Bounding the uncertainties in intake and elimination of PBDEs in the North American population

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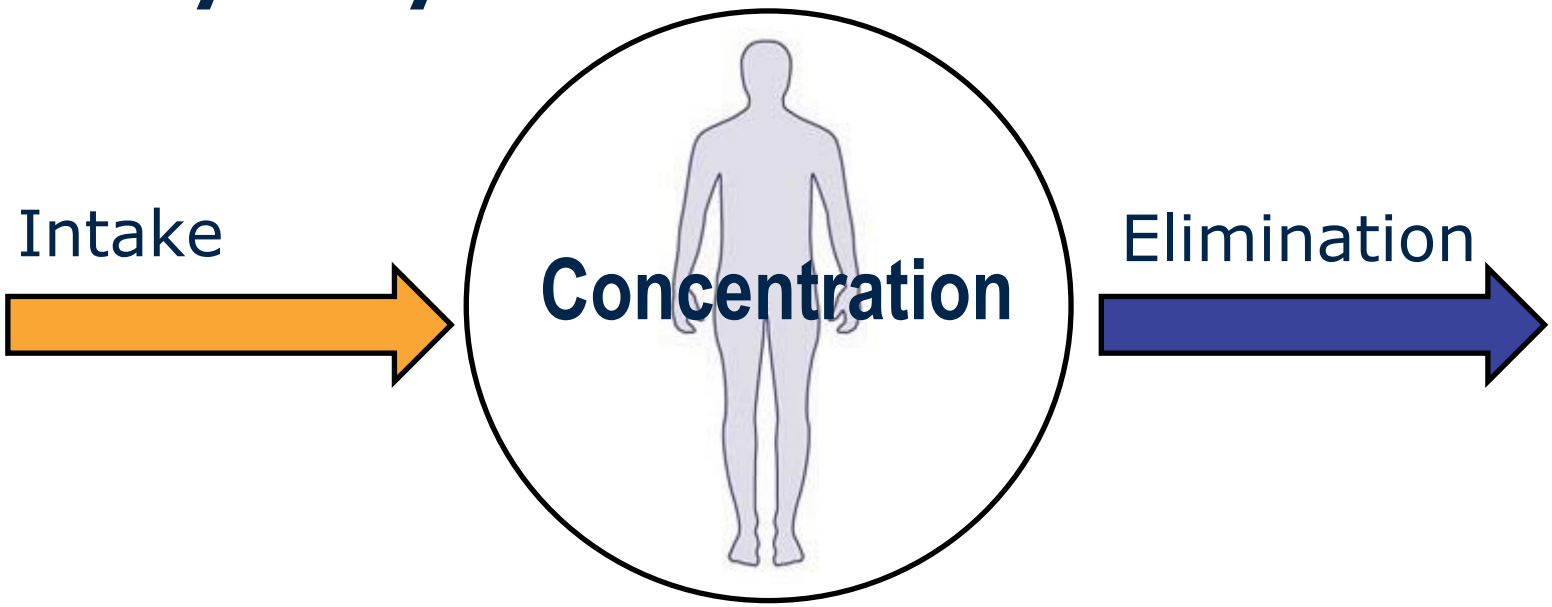
How much chemicals are accumulating in my body?



Exposure pathway studies, I

Experimental studies, k_e

Population pharmacokinetic model

(Ritter et al. EHP2011)

