



New Findings on Flame Retardants in Consumer Products, Dust and Biospecimens

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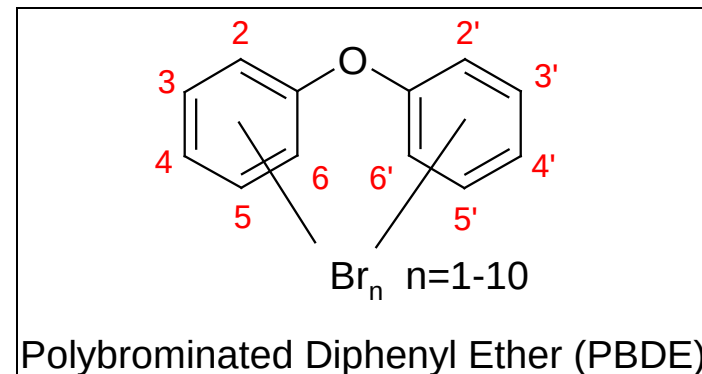
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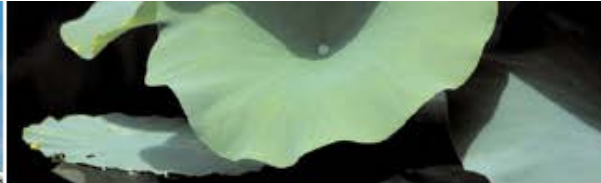
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Flame Retardants and CA TB 117

- 98% of World Market Demand for PentaBDE was in North America, primarily to meet TB 117
- Concern about persistence, bioaccumulation and potential toxicity led to voluntary phase-out in US in 2005; (banned in Europe in 2002)
- However, there are very limited data available on the flame retardants used as replacements for PentaBDE





PentaBDE Alternatives Assessment

2, 2, 4, 4, 6, 6 - Endpoint assigned using estimated values and professional judgment (Structure Activity Relationships)

Company	Chemical	% in Formulation ⁶	Human Health Effects							Ecotoxicity		Environmental		Potential Routes of Exposure							Reactive or Additive?	
			Cancer Hazard	Skin Sensitizer	Reproductive	Developmental	Neurological	Systemic	Genotoxicity	Acute	Chronic	Persistence	Bioaccumulation	Worker			General Population			Aquatic		
														Inhalation	Dermal	Ingestion	Inhalation	Dermal	Ingestion			
Albemarle	SAYTEX RZ-243																					
	Proprietary E Tetrabromophthalate diol diester		L	L	L*	L*	L	M*	L	L	H	L [▲]	L	N	Y	Y	N	N	Y	Y	Additive	
	Proprietary B Aryl phosphate		L	L	M*	M*	M	M*	L	H	H	L	M	N	Y	Y	N	Y	N	N	Additive	
	Triphenyl Phosphate CAS # 115-86-6		L	L	L	L	L	M	L	H	H	L	L	Y	Y	Y	Y	Y	Y	Y	Additive	
Ameribrom	FR513																					
	Tribromoneopentyl Alcohol CAS # 36483-57-5		M	L	M	M	M	M	M	M	M	L	L	Y	Y	Y	N	N	Y	Y	Reactive	
Great Lakes	Firemaster 550																					
	Proprietary F Halogenated aryl ester		L	L	M	M	L	M	L	H	H	L [▲]	L	N	Y	Y	N	Y	Y	Y	Additive	
	Proprietary G Triaryl phosphate, isopropylated		L	L	M*	M*	M	M*	L	H	H	L	M	N	Y	Y	N	Y	N	N	Additive	
	Triphenyl Phosphate CAS # 115-86-6		L	L	L	L	L	M	L	H	H	L	L	Y	Y	Y	Y	Y	Y	Y	Additive	
	Proprietary H Halogenated aryl ester		L	L	M	M	L	M	L	H	H	L [▲]	L	N	Y	Y	N	Y	Y	Y	Additive	
Great Lakes	Firemaster 552																					
	Proprietary F Halogenated aryl ester		L	L	M	M	L	M	L	H	H	L [▲]	L	N	Y	Y	N	Y	Y	Y	Additive	
	Proprietary G Triaryl phosphate, isopropylated		L	L	M*	M*	M	M*	L	H	H	L	M	N	Y	Y	N	Y	N	N	Additive	
	Triphenyl Phosphate CAS # 115-86-6		L	L	L	L	L	M	L	H	H	L	L	Y	Y	Y	Y	Y	Y	Y	Additive	
	Proprietary H Halogenated aryl ester		L	L	M	M	L	M	L	H	H	L [▲]	L	N	Y	Y	N	Y	Y	Y	Additive	

(Furniture Flame Retardancy Partnership V 1, EPA 2005)



What Types of FRs are Being Used to Meet TB 117 Today?

- With the phase-out of PentaBDE, what type of chemical flame retardants would be most common in residential furniture?
- Will these new/alternate FRs accumulate in indoor dust and air- leading to human exposure?
- What is known about health effects for these new flame retardants?



Screening Consumer Products for FR Chemicals:

Project 1- Baby Products

Project 2- Residential Couches



Project 1: Flame Retardants in Children's Products

ENVIRONMENTAL
Science & Technology

(2011)

ARTICLE
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Identification of Flame Retardants in Polyurethane Foam Collected from Baby Products

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Supporting Information

Sleep Positioners



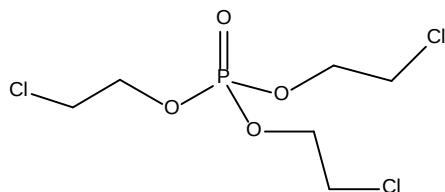
Car Seats



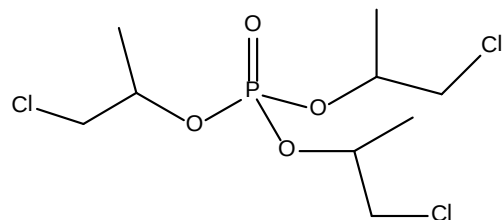
Nursing Pillow



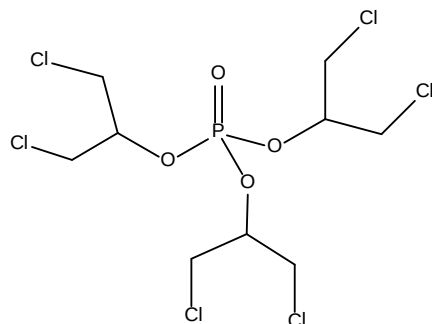
- 101 Baby products screened for flame retardant (FR) chemicals
- 80% contained a FR
- TDCPP, Firemaster 550 (FM 550), and “V6” most common FRs identified
- PentaBDE found in 5 samples
- Identified two new chlorinated organophosphate flame retardant mixtures
- Risk/exposure assessments do not consider exposure from use of these products
- Now 3 infant/juvenile products exempted from TB 117



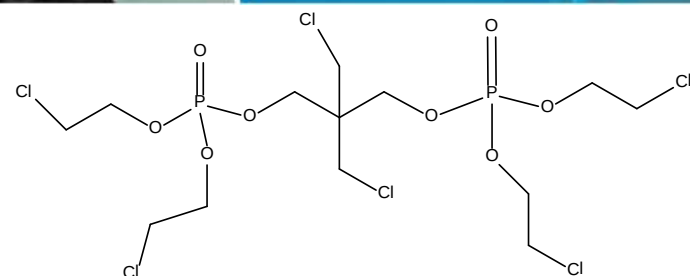
Tris (2-chloroethyl)phosphate
TCEP



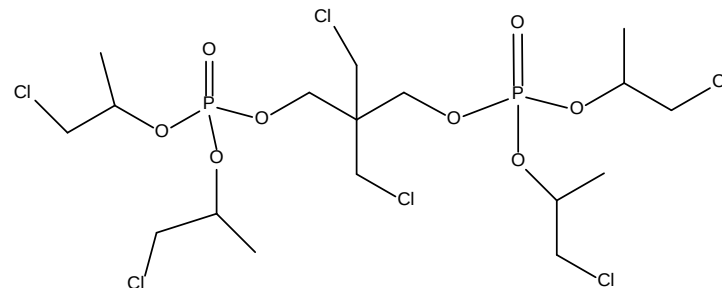
Tris (1-chloropropyl)phosphate
TCPP



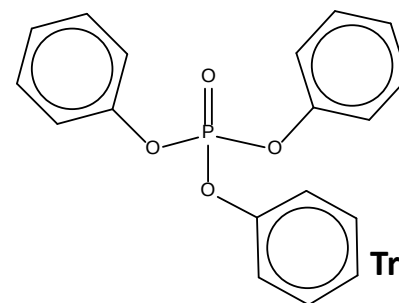
Tris (1,3-dichloroisopropyl)phosphate
TDCPP



