

```

%_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_anlsecondbio.sas;
%put NOTE: Purpose              : Analysis of Secondary Biomarkers of
Exposure - FAS;
%put NOTE: ;
%put NOTE: Input Data           : ADAM.ADBX;
%put NOTE: Output               : ;
%put NOTE: Macros Called        : _MPRINTTO;
%put NOTE: ;
%put NOTE: Programmed by        : cvn_vmurray;
%put NOTE: Creation Date        : 2014-06-11;
%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: 16JUN2014  VM          1) Use correct paramcd for hmpma;
%put NOTE:           2) Round up CV%;
%put NOTE: 23JUN2014  APH          3) Add baseline footnote;
%put NOTE:           4) Add correct units;
%put NOTE: 01Aug2014  AMH          5) Center Output;
%put NOTE: 01Aug2014  AMH          6) Add where clause used on dataset;
%put NOTE: 01Aug2014  AMH          7) Add and rather than , to appendix
reference;
%put NOTE: 01Aug2014  AMH          8) Change table numbering from
15.2.4.56 to 15.2.4.55;
%put NOTE: 05SEP2014  APH          9) Present standard errors instead of
CV% and amend footnotes;
%put NOTE: 11SEP2014  APH         10) Amend baseline footnote;
%put NOTE: 15SEP2014  APH         11) Add row for missing values;
%put NOTE:
=====;

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```

options notes source source2 nofullstimer validvarname=upcase missing=' '
NOQUOTELNMAX/*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,paramcd2,where,title,pop,popfl,tab,tabout,var);

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

/* 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;

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 (&paramcd) and avisitn=105 &where))
    out=adbxin;
    by SUBJID;
run;

data adbx1 /*missing*/; /* 11) APH 15SEP2014 */
    set adbxin;
    if aval not in (.,0) then do;
        logaval=log(aval);
        logbase=log(base);
/*          output adbx1;*/ /* 11) APH 15SEP2014 */
    end;
/*    else output missing;*/ /* 11) APH 15SEP2014 */
    if atpt not in ('08:00-10:00 PM' '') then delete;
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'"; /* 6) AMH 01Aug2014 */
%let tflno=L_15_04&tabout(&paramcd2);

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

proc sort data=adbx;by paramcd avalu;run;

options byline;

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

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

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```

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

data covparms;
set covparms;
dum=1;
run;

data diffs2;
merge diffs(where=(trtan=1)) 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);

ods rtf close;
ods results on;
ods path reset;

/*data counts*/
/*timepoints*/
proc univariate data=adbx noprint;
  by paramcd avalu;
  class trtan;
  var logaval;
  output out=num1 n=n1 NMISS=N2; /* 11) APH 15SEP2014 */
run;

/*Manipulate datasets for output all relevent stats on each row*/
/*_____*/
data tabout;
  length out $100 stat $100;
  set lsmeans(in=a) diffs2 num1(in=c);

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```

/*ordering columns of treatments*/
if _trtan=2 then colord=4;
else if _trtan=3 then colord=5;
else if trtan=1 then colord=1;
else if trtan=2 then colord=2;
else if trtan=3 then colord=3;
/* N row*/
if c then do;
    ord=1;
    stat='n';
    out=compress(put(n1,best.));
    output;
/* 11) APH 15SEP2014 */
    %IF "&PARAMCD2"="CO" %THEN %DO;
        ORD=0.5;
        STAT='Missing';
        OUT=COMPRESS(PUT(N2,BEST.));
        OUTPUT;
    %END;
/* 11) APH 15SEP2014 */
end;

