Health Effects of Halogenated Fire Retardants

Sarah Janssen, MD, PhD, MPH
Staff Scientist
Natural Resources Defense Council

Brominated Flame retardants

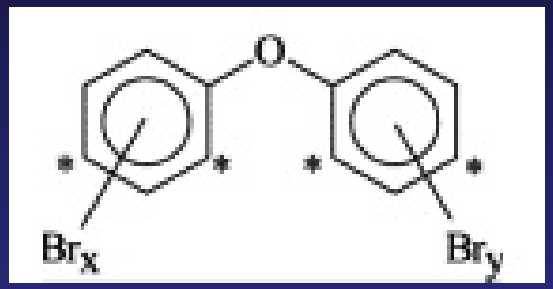
- Polybrominated biphenyls (PBBs)
- Polybrominated diphenyl ethers (**PBDE**s)
- Tetrabromobisphenol A (**TBBPA**)
- Hexabromocyclododecane (**HBCD**)
- 1,2-bis(2,4,6-tribromophenoxy) ethane (TBE)
- bis(2,4,6,-tribromphenoxy) ethane (BTBPE),
  2,4,6-tribromophenol (TBP)
- decabromodiphenyl ethane (DBDPE),
- brominated components in Firemaster 550 (FM 550):
  - 2-ethylhexyl 2,3,4,5-tetrabromobenzoate (TBB)
  - Bis (2-ethylhexyl) tetrabromophthalate (TBPH)
- Brominated Tris (Tris (2,3-dibromopropyl) phosphate)
- 1,2-Dibromo-4-(1,2-dibromoethyl)cyclohexane (TBECH)

Chlorinated Flame Retardants

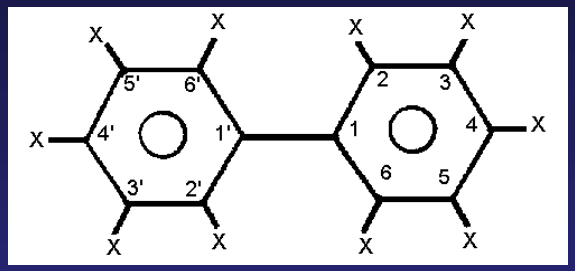
- Tris (1,3-dichloro-2-propyl) phosphate (TDCP)
- Tris(2-chloroisopropyl phosphate) (TCPP)
- Tris(2-chloroethyl) phosphate (TCEP)
- Chloroparaffins
- Bis(hexachlorocylocpentadieno)cycloocta ne (Dechlorane Plus)

- Hexachlorocyclopentadienyl-Dibromocyclooctane (HCDBCO)

