Code：

gender=as.numeric(para\_BP\_individual[2,i+1]) #1 for male, 2 for female

bw= as.numeric(para\_BP\_individual[1,i+1]) #body weight (kg)

QCC = as.numeric(para\_BP\_individual[3,i+1])

QliverC = as.numeric(para\_BP\_individual[4,i+1])

QskinC =as.numeric( para\_BP\_individual[7,i+1])

QgonadC=as.numeric(para\_BP\_individual[8,i+1])

QfatC = as.numeric(para\_BP\_individual[9,i+1])

QbrainC <- as.numeric(para\_BP\_individual[22,i+1])

QmuscleC <-as.numeric(para\_BP\_individual[24,i+1])

VplasmaC <-as.numeric(para\_BP\_individual[16,i+1])

VfatC <- as.numeric(para\_BP\_individual[15,i+1])

VliverC <- as.numeric(para\_BP\_individual[10,i+1])

VbrainC <- as.numeric(para\_BP\_individual[25,i+1])

VgonadC <- as.numeric(para\_BP\_individual[14,i+1])

VskinC <- as.numeric(para\_BP\_individual[13,i+1])

VrichC <- as.numeric(para\_BP\_individual[26,i+1])

VbodygC <- VplasmaC

VbodysC <- VplasmaC

MWBPS <- 250.27 # (g/mol) |Molecular weight

pliver <- 0.846 # | (liver/blood)

pfat <- 0.435 # | (fat/blood)

pslow <- 0.881 # | (slowly perfused/blood)

prich <- 0.810 # | (richly perfused/blood)

pgonad <- 0.843 # | (gonads/blood)

pbrain <- 0.810 # | (brain/blood)

pskin <- 1.43# | (skin/blood)

geC <- 3.5 # (1/h/bw^-0.25) |Gastric emptying of BPs

k0C <- 0 # (1/h/bw^-0.25) |Oral uptake of BPs from the stomach into the liver; set to 0

k1C <- 5 # (1/h/bw^-0.25) |Oral uptake of BPs from the small intestine into the liver

k4C <- 0 # (1/h/bw^-0.25) |Fecal elimination of BPs from small intestine after peroral administration; set to 0

kGIingC <- 50 # (1/h/bw^-0.25) |Transport of BPafG from enterocytes into serum

kGIinsC <- 50 # (1/h/bw^-0.25) |Transport of BPafS from enterocytes into serum

kmgutg <-555000 # (nM) |Glucuronidation of BPs in the gut

ksigutg <- 711000 # (nM) |Glucuronidation of BPs in the gut for substrate

vmaxgutgC <- 563 # (nmol/h/kg bw) |Glucuronidation of BPs in the gut

fgutg <- 1 # Correction factor of glucuronidation in the gut

kmguts <- 0.001 # (nM) |Sulfation of BPaf in the gut, not modeled

vmaxgutsC <- 0.001 # (nmol/h/bw^0.75 |Sulfation of BPf in the gut

fguts <- 0 # Correction factor of sulfation in the gut no sulfation in the gut assumed

met1g <- 0.33# |Fraction of BPs-G in the liver taken up directly into serum (set to 1 to deactivate EHR)

met1s <- 1 # |Fraction of BPAS in the liver taken up directly into serum

enterocytes <- 0.1223 # (L)

kmliver <-446000 # (nM) |Glucuronidation of BPs in the liver

vmaxliverC <- 7810 # (nmol/h/g liver) |Glucuronidation of BPs in the liver

fliverg <- 1

kmlivers <- 10100 # (nM) |Sulfation of BPA in the liver, set to the value for SULT1A1 (Takahito 2002)

vmaxliversC <- 149 #

flivers <- 1

EHRtime <- 0.00 # (h) |Time until EHR occurs

EHRrateC <- 2 # (1/h/bw^-0.25) |EHR of BPsg

k4C\_IV <- 0 # (1/h/bw^-0.25) |Fecal elimination of BPAG from the EHR compartment

