

```

options notes nosource;
proc datasets lib=work nolist memtype=data kill; quit;
* macro to save output and log to appropriate areas ;
%_mprintto;
%put NOTE:
=====;
%put NOTE: Covance Study Number : 000000106324;
%put NOTE: Client Protocol ID   : ZRHR-REXC-03-EU;
%put NOTE: Program Name        : d_2ADPC.sas;
%put NOTE: Purpose              : create ADPC dataset;
%put NOTE: ;
%put NOTE: Input Data           : STDLIB.ADPC SDTM.PC ADAM.PKMERGE
ADAM.ADSL SDTM.SV ADAM.ADEX ADAM.ADDX;
%put NOTE: Output               : ADAM.ADPC;
%put NOTE: Macros Called        : _MPRINTTO;
%put NOTE: ;
%put NOTE: Programmed by        : cvn_smulholl;
%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   SM        1) Add in PCHG and PCHGC;
%put NOTE: 27Jun2014   JM        2) INclude PKMERGE code in this
program;
%put NOTE: 27Jul2014   KB        3) Added in DTYPE for the BLQs;
%put NOTE: 27Jul2014   KB        4) Added a strip around PCHGC;
%put NOTE: 27Jul2014   KB        5) Amended formats of PARAM, PKDAY and
DEVN;
%put NOTE: 27Jul2014   KB        6) Removed WEIGHTBL from drop;
%put NOTE: 01AUG2014   JM        7) Fixed to not calculated chgs for
pre-baseline records ;
%put NOTE: 01AUG2014   JM        8) updated DEVWC;
%put NOTE: 13Sep2014   KB        9) Amended DEVN format;
%put NOTE: 13Sep2014   KB        10) Added ANL02FL;
%put NOTE: 13Sep2014   KB        11) Amended ABLFL;
%put NOTE: 15Sep2014   KB        12) Amended ANL02FL;
%put NOTE: 15Sep2014   KB        13) Added check for PCSTAT for ANL02FL;
%put NOTE: 15Sep2014   KB        14) Amended sorting for ANL02FL
derivation;
%put NOTE:
=====;
options notes source source2 nofullstimer validvarname=upcase missing='
';
ods _all_ close;
ods listing;

```

```

*=====;
* START OF PROGRAM CODE ;
*=====;
/*Include PKmerge program code*/
data checkarm;
    set adam.adsl(where=(armcd='SMABST'));
    keep usubjid;
run;

*code is based on pkmerge being produced prior to ADPC;
data adpc;
    merge sdtm.pc(where=(pctestcd in ('NIC' 'COT') and visit in ('DAY 5'
'DAY 6/DISCHARGE')) checkarm(in=a);
    by usubjid;
    if a then delete;          *abstinence arm not required in merge;
    length avalc units $20. param $120. PKDAY 8.; /* 5) KB 27Jul2014 */

    *results;
    aval=pcstresn;
    avalc=pcstresc;
    units=pcstresu;

    *parameter category;
    if not missing(pcstresu) then param=trim(pctest) ||'
('||trim(pcstresu)||')';
    else param=trim(pctest) ||' (ng/mL)'; * code in missing for transpose
;
    paramcd=pctestcd;

    if pctestcd='NIC' then
        paramn=1;
    else if pctestcd='COT' then
        paramn=2;
    else put 'PCTEST not recognised : ' pctestcd=;

    *treatment period;

    aperiod=1;

    *blq flag;
    if index(pcorres,'BLQ') then
        do;
            blqfl='Y';
            blqfn=1;
            aval=pcllloq/2;
        end;

    *test date and time;
    format adt date9. atm tod8. adtc $10. atmc $8.;
    adtc=compress(scan(pcdtc,1,'T'));
    atmc=compress(scan(pcdtc,2,'T'));

```

```

adt=input(adtc, yymmdd10.);

atm=input(atmc, time8.);

*visits and timepoints;
length avisit atpt $40 avisitn atptn ntime 8.;
avisit=propcase(visit);
avisitn=visitnum;

* times taken from protocol due to naimg convention in data (2h
intervals);
if upcase(pctpt)='T0 -15 MIN' then do;
    atpt='15 min < T0';
    atptn=0;
    ntime=0;
end;
else if compress(upcase(pctpt))='T1' then do;
    atpt='T0 + 2 h';
    atptn=1;
    ntime=2*60;
end;
else if compress(upcase(pctpt))='T2' then do;
    atpt='T0 + 4 h';
    atptn=2;
    ntime=4*60;
end;
else if compress(upcase(pctpt))='T3' then do;
    atpt='T0 + 6 h';
    atptn=3;
    ntime=6*60;
end;
else if compress(upcase(pctpt))='T4' then do;
    atpt='T0 + 8 h';
    atptn=4;
    ntime=8*60;
end;
else if compress(upcase(pctpt))='T5' then do;
    atpt='T0 + 10 h';
    atptn=5;
    ntime=10*60;
end;
else if compress(upcase(pctpt))='T6' then do;
    atpt='T0 + 12 h';
    atptn=6;
    ntime=12*60;
end;
else if compress(upcase(pctpt))='T7' then do;
    atpt='T0 + 14 h';
    atptn=7;
    ntime=14*60;
end;
else if compress(upcase(pctpt))='T8' then do;
    atpt='T0 + 16 h';
    atptn=8;

