

/*=====*

| Covance Study Number : COV- 106343 |

| Client Protocol ID : ZRHM-REXA-08-US |

| Program Name : t_anl_nc_pk.sas |

| Purpose : Table Analysis of plasma nicotine and cotinine PK |

| Input Data : ADBX ADSL |

| Output Data : T_15_02_04_22_01,22_02 |

| |

| Macros Called : |

| |

| Originally Performed by : Seroan Zheng |

| Date/Time billed : 05Jun2015 |

| |

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| Modification History |

| |

| Programmer : Serona Zheng |

| Date : 14Sep2015 |

| Reason for Change : Added UCPDGR1 ne " condition to select analysis subjects based on client comments|

+=====*/

options noquotelenmax;

***Create log file;

proc printto new

log="/cvn/projects/prj/development/000000106343/dev/tables/log/t_anl_nc_pk.log" ;

run;

```
%macro t_anl_nc(t_name=,l_name=,dsin=,conf1=,by_var1=,t_title=,t_title_l=);
```

```
%let pgrame=t_anl_nc_pk.sas;
```

```
%let table=&tflout.;
```

```
%let tflno=&t_name;
```

```
%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;
```

```
***Get raw data;
```

```
data anl1;
```

```
    set adam.&dsin;
```

```
    &conf1
```

```
    avisit = strip(avisit);
```

```
***Calculate LOG;
```

```
    if aval not in (.,0) then do;
```

```
        logaval=log(aval);
```

```
    end;
```

```

run;

proc sort data=anl1;by &by_var1;run;

***Get decimal length;

data temp;

    set anl1;

    declen=lengthn(scan(strip(put(aval, best.)),2,"."));

run;

proc sql;

    create table dectemp

    as select distinct paramn, max(declen) as declen

    from temp

    group by paramn;

    select max(declen) into: last

    from dectemp;

quit;

/*ods listing close;*/

%macro mix_nc(dsin_m,var=,dsout_m=,dsoutm_f=);

***Calculate STAT using MIXED model;

Proc mixed data=&dsin_m;

```

```

by &by_var1;

Class trtp sex UCPDGR1;

Model logaval = sex UCPDGR1 trtp;

Lsmean trtp / pdiff =control('mCC') alpha=0.05 cl;

ods output diffs = diffs;

ods output covparms = fit;

ods output lsmeans = lsmeans;

Run;

***prepare mean and ci for each group;

data lsmeans(where=(colord ne .));

    length out stat $100;

    merge lsmeans(in=a) dectemp;

    by paramn;

    if a;

***ordering columns of treatments*;

    if trtp='THSm2.2' then colord=1;

    else if trtp='mCC' then colord=2;

    %if &var=logaval %then %do;

        if estimate ne . then estimatee=exp(estimate);

        if lower ne . then lowere=exp(lower);

        if upper ne . then uppere=exp(upper);

    %end;

    %else %do;

        estimatee=estimate;

```

```

    lowere=Lower;

    uppere=Upper;

%end;

%do i=0 %to &last.;

    if declen=%eval(&i) then do;

        %let fmt= %sysevalf(12 + (&i +1 )*0.1);

        ***Gmean (CV%) row*;

    ord=2;

    stat='Geometric LS Mean (CV%)';

    if estimatee ne . then out=compress(put(round(estimatee,0.01),12.2));

    output;

    ord=3;

    stat='95% CI';

    if nmiss(lowere,uppere)=0 then out=compress(put(floor(100*lowere)/100,12.2))||',
'| |compress(put(ceil(100*uppere)/100,12.2));

    output;

    end;

%end;

run;

***prepare mean and ci for difference;

data diff;

    merge diffs(in=a where=(trtp='THSm2.2')) fit(in=b rename=(estimate=rootmse));

    by paramn paramcd param avisitn avisit;

