

```

%_mprintto;
options notes nosource;
proc datasets lib=work nolist memtype=data kill; quit;
/* Standard - leave this */
%let TFL_Part=%scan(&_SASPROGRAMFILE,-3,%str(/));

/* Standard - leave this */
data _null_;
    tmp="%TFL_Part";
    if tmp not in ("dev" "qc") then call symput("TFL_Part", "prod");
    call symput('TFLpath', compress("&_SASPROGRAMFILE",""));
run;
%put NOTE:
=====;
%put NOTE: Covance Study Number : 000000106324;
%put NOTE: Client Protocol ID   : ZRHR-REXC-03-EU;
%put NOTE: Program Name        : tl_anlprimbiosafas.sas;
%put NOTE: Purpose              : Analysis of Primary Biomarkers of
Exposure versus SA on Day 5,FAS;
%put NOTE: ;
%put NOTE: Input Data           : ADAM.ADBX;
%put NOTE: Output               : L_15_04_04_01(PRIMBIOA)
T_15_02_04_01(PRIMBIOA) ;
%put NOTE: Macros Called        : _MPRINTTO;
%put NOTE: ;
%put NOTE: Programmed by        : cvn_vmurray;
%put NOTE: Creation Date        : 2014-06-06;
%put NOTE: SAS Version          : 9.3;
%put NOTE: ;
%put NOTE: == Latest Run
=====;
%put NOTE: Run by                : &sysuserid;
%put NOTE: Date/Time             :
%sysfunc(putn(%sysfunc(date()),e8601da.))T%sysfunc(putn(%sysfunc(time()),
e86011z.));
%put NOTE: ;
%put NOTE: == Modification History
=====;
%put NOTE: Date      Initials   No. Reason;
%put NOTE: 10JUN2014  VM        1) Remove duplication on 'NOTE' in
first footnote and remove non breaking spaces;
%put NOTE:                               2) Add N=X to headers;
%put NOTE: 19JUN2014  VM        3) Amend rounding of CI and CV;
%put NOTE:                               4) Change ANOVA to ANCOVA;
%put NOTE: 23JUN2014  APH       5) Add baseline footnote;
%put NOTE:                               6) Amend units to pg/mg creat for
UMHBMCRE and USPMA;
%put NOTE: 24JUN2014  APH       7) centre output;
%put NOTE: 01Aug2014  AMH       8) Add where clause used on dataset to
listing ;
%put NOTE: 01Aug2014  AMH       9) Add and rather than , to appendix
reference;
%put NOTE: 12Sep2014  APH       10) Amend baseline footnote to match
REXC-04;

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%put NOTE:
=====;
options notes source source2 nofullstimer validvarname=upcase missing=' '
NOQUOTELENMAX/*turn off warnings about quoted strings too long*/;
ods _all_ close;
ods listing;

/*formats macro and appendix output macros*/
%include
"/cvn/projects/prj/development/000000106324/dev/adhoc/TMPLTMIX.sas";

*=====;
* START OF PROGRAM CODE ;
*=====;

*****;
* read in data ;
*****;
/* Calculate totals for products */

%macro table(paramcd,title,pop,popfl,tab,tabout,var);

/*2) VM10JUN2014*/

DATA ADSL;
    SET ADAM.ADSL(WHERE=(&popfl='Y'));
    IF INDEX(TRT01A,'THS 2.2') THEN COLORD=1;
    OUTPUT;
    IF INDEX(TRT01A,'CC') THEN COLORD=2;
    OUTPUT;
    IF INDEX(TRT01A,'SA') THEN COLORD=3;
    OUTPUT;
RUN;

PROC SORT DATA=ADSL NODUPKEY OUT=ADSL1;
    BY COLORD SUBJID;
RUN;

PROC FREQ DATA=ADSL1(WHERE=(NOT MISSING(COLORD))) NOPRINT;
    TABLE COLORD/ OUT =TOTALS2(DROP=PERCENT RENAME=(COUNT=TOTAL));
RUN;

DATA _NULL_;
    SET TOTALS2;
    CALL SYMPUT('TOT'||STRIP(PUT(COLORD,BEST.)),STRIP(PUT(TOTAL,BEST.)));
RUN;

proc sort data=adam.adbx(where=(anl02fl='Y' and &popfl='Y' and paramcd
