Environmental fate and toxicity of the PBDE flame retardants, with an emphasis on deca BDE

Seattle
March 20, 2008

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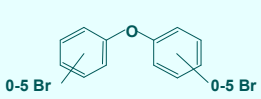
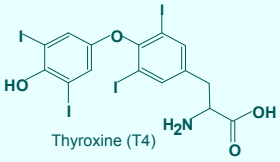
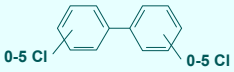
PCBs and PBDEs have similar structures



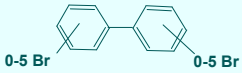
Polybrominated diphenyl ethers (PBDEs)



Thyroxine (T4)



Polychlorinated biphenyls (PCBs)



Polybrominated biphenyls (PBBs)

209 possible congeners
(combinations of Br placement)

Characteristics of PCBs

Persistent in the environment and transported long distances
Bioaccumulate and bioconcentrate up the food web
Toxic

- carcinogenic
- immunotoxic
- endocrine disruptors (including thyroid)
- developmental neurotoxicants
- developmental toxicants
- reproductive toxicants
- hepatotoxic
- large database, including humans

◆ **Banned in late 1970s**

Characteristics of PBDEs

Persistent in the environment and transported long distances
Bioaccumulate and bioconcentrate up the food web
Toxic

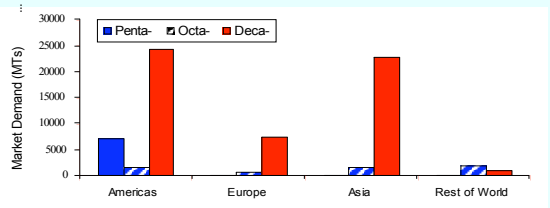
- developmental neurotoxicants
- carcinogenic
- endocrine disruptors
- reproductive toxicants
- hepatotoxic
- limited database, mostly animals

◆ **Used beginning in 1970s**

◆ **penta and octa BDE commercial mixtures withdrawn in 2004**

Demand for PBDEs is highest in Americas

metric tons, 2003



PBDE commercial mixtures

◆ Commercial penta mixture
- textiles, polyurethane foam, resins

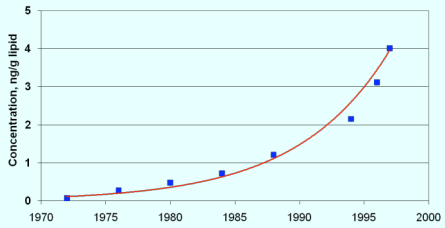
◆ Commercial octa mixture
- 2% DBDE
- additive in polymers for plastic housing, office equipment

◆ Commercial deca mixture
- TV casings primarily (~80% of deca use)
- textile backing
- electrical parts and wires

Congener	Commercial Product		
	Penta	Octa	Deca
BDE-47	26%		
BDE-99	50%		
BDE-100	~10%		
BDE-153	~5%	5%	
BDE-154	~5%	5%	
BDE-183		40%	
BDE-206		30-35%	
BDE-207		15%	
BDE-209			~98%

Data from Birnbaum and Staskal, 2004; Darnerud *et al.*, 2001; Huber and Ballschiffer, 2001; Hutzinger and Sundstrom, 1976; Sjödin *et al.*, 1998; WHO, 1994

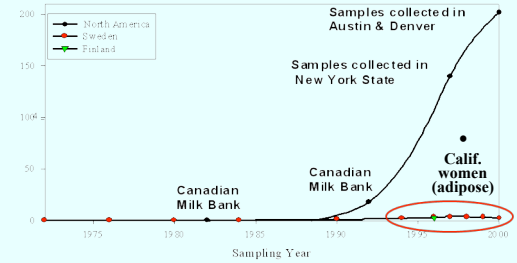
PBDEs in Swedish breast milk
The wake-up call



