

A Standard Adverse Event Summary Report Generation

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INTRODUCTION

In clinical trials, most adverse event summary reports display (1) the number of patients in each treatment group in whom the adverse event occurred, and (2) the rate of occurrence in each treatment group. According to <<Guideline for the Format and Content of the Clinical and Statistical Sections of New Drug Application>>, the Food and Drug Administration (FDA) requires that an adverse event(AE) summary report be identified each patient having each adverse event and each adverse event must be grouped in the table by individual patient number for some or all the controlled trials.

An example of FDA required AE summary tabular presentation is shown below, preparing thus a report is not as easy as it would appear.

This paper presents a SAS program that demonstrates how to use the SAS macro and PROC SQL to generate the AE summary report with a combination of summary data and individual patient number.

STEP-BY-STEP PROCEDURE

STEP 1. Subsetting A Data Set Adverse

A data set AEO is created by subsetting the original data set adverse and regrouping relation variable RE by assigning 1 (related to drug) or 2 (not related to drug).

An Example of Standard Adverse Event Summary Report

GENZYME CORPORATION
CAMBRIDGE, MASS.

STUDY NUMBER
PROJECT DESCRIPTION

AERPT
12:53/21JUN96

SUMMARY OF ADVERSE EVENTS

-- TX GROUP(N=60) --

BODY SYSTEM	ADVERSE EVENT	MILD		MODERATE		SEVERE		TOTAL	
		RELATED	NR	RELATED	NR	RELATED	NR	RELATED	NR
CV	TACHYCARDIA	0 (0.0%)	1 (1.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)		1 (1.6%)
			103						
DIG	CONSTIPATION	0 (0.0%)	3 (5.0%)	3 (5.0%)	4 (6.9%)	0 (0.0%)	0 (0.0%)	3 (5.0%)	7 (11.7%)
			115	903	701				
			401	905	713				
			509	909	1002				
					1104				
	DIARRHEA	0 (0.0%)	1 (1.6%)	0 (0.0%)	3 (5.0%)	0 (0.0%)	1 (1.6%)		5 (8.3%)
			723				720		
					102				
					104				
					813				
	HEARTEBURN	0 (0.0%)	5 (8.3%)	0 (0.0%)	3 (5.0%)	0 (0.0%)	0 (0.0%)		8 (13.3%)
			520		209				
			525		408				
			612		803				
			613						
			1012						

NR = not related .
RELATED = remote, possible, probable, definite.

STEP 2. Creating Six Patient Categories

As shown in the example above, adverse events are grouped by body system and each event is divided into defined severity (e.g., Mild, Moderate, Severe) and relationship to drug (e.g., related to drug, not related to drug) categories, therefore, six patient categories are required: Mild-Related, Mild-NR, Moderate-Related, Moderate-NR, Severe-Related, and Severe-NR.

%g_dsn macro splits AEO into six different category data sets AE1-AE6, and then merge the six data sets to a new data set AEGRP containing different category patient numbers.

STEP 3. Making The Duplicate Patient Number Empty

Since the process of the merging six data sets is a Match-Merge(with different number of observation in by group), duplicate patient numbers are produced. %del_dup macro is designed to make all duplicated patient numbers empty in each body system.

STEP 4. Obtaining Patient Counts and Percentages

%count macro runs three PROC SQL on counting total number of patients and percentages. Running the first PROC SQL to count total number of patients by treatment group and assigns the value to a global macro variable PTCNT. Running the second PROC SQL to count total number of patient and percentages for each AE in every category. Running third PROC SQL to sum total number of patients and percentages for each AE.

Finally, all data sets created by running PROC SQL are integrated into a new data set AEALL.

STEP 5. Producing the AE Summary Report

Since PROC REPORT gives SAS programmers a great deal of control over the format and layout of report, PROC REPORT was chosen to produce the AE summary report.

The SAS program is given in the Appendix.

SUMMARY

The AE standard summary report presents necessary data as well as individual patient number. It increases a review's ability to quickly understand the data presented, and it is very helpful for SAS programs and CRA to validate summary data.

The AE summary report can be regarded as standard AE report template. However, the AE summary report is *data driven* reporting(data drives the report structure), thus, AE report structure can be redefined based on the study design and the specific reporting needs of the study.

The author welcome comments and suggestions to generate this AE summary report with alternative approaches.

REFERENCES

1. Food and Drug Administration, *The Format and Content of the Clinical and Statistical Sections of New Drug Application*. pp.71-73.
2. SAS Institute, Inc., *SAS Guide to the SQL procedure:Usage and Reference, Version 6, First Edition*, Cary, NC. SAS Institute., 1989.

