

/*=====*

| Covance Study Number : COV- 106343 |
| Client Protocol ID : ZRHM-REXA-08-US |
| Program Name : t_anl_nc.sas |
| Purpose : Table Analysis of plasma nicotine and cotinine |
| Input Data : ADBX ADSL |
| Output Data : T_15_02_04_20_01,20_02 |

| |
| Macros Called : |

| |
| Originally Performed by : Seroan Zheng |
| Date/Time billed : 12May2015 |

| |

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| Modification History |

| |

| Programmer : Serona Zheng |

| Date : 14Sep2015 |

| Reason for Change : Added base ne . and 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.log" ;

run;

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

```
%let pgrame=t_anl_nc.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
```

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

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

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

```
        if base not in (.,0) then logbase=log(base);
```

```
    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=,base=,dsout_m=,dsoutm_f=);
```

```
***Calculate STAT using MIXED model;
```

```
Proc mixed data=&dsin_m;
```

```
    by &by_var1;
```

```

Class trtp sex UCPDGR1;

Model logaval = logbase 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)**2;*/
```

```
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;

***Create model result to lst file;

ods rtf

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

title "&t_title_1";

```

```
options orientation=landscape;
```

```
%mix_nc(dsin_m=anl1,var=logaval,base=logbase,dsout_m=anl_f);
```

```
ods rtf close;
```

```
data final1;
```

```
    set anl_f;
```

```
    logf = 1;
```

```
run;
```

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

```
data final2;
```

```
    set final1;
```

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

```
    if first.paramn then do; sum = 0; group + 1; end;
```

```
    sum +1;
```

```
    if sum > 9 then do;
```

```
        group +1;
```

```
        sum = 1;
```

```
    end;
```

```
    page = group;
```

```
run;
```

```
proc sort data=final2;by page logf paramn avisitn ord;run;
```

```
data final3;
```

```
    set final2;
```

```
by page logf paramn avisitn ord;  
if first.page then output;  
output;  
run;
```

```
data final;  
set final3;  
by page logf paramcd avisitn ord;  
if first.page then do;  
    call missing(stat,col1,col2,col4,avisitn);  
    id = 1;  
end;  
else do;  
    id = 2;  
    param = propcase(avisit);  
end;  
avisit = propcase(avisit);  
run;
```

```
data _null_;  
set final;  
by logf paramn;  
if last.paramn then call symput('tpage',strip(put(page,3.)));  
if first.logf then call symput('tpage' || strip(put(logf,best.)),strip(put(page,3.)));  
run;
```

```

%put &tpage;

data tflds.&tflno.;

    set final;

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 final end=eof;

```

```

where page=&i;

*** Amend title as needed;

_firtitl="&t_title";

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

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 paramn id avisitn param  ord stat col1 col2 col4;

define page      / order order=internal noprint;

define paramn    / order order = internal noprint;

define avisitn   / 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=3.5cm} 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";

%if &i < &tpage1 %then %do;

    define col4      / display style={just=c cellwidth=2.5cm} style(header)={just=center} "THSm2.2 -
mCC Difference";

    %end;

    %else %do;

    define col4      / display style={just=c cellwidth=2.7cm} style(header)={just=center} "THSm2.2 : mCC
$Ratio (%)";

    %end;

    break after page / page;

    compute after avisitn;

        line " ";

    endcomp;

    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;

%if &i < &tpage1 %then %do;

```

```

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

    line 'Note: Adjusted least squares (LS) means and confidence intervals (CIs) from an
ANCOVA model conducted with baseline value, study arm, sex and mCC consumption reported at
screening as fixed effect factors.';

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

    line ' ';

%end;

%else %do;

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 values with log-transformed baseline value,
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 ' ';

%end;

    line 'Appendix 15.3.3.3';

    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_20_01,
```

```
                l_name=L_15_04_04_20_01,
```

```
                dsin=adpc,
```

```
                conf1=%str(if (anl01fl = 'Y' and dtype ne 'LOCF' and base ne . and UCPDGR1 ne "
and ((pprot1fl = 'Y' and (avisitn in (101 102 103 104))) or (pprot2fl = 'Y' and avisitn =130)
```

```
                                or (pprot3fl = 'Y' and avisitn = 160) or (pprot4fl = 'Y' and
avisitn = 190 and atptn ne 10))) or (anl02fl = 'Y' and dtype ne 'LOCF' and pprot1fl = 'Y' and avisitn = 105
and atptn = 7);),
```

```
                by_var1=paramn paramcd param avisitn avisit,
```

```
                t_title=%str(Table 15.2.4.20.1 Analysis of Plasma Nicotine and Cotinine
Concentrations (ng/mL) over the 90 Days - PP Set),
```

```
                t_title_l=%str(Listing 15.4.4.20.1 Analysis of Plasma Nicotine and Cotinine
Concentrations (ng/mL) over the 90 Days - PP Set))
```

```
;
```

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

```
%t_anl_nc(      t_name=T_15_02_04_20_02,
```



```

l_name=L_15_04_04_20_02,

dsin=adpc,

conf1=%str(if (anl01fl = 'Y' and dtype ne 'LOCF' and base ne . and UCPDGR1 ne ''
and ((fasfl = 'Y' and (avisitn in (101 102 103 104))) or (fasfl = 'Y' and avisitn =130)

or (fasfl = 'Y' and avisitn = 160) or (fasfl = 'Y' and avisitn
= 190 and atptn ne 10))) or (anl02fl = 'Y' and dtype ne 'LOCF' and fasfl = 'Y' and avisitn = 105 and atptn =
7));),

by_var1=paramn paramcd param avisitn avisit,

t_title=%str(Table 15.2.4.20.2 Analysis of Plasma Nicotine and Cotinine
Concentrations (ng/mL) over the 90 Days - FAS),

t_title_l=%str(Listing 15.4.4.20.2 Analysis of Plasma Nicotine and Cotinine
Concentrations (ng/mL) over the 90 Days - FAS))

;

proc freq data=adam.adpc;

table avisitn*atpt*atptn / list missing;

run;

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,serv=dev,covstudyid=000000106343);
```