- No human poisoning episode
- Attention raised by analytical chemists

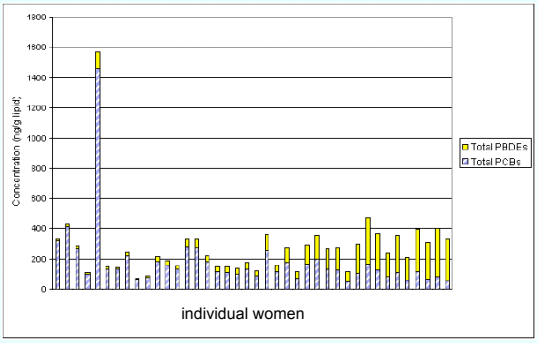
Norén & Meironyté, 1998

Concentrations of PBDEs in breast milk in North America are highest in the world



Canadian Milk Bank and New York State from Ryan and Patry 2000, Denver and Austin results from Fapke et al 2001, Swedish data from Meironyte Guvenius and Noren 2001, Finnish data from Strandman et al 2000

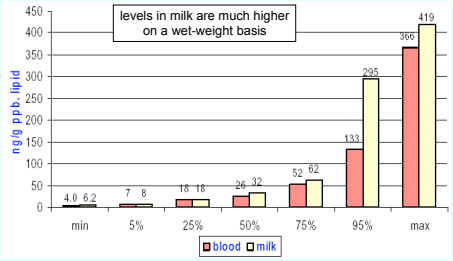
Total PBDEs and PCBs in Pacific Northwest breast milk samples
One-third of women have higher levels of PBDEs compared to PCBs



She *et al.*, 2005

PBDE levels in US women are similar in blood and milk

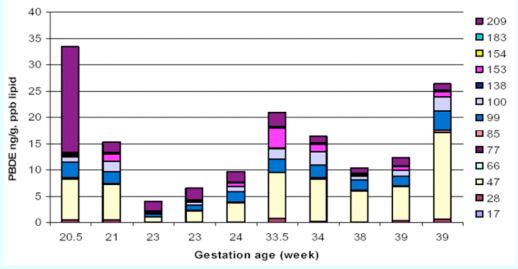
- 13 congeners
- other studies also document similarity of levels in blood and milk



blood (n=50), milk (n=62), 2005

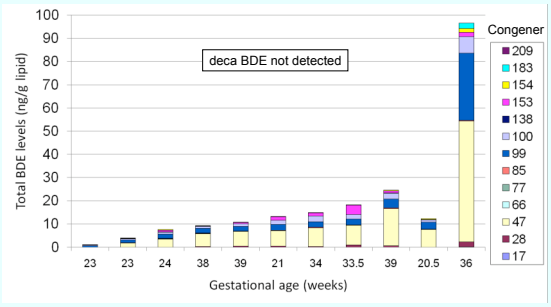
Schecter *et al.*

PBDEs, including deca BDE, cross the placenta and are found in fetal liver



Doucet *et al.*

PBDE levels in human fetal liver
(non-detects not included)



Schecter *et al.*, 2007

PBDEs in humans

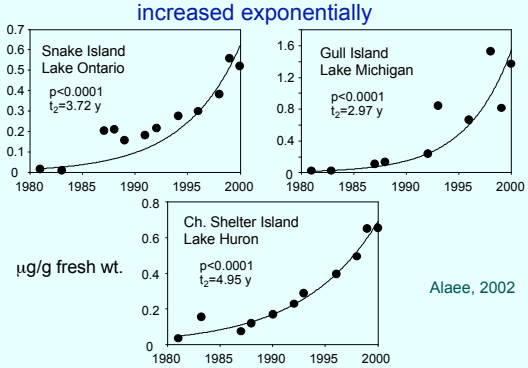
Increasing levels and changing congener pattern

- Levels in humans have increased exponentially since the 1970s
- Levels in humans in the U.S. highest in the world
- Excreted into breast milk and cross the placenta
- Highest concentrations were 47 and 99, presumably from penta BDE
- Currently 153 is dominant congener in some samples, perhaps from metabolism of deca BDE (and/or long half-life)
- Recent studies in Japan and Spain found deca BDE as the dominant congener in breast milk and umbilical cord serum

PBDEs in animals

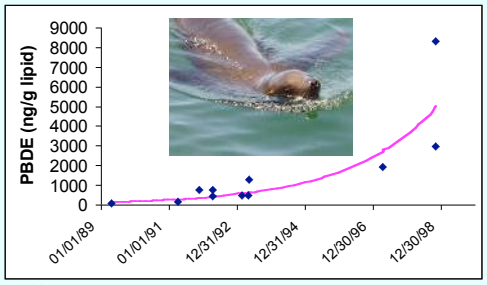
- Levels in wildlife are increasing exponentially around the world
- Found in fish in remote mountain lakes, Arctic mammals
- Animals and birds at the top of the food chain particularly affected
  - predatory fish, terrestrial and aquatic predatory birds (numerous species), herring gulls, whales, harbor seals, polar bears

