Supporting Information

APPLICATION OF BAYESIAN POPULATION PBPK MODELING AND MARKOV CHAIN MONTE CARLO SIMULATIONS TO PESTICIDE KINETICS STUDIES IN PROTECTED MARINE MAMMALS: DDT, DDE, DDD IN HARBOUR PORPOISES

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Supporting Information: Overview

Table S1. Parameters used for PBPK model calibration of male harbour porpoises. Table modified from Weijs et al. (2010b).

Parameter	Value/equation
Body Weight (BW; g)[a]	$1.387 \times BS^{2.076}$
Body Size (BS; cm)[b]	$142.4 \times (1-0.3751\ e^{(-0.000068 \times age)})$
Cardiac output (QC; L/hr)[c]	$(0.1017 \times (BW/1000)^{0.9988}) \times 60$
Compartment mass (g):	
blubber (V_F)[d]	$18.41 \times BW^{0.607}$
brain (V_B)[d]	$49.20 \times BW^{0.211}$
liver (V_L)[d]	$0.060 \times BW^{0.932}$
kidney (V_K)[d]	$0.002 \times BW^{1.137}$
muscle (V_R)	$(0.99 \times BW) - (V_F + V_B + V_L + V_K + V_{Blood})$
blood (V_{Blood})[e]	$0.143 \times BW$
Density (DENS; g/L):	
Blubber (F)[f]	920
Brain (B)[f]	1050
Liver (L)[f]	1040
Kidney (K)[f]	1050
Muscle (R)[f]	1040
Blood[g]	1068
Fractional blood flow (%)[h]:	
to blubber (Q_FC)	5
to brain (Q_BC)	12
to liver (Q_LC)	25
to kidney (Q_KC)	19
to muscle (Q_RC)	$100 - (Q_FC + Q_BC + Q_LC + Q_KC)$
Lipid percentage (FATPERC; %)[i]:	
blubber	92.85
liver	3.73
kidney	3.24
brain	11.49
blood	0.45
muscle	2.27
Daily consumption of milk (DCMILK; g/day)[k]	540
Daily consumption of fish (DC; g/day)[l]	$0.123 \times BW^{0.80}$

a-correlations developed using existing data from male harbour porpoises from the literature; b-Von Bertalanffy age dependent growth-curves developed using existing data male harbour porpoises from the literature; c-Altman and Dittmer (1971); d-McLellan et al. (2002); e-Reed et al. (2000); f-Maruyama et al. (2002); g-Dolfinarium Harderwijk, The Netherlands, personal communication; h-Williams and Leggett (1989), Brown et al. (1997); i-Weijs et al. (2010a); k-Oftedal (1997); l-Innes et al. (1987)

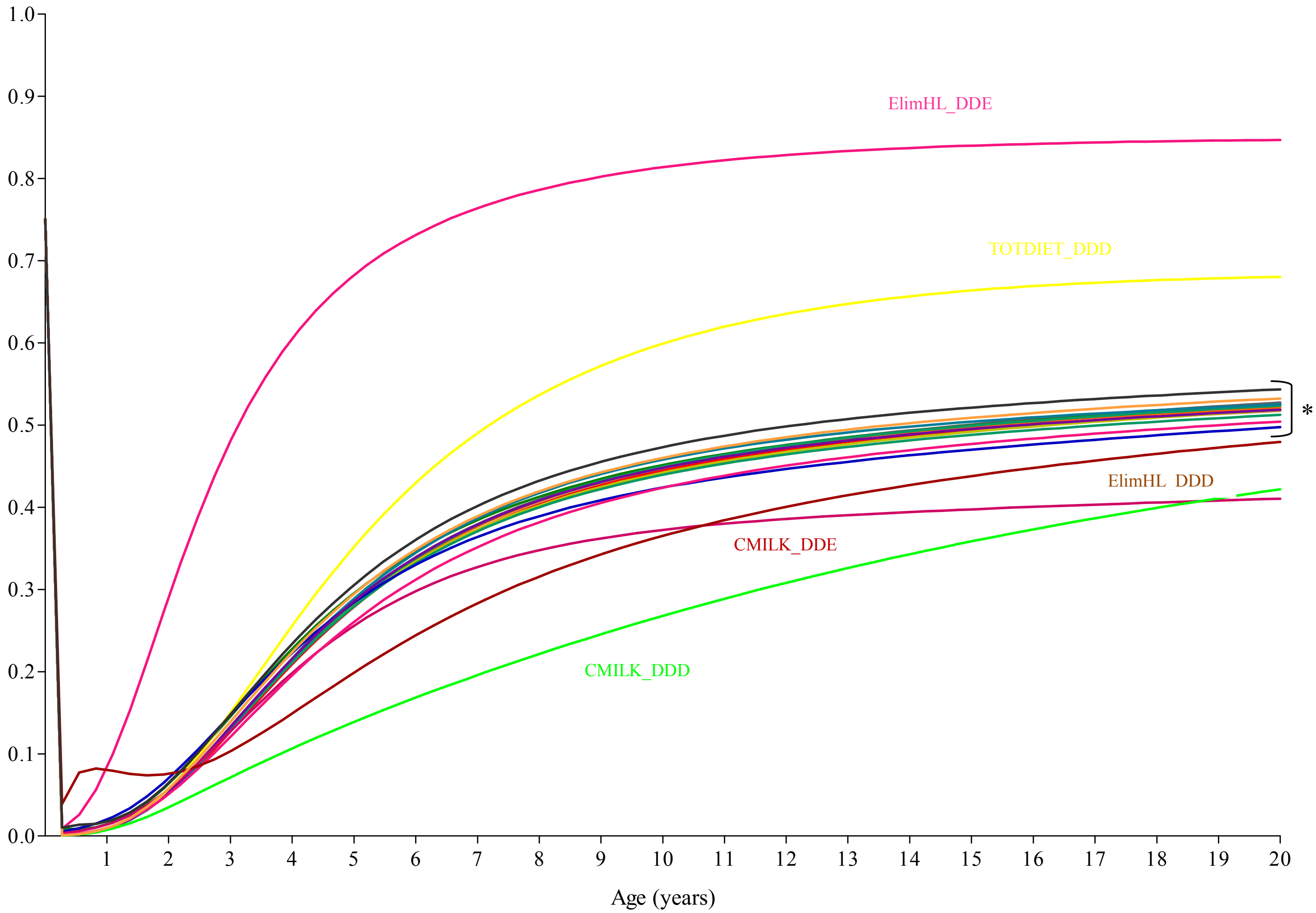
Table S2. Results of the Morris sensitivity test. The influence of changes in all 49 parameters was tested on the concentration of DDT, DDE and DDD in the blood, respectively, as this medium connects all compartments. Parameter ranges were broad, but arbitrarily chosen. The Morris test yields two sensitivity measures for each parameter: μ as an overall sensitivity measure and σ as an indication for a parameter interacting with other parameters or a parameter with a non-linear effect (McNally et al., 2011). According to the values of μ and σ, parameters were divided into 3 categories: I) *very sensitive* (values for μ and σ), II) *intermediate sensitive* (values for μ but σ values equal to zero) and III) *not sensitive* (extremely low values for μ or μ values equal to zero, σ values equal to zero). Parameters in grey were de-selected for the eFAST tests.