in ('CARBXHGB' 'UMHBMCRE' 'U3HPMCRE' 'USPMACRE') and avisitn=105))
    out=adbxin;
    by SUBJID;
run;

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data adbx1 missing;
  set adbxin;
  if atpt not in ('08:00-10:00 PM' '') then delete;
  if aval not in (.,0) then do;
    logaval=log(aval);
    logbase=log(base);
    output adbx1;
  end;
  else output missing;
run;

%fmt(datain=adbx1, start=trtan, label=trta, name=trt);

data adbx;
  set adbx1;
  format trtan trt. ;
/*   if trta not in ('THS 2.2' 'SA') then delete;*/
run;

title1 j=1 "PAGESPLIT"; /*do not change*/
title2 j=1 'Proc Mixed Procedure';
TITLE3 J=L "The where clause used on the dataset adam.adbx: &popfl.='Y'
and anl02fl='Y'"; /* 8) AMH 31Jul2014 */
%let tflno=L_15_04&tabout(PRIMBIOA);

%mixout1(fileout=/cvn/projects/prj/data/000000106324/TFL/&TFL_Part./&tflno);
options ps=20;

proc sort data=adbx;by paramcd;run;

options byline;

proc mixed data=adbx method=reml maxiter=200 order=internal;
  by paramcd;
  class trtan sexc ucpdgr1;
  model logaval = logbase*trtan*sexc*ucpdgr1 / outp=pred ;
  lsmeans trtan / diff=control('SA') alpha=0.05 cl ;

  ods output lsmeans=lsmeans(where=(trtan ne 2));
  ods output diffs=diffs(where=(trtan=1)) ;
  ods output covparms=covparms(rename=(estimate=residual));

run;

data diffs;
set diffs;
dum=1;
run;

data covparms;

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set covparms;
dum=1;
run;

data diffs2;
merge diffs covparms;
by paramcd dum;
run;

/*Residual Plots*/
title4 j=1 'Residual Plots';
options ps=27; /*change this for proc plot*/

proc rank data=pred out=resid normal=vw ;
  by paramcd;
  ranks nscore;
  var resid;
run;

proc plot data=resid hpercent=50;
  by paramcd;
  plot resid*pred / vref=0;
  plot resid*nscore;
run;
quit;

%mixout2(blankn=60, halfblnk=N,title=Listing 15.4.&tab &title - &pop);

/*data counts*/
/*timepoints*/
proc univariate data=adbx noprint;
  by paramcd;
  class trtan;
  var logaval;
  output out=num1 n=n1;
run;

/*Manipulate datasets for output all relevent stats on each row*/
/*_____*/
data tabout;
  length out $100 stat $100;
  set lsmeans(in=a) diffs2(in=b) num1(in=c);
  /*ordering columns of treatments*/
  if b then colord=3;
  else if trtan=1 then colord=1;
  else if trtan in (3) then colord=2;

  /* N row*/
  if c or d then do;
    ord=1;
    stat='n';
  end;
end;

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        out=compress(put(n1,best.));
        output;
    end;

    if a then do;
        /*Back transformation*/
        estimatee=exp(estimate);
        lower=exp(lower);
        uppere=exp(upper);

/*Gmean (CV%) row*/
        ord=2;
        stat='Geometric LS Mean (CV%)';
        out=compress(put(round(estimatee,0.01),8.2));
        output;
    /*95% CI row*/
        ord=3;
        stat='95% CI';
        out=compress(put(floor(100*lower)/100,8.2))||',
'||compress(put(ceil(100*upper)/100,8.2)); /*3) VM19JUN2014*/
        output;
    end;
    if b then do;
        /*Back transformation*/
        estimatee=exp(estimate);
        lower=exp(lower)*100; /*3) VM19JUN2014*/
        uppere=exp(upper)*100; /*3) VM19JUN2014*/
        geocv=sqrt((exp(residual)-1)*100**2);
/*Gmean (CV%) row*/
        ord=2;
        stat='Geometric LS Mean (CV%)';