```

```

        ntime=16*60;
    end;
    else if compress(upcase(pctpt))='T0+20H' then do;
        atpt='T0 + 20 h';
        atptn=9;
        ntime=20*60;
    end;
    else if compress(upcase(pctpt))='T0+24H' then do;
        atpt='T0 + 24 h';
        atptn=10;
        ntime=24*60;
    end;
    else put 'Check PCTPT as unable to map: ' usubjid= avisit= pctpt=;

    * PK Day;
    pkday=1; * within period;
    aday=pcdy;

    keep studyid usubjid pcseq pcspec pcstat pcreasnd param: avisit:
    atpt: pkday aperiod aval: aday blq: pcdtc adtc atmc adt atm
        ntime pcorres pclloq units;
run;

/*merge with adsl to get demographic and treatment related variables*/
proc sort data=adpc;
    by studyid usubjid;
run;

proc sort data=adam.adsl out=adsl;
    by studyid usubjid;
run;

*bring in day 5 product use times;
data ex;
    set adam.adex(where=(avisit='Day 5' and missing(dtype)));
    by usubjid avisit;
    if first.avisit;
    keep studyid usubjid astdtm;
run;

data dx;
    set adam.addx(where=(avisit='Day 5'));
    by usubjid avisit;
    if first.avisit;
    keep studyid usubjid astdtm;
run;

data doses;
    set ex dx;
    by usubjid;
run;

data pcl;

```

```

merge adsl adpc(in=a) doses;
by studyid usubjid;
if a;

* determine dose time by period;
format dosed datetime16.;

* treatment variables ;
if aperiod=1 then do;
    dosed=astdtm;
    trta=trt01a;
    trtan=trt01an;
    trtp=trt01p;
    trtpn=trt01pn;
end;
else put 'treatment not recognised : ' subjidn=;
run;

data pc2a;
    set pc1;

    if randfl='N' then delete; *only randomised population;

    * determine actual time post dose ;
    format drawn datetime16.;

    length pcdtc1 $19.;
    pcdtc1=pcdtc;
    if not missing(pcdtc) then drawn=input(pcdtc1,e8601dt.);

    *Create missing sample data/time and missing dose data/time
flags;
    if missing(dosed) then mddtfl='Y';

    if missing(drawn) or missing(pcdtc) then msdtfl='Y';

    *calculate actual time postdose;
    if not missing(dosed) and not missing(drawn) then
pactime=round((drawn-dosed)/(60),0.0001);

    * make any corrections for BST/DST ;
    format bst2013 dst2013 datetime13. sdate wdate date9. gstime
getime time5.;

    * time of start of day light saving #place #year specific for
#study;
    * otherwise set to early fictitious dates ;
    sdate='31MAR2013'd; * BST ;
    wdate='27OCT2013'd; * DST ;

    gstime='02:00:00'T;
    getime='03:00:00'T;
    bst2013=(sdate*24*60*60)+gstime;

```

```

dst2013=(wdate*24*60*60)+gstime;

if not missing(dosed) then do;
    if drawn>bst2013 and dosed<bst2013 then do;
        * if assay time after gmt time and dosed prior to
gmt time then decrease time by 1 hour ;
        clockfl='Y';
        pactime=pactime-1*60;
    end;
    else if drawn>dst2013 and dosed<dst2013 then do;
        * if assay time after gmt time and dosed prior to
gmt time then increase time by 1 hour;
        clockfl='Y';
        pactime=pactime+1*60;
    end;
    else clockfl=' ';
end;

run;

data pc2;
    set pc2a;

    *calculate deviation and derive deviation flag;
    attrib devn format=/*8.*/BEST. pctdev /*length=8*/FORMAT=best.; /* 5)
KB 27Jul2014 */ /* 9) KB 13Sep2014 */

    if ntime > 0 then do;
        if not missing(pactime) and not missing(ntime) then do;
            ddevn=(pactime-ntime); * in hours for below;
            devn=round(pactime-ntime,0.001); * now in minutes;
            pctdev=(ddevn*100)/ntime;
        end;
    end;

    * set negative pactime values to 0 at predose ;
    if index(atpt,'15 min < T0') then do;
        devn=round(pactime-ntime,0.001);
        pctdev=.;
    end;

    *Create PKDACTIM same as PACTIME. May need to alter at later stage ;
    format pkdactim 8.;
    if atptn=0 then pkdactim=0;
    else pkdactim=pactime*60;

run;

* analysis values and flags for PK MERGE dataset;
*study specific code below about handling BLQ values ;
*Identify the BLQ value;
data pc3 blqs;
    set pc2;
    keep subjidn paramn atptn aperiod aval;
    if missing(blqfl) and not missing(aval) then output pc3;

