

# An Overview of Research on Halogenated Fire Retardants

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## Fire Retardants Have Had a Lot of Publicity...

- Found in Breast Milk
- Potential Endocrine Disruptors
- Potential Developmental Neurotoxicants



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Thursday, September 23, 2003

**Newsline**

■ News ■ Money ■ Sports ■ Life

**Dollar slides — and stocks follow, 1, 5B**

	Close	Change
Dow Jones industrial average	9535.41	↓ 109.41
S&P 500	1874.62	↓ 31.08
Ind. 30-year yield	5.14%	▲ 0.07
USA TODAY Internet 50	100.04	▲ 1.85

**Flame retardant found in breast milk**

U.S. levels highest in the world, study says

By Elizabeth Weise  
USA TODAY

A toxic chemical used to make furniture, foam and electronics fire resistant is turning up in high amounts in the breast milk of women in the USA.

Two studies, one out today, found that all of the women tested were contaminated with polybrominated diphenyl ethers. Their PBDE levels were the highest in the world: 10 to 20 times higher than those in Europe, where the chemicals are being phased out.

The Environmental Working Group, a non-profit environmental research organization, tested the milk of 47 women. It found levels ranging from 9.5 to 1,078 parts per billion. The women were recruited via EWG's Web site.

It is not yet known how this chemical affects people; no studies have been done on what a safe level would be. But "this is another wake-up call," says Linda Birnbaum, director of the Environmental Protection Agency's experimental toxicology lab. Levels of PBDEs in humans are doubling every two to five years, she says.

A University of Texas-Houston study by Arnold Schechter, professor of environmental sciences, and Birnbaum found levels in breast milk from 5 to 418 parts per billion in 47 American women. It was published last month in *Environmental Health Perspectives*.

**What are PBDEs?**

Polybrominated diphenyl ethers are among the toughest flame retardancy standards, 3,000 people die in fires each year. The Chemical Manufacturers Association estimates the number would be up to 960 higher without such flame retardants.

**Mothers' Milk**

Record levels of toxic fire retardants found in American mothers' breast milk

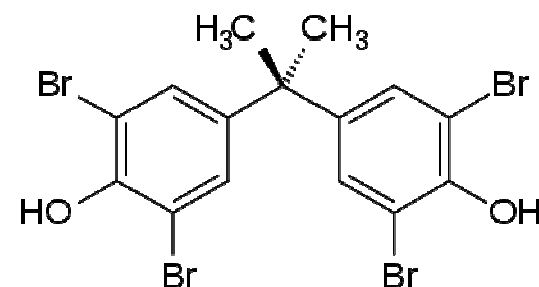
## Three Examples of Fire Retardants of Concern and the Research on Their Health Effects

- TBBPA, primarily used in electronics/circuit boards
- HBCD, used in electronics, textile backings, and as thermal insulation in buildings
- PBDEs, is or has been used in polymers, electronic equipment, textile backing, and flexible polyurethane foam

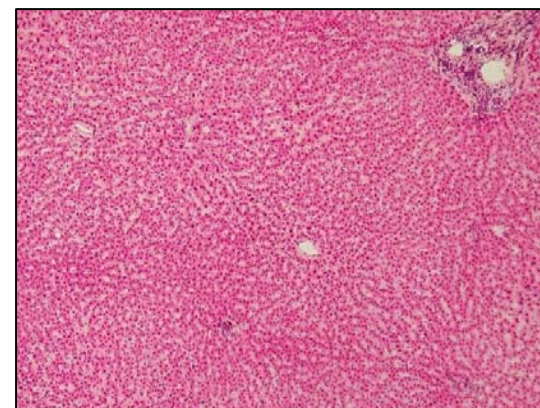


## TBBPA : Health Effects

- Immunotoxic – inhibits T cell activation
- Hepatotoxic – toxic to primary hepatocytes, destroys mitochondria, causes membrane dysfunction
- Neurotoxic – oxidative stress, inhibits dopamine uptake, generates free radicals, increases calcium
- Causes hearing deficits in rats following perinatal exposure