Parameter	Range	cBlood_DDT	cBlood_DDE	cBlood_DDD
PF_DDT	200 – 500	I	II	III
PR_DDT	0 – 15	I	I	I
PL_DDT	0.1 – 10	II	III	III
PB_DDT	0.1 – 20	II	III	III
PK_DDT	0.1 – 10	II	III	III
PF_DDE	200 – 500	III	II	III
PR_DDE	0 – 15	II	II	I
PL_DDE	0.1 – 10	III	II	III
PB_DDE	0.1 – 20	III	III	III
PK_DDE	0.1 – 10	III	II	III
PF_DDD	200 – 500	III	III	I
PR_DDD	0 – 15	II	II	II
PL_DDD	0.1 – 10	III	III	III
PB_DDD	0.1 – 20	III	III	III
PK_DDD	0.1 – 10	III	III	III
TOTDIET_DDT	10 – 60	I	I	II
CMILK_DDT	400 – 12 000	I	II	III
DCMILK	300 – 800	I	I	I
IN_DIET_DDT	0.5 – 1	I	I	I
IN_MILK_DDT	0.5 – 1	II	I	II
TOTDIET_DDE	50 – 150	III	II	III
CMILK_DDE	2700 – 51 200	III	II	III
IN_DIET_DDE	0.5 – 1	III	I	III
IN_MILK_DDE	0.5 – 1	III	II	III
TOTDIET_DDD	30 - 120	III	II	I
CMILK_DDD	2300 – 33 000	III	II	I
IN_DIET_DDD	0.5 – 1	III	II	I
IN_MILK_DDD	0.5 – 1	III	II	I
QLC	0.2 – 0.4	II	III	II
QFC	0.01 – 0.2	II	III	III
QBC	0.1 – 0.2	III	III	III
QKC	0.1 – 0.2	III	III	III
DENSL	1000 – 1200	II	II	II
FATPERCL	0.01 – 0.2	III	III	III
DENSF	850 – 1100	II	II	I
FATPERCF	0.65 – 0.99	III	III	III
DENSB	1000 – 1200	III	III	III
FATPERCB	0.03 – 0.3	III	III	III
DENSK	1000 – 1200	III	III	III
FATPERCK	0.01 – 0.15	III	III	III
DENSR	1000 – 1200	II	III	III
FATPERCR	0.01 – 0.15	III	III	III
DENSBlood	1000 – 1200	II	II	I
FATPERCBlood	0.0001 – 0.01	I	I	I
ElimHL_DDT	0.0001 – 7	I	II	I
ElimHL_DDE	0.0001 – 7	III	I	III

ElimHL_DDD	0.0001 – 7	III	III	I
PercDDT	0.1 – 0.7	III	II	I
PercDDD	0.01 – 0.5	III	II	III

