## E. Chloroprene PBPK Model Equations

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#Chloroprene PBPK Model
#Translated from the acslX model presented in Yang et al. 2012
#By Jerry Campbell 2019

States  = {
AI        ,
AX        ,
AM        ,
AMLU   ,
AMK     ,
ALU      ,
AL        ,
AK        ,
AS        ,
AR        ,
AF
};

Outputs = {
MASBAL ,
CLU      ,
CL        ,
CK        ,
CS        ,
CR        ,
CF        ,
CV  ,
CVLUM ,
ppm ,
AMP     ,
AMPLU ,
AMPK   ,
cvl ,
qcbal ,
vbal
};

Inputs = {EXPPULSE};

#BODY WEIGHT (kg)
    BW = 0.03 ;    # Body weight (kg)
```

```
#SPECIAL FLOW RATES
QPC = 29.1 ;    # Unscaled Alveolar Vent (L/h/kg^0.75)
QCC = 20.1 ;    # Unscaled Cardiac Output (L/h/kg^0.75)

#FRACTIONAL BLOOD FLOWS TO TISSUES
QLC = 0.161 ;  # Flow to Liver as % Cardiac Output (unitless)
QFC = 0.07  ;  # Flow to Fat as % Cardiac Output (unitless)
QSC = 0.159 ;  # Flow to Slow as % Cardiac Output (unitless)
QKC = 0.09  ;  # Flow to Kidney as % Cardiac Output (unitless)

#FRACTIONAL VOLUMES OF TISSUES
VLC = 0.055 ;     # Volume Liver as % Body Weight (unitless)
VLUC = 0.0073 ;  # Volume Lung as % Body Weight (unitless)
VFC = 0.1  ;        # Volume Fat as % Body Weight (unitless)
VRC = 0.08098 ;     # Volume Rapid Perfused as % Body Weight (unitless)
VSC = 0.384  ;      # Volume Slow Perfused as % Body Weight (unitless)
VKC = 0.0167 ;     # Volume Kidney as % Body Weight  (unitless)

#PARTITION COEFFICIENTS PARENT
PL = 1.26 ;   # Liver/Blood Partition Coefficient (unitless)
PLU = 2.38 ;   # Lung/Blood Partition Coefficient (unitless)
PF = 17.35 ;   # Fat/Blood Partition Coefficient (unitless)
PS = 0.59  ;  # Slow/Blood Partition Coefficient (unitless)
PR = 1.76 ;   # Rapid/Blood Partition Coefficient (unitless)
PB = 7.83 ;   # Blood/Air Partition Coefficient (unitless)
PK = 1.76 ;   # Kidney/Blood Partition Coefficient (unitless)

#KINETIC CONSTANTS
MW = 88.5  ;  # Molecular weight (g/mol)

# Metabolism in Liver
VMAXC = 7.95  ;  # Scaled VMax for Oxidative Pathway:Liver (mg/h/BW^0.75)
KM = 0.041  ;  # Km for Oxidative Pathway:Liver (mg/L)

# Metabolism in Lung
 VMAXCLU = 0.18;    # Scaled VMax for Oxidative Pathway:Lung (mg/h/BW^0.75)
KMLU = 0.26;       # Km for Oxidative Pathway:Lung (mg/L)
KFLUC = 0.0;         # Pseudo-first order clearance in lung (Km unidentifiable) (L/hr/BW^0.75)

# Metabolism in Kidney
VMAXCKid = 0.0 ;   # Scaled VMax for Oxidative Pathway:Kidney (mg/h/BW^0.75)
KMKD = 0.0  ;  # Km for Oxidative Pathway :Kidney
KFKIC = 0.079;    # Pseudo-first order clearance in kidney (Km unidentifiable) (L/hr/BW^0.75)
```

```
#DOSING INFORMATION
TSTOP = 7.0 ;    # Dosing stop time
CONC = 13.0 ;   # Initial concentration (ppm)


Dynamics {

# Scaled parameters

      QC = QCC*pow(BW,0.75) ;      #Cardiac output
      QP = QPC*pow(BW,0.75) ;      #Alveolar ventilation
      QL = QLC*QC   ;            #Liver blood flow
      QF = QFC*QC   ;            #Fat blood flow
      QS = QSC*QC   ;            #Slowly-perf tissue blood flow
      QK = QKC*QC   ;            #Kidney tissue blood flow

     QRC = 1-QLC-QKC-QFC-QSC ;     #Rapily Perfused tissues
      QR = QRC*QC          ;                  #Rapily-perf tissue blood flow