        out=compress(put(round(100*estimatee,0.01),8.2))||'
('||COMPRESS(PUT(CEIL(100*GEOCV)/100,8.2))||')'; /*3) VM19JUN2014*/
        output;
    /*95% CI row*/
        ord=3;
        stat='95% CI';
        out=compress(put(floor(100*lower)/100,8.2))||',
'||compress(put(ceil(100*upper)/100,8.2)); /*3) VM19JUN2014*/
        output;
    end;
run;

/*Add labels for all number variables*/
/*_____*/
data tabout1;
    set tabout;

/*Variable label*/
if paramcd='CARBXHGB' then do;var=1;varc='Evening COHb (%)
';end;
if paramcd='UMHBMCRE' then do;var=2;varc='Urinary MHBMA (pg/mg creat)
';end; /* 7) APH 23JUNE2014 */

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if paramcd='U3HPMCRE' then do;var=3;varc='Urinary 3-HPMA (ng/mg
creat)';end;
if paramcd='USPMACRE' then do;var=4;varc='Urinary S-PMA (pg/mg creat)
';end; /* 7) APH 23JUNE2014 */

run;

/*transpose for output*/
proc sort data=tabout1;
    by paramcd var varc ord colord;
run;

proc transpose data=tabout1(WHERE=(NOT MISSING(COLORD)))
out=ttabout(drop=_NAME_) prefix=col;
    by paramcd var varc ord stat;
    id colord;
    var out;
run;

/* Standard - macro for paging */
%macro outrtf(blankn=68, halfblnk=N, ref=);

%if &halfblnk=N %then %let halfblnk=;
%else %if &halfblnk=Y %then %let halfblnk=~;

/* Standard - just change the number to match the listing you're working
on. Also change the letters in the*/
/* bracket, eg ccb = current cigarette brands. Make sure to do this at
the top of the code too. */

    %let tflno=T_15_02&tabout(PRIMBIOSA);

/* Standard - leave this */
%let TFL_Part=%scan(&_SASPROGRAMFILE,-3,%str(/));

/* Standard - leave this */
data _null_;
    tmp="&TFL_Part";
    if tmp not in ("dev" "qc") then call symput("TFL_Part", "prod");
    call symput('TFLpath', compress("&_SASPROGRAMFILE",""));
run;

/*page numbers*/
data paging;
    set ttabout;
page=1;
%let tpage=1;
run;

/* Standard - leave this */

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options number nodate orientation=landscape papersize=&p_pgsz missing='
' NOQUOTELENMAX/*turn off warnings about quoted strings too long*/;
ods escapechar='`';
%let linetop = \brdrt\brdrs\brdrw30; * needs to be 1.5pt so calculated
in twips (1/20 pt) ;
%let linebot = \brdrb\brdrs\brdrw30;
%let linebot2 = \brdrb\brdrs\brdrw15;

ods path stdlib.tl06324 (read) ;
ods results off;
ods rtf toc_data/* contents*/
file="/cvn/projects/prj/data/000000106324/TFL/&TFL_Part./&tflno..rtf"
style=tl06324 startpage=yes headery=1440 footery=1440 ;
ods noproctitle;

%do i=1 %to &tpage;

ODS PROCLABEL = ' ';
title ;
footnote;
%let wd=0;

proc sort data=paging;by paramcd ord;run;

data comp;
    set paging end=eof;
    by paramcd ord;
    where page=&i;
    flag=1;
    _firtitl="Table 15.2.&tab    &title - &pop";
    _upcas=(length(_firtitl)-
length(compress(_firtitl,'ABCDEFGHIJKLMNOPQRSTUVWXYZ')))/2;
    len=&blankn.-length("(Page &i of &tpage)");
    if eof then do;
        call symput('_FSRTITL', trim(left(_firtitl)));
        call symput('_blankn', compress(put(len,best.)));
    end;
    drop _firtitl _upcas len;
run;

ods listing close;

* most set up in template others below;
* title arial 12pt bold with 12pt paragraph space below;
