Effects of bis(2,4,6-tribromophenoxy)ethane (BTBPE) in Mink (*Mustela vison*)

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Introduction

- Concentrations of brominated flame retardants (BFRs) have been monitored in the environment, wildlife, and humans
- BFRs can be persistent, bioaccumulate, undergo long range transport, and elicit adverse health effects
- Two commercial polybrominated diphenyl ether (PBDEs) BFRs (octa-BDE and penta-BDE) are no longer produced because of environmental concerns
- PentaBDE (DE-71) studies in mink indicate bioaccumulation in the liver and effects on reproduction and thyroid homeostasis
- Production and use of non-PBDE BFR alternatives, such as 1,2 bis(2,4,6-tribromophenoxy)ethane (BTBPE), have increased
- BTBPE has been detected in the environment including in fish and wildlife from the Great Lakes, e.g. herring gull eggs, lake trout

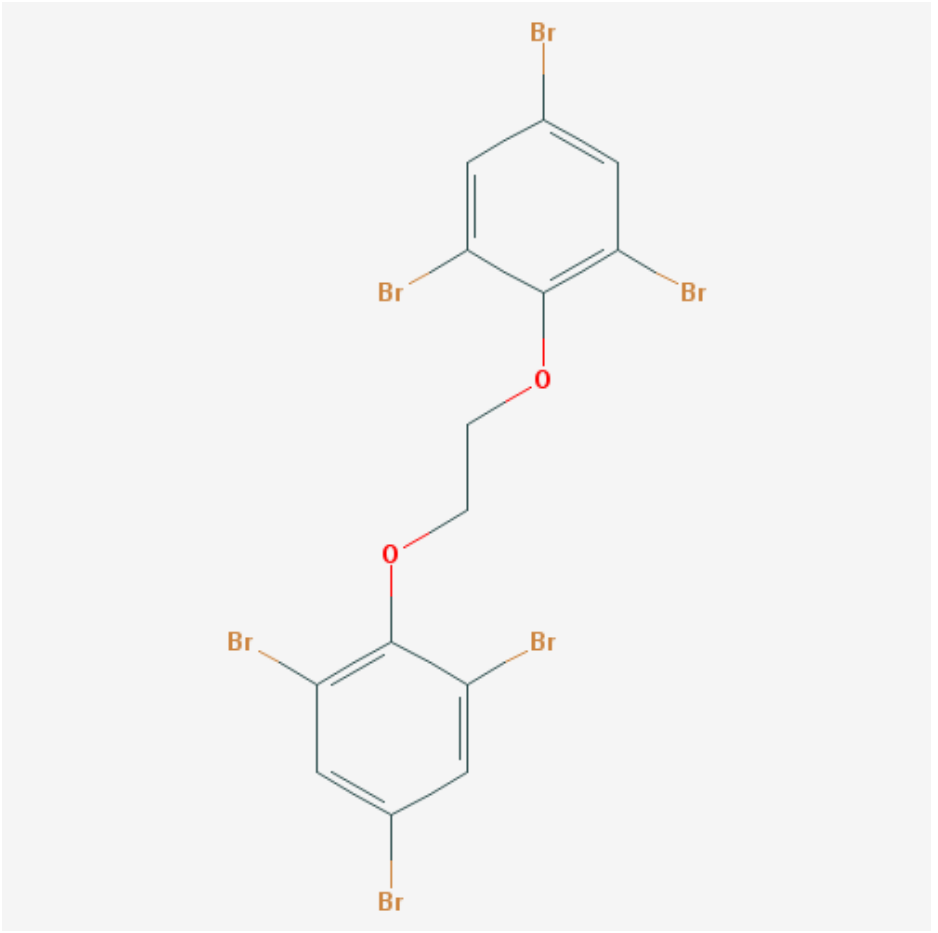
Objectives

- Assess effects of 1,2, bis (tribromophenoxy)-ethane (BTBPE: Great Lakes FF-680) in Mink
- Studies included:
  - Evaluate the reproductive effects in mink
- Evaluate BTBPE ecological risks to mink