```

```

        if not missing(blqfl) then output blqs;
run;

/* find last blq */
proc sort data=blqs out=lblq(rename=(atptn=lblqtm));
    by subjidn aperiod paramn atptn;
run;

data lblq2;
    set lblq(where=(lblqtm gt 0)) ;/* for 106324 by inspection of times
early blq between 0 and 1 ;
    by subjidn aperiod paramn lblqtm;

    check=1;
    if first.aperiod then fblqtm=lblqtm;
    retain fblqtm;
    check2=lag(check);
    checktm=lag(lblqtm);
    if (check2=1 and check=1) and (lblqtm=checktm+1) then output; /* 2
consecutive blq values after profile started */
run;

data lblq3;
    set lblq2;
    by subjidn aperiod paramn lblqtm;

    if last.aperiod ; /* assumption made that profile is single phase
and does not rise significantly */

    keep subjidn aperiod paramn lblqtm fblqtm;
run;

*Sort ;
proc sort data=pc3;
    by subjidn aperiod paramn atptn;
run;

*Take the first reading which is above BLQ and rename to first visit for
quantifiable values;
data pc3a;
    set pc3;
    by subjidn aperiod paramn atptn;

    if first.paramn;
    rename atptn=avisitnf;
    drop aval;
run;

/*Take the last reading which is above BLQ and rename to last visit for
quantifiable values*/
data pc3b;
    set pc3;
    by subjidn aperiod paramn atptn;

```

```

    lval=lag(atptn);

    if last.paramn; * last measureable value in a profile;
    rename atptn=avisitnl;
    drop aval;
run;

/*Sort the original dataset*/
proc sort data=pc2;
    by subjidn aperiod paramn atptn;
run;

*Merge and Assign flags;
data pc4;
    merge pc2(in=a) pc3a(in=b) pc3b(in=c) lblq3;
    by subjidn aperiod paramn;
    laval=lag(aval);
    pklevel=aval;

    *Create blq flags;
    if ((not missing(avisitnl) and (atptn ge avisitnl)) or (fblqtm le
atptn le lblqtm)) and blqfl='Y' then do;
        *pklevel=.; * all BLQ values to stay as 0.5*LLOQ;
        tblqfl='Y';
    end;*trailing blq flag at end of profile;

    * all blq values to stay at 0.5*llq re pkmerge requirements;
    *if atptn=0 and blqfl='Y' then pklevel=0; * re pk merge dataset
instructions for <T0;

    if index(atpt,'15 min < T0') and aval gt 0 and missing(blqfl) then
ppdosfl='Y'; *Positive value at pre-dose;

    if a and not b then fpblqfl='Y'; *full profile blq flag;

    if (atptn gt avisitnf) and (atptn le avisitnl) and blqfl='Y'
and missing(tblqfl) then do;
        eblqfl='Y';
    end; *Embedded blq flag ;

    * have non blq, quantifiable value that occurs after 2 blq
values that have occurred after 2 min for 106326 ;
    if missing(blqfl) and aval gt 0 and (not missing(lblqtm) and
atptn gt lblqtm) then do;
        *pklevel=.;* all BLQ values to stay as 0.5*LLOQ;
        lposfl='Y';
    end;*Late positive flag;
    * specific code for 106324 please remove if not this study;
    * strange profile - remove flags pending review;
    if index(usubjid,'0300') and paramcd='NIC' and tblqfl='Y'
then do;
        tblqfl=' ';
    end;