$$\frac{\partial n(t)}{\partial t} = I(t) - k_e \cdot n(t)$$

Intake, all exposure pathways

Elimination rate, k_e

Half-life = ln 2/k_e

Body burden – Biomonitoring

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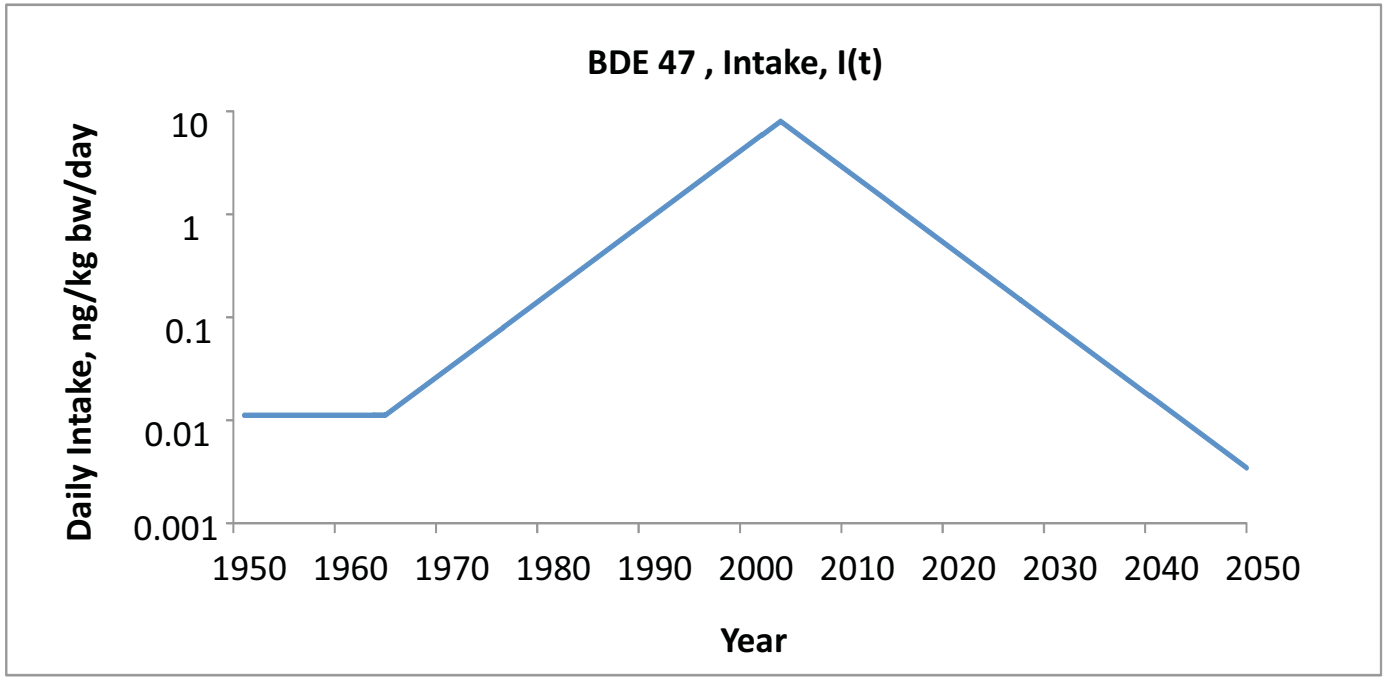
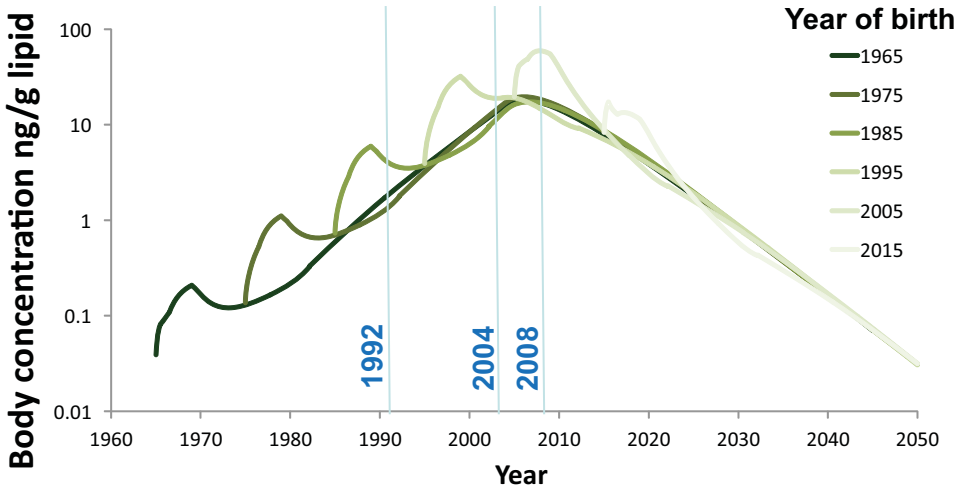
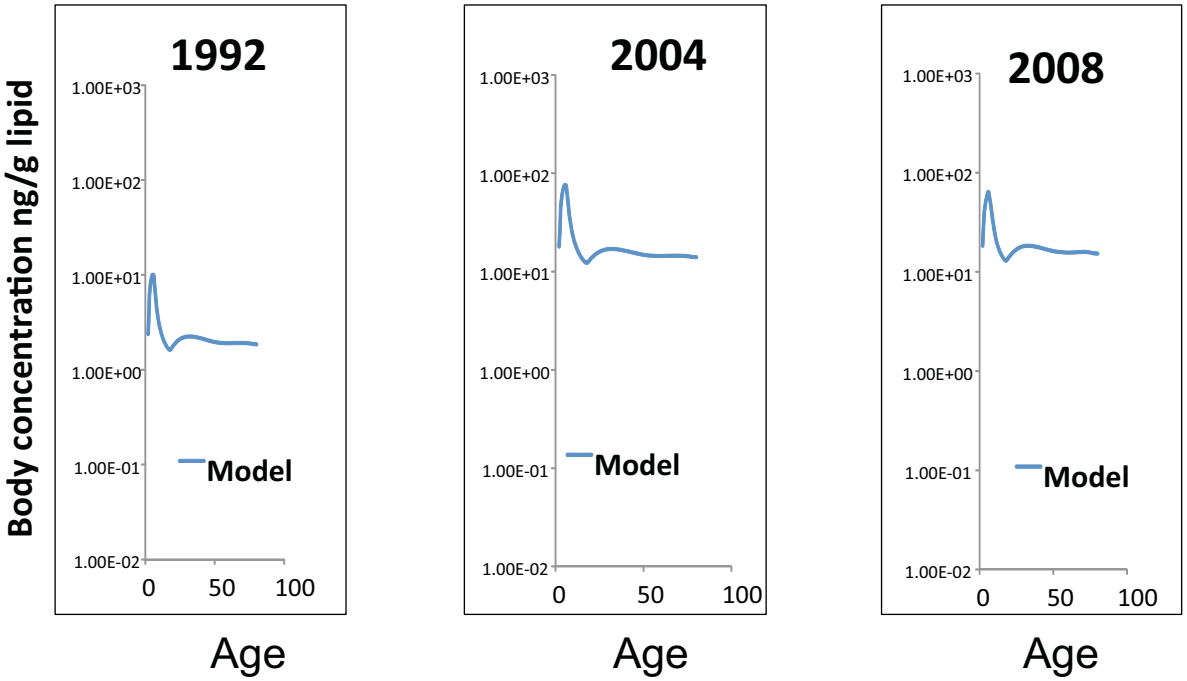
1. Intake level as function of time