BTBPE Chemical/Physical Properties

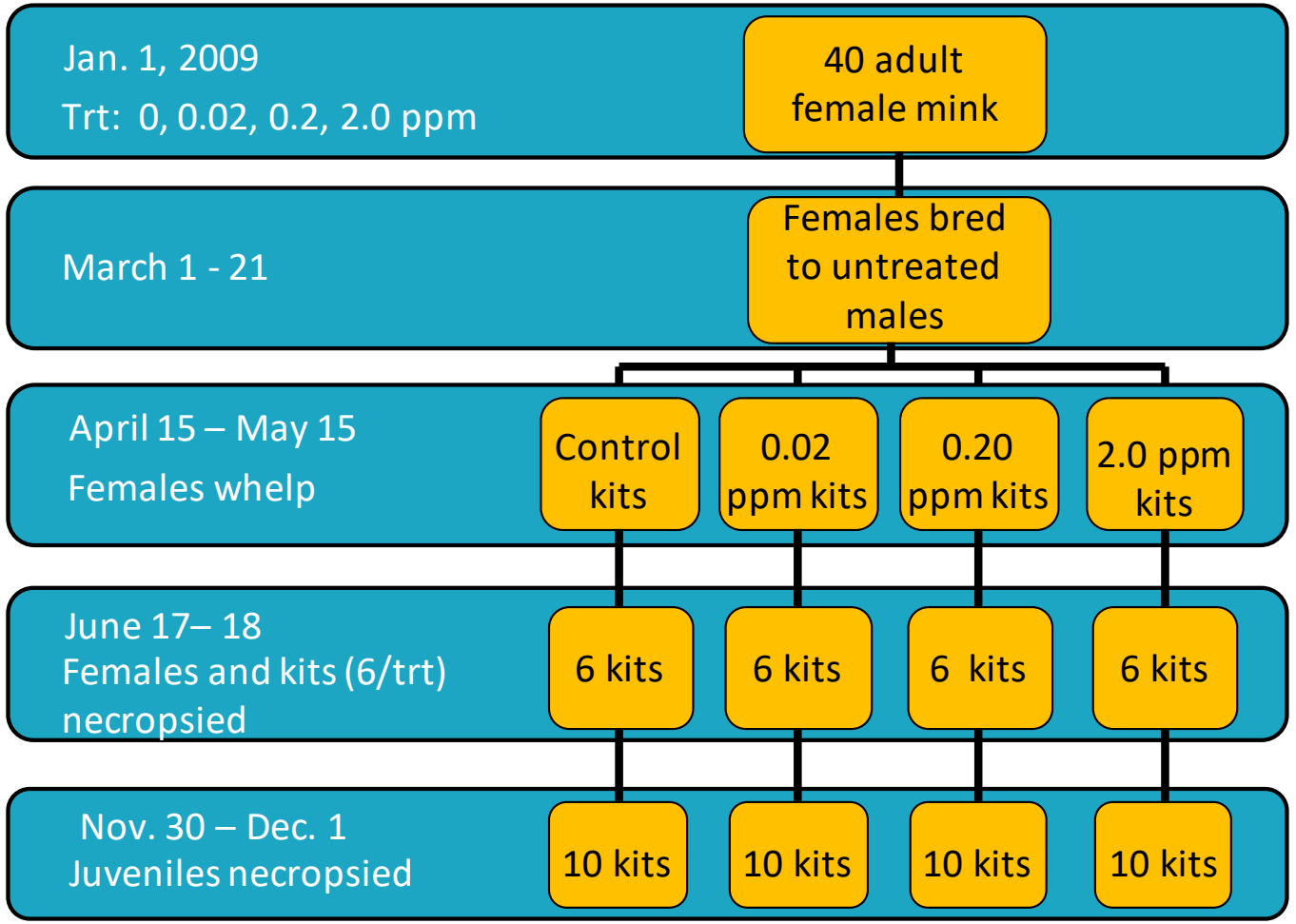
Parameters:

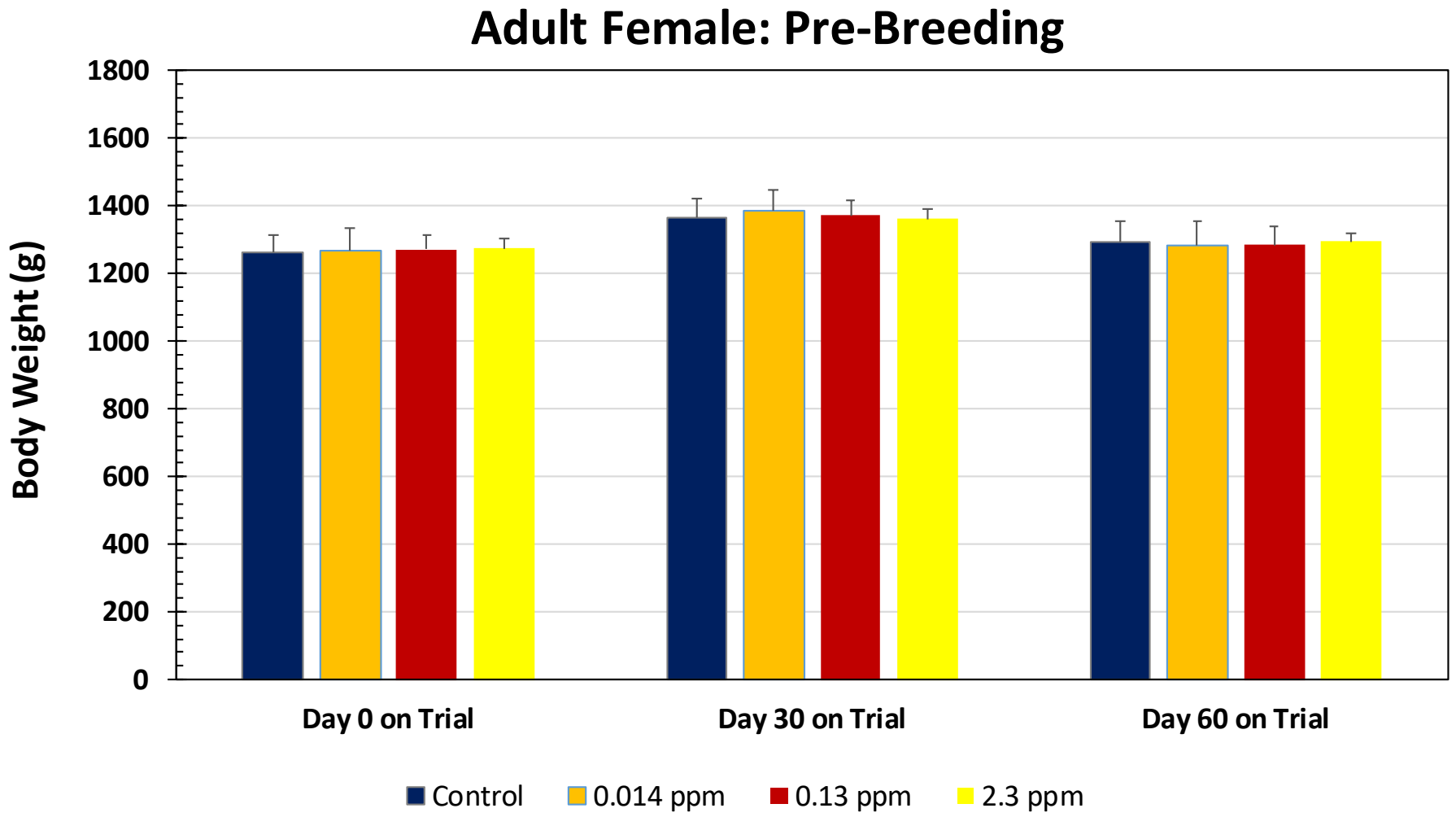
MW	687.6
B.P.	566 °C
V.P.	3.88E-10 Pa
WS.	2.23×10^{-4} mg/L
Log Kow	7.9
Log Koc	5.66
Log Kaw	-5.17