PBDEs in herring gull eggs in the Great Lakes have increased exponentially



Alaee, 2002

PBDEs in blubber of California seals has increased markedly over a short time



N=11

She et al., 2002

deca BDE in animals

- Found in top predators in terrestrial and aquatic food webs
  - concentrations often but not always low compared to other congeners
- Pattern is changing from lower-brominated to more highly brominated congeners
- Degradation and metabolism may result in underestimation of contribution of deca BDE to total body burden

deca BDE is accumulating in wildlife two examples

Grizzly Bears Along British Columbia
(Christensen et al., 2005)

Penta BDEs: 0.2 to 5 ppb lipid

Deca BDEs: 0.1 to 42 ppb lipid

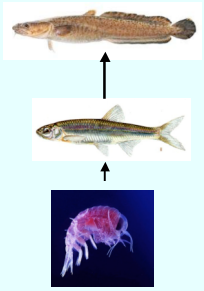
Terrestrial feeding bears have higher deca BDE concentrations in their tissues (as much as 90% of the burden was deca BDE)

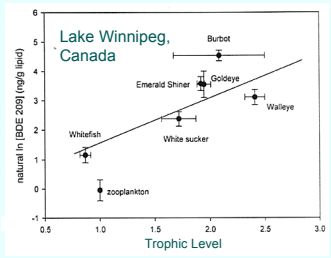
Red Foxes
(Voorspoels et al., 2006)
sampled ~30 individuals

Penta BDEs: 2 to 3 ppb lipid
Deca BDEs: <DL to 760 ppb lipid

deca BDE was the dominant congener (~80%) in almost half the foxes tested

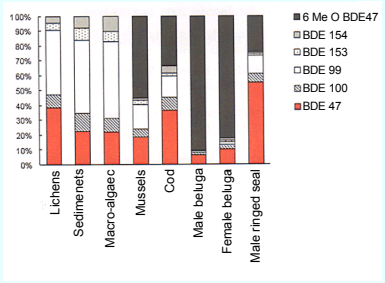
deca BDE accumulates in aquatic organisms and bioconcentrates up the trophic web

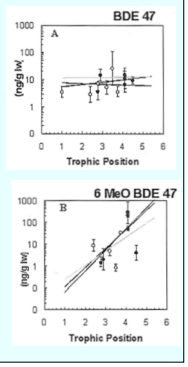




Law *et al.*, Environ. Toxicol. Chem., 2006

Another twist: BDE-47 is converted to a methoxy metabolite that bioconcentrates up the food web





Kelly and Ikonomou, 2006

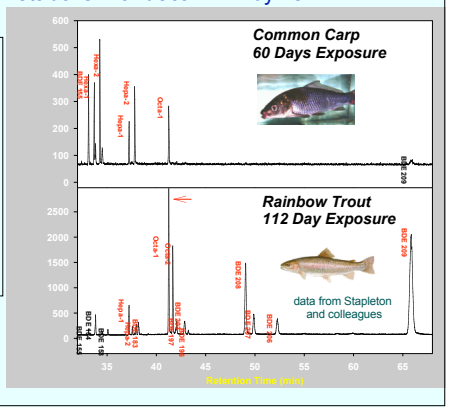
Metabolism of deca BDE

- deca BDE is absorbed, as much as >60% in some studies
- deca BDE is metabolized by fish and mammals to multiple congeners found in animal tissue
- Hydroxy- and methoxy- metabolites identified in experimental studies, wild animals and humans
  - more toxic than parent compound in some cases
- deca BDE or metabolites gets into brain
- Mice pups do not excrete PBDEs after single dose of BDE-47

Metabolism of deca BDE by fish

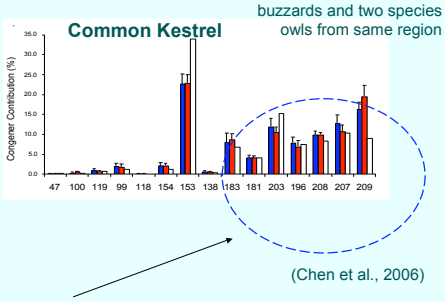
Same pattern observed In sunfish collected Downstream of a Wastewater treatment Facility in Virginia