kurinebpaC <- 0.04 # (L/h/bw^0.75)

kurinebpagC <-1.336 # (L/h/bw^0.75)

kurinebpasC <- 0.03 # (L/h/bw^0.75)

vreabsorptiongC <- 0

vreabsorptionsC<-0

kreabsorptiong<-9200

kreabsorptions<-9200

kenterobpagC <- 0.35 # (1/h/bw^-0.25) |EHR of Bps

kenterobpasC <- 0.0

QC <- QCC\*60 # (L/h) |Cardiac output according to ICRP

Qfat <- QfatC\*QC # (L/h) |Blood flow to the fat

Qliver <- QliverC\*QC # (L/h) |Blood flow to the liver

Qgonad <- QgonadC\*QC # (L/h) |Blood flow to the gonads

Qbrain <- QbrainC\*QC # (L/h) |Blood flow to the brain

Qskin=QskinC\*QC# (L/h) |Blood flow to the skin

Qslow <- QmuscleC\*QC # (L/h)|Blood flow to the slowly perfused tissues

Qrich <- QC-Qliver-Qbrain-Qfat-Qgonad-Qslow-Qskin

Vliver <- VliverC\*bw # (L) |Volume of the liver

Vfat <- VfatC\*bw # (L) |Volume of the fat

Vgonad <- VgonadC\*bw # (L) |Volume of the gonads

Vplasma <- VplasmaC\*bw # (L) |Volume of the plasma

Vbrain <- VbrainC\*bw # (L) |Volume of the brain

Vskin=VskinC\*bw # (L) |Volume of the skin

Vrich<- VrichC\*bw # (L) |Volume of the richly perfused tissues

Vslow <- bw-Vliver-Vfat-Vgonad-Vplasma-Vbrain-Vrich

Vbodyg<- VbodygC\*bw # (L) |Volume of the distribution for BPAG

Vbodys <- VbodysC\*bw # (L) |Volume of the distribution for BPAS

vmaxliversCnew <- vmaxliversC\*VliverC\*1000

vmaxliversCnew <- vmaxliversCnew\*bw/(bw^0.75)

vmaxliverCnew <- vmaxliverC\*VliverC\*1000

vmaxliverCnew <- vmaxliverCnew\*bw/(bw^0.75)

vmaxgutgCnew <- vmaxgutgC\*bw/(bw^0.75)

vreabsorptiong <- vreabsorptiongC\*bw^0.75 # (nmol/h) |vmax of renal resorption of BPAG

vreabsorptions <- vreabsorptionsC\*bw^0.75 # (nmol/h) |vmax of renal resorption of BPAS

EHRrate <- EHRrateC/(bw^0.25) # (1/h) |EHR of BPAG

k0 <- k0C/bw^0.25 # (1/h)|Uptake of BPA from the stomach into the liver

ge <- geC/bw^0.25 # (1/h)|Gastric emptying of BPA

k1 <- k1C/bw^0.25 # (1/h)|Uptake of BPA from small intestine into the liver

k4 <- k4C/bw^0.25 # (1/h)|Fecal excretion of BPA after peroral administration from small intestine

k4\_IV <- k4C\_IV/bw^0.25 # (1/h) |Fecal excretion of BPAG from the EHR compartment

vmaxliver <- vmaxliverCnew\*fliverg\*bw^0.75 # (nmol/h) |vmax of BPA glucuronidation in the liver

kGIing <- kGIingC/bw^0.25 # (1/h) |Uptake of BPAG from small intestine into serum

met2g <- 1.0-met1g # () |Fraction of BPAG formed subject to EHR

met2s <- 1.0-met1s # () |Fraction of BPAS formed subject to EHR

kurinebpa <- kurinebpaC\*bw^0.75 # (L/h)|Clearance of BPA via urine

kurinebpag <- kurinebpagC\*bw^0.75 #(L/h)|Clearance of BPAG via urine

kurinebpas <- kurinebpasC\*bw^0.75 #(L/h)|Clearance of BPAS via urine

vmaxlivers <- vmaxliversCnew\*flivers\*bw^0.75 # (nmol/h) |vmax of BPA sulfation in the liver