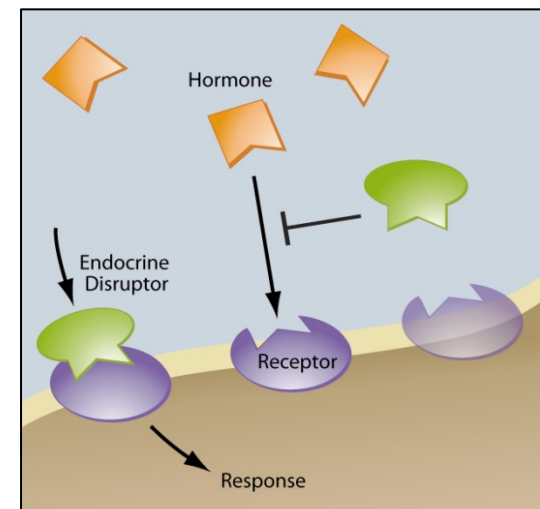
Hepatocyte - liver



*Courtesy: Department of Histology, Jagiellonian University Medical College*

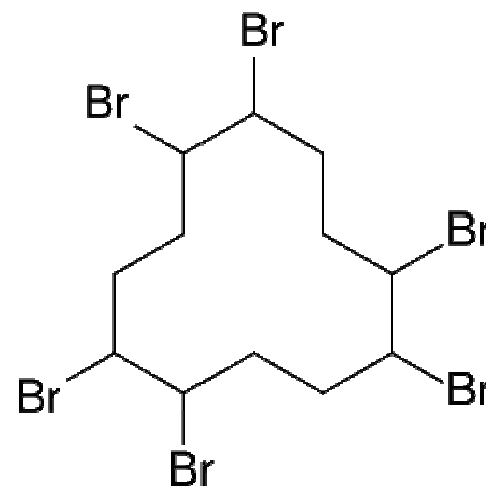
## Tetrabromobisphenol A (TBBPA): Health Effects (continued) – Endocrine Disruption

- AhR Effects – not relevant for commercial products (Contaminants? Combustion products?)
- Thyroid – Thyroid hormone agonist, antagonist, or no effect
- Estrogenic/Androgenic – inhibits sulfotransferase (decreases estrogen clearance), developmental effects including increased testis and pituitary weight



## HBDCD :Health Effects

- Mild acute toxicity, irritation, sensitization, mutagenicity (EU Commission, 2008)
- Liver hypertrophy: enzyme inducer (CAR/PXR)
- Repeated dose in rats increased liver weight, liver enzyme activity
- Two generation reproductive rat study showed decreased T4, increased TSH, reproductive effects, altered histology of ovary, decreased viability of pups (Ema, 2008)



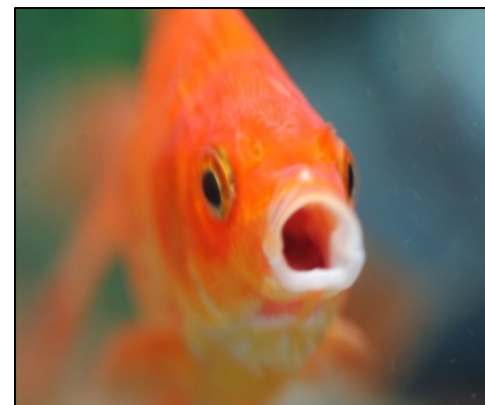
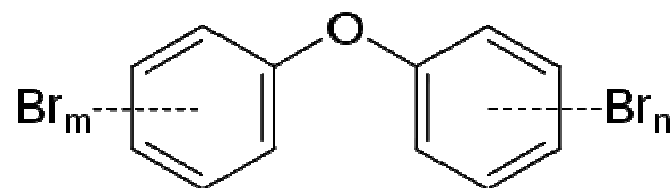
## Hexabromocyclododecane (HBCD): Health Effects (continued)