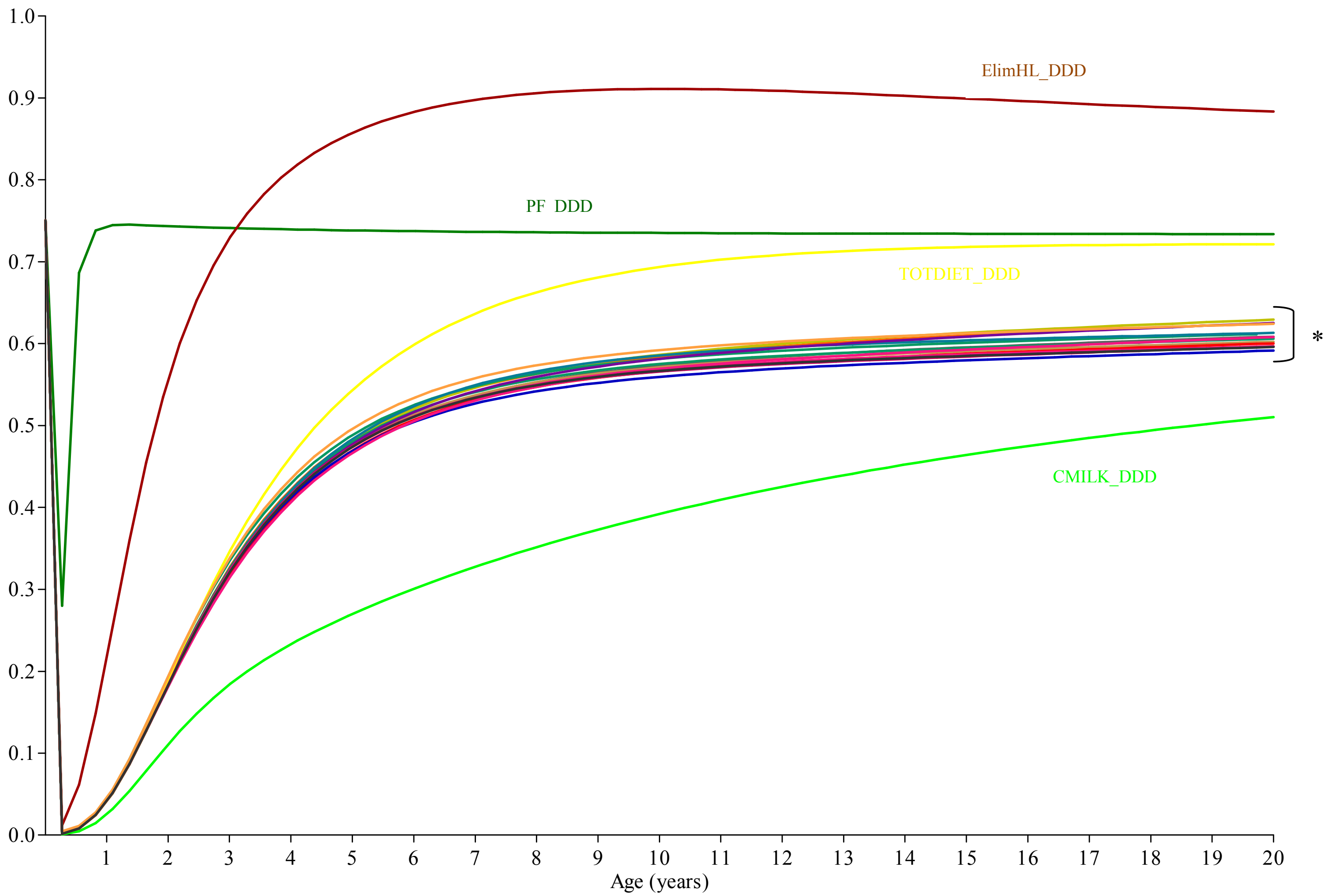
P – partition coefficient between blood and tissue; ElimHL – elimination half-life value; TOTDIET – concentration in the fish diet; CMILK – concentration in the milk diet

Figure S1. Results of the global sensitivity eFAST test on the concentration of *p,p'*-DDE in blood over the entire lifetime of the animals. X-axis represents the age of the animals expressed in years. Y-axis represents the sensitivity coefficients.