```



```

run;

proc sort data=pc4;
  by subjidn aperiod paramn avisitn;
run;

* find missing value reasons;
proc sort data=pc4(where=(not missing(pcstat))) out=reasnd(keep=pcreasnd)
nodupkey;
  by pcreasnd;
run;

data pc4a;
  set pc4;
  by subjidn aperiod paramn avisitn;
  * No result / missing sample flag ;
  if pcreasnd in ('IVR' 'NOT REPORTABLE' 'FAILED ANALYTICAL
INVESTIGATION' 'SVD' 'SVD-NICOTINE' 'SVD-COTININE') then nrfl='Y';
  else if not missing(pcreasnd) then misssfl='Y';

  if not missing(devn) then do;
    * pk group and statistics agreed that 15min window for prior to T0
still stands as per protocol - differs to SAP;

    if ntime=0 and not (-15 le devn le 0) then devnfl='Y';
    else if ntime gt 0 and abs(devn) gt 5 then devnfl='Y';

  end;

  if complfl = 'N' then withdfl='Y'; *withdrawn flag;
run;

data pc5;
  set pc4a;
run;

*get nicotine dose and unit; /*NO LONGER REQUIRED 1) SM 09Jun2014 */
/*
data ex;
  set sdtm.fa(where=(epoch='ADMI' and fatestd='NYIELD'));
  format nicu $8.;
  nicdose=fastresn;
  nicu=fastresu;
  keep usubjid nicdose nicu;
run;

data dx;
  set sdtm.dx;
  by usubjid visit;
  if visit='DAY 5' and first.visit;
  length nicu $8.;

```

```

        nicdose=0.5;  * assumption made that THS nicotine yield does not
differ between studies;
        nicu='mg';
        keep usubjid nicdose nicu;
run;

data ex1a;
    set ex dx;
run;

proc sort data=ex1a;
    by usubjid ;
run; /* /* 1) SM 09Jun2014 */

proc sort data=pc5;
    by usubjid aperiod aday;
run;

data pc6;
    /*merge*/SET pc5(in=a);* ex1a; /* 1) SM 09Jun2014 */
    by usubjid ;
    * if a; /* 1) SM 09Jun2014 */
run;

data pc7;
    set pc6;
    by usubjid aperiod pkday;

    *create pk merge specific variable;
    dosetime=0;
run;

* add onto library dataset ;
data final;
    set stdlib.pkmerge pc7;
    format pkday best12.;
run;

* check previous version to new data ;
* uncomment if not first run ;

proc sql;
    create table newpkmerge as
        select studyid, usubjid, subjidn, siteid,
            pcseq, param, paramcd, paramn, units, pcspec, pcstat,
pcreasnd ,
            avisit, avisitn, atpt, atptn, pkday, aperiod, ntime, pactime,
pkdactim, pcorres, aval, avalc, pklevel,
            fpblqfl, tblqfl, eblqfl, lposfl, ppdosfl, clockfl, devn,
pctdev, devnfl, anomfl, misssfl, nrfl,

```

```

        withdfl, aday, blqfl, blqfn, /*nicdose, nicu,*/exdose,
exdosu, pclloq, pcdtc, msdtfl, mddtfl, /* 1) SM 09Jun2014 */
        trtp, trtpn, trta, trtan, trtseqp, trtseqpn, trtseqa,
trtseqan
        from final
        order by usubjid, aperiod, paramn, avisitn, atptn;
quit;
/*End of Include PKmerge program code*/ /* 2) JM 27JUN2014*/

* pull in pkmerge data;
* for some studies this will contain only a subset of the data please
check SAP;
data pkmerge;
    set newpkmerge(rename=(param=oldparam units=avalu avalc=oldavalc
pactime=oldpactime)); /* 2) JM 27JUN2014*/
    format param /*$40.*/$120. avalc $200. pactime 8.; /* 5) KB 27Jul2014
*/
    param=trim(oldparam);
    avalc=trim(oldavalc);
    pactime=oldpactime;
    *test date and time;
    format adt date9. atm time5. adtm datetime13.;
    if not missing(pcdtc) and length(pcdtc) gt 10 then
adtm=input(pcdtc,e8601dt.);
    adt=input(scan(pcdtc,1,'T'),yymmdd10.);
    atm=input(scan(pcdtc,2,'T'),time8.);
    if avisit='Day 6' then avisit='Day 6/Discharge';
    drop studyid usubjid siteid /*weightbl*/ exdose exdosu trta: trtp:
trtseq: oldparam aday pcorres oldavalc oldpactime; /* 6) KB 27Jul2014 */
run;

* further code will be required to include cotinine data from SDTM.PC for
other studies;
* include here and then add into adpcl below;
* identify SA arm subjects;
data sa;
    set adam.adsl(where=(armcd='SMABST'));
    keep usubjid;
run;

*pick up data not used in PKmerge;
data pc;
    merge sdtm.pc sa(in=a);
    by usubjid;
    if a then sa=1;

    format avalc $200. aval best. avalu $20. param /*$40.*/$120. paramcd
$8. paramn subjidn 8.; /* 5) KB 27Jul2014 */
    subjidn=input(scan(usubjid,6,'-'),best.);

    *results;
    aval=pcstresn;
    avalc=pcstresc;