2. Body burden of a chemical as function of time



3. Body burden as function of age in samples collected at specific time



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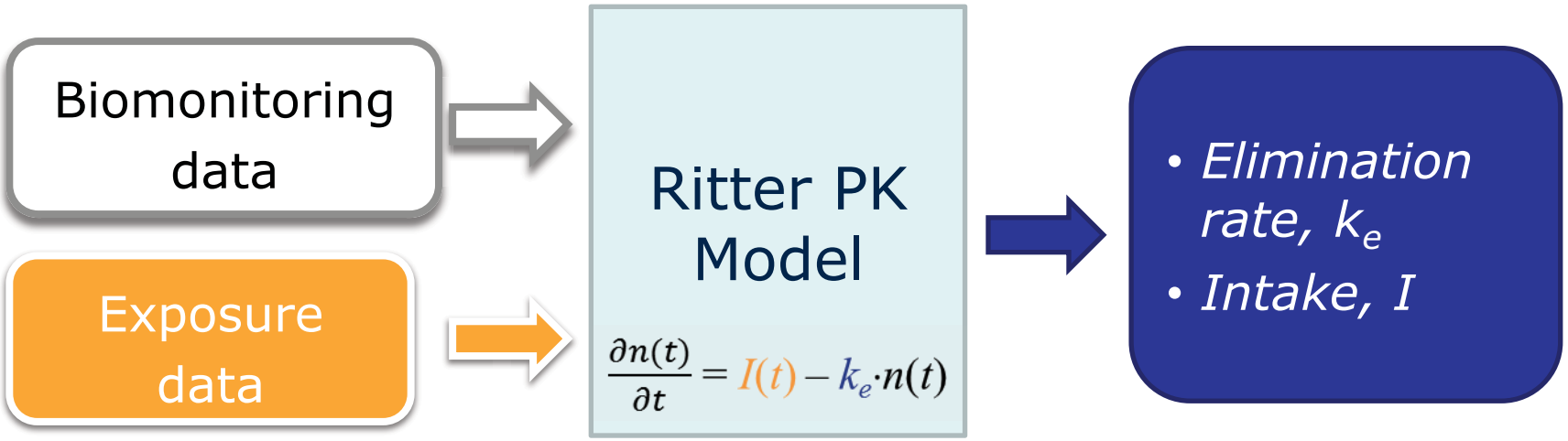
Population pharmacokinetic model