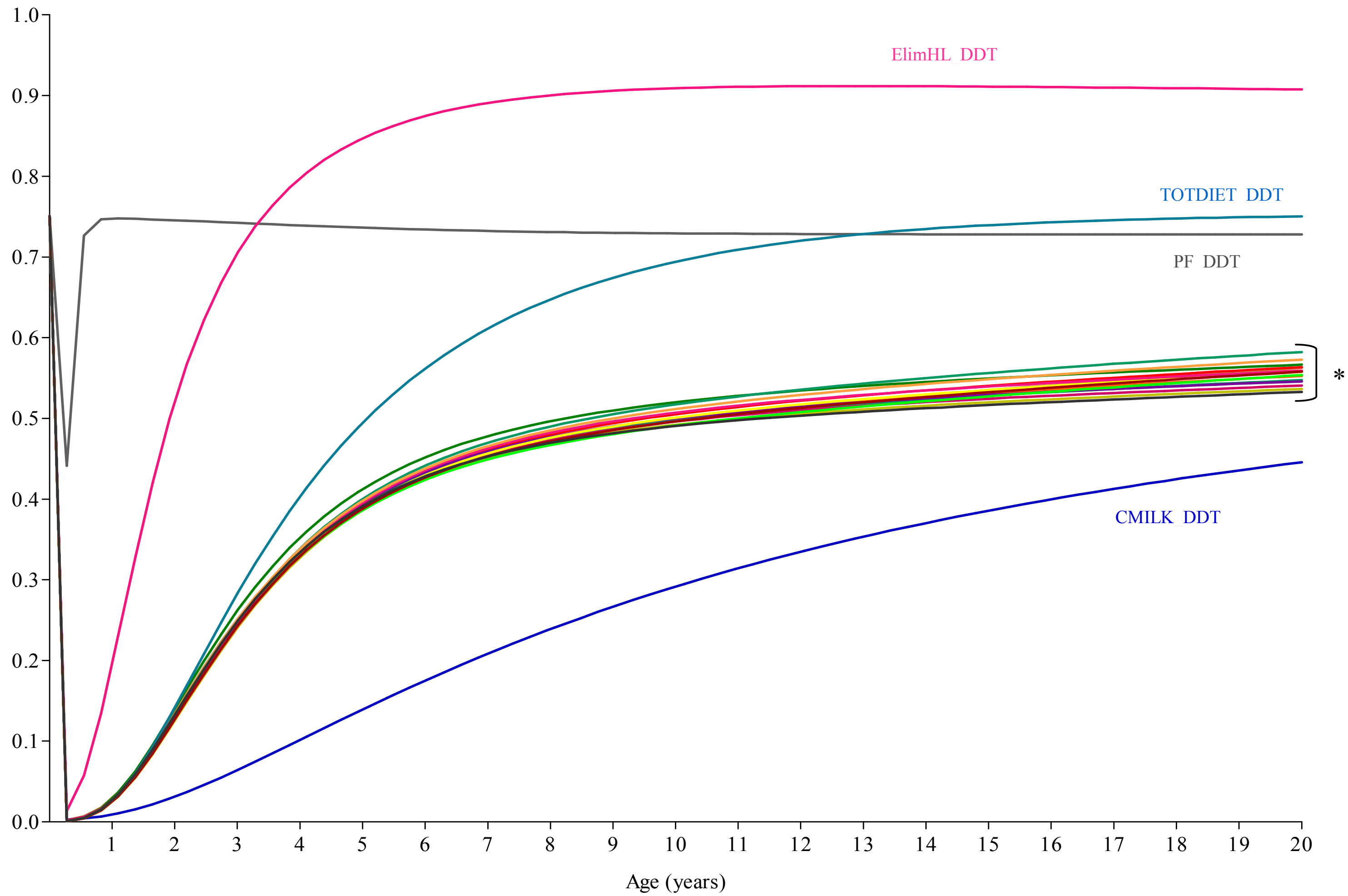
* - PF_DDT, PL_DDT, PR_DDT, PK_DDT, PB_DDT, PF_DDD, PR_DDD, PB_DDD, CMILK_DDT, TOTDIET_DDT, TOTDIET_DDE, ElimHL_DDT, PercDDD, PercDDT

Figure S2. Results of the global sensitivity eFAST test on the concentration of *p,p'*-DDD in blood over the entire lifetime of the animals. X-axis represents the age of the animals expressed years. Y-axis represents the sensitivity coefficients.



* - PF_DDT, PL_DDT, PR_DDT, PK_DDT, PB_DDT, PR_DDD, PB_DDD, CMILK_DDE, CMILK_DDT, TOTDIET_DDT, TOTDIET_DDE, ElimHL_DDT, ElimHL_DDE, PercDDD, PercDDT

Figure S3. Results of the global sensitivity eFAST test on the concentration of *p,p'*-DDT in blood over the entire lifetime of the animals. X-axis represents the age of the animals expressed in years. Y-axis represents the sensitivity coefficients.



* - PL_DDT, PR_DDT, PK_DDT, PB_DDT, PF_DDD, PR_DDD, PB_DDD, CMILK_DDE, CMILK_DDD, TOTDIET_DDD, TOTDIET_DDE, ElimHL_DDT, ElimHL_DDE, PercDDD, PercDDT

Codes of structural model (Berkeley Madonna)

NOTE: Parameters with the following description 'UPDATED WITH BAYESIAN APPROACH AND MCMC SIMULATIONS' can be found in Table 3 in the main manuscript.

COMMENT: Codes of the structural and statistical model (AcslX/Libero) are available upon request to the corresponding author.

