

```

%_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 : 000000106326;
%put NOTE: Client Protocol ID   : ZRHR-PK-05-JP;
%put NOTE: Program Name        : tl_anlpk432.sas;
%put NOTE: Purpose              : table and figure of sensitivity
analysis PK data;
%put NOTE: ;
%put NOTE: Input Data           : ADAM.ADPP;
%put NOTE: Output               : L_15_04_03_02(PK) T_15_02_03_02(PK) ;
%put NOTE: Macros Called        : _MPRINTTO;
%put NOTE: ;
%put NOTE: Programmed by        : cvn_ahall;
%put NOTE: Creation Date        : 2014-04-06;
%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: 24Jun2014  AMH        4) Conservative rounding of cv% 95% CI
;
%put NOTE: 24Jun2014  AMH        5) Small n in statistics row;
%put NOTE: 24Jun2014  AMH        6) correct gmean statistic to read:
Geometric LS Mean (CV%);
%put NOTE: 24Jun2014  AMH        7) Ammend footnotes;
%put NOTE: 24Jun2014  AMH        8) Ammend statistic labels;
%put NOTE: 24Jun2014  AMH        9) Ammend Table number +1;
%put NOTE: 24Jun2014  AMH        10) Add PK listing to reference list;
%put NOTE: 24Jun2014  AMH        11) Add number of subjects excluded to
start of table;
%put NOTE: 24Jun2014  AMH        12) Remove footnote reference for tmax;
%put NOTE: 24Jun2014  AMH        13) Add title indicating where clause
on dataset;
%put NOTE: 24Jun2014  AMH        14) Add input dataset where clasue to
listing;

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%put NOTE: 24Jun2014    AMH          15) Amend Menthol to menthol;
%put NOTE: 24Jun2014    AMH          16) Amend NNS footnote;
%put NOTE: 24Jun2014    AMH          17) TMAX on seperate page with seperate
header;
%put NOTE: 08Aug2014    AMH          18) Centre output) ;
%put NOTE: 08Aug2014    AMH          19) combine footnotes [2] and [3];
%put NOTE: 08Aug2014    AMH          20) correct footnotes [1] to 1 and [1]
to Note: 1: in footnote;
%put NOTE: 08Aug2014    AMH          21) Use different by statements for
each paramter;
%put NOTE: ;
%put NOTE:
=====;
options notes source source2 nofullstimer validvarname=upcase missing=' '
NOQUOTELNMAX/*turn off warnings about quoted strings to long*;;
ods _all_ close;
ods listing;

/*formats macro and appendix output macros*/
%include
"/cvn/projects/prj/development/000000106326/dev/adhoc/TMPLTMIX.sas";
/*Wilcoxon Signed Rank Macro*/
%include
"/cvn/projects/prj/development/000000106326/dev/adhoc/WSIGRANK.sas";

*=====;
* START OF PROGRAM CODE                                     ;
*=====;
/* Calculate totals for products */

data adsl;
    set adam.adsl(where=(pprotfl='Y'));
    if analgrln=1 then do;
        if index(trt01a,'THS 2.2') or index(trt02a,'THS 2.2') then
colord=1;
        output;
        if index(trt01a,'CC') or index(trt02a,'CC') then colord=2;
        output;
    end;
    else if analgrln=2 then do;
        if index(trt01a,'THS 2.2') or index(trt02a,'THS 2.2') then
colord=1;
        output;
        if index(trt01a,'NRT') or index(trt02a,'NRT') then colord=2;
        output;
    end;
    else if missing(analgrln) then delete;
run;

proc sort data=adsl nodupkey out=adsl1;
    by analgrln analgrl colord subjid;
run;

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proc freq data=adsl1(where=(not missing(colord))) noprint;
    table analgr1n*analgr1*colord/ out =totals2(drop=percent
rename=(count=total));
run;

data _null_;
    set totals2;
    call
symput('tot' || strip(put(colord,best.)) || strip(put(analgr1n,best.)),strip(