kGIins <- kGIinsC/bw^0.25 # (1/h) |Uptake of BPAS from small intestine into serum

vmaxgutg <- vmaxgutgCnew\*fgutg\*bw^0.75 # (nmol/h) |vmax of BPA glucuronidation in the gut

vmaxguts <- vmaxgutsC\*fguts\*bw^0.75 # (nmol/h) |vmax of BPA sulfation in the gut

kenterobpag<- kenterobpagC/bw^0.25 # (1/h) |EHR of BPA due to biliary excretion of BPAG

kenterobpas <- kenterobpasC/bw^0.25 # (1/h) |EHR of BPA due to biliary excretion of BPAS

oral\_intakerate=0

BSA= as.numeric(para\_BP\_individual[21,i+1])\*100 #m2-dm2 body skin area

if(gender==1) epi\_finger=545 else epi\_finger=460 #ICRP 89 P196 um

TSC = 185/100000 # Thickness of stratum corneum (um-dm). thick for palm

TVE = (epi\_finger-185)/100000 # Thickness of viable epidermis (um-dm).

SCDX = TSC / 10

if(gender==1) skin\_finger=1200+545 else skin\_finger=1095+460 #ICRP 89 P196 um

TFO=388/560\*skin\_finger/100000 #um-dm

DOSE=as.numeric(para\_BP\_individual[17,i+1])/MWBPS #(nmol/kg/d)

ABS=as.numeric(para\_BP\_individual[18,i+1]) #absorption fraction

DOSE\_d=DOSE\*ABS

AEXP=20/100 # Area of exposed skin (cm^2- dm2).

add\_peroid=1/60 #h

exp\_peroid=13/6 #h

VWELL=AEXP\*0.01 #L

FEXP=0.005 # FRACTION OF Area of exposed skin FOR HIAR

VTSC = AEXP \* TSC # ... (exposed) stratum corneum.L

VTVE = AEXP \* TVE # ... (exposed) viable epidermis.L

VTFO=AEXP\*FEXP\*TFO

HSCVE=19.45

HFOWell= 5.4

HSCwell= 5.4

DSC = 17.28E-9 # diffusion (cm^2/h- dm2)

PFO= 6.39E-5 #cm/h- dm

u1=5.7E-5

yini\_bps\_dermal <- unlist(c(data.frame(

dose=0,AFO=0,AWELL=0,

CSC01=0,CSC02=0,CSC03=0,CSC04=0,CSC05=0,CSC06=0,CSC07=0,CSC08=0,CSC09=0,

AVE=0,Input\_oral=0,

AST = 0,

AGImet = 0,

AGImets = 0,

AAO = 0,

ASI = 0,

Afeces = 0,

Aoral = 0,

AGIin = 0, AGIBPAg = 0, AGIins = 0,AGIBPAs = 0,

Askin=0,

Aplasma = 0,

AFat = 0,

Agonad = 0,

AM=0,AMs=0,

ABPA\_delayinbpag = 0,

ABPA\_delayinbpas = 0,

ALiver = 0,

Abrain = 0,

AR = 0,

AS = 0,

Aurinebpa = 0,

ABPAg\_prod = 0,

ABPAg\_prod\_delay = 0,

ABPAg\_prod\_gut = 0,

ABPAg\_prod\_delay\_gut=0,

ABPAs\_prod = 0,

ABPAs\_prod\_delay = 0,

ABPAs\_prod\_gut = 0,

ABPAs\_prod\_delay\_gut=0,

ABPA\_delayin= 0,

Afecesiv = 0,

ABPA\_delay = 0,

ABPA\_delayins = 0,

Afecesivs = 0,

ABPA\_delays = 0,

Areabsorption = 0,

Aurineg = 0,

Aurinebpag = 0,

Areabsorptions = 0,

Aurines = 0 ,

Aurinebpas = 0,

Abpac = 0,

Abpas = 0,

Vurine=0)))