* all headers to be arial 11pt bold;
* data arial 10pt;
* headers to be central, text values left aligned and numeric centered
around decimal point;
/* Update with your variables as needed */
proc report data = comp headline headskip missing nowd spanrows split =
'#'
%IF &I=1 %THEN %DO; CONTENTS=' ' %END; %ELSE %DO; CONTENTS=' ' %END;;

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column flag page var varc ord stat coll col2 col3;

define flag / order noprint;
  define page      / order order = internal noprint;
  define var       / order order = internal noprint;
  define varc      / group style={just=left cellwidth=2.5cm}
"Variable";
  define ord       / order order=internal noprint;
  define stat      / display style={just=left cellwidth=3cm}
"Statistic";
/*2) VM10JUN2014*/
  define coll      / display style={just=*d*/C cellwidth=3cm}
style(header)={just=center} "THS 2.2#(N=&tot1)";/* 7) APH 24JUN2014 */
  define col2      / display style={just=*d*/C cellwidth=3cm}
style(header)={just=center} "SA#(N=&tot3)";/* 7) APH 24JUN2014 */
  define col3      / display style={just=*d*/C cellwidth=3cm}
style(header)={just=center} "THS : SA Ratio#(%)";/* 7) APH 24JUN2014 */

break after page / page;

break before flag / page %IF &I=1 %THEN %DO;
  CONTENTS="&_FSRTITL" %END; %ELSE %DO; CONTENTS='' %END;;

compute before page / style={protectspecialchars=off};
  line "&linetop";
endcomp;

compute before _page_ / style={just=left protectspecialchars=off};
  line "\b\fs24\sa24&_FSRTITL." ; * \b = bold, \fs24 is font
size 12pt, \sa24 is space after 12pt;
  line "&linebot";
endcomp;

compute after var;
  line ' ';
endcomp;

compute after _page_ / style={just=left protectspecialchars=off}
pretext="&linetop."};
/*1) VM10JUN2014*/ /*4) VM19JUN2014*/
  line "Note: SA = Smoking abstinence; THS = Tobacco Heating
System.";
  line "Note: Adjusted geometric least squares (LS) means and
confidence intervals (CIs) from an ANCOVA model conducted on log-
transformed Day 5 values with log-transformed baseline value, study arm,
sex and CC consumption reported at screening as fixed effect factors.
Geometrical CV% of the ratio is estimated from the residual mean
squares.";
/*line "Baseline is defined as the last assessment prior to 06:29 AM on
Day 1";*/ /* 5) APH 23JUN2014 */ /* 10) APH 12SEP2014 */
  LINE "Baseline is defined as the last assessment prior to Day
1 product use for THS 2.2 and CC subjects and prior to 06:29 AM on Day 1
for SA subjects."; /* 10) APH 12SEP2014 */

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        line "Note: The urinary parameters are concentrations adjusted
for creatinine.";
        line "";
        line "Appendix &ref.";
        line "Path: &TFLpath." &_blankn.*"\~\~" "(Page &i of
&tpage)";
        line "Program Run: &sysdate   &sysuserid   Program Status:
&status";
        endcomp;

run;
%end;
ods rtf close;
ods results on;
ods path reset;

%mend outrtf;

%outrtf(blankn=60, halfblnk=N, ref=%str(15.4.&tab. and 15.3.3.1)); /* 9)
AMH 01Aug2014 */

%mend table;

%table(paramcd=,title=%str(Primary Biomarkers of Exposure versus SA on
Day 5),
pop=FAS,popfl=fasfl,tab=4.1,tabout=_04_01,var=);

*=====;
* END OF PROGRAM CODE                               ;
*=====;

```