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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_2ADBX.sas;
%put NOTE: Purpose : create ADBX dataset;
%put NOTE: ;
%put NOTE: Input Data : STDLIB.ADBX SDTM.LB SDTM.SUPPLB
ADAM.ADSL;
%put NOTE: Output : ADAM.ADBX;
%put NOTE: Macros Called : _MPRINTTO _MTOTPER _MPERALL _SCRAMBLE
CYP2A6 COUGH COHB UVOL CYP1A2 NEQ BIOM RISK;
%put NOTE: ;
%put NOTE: Programmed by : cvn_kbooth;
%put NOTE: Creation Date : 2014-05-02;
%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()),
e8601lz.));
%put NOTE: ;
%put NOTE: == Modification History
=====;
%put NOTE: Date Initials No. Reason;
%put NOTE: 13May2014 KB 1) Amended PARAMNs;
%put NOTE: 13May2014 KB 2) Amended BLQ values;
%put NOTE: 14May2014 KB 3) Amended repeats message in log;
%put NOTE: 14May2014 KB 4) Added apostrophe to TRANS3H test;
%put NOTE: 14May2014 KB 5) Amended truncation in PARAM for
NNAL;
%put NOTE: 14May2014 KB 6) Amended PARAMNs to match spec;
%put NOTE: 15May2014 KB 7) Amended PARCAT2 for CO and COHb;
%put NOTE: 15May2014 KB 8) Amended PARAM for UTRANSHY;
%put NOTE: 15May2014 KB 9) Amended PCHGC dp;
%put NOTE: 15May2014 KB 10) Removed reference to ASTDTM and
ASTDT;
%put NOTE: 15May2014 KB 11) Amended dataset reference;
%put NOTE: 15May2014 KB 12) Amended PBASE for subjects with
missing TRTSDTM;
%put NOTE: 15May2014 KB 13) AMended BASETYPE;
%put NOTE: 15May2014 KB 14) Amended ANL01FL for urine;
%put NOTE: 15May2014 KB 15) Removed avisit for PBASE
derivation;
%put NOTE: 16May2014 KB 16) Removed PBASE and ABLFL for LBALLs;
%put NOTE: 16May2014 KB 17) Added in new parameter for
biomarkers not done;

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%put NOTE: 16May2014	KB	18) Removed condition from AENDTM to populate for non missing LBENDTC;
%put NOTE: 01Jun2014	KB	19) Amended issue with missing units on parameter for NOT DONE tests;
%put NOTE: 01Jun2014	KB	20) Amended AQLFL for derived parameters;
%put NOTE: 02Jun2014	KB	21) Amended datasets due to updating windows for urine data and added windows to original urine data;
%put NOTE: 02Jun2014	KB	22) Added windows to CYP data;
%put NOTE: 03Jun2014	KB	23) Amended windows for CYP2A6 data;
%put NOTE: 03Jun2014	KB	24) Amended dataset label;
%put NOTE: 03Jun2014	KB	25) Amended formats of AVALC, ANRIND, ANRLO, ANRHI, ANL01FL and ANL02FL to match spec;
%put NOTE: 03Jun2014	KB	26) Amended TRANS3H PARAM;
%put NOTE: 04Jun2014	KB	27) Amended PARCAT2N for 24H URINE SAMPLE and amended LBALL tests for 24H URINE SAMPLE;
%put NOTE: 05Jun2014	KB	28) Amended ANL01FL for non-derived biomarkers;
%put NOTE: 05Jun2014	KB	29) Amended PCHG for biomarkers;
%put NOTE: 05Jun2014	KB	30) Amended ANL02FL for NOT DONE tests;
%put NOTE: 06Jun2014	KB	31) Added deviations for biomarker and CYP data;
%put NOTE: 06Jun2014	KB	32) Amended AEOEFL to only populate tests that are done;
%put NOTE: 09Jun2014	KB	33) Amended ANL01FL for urine data to refer to correct variables;
%put NOTE: 09Jun2014	KB	34) Removed LBENDTC for derived parameters;
%put NOTE: 09Jun2014	KB	35) Removed update 14;
%put NOTE: 09Jun2014	KB	36) Amended units for some biomarkers;
%put NOTE: 21Jun2014	KB	37) Amended PARAMNs;
%put NOTE: 21Jun2014	KB	38) Amended units for secondary biomarkers;
%put NOTE: 21Jun2014	KB	39) Amended UVOL to VOLUME due to change in SDTM and removed _ from PARAMCDs;
%put NOTE: 21Jun2014	KB	40) Amended informat error in log;
%put NOTE: 21Jun2014	KB	41) Amended AVALU for UNEQCRE;
%put NOTE: 21Jun2014	KB	42) Amended Day 6 due to change in visit structure;
%put NOTE: 22Jun2014	KB	43) AMended PARAM for PARAMN=65;
%put NOTE: 22Jun2014	KB	44) Added AMES 24 hour results;
%put NOTE: 22Jun2014	KB	45) Amended baseline for subject 55 MHBMA;
%put NOTE: 23Jun2014	KB	46) AMended data as per client comments;
%put NOTE: 23Jun2014	KB	47) Amended ABLFL for subject 55 MHBMA;
%put NOTE: 23Jun2014	KB	48) Added EXNOTRFL to the keep;
%put NOTE: 23Jun2014	KB	49) Amended PARAMNs for NEQ24U and NEQCRE;
%put NOTE: 24Jun2014	KB	50) Amended format of APERIODC and AVISITN;
%put NOTE: 24Jun2014	KB	51) Amended units of NEQCRE;
%put NOTE: 24Jun2014	KB	52) Amended warning regarding USUBJID length for merge;

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%put NOTE: 24Jun2014    KB    53) Amended rounding for derived
biomarkers;
%put NOTE: 31Jul2014    KB    54) Amended issue with missing BLQs;
%put NOTE: 31Jul2014    KB    55) Moved if condition;
%put NOTE: 01Aug2014    KB    56) Added to update 47;
%put NOTE: 01Aug2014    KB    57) Removed ANL01FL for records missing
AWHI;
%put NOTE: 01Aug2014    KB    58) Removed ABLFL for enrolled not
randomized subjects;
%put NOTE: 01Aug2014    KB    59) Added check to make sure AVAL and
AVALC are equal;
%put NOTE: 11Sep2014    KB    60) Amended PBASE to PBASEFL;
%put NOTE: 11Sep2014    KB    61) Amended PARAM for TRANS3H;
%put NOTE: 11Sep2014    KB    62) Amended ABLFL;
%put NOTE: 11Sep2014    KB    63) Removed study specific code from
previous run;
%put NOTE: 11Sep2014    KB    64) Amended DEVN & DEVWC;
%put NOTE: 11Sep2014    KB    65) Removed round function when
deriving base;
%put NOTE: 15Sep2014    KB    66) Amended PARAM for UFTRANSC and
UFTRANSH;
%put NOTE: 16Sep2014    KB    67) Amended PBASEFL;
%put NOTE: 16Sep2014    KB    68) Amended PBASEFL for CO 15 min prior
to T0;
%put NOTE: 17Sep2014    KB    69) Added code to fix an OpenCDISC
issue with one subjects CHG;
%put NOTE: 17Sep2014    KB    70) Amended PBASEFL to flag for greater
than or equal to trtsdtm and 06:30;
%put NOTE: 15Oct2014    KB    71) Amended AVALC issues;
%put NOTE: 15Oct2014    KB    72) Amended CHGC and PCHGC issues;
%put NOTE: 15Oct2014    KB    73) Added LBSEQ to key variables;
%put NOTE: 15Oct2014    KB    74) Added check on AVAL and AVALC due
to mismatches in AVAL in compare;
%put NOTE: 08Sep2015    JM    75) Added parameter BAP and derviation
parameters;
%put NOTE:
=====;
options notes source source2 nofullstimer validvarname=upcase missing='
';
ods _all_ close;
ods listing;

*=====;
* START OF PROGRAM CODE                                     ;
*=====;
%cyp2a6;
%cough;
%cohb;
%uvol;
%cypla2;
%neq;
%biom;
%risk;
%AMES; /* 44) KB 22Jun2014 */

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data all;
    set cyp2a lb_co8 lb_cohb7 lb_uvol5 cypdata3 /*neq5*/NEQ6
/*bioall12*/BIOALL3 /*riskall12*/RISKALL3 AMESALL3; /* 11) KB 15May2014 */
/* 16) KB 02Jun2014 */ /* 44) KB 22Jun2014 */
run;

proc sort data=all;
    by usubjid lbtestcd lbtest visitnum lbtpt;
run;

*****;
* bring in ADSL ;
*****;

data adsl;
    set adam.adsl;
    keep studyid usubjid subjid: siteid age sex: race height weightbl
bmi ucpdgr1 ucpdgrln nicogr1 nicogrln targr1 targrln
        enrfl scrffl complfl saffl fasfl pprotfl randfl trt: dthfl
enfl exfl fupfl cobl EXNOTRFL; /* 48) KB 23Jun2014 */
run;

