part of a standard application which provides a catalog of standard macros to help the programming of the Analysis Dataset (ADS) and the Submission Datasets (SDS)

OBJECTIVES OF THE MACRO

- Derive the PCSA in a standard way by choosing the study phase (1 or 2/3) and the domain (Laboratory data, vital signs or ECG)
- For laboratory data, flag the out of range values by choosing the reference values (original or standard)
- Derive the baseline status regarding the PCSA derivations
- Give the possibility to the user to re-run the PCSA derivations applicable at an old date. All the history of the PCSA definitions is stored in a system dataset.

PARAMETERS OF THE MACRO

```
%st_saflags(domain = <domain: LB or EG or VS>  
             ,phase  = <phase: 1 (for phase 1) or 3 (for phase 2/3)>  
             ,dsin   = <input dataset>
```

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```
,dsout      = <output dataset>
,dspcsa     = <system dataset for PCSA definitions>
,dsoutpcsa= <output dataset to store the PCSA definitions of the study parameters>
,dsref      = <system dataset to link macro-variables and values>
,cutoff     = <cut-off date to select version of the PCSA>
,lnrefer    = <ORG for original results or STD for standard results to derive the out of
range values>
,poptype    = <Y (for young population) or E (for elderly population)>
,debug      = <Y (to keep temporary datasets) or N (to delete temporary datasets)>
,no_lln     = <Laboratory parameters codes for which the lower normal range is not
expected>
,no_uln     = <Laboratory parameters codes for which the upper normal range is not
expected>
);
```

SYSTEM DATASETS DEFINING THE PCSA DEFINITIONS

All the PCSA definitions with the SAS® conditions are stored in an Excel file which is converted in a SAS® dataset.

Example:

_PCSA DT	_TEST3	_TEST4	_OC1	_PCSAID	_PHASE	_DOMAIN	_PCSAFL	_PCSAN	_PCSA	_PCSACOND
\$10	\$8	\$8	\$8	\$30	8	\$2	\$1	8	\$200	\$300
06/09/2000	CALKPH	ALP	ALP	ALP_+1	1	LB	+	1	>1.5 ULN	&stnrhi ne . and &stresn > (1.5 * &stnrhi)
01/05/2007	CALKPH	ALP	ALP	ALP_+1	1	LB	+	1	>=1.5 ULN	&stnrhi ne . and &stresn >= (1.5 * &stnrhi)
05/01/2009	CALKPH	ALP	ALP	ALP_+1	1	LB	+	1	>1.5 ULN	&stnrhi ne . and &stresn > (1.5 * &stnrhi)

SYSTEM DATASETS DEFINING THE MACRO-VARIABLES USED BY THE MACRO

As the macro uses a large number of macro-variables, these macro-variables are associated to their value through a SAS® dataset and thanks to the SAS® function FETCH.

Example:

macname	dssource	vardomain	varname	varlabel	vartype	varstatus	varcomm
\$10	\$10	\$2	\$20	\$200	\$3	\$6	\$200
sex	DSIN	LB	SEX	Sex	C	INPUT	M,F
race	DSIN	LB	RACE	Race	C	INPUT	CAUCASIAN, WHITE, BLACK, etc...
age	DSIN	LB	AGE	Age	N	INPUT	Year
testcd	DSIN	LB	LBTESTCD	Lab test	C	INPUT	GLU, CHOL, etc..
orresn	DSIN	LB	LBORRESN	Numeric result (original units)	N	INPUT	
ornrhi	DSIN	LB	LBORNRI	Reference range upper limit org units	N	INPUT	
ornrlo	DSIN	LB	LBORNRILO	Reference range lower limit org units	N	INPUT	
stunit	DSIN	LB	LBSTRESU	Standard units	C	INPUT	
stresn	DSIN	LB	LBSTRESN	Numeric result (standard units)	N	INPUT	
stnrhi	DSIN	LB	LBSTNRHI	Reference range upper limit std units	N	INPUT	
stnrlo	DSIN	LB	LBSTNRLO	Reference range lower limit std units	N	INPUT	
fasted	DSIN	LB	LBFAST	Fasting status	C	INPUT	Y N U Null

SAS® code:

```
%let ref_dsid=%sysfunc(open(_st_dsref(where=(vardomain="&domain."))));
%syscall set(ref_dsid);
%do %while(%sysfunc(fetch(&ref_dsid.))=0);
  data _null_;
    %let &macname.=%trim(%left(&varname.));
    %let l_&macname.=&varlabel.;
  run;
%end;
%let ref_rc=%sysfunc(close(&ref_dsid.));
```

A STANDARD BUT A FLEXIBLE MACRO

The flexibility of the macro is not due to the parameters of the macro only but also to the system datasets. The system datasets can be adapted by the users according to the specificities to their study.

By default the macro points on the system datasets of the application but the users can copy them in their study and bring some changes according to the study.

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SYSTEM DATASETS DEFINING THE PCSA DEFINITIONS

The users can add some parameters for which no PCSA is defined in the standard way.
If very specific population, the users can modify the conditions of the PCSA.
They can adapt the label of the PCSA.

SYSTEM DATASETS DEFINING THE MACRO-VARIABLES USED BY THE MACRO

The users can adapt the name of the input variables according to the structure of the raw data or change the name and the label of the output variables but never change the type of the input and output variables.

CONCLUSION

Even it is preferable to work in the standard way and even the flexibility of the macro must be used carefully, it is necessary to allow the adaptation by the users.

CONTACT INFORMATION

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

Claude Guyot
Sanofi-Aventis
1, avenue Pierre Brossolette
Chilly-Mazarin / 91385
Work Phone: 01.60.49.72.72
Email: claud.guyot@sanofi-aventis.com