para\_bps\_dermal <- unlist(c(data.frame(

oral\_intakerate,QC,Qfat,Qliver,Qgonad,Qbrain,

Qskin,

Qrich,Qslow,Vliver,Vfat,Vskin,Vgonad,Vplasma,Vbrain,

Vslow, Vrich,Vbodyg,Vbodys,

pliver,pfat,pslow, prich,pgonad,pbrain,pskin,kmgutg,ksigutg,kmguts,met1g,met1s,

enterocytes, kmliver, kmlivers,EHRtime,kreabsorptiong,kreabsorptions,vreabsorptiong,vreabsorptions,

EHRrate,k0, ge,k1, k4,k4\_IV,vmaxliver,kGIing, met2g,met2s,kurinebpa,kurinebpag, kurinebpas,vmaxlivers,

kGIins,vmaxgutg,vmaxguts,kenterobpag,kenterobpas,

DOSE\_d,VTVE,VTSC, VTFO,TFO,AEXP,SCDX,

HSCVE,HSCwell,HFOWell,PFO,

DSC,VWELL,exp\_peroid,u1,BSA,FEXP,add\_peroid

)))

PBTKmod\_bps <- function(t, y, parms)

{

with (as.list(c(y, parms)),

{

if(t<EHRtime){kentero=0}else{kentero=EHRrate}

if(t<=exp\_peroid){ OO\_S\_TP1=1} else { OO\_S\_TP1=0}

CA <- Aplasma/Vplasma

# Dermal Exposure Well

if(t<=add\_peroid) Rdose=DOSE\_d/(add\_peroid) else Rdose=0

CWELL= (AWELL/VWELL)\*OO\_S\_TP1 # ... skin exposure well (nmol/l)

CSC00 = CWELL \* HSCwell

CVE = AVE/ VTVE

CvVE = CVE / pskin

CSC10 = CVE \* HSCVE

JSC00 = -DSC \* (CSC01 - CSC00) / SCDX -u1\*CSC00 # ... outer surface of SC.

JSC10 = -DSC \* (CSC10 - CSC09) / SCDX -u1\*CSC10 # ... interface of SC with VE.

CFO=AFO/VTFO

CvFO=CFO/pskin

JFO=PFO\*(CWELL-CFO/HFOWell)

dAFO=JFO\*AEXP\*FEXP + Qskin\*(AEXP/BSA)\*0.25 \* (CA - CvFO)

dAWELL =(Rdose-JSC00\*AEXP\*(1-FEXP)-AEXP\*FEXP\*JFO)\*OO\_S\_TP1

dCSC01 = DSC \* (CSC00 - 2 \* CSC01 + CSC02) / (SCDX \* SCDX)+u1\*(CSC02-CSC00)/(2\*SCDX)

dCSC02 = DSC \* (CSC01 - 2 \* CSC02 + CSC03) / (SCDX \* SCDX)+u1\*(CSC03-CSC01)/(2\*SCDX)

dCSC03 = DSC \* (CSC02 - 2 \* CSC03 + CSC04) / (SCDX \* SCDX)+u1\*(CSC04-CSC02)/(2\*SCDX)

dCSC04 = DSC \* (CSC03 - 2 \* CSC04 + CSC05) / (SCDX \* SCDX)+u1\*(CSC05-CSC03)/(2\*SCDX)

dCSC05 = DSC \* (CSC04 - 2 \* CSC05 + CSC06) / (SCDX \* SCDX)+u1\*(CSC06-CSC04)/(2\*SCDX)

dCSC06 = DSC \* (CSC05 - 2 \* CSC06 + CSC07) / (SCDX \* SCDX)+u1\*(CSC07-CSC05)/(2\*SCDX)