      VL = VLC*BW     ;          #Liver volume
     VLU = VLUC*BW    ;          #Lung volume
      VF = VFC*BW     ;          #Fat tissue volume
      VS = VSC*BW     ;          #Slowly-perfused tissue volume
      VR = VRC*BW     ;          #Richly-perfised tissue volume
      VK = VKC*BW     ;          #kidney tissue volume

    ROBC = 1 - VLC - VLUC - VFC - VSC - VRC - VKC ;  #Rest of body un-perfused tissued for Monte Carlo
sims

# METABOLISM
    VMAX = VMAXC*pow(BW,0.75) ;      #Maximum rate of metabolism-Liver (mg/hr/kg-BW)
  VMAXLU = VMAXCLU*pow(BW,0.75) ;     #Maximum rate of metabolism-Lung (mg/hr/kg-BW)
    KFLU = KFLUC*pow(BW,0.75) ;
  VMAXKD = VMAXCKid*pow(BW,0.75) ;    #Maximum rate of metabolism-Kidney (mg/hr/kg-BW)
    KFKI = KFKIC*pow(BW,0.75) ;

# Exposure Control (mg/L)
     CIX = CONC*MW/24450 ;
      CI = CIX *EXPPULSE  ;

# Tissue Venous Concentrations (mg/L)
    CVLU = ALU/(VLU*PLU) ;
     CVL = AL/(VL*PL) ;
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    CVK = AK/(VK*PK) ;
    CVS = AS/(VS*PS) ;
    CVR = AR/(VR*PR) ;
    CVF = AF/(VF*PF) ;

# Concentration in Pulmonary/Arterial and venous blood Compartments (mg/L)
    CPU = (QP*CI+(QF*CVF + QL*CVL + QS*CVS + QR*CVR + QK*CVK))/(QP/PB+QC)  ;
     CX = CPU/PB ;
     CV = (QF*CVF + QL*CVL + QS*CVS + QR*CVR + QK*CVK)/QC ;
   CPUM = CPU*1000/MW ;
    RAI = QP*CI ;
    dt(AI) = RAI ;
    RAX = QP*CX ;
    dt(AX) = RAX ;

# Amount metabolized in Liver (mg)
    RAM = VMAX*CVL/(KM + CVL) ;
    dt(AM) = RAM ;

# Amount metabolized in Lung (mg)
    RAMLU = VMAXLU*CVLU/(KMLU + CVLU) + KFLU*CVLU ;
    dt(AMLU) = RAMLU ;

# Amount metabolized in Kidney (mg)
    RAMK = VMAXKD*CVK/(KMKD + CVK) + KFKI*CVK ;
    dt(AMK) = RAMK ;

# Amount in Lung Compartment (mg)
    RALU = QC*(CPU-CVLU) - RAMLU ;
    dt(ALU) = RALU ;

# Amount in Liver Compartment (mg)
    RAL = QL*(CVLU-CVL) - RAM ;
    dt(AL) = RAL ;

# Amount in Kidney Compartment (mg)
    RAK = QK*(CVLU-CVK) - RAMK ;
    dt(AK) = RAK ;

# Amount in Slowly Perfused Tissues (mg)
    RAS = QS*(CVLU - CVS) ;
    dt(AS) = RAS ;

# Amount in Rapidly Perfused Tissues (mg)
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```
    RAR = QR*(CVLU -CVR) ;
    dt(AR) = RAR ;

# Amount in Fat Compartment (mg)
    RAF = QF*(CVLU - CVF) ;
    dt(AF) = RAF ;

} # End of Dynamics

CalcOutputs {
# Mass-balance
          MASBAL = AI - AX - (AL+AM+AMLU+ALU+AK+AMK+AS+AR+AF) ;
          #Tissue Concentrations (mg/L)
           CLU = ALU/VLU ;
       CL = AL/VL ;
       CK = AK/VK ;
       CS = AS/VS ;
       CR = AR/VR ;
       CF = AF/VF ;
#Concentrations for plots
          CVLUM = CVLU*1000/MW ;  #(umol/L)
#Dose metrics
  ppm = CONC ;
  AMP = ((AM*1000/MW)/(VL*1000))/(TSTOP/24) ;
 AMPLU = ((AMLU*1000/MW)/(VLU*1000))/(TSTOP/24) ;
  AMPK = ((AMK*1000/MW)/(VK*1000))/(TSTOP/24) ;

  cvl = CVL ;

#Blood Flow balance
  qcbal = QC - QL - QF - QS - QK - QR ;
#Tissue Volume balance
   vbal = BW*(1-ROBC) - VL - VLU - VF - VS - VK - VR ;

} # End of CalcOutputs

End.
```