**2,2-bis(chloromethyl)propane-
1,3-diyl tetrakis(2-chloroethyl)bis(phosphate)**
"V6"



**2,2-bis(chloromethyl)propane-
1,3-diyl tetrakis(1-chloropropan-2-yl)bis(phosphate)**
"U-OPFR"



Triphenylphosphate
TPP



V6 Levels In Baby Products And Dust (Fang et al. 2013)

Table 2. Summary Statistics for V6 measurements in Baby products (n = 101), House Dust (n = 20) and Car Dust Samples (n = 20)

	Baby Products (10 ⁶ ng/g)		House dust (ng/g)		Car dust (ng/g)	
	V6	TCEP	V6	TCEP	V6	TCEP
% detect	NA	NA	70%	48%	95%	95%
Concentration	46.5 ±12.0 ^a	3.6 ± 1.6 ^a	12.5 ^c	50.2 ^c	103.0 ^c	1080.0 ^c
Range	24.5 – 59.4 ^b	1.1 –5.9 ^b	< 5 – 1,110	< 20 – 1350	< 5 – 6,160	< 20 – 50,120

^aAverage was calculated based on 12 baby products in which V6 was detected (Average ± SD). ^bRange is only from the 12 baby products in which V6 was measured. ^cMedian. NA indicates not applicable.

**** TCEP and V6 levels in dust significantly associated**



Project 2: Flame Retardants in Couches

ENVIRONMENTAL
Science & Technology

(2012)

Article
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Novel and High Volume Use Flame Retardants in US Couches Reflective of the 2005 PentaBDE Phase Out

Heather M. Stapleton,^{*,†} Smriti Sharma,[‡] Gordon Getzinger,[‡] P. Lee Ferguson,[‡] Michelle Gabriel,[§] Thomas F. Webster,[‡] and Arlene Blum[§]

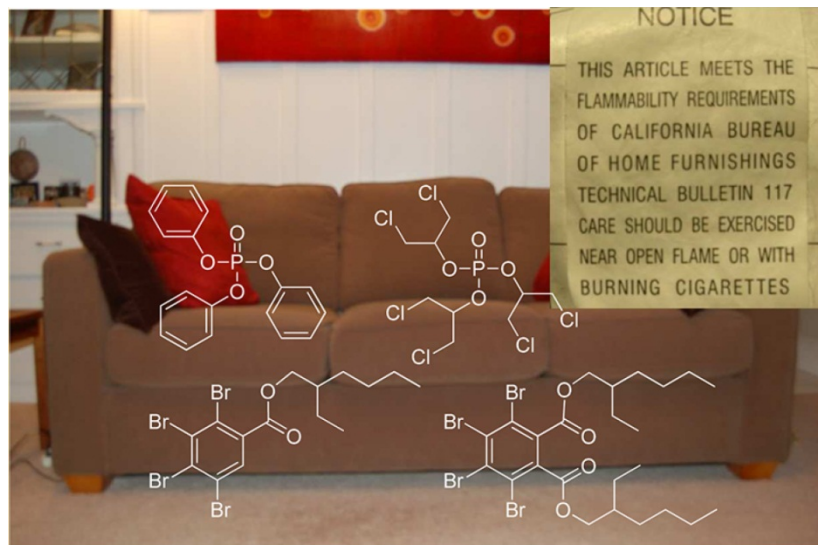
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[§]Department of Chemistry, University of California, and Green Science Policy Institute, Berkeley, California, United States

Supporting Information

- 102 foam samples collected from residential couches in the US
- Information on year of purchase, state where couch purchased, and presence of TB 117 label recorded
- Samples purchased between 1985-2010
- 87 of 102 samples contained a FR
- TDCPP, PentaBDE, and Firemaster 550 (FM 550) most common FRs identified
- Identified two new organophosphate flame retardant mixtures





Flame Retardant Detection and Measurement:

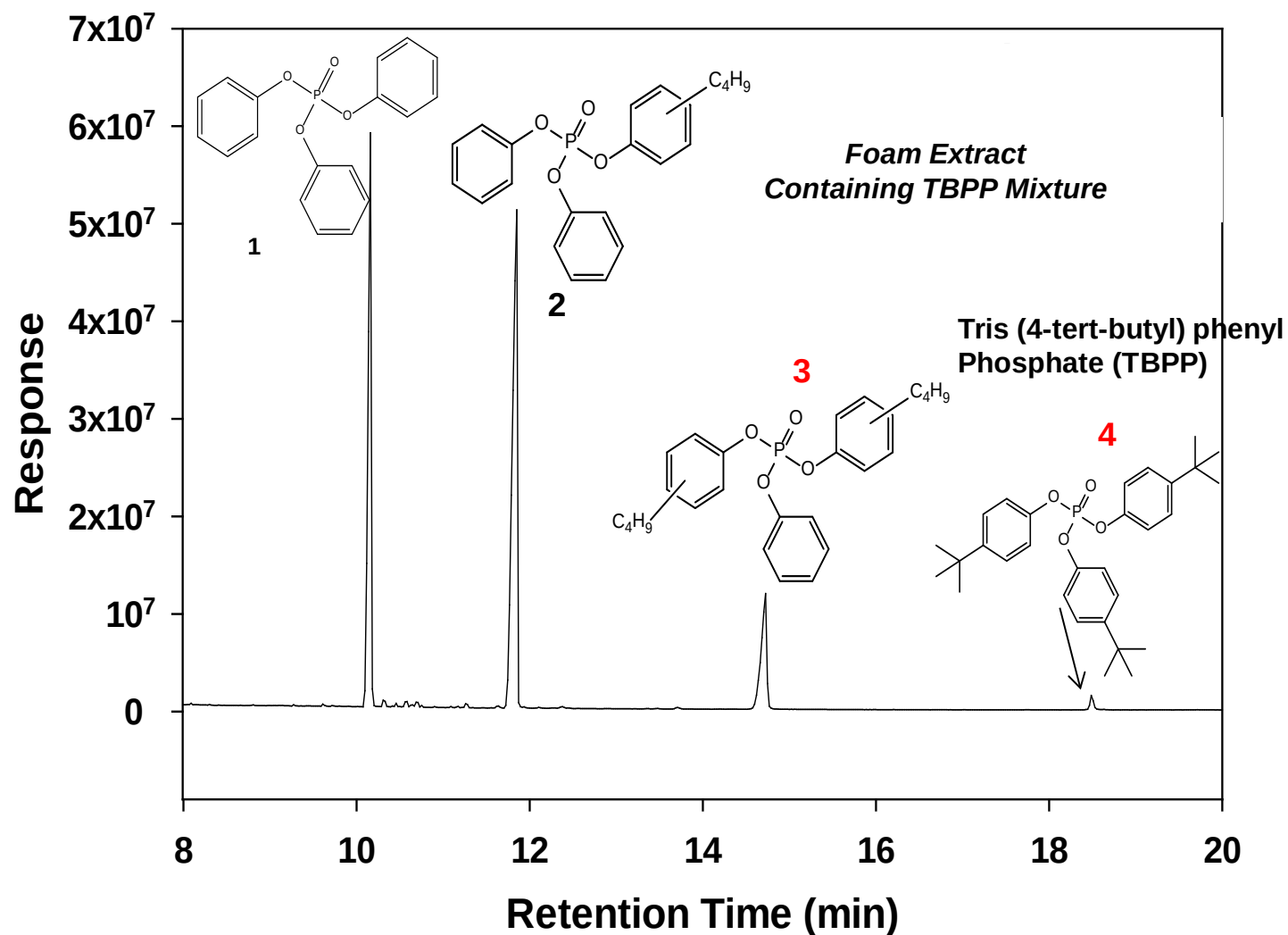
Table 1. Flame Retardant (FR) Measurements and Descriptive Statistics of Polyurethane Foam Samples ($n = 102$). (Values in parenthesis represent percentage of the total number of samples for that specific column)