```

```

        if a;

run;

data diff;

    length out stat $100;

    merge diff(in=a) dectemp(in=c);

    by paramn;

    if a;

***ordering columns of treatments*;

    if _trtp='mCC' then colord=4;

    %if &var=logaval %then %do;

        if estimate ne . then estimatee=exp(estimate);

        if lower ne . then lowere=exp(lower);

        if upper ne . then uppere=exp(upper);

        MSE=rootmse;

        if mse ne . then CV_=100*sqrt(exp(MSE)-1);

        if cv_ ne . then cv = put(ceil(CV_*100)/100,12.2);

    %do i=0 %to &last.;

        if declen=%eval(&i) then do;

            %let fmt= %sysevalf(12 + (&i +1 )*0.1);

            ord=3;

            stat='95% CI';

            if lowere ne . and uppere ne . then
out=compress(put(floor(100*lowere*100)/100,12.2))||',
'||compress(put(ceil(100*uppere*100)/100,12.2));

```

```

        output;

        ord=2;

        stat='Geometric LS Mean (CV%)';

        if estimatee ne . then
out=compress(put(round(100*estimatee,0.01),12.2))||' ('||COMPRESS(cv)||');

        output;

        end;

    %end;

%end;

%else %do;

    estimatee=estimate;

    lowere=Lower;

    uppere=Upper;

    %do i=0 %to &last.;

        if declen=%eval(&i) then do;

            %let fmt= %sysevalf(12 + (&i +1 )*0.1);

            ord=3;

            stat='95% CI';

            if lowere ne . and uppere ne . then
out=compress(put(floor(100*lowere)/100,12.2))||', '||compress(put(ceil(100*uppere)/100,12.2));

            output;

        end;

    end;

    ord=2;

    stat='Geometric LS Mean (CV%)';

    if estimatee ne . then
out=compress(put(round(100*estimatee,0.01),12.2));

    end;

```

```

                                %end;

                                %end;

run;

***Calculate N;

proc univariate data=&dsin_m noprint;

    by paramn paramcd param avisitn avisit;

    class trtp;

    var &var;

    output out=num1 n=n1;

run;

data num1;

    length trtp $7;

    set num1(rename=(trtp=trtp1));

    trtp = trtp1;

    drop trtp1;

run;

data num1;

    merge num1(in=a) dectemp;

    by paramn;

    if a;

***ordering columns of treatments*;

    if trtp='THSm2.2' then colord=1;

    else if trtp='mCC' then colord=2;

```



```

ord=1;

stat='n';

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

    if colord ne .;

run;

data tabout;

    set lsmeans diff num1;

    by &by_var1;

run;

proc sort data=tabout; by &by_var1 ord stat;run;

proc transpose data=tabout out=&dsout_m.(drop=_NAME_) prefix=col;

    by &by_var1 ord stat;

    id colord;

    var out;

run;

%mend;

%macro hdoges;

***Calculate difference median and 95% CI for two group;

```

```
proc sort data=anl1 out=anl_t;where paramcd in ('NTMAX' 'CTMAX');by paramn avisitn paramcd param  
avisit descending trtp;run;
```

```
proc npar1way hl alpha=0.05 data=anl_t median;
```

```
    by paramn avisitn paramcd param avisit;
```

```
    class trtp;
```

```
    var aval;
```

```
    ods output hodgelehmann=hlmed_d;
```

```
run;
```

```
data hlmed_d(keep=paramn avisitn paramcd param avisit stat out ord colord);
```

```
    length out stat $100;
```

```
    set hlmed_d;
```

```
    stat = 'Median';
```

```
    ord = 2;
```

```
    colord = 4;
```

```
    if shift =0 then out = compress(put(round(shift,0.01),12.2));
```

```
    else out = compress(put(round(-shift,0.01),12.2));
```

```
    output;
```

```
    stat = "95% CI";
```

```
    colord = 4;
```

```
    ord = 3;
```

```
    if lowercl ne . and uppercl ne . then out=compress(put(floor(100*-uppercl)/100,12.2))||',  
'||compress(put(ceil(100*-lowercl)/100,12.2));
```

```
    output;
```

```
run;
```

```
***HL Estimator & 95% CI for each group***;
```

```
proc sort data=anl_t;by paramn avisitn paramcd param avisit trtp;run;
```

```

data anl_t1;

    set anl_t;

    by paramn avisitn paramcd param avisit trtp;

    if first.trtp then rec=0;

    rec+1;

run;

proc sort data=anl_t1;by paramn avisitn paramcd param avisit trtp rec;run;

proc sql;

    ***Calculate n;

    create table totsbj as

        select distinct paramn,avisitn,paramcd, param, avisit, trtp, compress(put(count(distinct
usubjid),8.)) as out length=100, 'n' as stat length=100, 1 as ord from anl_t group by
paramn,avisitn,paramcd, param, avisit, trtp;

    ***Sample size of trt1/trt2***;

    create table tsubj as

        select distinct paramn,avisitn,paramcd, param, avisit, trtp, count(distinct usubjid) as
tsubj from anl_t group by paramn,avisitn,paramcd, param, avisit, trtp;

    ***Calculate the Uk/Walsh average in trt1/trt2***;

    create table hlrnk as

        select t1.paramn,t1.avisitn,t1.paramcd, t1.param, t1.avisit, t1.trtp,t1.aval as aval1,
t2.aval as aval2,((t1.aval+t2.aval)/2) as hlrnk from anl_t1 t1, anl_t1 t2

        where t1.paramcd=t2.paramcd and t1.trtp=t2.trtp and t1.avisitn=t2.avisitn and
t1.rec<=t2.rec order by t1.paramn,t1.avisitn, t1.trtp;

quit;

***Median of HL Estimator ***;