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{--------------------PHYSIOLOGICAL PARAMETERS--------------------}

BW=1.387*BS**2.076
{body weight (g), body size-dependent; Weijs et al., 2010b}

BS=142.4*(1-0.3751*exp(-0.000068*TIME))
{body size or body length (cm), age-dependent; Weijs et al., 2010b}

VF=18.41*BW**0.607
{Mass of fat (g), body weight-dependent; McLellan et al., 2002}
VFL=VF/DENSF
{Volume of fat (L)}
DENSF=920
{density of fat (human) =0.92 g/mL, Maruyama et al., 2002}

VB=49.20*BW**0.211
{Mass of brain (g), body weight-dependent; McLellan et al., 2002}
VBL=VB/DENSB
{Volume of brain (L)}
DENSB=1050
{density of brain (human) =1.05 g/mL; Maruyama et al., 2002}

VL=0.060*BW**0.932
{Mass of liver (g), body weight-dependent; McLellan et al., 2002}
VLL=VL/DENSL
{Volume of liver (L)}
DENSL=1040
{density of liver (human) =1.04 g/mL; Maruyama et al., 2002}

VK=0.002*BW**1.137
{Mass of kidney (g), body weight-dependent; McLellan et al., 2002}
VKL=VK/DENSK
{Volume of kidney (L)}
DENSK=1050
{density of kidney (human)=1.05 g/mL; Maruyama et al., 2002}

VBlood=0.143*BW
{Mass of blood (g), body weight dependent; Reed et al., 2000}
VBloodL=VBlood/DENSBlood
{Volume of blood (L)}
DENSBlood=1068
{density of blood (bottlenose dolphin; n=3; Harderwijk, personal communication)=1.068 g/mL}

VR=(0.99*BW)-VBlood-VK-VL-VB-VF
{Compartment for 'Rest of the body'; under the assumption that 1% of the body is pharmacokinetically inactive}
VRL=VR/DENSR
{Volume of rest of the body (muscle) (L)}
DENSR=1040
{Density of muscle (human)=1.04 g/mL, Maruyama et al., 2002. The 'muscle' is the biggest part of 'the rest of
the body' compartment and muscle parameters are therefore used when needed}

FATPERCF=0.9285
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{average fatpercentage of blubber; data from male porpoises Black Sea; Weijs et al., 2010a }
FATPERCK=0.0324
{average fatpercentage of kidney; data from male porpoises Black Sea; Weijs et al., 2010a}
FATPERCL=0.0373
{average fatpercentage of liver; data from male porpoises Black Sea; Weijs et al., 2010a}
FATPERCB=0.1149
{average fatpercentage of brain; data from male porpoises Black Sea; Weijs et al., 2010a}
FATPERCBlood=0.0045
{fatpercentage of blood; Maruyama et al., 2002}
FATPERCR=0.0227
{average fatpercentage of muscle; data from male porpoises Black Sea; Weijs et al., 2010a}

QC=(0.1017*(BW/1000)**0.9988)*60
{Cardiac output (L/hr); Equation from Altman and Dittmer, 1971}

QFC=0.05
{ fat blood flow (human) - portion of total, fractional blood flow to fat, Williams and Leggett, 1989 and Brown et al., 1997; percentage }
QF=QFC*QC
{L/hr}

QLC=0.25
{ liver blood flow (human) - portion of total, fractional blood flow to liver, Williams and Leggett, 1989 and Brown et al., 1997; percentage }
QL=QLC*QC
{L/hr}

QBC=0.12
{ brain blood flow (human) - portion of total, fractional blood flow to brain, Williams and Leggett, 1989 and Brown et al., 1997; percentage }
QB=QBC*QC
{L/hr}

QKC=0.19
{ kidney blood flow (human) - portion of total, fractional blood flow to kidney, Williams and Leggett, 1989 and Brown et al., 1997; percentage }
QK=QKC*QC
{L/hr}

QRC=100-QFC-QLC-QBC-QKC
{ muscle blood flow (human) - portion of total, fractional blood from to muscle, Williams and Leggett, 1089 and Brown et al., 1997. Constant is 17%, however recalculated to meet assumptions of mass balance; percentage}
QR=QRC*QC
{L/hr}

PF_DDT=331.0
{Fat/blood partition coefficient; UPDATED WITH BAYESIAN APPROACH AND MCMC SIMULATIONS}
PL_DDT=0.2
{Liver/blood partition coefficient; UPDATED WITH BAYESIAN APPROACH AND MCMC SIMULATIONS}
PB_DDT=1.5
{Brain/blood partition coefficient; UPDATED WITH BAYESIAN APPROACH AND MCMC SIMULATIONS}
PK_DDT=0.9
{Kidney/blood partition coefficient; UPDATED WITH BAYESIAN APPROACH AND MCMC SIMULATIONS}
PR_DDT=3.5
{Rest of the body/blood partition coefficient; UPDATED WITH BAYESIAN APPROACH AND MCMC SIMULATIONS; Rest of the body here is actually 'muscle'}

PF_DDD=400.8
{Fat/blood partition coefficient; UPDATED WITH BAYESIAN APPROACH AND MCMC SIMULATIONS}
PL_DDD=7.9
{Liver/blood partition coefficient; UPDATED WITH BAYESIAN APPROACH AND MCMC SIMULATIONS}
PB_DDD=3.0
{Brain/blood partition coefficient; UPDATED WITH BAYESIAN APPROACH AND MCMC SIMULATIONS}
PK_DDD=4.6
{Kidney/blood partition coefficient; UPDATED WITH BAYESIAN APPROACH AND MCMC SIMULATIONS}
PR_DDD=15.0
{Rest of the body/blood partition coefficient; UPDATED WITH BAYESIAN APPROACH AND MCMC SIMULATIONS; Rest of the body here is actually 'muscle'}