*****;
* bring in SUPPLB ;
*****;

data supplb;
    set sdtm.supplb;
    attrib qval2 format=$2. USUBJID2 LENGTH=$24; /* 52) KB 24Jun2014 */

    qval2=qval;
    USUBJID2=USUBJID; /* 52) KB 24Jun2014 */
    RENAME USUBJID2=USUBJID; /* 52) KB 24Jun2014 */
    drop qval USUBJID; /* 52) KB 24Jun2014 */
run;

proc transpose data=supplb out=supplb2(drop = _:);
    var qval2;
    by usubjid idvarval;
    id qnam;
    idlabel qlabel;
run;

data supplb3(drop = idvarval);
    set supplb2;
    lbseq = input(idvarval, best.);
run;

proc sort data=supplb3;
    by usubjid lbseq;
run;

*****;

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* bring in LB      ;
*****;

*select relevant safety data only ;
proc sort data = sdtm.lb out = lb(where = (lbcat in ('BIOMARKERS' 'ENZYME
ACTIVITY')));
    by usubjid lbtestcd lbtest visitnum lbtpt;
run;

* check parameters and units to SAP;
* all original and standardised units match so only keep 1 set of data ;
proc sort data = lb out=lbchk(keep = lbcat lbscat lbtestcd lbtest
lborresu lbstresu) nodupkey;
    by lbcat lbscat lbtestcd lbtest lborresu lbstresu;
run;

* check for unscheduled observations;
proc sort data = lb(where = (index(upcase(visit),'UNSCHEDULED')) out =
uns nodupkey;
    by usubjid visitnum visit lbtpt lbtptnum lbdtc;
run;

*Check that all data in LB is captured in biomarker macros;
data lbbio lbbio2 lbbio2a;
    merge all(in=a) lb(in=b);
    by usubjid lbtestcd lbtest visitnum lbtpt;

    if a and b then output lbbio;
    else if b and not a then output lbbio2;
    else if a and not b then output lbbio2a;
run;

data lbbio3;
    set lbbio lbbio2 lbbio2a;
run;

/* 46) START KB 23Jun2014 */
DATA LBBIO4;
    SET LBBIO3(WHERE=(LBTESTCD IN ('S_BMA' 'HEMA' 'MHBMA' 'S_PMA') AND
LBSTAT NE 'NOT DONE'));

    IF INDEX(LBSTRESC,'BLQ')=0 THEN DO;

LBSTRESN=ROUND(LBSTRESN*1000,/*0.000000000000000001*/0.000000000000000000
0000000000001); /* 53) KB 24Jun2014 */ /* 71) KB 15Oct2014 */
    LBSTRESC=STRIP(PUT(LBSTRESN,BEST32.));
    END;
    IF INDEX(LBSTRESC,'BLQ') THEN DO;
        LBSTRESN =
(INPUT(TRANWRD(SCAN(LBSTRESC,2,'(',')',''),BEST.)*1000)/2;
        LBSTRESC
=STRIP('BLQ('&') || STRIP(PUT(LBSTRESN*2,BEST.)) || STRIP('&')');
    END;
    LBTESTCD=STRIP('D') || STRIP(LBTESTCD);

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PARAMTYP='DERIVED';
DTYPE='FUNCTION';

LBSTRESU=STRIP('pg/mL');

KEEP STUDYID USUBJID VISITNUM VISIT LBDTC LBENDTC LBTPT LBSTRESU
LBCAT LBSCAT LBTESTCD LBSTRESN LBSTRESC LBTEST PARAMTYP DTYPE;
RUN;

DATA LBBIO5;
    SET LBBIO3 LBBIO4;
RUN;
/* 46) END KB 23Jun2014 */

proc sort data=/*lbbio3*/LBBIO5; /* 46) KB 23Jun2014 */
    by usubjid lbseq;
run;

* combine with supplb ;
data lb2;
    merge /*lbbio3*/LBBIO5(in = a) supplb3;    /* 46) KB 23Jun2014 */
    by usubjid lbseq;
    if a;

    format paramcd $8. parcat1 parcat2 $80. avisit avalcat1 $40. param
$200. paramn parcat1n parcat2n 8. aval /*AVISITN*/ /*best.*/BEST32.
AVISITN 8.    /* 25) KB 03Jun2014 */ /* 50) KB 24Jun2014 */ /* 53) KB
24Jun2014 */
    avalc $200. anrind anrlo anrhi /*$40.*/$50. adt date9. adm
datetime13. atm time5. bloqfl aulqfl aqlfl $2. atoxgr $20. avalu $40.; /*
25) KB 03Jun2014 */

    * Parameter variables;
    if index(lbtest,'CYP2A6')=0 and index(lbtest,'CYP1A2')=0 then do;
        param=left(trim(lbtest));
    end;
    else do;
        param=left(trim(lbtest));
    end;
    if index(lbtestcd,'-') then lbtestcd=compress(lbtestcd,'-');
    IF INDEX(LBTESTCD,'_') THEN LBTESTCD=COMPRESS(LBTESTCD,'_'); /* 39)
KB 21Jun2014 */
    paramcd=lbtestcd;
    if paramcd in ('3HPMACRE' '3HPMA24U' 'HMPMACRE' 'HMPMA24U' 'MHBMACRE'
'MHBM24U' 'TXB2_D11') then do;
        paramcd=tranwrd(paramcd,'3HPMACRE','3HPMCRE');
        paramcd=tranwrd(paramcd,'3HPMA24U','3HPM24U');
        paramcd=tranwrd(paramcd,'HMPMACRE','HMPMCRE');
        paramcd=tranwrd(paramcd,'HMPMA24U','HMPM24U');
        paramcd=tranwrd(paramcd,'MHBMACRE','MHBMCRE');
        paramcd=tranwrd(paramcd,'MHBM24U','MHBM24U');
        paramcd=tranwrd(paramcd,'TXB2_D11','TXB2D11');
    end;

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/* 46) START KB 23Jun2014 */
  IF PARAMCD IN ('HEMA' 'SBMA' 'SPMA' 'MHBMA') THEN DO;
    PARAMCD=STRIP('O') || STRIP(LBTESTCD);
  END;
  IF PARAMCD IN ('HEMA' 'DSBMA' 'DSPMA' 'DMHBMA') THEN DO;
    PARAM=STRIP(PARAM) || ' ' || STRIP('(Derived)');
  END;
/* 46) END KB 23Jun2014 */
  if paramcd not in ('CO' 'CARBXHGB' /*'UVOL'*/'VOLUME' 'COT'
'COTININE' 'TRANS3H' 'CYP2A6' 'HCOT' 'CAF' 'CAFFEINE' 'PXC' 'PX' 'CYP1A2'
'LBALL' 'CREAT') then do; /* 39) KB 21Jun2014 */
    paramcd=strip('U') || strip(paramcd);
  end;
  parcat1=lbcats;
  parcat2=lbscats;

  if paramcd = 'LBALL' then do;
    if parcat2 ne '' then do;
      param = strip(param) || ' (' || strip(parcat2) || ')';
    end;
  else do;
    param = strip(param) || ' (' || strip(parcat1) || ')';
  end;
  paramcd = substr(parcat1,1,1) || strip(paramcd);
  if parcat2='CYTOCHROME 2A6' then do;
    paramcd=strip(paramcd) || '1';
  end;
  else if parcat2='CYTOCHROME 1A2' then do;
    paramcd=strip(paramcd) || '2';
  end;
end;

  IF INDEX(PARAM,'(BIOMARKERS OF EXPOSURE)') THEN PARAMCD='BELBALL'; /*
17) KB 16May2014 */
  IF INDEX(PARAM,'(24H URINE SAMPLE)') THEN PARAMCD='ULBALL'; /* 27) KB
04Jun2014 */

  if paramcd='CO' then paramn=1;
  else if paramcd='CARBXHGB' then paramn=2;
  else if paramcd='COTININE' then paramn=3;
  else if paramcd='TRANS3H' then paramn=4;
  else if paramcd='CYP2A6' then paramn=5;
  else if paramcd='COT' then paramn=6;
  else if paramcd='HCOT' then paramn=7;
  else if paramcd=/*'UVOL'*/'VOLUME' then paramn=8; /* 39) KB 21Jun2014
*/
/* 37) START KB 21Jun2014 */
  else if paramcd='U1NA' then paramn=/*10*/9;
  else if paramcd='U1NACRE' then paramn=/*11*/10;
  else if paramcd='U1NA24U' then paramn=/*12*/11;
  else if paramcd='U1OHP' then paramn=/*13*/12;
  else if paramcd='U1OHPCRE' then paramn=/*14*/13;
  else if paramcd='U1OHP24U' then paramn=/*15*/14;
  else if paramcd='U2NA' then paramn=/*16*/15;