(LaGuardia et al., 2005)



Congener profiles in wildlife suggest metabolism of deca BDE

Similar patterns observed in buzzards and two species of owls from same region

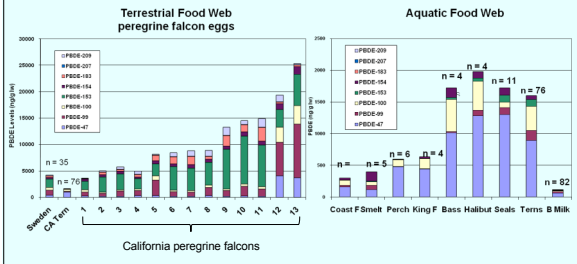


(Chen et al., 2006)

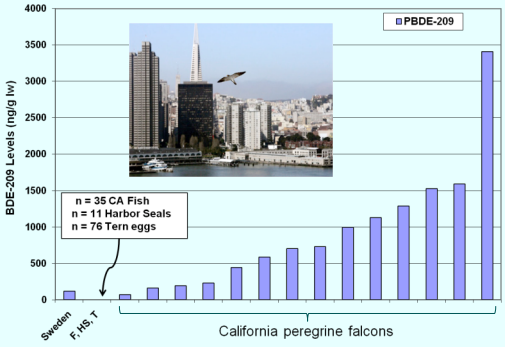
Evidence of accumulation and metabolism of Deca BDE

Congener pattern in terrestrial and aquatic food webs

San Francisco Bay



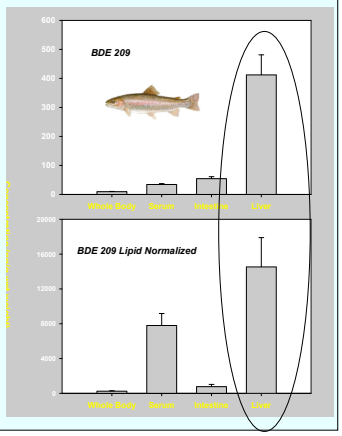
BDE-209 in “aquatic” vs “terrestrial” food webs



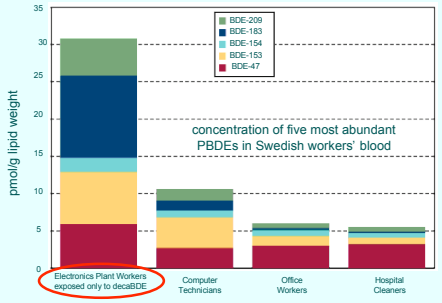
Kim Hooper

Tissue distribution of deca BDE is different from other congeners

- BDE 209 preferentially accumulates in liver and in serum. This has the potential to induce greater toxicity than if it was accumulating in fat tissues (Stapleton et al)
- Similar to Findings by Morck et al. (2003) and Kierkegaard et al. (1999) exposing rats and rainbow trout to BDE 209, respectively



deca BDE is metabolized by humans to toxic congeners



Exposure to deca BDE for years resulted in higher levels of deca, 183, 153, and 47. This suggests metabolism of deca BDE to other congeners.

Other potential metabolites of deca BDE were not measured.

Thuresson *et al.*, 2005

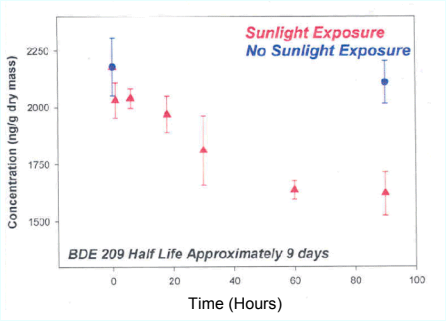
deca BDE in the environment

- Undergoes long-range transport, including into the Arctic (levels of PBDEs highest near cities)
- Levels of PBDEs in sediment have increased by several orders of magnitude since the 1970s
  - deca is dominant congener, >90% in many cases
- High levels in sewage sludge, deca dominant
  - one-half of sludge used as fertilizer
- High levels near waste dumps, dibenzofurans produced during burning