PF_DDE=450.0
{Fat/blood partition coefficient;ATSDR, 2002}
PL_DDE=7.0
{Liver/blood partition coefficient; ATSDR, 2002}
PB_DDE=6.0
{Brain/blood partition coefficient; ATSDR, 2002}
PK_DDE=6.0
{Kidney/blood partition coefficient; ATSDR, 2002}
PR_DDE=12.0
{Rest of the body/blood partition coefficient; ATSDR, 2002; Rest of the body here is actually 'muscle'}

{--------------------DOSING--------------------}

TOTDIET_DDT=33.88
{Tanabe et al., 1997a and b; unit ng/g ww (wet weight)}
IN_DDT=0.98
{Assimilation efficiency; Thomas et al., 2005}
DC=(0.123*(BW/1000)**0.80)*1000
{Daily Consumption (g/day) for porpoises according to Innes et al. (1987)}
DIET_DDT=(DC*IN_DDT*TOTDIET_DDT)/24
{ng/hr ///// no unit*g/day*ng/g= ng/day divided by 24 hrs=ng/hr}
LACTATION_DDT=(IN_DDT*DCMILK*CMILK_DDT)/24
{the same unit as DIET = ng/hr}
DCMILK=540
{Daily Milk Consumption (g/day) for porpoises during lactation according to Oftedal (1997)}
FATPERCMILK=0.2994
{Fat percentage of milk of harbour porpoises; own analyses of Black Sea animals; Table 1 (main manuscript)}
CMILK_DDT=779.3
{ng/g; own analyses of Black Sea animals}
DOSE_DDT=IF TIME<=2920 THEN LACTATION_DDT ELSE DIET_DDT
{switch from milk-diet to fish-diet after 4 months (2920 hours) lactation}

TOTDIET_DDD=68.87
{Tanabe et al., 1997a and b; unit ng/g ww (wet weight)}
IN_DDD=0.99
{Assimilation efficiency; Thomas et al., 2005; this is a percentage }
DIET_DDD=(DC*IN_DDD*TOTDIET_DDD)/24
{ng/hr ///// no unit*g/day*ng/g= ng/day divided by 24 hrs=ng/hr}
LACTATION_DDD=(IN_DDD*DCMILK*CMILK_DDD)/24
{the same unit as DIET = ng/hr}
CMILK_DDD=1628.6
{ng/g; own analyses of Black Sea animals}

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DOSE_DDD=IF TIME<=2920 THEN LACTATION_DDD ELSE DIET_DDD
{switch from milk-diet to fish-diet after 4 months (2920 hours) lactation}

TOTDIET_DDE=114.79
{Tanabe et al., 1997a and b; unit ng/g ww (wet weight)}
IN_DDE=0.97
{Assimilation efficiency; Thomas et al., 2005; this is a percentage, so no unit}
DIET_DDE=(DC*IN_DDE*TOTDIET_DDE)/24
{ng/hr ///// no unit*g/day*ng/g= ng/day divided by 24 hrs=ng/hr}
LACTATION_DDE=(IN_DDE*DCMILK*CMILK_DDE)/24
{the same unit as DIET = ng/hr}
CMILK_DDE=2011.7
{ng/g; own analyses of Black Sea animals}
DOSE_DDE=IF TIME<=2920 THEN LACTATION_DDE ELSE DIET_DDE
{switch from milk-diet to fish-diet after 4 months (2920 hours) lactation}



{--------------------MASS-BALANCE EQUATIONS DDT--------------------}

AF_DDT'=QF*(CBlood_DDT-CVF_DDT)
CVF_DDT=CF_DDT/PF_DDT
CF_DDT=AF_DDT/VFL
CFG_DDT=CF_DDT/(DENSF*FATPERCF)
init AF_DDT=CFoetusF_DDT*DENSF*VFL
CFoetusF_DDT=918.8

AR_DDT'=QR*(CBlood_DDT-CVR_DDT)
CVR_DDT=CR_DDT/PR_DDT
CR_DDT=AR_DDT/VRL
CRG_DDT=CR_DDT/(DENSR*FATPERCR)
init AR_DDT=CFoetusR_DDT*DENSR*VRL
CFoetusR_DDT=0.000001

AL_DDT'=(QL*(CBlood_DDT-CVL_DDT)-HepMet_DDT+DOSE_DDT)
CVL_DDT=CL_DDT/PL_DDT
CL_DDT=AL_DDT/VLL
CLG_DDT=CL_DDT/(DENSL*FATPERCL)
init AL_DDT=CFoetusL_DDT*DENSL*VLL
CFoetusL_DDT=0.000001