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

/*Gmean (CV%) row*/
    ord=2;
    stat='Geometric LS Mean (SE)`{SUPER 1}'; /* 9) APH 05SEO2014 */
    out=compress(put(round(estimatee,0.01),8.2));
    output;
/*95% CI row*/
    ord=3;
    stat='95% CI';
    out=compress(put(floor(100*lowere)/100,8.2))||',
'||compress(put(ceil(100*uppere)/100,8.2));
    output;
end;
if colord in (4 5) then do;
/*Back transformation*/
estimatee=exp(estimate)*100;
lowere=exp(lower)*100;
uppere=exp(upper)*100;
geocv=sqrt((exp(residual)-1)*100**2);
/*Gmean (CV%) row*/
    ord=2;
    stat='Geometric LS Mean (SE)`{SUPER 1}'; /* 9) APH 05SEO2014 */
    out=compress(put(round(estimatee,0.01),8.2))||'
('||COMPRESS(PUT(CEIL(1000*STDERR)/1000,8.3))||')'; /*2) VM16JUN2014*/
/* 9) APH 05SEO2014 */
    output;
/*95% CI row*/

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        ord=3;
        stat='95% CI';
        out=compress(put(floor(100*lowere)/100,8.2))||',
' ||compress(put(ceil(100*uppere)/100,8.2));
        output;

    end;
run;

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

/*Variable label*/
if index(paramcd,'24U') then do;var=1;varc="Urinary Quantity over 24
hours ("||STRIP(AVALU)||") ";end; /* 4) APH 23JUN2014 */
if index(paramcd,'CRE') then do;var=2;varc="Concentration Adjusted for
Creatinine ("||STRIP(AVALU)||") ";end; /* 4) APH 23JUN2014 */
VARC=TRANWRD(VARC,'µ','\uc2\u956 mu');/* 4) APH 23JUN2014 */
run;

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

proc transpose data=tabout1 out=ttabout(drop=_NAME_) prefix=col;
    by paramcd var varc ord stat;
    id colord;
    var out;
run;

/* Standard - macro for paging */
%macro outrtf(blankn=60, 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(&paramcd2);

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

/* Standard - leave this */
data _null_;
    tmp="&TFL_Part";

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```

        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 */
options number nodate orientation=landscape papersize=&p_pgsz missing='
' NOQUOTELNMAX/*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 1;

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;;
    column flag page var
    %if "&paramcd2" ne "CO" %then %do;
    varc
    %end;
    ord stat col1 col2 col3 col4 col5;

define flag / order noprint;
    define page          / order order = internal noprint;
    define var           / order order = internal noprint;
    %if "&paramcd2" ne "CO" %then %do;
        define varc      / group style={just=left cellwidth=2.5cm}
"Variable";
        %end;
    define ord           / order order=internal noprint;
    define stat          / display style={just=left cellwidth=3.5cm}
"Statistic";
    /*2) VM10JUN2014*/
    define col1          / display style={just=c/*d*/ cellwidth=2.1cm}
style(header)={just=center} "THS 2.2#(N=&tot1)";
    define col2          / display style={just=c/*d*/ cellwidth=2.1cm}
style(header)={just=center} "CC#(N=&tot2)";
    define col3          / display style={just=c/*d*/ cellwidth=2.1cm}
style(header)={just=center} "SA#(N=&tot3)";
    define col4          / display style={just=c/*d*/ cellwidth=2.1cm}
style(header)={just=center} "THS : CC Ratio#(%)";
    define col5          / display style={just=c/*d*/ cellwidth=2.1cm}
style(header)={just=center} "THS : SA Ratio#(%)"; /* 5) AMH 01Aug2014 */

    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."};
  line "Note: CC = Conventional cigarettes; 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.";*/ /* 9) APH 05SEP2014 */