put(total,best.)));
run;

*****;
* read in data ;
*****;
proc sort data=adam.adpp(where=(
paramcd in ('AUCIFO','AUCINT','LAMZHL','TMAX','CMAX','AUCLST')
and aval not in (.,0) and crit3fl ne 'Y' and pprotfl='Y'))
    out=adpp;
    by subjid paramcd;
run;

/*Count number of datapoints for each subject and parameter*/
proc sql;
create table adpp1 as
select *, count(distinct trtan) as trtcount
from adpp
group by analgr1n, paramcd, subjid
order by subjid;

quit;

/*Subjects with T0 > 5% of Cmax */
proc sql;
create table subexc as
select distinct subjid
from adpp
where crit4fl='Y';
CREATE TABLE SUBEXC1 AS /* 11) AMH 24Jun2014 */
SELECT ANALGR1N, TRTAN, COUNT(DISTINCT SUBJID) AS COUNTS
FROM ADPP
WHERE CRIT4FL='Y'
GROUP BY ANALGR1N, TRTAN;
quit;

/* take logs and exclude subjects with <2 timepoints T0 > 5% of Cmax*/
data adpp2 noanal;
ATTRIB BYCLAUSE LENGTH=$100; /* 20) AMH 02Jul2014 */
merge adpp1 subexc(in=a);
by subjid;
if not a;
IF PARAMCD IN ('AUCIFO','LAMZHL') THEN BYCLAUSE="crit3fl ne 'Y'";

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ELSE BYCLAUSE="anl01fl='Y'"; /* 20) AMH 08Aug2014 */
    if paramcd='AUCIFO' then param=tranwrd(param,'(0-inf)', '{sub(0-
inf)}');
    else if paramcd='AUCINT' then param=tranwrd(param,"(0-t)"," {sub(0-
t)}");
    else if paramcd='TMAX' then
param=tranwrd(strip(tranwrd(param,'max',' {sub max}'))/'*||'
[1]'/','T','t');/* 12) AMH 24Jun2014 */
    else if paramcd='LAMZHL' then param=tranwrd(param,'1/2',' {sub
1/2}');
    else if paramcd='CMAX' then param=tranwrd(param,'max',' {sub max}');
    else if paramcd='AUCLST' then param=tranwrd(param,'(0-
last)', '{sub(0-last)}');
    if trtcount>1 then do;
        logaval=log(aval);
        output adpp2;
    end;
    else output noanal;
run;

```

```

PROC SORT DATA=ADPP1; BY SUBJID APERIOD; RUN;
PROC SORT DATA=SUBEXC; BY SUBJID; RUN;

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```

DATA EXCLUDE;
MERGE ADPP1 SUBEXC(IN=A);
IF A;
BY SUBJID;
RUN;

```

```

PROC SQL;
CREATE TABLE TOTEXC AS
SELECT ANALGR1N, TRTAN, COUNT(DISTINCT SUBJID) AS COUNTS
FROM EXCLUDE
GROUP BY ANALGR1N, TRTAN;
quit;

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/*treatment and parameter formats to display text rather than numbers for
listing*/

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```

/* 11) AMH 24Jun2014 */
DATA PARAMLAB;
SET ADPP2 END=A;
OUTPUT;
IF A THEN DO;
PARAMN=0;
PARAM='Number of subjects excluded';
OUTPUT;
END;
RUN;
%FMT(DATAIN=PARAMLAB, START=PARAMN, LABEL=PARAM, NAME=PARAM);
/*%fmt(datain=adpp2, start=paramn, label=param, name=param);*/
%fmt(datain=adpp2, start=trtan, label=trta, name=trt);
%fmt(datain=adpp2, start=trta, label=trtan, name=trta);

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```

data adppmod;
    set adpp2;
    format paramn param. trtan trt. ;
run;

proc sort data=adppmod; by analgrln paramn trtan subjid; run;

title1 j=1 "PAGESPLIT"; /*do not change*/
title2 j=1 'Group #byvall, Parameter: #byval2';
title3 j=1 'Proc GLM Procedure';
/*TITLE4 J=L "The where clause used on the dataset adam.adpp: crit3fl ne
'Y' and pprotfl='Y'"; *//* 13) AMH 24Jun2014 */
TITLE4 J=L "The where clause used on the dataset adam.adpp: pprotfl='Y',
#BYVAL3 and crit4fl='Y'"; /* 20) AMH 08Aug2014 */
/*%let tflno=L_15_04_04_03(PK);*/
%let tflno=L_15_04_04_03_02(PK); /* 9) AMH 24Jun2014 */

%mixout1(fileout=/cvn/projects/prj/data/000000106326/TFL/&TFL_Part./&tflno);
options ps=28;