```

```

    avalu=pcstresu;

    *parameter category;
    if not missing(pcstresu) then param=trim(pctest) ||'
(|||trim(pcstresu)|||)';
    else param=trim(pctest) ||' (ng/mL)'; * code in missing for transpose
;
    paramcd=pctestcd;

    if pctestcd='NIC' then
        paramn=1;
    else if pctestcd='COT' then
        paramn=2;
    else put 'PCTEST not recognised : ' pctestcd=;

    *treatment period;
    format aperiod 8.;
    aperiod=1;

    *blq flag;
    if index(pcstresc,'BLQ') then
        do;
            blqfl='Y';
            blqfn=1;
            aval=pcilloq/2;
        end;

    *test date and time;
    format adt date9. atm tod5. adtm datetime13.;
    length pcdtc1 $19.;
    pcdtc1=pcdtc;
    if not missing(pcdtc) and length(pcdtc) gt 10 then
adtm=input(pcdtc1,e8601dt.);
    adt=input(scan(pcdtc,1,'T'),yymmdd10.);
    atm=input(scan(pcdtc,2,'T'),time8.);

    *visits and timepoints;
    format avisit atpt $40. avisitn atptn ntime 8.;
    avisit=propcase(visit);
    avisitn=visitnum;

    * times taken from protocol due to naimg convention in data (2h
intervals);
    if upcase(pctpt)='T0 -15 MIN' then do;
        atpt='15 min < T0';
        atptn=0;
        ntime=0;
    end;
    else if compress(upcase(pctpt))='T1' then do;
        atpt='T0 + 2 h';
        atptn=1;
        ntime=2*60;
    end;

```

```

else if compress(upcase(pctpt))='T2' then do;
    atpt='T0 + 4 h';
    atptn=2;
    ntime=4*60;
end;
else if compress(upcase(pctpt))='T3' then do;
    atpt='T0 + 6 h';
    atptn=3;
    ntime=6*60;
end;
else if compress(upcase(pctpt))='T4' then do;
    atpt='T0 + 8 h';
    atptn=4;
    ntime=8*60;
end;
else if compress(upcase(pctpt))='T5' then do;
    atpt='T0 + 10 h';
    atptn=5;
    ntime=10*60;
end;
else if compress(upcase(pctpt))='T6' then do;
    atpt='T0 + 12 h';
    atptn=6;
    ntime=12*60;
end;
else if compress(upcase(pctpt))='T7' then do;
    atpt='T0 + 14 h';
    atptn=7;
    ntime=14*60;
end;
else if compress(upcase(pctpt))='T8' then do;
    atpt='T0 + 16 h';
    atptn=8;
    ntime=16*60;
end;
else if compress(upcase(pctpt))='T0+20H' then do;
    atpt='T0 + 20 h';
    atptn=9;
    ntime=20*60;
end;
else if compress(upcase(pctpt))='T0+24H' then do;
    atpt='T0 + 24 h';
    atptn=10;
    ntime=24*60;
end;
else if not missing(pctpt) then put 'Check PCTPT as unable to map: '
usubjid= avisit= pctpt=;

* deviation from window;
format devn /*8.*/BEST.; /* 9) KB 13Sep2014 */
if a and avisit='Day 6/Discharge' then do; * SA arm only;
    if atm lt '08:00't then devn=(atm-'08:00't)/60;
    else if atm gt '10:00't then devn=(atm-'10:00't)/60;
    else devn=0;

```

```

end;
else do; *all other;
    if atm lt '20:00't then devn=(atm-'20:00't)/60;
    else if atm gt '22:00't then devn=(atm-'22:00't)/60;
    else devn=0;
end;

keep usubjid subjidn pcseq pcspec pcstat pcreasnd param: avisit:
atpt: aperiod aval: pcdtc adt atm adtm
    ntime pcorres pcloq devn sa blqfl;

if a and avisit in ('Day 5' 'Day 6/Discharge') then output; * SA
data not included in pkmerge;
else if not(avisit in ('Day 5' 'Day 6/Discharge')) then output; * all
other data not in Day 5 and Day 6;
run;

data adpcl;
set pkmerge pc;
format pnomtime best.;
pnomtime=ntime;
format devwc $10. /*ablfl $2.*; /* 11) KB 13Sep2014 */
*character deviation from window;
* study specific code - please check;
if not missing(devn) then do;
    if atpt='15 min < T0' /*and not (-15 le devn le 0)* / then do;
/*8) JM 01AUG2014*/
        if devn lt -15 then devwc=compress(put(devn+15,best.))||'
min';
        else if devn gt 0 then
devwc='+'||compress(put(devn,best.))||' min';
        end;
        else if not missing(atpt) then do; * REXC studies have window of
>5 min for all other timepoints;
            if not missing(devn) and devn lt 0 then
devwc=compress(put(devn,best.))||' min';
            else if devn gt 5 then devwc='+'||compress(put(devn-
5,best.))||' min';
            end;
            else if not missing(devn) then do;
                if not missing(devn) and devn lt 0 then
devwc=compress(put(devn,best.))||' min';
                else if devn gt 0 then devwc='+'||compress(put(devn-
5,best.))||' min';
                end;
            end;
end;
/* if avisit='Day 0' then ablfl='Y';*/ /* 11) KB 13Sep2014 */
run;

/* 11) START KB 13Sep2014 */
DATA SV;
SET SDTM.SV(WHERE=(VISIT=('DAY 1')));
FORMAT DAY DATE9.;