dCSC07 = DSC \* (CSC06 - 2 \* CSC07 + CSC08) / (SCDX \* SCDX)+u1\*(CSC08-CSC06)/(2\*SCDX)

dCSC08 = DSC \* (CSC07 - 2 \* CSC08 + CSC09) / (SCDX \* SCDX)+u1\*(CSC09-CSC07)/(2\*SCDX)

dCSC09 = DSC \* (CSC08 - 2 \* CSC09 + CSC10) / (SCDX \* SCDX)+u1\*(CSC10-CSC08)/(2\*SCDX)

dAVE = JSC10 \* AEXP\*(1-FEXP) + Qskin\*(AEXP/BSA)\*0.75\*(CA - CvVE)

if(t<=0.1 && t>=0){onoff\_oral =1} else{onoff\_oral =0}

dInput\_oral=oral\_intakerate\*onoff\_oral

Cgut <- ASI/enterocytes

dAST <- dInput\_oral-k0\*AST-ge\*AST

RAGImet <- vmaxgutg\*Cgut/(kmgutg+Cgut\*(1+Cgut/ksigutg))

RAGImets <- vmaxguts\*Cgut/(kmguts+Cgut)

RAAO <- k1\*ASI

dASI <- ge\*AST-RAGImet-RAAO-RAGImets

RAfeces <- k4\*ASI

RAoral <- k0\*AST+RAAO

RAGIin <- kGIing\*AGIBPAg

RAGIBPAg <- RAGImet - RAGIin

RAGIins <- kGIins\*AGIBPAs

RAGIBPAs <- RAGImets - RAGIins

Cskin <- Askin/(Vskin-VTSC-VTVE-VTFO)

CVskin <- Askin/((Vskin-VTSC-VTVE-VTFO)\*pskin)

CFat <- AFat/Vfat

CVFat <- AFat/(Vfat\*pfat)

Cgonad <- Agonad/Vgonad

CVgonad <- Agonad/(Vgonad\*pgonad)

CLiver <- ALiver/Vliver

CVLiver <- ALiver/(Vliver\*pliver)

Cbrain <- Abrain/Vbrain

CVbrain <- Abrain/(Vbrain\*pbrain)

CR <- AR/Vrich #

CVR <- AR/(Vrich\*prich) #

CVS <- AS/(Vslow\*pslow) # (nmol/L)

CS <- AS/Vslow #

CV <-(CVLiver\*Qliver+

CVskin\*(Qskin\*(1-AEXP/BSA)) +

CvVE\*(Qskin\*(AEXP/BSA)\*0.75)+

CvFO\*(Qskin\*(AEXP/BSA)\*0.25)+

+CVFat\*Qfat+CVR\*Qrich+CVS\*Qslow+

CVgonad\*Qgonad+CVbrain\*Qbrain)/QC #

dAskin <- Qskin\*(1-AEXP/BSA)\*(CA-CVskin)

dAplasma <- QC\*(CV-CA) -kurinebpa\*CV

dAfat <- Qfat\*(CA-CVFat)

dAgonad <- Qgonad\*(CA-CVgonad)

RAM <- vmaxliver\*CVLiver/(kmliver+CVLiver)

RAMs <- vmaxlivers\*CVLiver/(kmlivers+CVLiver)