flame retardant	number of detects	average FR level (mg/g)	purchased prior to 2005 ^a	purchased 2005 or later ^a	purchased in California ^b	purchased outside California ^b	yes TB 117 ^c	no TB 117 ^c
PentaBDE	17	20.23 ^d	16 (39%)	1 (2%) ^e	7 (29%)	9 (12%)	9 (14%)	8 (24%)
TDCPP	42	44.87	10 (24%)	32 (52%)	10 (42%)	30 (41%)	33 (50%)	9 (26%)
FM 550	13	19.76 ^f	2 (5%)	11 (18%)	3 (13%)	8 (11%)	12 (18%)	1 (3%)
V6/TCEP	1	41.77 ^g	0	1 (2%)	1 (4%)	0	1 (2%)	0
TBPP mix	8	7.90 ^h	0	8 (13%)	1 (4%)	7 (10%)	6 (9%)	1 (3%)
MPP mix	2	3.23 ⁱ	0	2 (3%)	0	2 (3%)	1 (2%)	1 (3%)
TDCPP and PentaBDE	2	22.64	2 (5%)	0	1 (4%)	1 (1%)	1 (2%)	1 (3%)
TDCPP and FM 550	2	19.06	0	2 (3%)	0	2 (3%)	2 (3%)	0
FR < 0.2 mg/g	3 ^j	0.11	1 (2%)	2 (3%)	0	3 (4%)	0	2 (6%)
none detected	12	-	10 (24%)	2 (3%)	1 (4%)	11 (15%)	1 (2%)	11 (32%)
totals	102		41	61	24	73	66	34

- Average Concentration in foam approximately 4-5% by weight of foam (40-50 mg/g)
- Significant increase in FR applications since 2005
- Significant increase in diversity of FR chemicals in furniture since 2005
- 62% of samples without a TB 117 label still contained FRs
- California TB 117 has become a *de facto* standard for the US

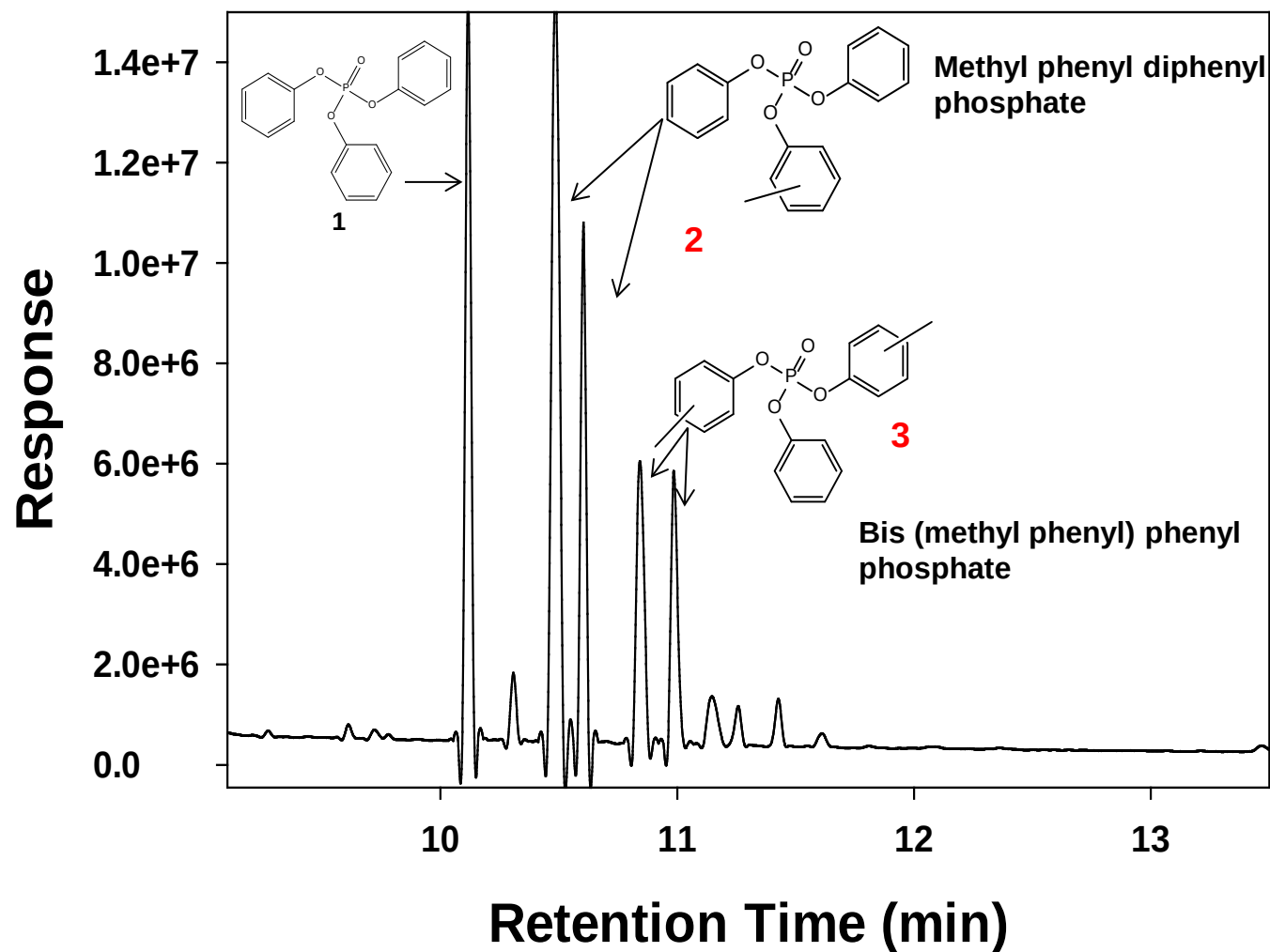


TBPP Flame Retardant Mix (n=8)





MPP Flame Retardant Mix (n=2)





FR Applications in Consumer Products



1. Textiles Used in Curtains (Kajiwara et al 2009):

10 Japanese Polyester Samples Analyzed

- 9 Contained Hexabromocyclododecane (HBCD)
Concentrations ranging from 22 – 43 mg/g (2-4%)**
- 1 sampled was treated with BDE-209
Concentration was 114 mg/kg (11.4 %)**

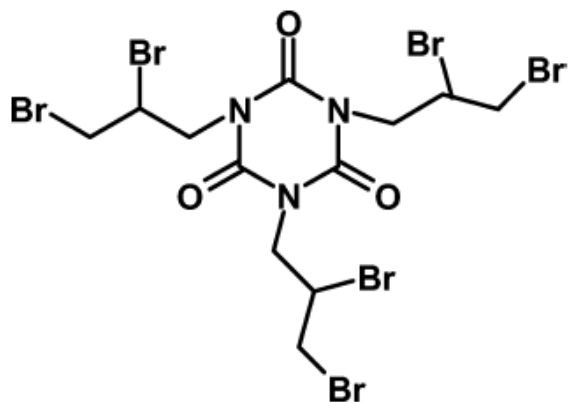


2. TV Casings containing high impact polystyrene (Kajiwara et al. 2008):

- 1 TV Case contained BDE-209 and low levels of dibenzofurans
Concentration was 96 ± 7.4 mg/g (9.6%)**