- DNT effects in mice – spontaneous behavior, learning and memory deficits (Eriksson, 2006)
- *In Vitro* effects – anti-androgen, aromatase inhibitor, interactions with steroid hormone receptors; potentiates T3 effects in rat pituitary cell line/T-screen; neurotoxic to rat cerebellar granule cells; inhibits depolarization-evoked intracellular Ca<sup>++</sup> increase and neurotransmitter release



## PBDEs: Ecotoxicity

- Highly toxic to invertebrates
- Endocrine disruption in frogs, decreases testosterone, increases estradiol, increases phenotypic female frogs
- Developmentally toxic to fish, tail asymmetry, delayed hatching, behavioral changes, learning
- Baltic porpoise die-off related to lymphoid depletion



## Polybrominated Diphenyl Ethers (PBDEs): Ecotoxicity (continued)

- Depletion of vitamin E in duck eggs
- Altered reproductive behaviors in Kestrels at environmental levels and decreased reproductive success
- PBDE levels measured in fish, sea turtles, birds, mammalian wildlife and domestic animals
- Decreases in T4/retinoids, and increases oxidative stress in Kestrels



## Polybrominated Diphenyl Ethers (PBDEs): Endocrine Disrupting Effects

- Some PBDEs may be anti-estrogenic, others estrogenic
- Laboratory animal studies have shown decreased weight of epididymis, seminal vesicles and ventral prostate, decreased LH, sperm head deformities
- Decreased testosterone
- *In vitro* studies have shown antiandrogenic, non-competitive inhibition



## Polybrominated Diphenyl Ethers (PBDEs) and Hyperthyroidism

- Effects shown in both cats and humans
- Histologic changes, benign hyperplasia, benign nodular hyperplasia, TNG, TMNG
- No evidence of auto-antibodies, i.e. not Graves' disease
- In cats, age of onset – older than 8 years of age, mean 14 years of age
- Insidious onset
- Cause unknown



## PBDE Developmental and Reproductive Effects

- DE71 – pubertal exposures
- Delay in puberty
- Effects on male organs
- Anti-androgenic *in vitro*, especially BDE 100, 47
- BDE-99 and PBDE-47 – *in utero* exposures
- Delay in puberty
- Ovarian toxicity
- Male organ effects and decreased sperm



## PBDE Developmental Neurotoxicity

- DE-71, in rats, causes deficits in sensory and cognitive function
- Altered sex-dependent behaviors
- Effects on thyroid, cholinergic, and dopaminergic systems
- BDE-99, 209, 47, 153, 203, and 206 in mice and rats
- Infantile exposure during a period of “rapid brain growth” causes learning effects
- Perinatal exposure causes delay in sensory development
- Additive effects observed following co-exposure of BDE-99 and PCB-52, PFOA or MeHg, in mice



## PBDE Developmental Neurotoxicity (continued)

- A number of mechanisms may be at work
- Depression in serum T4
- Anti-cholinergic/anti-dopaminergic
- Alterations in key proteins involved in normal brain maturation
- Detrimental effects on cytoskeletal regulation and neuronal maturation
- Oxidative stress
- PBDEs alter cell signaling in vitro – DE71, BDEs 47, 99, 153
- Altered PKC and calcium homeostasis associated with learning, memory
- Altered phorbol ester binding



## NIEHS and NTP DE71 Studies

- DE71 subchronic studies using F344/N rats and B6C3F1 mice
- Primary toxicity to liver (hepatocytic hypertrophy, fatty change, single cell necrosis)
- Thyroid effects in rats
- DE71 *in utero*/postnatal/adult exposure cancer study in Wistar rats (ongoing)
- DE71 2-year traditional cancer study in B6C3F1 mice (ongoing)
- DE71 administered by oral gavage in corn oil



## Developmental Effects of DBDE

- Developmental Reproductive Toxicity – decrease in sperm function, increase in oxidative stress
- Developmental Immunotoxicity – continuous exposure to high-dose PBDE-209 in female rats during pregnancy and lactation results in possible adverse effect on the immune function of offspring
- Changes in lymphocyte subsets
- Developmental Neurotoxicity – permanent effects on behavior, learning and memory