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else if paramcd='U2NACRE' then paramn=/*17*/16;
else if paramcd='U2NA24U' then paramn=/*18*/17;
else if paramcd='U3HPMA' then paramn=/*19*/18;
else if paramcd='U3HPMCRE' then paramn=/*20*/19;
else if paramcd='U3HPM24U' then paramn=/*21*/20;
else if paramcd='U4ABP' then paramn=/*22*/21;
else if paramcd='U4ABPCRE' then paramn=/*23*/22;
else if paramcd='U4ABP24U' then paramn=/*24*/23;
else if paramcd='UCEMA' then paramn=/*25*/24;
else if paramcd='UCEMACRE' then paramn=/*26*/25;
else if paramcd='UCEMA24U' then paramn=/*27*/26;
else if paramcd='UCOTG' then paramn=/*28*/27;
else if paramcd='UCOTGC' then paramn=/*29*/28;
else if paramcd='CREAT' then paramn=/*30*/29;
else if paramcd='UFCOT' then paramn=/*31*/30;
else if paramcd='UFCOTC' then paramn=/*32*/31;
else if paramcd='UFNIC' then paramn=/*33*/32;
else if paramcd='UFNICC' then paramn=/*34*/33;
else if paramcd='UFTRANSC' then paramn=/*35*//*36*/34; /* 6) KB
14May2014 */
else if paramcd='UFTRANSH' then paramn=/*36*/35; /* 6) KB 14May2014
*/
else if paramcd=/'UHEMA'/'UOHEMA' then paramn=/*37*/36; /* 46) KB
23Jun2014 */
/* 46) START KB 23Jun2014 */
ELSE IF PARAMCD='UDHEMA' THEN PARAMN=37;
else if paramcd='UHEMACRE' then paramn=/*38*//*37*/38;
else if paramcd='UHEMA24U' then paramn=/*39*//*38*/39;
else if paramcd='UHMPMA' then paramn=/*40*//*39*/40;
else if paramcd='UHMPMCRE' then paramn=/*41*//*40*/41;
else if paramcd='UHMPM24U' then paramn=/*42*//*41*/42;
else if paramcd=/'UMHBMA'/'UOMHBMA' then paramn=/*43*//*42*/43;
ELSE IF PARAMCD='UDMHBMA' THEN PARAMN=44;
else if paramcd='UMHBMCRE' then paramn=/*44*//*43*/45;
else if paramcd='UMHBM24U' then paramn=/*45*//*44*/46;
else if paramcd='UNEQ24U' then paramn=/*46*//*47*//*46*//*47*/48; /*
1) KB 13May2014 */ /* 49) KB 23Jun2014 */
else if paramcd='UNEQCRE' then paramn=/*47*//*46*//*45*//*48*/47; /*
1) KB 13May2014 */ /* 49) KB 23Jun2014 */
else if paramcd='UNICG' then paramn=/*48*//*47*/49;
else if paramcd='UNICGC' then paramn=/*49*//*48*/50;
else if paramcd='UNNAL' then paramn=/*50*//*49*/51;
else if paramcd='UNNALCRE' then paramn=/*51*//*50*/52;
else if paramcd='UNNAL24U' then paramn=/*52*//*51*/53;
else if paramcd='UNNN' then paramn=/*53*//*52*/54;
else if paramcd='UNNNCRE' then paramn=/*54*//*53*/55;
else if paramcd='UNNN24U' then paramn=/*55*//*54*/56;
else if paramcd='UOTOL' then paramn=/*56*//*55*/57;
else if paramcd='UOTOLCRE' then paramn=/*57*//*56*/58;
else if paramcd='UOTOL24U' then paramn=/*58*//*57*/59;
else if paramcd=/'USBMA'/'UOSBMA' then paramn=/*59*//*58*/60;
ELSE IF PARAMCD='UDSBMA' THEN PARAMN=61;
else if paramcd='USBMACRE' then paramn=/*60*//*59*/62;
else if paramcd='USBMA24U' then paramn=/*61*//*60*/63;

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else if paramcd=/'USPMA'/'UOSPMA' then paramn=/'62*//*61*/64;
ELSE IF PARAMCD='UDSPMA' THEN PARAMN=65;
else if paramcd='USPMACRE' then paramn=/'63*//*62*/66;
else if paramcd='USPMA24U' then paramn=/'64*//*63*/67;
else if paramcd='UTRANSHC' then paramn=/'65*//*64*/68;
else if paramcd='UTRANSHY' then paramn=/'66*//*65*/69;
else if paramcd='UAMES' then paramn=/'67*//*66*/70;
    ELSE IF PARAMCD='UBAP' THEN PARAMN=111; /*75) JM 08SEP2015*/
ELSE IF PARAMCD='UBAPCRE' THEN PARAMN=112; /*75) JM 08SEP2015*/
ELSE IF PARAMCD='UBAP24U' THEN PARAMN=113; /*75) JM 08SEP2015*/

/* 44) START KB 22Jun2014 */
ELSE IF PARAMCD='UAMES24U' THEN PARAMN=/'67*/71;
else if paramcd='UPGF2A' then paramn=/'68*//*67*//*68*/72;
else if paramcd='UPGF2CRE' then paramn=/'69*//*68*//*69*/73;
else if paramcd='UPGF224U' then paramn=/'70*//*69*//*70*/74;
else if paramcd='UTXB2D11' then paramn=/'71*//*70*//*71*/75;
else if paramcd='UTXB2CRE' then paramn=/'72*//*71*//*72*/76;
else if paramcd='UTXB224U' then paramn=/'73*//*72*//*73*/77;
else if paramcd='CAF' then paramn=/'74*//*73*//*74*/78;
else if paramcd='CAFFEINE' then paramn=/'75*//*74*//*75*/79;
else if paramcd='CYP1A2' then paramn=/'76*//*75*//*76*/80;
else if paramcd='PX' then paramn=/'77*//*76*//*77*/81;
else if paramcd='PXC' then paramn=/'78*//*77*//*78*/82;
/* 46) END KB 23Jun2014 */
/* 37) END KB 21Jun2014 */
/* 44) END KB 22Jun2014 */
ELSE IF PARAMCD='ULBALL' THEN PARAMN=94; /* 27) KB 04Jun2014 */
else if paramcd='ELBALL1' then paramn=95;
else if paramcd='ELBALL2' then paramn=96;
ELSE IF PARAMCD='BELBALL' THEN PARAMN=97; /* 17) KB 16May2014 */
else if paramcd='BLBALL' then paramn=98;
else if paramcd='LBALL' then paramn=99;
else put "USER WA" "RNING: Check PARAMCDs " paramcd;

/* 7) START KB 15May2014 */
IF PARAMCD IN ('CO' 'CARBXHGB') THEN DO;
    PARCAT2='BIOMARKERS OF EXPOSURE';
END;
/* 7) END KB 15May2014 */

if parcat1='BIOMARKERS' then parcat1n=1;
if parcat1='ENZYME ACTIVITY' then parcat1n=2;
if parcat2='BIOMARKERS OF EXPOSURE' then parcat2n=1;
if parcat2='CYTOCHROME 2A6' then parcat2n=2;
if parcat2='CYTOCHROME 1A2' then parcat2n=3;
IF PARCAT2='24H URINE SAMPLE' THEN PARCAT2N=4; /* 27) KB 04Jun2014
*/

    * analysis variables ;
    aval = lbstresn;
    if index(lbstresc, 'BLQ')=0 then avalc = propcase(lbstresc);
/*    if not missing(aval) and index(avalc, 'BLQ')=0 then
aval=input(avalc,best32.);*/