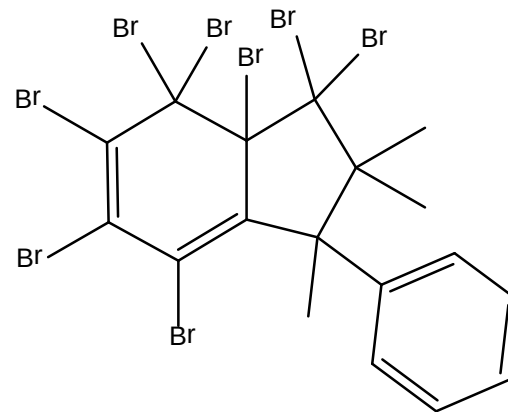
New Flame Retardants Identified in the Environment:



Tris (2,3-dibromopropyl) isocyanurate (TBC)

Detected in the environment
(Ruan et al. 2009; Zhu et al. 2012)

Used in polypropylene, polyethylene, and polystyrene



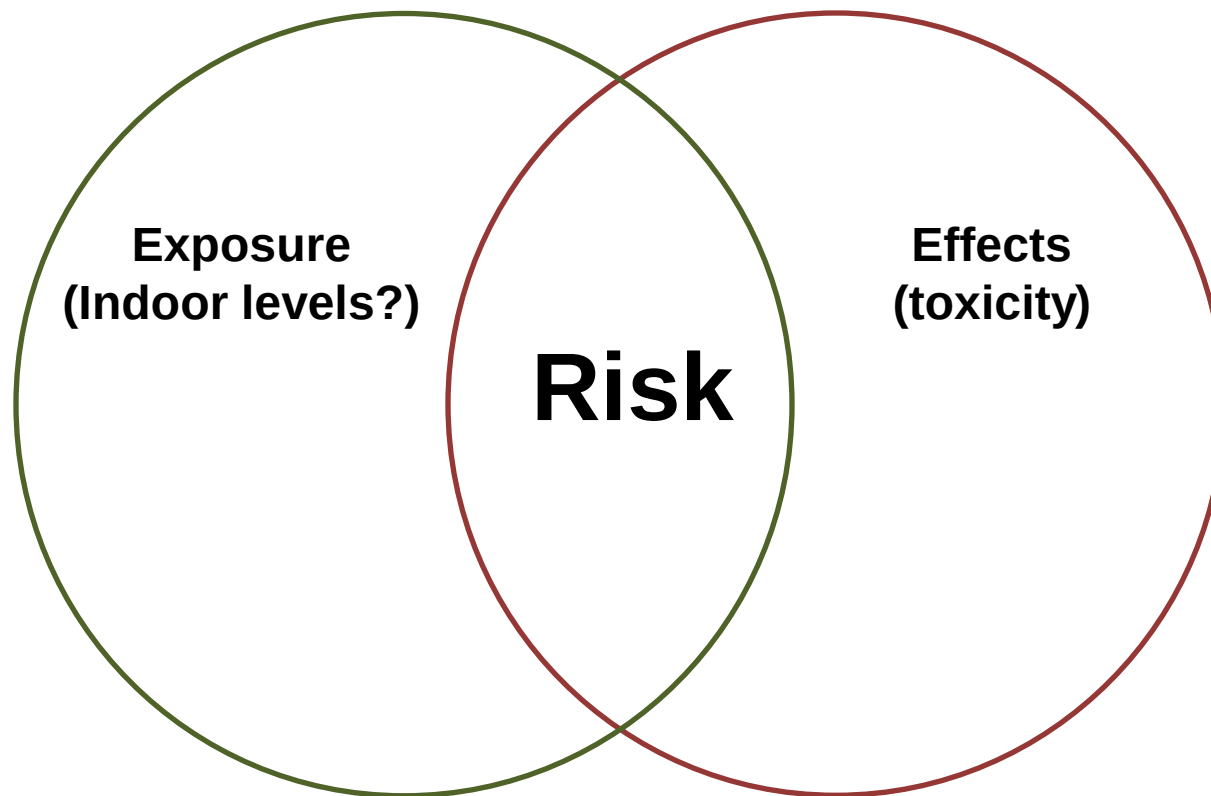
Octabromotrimethylphenylindane (OBIND)

Detected in bird eggs
(Guerra et al. 2012)

Used in most plastics



FR Human Health Risk Assessment



Risk is a function of both exposure and toxicity



**Are These Alternate Flame Retardants
Present in Indoor Dust and are People
Exposed to Them?**



Flame Retardants Measured in CA Dust (2011)

(Values are in ppb; n=16)

Flame Retardant	% Detect	Minimum	Median	Maximum	Time Trend
BDE 47	100	140	1,000	17,000	↓
BDE 209	100	110	1,200	8,500	→
TCEP	100	330	2,700	110,000	↓
TCPP	100	490	2,200	140,000	→
TDCPP	100	920	2,100	44,000	→
TPP	100	790	2,800	36,000	→
TBB	100	45	100	5,900	↑
TBPH	94	<2	260	3,800	↑
TBBPA	100	22	200	2,000	→
HBCD	100	39	160	1,800	→
BTBPE	100	3	12	130	↓

FM 550

Source: Dodson et al 2012

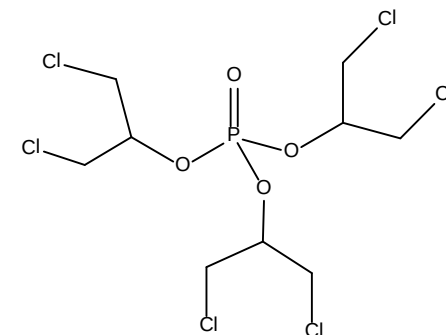


TDCPP and Firemaster 550

What are the Health Concerns?



TDCPP



- TDCPP was used as a FR in children's pajamas in the 1970s
- Studies conducted at UC Berkeley found that TDCPP and its brominated analogue were both mutagens (Gold et al 1978, Blum et al 1977)
- Studies conducted by the National Toxicology Program also found increased incidence of tumors in rats exposed to TDCPP over 2 years (NTP, 2000);
- CPSC issued a 2006 report estimating that exposure to TDCPP from residential furniture was greater than acceptable daily dose (Babich, 2006)
- Studies conducted in my laboratory suggest TDCPP may also be a neurotoxicant with similar toxic effects observed in chlorinated organophosphate pesticides (Dishaw et al. 2011).
- TDCPP has been used in tents to meet CPAI 84 (Stapleton et al. unpublished data)



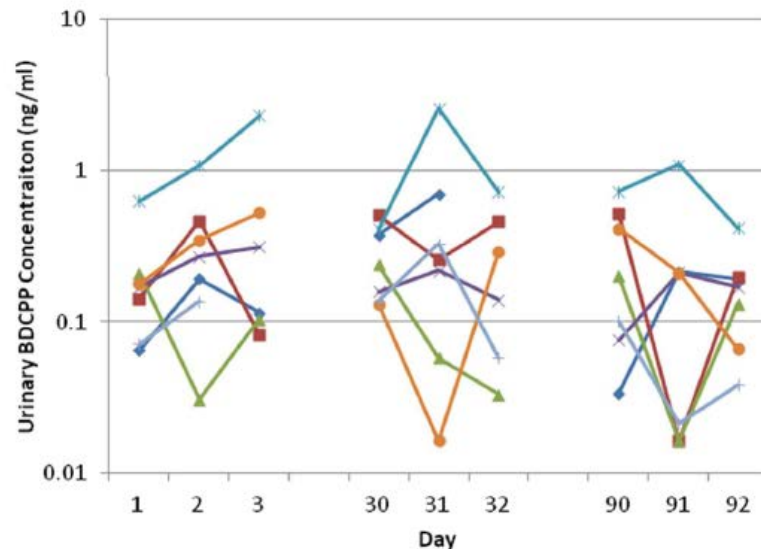
TDCPP Urinary Metabolite Levels

- TDCPP is metabolized in humans to bis (1,3-dichloro-isopropyl) phosphate (BDCPP) by cytochrome P450s (Cooper et al., in draft)
- Our laboratory developed a method to measure urinary levels of BDCPP (Cooper et al. 2011)
- Urinary BDCPP levels measured in two cohort studies:
 - 45 Men in fertility study (2002-2007); repeated measures and associations with dust TDCPP levels (Meeker et al., 2013)
 - Male and Female office workers (2009); associations with dust TDCPP levels (Carignan et al., 2013)