PBDEs in the N. America population

Biomonitoring Data, *n(t)*

- Canada and US general population, 1982 to 2009
- Serum and milk samples
- 10 studies (*Ryan 2000 and 2002; Schecter et al. 2005 and 2010; Sjodin et al. 2008;Johnson et al. 2010; Watkins et al. 2011)*

Exposure data, *I(t)*

- Total exposure pathways (dietary, dust/soil ingestion, inhalation, dermal etc)
- 2 studies (*Lorber 2008; Trudel et al. 2011)*

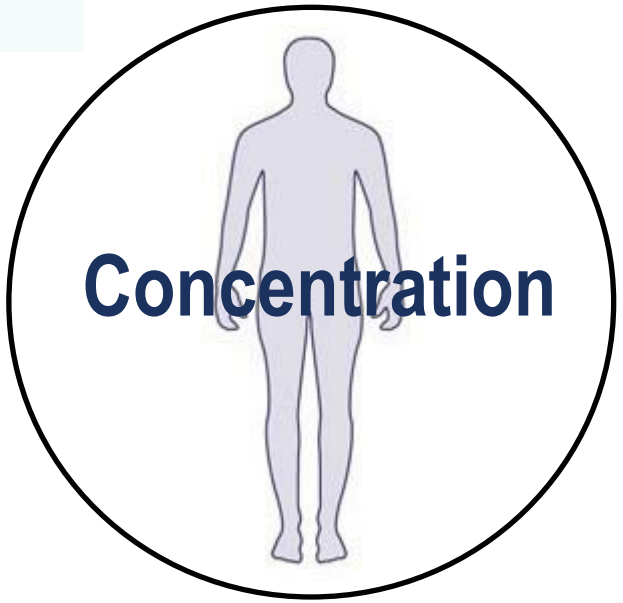
Model to fit both biomonitoring and exposure data – BDE47

	Model	Measured
$I(t_{2004})$, ng/kg bw/day	1.11	0.44, 1.98
$t_{1/2}$ (yrs)	440000	1.4 to 3