```

```
proc univariate data=hrank noprint;
```

```
    var hrank;
```

```
    by paramn avisitn paramcd param avisit trtp;
```

```
    output out=hlmed median=hlmed;
```

```
run;
```

```
***Calculate the position of lower/upper CL ***;
```

```
data clpos;
```

```
    set tsubj;
```

```
    by paramn avisitn paramcd param avisit trtp;
```

```
    ***Calculate K value***;
```

```
    kval=round((0.5+(Tsubj*(tsubj+1)/4)+probit(0.05/2)*sqrt(tsubj*(tsubj+1)*(tsubj+2)/24)),1);
```

```
    ukval=(tsubj*(tsubj+1)/2)+1-kval;
```

```
run;
```

```
data hrank1;
```

```
    merge clpos hrank;
```

```
    by paramn avisitn paramcd param avisit trtp;
```

```
run;
```

```
proc sort data=hrank1;by paramn avisitn paramcd param avisit trtp hrank;run;
```

```
***CL of Hodges-Lehmann estimator***;
```

```
data hlcl(keep=paramcd trtp lowercl uppercl paramn param avisitn avisit);
```

```
    set hrank1;
```

```

by paramn avisitn paramcd param avisit trtp hlrnk;

retain lowercl uppercl;

***Initial record number and lower/upper CL***;

if first.trtp then do;rec=0;lowercl=.;uppercl=.;end;

rec+1;recn=rec; ***Record No. of HLRANK per by-group;

if recn=kval then lowercl=hlrank;

if recn=ukval then uppercl=hlrank;

if last.trtp;

run;

data hlcl_m;

merge hlcl hlmed;

by paramn avisitn paramcd param avisit trtp;

run;

data hlcl_m(keep=paramcd trtp stat ord out paramn param avisitn avisit);

length out stat $100;

set hlcl_m;

stat = 'Median';

ord = 2;

out = compress(put(round(hlmed,0.01),12.2));

output;

stat = "95% CI";

ord = 3;

if lowercl ne . and uppercl ne . then out=compress(put(floor(100*lowercl)/100,12.2))||',
'| |compress(put(ceil(100*uppercl)/100,12.2));

output;

```

```

run;

data hlcl_f;

    set totsbj hlcl_m hlmed_d;

    if trtp='THSm2.2' then colord=1;

    else if trtp='mCC' then colord=2;

run;

proc sort data=hlcl_f; by paramn avisitn paramcd param avisit ord stat;run;

proc transpose data=hlcl_f out=hlcl_f(drop=_NAME_) prefix=col;

    by paramn avisitn paramcd param avisit ord stat;

    id colord;

    var out;

run;

%mend;

***Create model result to lst file;

ods rtf

file="/cvn/projects/prj/data/000000106343/TFL/dev/Tables/&l_name..rtf";

title "&t_title_l";

options orientation=landscape;

%mix_nc(dsin_m=anl1(where=(paramcd in ('NCAVG' 'NCMAX' 'CAVG'
'CCMAX'))),var=logaval,dsout_m=anl_f);

%hdoges;