TDCPP Urinary Metabolite Levels

Population	Sample Number	% Detect	Range (pg/mL)	Geomean (pg/mL)	Reference
Men (2002-2007)	45	91	<MDL- 25,000	130	Meeker et al., 2013
Men and Women (2009)	29	100	62-1760	408	Carignan et al., 2013

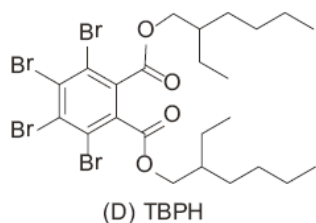
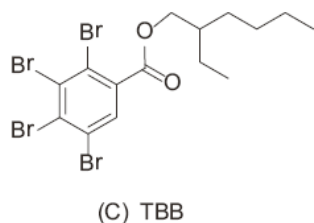
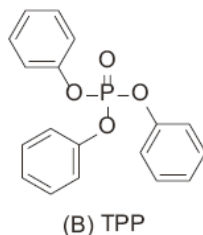
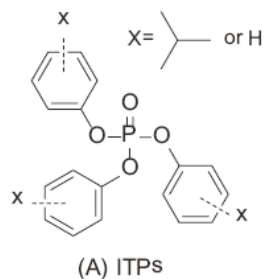


Repeated measurements of BDCPP
In 7 men over 3 month period

Intraclass correlation coefficient: 0.62



Firemaster 550 (FM 550)

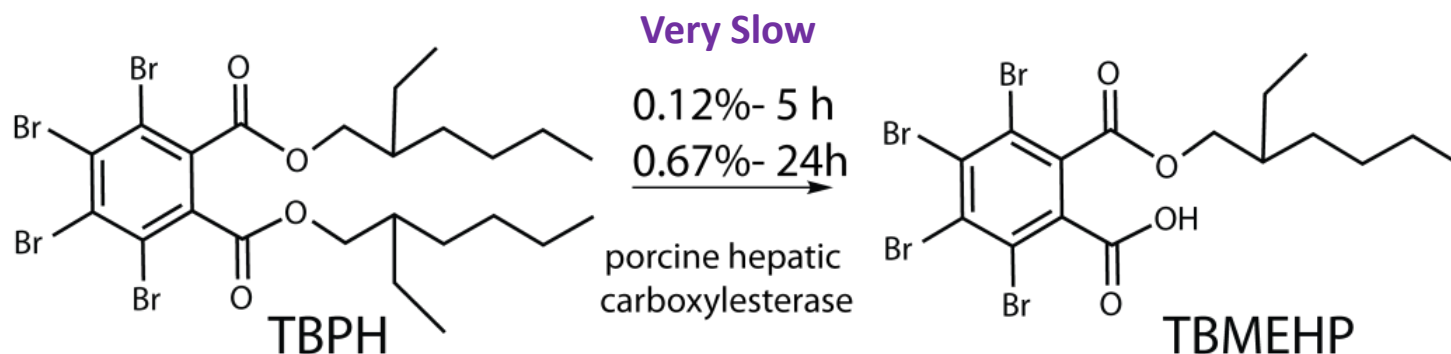
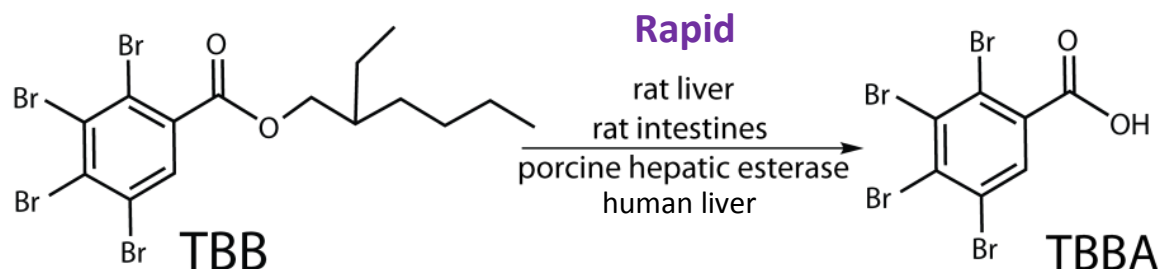


- Manufactured by Chemtura
- Advertised as replacement for PentaBDE
- EPA Issued Consent Order for More Testing in 2005, but only tested effects of two brominated components
- Before 2012, no studies on health effects of FM 550 in rodents/mammals
- No human biomarker available yet.....



FM 550 In Vitro Metabolism

(Roberts et al., 2012)

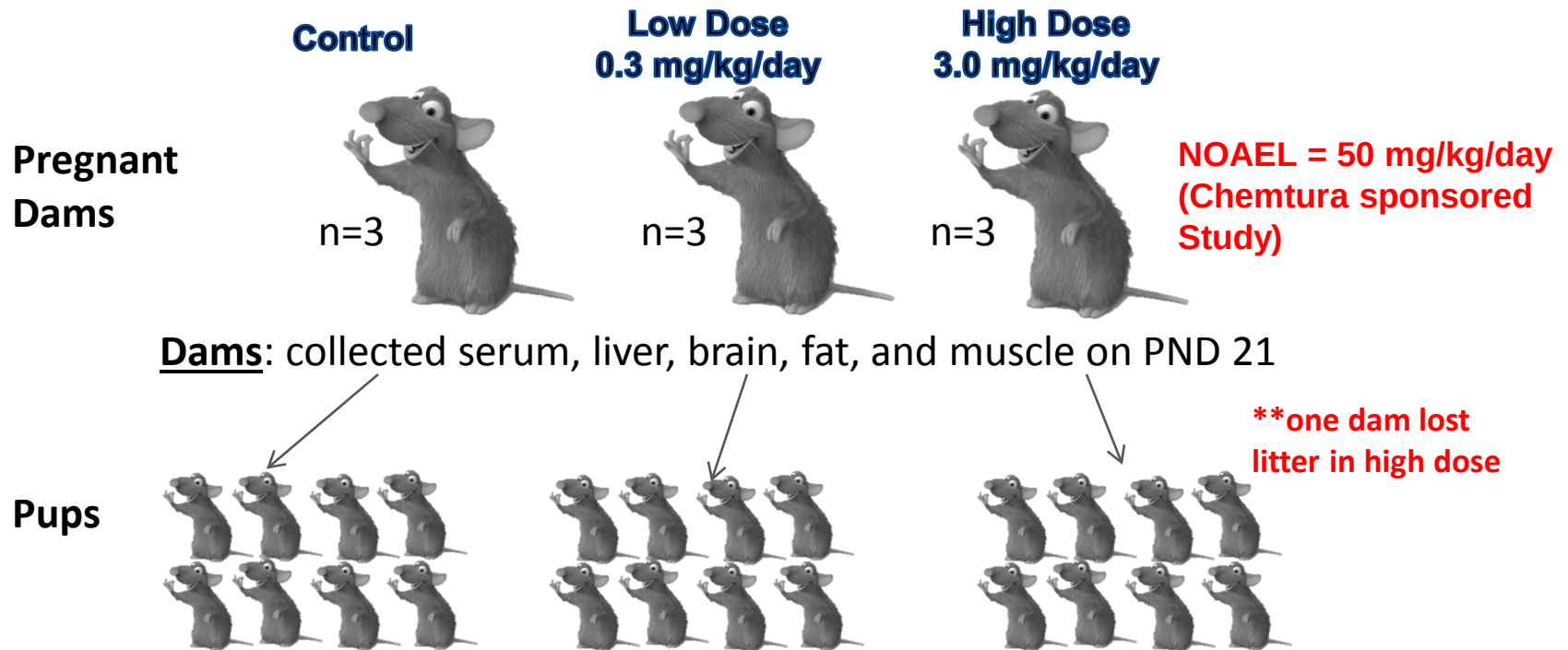


**Triphenyl phosphate (TPP) also rapidly metabolized to OH-TPPs and diphenyl phosphate
In human liver microsomal fractions – manuscript in draft.