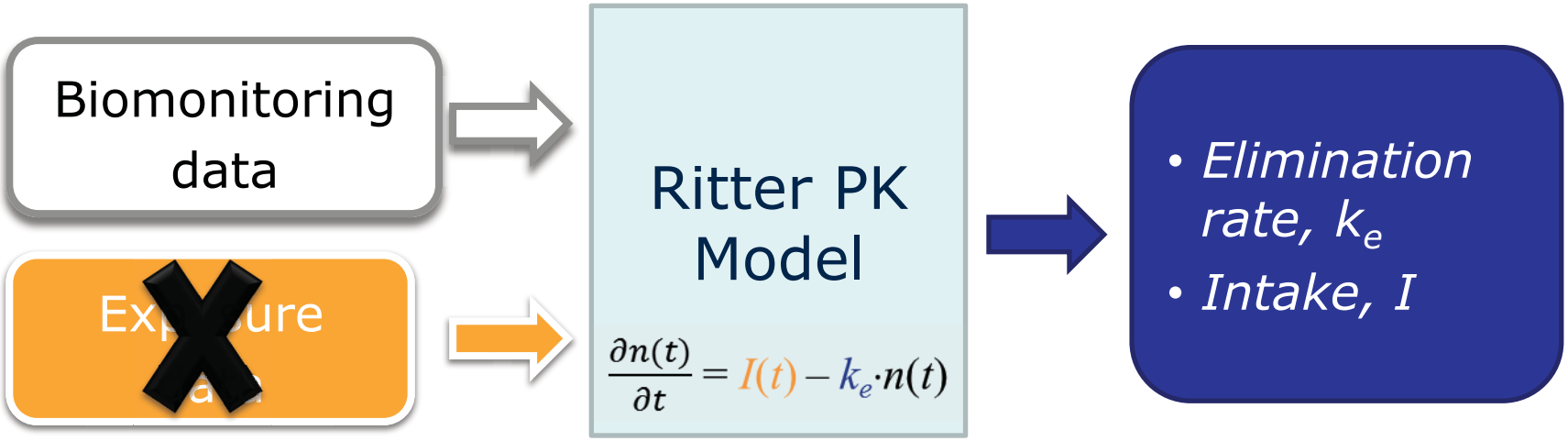
Low intake
Long half-live

OR

High intake
Short half-live



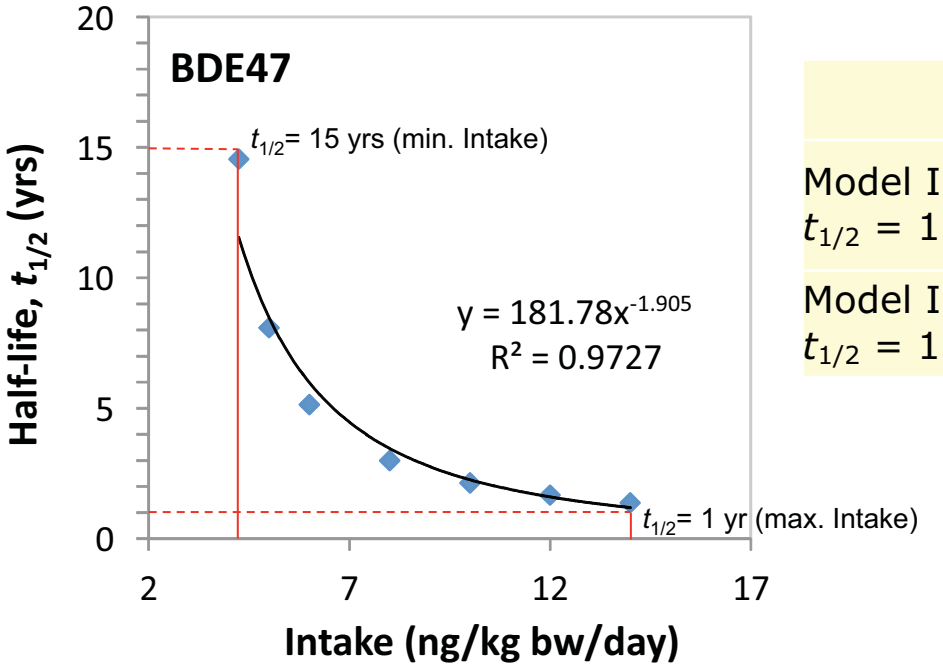
Population pharmacokinetic model



- Fit the model to the biomonitoring data only
- Constrain the half-lives to less than 15 years