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ELSE AVALC=STRIP(LBSTRESC); /* 54) KB 31Jul2014 */
if paramcd='COT' then avalu=strip('nmol/L');
else if paramcd='HCOT' then avalu=strip('nmol/L');
else if paramcd='CYP2A6' then avalu=strip('%');
else if paramcd='CAF' then avalu=strip('nmol/L');
else if paramcd='PXC' then avalu=strip('nmol/L');
else if paramcd='CYP1A2' then avalu=strip('%');
ELSE IF PARAMCD='UNEQCRE' THEN AVALU=STRIP('/*mg / mg/dL
creat'*/'/*Âµg/mg creat'*/'mg/g creat'); /* 41) KB 21Jun2014 */ /* 46)
KB 23Jun2014 */ /* 51) KB 24Jun2014 */
else if paramcd in ('U1NACRE' 'U1OHPCRE' 'U2NACRE' 'U4ABPCRE'
'UNNALCRE' 'UNNNCRE' 'UOTOLCRE' 'UPGF2CRE' 'UTXB2CRE') then
avalu=strip('/*pg/mL / mg/dL creat'*/'pg/mg creat'); /* 38) KB 21Jun2014
*/
else if paramcd in ('/*U3HPMCRE'*/ 'UCEMACRE' /*'UHEMACRE'*/
'UHMPMCRE' /*'UMHBMCRE'*/ /*'USBMACRE'*/ /*'USPMACRE'*/) then
avalu=strip('/*ng/mL / mg/dL creat'*/'ng/mg creat'); /* 36) KB 09Jun2014
*/ /* 38) KB 21Jun2014 */ /* 46) KB 23Jun2014 */
ELSE IF PARAMCD IN ('U3HPMCRE' /*'UMHBMCRE' 'USPMACRE'*/) THEN
AVALU=STRIP('ng/mg creat'); /* 36) KB 09Jun2014 */ /* 46) KB 23Jun2014
*/
else if paramcd in ('U1NA24U' 'U1OHP24U' 'U2NA24U' 'U4ABP24U'
'UNNAL24U' 'UNNN24U' 'UOTOL24U' 'UPGF224U' 'UTXB224U') then
avalu=strip('/*pg'*/'ng'); /* 38) KB 21Jun2014 */
else if paramcd in ('/*U3HPM24U'*/ 'UCEMA24U' /*'UHEMA24U'*/
'UHMPM24U' /*'UMHBM24U'*/ /*'USBMA24U'*/ /*'USPMA24U'*/) then
avalu=strip('/*ng'*/'Âµg'); /* 36) KB 09Jun2014 */ /* 38) KB 21Jun2014
*/ /* 46) KB 23Jun2014 */
ELSE IF PARAMCD IN ('U3HPM24U' /*'UMHBM24U' 'USPMA24U'*/) THEN
AVALU=STRIP("Âµg"); /* 36) KB 09Jun2014 */ /* 46) KB 23Jun2014 */
ELSE IF PARAMCD='UAMES24U' THEN AVALU=STRIP("REV/24h"); /* 44) KB
22Jun2014 */
/* 46) START KB 23Jun2014 */
ELSE IF PARAMCD IN ('UDSPMA' 'UDMHBMA' 'UDHEMA' 'UDSBMA') THEN
AVALU=STRIP('pg/mL');
ELSE IF PARAMCD IN ('UMHBM24U' 'USPMA24U' 'USBMA24U' 'UHEMA24U') THEN
AVALU=STRIP('ng');
ELSE IF PARAMCD IN ('UMHBMCRE' 'USPMACRE' 'UHEMACRE' 'USBMACRE') THEN
AVALU=STRIP('pg/mg creat');
/* 46) END KB 23Jun2014 */
/* 75) START JM 08SEP2015 */
ELSE IF PARAMCD IN ('UBAP24U') THEN AVALU=STRIP('pg');
ELSE IF PARAMCD IN ('UBAPCRE') THEN AVALU=STRIP('fg/mg creat');
/* 75) END JM 08SEP2015 */
else avalu = strip(lbstresu);

if avalu ne '' then do;
param=left(trim(param)) || ' (' || left(trim(avalu)) || ')';
end;

if paramcd='CO' then do;
if missing(aval) then avalcat1='';
else if not missing(aval) and aval le 10 then avalcat1='<=10';
else avalcat1='>10';

```

```

end;
else if paramcd='CARBXHGB' then do;
    if missing(aval) then avalcat1='';
    else if not missing(aval) and aval le 2 then avalcat1='<=2';
    else avalcat1='>2';
end;

atoxgr=propcase(lbttoxgr);
anrind = strip(lbnrind);
if missing(lbstnrc) then anrlo = strip(lbstnrlo);
else if not missing(lbstnrc) then anrlo = strip(lbstnrc);
anrhi = strip(lbstnrhi);

*loq flags;
if index(lbstresc,'<') then do;
    bloqfl = 'Y';
    aval = /*0.5 *
input(scan(lbstresc,2),best.)/INPUT(TRANWRD(SCAN(LBSTRESC,2,'(',')',''),
,BEST.)/2; * following section 11.1.5 of SAP relating to biomarkers; /*
2) KB 13May2014 */
    aqlfl = 'Y';
end;
if index(lbstresc,'>') then do;
    aulqfl = 'Y';
    aval = input(scan(lbstresc,2),best.);
    aqlfl = 'Y';
end;

/* 20) START KB 01Jun2014 */
IF BLQFLG='Y' THEN DO;
    AQLFL='Y';
    BLOQFL='Y';
END;
/* 20) END KB 05Jun2014 */

* visit details ;
avisit = propcase(visit);
avisitn = visitnum;

* dates;
if length(lbdtc) gt 10 /*and paramcd ne 'UVOL'*/ then do; /* 10) KB
15May2014 */
/*      adtm = input(lbdtc,e8601dt.);*/

ADTM=DHMS(INPUT(SCAN(LBDTC,1,'T'),YYMMDD10.),HOUR(INPUT(SCAN(LBDTC,2,'T')
,TIME5.)),MINUTE(INPUT(SCAN(LBDTC,2,'T'),TIME5.)),0); /* 40) KB 21Jun2014
*/
    adt = datepart(adtm);
    atm = timepart(adtm);
end;
else if length(lbdtc) = 10 then adt = input(lbdtc,yyymmdd10.);

IF PARAM='Trans-3 Hydroxycotinine (ng/mL)' THEN PARAM="Trans-
3'Hydroxycotinine (ng/mL)"; /* 4) KB 14May2014 */

```

```

/* 5) START KB 14May2014 */
  IF PARAMCD IN ('UNNAL' 'UNNAL24U' 'UNNALCRE') THEN DO;
    PARAM=TRANWRD(PARAM,'3-pyridyl', '3-pyridyl');
  END;
/* 5) END KB 14May2014 */
/* 8) START KB 15May2014 */
  IF PARAMN=/*66*///*65*/69 THEN DO; /* 43) KB 22Jun2014 */ /* 46) KB
23Jun2014 */
    PARAM="Trans-3'-Hydroxycotinineglucuronide (ng/mL)";
  END;
/* 8) END KB 15May2014 */

run;

/* 19) START KB 01Jun2014 */
PROC SORT DATA=LB2(WHERE=(LBSTAT NE 'NOT DONE' AND
INDEX(PARAMCD,'LBALL')=0)) OUT=UNITS(KEEP=PARAMCD AVALU
RENAME=(AVALU=UNITS)) NODUPKEY;
  BY PARAMCD AVALU;
RUN;

PROC SORT DATA=LB2;
  BY PARAMCD;
RUN;

DATA LB2U;
  MERGE LB2 UNITS;
  BY PARAMCD;

  IF LBSTAT EQ 'NOT DONE' AND INDEX(PARAMCD,'LBALL')=0 THEN DO;
    PARAM=LEFT(TRIM(PARAM)) || ' (' || LEFT(TRIM(UNITS)) || ')';
  END;

  DROP UNITS;
RUN;
/* 19) END KB 01Jun2014 */

proc sort data = /*lb2*/LB2U; /* 19) KB 01Jun2014 */
  by usubjid paramn avisitn atptn;
run;

*****;
* Combine ADSL and BX data *;
*****;
* treatment period;
*_mtotper;

data sllb;
  merge adsl /*lb2*/LB2U(in = a); /* 19) KB 01Jun2014 */
  by usubjid;
  if a; * only include subjects with data ;
  format aperiod trtan trtpn aday astday 8. trta trtp $40. aperiodc
/*$8.*/$10. /*pbase*/PBASEFL $2. /*astdt*/ aendt date9. /*asttm*/ aentm

```

```

time5. /*astdtm*/ aendtm datetime13. ANL01FL $2.; /* 10) KB 15May2014 */
/* 25) KB 03Jun2014 */ /* 50) KB 24Jun2014 */ /* 60) KB 11Sep2014 */
    aday = adt - trtsdt + 1;
    astday = adt - trtsdt + 1;
    * allocate tretament and period;
    %_mperall(dvar1 = adtm, dvar2 = adt);

    if not missing(aperiod) then do;
        aperiodc = 'Period ' || put(aperiod,1.);
    end;

/*      if paramcd='UVOL' then do;*/ /* 18) KB 16May2014 */
/* 10) START KB 15May2014 */
/*          if length(lbdtc) gt 10 then do;*/
/*              astdtm = input(lbdtc,e8601dt.);*/
/*              astdt = datepart(astdtm);*/
/*              asttm = timepart(astdtm);*/
/*          end; */
/*          else if length(lbdtc) = 10 then astdt =
input(lbdtc,ymmdd10.); */
/* 10) END KB 15May2014 */
        if NOT MISSING(LBENDTC) AND length(lbendtc) gt 10 then do; /* 18)
KB 16May2014 */
/*              aendtm = input(lbendtc,e8601dt.);*/