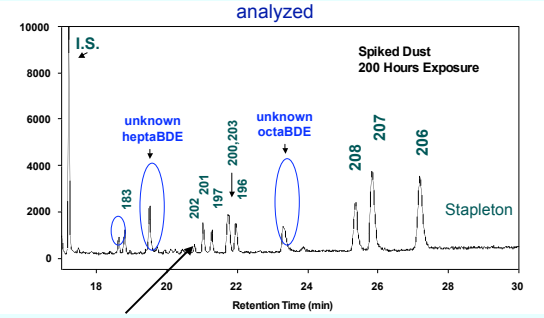
deca BDE in the environment

- Undergoes relatively rapid degradation by sunlight to other PBDEs (congeners with fewer bromine atoms)
- Degraded by microorganisms in sediment
  - products may include congeners routinely found in the environment
- Suggests contribution of deca BDE to levels in the environment, animals and humans is underestimated

Deca BDE is rapidly debrominated in dust, sand, or sediment exposed to sunlight

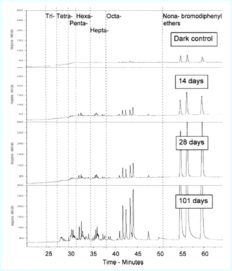


deca BDE is debrominated, included to congeners not usually analyzed

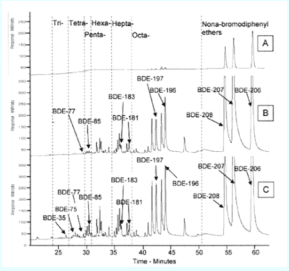


Degradation products not found in any commercial mixtures:
Indicators of DecaBDE debromination
BDE 202 has been measured in house dust (Allen et al., 2006)

Photodegradation of DecaBDE By sunlight under natural conditions produces multiple congeners



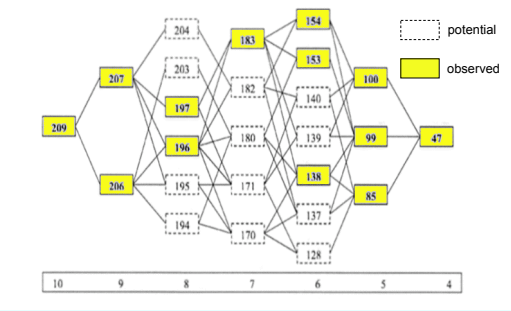
GC-ECD chromatograms showing appearance of PBDE congeners after sunlight irradiation of BDE-209



GC-ECD chromatograms of concentrated dark control (A) and sunlight-irradiated kaolinit (B) and montrmorillonite (C) at 56 days

Ahn *et al.*, Environ. Sci. Technol., 2006

Photopic debromination of decaDBE in hexane produces a number of intermediates found in the environment and animals, including 153, 99, and 47



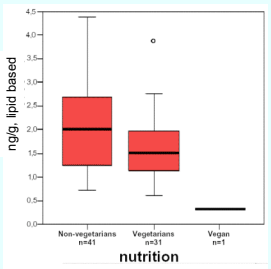
Cruz *et al.*, Environ. Sci. Technol., 2004

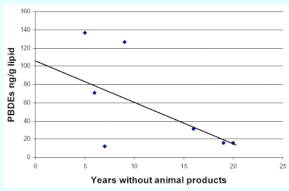
Sources of PBDE Exposure in Humans

PBDEs are found in human food

- Highest levels are found in fish
- PBDEs also found in meat and dairy products
- deca BDE is present, usually but not always at low levels
  - occasionally deca is the dominant congener
- Highest exposure is through meat

Consumption of animal products predicts PBDE breast milk levels





r=-0.6, $p < 0.05$

Schecter *et al.*

Paepke *et al.*

decaBDE is metabolized by cattle
source of human exposure

- decaBDE is in silage fed to dairy cows
  - deca BDE found in fat, muscle, liver, and kidney
  - significant accumulation of hepta-, octa-, and nona BDE congeners despite absence in food
  - higher levels in fat and muscles, suggests source of exposure to humans
- Humans may ingest deca BDE from food, or indirectly via metabolism by the animals we eat

(Kierkegaard *et al.*, 2007)