proc glm data=adppmod(where=(paramcd ne 'TMAX')) order=internal;
by analgrln paramn BYCLAUSE; /* 20) AMH 08Aug2014 */
class trtan subjid trtseqa aperiodc;
model logaval= trtseqa subjid(trtseqa) aperiodc trtan ;
lsmeans trtan / pdiff alpha=0.05 cl;
output out=pred p=pred r=resid;
ods output lsmeancl=lsmeans;
ods output lsmeandiffcl=diffs;
ods output FitStatistics=mse;
run;

proc glm data=adppmod(where=(paramcd ne 'TMAX' and analgrln=2))
order=internal;
by analgrln paramn BYCLAUSE; /* 17) AMH 07Aug2014 */
class trtan subjid trtseqa aperiodc;
model logaval= trtseqa subjid(trtseqa) aperiodc trtan ;
lsmeans trtan / pdiff=controlu('NRT gum') alpha=0.025 cl;
ods output lsmeans=pval;
run;

/*Residual Plots*/
title3 j=1 'Residual Plots';
options ps=26; /*change this for proc plot*/

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

proc plot data=resid hpercent=50;

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by analgr1n paramn BYCLAUSE; /* 20) AMH 08Aug2014 */
plot resid*pred / vref=0;
plot resid*nscore;
run;
quit;

%mixout2(blankn=70, halfblnk=Y,title=Listing 15.4.4.3.2 Supportive
Analysis of Pharmacokinetic Parameters of Nicotine Excluding Subject with
T`{sub 0} Value >5% of Their C`{sub max} Value - PK Population);
/* 9) AMH 24Jun2014 */

/*data counts*/
proc univariate data=adppmod(where=(paramcd ne 'TMAX')) noprint;
  by analgr1n paramn;
  class trtan;
  var logaval;
  output out=num1 n=n1;
run;

data diffs1;
  merge diffs mse pval(keep=analgr1n paramn probtdiff
where=(missing(probtdiff)=0));
  by analgr1n paramn;
run;

/*Manipulate datasets for output all relevent stats on each row*/
/* _____ */
data tabout;
  length out $100 stat $100;
  set lsmeans(in=a rename=(trtan=treat)) diffs1(in=b) num1(in=c)
TOTEXC(IN=D) ; /* 11) AMH 24Jun2014 */
  IF D THEN DO;
    IF TRTAN=4 THEN COLORD=1;
    ELSE COLORD=2;
    PARAMN=0;
    OUT=COMPRESS(PUT(COUNTS,BEST.));
    OUTPUT;
    END;
  ELSE DO;
if a then trtan=input(treat,$trta.);
/*ordering columns of treatmnts*/
if b then colord=3;
else if trtan=4 then colord=1;
else colord=2;

/* N row*/
  if c then do;
    ord=1;
    stat=/'N'*/'n'; /* 5) AMH 24Jun2014 */
    out=compress(put(n1,best.));
    output;
  end;
end;

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        if a or b then do;
        /*Back transformation*/
        if a then estimatee=exp(lsmean);
        if b then estimatee=exp(difference);
        lower=exp(lowercl);
        uppers=exp(uppercl);
        geocv=100*sqrt(exp(rootmse**2)-1);
        /*Gmean (CV%) row*/
        ord=2;
        stat=/'GMean (CV%)'*/'Geometric LS Mean (CV%)`{SUPER 1}'; /* 5)
AMH 24Jun2014 */ /* 7) AMH 24Jun2014 */ /* 20) AMH 08Aug2014 */
        if colord=3 then
        out=compress(put(round(100*estimatee,0.01),8.2))||'
('||compress(put(/*round(geocv,0.01)*CEIL(GEOCV*100)/100,8.2))||')'; /*
4) AMH 24Jun2014 */
        else out=compress(put(round(estimatee,0.01),8.2));
        output;
        /*95% CI row*/
        ord=3;
        stat='95% CI';
        if colord=3 then
        out=compress(put(/*round(100*lower,0.01)*FLOOR(100*100*LOWERE)/100,8.2)
)||',
'||compress(put(/*round(100*uppers,0.01)*CEIL(100*100*UPPERS)/100,8.2));
/* 4) AMH 24Jun2014 */
        else
        out=compress(put(/*round(lower,0.01)*FLOOR(100*LOWERE)/100,8.2))||',
'||compress(put(/*round(uppers,0.01)*CEIL(100*UPPERS)/100,8.2)); /* 4)
AMH 24Jun2014 */
        output;
        /*Precision Pvalue row*/
        /*P-value*/
        if b and analgrln=2 then do;