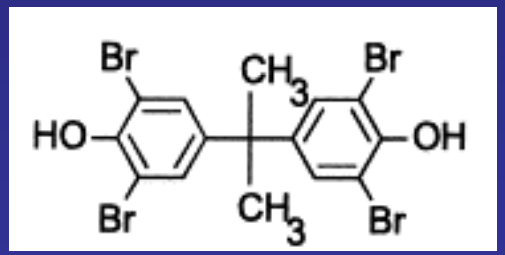
Structural similarities



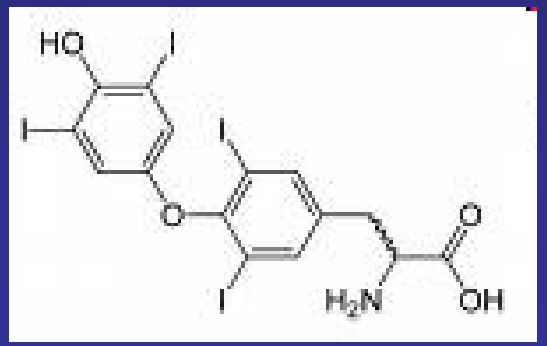
PBDEs



PBB/PCBs

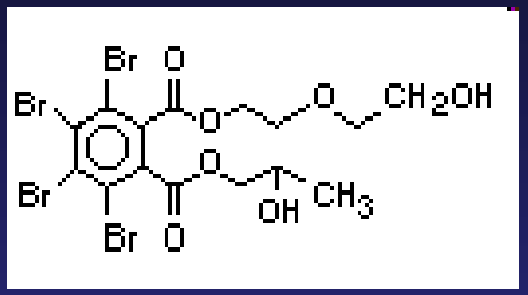


TBBPA

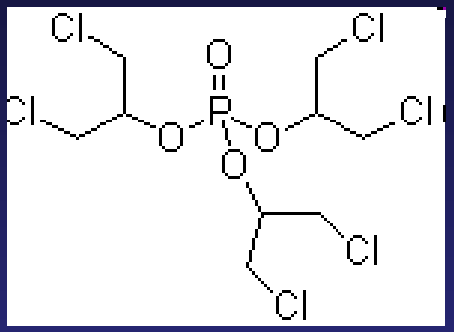


Thyroid hormone

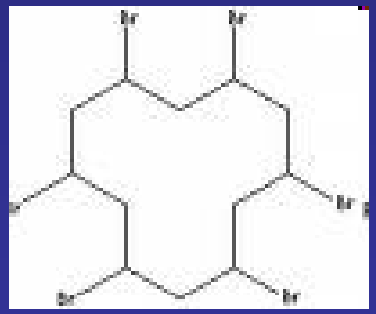
Structural dis-similarities



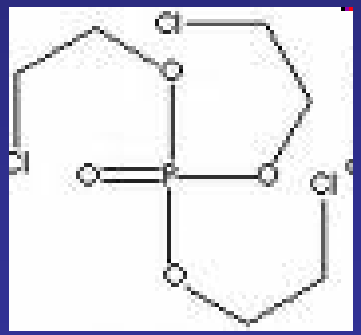
TBPH



TDCPP



HBCD



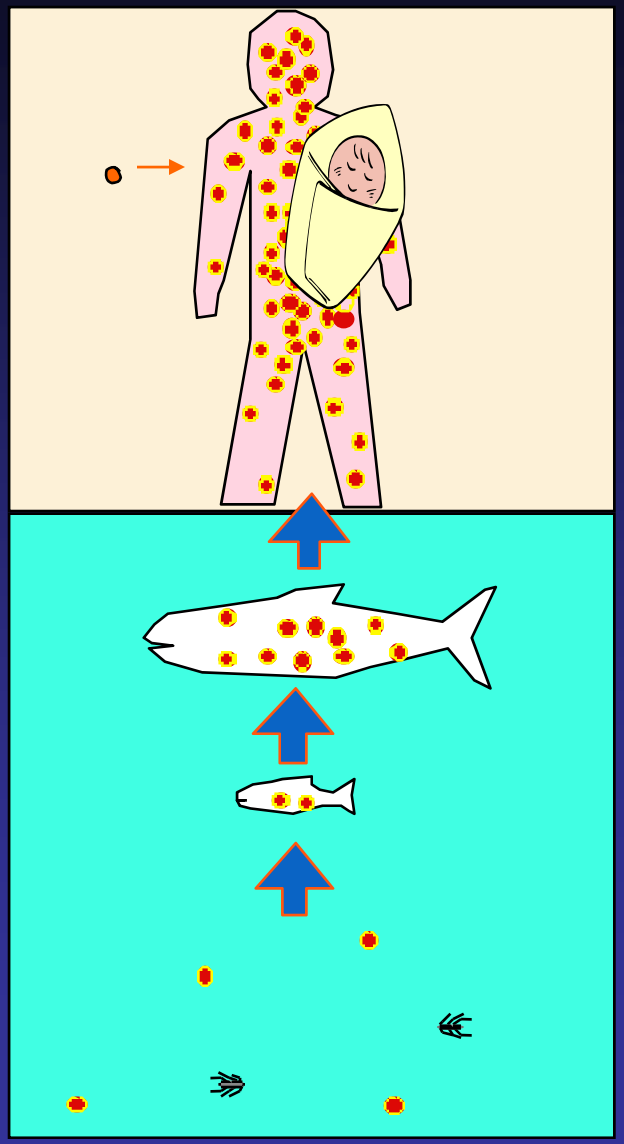
TCEP

Some HFRs are Persistent, Bioaccumulative, Toxicants

PBTs:

- **Persistent** (resist breakdown) in the environment
- **Bioaccumulative** (resist metabolism and accumulate up the food chain)
- **Toxicants -** endocrine disruption**,** neuro-, immuno-, and reproductive toxicity