Indoor air is a major source of PBDE exposure

Deca BDE is inhaled In indoor air

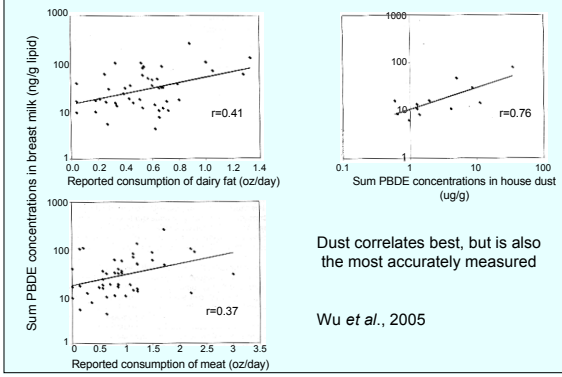
Presence of personal "Dust Clouds" results in higher exposure than predicted by large volume air samplers

GM PBDE Concentrations in Air (pg/m^3)

Congener	Personal	Bedroom	Main living area
BDE 17	7.6	8.1	7.0
BDE 28/33	29.6	27.3	25.4
BDE 47	226.8	157.9 **	145.1 **
BDE 49	9.1	6.0 **	7.2
BDE 66	3.7	3.5	3.5
BDE 85/155	3.8	2.7	2.5
BDE 99	110.8	66.9 **	60.3 **
BDE 100	22.2	14.4 **	12.0 **
BDE 153	8.6	4.0 **	3.5 **
BDE 154	9.1	6.1 **	5.2 **
BDE 209	173.6	94.8 **	94.2 **
∑BDE	765.7	460.4	452.8
∑BDE (no 209)	469.1	324.7	288.6

Allen et al., 2007
20 participants from Boston, MA

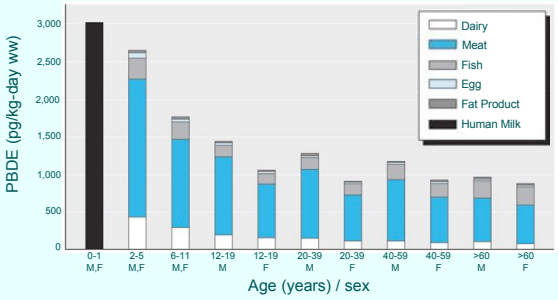
Dust, meat and dairy are all correlated with breast milk PBDEs



Dust correlates best, but is also the most accurately measured

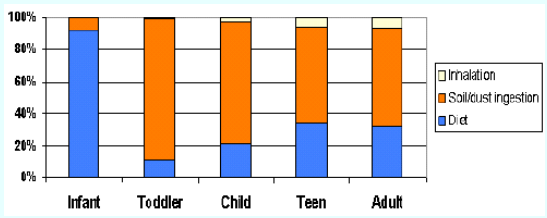
Wu *et al.*, 2005

Source and intake of PBDEs from food depends on age



Schecter *et al.*, Environ. Health Perspect., 2006, US population

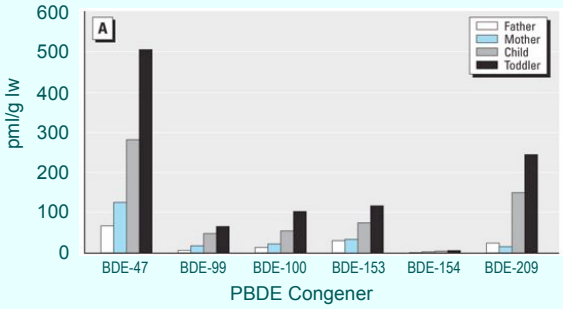
Relative contribution from different pathways is also age-dependent



% contributions from inhalation, soil/dust ingestion and diet to "average" Canadian exposure to total PBDEs

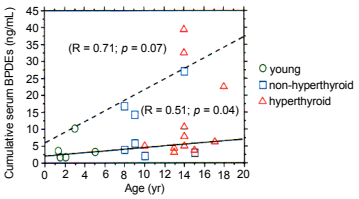
Jones-Otazo *et al.*, 2005, Canada

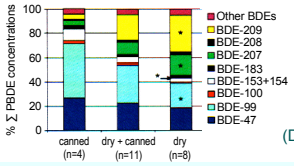
PBDE serum concentrations in a family
levels in the toddler rival occupational exposure