```

```

        DAY=INPUT(SCAN(SVSTDTC,1,'T'),YYMMDD10.);
        KEEP USUBJID DAY;
RUN;

DATA ABLFL;
    SET ADPC1(WHERE=(AVISIT IN ('Screening' 'Day -2' 'Day -1' 'Day 0'
'Day 1') AND PCSTAT NE 'NOT DONE'));

    KEEP USUBJID PARAMCD AVISIT ATPTN ADTM ATPT;
RUN;

PROC SORT DATA=ABLFL;
    BY USUBJID;
RUN;

DATA ABLFL2;
    MERGE ABLFL(IN=A) SV;
    BY USUBJID;
    IF A;
RUN;

DATA ADSLTM;
    SET ADAM.ADSL;
    WHERE TRT01A IN ('CC' 'THS 2.2' 'SA');

    KEEP USUBJID TRTSDTM TRT01A;
RUN;

DATA ABLFL2A;
    MERGE ABLFL2(IN=A) ADSLTM;
    BY USUBJID;
    IF A;
RUN;

PROC SORT DATA=ABLFL2A;
    BY USUBJID PARAMCD ADTM;
RUN;

DATA ABLFL3;
    SET ABLFL2A;

    IF TRT01A='SA' THEN DO;
        IF DAY NE . THEN DO;
            IF ADTM<DHMS(DAY,6,30,0) AND
INDEX(UPCASE(AVISIT),'UNSCHED')=0 AND INDEX(UPCASE(ATPT),'UNSCHED')=0
THEN ABLFL2='Y';
            END;
        ELSE IF DAY EQ . THEN DO;
            IF INDEX(UPCASE(AVISIT),'UNSCHED')=0 AND
INDEX(UPCASE(ATPT),'UNSCHED')=0 THEN ABLFL2='Y';
            END;
        END;
    ELSE IF TRT01A IN ('CC' 'THS 2.2') THEN DO;

```

```

        IF ADTM<TRTSDTM AND INDEX(UPCASE(AVISIT),'UNSCHED')=0 AND
INDEX(UPCASE(ATPT),'UNSCHED')=0 THEN ABLFL2='Y';
        END;
        ELSE IF MISSING(TRT01A) THEN DO;
            IF INDEX(UPCASE(AVISIT),'UNSCHED')=0 AND
INDEX(UPCASE(ATPT),'UNSCHED')=0 THEN ABLFL2='Y';
            END;
RUN;

PROC SORT DATA=ABLFL3(WHERE=(ABLFL2='Y')) OUT=ABLFL4;
    BY USUBJID PARAMCD ADTM;
RUN;

DATA ABLFL5(WHERE=(ABLFL='Y'));
    SET ABLFL4;
    BY USUBJID PARAMCD ADTM;
    FORMAT ABLFL $2.;

    IF LAST.PARAMCD THEN ABLFL='Y';

    KEEP USUBJID PARAMCD AVISIT ABLFL;
RUN;

PROC SORT DATA=ABLFL5;
    BY USUBJID PARAMCD AVISIT;
RUN;

PROC SORT DATA=ADPC1;
    BY USUBJID PARAMCD AVISIT;
RUN;

DATA ADPC2A;
    MERGE ADPC1 ABLFL5;
    BY USUBJID PARAMCD AVISIT;
RUN;
/* 11) END KB 13Sep2014 */

data adpc2;
    set /*adpc1*/ADPC2A; /* 11) KB 13Sep2014 */
    format bloqfl $2.;
    bloqfl=blqfl;
run;

proc sort data=adpc2;
    by subjidn pcseq;
run;

* bring in pc data for day ;
data pc;
    set sdtm.pc;

    format subjidn 8.;
    subjidn=input(scan(usubjid,6,'-'),best.);
    keep pcseq pcdy subjidn epoch;