        ord=4;
        stat='P-value (one-sided)';
        IF PROBTDIFF<0.002 THEN OUT='<0.001'; /* 1) AMH 03Jun2014 */
        ELSE
        out=compress(put(probtdiff,8.3/*pvalue6.3*/)); /* 1) AMH
03Jun2014 */
        if paramn=8 then delete;
        output;
        end;
        if b and analgrln=1 and paramn<3 then do;
        ord=4;
        stat='Precision';
        out=compress(put(/*round*/ceil(100*100*max(abs(estimatee-
lower),abs(estimatee-uppers))/100/*,0.01)*/,8.2)); /* 2) AMH
24Jun2014 */
        output;
        end;

    end;
END;

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```

run;

/*transpose for output*/
proc sort data=tabout;
    by analgrln paramn ord colord;
run;

proc transpose data=tabout out=ttabout(drop=_NAME_) prefix=col;
    by analgrln paramn ord stat;
    id colord;
    var out;
run;

/*Tmax analysis*/

data tmax;
set adppmod(where=(paramcd='TMAX'));
vol=subjidn;
if analgrln=1 and trtan=4 then trtan=3;
run;

%wsigrank(dset=tmax, out=tmaxout, by=analgrln paramn, var=aval,
from=trtan, test=3:4, refs=5:7,
                                label=THS 2.2 Menthol - mCC      :THS 2.2 Menthol - NRT
gum, ci=95);

data tabout1;
length col1 $100 col2 $100 col3 $100 stat $100;
set tmaxout ;
TMAX=1; /* 17) AMH 24Jun2014 */
/*ordering columns of treatments*/
/* N row*/
ord=1;
stat=/'N'/'n'; /* 5) AMH 24Jun2014 */
col1=compress(put(n,best.));
col2=compress(put(n,best.));
col3='';
output;
/*Gmean (CV%) row*/
ord=2;
stat=/'GMean (CV%)'/'Median'/'`{SUPER [2]}'*/; /* 7) AMH
24Jun2014 */ /* 8) AMH 24Jun2014 */ /* 19) AMH 08Aug2014 */
col1=compress(put(round(medtest,0.01),8.2));
col2=compress(put(round(medref,0.01),8.2));
col3=compress(put(round(estimate,0.01),8.2));
output;
/*95% CI row*/
ord=3;
stat='95% CI`{SUPER 2}'; /* 7) AMH 24Jun2014 */ /* 19) AMH
08Aug2014 */ /* 20) AMH 08Aug2014 */
col1='';
col2='';

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col3=compress(put(/*round(lower,0.01)*/FLOOR(100*LOWER)/100,8.2))||',
'||compress(put(/*round(upper,0.01)*/CEIL(100*UPPER)/100,8.2)); /* 4) AMH
24Jun2014 */
    output;
    /*P-value*/
if analgrln=2 then do;
    ord=4;
    stat='P-value (one-sided)';
    col1='';
    col2='';
    if probt<0.002 then col3='<0.001';
    else col3=compress(put(probt/2,8.3));

    output;
end;

run;

data allout;
set ttabout tabout1;
run;

proc sort data=allout; by analgrln TMAX paramn ord; run;

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

/* treatment column headers and footnotes */
/*group 1*/
%let col11=THS 2.2 Menthol#(N=&tot11);
%let col21=mCC#(N=&tot21);
%let col31=THS 2.2 Menthol:mCC#Ratio (%);
%let foot1=%str(mCC = menthol conventional cigarettes); /* 15) AMH
22JUN2014 */
%let foot11=mCC;

/*group 2*/
%let col12=THS 2.2 Menthol#(N=&tot12);
%let col22=NRT gum#(N=&tot22);
%let col32=THS 2.2 Menthol#:NRT gum Ratio (%);
%let foot2=%str(NRT gum = Nicotine Replacement Therapy gum); /* 16) AMH
22JUN2014 */
%let foot12=NRT gum;

%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. */

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/*      %let tflno=T_15_02_04_03(PK);*/
      %let tflno=T_15_02_04_03_02(PK); /* 9) AMH 24Jun2014 */

/* 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 allout;
    by analgrln TMAX paramn; /* 17) AMH 24Jun2014 */
    retain page count;
    if first.paramn then count + 1;
    if count>3 or first.analgrln OR FIRST.TMAX then do; page+1; /* 17)
AMH 24Jun2014 */
    count=1;
    end;
