

/\*=====\*

| Covance Study Number : COV- 106331 |

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

| Program Name : t\_anl\_cyp.sas |

| Purpose : Table Analysis of CYP1A2 and CYP2A1 |

| Input Data : ADBX ADSL |

| Output Data :

T\_15\_02\_04\_24\_01,24\_01\_01,24\_02,24\_02\_01,63\_01,63\_01\_01,63\_02,63\_02\_01|

| |

| Macros Called : |

| |

| Originally Performed by : Seroan Zheng |

| Date/Time billed : 12May2015 |

| |

+=====+

| Modification History |

| |

| Programmer : Serona Zheng |

| Date : 08Sep2015 |

| Reason for Change : Change footnote |

| |

| 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 notes;
```

```
***Create log file;
```

```
proc printto new
```

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

```
run;
```

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

```
%let pgname=t_anl_cyp.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;

%if &t_name=T_15_02_04_25_01_01 or &t_name=T_15_02_04_25_02_01 %then %do;

```

```

data dectemp;

    set dectemp;

    declen = 1;

run;

proc sql;

    select max(declen) into: last

    from dectemp;

quit;

%end;

ods listing close;

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

options linesize=max;

***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;

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

ods output diffs = diffs;

```

```

ods output covparms = fit;

ods output lsmeans = lsmeans;

Run;

options linesize=132;

***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;

    else if trtp='SA' then colord=3;

%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,1/10**(declen+1)),&fmt.));

    output;

    ord=3;

    stat='95% CI';

    if nmiss(lowere,uppere)=0 then
out=compress(put(floor(10**(declen+1)*lowere)/10**(declen+1),&fmt.))||',
'| | compress(put(ceil(10**(declen+1)*uppere)/10**(declen+1),&fmt.));

        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 _trtp='SA' then colord=5;

    %if &var=logaval %then %do;

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

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

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

/*      MSE=(rootmse)**2;*/

        MSE = rootmse;

        CV_=100*sqrt(exp(MSE)-1);

        cv = put(ceil(CV_*100)/100,12.2);

        ord=3;

stat='95% CI';

        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%)';

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

        output;

    %end;

    %else %do;

        estimatee=estimate;

        lowere=Lower;

        uppere=Upper;

    ord=3;

    stat='95% CI';

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

        output;

    ord=2;

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

        out=compress(put(round(100*estimatee,0.01),12.2));

    %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;
```

```
    else if trtp='SA' then colord=3;
```

```
ord=1;
```

```
stat='n';
```

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

```
    if colord ne .;
```

```
run;
```

```
*p-value;
```

```
data pval1;
```

```

length out stat $100;

set diffs(keep=paramn paramcd param avisitn avisit trtp _trtp probt);

by paramcd avisitn avisit;

where trtp="THSm2.2";

***ordering columns of treatments*;

if first.avisitn then colord=4;

if last.avisitn then colord=5;

ord=4;

stat='p-value (one-sided)';

if probt = <.0001 then out="<0.001";

else do;

pval_=probt/2;

if pval_ < 0.001 then out="<0.001";

else if pval_ > 0.999 then out=">0.999";

else if 0.001 < pval_ < 0.999 then out=put(pval_,5.3);

end;

run;

data tabout;

set lsmeans diff num1 pval1;

by &by_var1;

run;

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

```

```
/*data &dsoutf;*/
```

```
/*      set tabout;*/
```

```
/*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" ;
```

```
run;
```

```
title "&t_title_1";
```

```
%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 > 8 then do;  
        group +1;  
        sum = 1;  
    end;  
    page = group;  
run;
```

```
data pval1;  
    set pval1;  
    if trtp = 'THSm2.2' and _trtp = 'mCC' and avisitn in (105 106) then call symput('pvalue',  
strip(put(pval_8.3)));  
run;  
%put &pvalue;  
data final;  
    set final2;
```

```

        if avisitn in (105 106 190) and stat = 'p-value (one-sided)' then call missing(col5);

        %if &pvalue > 0.025 %then %do;

            if avisitn in (190) and stat = 'p-value (one-sided)' then delete;

        %end;

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;
```

```
    call symput('param',param);
```

```
    _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 avisitn avisit ord stat col1 col2 col3 col4 col5;
```

```
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;*/
```

```
%if &t_name=T_15_02_04_24_01 or &t_name=T_15_02_04_24_01_01 or  
&t_name=T_15_02_04_24_02 or &t_name=T_15_02_04_24_02_01 %then %do;
```

```
define avisit / order style={just=left cellwidth=2cm} style(header)={just=left} "Variable" ;
```