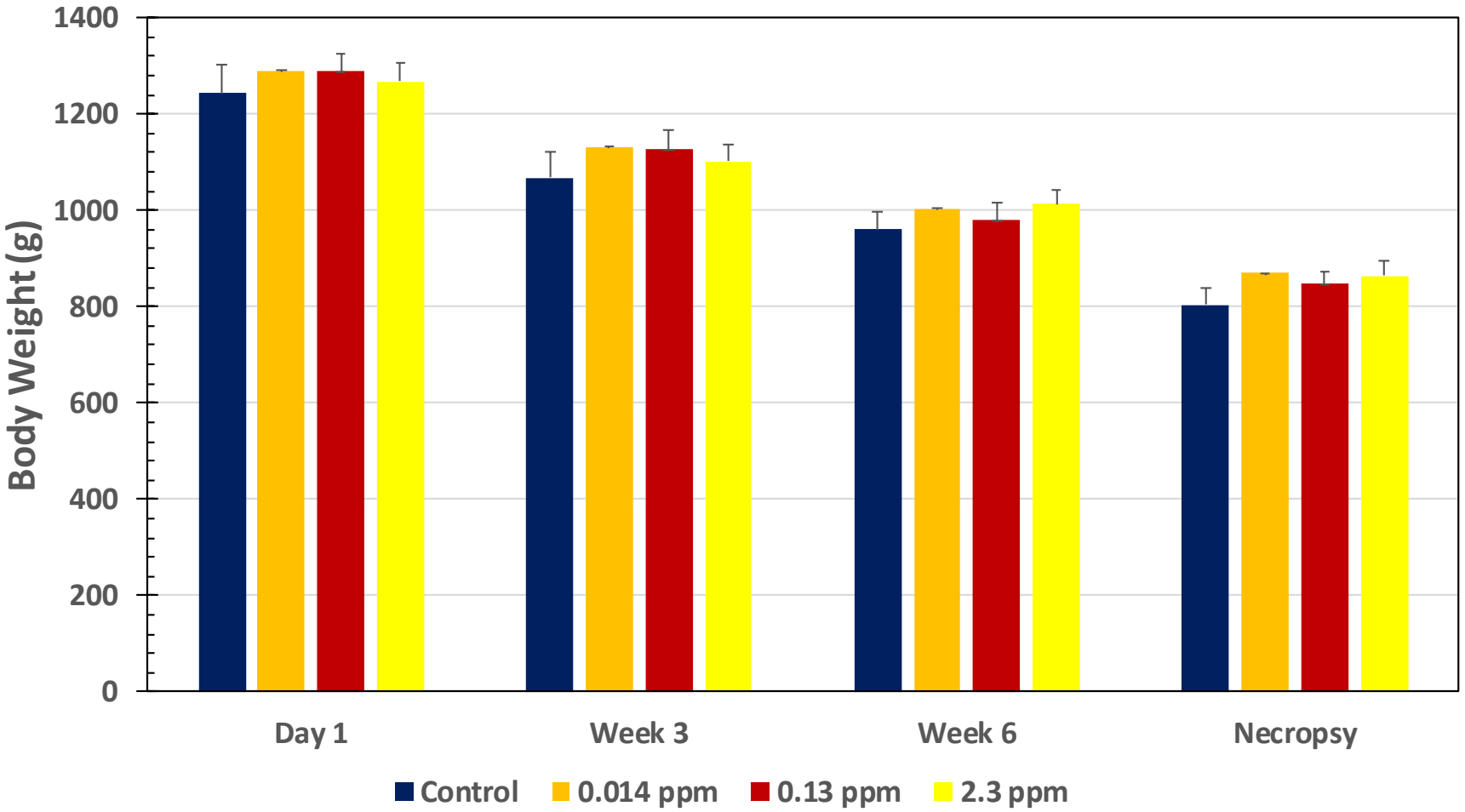
Reproduction Study

Experimental Design




Adult Female: Pre-Breeding
Body Weight (g)
1800
1600
1400
1200
1000
800
600
400
200
0
Day 0 on Trial
Day 30 on Trial
Day 60 on Trial
Control
0.014 ppm
0.13 ppm
2.3 ppm