FM 550 Reproductive Study (Patisaul et al., 2013; DOI: 10.1002/jbt.21439)

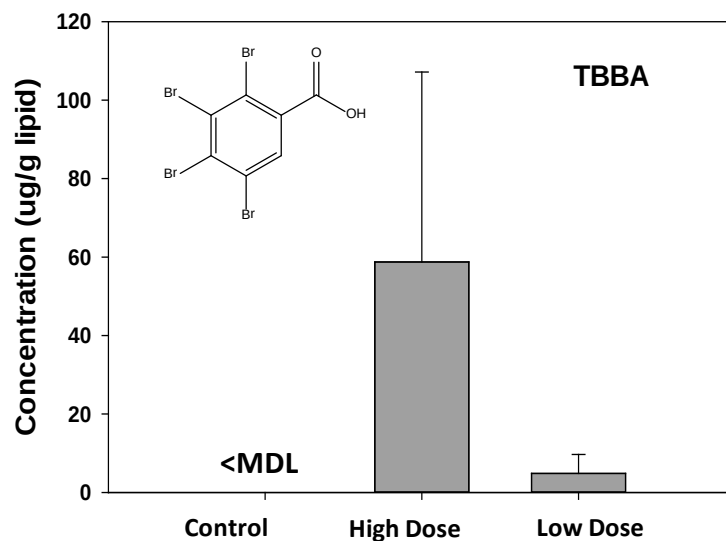
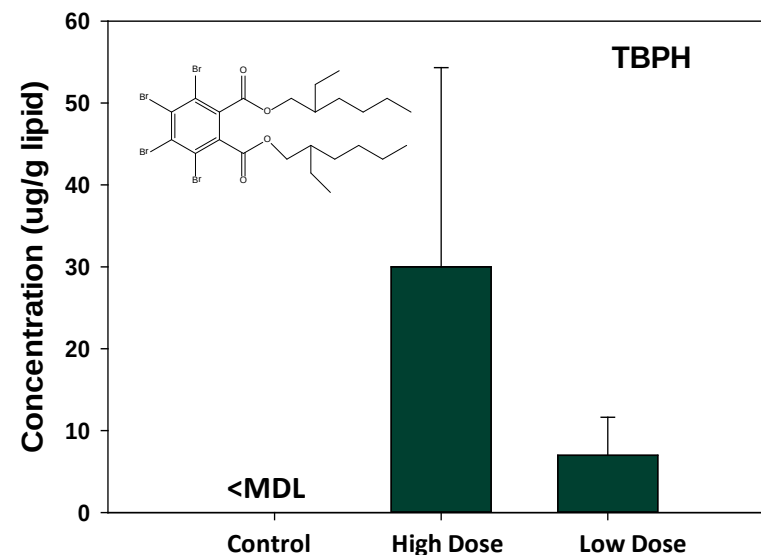
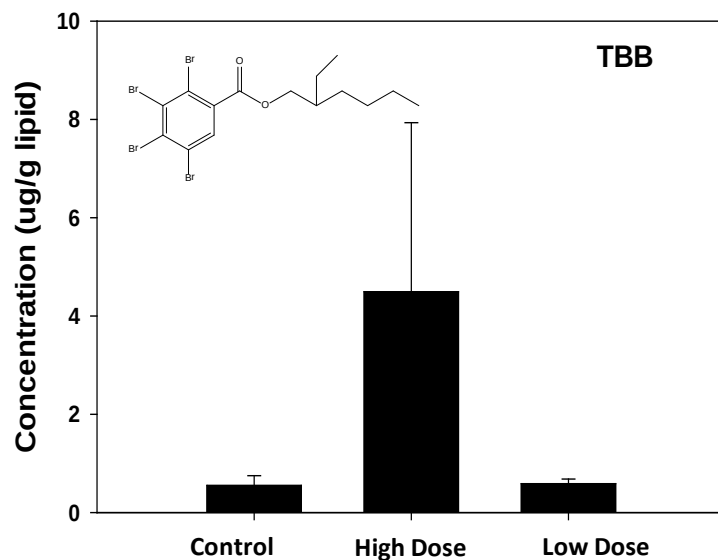
Pregnant rats exposed to FM 550 or control from Gestational Day 6 to Postnatal Day 21



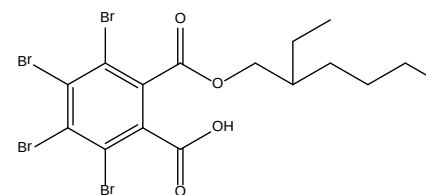
Pups: - Collected serum (limited), liver, brain, fat, and muscle from pups on PND 21, and 7 months of age
- Assessed reproductive development, behavior and growth



Liver Tissue in Dams on PND 21:

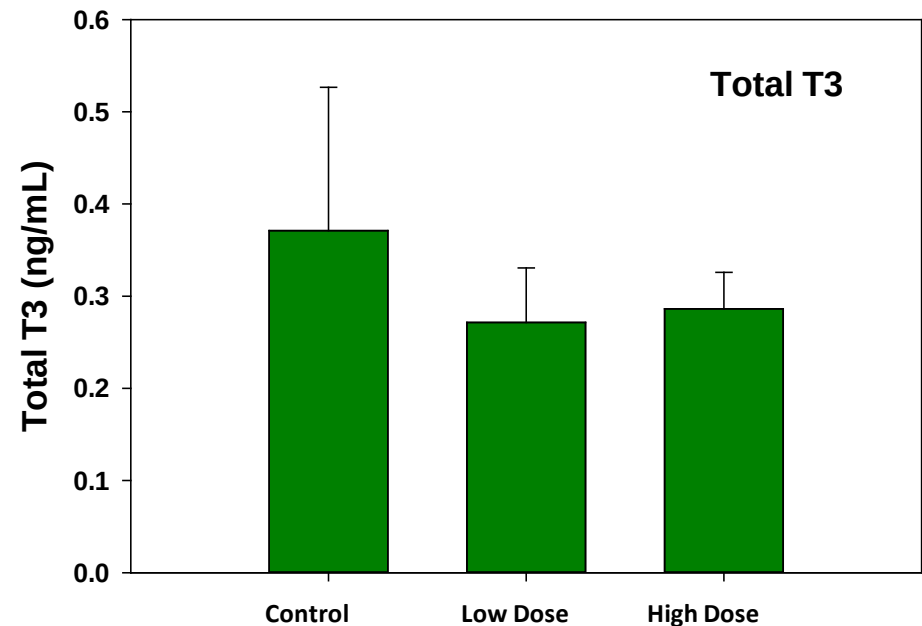
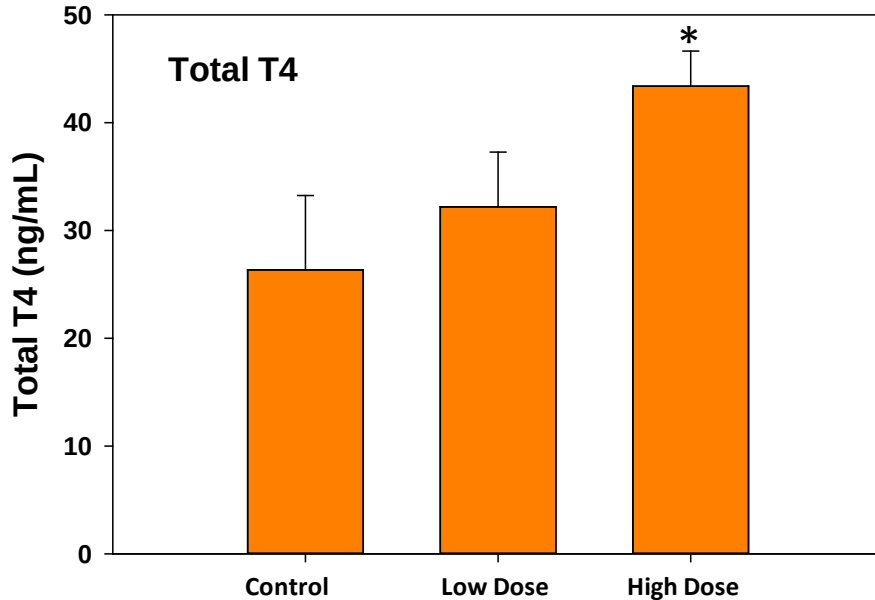