Fischer *et al.*, Environ. Health Perspect., 2006

PBDE levels in cats increases with age
levels are 10-100 times humans





congener profile depends on food type

(Dye et al, 2007)

PBDEs are toxic to multiple systems in animals

- More toxicity data have been published recently
- Decrease thyroid hormone, including deca BDE
- Interfere with reproductive hormones and function, including deca BDE
  - Anti-androgenic, estrogenic depending on congener
- Suppress immune function
- Change regulation of liver enzymes, which interferes with multiple hormones and other biochemical processes
- deca BDE causes cancer in rodents at high doses

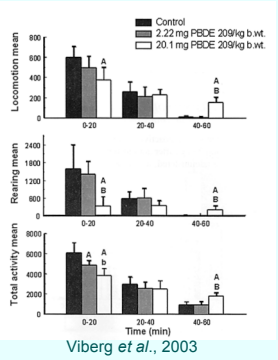
PBDEs produce changes in brain function following developmental exposure

- PBDEs, including deca BDE, produce changes in brain chemistry and the function of multiple neurochemical pathways
- PBDEs, including deca BDE, produce changes in behavior in multiple studies
  - motor activity
  - learning
  - delayed normal sensorimotor development early in life
  - cognitive effects later in life not present in young adulthood (Markowski, Rice et al, unpublished)
- PBDEs, including deca BDE, interact with other environmental chemicals to produce greater toxicity

Deca and other BDEs produce neurotoxicity following postnatal exposure

- Swedish group studied motor activity in mice dosed on postnatal day 3, 10, or 19
  - congeners 47, 99, 153, 183, 203, 206, and 209 all produced similar effects on motor activity
  - effects on learning observed with 203, 206, or 153 but not 183
  - PCB + BDE are additive in producing motor effects
  - decaBDE + PFOA also interacted
  - BDE-99 or PCBs interact with methylmercury
- Congeners 47, 99, 153, 183, 203, 206 are all potential breakdown products or metabolites of 209 (deca)

Motor activity during adulthood following decaBDE exposure, single dose on PND 10



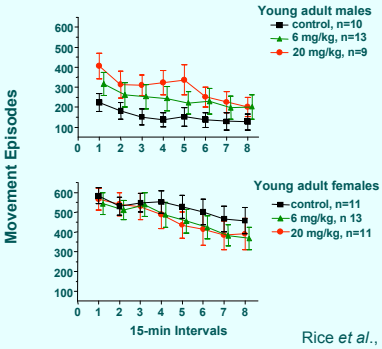
All their mouse data from the various congeners look about like this

Viberg *et al*., 2003

Postnatal decaBDE study in mice
University of Southern Maine/Maine CDC

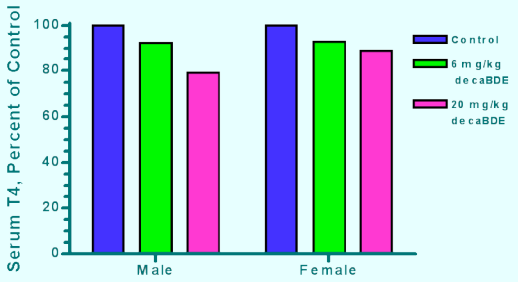
- Mice exposed on postnatal days 2-15 with 6 or 20 mg/kg/day
  - female and male littermates assessed preweaning, young adulthood, one year of age
- **F**unctional **O**bservation **B**attery
  - development of sensorimotor integration
  - retarded development of grip strength and palpebral (blink) reflex, increased reaction to handling at lower dose
- Increased activity in males in early adulthood
- Decreased thyroid levels after weaning

Postnatal decaBDE exposure increased activity in young but not old male mice



Rice *et al*., 2007

Postnatal exposure to decaBDE decreased thyroid hormone at 21 days of age



PBDEs may have effects on reproduction and development in humans

Chao *et al*., 2006

- Deca BDE levels in breast milk predicted lower birth weight and length, smaller head circumference
- Deca BDE was associated with decreased cycle length and decreased duration of menstrual bleeding
- Deca BDE levels in breast milk predicted more adverse outcomes than other congeners
- Animal studies document change: in LH, estradiol, testosterone, reduction in ovarian follicle