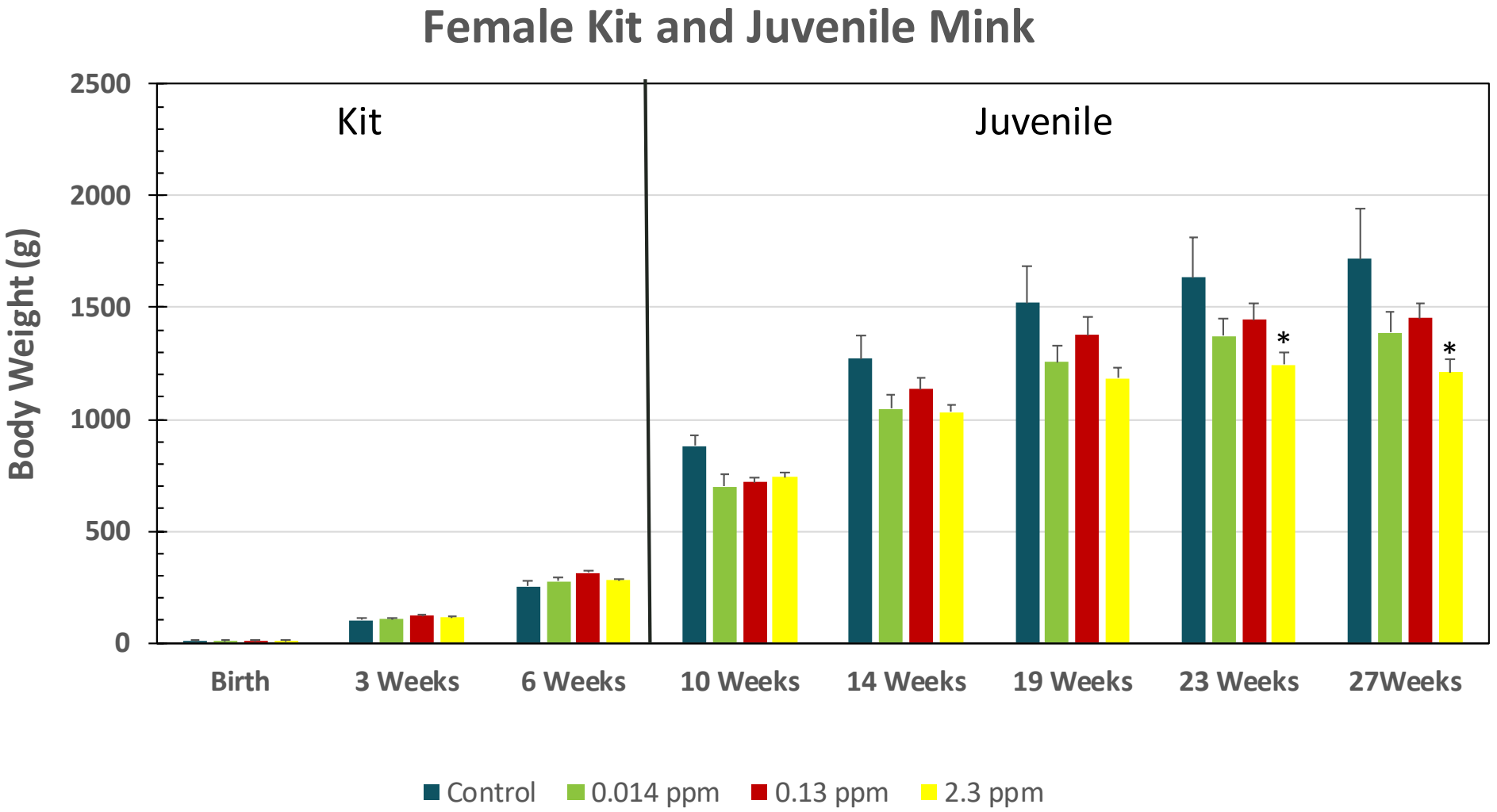
Adult Female: Whelping and Necropsy

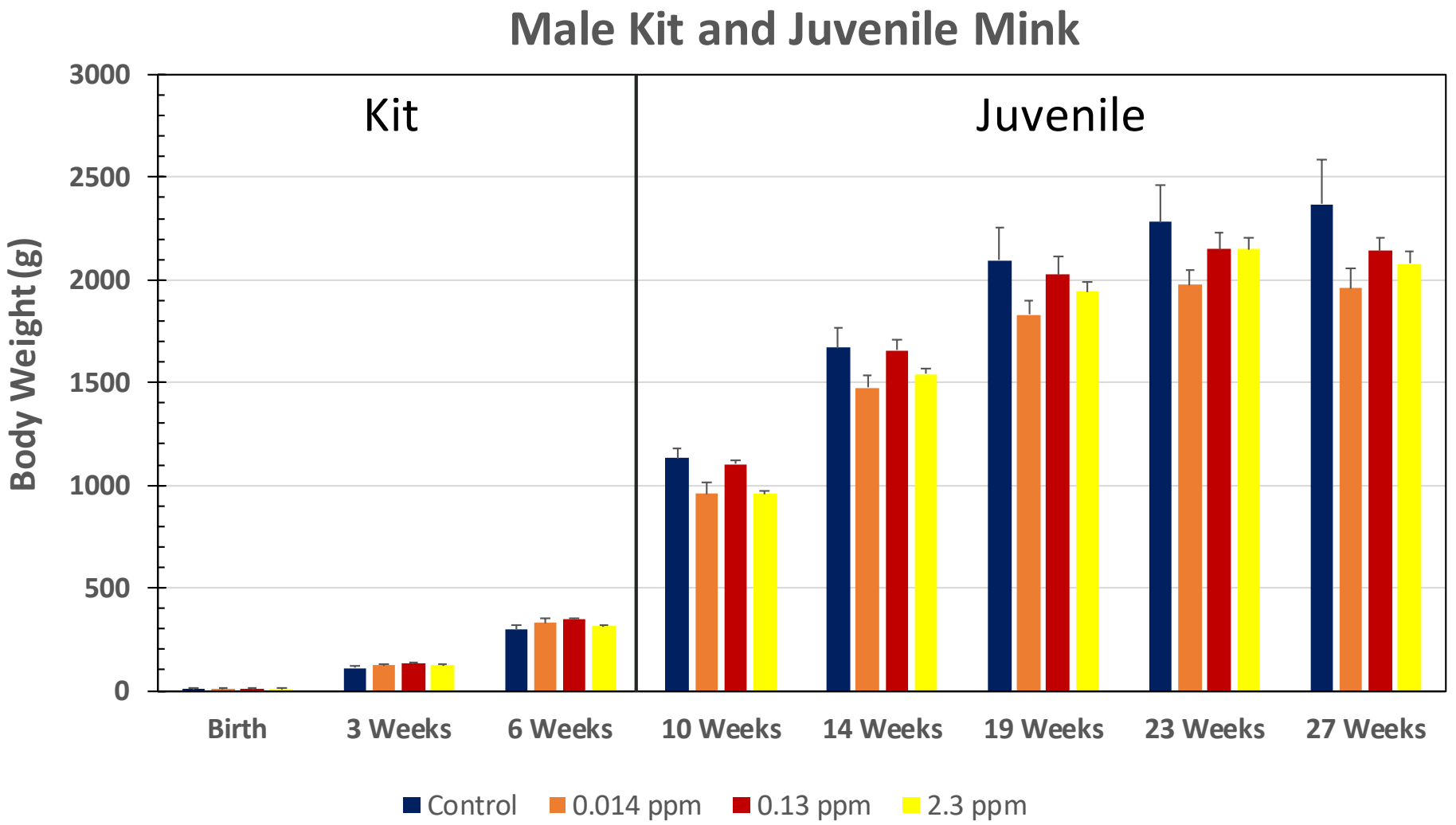


Effect of 1,2 bis (2,4,6-tribromophenoxy) ethane (BTBPE) on mink reproduction

Diet mg/kg	# Females Welped/ #Bred	Total Kits Whelped	Live Kits Whelped	Kit Survivability (%)		
				Birth	Week 3	Week 6
0	8/10	7.9 ± 0.78	7.4 ± 0.76	94 (84-104)	87 (68-107)	86 (67-105)
0.014	8/10	7.0 ± 0.78	5.4 ± 0.76	81 (62-99)	88 (74-103)	88 (74-103)
0.13	10/10	7.7 ± 0.70	6.8 ± 0.68	89 (75-103)	94 (86-101)	93 (83-102)
2.3	10/10	8.9 ± 0.74	7.6 ± 0.72	86 (73-99)	82 (68-95)	82 (68-95)
P-value		0.3774	0.1814	0.5610	0.3696	0.4215

[1] Data presented as mean with standard error
[2] Data presented as mean with 95% confidence interval in parenthesis
Dietary feed concentrations given as wet weight


Female Kit and Juvenile Mink
Kit
Juvenile
Body Weight (g)
2500
2000
1500
1000
500
0
Birth
3 Weeks
6 Weeks
10 Weeks
14 Weeks
19 Weeks
23 Weeks
27Weeks
*
*
Control
0.014 ppm
0.13 ppm
2.3 ppm