## PBDE Effects in People

- Cryptorchidism (undescended testicles)
- Reproductive hormone effects – decrease in androgens, increase in FSH and Inhibin
- Increase in testosterone (BDE-47)
- Decrease in sperm quality
- Diabetes
- Thyroid Homeostasis – decrease TSH, decrease TT3, elevated T4, elevated rT3



## Regulation of Brominated Flame Retardants

- TBBPA – not regulated
- HBCD banned in Norway, European Union “SVHC”
- PBDEs – Penta/Octa Commercial Products – voluntarily withdrawn in U.S. at end of 2004, bans in several U.S. states, SNUR in place; Europe banned July 31, 2004, use stopped in many EU countries about ten years ago; targeted for elimination under the Stockholm Convention May 9, 2009.
- Deca Product – US – HPV, banned in Washington State and Maine, proposed bans in many other states; Canada ban upheld March 30, 2009; banned in Sweden January 2007; banned in EU July 2008.



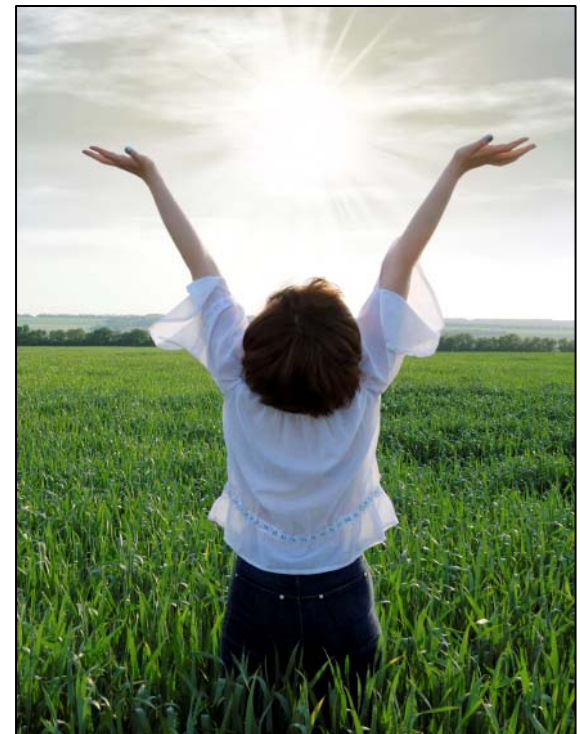
## Considerations for Flame Retardant Alternatives

- Alternative chemicals other than BFRs or other classes of FRs
- Minimize potential for hazard and exposure
- Low persistence and bioaccumulation, for breakdown products as well as parent chemicals
- Low toxicity, less potential for harm when exposure occurs
- Low exposure, less potential for release



## Other Considerations for Flame Retardant Alternatives

- Aesthetic and performance considerations: appearance, durability, fire safety
- Process equipment cost
- Alternative technologies, barriers, surface treatments, graphite-impregnated foams
- The main consideration:  
**Minimize risk to human health and the environment!**



## Recent PBDE Policy Developments

- Europe – Inclusion of Deca in RoHS reinstated, bans use in electronics
- Sweden – Reversed a ban on Deca in textile, furniture, and some cables, but this reversal was challenged by EU
- Norway – Implemented a ban on Deca in textiles, furniture, insulation (non-transportation); also bans manufacture, import, sales
- Canada – Bans Deca manufacture, though import, sale and use are unrestricted



## Recent PBDE Policy Developments (continued)

- **Targeted for elimination under Stockholm Convention, May 9, 2009**
- POPS Treaty review committee: listing for commercial Octa should not include the octa- and nona-congeners
- Recommended listing the hexa- and hepta-BDEs present in commercial Octa, BDEs 153, 154, 175, and 183 as markers for enforcement purposes
- Recommendations for listing of congeners related to commercial Pena and Octa was considered at 4th Conference of Parties, May 2009



## Thank You for Your Attention

- I will be happy to answer questions as the chairperson sees fit.
- I welcome your questions on an informal basis after the session is over.