  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.";
/* 9) APH 05SEP2014 */
/*      line "Baseline is defined as the last assessment prior to 06:29
AM on Day 1"; */ /* 3) 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 */
  line "Note: 1 = Standard errors presented from analysis performed
on the log`{SUB e} scale."; /* 9) APH 05SEP2014 */
  %if "&paramcd2" ne "CO" %then %do;
    line "Note: Collection over 24 hours starting on the Day stated
in the title.";
  %end;
  %if "&paramcd2"="CO" %then %do;
    line "Note: The evening value on day 5 is analyzed.";
  LINE "Note: Missing numbers show number of observations missing
at a timepoint where the subject was still on the study due to 0 values
recorded, which cannot be log-transformed."; /* 11) APH 15SEP2014 */
  %end;
  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 15.3.3.2)); /* 8)
AMH 01Aug2014 */
```

```
%mend table;
```

```
%table(paramcd=%str('CO'),paramcd2=CO,where=%str(and atpt='08:00-10:00
PM'),title=%str(Analysis of Exhaled CO (ppm) on Day 5),
pop=FAS,popfl=fasfl,tab=4.6,tabout=_04_06);
```

```
%table(paramcd=%str('U1OHP24U'
'U1OHPCRE'),paramcd2=U1OHP,where=,title=%str(Analysis of Urinary 1-OHP on
Day 5),
pop=FAS,popfl=fasfl,tab=4.9,tabout=_04_09 );
```

```
%table(paramcd=%str('UNNN24U'
'UNNNCRE'),paramcd2=NNN,where=,title=%str(Analysis of Urinary Total NNN
on Day 5),
pop=FAS,popfl=fasfl,tab=4.11,tabout=_04_11);
```

```
%table(paramcd=%str('U4ABP24U'
'U4ABPCRE'),paramcd2=4ABP,where=,title=%str(Analysis of Urinary 4-ABP on
Day 5),
pop=FAS,popfl=fasfl,tab=4.13,tabout=_04_13);
```

```
%table(paramcd=%str('U1NA24U'
'U1NACRE'),paramcd2=1NA,where=,title=%str(Analysis of Urinary 1-NA on Day
5),
pop=FAS,popfl=fasfl,tab=4.15,tabout=_04_15);
```

```
%table(paramcd=%str('U2NA24U'
'U2NACRE'),paramcd2=2NA,where=,title=%str(Analysis of Urinary 2-NA on Day
5),
pop=FAS,popfl=fasfl,tab=4.17,tabout=_04_17);
```

```
%table(paramcd=%str('UOTOL24U'
'UOTOLCRE'),paramcd2=OTOL,where=,title=%str(Analysis of Urinary o-
toluidine on Day 5),
pop=FAS,popfl=fasfl,tab=4.19,tabout=_04_19);
```

```
%table(paramcd=%str('UCEMA24U'
'UCEMACRE'),paramcd2=CEMA,where=,title=%str(Analysis of Urinary CEMA on
Day 5),
pop=FAS,popfl=fasfl,tab=4.21,tabout=_04_21);
```

```
%table(paramcd=%str('UHEMA24U'
'UHEMACRE'),paramcd2=HEMA,where=,title=%str(Analysis of Urinary HEMA on
Day 5),
pop=FAS,popfl=fasfl,tab=4.23,tabout=_04_23);
```

```
/*Need to add in table 25 when the data is available*/
```

```
%table(paramcd=%str('UHMPM24U'
'UHMPMCRE'),paramcd2=HMPMA,where=,title=%str(Analysis of Urinary HMPMA on
Day 5),
```

```

pop=FAS,popfl=fasfl,tab=4.27,tabout=_04_27);

%table(paramcd=%str('USBMA24U'
'USBMACRE'),paramcd2=SBMA,where=,title=%str(Analysis of Urinary S-BMA on
Day 5),
pop=FAS,popfl=fasfl,tab=4.29,tabout=_04_29);

%table(paramcd=%str('UNNAL24U'
'UNNALCRE'),paramcd2=NNAL,where=,title=%str(Analysis of Urinary Total
NNAL on Day 5),
pop=FAS,popfl=fasfl,tab=4.31,tabout=_04_31);

%table(paramcd=%str('UNEQ24U'
'UNEQCRE'),paramcd2=NEQ,where=,title=%str(Analysis of Urinary NEQ on Day
5),
pop=FAS,popfl=fasfl,tab=4.33,tabout=_04_33);

%table(paramcd=%str('UPGF224U'
'UPGF2CRE'),paramcd2=PGF2,where=,title=%str(Analysis of Urinary 8-epi-
PGF2 Alpha on Day 5),
pop=FAS,popfl=fasfl,tab=4.53,tabout=_04_53);

%table(paramcd=%str('UTXB224U'
'UTXB2CRE'),paramcd2=11DTXB2,where=,title=%str(Analysis of Urinary 11-
DTX-B2 on Day 5),
pop=FAS,popfl=fasfl,tab=4.55,tabout=_04_55); /* 8) AMH 01Aug2014 */
*=====;
* END OF PROGRAM CODE ;
*=====;

```