    if last.analgrln then call symput("tpage",compress(put(page,best.)));
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.tl06326 (read) ;
ods results off;
ods rtf toc_data/* contents*/
file="/cvn/projects/prj/data/000000106326/TFL/&TFL_Part./&tflno..rtf"
style=tl06326 startpage=yes headery=1440 footery=1440 ;
ods noproctitle;

%do i=1 %to &tpage;

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

data comp;

```

```

set paging end=eof;
by paramn ord;
  where page=&i;
  flag=1;
  IF TMAX=1 AND ANALGR1N=1 THEN call symput('COL31', 'THS 2.2
Menthol -#mCC (min)'); /* 17) AMH 24Jun2014 */
  IF TMAX=1 AND ANALGR1N=2 THEN call symput('COL32', 'THS 2.2 Menthol
-#NRT gum (min)'); /* 17) AMH 24Jun2014 */
  call symput('grp',compress(put(analgr1n,best.)));
  /* Amend title as needed */
  _firtitl="Table 15.2.4.3.2 Supportive Analysis of
Pharmacokinetic Parameters of Nicotine Excluding Subject with T`{sub 0}
Value >5% of Their C`{sub max} Value - PK Population"; /* 2) AMH
27May2014 */
  _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 paramn ord stat ("Group-&grp PK &linebot." coll
col2 col3);

  define flag / order noprint;
    define page / order order = internal noprint;
    define paramn / group order=internal style={just=left
cellwidth=3.5cm} "Variable";
    define ord / order order=internal noprint;
    define stat / display style={just=left cellwidth=3.5cm}
"Statistic";
    define coll / display style={just=C/*d*/ cellwidth=3cm}
style(header)={just=center} "&&coll&grp";
    define col2 / display style={just=C/*d*/ cellwidth=3cm}
style(header)={just=center} "&&col2&grp";
    define col3 / display style={just=C/*d*/ cellwidth=3cm}
style(header)={just=center} "&&col3&grp"; /* 18) AMH 08Aug2014 */

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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 paramn;
    line " ";
endcomp;

compute after _page_ / style={just=left protectspecialchars=off
pretext="&linetop."};
/*      line 'Note: GMean and 95%CI are the adjusted geometric least
squares means and confidence intervals from an ANOVA model conducted on
log-transformed data with sequence, subject within sequence, period and
product exposure as fixed effect factors. Geometrical CV% of the ratio is
estimated from the residual mean square error.';*/
    line "Note:  &&foot&grp; THS = Tobacco Heating System.";
/*      line "[1] For t`{SUB max} the medians for each product and the
median difference and 95% confidence interval between THS 2.2 and CC is
reported. The 95% CI is based on the Hodges-Lehmann estimate.";*/ /* 2)
AMH 27May2014 */
LINE 'Note: 1: Geometric LS Mean and 95% CI are the adjusted geometric
least squares means based on an ANOVA model. Geometrical CV% of the ratio
is estimated only for the ratio. Precision is the largest difference
between the 95% CI bounds and the mean';
LINE "Note: 2: 95% CI are estimated only for the median difference based
on the Hodges-Lehmann estimate."; /* 19) AMH 08Aug2014 */
/*LINE "[2] Median Difference presented for THS 2.2 - &&footl&grp."; */
/*LINE "[3] The 95% CI is based on the Hodges-Lehmann estimate. ";*/
    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 ;

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```
%outrtf(blankn=69, halfblnk=Y, ref=15.4.4.3.2 and 15.3.3.1); /* 10) AMH  
24Jun2014 */  
/* 9) AMH 24Jun2014 */
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```
proc printto ; run;  
*=====;  
* END OF PROGRAM CODE ;  
*=====;
```