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Appendix. An Standard Adverse Event Summary Report Program

```

*****
*
* Program name: AERPT.SAS
* Date: : 07/19/95
* Programmer : Frank Liu
* Purpose : To generate adverse event summary report presenting:
*          1. total number of categorized patients and percentages for each
*          adverse event;
*          2. individual patient number for each adverse event in every
*          category.
* Revised : 06/26/96
*
*****;

%include '_STANDARD.SAS';

/* Monte Jarvis has developed the _standard.sas including:
1. _title macro creating left- and right- justified,
centered titles and footnotes;
2. various library definitions. */

options symbolgen mprint macrogen source source2 missing=' ';

title4 'SUMMARY OF ADVERSE EVENTS';

-----*
* CODING INFOMATION
*
* SEVERITY 1 = MILD RELATION 0 = NOT RELATED
*          2 = MODERATE 1 = REMOTE
*          3 = SEVERE 2 = POSSIBLE
*          9 = UNKNOWN 3 = PROBABLE
*                   4 = DEFINITE
*                   9 = UNKNOWN
-----*

data ae0;
set ssd.adverse (keep=patid body ae noaes severity relate);
tx = put(patid,tx.);
if noaes ne 'X' then
do;
if relate = 0 then
re=2;
else
if relate not in (0,9) then
re=1;
end;
if severity in (1,2,3);
run;

-----*
* The macro g_dsn to create six datasets (six patient categories), each includes
* different type of patid
-----*

```

```

%macro g_dsn;

%do i=1 %to 3;
  %do j=1 %to 2;
    %if &i=1 %then
      %let m=&j;
    %if &i=2 %then
      %let m=%eval(&i+&j);
    %if &i=3 %then
      %let m=%eval(&i+&j+1);

    proc sql;
      create table ae&m as
        select distinct
          tx,
          body,
          ae,
          patid as p&m
        from ae0
        where severity=&i and
              re=&j
        order by 1,2,3;
      quit;

  %end;
%end;

data aegrp;
  merge ae1 ae2 ae3 ae4 ae5 ae6;
  by tx body ae;
run;

%mend;

*-----*
* The macro del_dup to make duplicate patid empty. The duplicat data was brought *
* by merging. *
*-----*

%macro del_dup;

  %do i=1 %to 6;

    proc sort data=aegrp;
      by tx body ae p&i;
    run;

    data aegrp(drop=pp&i p&i);
      set aegrp;
      by tx body ae p&i;
      if first.p&i then
        do;
          pp&i=p&i;
          retain pp&i;
          pt&i=put(p&i,5.);
        end;
      if not first.p&i and p&i=pp&i
        then pt&i=' ';
  %end;

```

```

run;

%end;
%mend;

*-----*
*       The macro count to count total number of patients and percentages by tx,   *
*       body and ae.                                                                *
*-----*

%macro count;

%do i=1 %to 2;

proc sql noprint;
  select count(distinct patid) into:ptcnt&i /* Create the global macro var */
  from ae0 /* for the total number of patid */
  where tx="&i"; /* in each category */
quit;

%do k=1 %to 6;

proc sql;
create table aep&k as
select tx,
       body,
       ae,
       put(count(distinct pt&k),3.)||' ('||
       trim(left(put((count(distinct pt&k)/&&ptcnt&i)*100,4.1)))||'%)' as pt&k,
from aegrp
where tx="&i"
group by 1,2,3;

%end;

%do j=1 %to 2;

proc sql;
create table ae0&j as
select tx,
       body,
       ae,
       put(count(distinct patid),3.)||' ('||
       trim(left(put((count(distinct patid)/&&ptcnt&i)*100,4.1)))||'%)'
as tot&j
from ae0
where re=&j and tx="&i"
group by 1,2,3;
quit;

%end;

data aegrp&i;
merge ae01 ae02;
by tx body ae;
run;

```

```

data ae&i;
  merge aep1 aep2 aep3 aep4 aep5 aep6 aegrp&i;
  by tx body ae;
run;
%end;

data aeall;
  merge ae1 ae2;
  by tx body ae;
run;

proc format;
  value $txfmt
    '1' = "HAL-F (N=%left(&ptcnt1))"
    '2' = "NO TX (N=%left(&ptcnt2))"
  ;
run;

%mend;

/*-----CALING MACRO-----*/

%g_dsn;

%deldup;

%count;

/*-----*/
*-----*
*      Create a empty obs to insert after the first obs of every body system      *
*-----*

proc sql;
  create table aeall as
  select *
  from aeall
  union
  select tx,
         body,
         ae,
         ' ' as pt1,
         ' ' as pt2,
         ' ' as pt3,
         ' ' as pt4,
         ' ' as pt5,
         ' ' as pt6,
         ' ' as tot1,
         ' ' as tot2
  from aeall
quit;

proc sort data=aeall;
  by tx body ae descending pt1 pt2 pt3 pt4 pt5 pt6 tot1 tot2;
run;

```

```

data ae;
  set aeall aegrp;
  by tx body ae;
run;

options nobyline;

title6 "-- TREATMENT GROUP #byval(tx) --";
title8
'_____';

footnotel
'_____';

footnote3 'NR = not related .';
footnote4 'RELATED = remote, possible, probable, definite.';

proc report data=ae headskip headline spacing=1 split='|';
  by tx;
  column body ae
          (' MILD |__' pt1 pt2 )
          (' MODERATE |__' pt3 pt4)
          (' SEVERE |__' Pt5 Pt6)
          (' TOTAL |__' TOT1 TOT2);

  define body / display order width=7 'BODY|SYSTEM';
  define ae / display order width=26 flow ' ADVERSE EVENT';
  define pt1 / display center 'RELATED' width=11;
  define pt2 / display center 'NR' width=11;
  define pt3 / display center 'RELATED' width=11;
  define pt4 / display center 'NR' width=11;
  define pt5 / display center 'RELATED' width=11;
  define pt6 / display center 'NR' width=11;
  define tot1 / display center 'RELATED' width=11;
  define tot2 / display center 'NR' width=11;
  format tx $txfmt.;

break after ae/skip;
run;

endsas;

```