Male Kit and Juvenile Mink
Kit
Juvenile
Body Weight (g)
3000
2500
2000
1500
1000
500
0
Birth
3 Weeks
6 Weeks
10 Weeks
14 Weeks
19 Weeks
23 Weeks
27 Weeks
Control
0.014 ppm
0.13 ppm
2.3 ppm

Effects of dietary 1,2 bis(2,4,6-tribromophenoxy) ethane (BTBPE) on plasma triiodothyronine (T3) and thyroxine (T4) in adult female mink

Diet (mg/kg)	T3 (ng/ml)	T4 (ng/ml)	T3/T4
Control	16 ± 3.3 [A]	102 ± 13 [A]	0.15 ± 0.023 [A]
0.014	16 ± 3.2 [A]	59 ± 4.4 [B]	0.27 ± 0.048 [B]
0.13	16 ± 2.8 [A]	100 ± 7.1 [A]	0.16 ± 0.035 [A]
2.3	31 ± 8.9 [B]	100 ± 5.8 [A]	0.31 ± 0.094 [B]
P-value	0.019	0.0035	0.036

Data are presented as geomeans and standard errors
Values with different superscripts within the same column are significantly different ($p < 0.05$)

Hepatic and adipose BTBPE concentrations in juvenile mink

Diet (mg/kg)	Liver (ug/kg, ww)		Adipose (ug/kg, ww)
	Male	Female	
Control	<0.035	<0.035	<0.012 [A]
0.014	na	na	1.4 ± 016 [A]
0.13	<0.035	<0.035	11 ± 1.1 [A]
2.3	0.077 ± 0.033	0.23 ± 0.033	205 ± 17 [B]
p-value treatment	0.0010		<0.0001

Data are presented as geomeans and standard errors
Values with different superscripts within the same column are significantly different (p <0.05)

Ecological Relevance?

Derivation of Safe Water Concentrations for the Protection of Wildlife

$$\text{Wildlife Value} = \frac{\dfrac{\text{Test Dose}}{\text{Uncertainty Factor}} \; x \; BW}{W + \sum\left(F_{TLi} \; \text{xBAF}_{TLi}^{WL}\right)}$$

Baseline Bioaccumulation Factor (BAF)

Definition

- For organic chemicals, is based on the concentration of freely dissolved chemical in the ambient water and takes into account the partitioning of the chemical within the organism.
- Mathematically determined as the total concentration in tissue divided by concentration in water
- Can be derived from:
  - Field-measured BAFs
  - Biota-Sediment Accumulation Factors (BSAF)
  - Bioconcentration Factors (BCF) and Trophic Magnification factors (TFM)

Bioaccumulation Factors

- Wu JP et al. (2011). Environ. Inter. 37:210-215
  - Natural pond near an E-recycling facility in China
  - Species included invertebrates, fish and reptile
  - BAFs were species-specific
    - Log BAFs ranged from 2.85-5.98, **average=4.25**
- LaGuardia MJ et al. (2012). Environ. Sci. Technol. 46: 5798-5805
  - Accumulation measured mussels and gastropods
    - Log BAFs ranged from **5.0 to 5.8**
    - Log BSAFs ranged from **-1.12 to -0.3**

BTBPE Biomagnification Factors

- Poma G et al. (2014) Sci. Total Environ. 481:401-408
  - BTBPE measured in zooplankton and fish in Lake Maggione, Italy
    - BMFs based on zooplankton and fish muscle concentrations (Lipid)
    - BMF based on trophic level normalized data
    - BMFs ranged from 0.3 to 0.6, **average = 0.3**

- Tomy GT et al. (2007) Environ. Sci. Technol. 41: 4913-4918
  - Kinetic study where rainbow trout were fed BTBPE in the diet
    - BMFs based on diet and muscle concentrations
    - BMFs ranged from 1.1 to 5.2, **average = 2.3**
- Law K et al. (2006) Environ. Sci. Technol 25: 2177-2186
  - BTBPE measured in zooplankton, mussels, and fish in Lake Winnipeg
    - BMFs based on muscle tissue of mussels and fish
    - BMFs ranged from 0.1 to 2.5, **average= 0.9**

Food Chain Magnification Factors

- Wu JP et al. (2010). Environ. Sci. Technol. 44:5490
  - China freshwater lake near E-recycling area
  - Aquatic based, no wildlife. **TMF=0.40**
- Law K et al. (2006). Environ. Toxicol. Chem. 25:2177
  - Lake Winnipeg-Aquatic only
  - **TMF = 1.86**

Uncertainty Factors for a Mink and Otter Exposed to BTBPE

US EPA Great Lakes Initiative (GLI)

UNCERTAINTY FACTORS (UF)	Values
Inter-taxon Extrapolation (UF_A)	1
Exposure Duration (UF_L)	1
Toxicological Endpoint (UF_S)	5
UF for TRV	UF= (1 x 1 x 5) = 5