RABPA\_delayinbpag <- ABPA\_delay\*kenterobpag

RABPA\_delayinbpas <- ABPA\_delays\*kenterobpas

dALiver <- Qliver\*(CA-CVLiver)+RAoral-RAM-RAMs+RABPA\_delayinbpag+RABPA\_delayinbpas

dAbrain <- Qbrain\*(CA-CVbrain) # (nmol/h)

dAR <- Qrich\*(CA-CVR)

dAS <- Qslow\*(CA-CVS)

dAurinebpa <- kurinebpa\*CV

RABPAg\_prod <- met1g\*RAM # (nmol/h) |Taken up into systemic circulation

RABPAg\_prod\_delay <- met2g\*RAM # (nmol/h) |Excreted into bile

RABPAg\_prod\_gut<- met1g\*RAGIin # (nmol/h)|Taken up into systemic circulation

RABPAg\_prod\_delay\_gut <- met2g\*RAGIin # (nmol/h) |Excreted into bile

RABPAs\_prod <- met1s\*RAMs # (nmol/h) |Taken up into systemic circulation

RABPAs\_prod\_delay <- met2s\*RAMs # (nmol/h) |Excreted into bile

RABPAs\_prod\_gut<- met1s\*RAGIins # (nmol/h)|Taken up into systemic circulation

RABPAs\_prod\_delay\_gut <- met2s\*RAGIins # (nmol/h) |Excreted into bile

RABPA\_delayin <- ABPA\_delay\*kentero

RAfecesiv <- ABPA\_delay\*k4\_IV

RABPA\_delay <- RABPAg\_prod\_delay+RABPAg\_prod\_delay\_gut-RABPA\_delayin-

RAfecesiv-RABPA\_delayinbpag

RABPA\_delayins <- ABPA\_delays\*kentero

RAfecesivs <- ABPA\_delays\*k4\_IV

RABPA\_delays <- RABPAs\_prod\_delay+RABPAs\_prod\_delay\_gut-RABPA\_delayins-

RAfecesivs-RABPA\_delayinbpas

Cbpac <- Abpac/(Vbodyg+1E-34)

Cbpas <- Abpas/(Vbodys+1E-34)

RAreabsorption <- vreabsorptiong\*Cbpac/(kreabsorptiong+Cbpac)

dAurineg <- kurinebpag\*Cbpac

RAurinebpag <- kurinebpag\*Cbpac-RAreabsorption

RAreabsorptions <- vreabsorptions\*Cbpas/(kreabsorptions+Cbpas)

dAurines <- kurinebpas\*Cbpas

RAurinebpas <- kurinebpas\*Cbpas-RAreabsorptions

RAbpac <- RABPAg\_prod+RABPAg\_prod\_gut+RABPA\_delayin-RAurinebpag

RAbpas <- RABPAs\_prod+RABPA\_delayins+RABPAs\_prod\_gut-RAurinebpas

dVurine=1.5/24

dydt <-

c(Rdose,dAFO,

dAWELL,dCSC01,dCSC02,dCSC03,dCSC04,dCSC05,dCSC06,

dCSC07,dCSC08,dCSC09,dAVE,dInput\_oral,

dAST,RAGImet,RAGImets,RAAO,dASI,

RAfeces,RAoral, RAGIin,RAGIBPAg,RAGIins,RAGIBPAs,

dAskin,dAplasma,dAfat,dAgonad,RAM,RAMs,RABPA\_delayinbpag,RABPA\_delayinbpas,

dALiver,dAbrain, dAR,dAS,dAurinebpa,

RABPAg\_prod,RABPAg\_prod\_delay,RABPAg\_prod\_gut,RABPAg\_prod\_delay\_gut,

RABPAs\_prod,RABPAs\_prod\_delay,RABPAs\_prod\_gut,RABPAs\_prod\_delay\_gut,

RABPA\_delayin,RAfecesiv,RABPA\_delay,RABPA\_delayins,RAfecesivs,RABPA\_delays,

RAreabsorption,dAurineg,RAurinebpag,

RAreabsorptions,dAurines,RAurinebpas,

RAbpac,RAbpas,dVurine)

conc <- c(CV=CV,CWELL=CWELL)

res <- list(dydt, conc)

return(res)

})}

zeit <- seq(0,75, 0.1) # (h) time

BPS1<-ode(y=yini\_bps\_dermal, func=PBTKmod\_bps,

times=zeit, parms=para\_bps\_dermal, method="lsoda")