AENDTM=DHMS(INPUT(SCAN(LBENDTC,1,'T'),YMMDD10.),HOUR(INPUT(SCAN(LBENDTC,
2,'T'),TIME5.)),MINUTE(INPUT(SCAN(LBENDTC,2,'T'),TIME5.)),0); /* 40) KB
21Jun2014 */
            aendt = datepart(aendtm);
            aentm = timepart(aendtm);
        end;
        else if length(lbendtc) = 10 then aendt = input(lbendtc,ymmdd10.);
/*      end; */ /* 18) KB 16May2014 */

/* 14) START KB 15May2014 */
    IF AWLO NE . THEN DO;
        if paramcd /*ne 'UVOL'*/IN('CO' 'CARBXHGB') then do; /* 14) KB
15May2014 */
            if awlo <= adtm <= awhi and (paramcd not in ('ULBALL'
'ELBALL1' 'ELBALL2' 'LBALL' 'BLBALL' 'BELBALL')) then anl01fl='Y'; /*
17) KB 16May2014 */ /* 27) KB 04Jun2014 */
            end;

            /* 14) START KB 15May2014 */
            /*      if paramcd eq 'UVOL' then do;*/
            /*          if (awlo - dhms(0,0,20,0)) <= /*astdtm*/ADTM <= (awlo +
dhms(0,0,20,0)) then anl01fl='Y';*/ /* 10) KB 15May2014 */
            /*          else anl01fl='';*/
            /*          if (awhi - dhms(0,0,20,0)) <= aendtm <= (awhi +
dhms(0,0,20,0)) then anl01fl='Y';*/
            /*          else anl01fl='';*/
            /*      end;*/
/* 35) START KB 09Jun2014 */
/*      IF PARAMCD NOT IN ('CO' 'CARBXHGB') THEN DO;*/

```

```

/*          IF LBSTAT NE 'NOT DONE' THEN ANL01FL='Y';*/
/*          END;*/
/* 35) END KB 09Jun2014 */
/* 14) END KB 15May2014 */
END;
/* 14) END KB 15May2014 */

    if not missing(adtm) AND NOT MISSING(TRTSDTM) /*and avisit='Day 1'*/
AND MISSING(AENDTM) then do; /* 12) KB 15May2014 */ /* 15) KB 15May2014
*/ /* 67) KB 16Sep2014 */
        if adtm/*>*/>=trtsdtm then /*pbase*/PBASEFL='Y'; /* 60) KB
11Sep2014 */ /* 70) KB 17Sep2014 */
        else /*pbase*/PBASEFL=''; /* 60) KB 11Sep2014 */
    end;
/* 67) START KB 16Sep2014 */
    ELSE IF NOT MISSING(ADTM) AND NOT MISSING(TRTSDTM) AND NOT
MISSING(AENDTM) THEN DO;
        IF AENDTM/*>*/>=TRTSDTM THEN PBASEFL='Y'; /* 70) KB 17Sep2014 */
        ELSE PBASEFL='';
    END;
/* 67) END KB 16Sep2014 */
    IF MISSING(TRTSDTM) THEN /*PBASE*/PBASEFL=''; /* 12) KB 15May2014 */
/* 60) KB 11Sep2014 */

/* 68) START KB 16Sep2014 */
    IF PARAMCD='CO' THEN DO;
        IF PBASEFL='' AND ATPT='15 min < T0' AND CHG NE . THEN
PBASEFL='Y';
    END;
/* 68) END KB 16Sep2014 */

run;

proc sort data=sllb;
    by usubjid paramcd avisit atpt;
run;

data sllb2;
    set sllb;
    by usubjid paramcd avisit atpt;
    format /*pbase*//*PBASEFL*/ ANL02FL $2.; /* 25) KB 03Jun2014 */ /*
60) KB 11Sep2014 */ /* 67) KB 16Sep2014 */

    if first.atpt and upcase(index(avisit,'UNSCH'))=0 and paramcd not
in('ULBALL' 'LBALL' 'BLBALL' 'ELBALL1' 'ELBALL2' 'BELBALL') AND LBSTAT NE
'NOT DONE' then anl02fl='Y'; /* 17) KB 16May2014 */ /* 27) KB 04Jun2014
*/ /* 30) KB 05Jun2014 */

/* 67) START KB 16Sep2014 */
/* if paramcd ne*/ /*'UVOL'*//*'VOLUME' then do; *//* 39) KB 21Jun2014
*/
    /* if adtm>trtsdtm or avisit='Day 1' then*/
/*pbase*//*PBASEFL='Y'; */ /* 60) KB 11Sep2014 */
/*    end;*/

```

```

/*      else do;*/
/*      if*/ /*astdtm*/ /*ADTM>trtsdtm or avisit='Day 1' then*/
/*pbase*/ /*PBASEFL='Y';*/ /* 10) KB 15May2014 */ /* 60) KB 11Sep2014 */
/*      end;      */
/*      IF MISSING(TRTSDTM) THEN*/ /*PBASE*/ /*PBASEFL=''; */ /* 12) KB
15May2014 */ /* 60) KB 11Sep2014 */
/* 67) END KB 16Sep2014 */

run;

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

data sllb4;
    set sllb2;
    format devwc $10. devn 8.;

    if paramcd in ('CO' 'CARBHXGB') then do;

        lbdtc2=input(scan(lbdtc,1,'T'),yymmdd10.);
        lbdtc3=input(scan(lbdtc,2,'T'),time5.);
        adtmtest=dhms(lbdtc2,hour(lbdtc3),minute(lbdtc3),0);

        if lbstat ne 'NOT DONE' then do;
            if adtmtest<awlo then do;
                devn=floor((adtmtest-awlo)/60);
                devwc=compress(put(floor((adtmtest-awlo)/60),best.));
            end;
            else if adtmtest>awhi then do;
/*                devn=ceil((adtmtest-awhi)/60);*/
/*                devwc=compress(put(ceil((adtmtest-awhi)/60),best.));*/
                DEVN=CEIL(((ADTMTEST+59)-AWHI)/60); /* 64) KB 11Sep2014 */
                DEVWC=COMPRESS(PUT(CEIL(((ADTMTEST+59)-AWHI)/60),BEST.)); /*
64) KB 11Sep2014 */
            end;
        end;

        if not missing(devwc) then do;
            if index(devwc,'-')=0 then devwc=cats(cats('+',devwc),' min');
            else if index(devwc,'-') then devwc=cats(devwc,' min');
        end;
    end;

/*      if paramtyp='DERIVED' then lbdtc='';*/
run;

/* 62) START KB 11Sep2014 */
DATA SV;
    SET SDTM.SV(WHERE=(VISIT=('DAY 1')));
    FORMAT DAY DATE9.;

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

```

```

KEEP USUBJID DAY;
RUN;

DATA SLLB4A;
    MERGE SLLB4 (IN=A) SV;
    BY USUBJID;
    IF A;
RUN;

DATA SLLB4B;
    SET SLLB4A;
    WHERE /*BASE EQ . AND PARAMCD NE 'CO'*/BLFL NE 1 AND LBSTAT NE 'NOT
DONE'; /* 66) KB 15Sep2014 */

    IF PARAMCD IN ('HCOT' 'TRANS3H' 'CYP2A6' 'PX' 'COTININE' 'COT'
'CAFFEINE') THEN DO;
        IF TRTA='SA' THEN DO;
            IF DAY NE . THEN DO;
                IF ADTM<DHMS(DAY,6,30,0) AND
INDEX(UPCASE(VISIT),'UNSCHED')=0 THEN ABLFL2='Y';
            END;
            ELSE IF DAY EQ . THEN DO;
                IF INDEX(UPCASE(VISIT),'UNSCHED')=0 THEN ABLFL2='Y';
            END;
        END;
        ELSE IF TRTA IN ('CC' 'THS 2.2') THEN DO;
            IF ADTM<TRTSDTM AND INDEX(UPCASE(VISIT),'UNSCHED')=0 THEN
ABLFL2='Y';
        END;
        ELSE IF MISSING(TRTA) THEN DO;
            IF INDEX(UPCASE(VISIT),'UNSCHED')=0 THEN ABLFL2='Y';
        END;
    END;
    ELSE DO;
        IF NOT MISSING(AENDTM) THEN DO;
            IF TRTA='SA' THEN DO;
                IF DAY NE . THEN DO;
                    IF AENDTM<DHMS(DAY,6,30,0) AND
INDEX(UPCASE(VISIT),'UNSCHED')=0 THEN ABLFL2='Y';
                END;
                ELSE IF DAY EQ . THEN DO;
                    IF INDEX(UPCASE(VISIT),'UNSCHED')=0 THEN ABLFL2='Y';
                END;
            END;
            ELSE IF TRTA IN ('CC' 'THS 2.2') THEN DO;
                IF AENDTM<TRTSDTM AND INDEX(UPCASE(VISIT),'UNSCHED')=0
THEN ABLFL2='Y';
            END;
            ELSE IF MISSING(TRTA) THEN DO;
                IF INDEX(UPCASE(VISIT),'UNSCHED')=0 THEN ABLFL2='Y';
            END;
        END;
    END;
END;
RUN;

```