Hepatic TBMEHP <MDL





Thyroid Hormones in Dam Serum PND 21



Bars represent mean $\pm$ 1 standard error

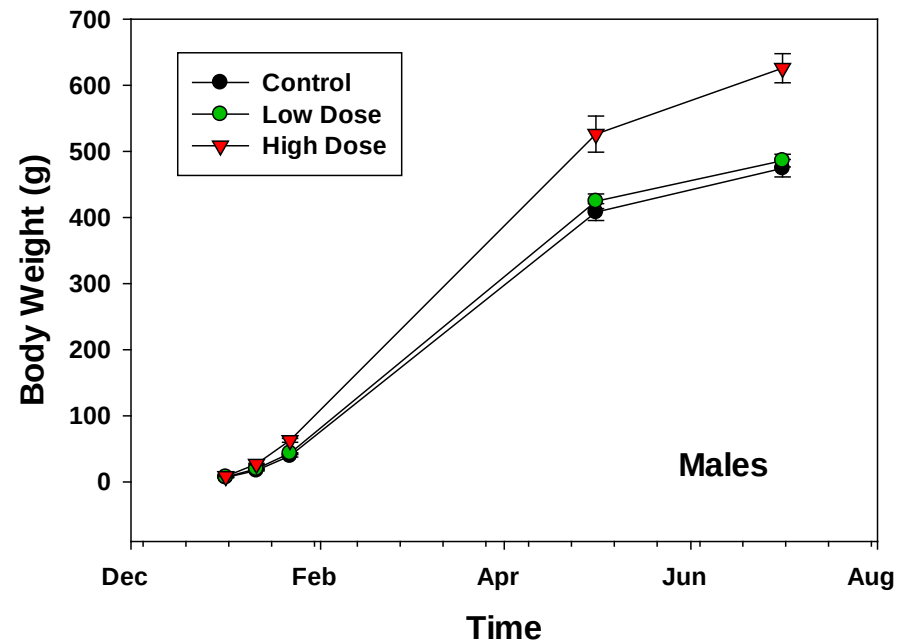
Data were analyzed using ANOVA and Dunnett's post-hoc when appropriate

* Indicates significant difference from control of $p < 0.05$

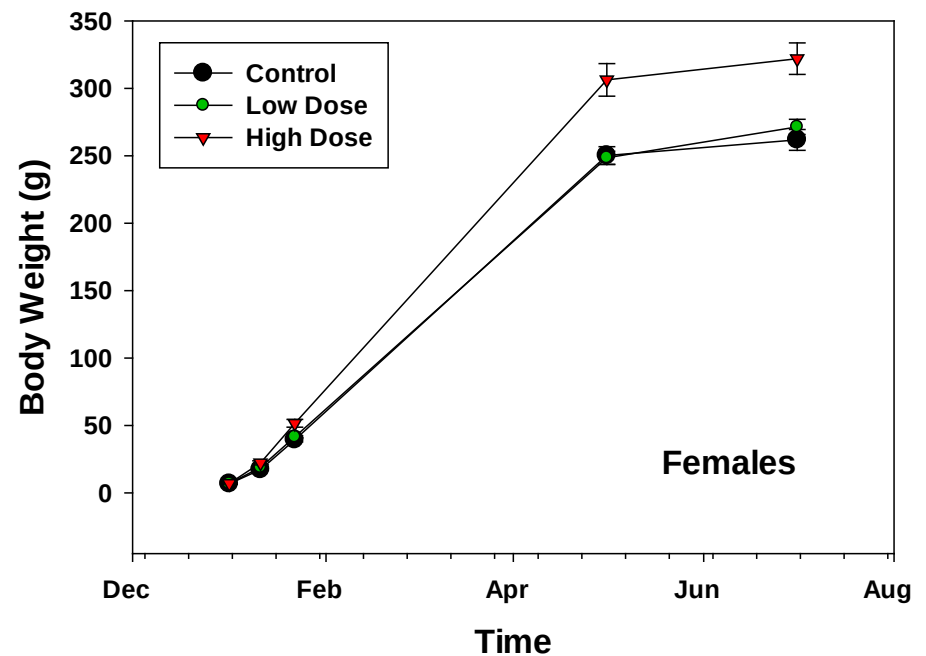
n=3 unless otherwise noted



Pup Body Weight



*Males in high dose significantly heavier than controls starting at PND 10



*Females in high dose significantly heavier than controls starting at PND 21

Bars represent mean $\pm$ 1 standard error

* Indicates significant difference from control of $p < 0.05$
n=3 unless otherwise noted



Findings from FM 550 Rodent Exposure Study:

- TBB and TBPH did accumulate in female rats and their pups exposed during pregnancy and lactation; the metabolite of TBB (TBBA) accumulated more than TBB
- Significant increases in serum thyroxine were observed in dams exposed to 3 mg/kg/day; while pups displayed a suggestive decrease in thyroxine
- Effects on cardiac function were observed in male rats (increased ventricular wall thickness in heart)
- Female pups from high dose group had an early vaginal opening, were more anxious in behavioral tests, and were in persistent estrous cycle ($p < 0.01$)
- Male pups were 32% heavier than controls at 7 months of age and female pups were 23% heavier than controls ($p < 0.01$)
- What is the true NOAEL for FM 550? Should FM 550 or its components be considered an endocrine disruptor or chemical obesogen?



Human Biomonitoring



Appropriate Tissues for Biomonitoring

Blood/Serum	Breast Milk	Urine
PBDEs (All) OH-BDEs Brominated Phenols MeO-BDEs HBCD TBBPA BTBPE DBDPE Dechlorane Plus FM 550??	PentaBDEs HBCD	TCEP → BCEP TCPP → BCPP TDCPP → BDCPP TPP → DPP FM 550 Metabolites

*May also be present as conjugates in urine

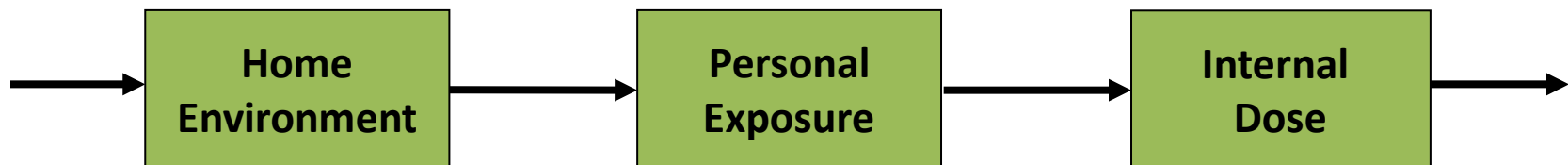
**Method development needed



PBDE Exposure Pathway

Dust and diet are known to be the greatest exposure pathway among the general population. However, children are receiving significantly higher exposures likely due to greater dust exposure.