```
%end;
```

```
%else %do;
```

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

```
%end;
```

```
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=2.5cm} style(header)={just=center} "mCC";
```

```
define col3 / display style={just=c cellwidth=2.5cm} style(header)={just=center} "SA";
```

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

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

```

        define col5      / display style={just=c cellwidth=2.5cm} style(header)={just=center} "THSm2.2 -
SA Difference";

        %end;

        %else %do;

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

        define col5      / display style={just=c cellwidth=2.7cm} style(header)={just=center} "THSm2.2 : SA
$Ratio (%)";

        %end;

        break after page / page;

        compute after avisitn;

                line " ";

        endcomp;

        compute before page / style={just=left protectspecialchars=off fontsize=10pt};

                line "&linetop";

                line "&param";

                line "";

        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.';

    %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.';

    %end;

    line 'Note: p-value for one-sided test for comparison between THSm2.2 and mCC. P-
value at Day 90 is evaluated only if p-value at Day 5 is significant.';

    line ' ';

    line "Appendix: &appendix";

    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 path show;*/
```

```
%mend;
```

```
***For table 15.2.4.24.1;
```

```
%t_anl_cyp( t_name=T_15_02_04_24_01,
```

```
l_name=L_15_04_04_24_01,
```

```
dsin=adbx,
```

```
conf1=%str(if anl02fl = 'Y' and dtype ne 'LOCF' and paramcd = 'CYP1A2' and base  
ne . and UCPDGR1 ne " and ((pprot1fl = 'Y' and avisitn = 105)
```

```
or (pprot4fl = 'Y' and avisitn = 190)));,
```

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

```
t_title=%nrbquote(Table 15.2.4.24.1 Analysis of CYP1A2 Activity (%) - PP Set),
```

```
t_title_l=%nrbquote(Listing 15.4.4.24.1 Analysis of CYP1A2 Activity (%) - PP Set),
```

```
appendix=%str(15.3.4.1)
```

```
);
```

```
***For table 15.2.4.24.1.1;
```

```
%t_anl_cyp( t_name=T_15_02_04_24_01_01,
```

```
l_name=L_15_04_04_24_01_01,
```

```
dsin=adbx,
```

```
conf1=%str(if anl03fl = 'Y' and dtype ne 'LOCF' and paramcd = 'CYP1A2' and base  
ne . and UCPDGR1 ne " and ((pprot1fl = 'Y' and avisitn = 105)
```

```
or (pprot4fl = 'Y' and avisitn = 190)));,
```

```

        by_var1=paramn paramcd param avisitn avisit,

        t_title=%nrquote(Table 15.2.4.24.1.1 Analysis of CYP1A2 Activity (%) Excluding
Assessments within 5 Half-Lives of a Concomitant Medication Affecting CYP1A2 Activity - PP Set),

        t_title_l=%nrquote(Listing 15.4.4.24.1.1 Analysis of CYP1A2 Activity (%)
Excluding Assessments within 5 Half-Lives of a Concomitant Medication Affecting CYP1A2 Activity - PP
Set),

        appendix=%str(15.3.4.1)

```

```
);
```

\*\*\*For table 15.2.4.24.2;

```

%t_anl_cyp(    t_name=T_15_02_04_24_02,

                l_name=L_15_04_04_24_02,

                dsin=adbx,

                conf1=%str(if anl02fl = 'Y' and dtype ne 'LOCF' and paramcd = 'CYP1A2' and base
ne . and UCPDGR1 ne " and ((fasfl = 'Y' and avisitn = 105)

                or (fasfl = 'Y' and avisitn = 190))),

                by_var1=paramn paramcd param avisitn avisit,

                t_title=%nrquote(Table 15.2.4.24.2 Analysis of CYP1A2 Activity (%) - FAS),

                t_title_l=%nrquote(Listing 15.4.4.24.2 Analysis of CYP1A2 Activity (%) - FAS),

                appendix=%str(15.3.4.1)

);

```

\*\*\*For table 15.2.4.24.1.2;

```

%t_anl_cyp(    t_name=T_15_02_04_24_02_01,

                l_name=L_15_04_04_24_02_01,

                dsin=adbx,

```

```

        conf1=%str(if anl03fl = 'Y' and dtype ne 'LOCF' and paramcd = 'CYP1A2' and base
ne . and UCPDGR1 ne '' and ((fasfl = 'Y' and avisitn = 105)

        or (fasfl = 'Y' and avisitn = 190)));),

        by_var1=paramn paramcd param avisitn avisit,

        t_title=%nrquote(Table 15.2.4.24.2.1 Analysis of CYP1A2 Activity (%) Excluding
Assessments within 5 Half-Lives of a Concomitant Medication Affecting CYP1A2 Activity - FAS),

        t_title_l=%nrquote(Listing 15.4.4.24.2.1 Analysis of CYP1A2 Activity (%)
Excluding Assessments within 5 Half-Lives of a Concomitant Medication Affecting CYP1A2 Activity - FAS),

        appendix=%str(15.3.4.1)