```
PROC SORT DATA=SLLB4B(WHERE=(ABLFL2='Y')) OUT=SLLB4C;
  BY USUBJID PARAMCD VISITNUM ADTM AENDTM;
RUN;
```

```
DATA SLLB4D(WHERE=(ABLFL='Y'));
  SET SLLB4C;
  BY USUBJID PARAMCD VISITNUM ADTM AENDTM;
  FORMAT ABLFL $2.;

  IF LAST.PARAMCD AND NOT MISSING(ADTM) THEN ABLFL='Y';

  KEEP USUBJID VISIT ABLFL PARAMCD VISITNUM;
RUN;
```

```
PROC SORT DATA=SLLB4A;
  BY USUBJID PARAMCD VISITNUM VISIT;
RUN;
PROC SORT DATA=SLLB4D(RENAME=(ABLFL=ABLFL4));
  BY USUBJID PARAMCD VISITNUM VISIT ;
RUN;
```

```
DATA SLLB4DA;
  MERGE SLLB4D SLLB4A;
  BY USUBJID PARAMCD VISITNUM VISIT;
RUN;
```

```
DATA SLLB4DB;
  SET SLLB4DA;

  IF NOT MISSING(ABLFL4) THEN ABLFL=ABLFL4;
  DROP ABLFL4;
RUN;
```

```
/* 62) END KB 11Sep2014 */
```

```
data baselines;
  /* set sllb4(where=((paramcd ne ('CO') and base eq . and avisit='Day
0' and lbstat ne 'NOT DONE') OR (PARAMCD IN ('UOMHBMA' 'UDMHBMA') AND
USUBJID='ZRHR-REXC-03-EU-BIO-0055' AND AVISIT='Day -1')));*/ /* 45) KB
22Jun2014 */
```

```
  SET SLLB4DB; /* 62) KB 11Sep2014 */
  WHERE ABLFL='Y' AND /*PARAMCD NE 'CO' AND BASE EQ .*/BLFL NE 1 AND
LBSTAT NE 'NOT DONE'; /* 62) KB 11Sep2014 */ /* 66) KB 15Sep2014 */
  format base2 /*best.*/BEST32. BASETYP2 $40.; /* 13) KB 15May2014 */
/* 53) KB 24Jun2014 */
```

```
  IF USUBJID='ZRHR-REXC-03-EU-BIO-0055' AND PARAMCD IN ('UOMHBMA'
'UDMHBMA') AND VISIT='DAY 0' THEN DELETE; /* 46) KB 23Jun2014 */
  base2=/*ROUND(*/aval/*,0.00000000000000001)*/; /* 53) KB 24Jun2014 */
/* 65) KB 11Sep2014 */
  /* IF PARAMCD IN ('UOMHBMA' 'UDMHBMA') AND USUBJID='ZRHR-REXC-03-EU-
BIO-0055' AND AVISIT='Day -1' THEN BASETYP2='DAY -1';*/ /* 45) KB
22Jun2014 */ /* 46) KB 23Jun2014 */
```

```

/* ELSE BASETYP2='DAY 0'; */ /* 13) KB 15May2014 */ /* 45) KB 22Jun2014
*/
BASETYP2=STRIP(VISIT); /* 62) KB 11Sep2014 */

BLFL2=1; /* 66) KB 15Sep2014 */

keep usubjid paramcd base2 BASETYP2 BLFL2; /* 13) KB 15May2014 */ /*
66) KB 15Sep2014 */
run;

proc sort data=/*sllb4*/SLLB4DB; /* 62) KB 11Sep2014 */
by usubjid paramcd;
run;

data sllb5;
merge /*sllb4*/SLLB4DB baselines(in=a); /* 62) KB 11Sep2014 */
by usubjid paramcd;
if a and base=. then base=base2;
IF A AND BASETYPE=' ' THEN BASETYPE=BASETYP2; /* 13) KB 15May2014 */
IF A AND BLFL=. THEN BLFL=BLFL2; /* 67) KB 16Sep2014 */

if a and avisit not in ('Day 0' 'Day -1') then do;
chg=aval-base; /* 53) KB 24Jun2014 */
/* chgc=strip(put(chg,BEST32.)); */
CHGC=STRIP(PUT(ROUND(AVAL-BASE,0.0000000000000001),BEST32.)); /*
72) KB 15Oct2014 */
if base ne 0 then do;
pchg=(chg/base)*100; /* 53) KB 24Jun2014 */

PCHGC=STRIP(PUT(ROUND((CHG/BASE)*100,0.0000000000000001),BEST32.)); /*
72) KB 15Oct2014 */
end;
/* 29) START KB 05Jun2014 */
ELSE DO;
PCHG=(CHG/1)*100; /* 53) KB 24Jun2014 */

PCHGC=STRIP(PUT(ROUND((CHG/1)*100,0.0000000000000001),BEST32.)); /* 72)
KB 15Oct2014 */
END;
/* 29) END KB 05Jun2014 */
/*pchg=strip(put(pchg,/*best.*/ /*8.1*/ /*BEST32.)); */ /* 9) KB
15May2014 */ /* 53) KB 24Jun2014 */
end;

/*if paramcd not in (/*'UVOL'*/ /*'VOLUME' 'CO' 'CARBHXGB' 'CREAT')
and avisit='Day 0' then ablfl='Y'; */ /* 39) KB 21Jun2014 */ /* 62) KB
11Sep2014 */ /* 62) KB 11Sep2014 */

run;

proc sort data=sllb5;
by usubjid paramcd visitnum;
run;

```

```

data eos;
    set sllb5(where=(paramcd not in ('CO' 'CARBXHGB' 'ELBALL1' 'ELBALL2'
'BLBALL' 'BELBALL' 'ULBALL') AND LBSTAT NE 'NOT DONE')); /* 17) KB
16May2014 */ /* 27) KB 04Jun2014 */ /* 32) KB 06Jun2014 */
    by usubjid paramcd visitnum;
    format aeofl $2.;

    if last.paramcd and last.visitnum then do;
        aeofl='Y';
        OUTPUT; /* 3) KB 14May2014 */
    end;

    keep usubjid paramcd visitnum aeofl;
run;

data sllb5a;
    merge sllb5 eos;
    by usubjid paramcd visitnum;
run;

data eos2;
    set sllb5a(where=(aeofl='Y'));
    format eoe best.;

    eoe=aval;

    keep usubjid paramcd eoe;
run;

proc sort data=sllb5a;
    by usubjid paramcd;
run;

PROC SORT DATA=EOS2 DUPOUT=EOS3 NODUPKEY;
    BY USUBJID PARAMCD;
RUN;

data sllb5b;
    merge sllb5a eos2;
    by usubjid paramcd;

    if index(avalc,'Blq') then avalc=tranwrd(avalc,'Blq','BLQ');

    /*IF*/ /*PBASE*/ /*PBASEFL='' AND AVISIT IN ('Day 1' 'Day 2' 'Day 3'
'Day 4' 'Day 5'*/ /*'Day 6'*/ /*'Day 6/Discharge') AND
INDEX(PARAMCD,'LBALL')=0 THEN /*PBASE*/ /*PBASEFL='Y'; */ /* 12) KB
15May2014 */ /* 42) KB 21Jun2014 */ /* 60) KB 11Sep2014 */ /* 67) KB
16Sep2014 */

    /* 16) START KB 16May2014 */
    IF PARAMCD IN ('BLBALL' 'ELBALL1' 'ELBALL2' 'LBALL' 'BELBALL'
'ULBALL') THEN DO; /* 27) KB 04Jun2014 */
        /*PBASE*/PBASEFL=''; /* 60) KB 11Sep2014 */
        ABLFL='';

```

```

        END;
/* 16) END KB 16May2014 */
/*      keep &keepvars; */ /* 67) KB 16Sep2014 */
run;

/* 22) START KB 02Jun2014 */
/* 23) START KB 03Jun2014 */
DATA EXTIMES;
    SET SDTM.EX(WHERE=(VISIT IN ('DAY 0')));
    FORMAT AVISIT $40.;
    AVISIT=PROPCASE(VISIT);
    KEEP USUBJID AVISIT EXSTDTC;
RUN;

PROC SORT DATA=EXTIMES;
    BY USUBJID AVISIT EXSTDTC;
RUN;

DATA EXTIMES2;
    SET EXTIMES;
    BY USUBJID AVISIT EXSTDTC;
    IF FIRST.AVISIT AND FIRST.EXSTDTC;
RUN;

PROC SORT DATA=EXTIMES2;
    BY USUBJID AVISIT;
RUN;

PROC SORT DATA=SLLB5B;
    BY USUBJID AVISIT;
RUN;