CLint_DDT=0.06315
{Biotransformation in liver; calculated according Verner et al. (2009) using an elimination half life of 4.8 years;
UPDATED WITH BAYESIAN APPROACH AND MCMC SIMULATIONS}
Eh_DDT=(CLint_DDT*VLL)/(CLint_DDT*VLL+QL)
HepMet_DDT=QL*Eh_DDT*CBlood_DDT

AK_DDT'=QK*(CBlood_DDT-CVK_DDT)
CVK_DDT=CK_DDT/PK_DDT
CK_DDT=AK_DDT/VKL
CKG_DDT=CK_DDT/(DENSK*FATPERCK)
init AK_DDT=CFoetusK_DDT*DENSK*VKL
CFoetusK_DDT=4.7

AB_DDT'=QB*(CBlood_DDT-CVB_DDT)
CVB_DDT=CB_DDT/PB_DDT
CB_DDT=AB_DDT/VBL
CBG_DDT=CB_DDT/(DENSB*FATPERCB)
init AB_DDT=CFoetusB_DDT*DENSB*VBL
CFoetusB_DDT=3.9
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ABlood_DDT'=QF*CVF_DDT+QR*CVR_DDT+QL*CVL_DDT+QK*CVK_DDT+QB*CVB_DDT-
(QF+QR+QL+QK+QB)*CBlood_DDT
CBlood_DDT=ABlood_DDT/VBloodL
CBloodG_DDT=CBlood_DDT/(DENSBlood*FATPERCBlood)
init ABlood_DDT=CFoetusBlood_DDT*DENSBlood*VBloodL
CFoetusBlood_DDT=0.000001

ABioaccumulation_DDT'=Dose_DDT-HepMet_DDT
init ABioaccumulation_DDT=CFoetusF_DDT*DENSF*VFL+CFoetusR_DDT*DENSR*VRL+
CFoetusL_DDT*DENSL*VLL+CFoetusK_DDT*DENSK*VKL+CFoetusB_DDT*DENSB*VBL+CFoetusBlo
od_DDT*DENSBlood*VBloodL

{--------------------MASS BALANCE--------------------}

TOTAL_DDT=ABioaccumulation_DDT
CALCULATION_DDT=AF_DDT+AR_DDT+AL_DDT+AB_DDT+AK_DDT+ABlood_DDT
MASSBALANCE_DDT=(TOTAL_DDT-CALCULATION_DDT)/(TOTAL_DDT+1E-30)*100



{--------------------MASS-BALANCE EQUATIONS DDD--------------------}

AF_DDD'=QF*(CBlood_DDD-CVF_DDD)
CVF_DDD=CF_DDD/PF_DDD
CF_DDD=AF_DDD/VFL
CFG_DDD=CF_DDD/(DENSF*FATPERCF)
init AF_DDD=CFoetusF_DDD*DENSF*VFL
CFoetusF_DDD=2943.8

AR_DDD'=QR*(CBlood_DDD-CVR_DDD)
CVR_DDD=CR_DDD/PR_DDD
CR_DDD=AR_DDD/VRL
CRG_DDD=CR_DDD/(DENSR*FATPERCR)
init AR_DDD=CFoetusR_DDD*DENSR*VRL
CFoetusR_DDD=0.000001

AL_DDD'=(QL*(CBlood_DDD-CVL_DDD)-HepMet_DDD+DOSE_DDD+PercDDT*HepMet_DDT)
CVL_DDD=CL_DDD/PL_DDD
CL_DDD=AL_DDD/VLL
CLG_DDD=CL_DDD/(DENSL*FATPERCL)
init AL_DDD=CFoetusL_DDD*DENSL*VLL
CFoetusL_DDD=37.6

PercDDT=0.502
{UPDATED WITH BAYESIAN APPROACH AND MCMC SIMULATIONS}

CLint_DDD=0.111919
{Biotransformation in liver; calculated according Verner et al. (2009) using an elimination half life of 3.6 years;
UPDATED WITH BAYESIAN APPROACH AND MCMC SIMULATIONS}
Eh_DDD=(CLint_DDD*VLL)/(CLint_DDD*VLL+QL)
HepMet_DDD=QL*Eh_DDD*CBlood_DDD

AK_DDD'=QK*(CBlood_DDD-CVK_DDD)
CVK_DDD=CK_DDD/PK_DDD
CK_DDD=AK_DDD/VKL
CKG_DDD=CK_DDD/(DENSK*FATPERCK)
init AK_DDD=CFoetusK_DDD*DENSK*VKL
CFoetusK_DDD=35.5
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AB_DDD'=QB*(CBlood_DDD-CVB_DDD)
CVB_DDD=CB_DDD/PB_DDD
CB_DDD=AB_DDD/VBL
CBG_DDD=CB_DDD/(DENSB*FATPERCB)
init AB_DDD=CFoetusB_DDD*DENSB*VBL
CFoetusB_DDD=27.6