PBDEs may have effects on development in humans

- PBDEs in breast milk associated with cryptorchidism (undescended testes) (Main *et al*., 2007)
  - deca BDE was not measured
  - PBDEs reduce ano-genital distance in animal studies
- multiple epidemiological studies planned or ongoing
- multimillion-dollar multiple year studies have not been done for PBDEs as was done for PCBs

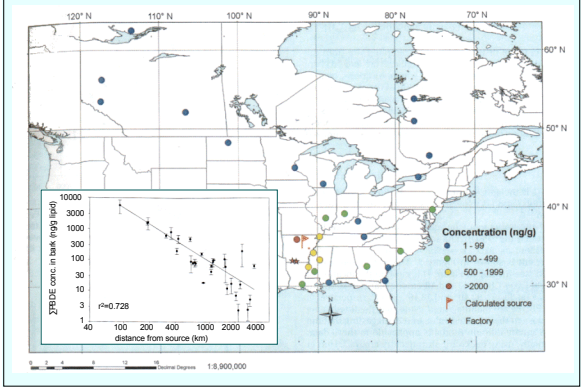
Past and future contribution of decaBDE to the observed congener pattern in humans

- Initially most prevalent congeners were 47, 99
  - from the penta and octa commercial mixtures
- Currently 153 is becoming dominant
  - from penta and octa mixture, deca metabolism or breakdown in the environment
- If deca remains in commerce
  - increasing levels of 47, 99, 153, and more highly brominated compounds, all toxic
  - Also methoxy and hydroxy compounds, more toxic than the parent compound in some cases
    - particularly affect sex hormones

deca BDE: A Cautionary Tale

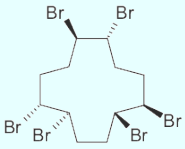
- Assertion
  - deca BDE will not be persistent or transported
  - big molecule, low volatility
- Reality
  - transported long distances, degraded in the environment to toxic congeners
- Assertion
  - decaBDE will not be absorbed, and will not bioconcentrate
- Reality
  - decaBDE is absorbed, metabolites and possibly parent can bioconcentrate, present in human food chain
- Assertion
  - decaBDE is not toxic
- Reality
  - may be largely true for parent compound based on *in vitro* studies
  - toxic to multiple systems *in vivo*
  - metabolites and degradation products are toxic

North American PBDE gradient from bromine factories in Arkansas



There are lots of other brominated flame retardants…

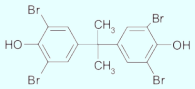
Hexabromocyclododecane (HBCD)



- high production volume chemical
- ubiquitous contaminant in environment and wildlife with levels similar to PBDEs
- environmental levels are increasing
- undergoes long-range transport
- interferes with thyroid hormones, brain development, liver metabolism, reproduction
- found in human tissue, including umbilical cord blood

There are lots of other brominated flame retardants…

Tetrabromobisphenol A (TBBP-A)



- largest-selling brominated flame retardant
- found in environment and wildlife
- bioaccumulates and undergoes long-range transport
- toxic to aquatic organisms
- produces many of same toxic effects as PBDEs, PCBs, HBCD
- degraded in the environment to bisphenol A, a potent endocrine disruptor

Still other flame retardants also present in homes and the environment… some not even identified

State initiatives

- States acted in response to lack of federal leadership
- Commercial penta- and octa-BDE banned in 10 states after 2003
  - Maine, Hawaii, California, Maryland, Michigan, Washington, Oregon, Illinois, New York, Rhode Island
- Commercial penta- and octa-BDE voluntarily withdrawn by industry in U.S. December 31, 2004
- Bills to ban decaBDE passed in Washington and Maine in 2007
- Bills to ban decaBDE pending in California, Illinois, New York, Hawaii, Michigan, Minnesota, Montana
  - little chance of passage for most bills

State of Maine bills banning PBDEs

- 2004 – penta- and octa- banned as of January 1, 2006
  - deca provisionally banned if safer alternatives identified
  - annual reports by MeCDC and DEP 2005, 2006, 2007
- May 2007
  - deca banned - mattresses and furniture January 1, 2008; televisions and other plastic-case electronics January 1, 2010
  - exceptions for cars, wiring and cable, industrial or manufacturing processes
  - report every two years on flame retardants by CDC and DEP
  - DEP Commissioner can remove other flame retardants if safer alternative exists and State Fire Marshall determines it meets safety standards