/* 23) END KB 03Jun2014 */
DATA SLLB5C;
    /*SET*/MERGE SLLB5B EXTIMES2; /* 23) KB 03Jun2014 */
    BY USUBJID AVISIT; /* 23) KB 03Jun2014 */

    IF PARAMCD IN ('HCOT' 'COT' 'COTININE' 'TRANS3H' 'CYP2A6') THEN DO;
        AWLO=.;
/* 23) START KB 03Jun2014 */
        IF AVISIT='Day 0' THEN DO;

AWHI=/*TRTSDTM*/DHMS(INPUT(SCAN(EXSTDTC,1,'T'),YYMMDD10.),HOUR(INPUT(SCAN
(EXSTDTC,2,'T'),TIME5.)),MINUTE(INPUT(SCAN(EXSTDTC,2,'T'),TIME5.)),0); /*
23) KB 03Jun2014 */
        END;
        ELSE IF AVISIT=/'Day 6'/'Day 6/Discharge' THEN DO; /* 42) KB
21Jun2014 */
            AWHI=DHMS(ADT,6,30,0);
        END;
/* 23) END KB 03Jun2014 */
        AWRANGE=STRIP("<")||STRIP(PUT(AWHI,DATETIME13.));

/* 28) START KB 05Jun2014 */

```

```

        IF AWLO <= ADTM <= AWHI AND LBSTAT NE 'NOT DONE' THEN
ANL01FL='Y';
/* 28) END KB 05Jun2014 */

/* 31) START KB 06Jun2014 */
        IF LBSTAT NE 'NOT DONE' THEN DO;
            IF ADTM<AWLO THEN DO;
                DEVN=FLOOR((ADTM-AWLO)/60);
                DEVWC=COMPRESS(PUT(FLOOR((ADTM-AWLO)/60),BEST.));
            END;
            ELSE IF ADTM>AWHI THEN DO;
/*                DEVN=CEIL((ADTM-AWHI)/60); */
/*                DEVWC=COMPRESS(PUT(CEIL((ADTM-AWHI)/60),BEST.)); */
                DEVN=CEIL(((ADTM+59)-AWHI)/60); /* 64) KB 11Sep2014 */
                DEVWC=COMPRESS(PUT(CEIL(((ADTM+59)-AWHI)/60),BEST.));
/* 64) KB 11Sep2014 */
            END;
        END;

        IF NOT MISSING(DEVWC) THEN DO;
            IF INDEX(DEVWC,'-')=0 THEN DEVWC=CATS(CATS('+',DEVWC),'
min');
            ELSE IF INDEX(DEVWC,'-') THEN DEVWC=CATS(DEVWC,' min');
        END;
/* 31) END KB 06Jun2014 */

        END;
        DROP EXSTDTC; /* 23) KB 03Jun2014 */
RUN;

DATA SU;
    SET SDTM.SU(WHERE=(SUTRT='CAFFEINE'));
    FORMAT AVISIT $40.;

    IF EPOCH='BASELINE' THEN AVISIT='Day 0';
    ELSE IF EPOCH='PRODUCT USE CONFINEMENT' THEN AVISIT='Day 5';
    KEEP USUBJID SUSTDTC AVISIT;
RUN;

PROC TRANSPOSE DATA=SU OUT=SU2(DROP=_NAME_ _LABEL_);
    BY USUBJID;
    VAR SUSTDTC;
    ID AVISIT;
RUN;

DATA SLLB5D;
    MERGE SLLB5C SU2;
    BY USUBJID;

    IF PARAMCD IN ("CAF" "CAFFEINE" "PX" "PXC" "CYP1A2") THEN DO;
        IF INDEX(DAY_0,'--')=0 THEN DO;
            IF AVISIT='Day 0' THEN DO;
AWLO=DHMS(INPUT(SCAN(DAY_0,1,'T'),YYMMDD10.),HOUR(INPUT(SCAN(DAY_0,2,'T')

```

```

, TIME5.)), MINUTE (INPUT (SCAN (DAY_0, 2, 'T'), TIME5.)), 0) + DHMS (0, 6, 0, 0) -
DHMS (0, 0, 15, 0);

AWHI= DHMS (INPUT (SCAN (DAY_0, 1, 'T'), YYMMDD10.), HOUR (INPUT (SCAN (DAY_0, 2, 'T')
, TIME5.)), MINUTE (INPUT (SCAN (DAY_0, 2, 'T'), TIME5.)), 0) + DHMS (0, 6, 0, 0) + DHMS (0
, 0, 15, 0);

                AWRANGE=STRIP (PUT (AWLO, DATETIME13.)) || '-'
' || STRIP (PUT (AWHI, DATETIME13.));
        END;
    END;
    IF INDEX (DAY_5, '--')=0 THEN DO;
        IF AVISIT='Day 5' THEN DO;

AWLO= DHMS (INPUT (SCAN (DAY_5, 1, 'T'), YYMMDD10.), HOUR (INPUT (SCAN (DAY_5, 2, 'T')
, TIME5.)), MINUTE (INPUT (SCAN (DAY_5, 2, 'T'), TIME5.)), 0) + DHMS (0, 6, 0, 0) -
DHMS (0, 0, 15, 0);

AWHI= DHMS (INPUT (SCAN (DAY_5, 1, 'T'), YYMMDD10.), HOUR (INPUT (SCAN (DAY_5, 2, 'T')
, TIME5.)), MINUTE (INPUT (SCAN (DAY_5, 2, 'T'), TIME5.)), 0) + DHMS (0, 6, 0, 0) + DHMS (0
, 0, 15, 0);

                AWRANGE=STRIP (PUT (AWLO, DATETIME13.)) || '-'
' || STRIP (PUT (AWHI, DATETIME13.));
        END;
    END;

/* 28) START KB 05Jun2014 */
    IF AWLO <= ADTM <= AWHI AND LBSTAT NE 'NOT DONE' THEN
ANL01FL='Y';
/* 28) END KB 05Jun2014 */

/* 31) START KB 06Jun2014 */
    IF LBSTAT NE 'NOT DONE' THEN DO;
        IF ADTM<AWLO THEN DO;
            DEVN=FLOOR ((ADTM-AWLO)/60);
            DEVWC=COMPRESS (PUT (FLOOR ((ADTM-AWLO)/60), BEST.));
        END;
        ELSE IF ADTM>AWHI THEN DO;
/*            DEVN=CEIL ((ADTM-AWHI)/60); */
/*            DEVWC=COMPRESS (PUT (CEIL ((ADTM-AWHI)/60), BEST.)); */
            DEVN=CEIL ((ADTM+59)-AWHI)/60; /* 64) KB 11Sep2014 */
            DEVWC=COMPRESS (PUT (CEIL ((ADTM+59)-AWHI)/60), BEST.); /* 64)
KB 11Sep2014 */
        END;
    END;

    IF NOT MISSING (DEVWC) THEN DO;
        IF INDEX (DEVWC, '-')=0 THEN DEVWC=CATS (CATS ('+', DEVWC), '
min');
        ELSE IF INDEX (DEVWC, '-') THEN DEVWC=CATS (DEVWC, ' min');
    END;
/* 31) END KB 06Jun2014 */

END;

```

```

        DROP DAY_0 DAY_5;
RUN;

DATA SLLB5E;
    SET SLLB5D;
    FORMAT AVAL2   BASE2   BEST32.; /* 35) KB 24Jun2014 */

    IF AWRANGE='' THEN DO;
/*      IF LBENDTC NE '' THEN DO; /* 55) KB 31Jul2014 */
        IF PARAMCD NE 'CO' THEN DO; /* 55) KB 31Jul2014 */
            ADT1=INPUT(SCAN(LBDTC,1,'T'),YYMMDD10.);
            AWLOUS=DHMS(ADT1,6,0,0);
            AWLOUE=DHMS(ADT1,7,0,0);
        END; /* 55) KB 31Jul2014 */

            IF LBENDTC NE '' THEN DO; /* 55) KB 31Jul2014 */
                ADT2=INPUT(SCAN(LBENDTC,1,'T'),YYMMDD10.);

                AWHIUS=DHMS(ADT2,5,59,0);
                AWHIUE=DHMS(ADT2,6,59,0);
            END; /* 55) KB 31Jul2014 */

            AWLO=AWLOUS;
            AWHI=AWHIUE;

            IF NOT MISSING(AWLO) AND NOT MISSING(AWHI) THEN DO;
                AWRANGE=PUT(AWLO,DATETIME13.) || '-' ||
PUT(AWHI,DATETIME13.);
            END;

/* 28) START KB 05Jun2014 */
        IF (AWLO <= ADTM AND AENDTM<=AWHI) AND AENDTM NE . /*<= AWHI*/
AND (PARAMCD NOT IN ('ULBALL' 'ELBALL1' 'ELBALL2' 'LBALL' 'BLBALL'
'BELBALL')) AND LBSTAT NE 'NOT DONE' THEN ANL01FL='Y'; /* 33) KB
09Jun2014 */ /* 55) KB 31Jul2014 */
        IF MISSING(AWHI) THEN ANL01FL=''; /* 57) KB 01Aug2014 */
/* 28) END KB 05Jun2014 */