```

```
ods rtf close;
```

```
data final1;
```

```
    set anl_f hlcl_f;
```

```
    logf = 1;
```

```
run;
```

```
proc sort data=final1;by logf paramn avisitn ord;run;
```

```
data final2;
```

```
    set final1 end=last;
```

```
    by logf paramn avisitn ord;
```

```
    if paramcd in ('NCAVG' 'NCMAX' 'NTMAX') then do;
```

```
        param1 = 'Nicotine';
```

```
        page = 1;
```

```
    end;
```

```
    else if paramcd in ('CCAUG' 'CCMAX' 'CTMAX') then do;
```

```
        param1 = 'Cotinine';
```

```
        page = 2;
```

```
    end;
```

```
    if index(paramcd,'AVG') then param = "C\sub avg\nosupersub(ng/mL)";
```

```
    else if index(paramcd,'CMAX') then param = "C\sub peak\nosupersub(ng/mL)";
```

```
    else if index(paramcd,'TMAX') then param = "t\sub peak\nosupersub(h)\super (1)\nosupersub";
```

```
    if paramn in (1 2 4 5) then id = 1;
```

```
    else if paramn in (3 6) then id = 2;
```

```
if last then call symputx("tpage", page);
```

```
run;
```

```
data final2;
```

```
    set final2;
```

```
    if paramcd in ('NTMAX' 'CTMAX') and stat = '95% CI' then call missing(col1,col2);
```

```
run;
```

```
%put &tpage;
```

```
data tflds.&tflno.;
```

```
    set final2;
```

```
run;
```

```
options number nodate mprint mlogic orientation=landscape /* papersize=&p_pgsz */ missing=' ';
```

```
%let linetop = \brdrt\brdrs\brdrw30; * needs to be 1.5pt so calculated in twips (1/20 pt) ;
```

```
%let linebot = \brdrb\brdrs\brdrw30;
```

```
ods escapechar='$';
```

```
ods path stdlib.t106343 (read) ;
```

```
ods results off;
```

```
ods rtf toc_data file="/cvn/projects/prj/data/000000106343/TFL/dev/Tables/&tflno..rtf" style=t106343
```

```
startpage=yes headery=1440 footery=1440 ;
```

```
ods noproctitle;
```

```
%do i=1 %to &tpage;
```



```
title ;
```

```
footnote;
```

```
%let wd=0;
```

```
ods proclabel=' ';
```

```
data comp;
```

```
    set final2 end=eof;
```

```
    where page=&i;
```

```
    *** Amend title as needed;
```

```
    _firtitl="&t_title";
```

```
    call symput('_FSRTITL', trim(left(_firtitl)));
```

```
    call symput('param1', strip(param1));
```

```
    drop _firtitl ;
```

```
run;
```

```
* 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;
```

```
proc report data = comp missing headline headskip missing nowd split = '$' %if &i=1 %then %do;  
contents=' ' %end; %else %do; contents=" " %end;; ;
```

```
    column page param1 id param ord stat col1 col2 col4;
```

```

define page      / order order=internal noprint;

define param1    / order order = internal noprint;

define ord       / order order=internal noprint;

define id        / order order=internal noprint;


define param      / order style={just=left cellwidth=3cm} style(header)={just=left} "Variable" ;

define stat       / display style={just=left cellwidth=3cm} style(header)={just=left} "Statistic";

define col1       / display style={just=c cellwidth=2cm} style(header)={just=center} "THSm2.2";

define col2       / display style={just=c cellwidth=2cm} style(header)={just=center} "mCC";


define col4       / display style={just=c cellwidth=3.5cm} style(header)={just=center} "THSm2.2 : mCC
Ratio (%)";


break after page / page;

compute before param1 / style={just=left fontweight=bold fontsize=11pt
protectspecialchars=on};

line "";

line "&param1";

endcomp;

compute before id / style={just=left fontweight=bold fontsize=11pt protectspecialchars=on};

line _a1 =
"
_____";

line _a2 = "Variable          Statistic
THSm2.2 - mCC Difference (h)";

