Macro to manage the PCSA

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PhUSE 2009 – Basel
Paper CS02
Agenda

- Standardization of the PCSA definition
  - What are the PCSA?
  - Who defines the PCSA in Sanofi-Aventis?

- Macro to derive the PCSA
  - Objectives of the macro
  - Parameters of the macro
  - Two system datasets
    - PCSA conditions
    - Macro-variables used in the macro

- CALL SET Routine and FETCH Function
Standardization of the PCSA definition

What are the PCSA?

Potentially Clinically Significant Abnormalities

Definition

- A Potentially Clinically Significant Abnormality is a major deviation in comparison with the normal limits for:
  - Laboratory data (clinical chemistry and hematology)
  - Electrocardiogram parameters
  - Vital signs

A PCSA leads to a close surveillance in the clinical studies
Standardization of the PCSA definition

Who defines the PCSA in Sanofi-Aventis?

Pharmacovigilance (PV)

- Only one unit per parameter
- Homogeneization of the labels

Biostatistics & Programming (B&P)

How to enter PCSA in the database?
How to standardize the PCSA?
How to analyse the PCSA?
From baseline or not?
How to report PCSA in CSR?
Macro to derive the PCSA

Objective of the macro

- Derive the PCSA variables in the Analysis DataSets (ADS) in a standard way for Laboratory Data, ECG and Vital Signs
  - Label of PCSA
  - Flags
  - Status at baseline
- For laboratory data, flag the out of range values
- Allow to re-run and derive the PCSA variables with previous versions of PCSA definition
Macro to derive the PCSA

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>
    ,dsout    = <output dataset>
    ,dsoutpcsa= <output dataset to store the PCSA definitions of the study parameters>
    ,dspcsa   = <system dataset for PCSA definitions>
    ,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)>
);
Macro to derive the PCSA

- Two system datasets
  - PCSA Definitions

```plaintext
%st_sflags(
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    ,phase        = <phase: 1 (for phase 1) or 3 (for phase 2/3)>
    ,dsin         = <input dataset>
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    ,poptype      = <Y (for young population) or E (for elderly population)>
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);
```
System Dataset: PCSA Definitions

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<th>D</th>
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%st_saflags(
    domain = <domain: LB or EG or VS>,
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    lnrefer = <OR for original results or STD for standard results to derive the out of range values>,
    lnrefer = <OR for original results or STD for standard results to derive the out of range values>,
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    debug = Y (to keep temporary datasets) or N (to delete temporary datasets);
## System Dataset: PCSA Definitions

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### PCSA Definitions

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<thead>
<tr>
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</tbody>
</table>

\[
(\text{age} \geq 12 \text{ or } \text{age} > 12) \text{ and upcase(\text{stunit}) = 'UMOL/L' and } \text{stresn} \geq 150
\]

\[
30 \leq \text{chgbklr} < 100
\]

\[
\text{stnhr ne. and } \text{stresn} > (2 \times \text{stnhr})
\]
Macro to derive the PCSA

Two system datasets

PCSA Definitions

Macro-variables used in the macro

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CALL SET Routine and FETCH Function

**SAS® definitions:**

- **CALL SET Routine**
  Links SAS data set variables to DATA step or macro variables that have the same name and data type

- **FETCH Function**
  Reads the next nondeleted observation from a SAS data set into the Data Set Data Vector (DDV)
CALL SET Routine and FETCH Function

Part 1: Creation of macro-variables

%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.=&varname.;
    %let l_&macname.=&varlabel.;
  run;
%end;
%let ref_rc=%sysfunc(close(&ref_dsid.));
### CALL SET Routine and FETCH Function

```sas
%let &macname.=&varname.;
%let l_&macname.=&varlabel.;
```

<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
<th>C</th>
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<th>varname</th>
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<td>SEX</td>
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<td>LBTESTCD</td>
<td>Lab test</td>
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<tr>
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<td>Numeric result (original units)</td>
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<tr>
<td>LBORNRI</td>
<td>Reference range upper limit org units</td>
</tr>
<tr>
<td>LBORNROI</td>
<td>Reference range lower limit org units</td>
</tr>
<tr>
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<td>Standard units</td>
</tr>
<tr>
<td>LBSTRESN</td>
<td>Numeric result (standard units)</td>
</tr>
<tr>
<td>Baseline status for PCSA analysis</td>
<td></td>
</tr>
</tbody>
</table>

```
%let sex=SEX;
%let l_sex=Sex;
%let race=RACE;
%let l_race=Race;
%let age=AGE;
%let l_age=Age;
%let testcd=LBTESTCD;
%let l_testcd=Lab test;
%let orresn=LBORRESN;
%let l_orresn=Numeric result (original units);
```
CALL SET Routine and FETCH Function

Part 2: Resolution of the macro-variables

%let id_pcsa=%sysfunc(open(_st_pcsa,i));
%if &id_pcsa. gt 0 %then %do;
  %syscall set(id_pcsa);
data _st_temp;
  length pcsa $200 pcsafl $1 pcsan 8 pcsaid $30;
  set _st_dsin;
  %do %while(%sysfunc(fetch(&id_pcsa.))=0);
    if trim(&testcd.)="&_oc1." then do;
      if &_pcsacond. then do;
        pcsa   =trim("&_pcsa.");
        pcsafl =trim("&_pcsafl.");
        %if &_pcsan. ne . %then %str(pcsan =%eval(_pcsan.));
        %else %str(pcsan= .);
        pcsaid=trim("&_pcsaid.");
        output;
      end;
    end;
  %end;
run;
%end;
%let rc_pcsa=%sysfunc(close(&id_pcsa.));
CALL SET Routine and FETCH Function

%do %while(%sysfunc(fetch(&id_pcsa.))=0);
  if trim(&testcd.)="&_oc1." then do;
    if &pcsac. then do;
      pcsa =trim("&_pcsac.");
      pcsafl =trim("&_pcsafl.");
      %if &_pcsan. ne . %then %str(pcsan =%eval(&_pcsan.));
      %else %str(pcsan=.);
      pcsaid=trim("&_pcsaid.");
      output;
    end;
  end;
%end;

if trim(&testcd.)="ALP" then do;
  if &stnrhi ne . and &stresn > (1.5 * &stnrhi) then do;
    pcsa =trim("> 1.5 ULN");
    pcsafl =trim("+");
    pcsan =1;
    pcsaid=trim("ALP_+1");
    output;
  end;
end;

if trim(&testcd.)="ALP" then do;
  if &stnrhi ne . and &stresn <= (1.5 * &stnrhi) then do;
    pcsa =trim("0");
    pcsafl =trim("0");
    pcsan =0;
    pcsaid=trim("ALP_0");
    output;
  end;
end;
Conclusion

- The standardization of the PCSA definitions and the automation of their computation with a unique macro ensure an homogeneity of the PCSA analysis through all the therapeutic areas world-wide.
- The CALL SET routine and the function FETCH allow to manage an important number of macro-variables and SAS® conditions/instructions thanks to system datasets...
- ... and these system datasets simplify also the updates of the PCSA definitions.
To finish ...

- Thank you to all the persons who have worked or who work always on this macro:
  - Fabienne Rouillé
  - Yvane Boudraa
- And especially
  - Gérard Capdevielle who is the father of this macro
Thank you for your attention ...
... and see you next year !!

Questions ? ? ?

Contact:
claude.guyot@sanofi-aventis.com
(33) 1 69 79 72 72