Model to fit biomonitoring data only and constrain half-lives < 15 yrs

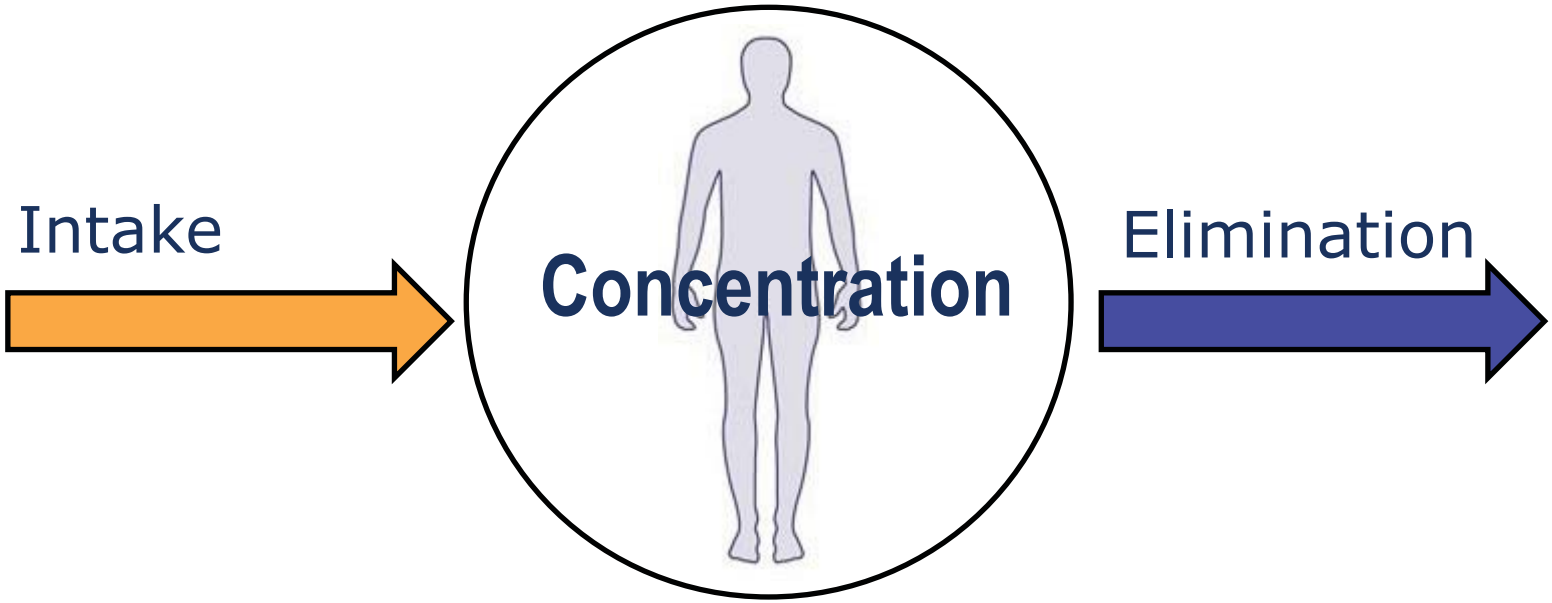
BDE47						Measured
$I(t_{2004})$, ng/kg bw/day	14	10	8	6	4.2	0.44 1.98
$t_{1/2}$ (yrs)	1.37	2.1	3.0	5.1	14.5	1.4 to 3



	BDE47
Model Intake at 2004 (minimum) $t_{1/2}$ = 15 yrs	3.70
Model Intake at 2004 (maximum) $t_{1/2}$ = 1 yr	15.3

Conclusion

- *Modeled intake is higher than measured*
- *Discrepancy between exposure and biomonitoring data*
- *Need better understanding and characterization of exposures*



Work Plan

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- Prepare manuscript
- Apply the Ritter PK model to European population
- Secondment at IVL, NIPH and visit to Birmingham

Meetings:

Nordic Environmental Chemistry Conference 2012

Dioxin 2012

Publication (related to INFLAME):

Wong et al. Fate of brominated flame retardants and organochlorine pesticides in urban soil: volatility and degradation. Environ. Sci. Technol., 2012, 46, 2668-2674.