PBTs and the Food Chain



← Vulnerable periods of development

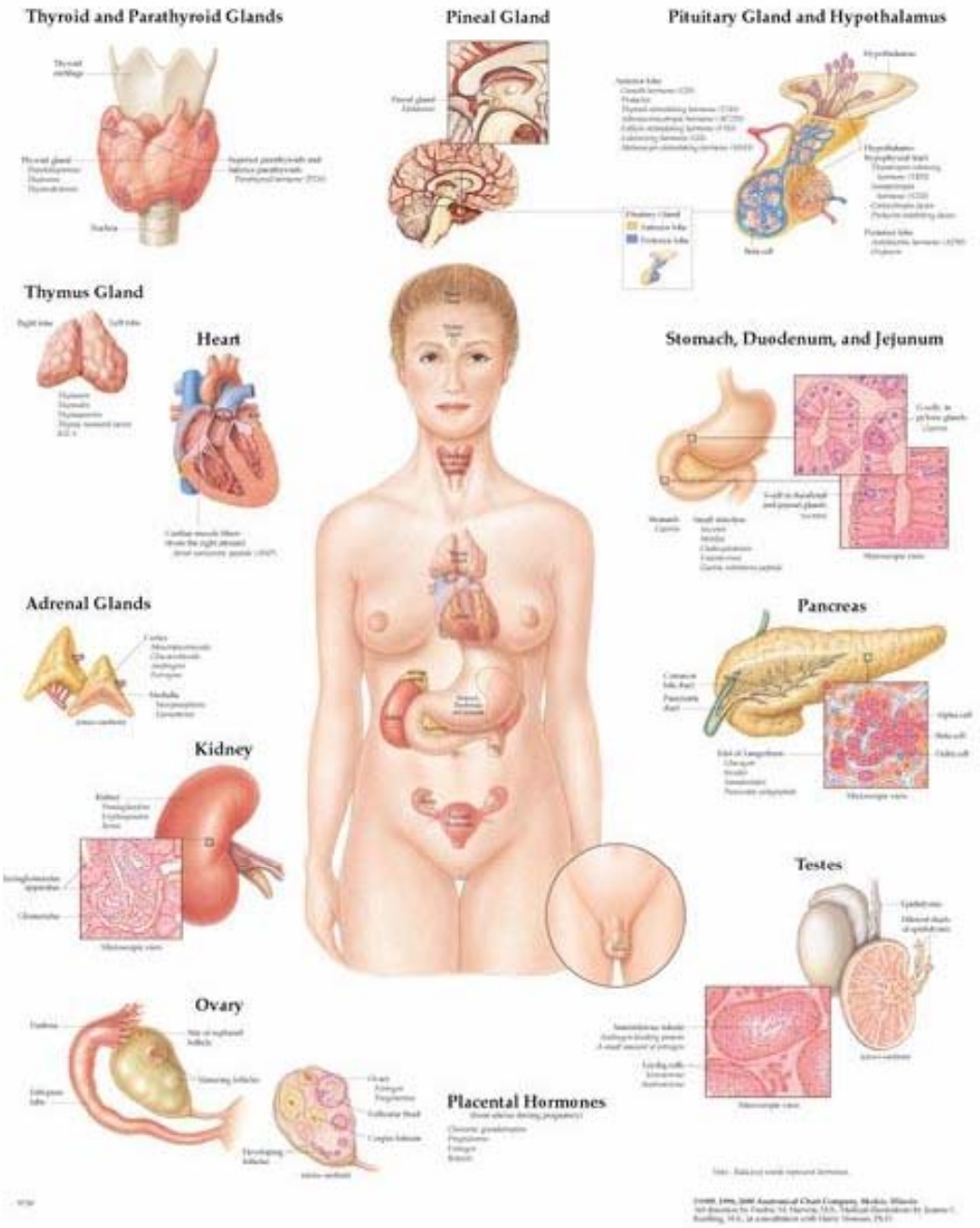
← Bioconcentration

← Persistence

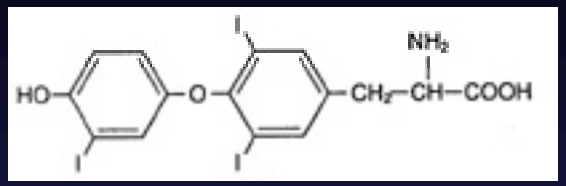
Potential Health Effects of HFRs

- No acute toxicity
- Chronic toxicity
  - Endocrine disruption
    - Neurodevelopment
    - Reproductive system effects
  - Immune suppression
  - Carcinogenicity

THE ENDOCRINE SYSTEM



Endocrine Disruption: Interference with Thyroid Hormone Action

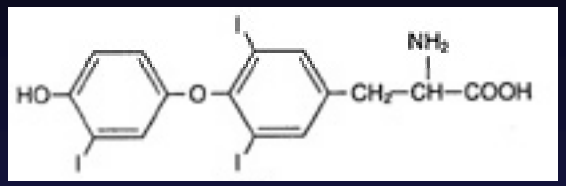


- Interference with thyroid hormone function in fetuses and young children up to age 2-3 can affect brain development.

- Historically, exposures to PCBs, has been associated with
  alterations in thyroid hormone function and lower IQ, lower reading comprehension, and behavioral abnormalities in children

- Exposures to some BFRs has been shown to cause

Endocrine Disruption: Interference with Thyroid Hormone Action - PBDEs

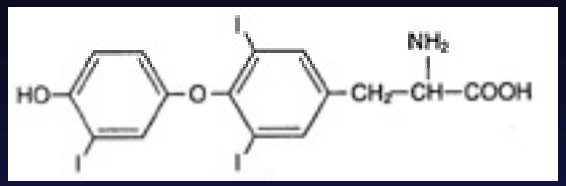


- In fish and rodents, PBDEs have been shown to cause a lowering of thyroid hormone levels.