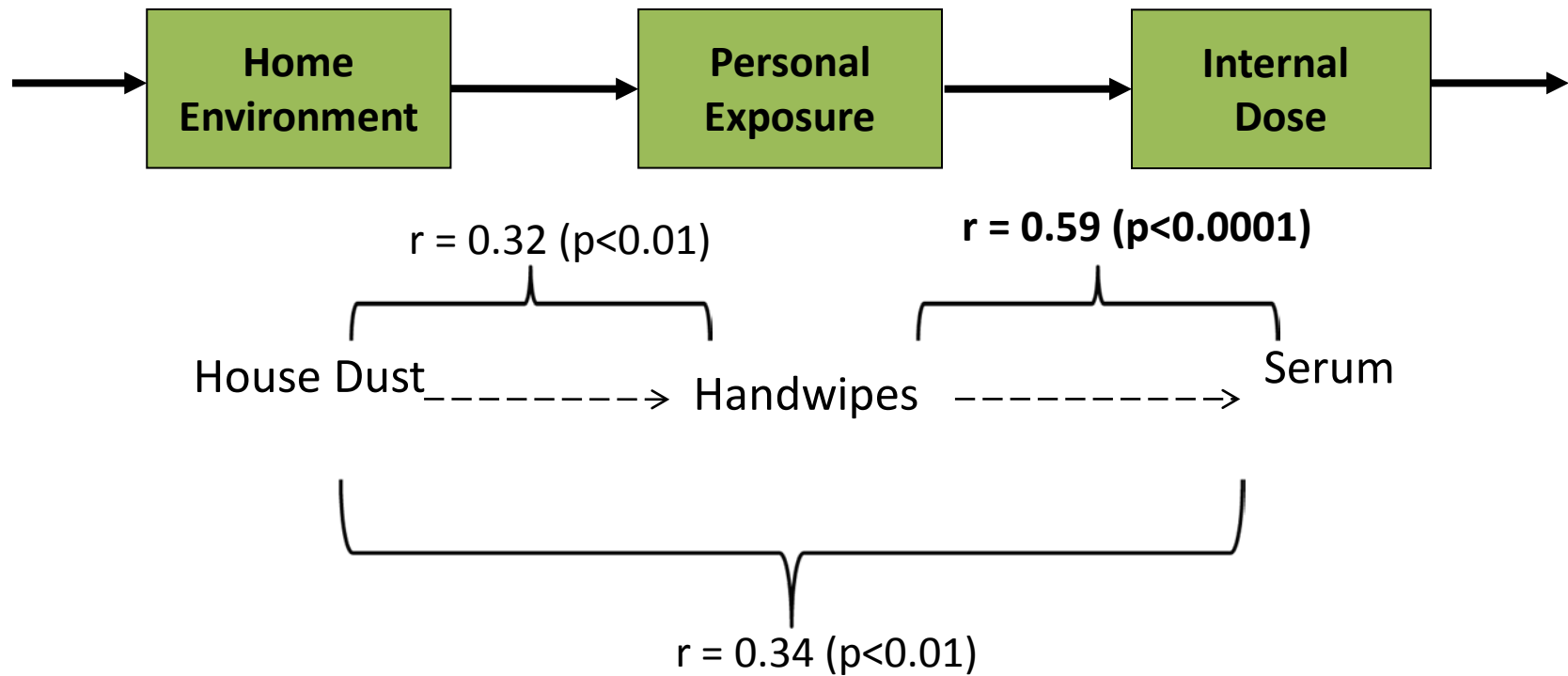
(Wu et al. 2007; Johnson et al. 2010; Rose et al. 2010; Stapleton et al. 2012)





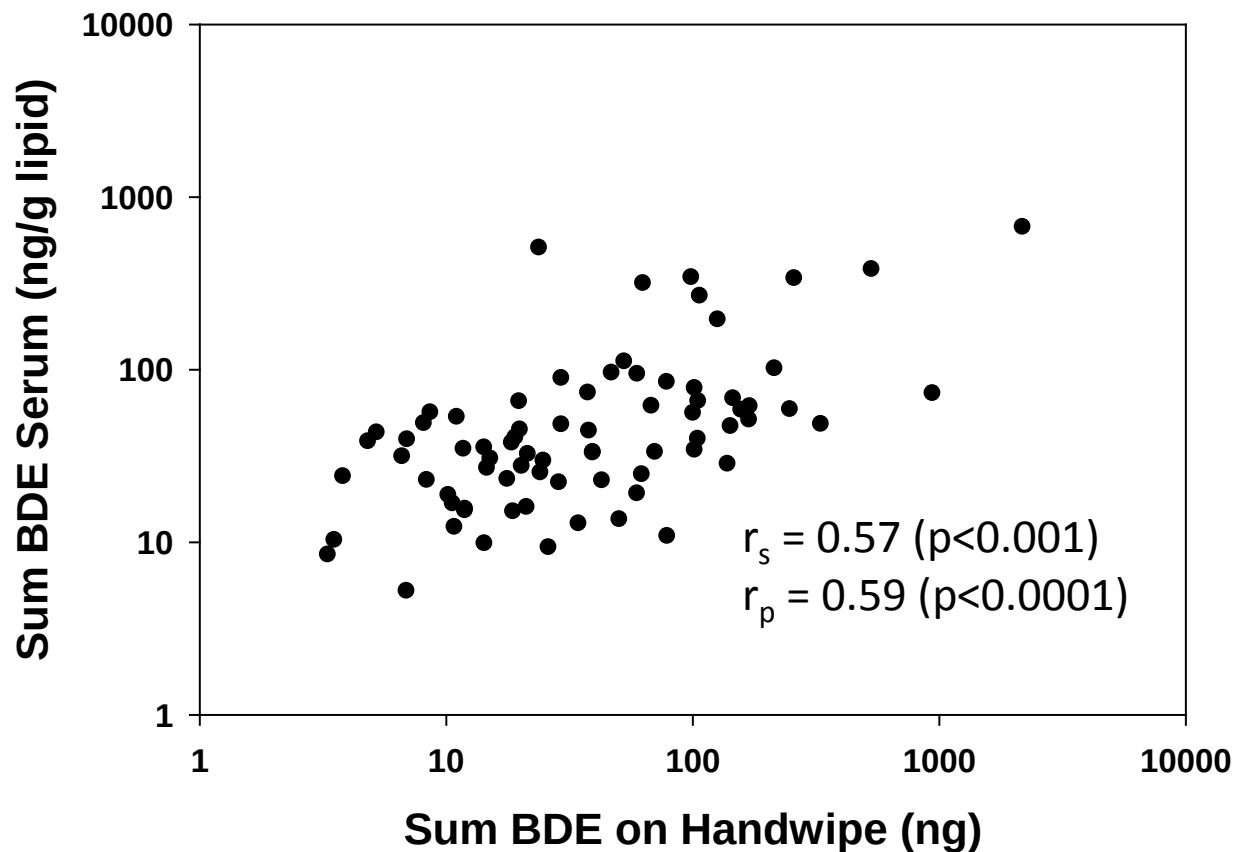
PBDE Exposure Among Toddlers

North Carolina Toddler Cohort (2009-2011): 83 children





***PBDE Residues on Your Hands Are Related
to What's in Your Body
(Stapleton et al. 2012)***





Should We Consider Handwipes as an Exposure Metric?



- Hand wipes are easy to collect and easy to store
- Hand wipes have fewer matrix interferences than biological samples
- Hand wipes may provide a more complete picture of indoor “exposome”



Conclusions and Considerations:

- While PBDEs are being phased out, new flame retardant chemicals are increasingly detected in indoor environments
- The primary flame retardants used to meet TB 117 currently are TDCPP, Firemaster 550 (FM 550), and organophosphate mixtures
- More studies on human health effects related to TDCPP and FM 550 exposure may be warranted
- More data on children's exposure to multiple classes of flame retardants is needed
- Collection and analysis of hand wipes may provide useful measures of exposure to larger classes of compounds



Acknowledgments

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Primary Collaborators:

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Dr. Arlene Blum (Green Science Policy Institute)

Dr. Andreas Sjödín (CDC)

Dr. John Meeker (University of Michigan)

Dr. Marie Lynn Miranda (University of Michigan)

Dr. Heather Patisaul (N.C. State)