```



```

run;

proc sort data=pc;
  by subjidn pcseq;
run;

data adpc3;
  merge pc adpc2;
  by subjidn pcseq;
run;

*bring in screening date;
data sv;
  set sdtm.sv(where=(visit='SCREENING'));
  format scrndt date9.;
  scrndt=input(svstdtc, yymmdd10.);
  format subjidn 8.;
  subjidn=input(scan(usubjid,6,'-'),best.);
  keep scrndt subjidn;
run;

* bring in adsl for T0 and subject level data;
data adsl;
  merge adam.adsl adpc3(in=a drop=usubjid) sv;
  by subjidn;
  if a;
  format anl01fl $2. aexreas $200.;
  *inclusion in summary tables and figures;
  if fasfl='Y' then anl01fl='Y'; * to be amended after lock in ADSL;
  if fasfl='N' then aexreas=trim(fasreas); * SAP section 12.6.2.2;

  format aperiodc $10.;
  aperiodc='Period '||compress(put(aperiod,1.));

  format trta trtp $40. trtan trtpn 8.;

  if aperiod=1 then do;
    trta=trt01a;
    trtp=trt01p;
    trtan=trt01an;
    trtpn=trt01pn;
  end;
run;

*need first product use dates and times;
*included all so that there is needed;
data exdx;
  set adam.adex adam.addx;
  if astday ge 0;
  keep subjidn astdt astdtm astday;
run;

proc sort data=exdx;

```

```

    by subjidn astday astdtm;
run;

data exdx2;
    set exdx;
    by subjidn astday;
    if first.astroday;
run;

proc transpose data=exdx2 out=teidx prefix=tr;
    var astdtm;
    by subjidn;
    id astroday;
run;

data adpc4;
    merge adsl(in=a) teidx;
    by subjidn;
    if a;
    format aday 8.;
    aday=adt-trtsdt+1;

    * windows;
    if aperiod=1 and not missing(tr5) then trtstart=tr5;* specific for
REXC where pkday = day 5;
    format awlo awhi datetime13. awrange $50.;
    if not missing(trtstart) and avisit in ('Day 5' 'Day 6/Discharge')
then do;
    if atptn=0 then do;
        awlo=trtstart-'00:15't;
        awhi=trtstart;
    end;
    else if atptn=1 then do; /* 2 h */
        awlo=trtstart+'02:00't;
        awhi=trtstart+'02:05't;
    end;
    else if atptn=2 then do; /* 4 h */
        awlo=trtstart+'04:00't;
        awhi=trtstart+'04:05't;
    end;
    else if atptn=3 then do; /* 6 h */
        awlo=trtstart+'06:00't;
        awhi=trtstart+'06:05't;
    end;
    else if atptn=4 then do; /* 8 h */
        awlo=trtstart+'08:00't;
        awhi=trtstart+'08:05't;
    end;
    else if atptn=5 then do; /* 10 h */
        awlo=trtstart+'10:00't;
        awhi=trtstart+'10:05't;
    end;
    else if atptn=6 then do; /* 12 h */
        awlo=trtstart+'12:00't;

```

```

        awhi=trtstart+'12:05't;
    end;
    else if atptn=7 then do; /* 14 h */
        awlo=trtstart+'14:00't;
        awhi=trtstart+'14:05't;
    end;
    else if atptn=8 then do; /* 16 h */
        awlo=trtstart+'16:00't;
        awhi=trtstart+'16:05't;
    end;
    else if atptn=9 then do; /* 20 h */
        awlo=trtstart+'20:00't;
        awhi=trtstart+'20:05't;
    end;
    else if atptn=10 then do; /* 24 h */
        awlo=trtstart+'24:00't;
        awhi=trtstart+'24:05't;
    end;
    end; * of trtstart;
    else if missing(atpt) then do;
        if avisit='Day 6/Discharge' then do;
            awlo=dhms(adl,8,0,0);
            awhi=dhms(adl,10,0,0);
        end;
        else do;
            awlo=dhms(adl,20,0,0);
            awhi=dhms(adl,22,0,0);
        end;
    end;

    end;
    if not missing(awlo) then awrange=put(awlo,datetime16.) || '-
'||put(awhi,datetime16.);
run;

```

```

/* 3) START KB 27Jul2014 */
DATA DUPLIT_;
    SET ADPC4;
    WHERE BLOQFL='Y';
    FORMAT DTYPE $20.;
    AVAL = 0.5 * PCLLOQ;
    AVALC=COMPRESS(PUT(AVAL,BEST.));
    DTYPE='BLQHALF';
    AQLFL = 'Y';
    DROP PCLLOQ PCSEQ PCDTC PCSPEC PCORRES PCDY;
RUN;