- In cats, preliminary data - increase in thyroid hormone.

(Darnerud, 2003; van der Ven, 2006, Dye, 2007, Turyk, 2008)

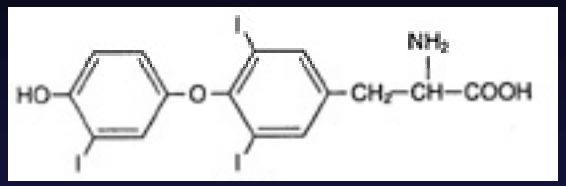
Endocrine Disruption: Interference with Thyroid Hormone Action - PBDEs



- Humans?
  - One study of manufacturing workers exposed to PBDEs and PBBs found an increased incidence of hypothyroidism
  - BDE exposure in sports fisherman was associated with increased thyroglobulin antibodies and increased T(4) in adult males.

(Darnerud, 2003; van der Ven, 2006, Dye, 2007, Turyk, 2008)

Endocrine Disruption: Interference with Thyroid Hormone Action



- Other brominated flame retardants?

  HBCD
  TBBPA
  BTBPE metabolite - 2,4,6-tribromophenol

(Hamers 2006; Suzuki et al., 2008; Van der Ven et al., 2008).).

Neurodevelopmental Outcomes

- Exposure to PBDEs during critical windows of brain development results in decreased memory and learning that worsens with age and is irreversible. (Viberg, 2003)
- Higher brominated BDEs - impairs spontaneous behavior and learning and memory functions of adult mice.
- Co-exposure of PBDEs with another known neurotoxicants – PCBs, MeHg results in an additive effect. (Eriksson, 2006; Fischer, 2008)

Neurodevelopmental Outcomes (cont'd)

- HBCD exposure causes changes in memory and learning in rodent studies and is toxic to cerebellar cells. (Eriksson, 2006)
- Brominated flame retardants (TBBPA, PBDE and HBCD) alter levels of the neurotransmitters, glutamate, dopamine and VP. (Mariussen and Fonnum, 2003).

Reproductive System Effects

- Penta-BDE exposure results in delayed puberty and abnormal gonadal development in rodents.
- Penta-BDE exposure at levels similar to those found in humans was associated with decreased sperm counts in rodents.
- Deca-BDE exposure is associated with abnormal sperm function.
- HBCD exposure resulted in suppression of egg development and decreased fertility.

(Kuriyama, et al. 2005; Lilienthal, et al. 2005; Tseng, et al. 2006; Ema, 2008)

Endocrine Disruption

- PBDEs interfere with expression of estrogen-regulated genes in prostate and brain tissue. (Lichteinsteiger, 2003 and 2004)
- TBBPA estrogenic activity (Kitamura et al., 2005).
- Anti-androgenic effects
  - PBDEs
  - 2, 4, 6 - TBP
  - TBPH ?
    - brominated analogue of phthalate DEHP
- Androgenic effects
  - TBECH

Immune Suppressing Effects

- Suppression of the immune system can lead to an increased rate of infections.

- PBDEs have been shown to cause immune suppression in mice.

- TBBPA also has been shown to inhibit T-cell function - a vital part of the immune response.

Carcinogenicity

- Of all the PBDEs, only Deca has been tested for carcinogenicity.
- **Deca-BDE** has been associated with an increase in liver tumors and thyroid tumors in rodent studies.
- US EPA considers **decaBDE** a possible human carcinogen (http://cfpub.epa.gov/iris/quickview.cfm?substance_nmbr=0035)
- **HBCD** has been associated with liver tumors.

Carcinogenicity cont'd

Prop 65 list of carcinogens recognized by California

- Tris (2,3-dibromopropyl) phosphate (TRIS)
- tris(2-chloroethyl)phosphate (TCEP)
- Chlorinated paraffins.

Because of structural similarities to other chlorinated chemicals – many other chlorinated flame retardants are suspected carcinogens

Potential Human Health Risks

- Increasing body burdens in humans are approaching levels found to cause harm.
- Doses found to cause developmental neurotoxicity and reproductive toxicity are within 10-fold of the levels in human blood and breast milk.

Potential Human Health Risks

- There is little to no toxicity data available for many of the flame retardants being used to replace PBDEs in consumer products
- Concerns that widespread exposure in environment and homes is leading to ubiquitous human exposure
- Health impacts are unknown

Research Gaps

- We need more human data on effects of persistent HFRs in consumer products
- We need more toxicity information – animal and human data on replacement HFRs
- We need more research and information that is readily available to consumers about non-toxic alternatives
- Chemical Policy Reform