Model Parameters

Bioaccumulation Factors

Trophic Magnification Factor (TMF):	1.1
BCF*	490
Trophic Level 3 BAF:	539
Trophic Level 4 BAF:	593
Biomagnification Factor (BMF):	1.2

Toxicity Data

Test Dose (mg BTBPE/kg bw/day):	0.29
Total Uncertainty Factor:	5

***Based Gobas and Arnot upper trophic level species**

Exposure Parameters for Three Surrogate Mammalian Species Identified for Deriving Wildlife Values

Species	Adult Body wt. (kg)	Water ingestion rate (L/day)	Food ingestion rate of each prey in each trophic level (kg/day)	Trophic level of prey (% diet)
Mink	0.80	0.081	TL3: 0.159 Other: 0.0177	Fish: 90 (TL3: 90) Other: 10
Otter	7.4	0.600	TL3: 0.977 TL4: 0.244	Fish: 100 (TL3: 80; TL4: 20)

Note: TL3 or TL4 = trophic level 3 or 4 fish; PB= piscivorous birds; Other = non-aquatic birds and mammals

BTBPE Wildlife Values for Aquatic Mammals

Species	Wildlife Value (ng BTBPE/L)
Mink	560
Otter	660
Geometric Mean	610

Calculation of Toxicity Reference Value (TRV) for Mink

Dietary-based TRV for BTBPE in Mink

General TRV Equation

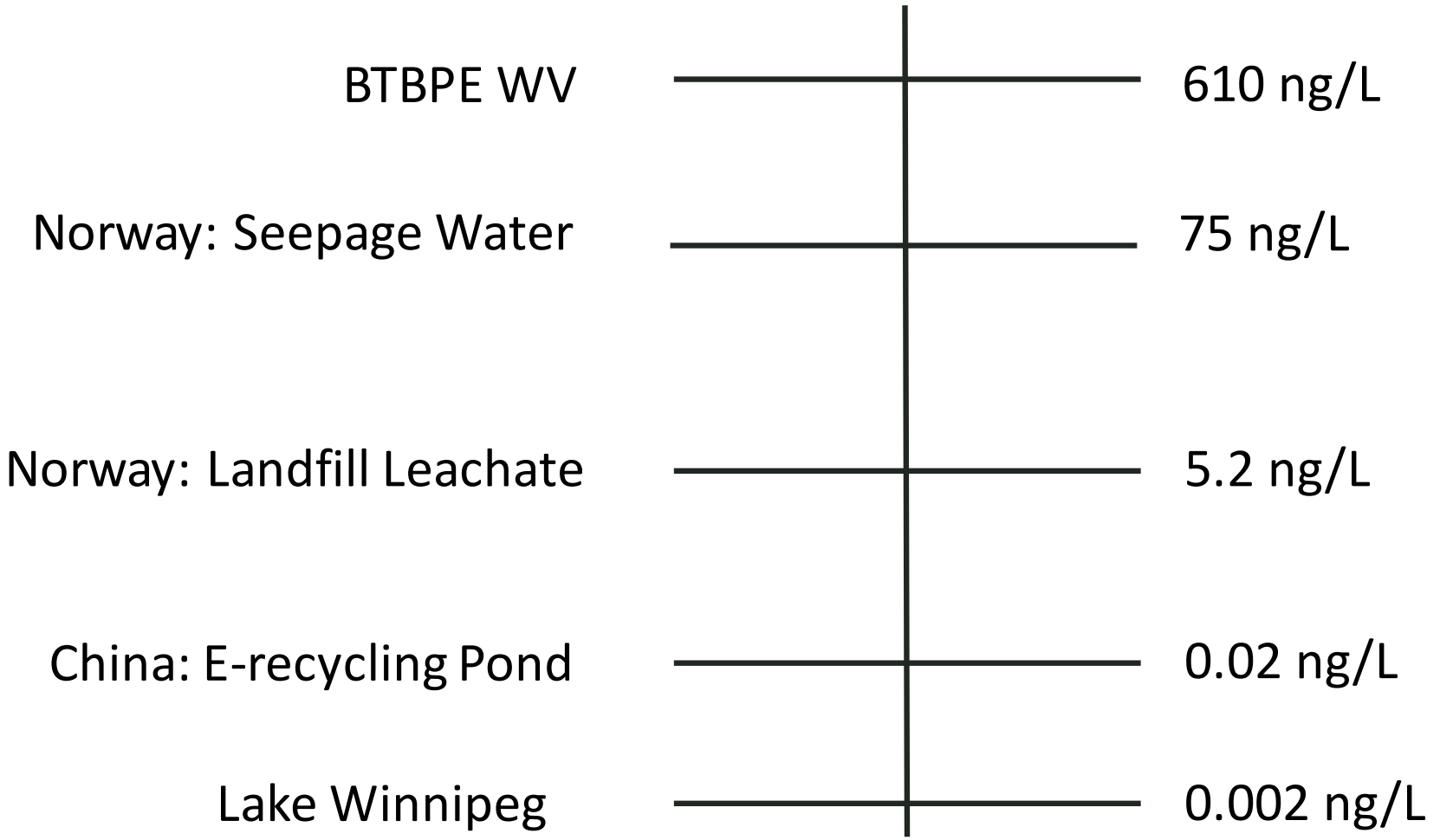
$$\text{TRV} = \frac{\text{NOAEL Daily Dose for BTBPE (mg/kg/d)}}{\text{Overall UF}} = \text{mg BTBPE/kg/day}$$