```

```

line_a3 =
"
_____";

if id = 1 then len = 0;

else len = 255;

line line_a1 $varying24. len;

line line_a2 $varying24. len;

line line_a3 $varying24. len;

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 _page_ / style={just=left protectspecialchars=off pretext="&linetop."};

line "Note: Adjusted geometric least squares (LS) means and confidence intervals (CIs)
from an ANCOVA model conducted on log-transformed Day 5 values with study arm, sex and mCC
consumption reported at screening as fixed effect factors. Geometrical CV% of the ratio is estimated
from the residual mean squares.";

line 'Note: mCC = Menthol Conventional cigarettes; SA = Smoking abstinence; THSm2.2
= Tobacco Heating System 2.2 Menthol.';

line "(1): For t\sub peak\nosupersub the medians for each product and the median
difference and 95% confidence interval between THS 2.2 Menthol and mCC is reported. The 95% CI is
based on the Hodges-Lehmann estimate. ";

line ' ';

line 'Appendix 15.3.3.4';

```

```

line "Study ID: ZRHM-REXA-08-US" " " "Program: &pgname" " " "Status: &status"
" "&sysdate" " "(Page &i of &tpage)";

```

```

endcomp;

```

```

run;

```

```

ods path WORK.TEMPLAT(UPDATE)

```

```

SASUSER.TEMPLAT(READ)

```

```

SASHELP.TMPLMST(READ) ;

```

```

%end;

```

```

ods rtf close;

```

```

ods listing;

```

```

title " ";

```

```

footnote " ";

```

```

/* ods path show;*/

```

```

%mend;

```

```

***For table 15.2.4.20.1;

```

```

%t_anl_nc( t_name=T_15_02_04_22_01,

```

```

l_name=L_15_04_04_22_01,

```

```

dsin=adpp,

```

```

conf1=%str(if anl01fl = 'Y' and pprot1fl = 'Y' and avisitn = 105 and UCPDGR1 ne

```

```

");),

```

```

by_var1=paramn paramcd param avisitn avisit,

```

```

t_title=%str(Table 15.2.4.22.1 Analysis of Plasma Nicotine and Cotinine
Concentration PK Parameters on Day 5 - PP Set),

```

```
                t_title_l=%str(Listing 15.4.4.22.1 Analysis of Plasma Nicotine and Cotinine  
Concentration PK Parameters on Day 5 - PP Set))
```

```
;
```

```
***For table 15.2.4.20.1;
```

```
%t_anl_nc(      t_name=T_15_02_04_22_02,  
                l_name=L_15_04_04_22_02,  
                dsin=adpp,  
                conf1=%str(if anl01fl = 'Y' and fasfl = 'Y' and avisitn = 105 and UCPDGR1 ne ";),  
                by_var1=paramn paramcd param avisitn avisit,  
                t_title=%str(Table 15.2.4.22.2 Analysis of Plasma Nicotine and Cotinine  
Concentration PK Parameters on Day 5 - FAS),  
                t_title_l=%str(Listing 15.4.4.22.2 Analysis of Plasma Nicotine and Cotinine  
Concentration PK Parameters on Day 5 - FAS))
```

```
;
```

```
ods path WORK.TEMPLAT(UPDATE)
```

```
SASUSER.TEMPLAT(READ)
```

```
SASHELP.TMPLMST(READ) ;
```

```
proc printto ;
```

```
run;
```

```
ods listing;
```

```
options quotelenmax;
```

```
/*proc datasets kill lib=work memtype=data;run;*/
```

***check the log, if there is any findings, please make sure to resolve;

```
%m_chklog(TFL_part=dev,pgm_type=tables,pgm_name=t_anl_nc_pk,serv=dev,covstudyid=000000106343);
```