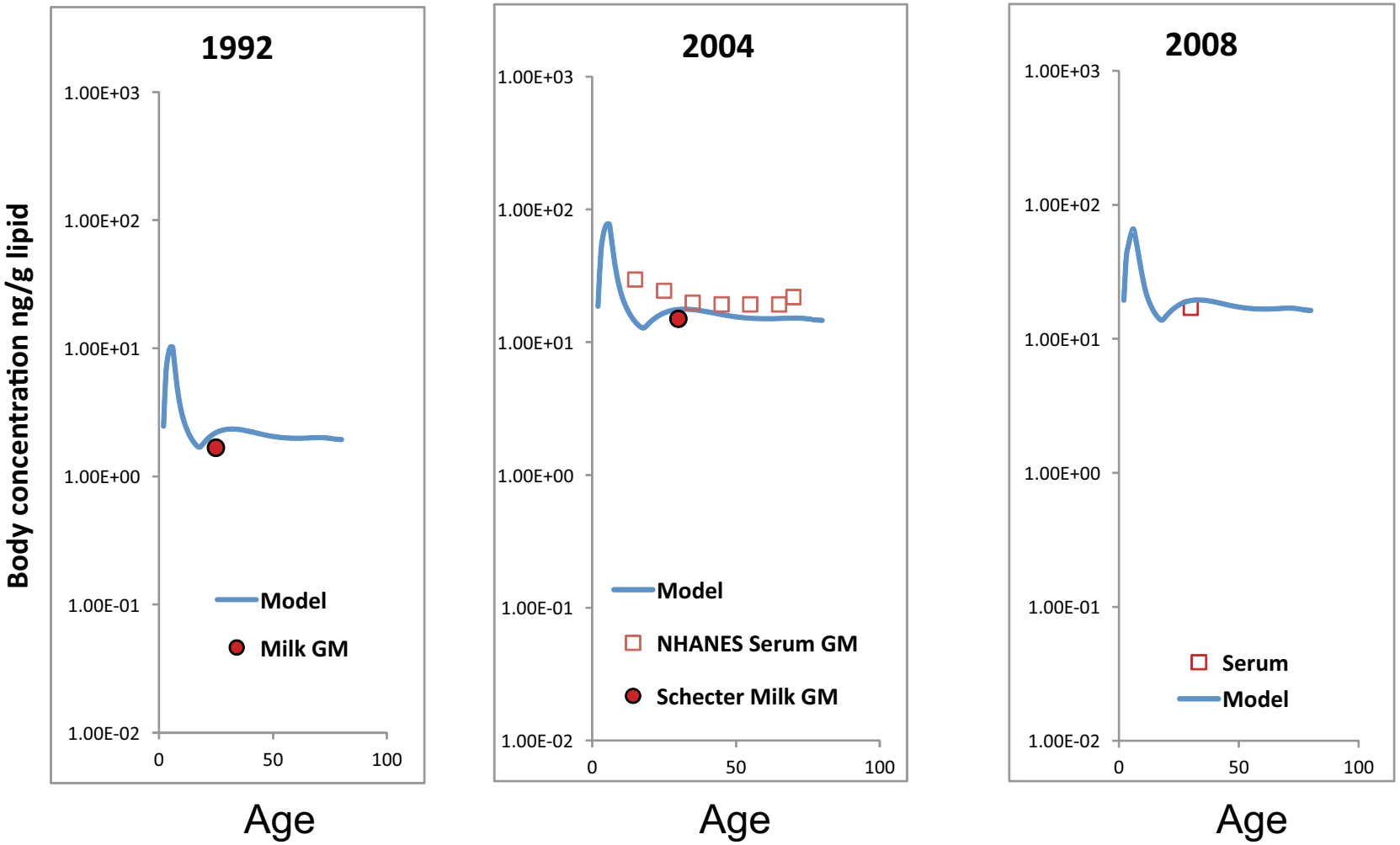
- enantioselective degradation of TBECH, TBCO, DPTE

Results – Model vs. Empirical intakes

	BDE47	**BDE99**	**BDE100**	**BDE153**	**Reference**
Empirical intake	1.98	2.19	0.83	0.23	Lorber, 2008
Empirical intake	0.442	0.476	0.187	0.051	Trudel et al., 2011
Model Intake at 2004 (minimum) $t_{1/2}$ = 15 yrs	*3.70*	*1.10*	*0.85*	*0.76*	*Present study*
Model Intake at 2004 (maximum) $t_{1/2}$ = 1 yr	*15.3*	*4.4*	*3.7*	*3.0*	*Present study*
Half-lives (yrs)	1.4 to 3	0.77 to 5.4	1.8-2.9	6.5-12	Geyer et al., 2004, Trudel et al., 2011