```

```

DATA ADPC4A;
    SET ADPC4(IN=A) DUPLIT_ ;
    FORMAT ANL01FL $2.;
    IF A AND AVALC='BLQ' THEN CALL MISSING (AVAL, ANL01FL);

    IF AVALC='BLQ' AND ABLFL='Y' THEN ABLFL='';
RUN;
/* 3) END KB 27Jul2014 */

```

```

*change from baseline;
proc sort data=/*adpc4*/ADPC4A; /* 3) KB 27Jul2014 */
  by subjidn paramn avisitn atptn;
run;

data base(rename=(aval=base));
  set /*adpc4*/ADPC4A(where=(ablfl='Y')); /* 3) KB 27Jul2014 */
  keep subjidn paramn aval;
run;

data change;
  merge /*adpc4*/ADPC4A base; /* 3) KB 27Jul2014 */
  by subjidn paramn;
  format chg pchg best. pchgc $20.;
  chg=aval-base;
  PCHG=(CHG/BASE)*100; /* 1) SM 16Jun2014 */
  PCHGC=STRIP(PUT(ROUND(PCHG,0.1),8.1)); /* 1) SM 16Jun2014 */ /* 4)
KB 27Jul2014 */
run;

/* 10) START KB 13Sep2014 */
DATA CHANGE2;
  SET CHANGE;
/* 12) KB 15Sep2014 */
  IF AVISIT='Day 5' AND PCSTAT NE 'NOT DONE' THEN DO;
/* 12) START KB 15Sep2014 */
/* 12) IF DHMS(ADT,20,0,0)<=ADTM<=DHMS(ADT,21,30,0) THEN
ANL02FL='Y';*/
/* 12) IF AVALC='BLQ' THEN ANL02FL='';*/

  DEVTIME=ADTM-DHMS(ADT,20,0,0);
  IF DEVTIME LT 0 THEN DEVTIME=-1*DEVTIME;
/* 12) END KB 15Sep2014 */
  END;
RUN;
/* 10) END KB 13Sep2014 */

/* 12) START KB 15Sep2014 */
PROC SORT DATA=CHANGE2(WHERE =(NOT MISSING(DEVTIME))); /* 14) KB
15Sep2014 */
  BY SUBJIDN PARAMN AVISITN DEVTIME DESCENDING DTYPE;
RUN;

DATA CHANGE3(WHERE=(ANL02FL='Y')); /* 14) KB 15Sep2014 */
  SET CHANGE2;
  BY SUBJIDN PARAMN AVISITN DEVTIME DESCENDING DTYPE;
  FORMAT ANL02FL $2.;

  IF FIRST.AVISITN AND AVISIT='Day 5' AND PCSTAT NE 'NOT DONE' THEN
ANL02FL='Y'; /* 13) KB 15Sep2014 */

```

```

        KEEP USUBJID ANL02FL AVISITN AVISIT ATPTN ATPT PARAMCD DTYPE; /* 14)
KB 15Sep2014 */
RUN;
/* 12) END KB 15Sep2014 */

/* 14) START KB 15Sep2014 */
PROC SORT DATA=CHANGE;
    BY USUBJID PARAMCD AVISITN AVISIT ATPTN ATPT DTYPE;
RUN;

PROC SORT DATA=CHANGE3;
    BY USUBJID PARAMCD AVISITN AVISIT ATPTN ATPT DTYPE;
RUN;

DATA CHANGE4;
    MERGE CHANGE CHANGE3;
    BY USUBJID PARAMCD AVISITN AVISIT ATPTN ATPT DTYPE;
RUN;
/* 14) END KB 15Sep2014 */

proc sql noprint;
    select name into: keepvars separated by " " from sashelp.vcolumn
where libname = "STDLIB" and memname = "ADPC";
quit;

options replace;

data adpc;
    set stdlib.adpc /*change*//*CHANGE2*//*CHANGE3*/CHANGE4; /* 10) KB
13Sep2014 */ /* 12) KB 15Sep2014 */ /* 14) KB 15Sep2014 */
    if pcstat ne 'NOT DONE' and adtm<=TRTSDTM then call missing(chg,
pchgc, pchgc); /*7) JM 01AUG2014*/
    if missing(atpt) then call missing(DEVN, DEVWC); /*8) JM
01AUG2014*/
    format PKDAY 8.;
    keep &keepvars;
run;

proc sort data = adpc out = adam.adpc(label= 'Pharmacokinetic
Concentration Analysis Dataset');
    by USUBJID APERIOD AVISITN PARAMCD ATPTN PCSEQ DTYPE;
run;

proc printto; run;
*=====;
* END OF PROGRAM CODE;
*=====;

```