ABlood_DDD'=QF*CVF_DDD+QR*CVR_DDD+QL*CVL_DDD+QK*CVK_DDD+QB*CVB_DDD-(QF+QR+QL+QK+QB)*CBlood_DDD
CBlood_DDD=ABlood_DDD/VBloodL
CBloodG_DDD=CBlood_DDD/(DENSBlood*FATPERCBlood)
init ABlood_DDD=CFoetusBlood_DDD*DENSBlood*VBloodL
CFoetusBlood_DDD=0.000001

ABioaccumulation_DDD'=Dose_DDD-HepMet_DDD+PercDDT*HepMet_DDT
init ABioaccumulation_DDD=CFoetusF_DDD*DENSF*VFL+CFoetusR_DDD*DENSR*VRL+CFoetusL_DDD*DENSL*VLL+CFoetusK_DDD*DENSK*VKL+CFoetusB_DDD*DENSB*VBL+CFoetusBlood_DDD*DENSBlood*VBloodL

{--------------------MASS BALANCE--------------------}

TOTAL_DDD=ABioaccumulation_DDD
CALCULATION_DDD=AF_DDD+AR_DDD+AL_DDD+AB_DDD+AK_DDD+ABlood_DDD
MASSBALANCE_DDD=(TOTAL_DDD-CALCULATION_DDD)/(TOTAL_DDD+1E-30)*100

{--------------------MASS-BALANCE EQUATIONS DDE--------------------}

AF_DDE'=QF*(CBlood_DDE-CVF_DDE)
CVF_DDE=CF_DDE/PF_DDE
CF_DDE=AF_DDE/VFL
CFG_DDE=CF_DDE/(DENSF*FATPERCF)
init AF_DDE=CFoetusF_DDE*DENSF*VFL
CFoetusF_DDE=3351.6

AR_DDE'=QR*(CBlood_DDE-CVR_DDE)
CVR_DDE=CR_DDE/PR_DDE
CR_DDE=AR_DDE/VRL
CRG_DDE=CR_DDE/(DENSR*FATPERCR)
init AR_DDE=CFoetusR_DDE*DENSR*VRL
CFoetusR_DDE=0.000001

AL_DDE'=QL*(CBlood_DDE-CVL_DDE)-HepMet_DDE+DOSE_DDE+((1.0-PercDDT)*HepMet_DDT)+(PercDDD*HepMet_DDD)
CVL_DDE=CL_DDE/PL_DDE
CL_DDE=AL_DDE/VLL
CLG_DDE=CL_DDE/(DENSL*FATPERCL)
init AL_DDE=CFoetusL_DDE*DENSL*VLL
CFoetusL_DDE=50.5

PercDDD=0.10
{UPDATED WITH BAYESIAN APPROACH AND MCMC SIMULATIONS}

CLint_DDE=0.036037
{Biotransformation in liver; calculated according Verner et al. (2009) using an elimination half life of 11.8 years; UPDATED WITH BAYESIAN APPROACH AND MCMC SIMULATIONS}
Eh_DDE=(CLint_DDE*VLL)/(CLint_DDE*VLL+QL)
HepMet_DDE=QL*Eh_DDE*CBlood_DDE

```
AK_DDE'=QK*(CBlood_DDE-CVK_DDE)
CVK_DDE=CK_DDE/PK_DDE
CK_DDE=AK_DDE/VKL
CKG_DDE=CK_DDE/(DENSK*FATPERCK)
init AK_DDE=CFoetusK_DDE*DENSK*VKL
CFoetusK_DDE=43.3

AB_DDE'=QB*(CBlood_DDE-CVB_DDE)
CVB_DDE=CB_DDE/PB_DDE
CB_DDE=AB_DDE/VBL
CBG_DDE=CB_DDE/(DENSB*FATPERCB)
init AB_DDE=CFoetusB_DDE*DENSB*VBL
CFoetusB_DDE=42.0

ABlood_DDE'=QF*CVF_DDE+QR*CVR_DDE+QL*CVL_DDE+QK*CVK_DDE+QB*CVB_DDE-
(QF+QR+QL+QK+QB)*CBlood_DDE
CBlood_DDE=ABlood_DDE/VBloodL
CBloodG_DDE=CBlood_DDE/(DENSBlood*FATPERCBlood)
init ABlood_DDE=CFoetusBlood_DDE*DENSBlood*VBloodL
CFoetusBlood_DDE=0.000001

ABioaccumulation_DDE'=Dose_DDE-HepMet_DDE+((1.0-PercDDT)*HepMet_DDT)+
(PercDDD*HepMet_DDD)
init ABioaccumulation_DDE=CFoetusF_DDE*DENSF*VFL+CFoetusR_DDE*DENSR*VRL+
CFoetusL_DDE*DENSL*VLL+CFoetusK_DDE*DENSK*VKL+CFoetusB_DDE*DENSB*VBL+CFoetusBlo
od_DDE*DENSBlood*VBloodL

{--------------------MASS BALANCE--------------------}

TOTAL_DDE=ABioaccumulation_DDE
CALCULATION_DDE=AF_DDE+AR_DDE+AL_DDE+AB_DDE+AK_DDE+ABlood_DDE
MASSBALANCE_DDE=(TOTAL_DDE-CALCULATION_DDE)/(TOTAL_DDE+1E-30)*100
```

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