Mink-based Dietary TRV

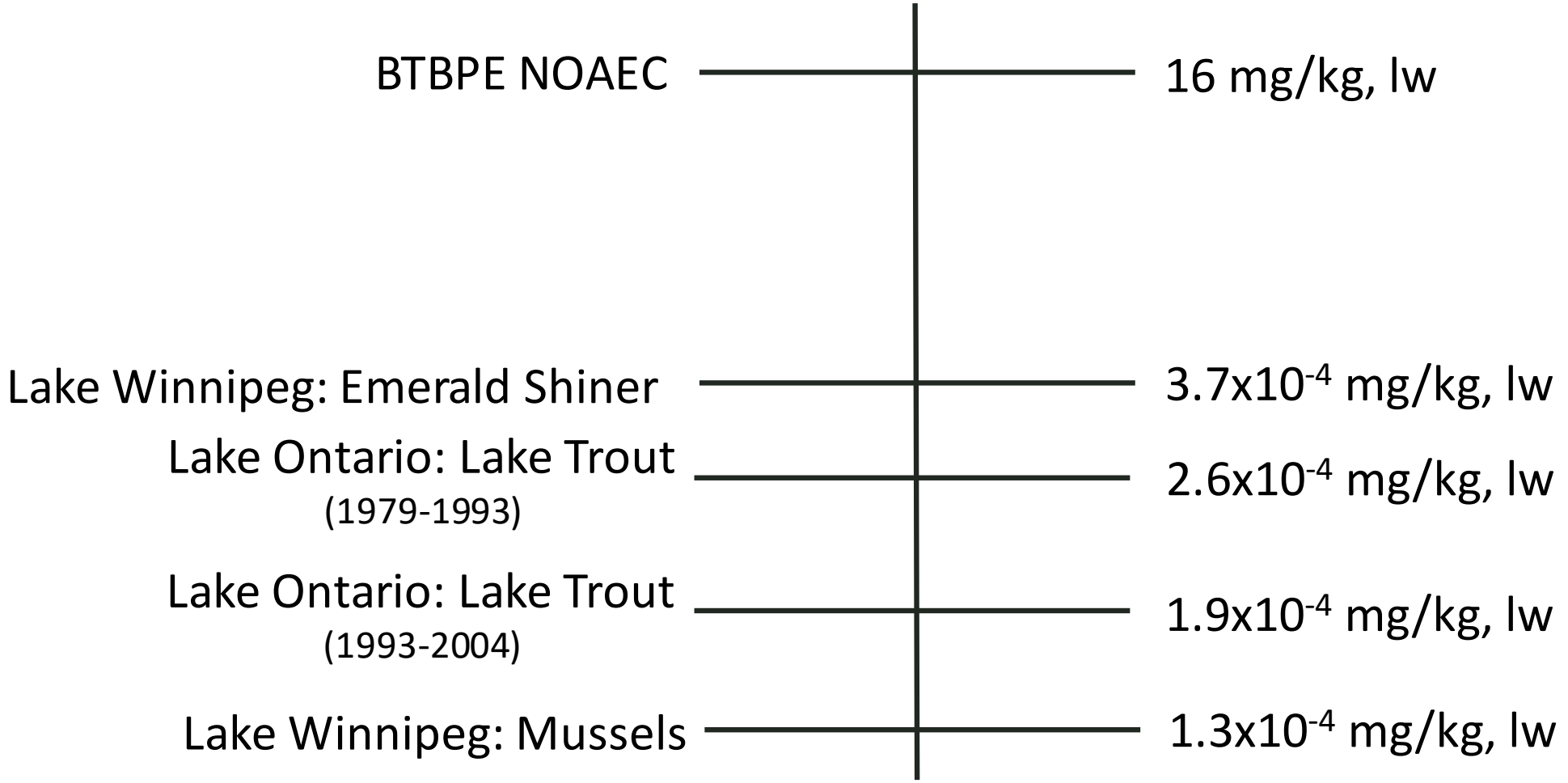
$$\text{TRV} = \frac{0.29 \text{ mg BTBPE /kg/d}}{5} = \mathbf{0.058\ mg\ BTBPE/kg/day}$$

Ecological Risks?

BTBPE Water Concentrations



BTBPE Fish Concentrations



Conclusions

- BTBPE had no effect on reproductive performance of mink and survivability and growth of their offspring.
- BTBPE affected thyroid hormone homeostasis although not in a BFR dose dependent manner.
- BTBPE detected in adipose tissue but not liver, suggesting effective clearance from the liver and bioaccumulation in the fat.
- BTBPE was significantly less toxic than DE-71 where total reproductive failure occurred at 0.25 ug/kg/day.
- BTBPE poses minimal risk to wildlife including mink.

Thank You

Questions?