);

```

\*\*\*For table 15.2.4.63.1;

```

%t_anl_cyp(    t_name=T_15_02_04_63_01,

                l_name=L_15_04_04_63_01,

                dsin=adbx,

                conf1=%str(if anl02fl = 'Y' and dtype ne 'LOCF' and paramcd = 'CYP2A6' and base
ne . and UCPDGR1 ne '' and ((pprot1fl = 'Y' and avisitn = 106)

                or (pprot4fl = 'Y' and avisitn in (190 191)));),

                by_var1=paramn paramcd param avisitn avisit,

                t_title=%nrquote(Table 15.2.4.63.1 Analysis of CYP2A6 Activity (%) - PP Set),

                t_title_l=%nrquote(Listing 15.4.4.63.1 Analysis of CYP2A6 Activity (%) - PP Set),

                appendix=%str(15.3.6.20)

);

```

\*\*\*For table 15.2.4.63.1.1;

```

%t_anl_cyp(  t_name=T_15_02_04_63_01_01,

              l_name=L_15_04_04_63_01_01,

              dsin=adbx,

              conf1=%str(if anl03fl = 'Y' and dtype ne 'LOCF' and paramcd = 'CYP2A6' and base
ne . and UCPDGR1 ne " and ((pprot1fl = 'Y' and avisitn = 106)

              or (pprot4fl = 'Y' and avisitn = 190)));),

              by_var1=paramn paramcd param avisitn avisit,

              t_title=%nrquote(Table 15.2.4.63.1.1 Analysis of CYP2A6 Activity (%) Excluding
Assessments within 5 Half-Lives of a Concomitant Medication Affecting CYP2A6 Activity - PP Set),

              t_title_l=%nrquote(Listing 15.4.4.63.1.1 Analysis of CYP2A6 Activity (%)
Excluding Assessments within 5 Half-Lives of a Concomitant Medication Affecting CYP2A6 Activity - PP
Set),

              appendix=%str(15.3.6.20)

);

```

\*\*\*For table 15.2.4.63.2;

```

%t_anl_cyp(  t_name=T_15_02_04_63_02,

              l_name=L_15_04_04_63_02,

              dsin=adbx,

              conf1=%str(if anl02fl = 'Y' and dtype ne 'LOCF' and paramcd = 'CYP2A6' and base
ne . and UCPDGR1 ne " and ((fasfl = 'Y' and avisitn = 106)

              or (fasfl = 'Y' and avisitn in (190 191))));),

              by_var1=paramn paramcd param avisitn avisit,

              t_title=%nrquote(Table 15.2.4.63.2 Analysis of CYP2A6 Activity (%) - FAS),

              t_title_l=%nrquote(Listing 15.4.4.63.2 Analysis of CYP2A6 Activity (%) - FAS),

```

```

        appendix=%str(15.3.6.20)

);

***For table 15.2.4.63.1.2;

%t_anl_cyp(    t_name=T_15_02_04_63_02_01,

               l_name=L_15_04_04_63_02_01,

               dsin=adbx,

               conf1=%str(if anl03fl = 'Y' and dtype ne 'LOCF' and paramcd = 'CYP2A6' and base
ne . and UCPDGR1 ne '' and ((fasfl = 'Y' and avisitn = 106)

               or (fasfl = 'Y' and avisitn = 190))),

               by_var1=paramn paramcd param avisitn avisit,

               t_title=%nrquote(Table 15.2.4.63.2.1 Analysis of CYP2A6 Activity (%) Excluding
Assessments within 5 Half-Lives of a Concomitant Medication Affecting CYP2A6 Activity - FAS),

               t_title_l=%nrquote(Listing 15.4.4.63.2.1 Analysis of CYP2A6 Activity (%)
Excluding Assessments within 5 Half-Lives of a Concomitant Medication Affecting CYP2A6 Activity - FAS),

               appendix=%str(15.3.6.20)

);

proc printto ;

run;

ods path WORK.TEMPLAT(UPDATE)

SASUSER.TEMPLAT(READ)

SASHELP.TMPLMST(READ) ;

```

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\_cyp,serv=dev,covstudyid=000000106343)  
;