/* 31) START KB 06Jun2014 */
        IF LBSTAT NE 'NOT DONE' THEN DO;
            IF ADTM<AWLO THEN DO;
                DEVN=FLOOR((ADTM-AWLO)/60);
                DEVC=COMPRESS(PUT(FLOOR((ADTM-AWLO)/60),BEST.));
            END;
            ELSE IF AENDTM>AWHI AND AENDTM NE . THEN DO; /* 55) KB
31Jul2014 */
/*      DEVN=CEIL((AENDTM-AWHI)/60); */
/*      DEVC=COMPRESS(PUT(CEIL((AENDTM-AWHI)/60),BEST.)); */
            DEVN=CEIL(((AENDTM+59)-AWHI)/60); /* 64) KB 11Sep2014 */
            DEVC=COMPRESS(PUT(CEIL(((AENDTM+59)-AWHI)/60),BEST.)); /*
64) KB 11Sep2014 */
            END;
        END;
END;

```

```

        IF NOT MISSING(DEVWC) THEN DO;
            IF INDEX(DEVWC, '-')=0 THEN DEVWC=CATS(CATS('+',DEVWC), '
min');
            ELSE IF INDEX(DEVWC, '-') THEN DEVWC=CATS(DEVWC, ' min');
        END;
/* 31) END KB 06Jun2014 */
/*      END;*/ /* 55) KB 31Jul2014 */
END;

/* IF PARAM='Trans-3 Hydroxycotinine (ng/mL)' THEN PARAM="Trans-
3'Hydroxycotinine (ng/mL)";*/ /* 26) KB 03Jun2014 */
    IF PARAMCD='TRANS3H' THEN PARAM="Trans-3'hydroxycotinine (ng/mL)"; /*
61) KB 11Sep2014 */
    IF PARAMCD IN ('UFTRANSC') THEN PARAM=TRANWRD(PARAM, "3'-
Hydroxycotinine", "3'-hydroxycotinine"); /* 66) KB 15Sep2014 */
    IF PARAMCD IN ('UFTRANSH') THEN PARAM=TRANWRD(PARAM, "3'-
Hydroxycotinine", "3'-hydroxycotinine"); /* 66) KB 15Sep2014 */
    IF PARAMCD IN ('UTRANSHC' 'UTRANSHY') THEN PARAM=TRANWRD(PARAM, "3'-
Hydroxycotinine", "3'-hydroxycotinine"); /* 66) KB 15Sep2014 */

    IF PARAMTYP='DERIVED' AND LBENDTC NE '' THEN LBENDTC=''; /* 34) KB
09Jun2014 */

    IF PARAMTYP='DERIVED' THEN LBDTC=''; /* 46) KB 23Jun2014 */
    IF PARAMCD IN ('UOMHBMA' 'UOSPMA' 'UOHEMA' 'UOSBMA') THEN ANL02FL='';
/* 46) KB 23Jun2014 */

/* IF USUBJID='ZRHR-REXC-03-EU-BIO-0055' AND AVISIT='Day -1' AND
PARAMCD='UOMHBMA' THEN ABLFL='Y';*/ /* 47) KB 23Jun2014 */ /* 63) KB
11Sep2014 */
/*IF USUBJID='ZRHR-REXC-03-EU-BIO-0055' AND AVISIT='Day -1' AND
PARAMCD*/ /*=*/ /* IN ('UDMHBMA' 'UMHBM24U' 'UMHBMCRE') THEN ABLFL='Y';*/
/* 47) KB 23Jun2014 */ /* 56) KB 01Aug2014 */ /* 63) KB 11Sep2014 */
/* IF USUBJID='ZRHR-REXC-03-EU-BIO-0055' AND AVISIT='Day 0' AND
PARAMCD='UOMHBMA' THEN ABLFL=''; */ /* 47) KB 23Jun2014 */ /* 63) KB
11Sep2014 */

/* 53) START KB 24Jun2014 */
    IF INDEX(AVALC, 'BLQ')=0 THEN DO;
        AVAL2=INPUT(AVALC, BEST32.);
    END;
    ELSE AVAL2=AVAL;

    IF ABLFL='Y' AND INDEX(AVALC, 'BLQ')=0 THEN DO;
        BASE2=INPUT(AVALC, BEST32.);
    END;
    ELSE IF ABLFL='Y' THEN BASE2=AVAL;
    ELSE BASE2=BASE;

    RENAME AVAL2=AVAL BASE2=BASE;
    DROP AVAL BASE;
/* 53) END KB 24Jun2014 */

```



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/* 58) START KB 01Aug2014 */
  IF TRTA='Enrolled not randomized' THEN DO;
    ABLFL='';
    BASE2=.;
    BASETYPE='';
    ABLAMFL='';
    ABLPMFL='';
  END;
/* 58) END KB 01Aug2014 */

  IF BLFL NE 1 AND PBASEFL='Y' THEN PBASEFL=''; /* 67) KB 16Sep2014 */

/*      KEEP &KEEPVARS;*/
RUN;
/* 22) END KB 02Jun2014 */

/* 69) START KB 17Sep2014 */
data SLLB5EA;
  set SLLB5E;

  ATTRIB AVALCHECK BASECHECK LENGTH = $200;

  *Round AVAL and BASE to 12dp - this is used to check number of DP to
  confirm we are not reviewing precision for unrounded values;
  AVALCHECK = STRIP(PUT(ROUND(AVAL,0.000000000001),BEST32.));
  BASECHECK = STRIP(PUT(ROUND(BASE,0.000000000001),BEST32.));

  *If after rounding the number of DP is < 12, then there is a possible
  precision issue;
  *Code then checks whether BASE = AVAL and therefore CHG should be 0;
  IF LENGTH(SCAN(AVALCHECK,2,".")) LT 12 AND
  LENGTH(SCAN(BASECHECK,2,".")) LT 12 AND ROUND(AVAL,0.000000000001) =
  ROUND(BASE,0.000000000001) AND CHG NE . AND CHG NE 0 THEN DO;
    *Identify subject, parameter and visit, so that each case can be
    individually reviewed prior to removing the precision error;
    *Code will flag a warning if it occurs for any new cases;
    IF USUBJID = "ZRRH-REXC-03-EU-BIO-0035" AND PARAMCD = "U1NA24U" AND
    AVISIT = "Day 2" THEN DO;
      BASE = INPUT(AVALC, BEST32.);
      CHG = 0;
      CHGC = "0";
      PCHG = 0;
      PCHGC = "0";
    END;
    ELSE PUT "WAR" "NING: Check for SAS precision error " USUBJID=
    PARAMCD= AVISIT=;
  END;
RUN;
/* 69) END KB 17Sep2014 */

/* 53) START KB 24Jun2014 */
DATA SLLB5F;
  SET /*SLLB5E*/SLLB5EA; /* 69) KB 17Sep2014 */
  KEEP &KEEPVARS;

```

```

RUN;
/* 53) END KB 24Jun2014 */

/* 59) START KB 01Aug2014 */
DATA TEST;
    SET SLLB5F;
    IF INDEX(AVALC,'BLQ')=0 THEN DO;
        IF INPUT(AVALC,BEST32.) NE AVAL THEN OUTPUT;
    END;
RUN;
/* 59) END KB 01Aug2014 */

/* 74) START KB 15Oct2014 */
DATA TEST2;
    SET SLLB5F;

    IF INDEX(AVALC,'BLQ')=0 THEN DO;
        XVAR=ROUND(AVAL,0.0000000001);
        YVAR=ROUND(INPUT(AVALC,BEST32.),0.0000000001);
    END;

    IF XVAR NE YVAR THEN PUT "USER WARN" "ING: AVAL and AVALC do not
match!";
RUN;
/* 74) END KB 15Oct2014 */

*****;
* create output dataset ;
*****;

options replace;

data adbx;
    set stdlib.adbx /*sllb5b*//*SLLB5E*/SLLB5F; /* 22) KB 02Jun2014 */
/* 53) KB 24Jun2014 */
    if lbstat='NOT DONE' then call missing(base, AWLOUS, AWLOUE,
AWHIUS, AWHIUE, AWRANGE, AWLO, AWHI, DEVN, DEVWC, ablfl,
/*pbase*/PBASEFL, basetype); /* 60) KB 11Sep2014 */
run;

proc sort data = adbx out = adam.adbx(label = /*'Biomarker Analysis
Dataset'*/'Biomarker Exposure Analysis Dataset'); /* 24) KB 03Jun2014 */
    by usubjid avisitn parcat1 paramcd atptn adtm LBSEQ; /* 73) KB
15Oct2014 */
run;

options noreplace;

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

```