

SUPPLEMENTARY DATA

INITIAL

constant BW = 70. ! Body weight (kg)
constant conc = 0 ! Exposition dose (ppm)
constant MW = 0 ! Molecular weight
constant SV = 24.450 ! Standard volume mL/mol
constant DUREE= 0 ! Exposure lenght (h)
constant periode = 0 ! Period between two exposures (h)

! Tissue volumes (fraction of body weight)

constant VLc = 0.026 ! Liver (fraction of body weight)
constant VRc = 0.05 ! Richly perfused tissues (fraction of body weight)
constant VSc = 0.62 ! Poorly perfused tissues (fraction of body weight)
constant VFc = 0.19 ! Fat (fraction of body weight)

VL = VLc*BW ! Liver (L)
VR = VRc*BW ! Richly perfused tissues (L)
VS = VSc*BW ! Poorly perfused tissues (L)
VF = VFc*BW ! Fat (L)

! Flows

constant $QP_c = 18$! Alveolar ventilation (L/h/kg)

constant $QC_c = 18$! Cardiac output (L/h/kg)

$QP = QP_c \cdot BW^{0.74}$! Alveolar ventilation (L/h)

$QC = QC_c \cdot BW^{0.74}$! Cardiac output (L/h)

constant $QL_c = 0.26$! Liver (fraction of QC)

constant $QR_c = 0.44$! Richly perfused tissues (fraction of QC)

constant $QSc = 0.25$! Poorly perfused tissues (fraction of QC)

constant $QFc = 0.05$! fat (%QC)

$QL = QL_c \cdot QC$! Liver (L/h)

$QR = QR_c \cdot QC$! Richly perfused tissues (L/h)

$QS = QSc \cdot QC$! Poorly perfused tissues (L/h)

$QF = QFc \cdot QC$! fat (L/h)

! Partition coefficients (PCs)

constant $PB = 0.0$! Blood:air

constant $PLB = 0.0$! Liver:blood

constant PRB = 0.0 ! RPT:blood

constant PSB = 0.0 ! PPT:blood

constant PFB = 0.0 ! Fat:blood

! Metabolism constants

constant logclint = 0.0 ! log CLint (L PL/h/kg)

CLintPL = 10**logclint ! CLint L PL/h/kg

constant pplb = 0.0 ! Phospholipids:blood PC

CLint = CLintPL * pplb * BW**0.75 ! CLint (L bloob/h)

constant KFC = 0.0 ! First order metabolism (h-kg)-1

KF = KFC * BW**0.3 ! First order metabolism (h-1)

! Hepatic clearance based on CLint and Kf

CLH = QL * (CLINT + KF * VL)/(QL + CLINT + KF * VL)

! Hepatic clearance based extraction ratio (E)

constant E = 0.0 ! Extraction ratio

! CLH = QL * E

END ! INITIAL

DYNAMIC

! Exposure scenario

JOURNE=PULSE(0.,periode,DUREE) ! 24 h exposure

CI=JOURNE*conc *MW / SV /1000 ! Inhaled concentration (mg/L)

! Blood concentrations

CA = (CI*QP+QC*CV)/(QC+QP/PB) ! Arterial mg/L

CV = (QL*CVL+QR*CVR+QS*CVS+QF*CVF)/QC ! Venous mg/L

AUC = INTEG(CV, 0.0) ! Venous blood area under the curve (mg/L-h)

CALV = CA/PB*SV/MW*1000 ! Alveolar air PPM

! Tissue compartments

! Liver

rAL = QL*(CA-CVL) - CLH * CA ! Rate of amount (mg/h)

AL = integ (rAL,0.0) ! Amount (mg)

CL = AL/VL ! Liver concentration (mg/L)

CVL = CL/PLB ! Liver venous blood concentration (mg/L)

! Richly perfused tissues

$rAR = QR*(CA-CVR)$! Rate of amount (mg/h)

$AR = \text{integ}(rAR, 0.0)$! Amount (mg)

$CR = AR/VR$! Richly perfused tissues concentration (mg/L)

$CVR = CR/PRB$! Richly perfused tissues venous blood concentration (mg/L)

! Slowly perfused tissues

$rAS = QS*(CA-CVS)$! Rate of amount (mg/h)

$AS = \text{integ}(rAS, 0.0)$! Amount (mg)

$CS = AS/VS$! Poorly perfused tissues concentration (mg/L)

$CVS = CS/PSB$! Poorly perfused tissues venous blood concentration (mg/L)

! Fat

$rAF = QF*(CA-CVF)$! Rate of amount (mg/h)

$AF = \text{integ}(rAF, 0.0)$! Amount (mg)

$CF = AF/VF$! Fat concentration (mg/L)

$CVF = CF/PFB$! Fat venous blood concentration (mg/L)

END ! DYNAMIC