- Model intakes are great than empirical data

BDE47, Intake = 8 ng/kg bw/day, $t_{1/2}$ = 3 years



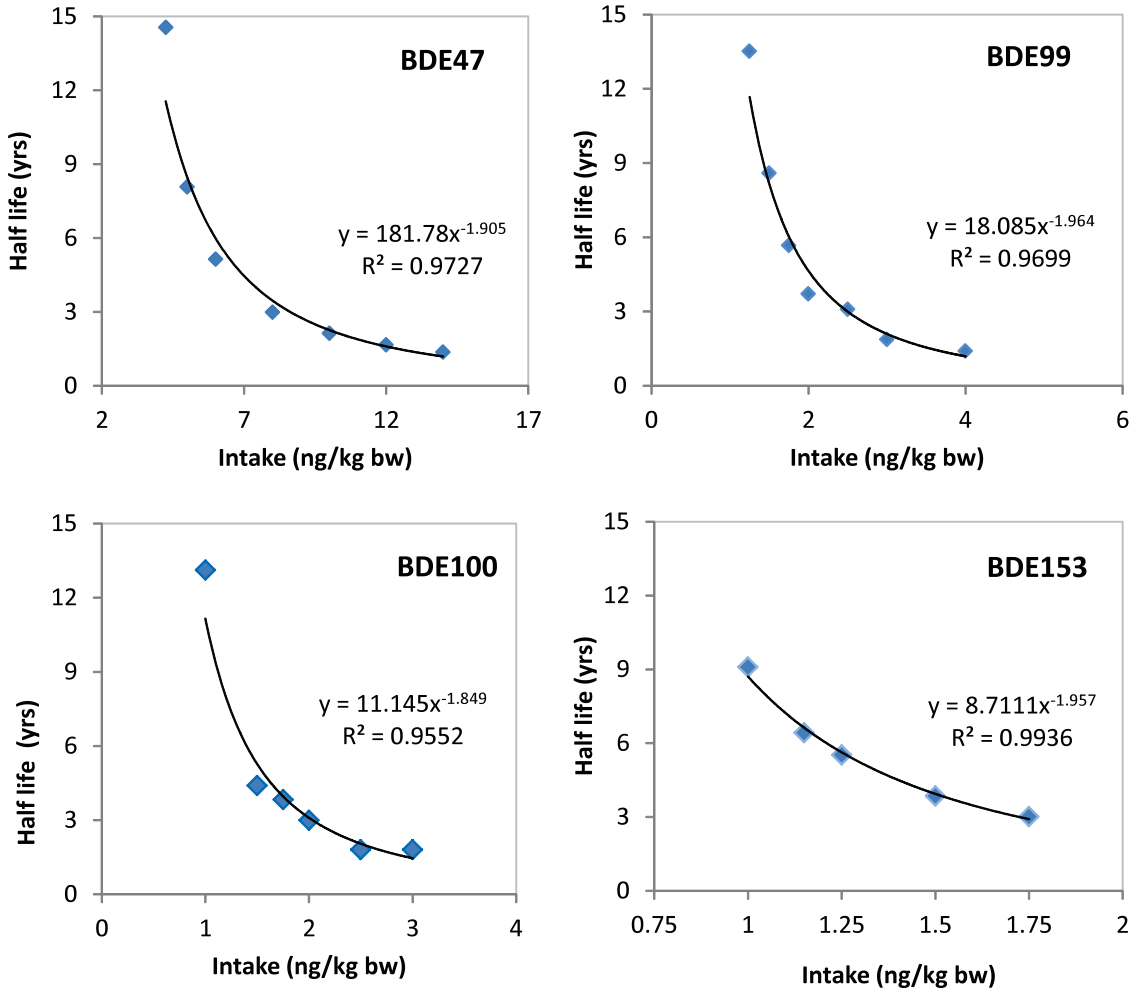
The Ritter Model

$$\frac{\partial n(t)}{\partial t} = I(t) - k \cdot n(t)$$

Intake: $I(t) = u \times E_a \times M_{bw}(t_{age}) \times I_{ref}(t) \times P(t_{age})$

$$\frac{dC(t^{age})}{dt} = -(k_{elim} + \frac{M_{lip}'(t^{age})}{M_{lip}(t^{age})}) \cdot C(t^{age}) + \frac{I(t^{age}, t^{birth} = const.)}{M_{lip}(t^{age})}$$

Model to fit biomonitoring data only and constrain half-lives < 15 yrs



BDE47, Intake = 8 ng/kg bw/day, $t_{1/2}$ = 3 years