

BROMINATED AND CHLORINATED ORGANIC CHEMICAL COMPOUNDS USED AS FLAME RETARDANTS

Materials for the December 4-5, 2008 Meeting of the California Environmental Contaminant Biomonitoring Program (CECBP) Scientific Guidance Panel (SGP)

Agenda Item: "Consideration of Potential Designated Chemicals"

Introduction:

Many brominated and chlorinated compounds have been shown to persist in the environment and have been associated with adverse health effects including cancer, reproductive and developmental toxicity and endocrine disruption. A number of brominated and chlorinated organic chemical compounds are used as flame retardants (BFRs and CFRs). The underlying structures of BFRs and CFRs vary widely and include: straight-chain paraffins, cycloaliphatic hydrocarbons, aromatic hydrocarbons and organophosphate compounds.

Flame retardants can be either reactive or additive. Additive flame retardants are incorporated into a product but are not chemically bound, so that over time they migrate out of the product and into the environment (e.g., house dust, sewage sludge, food chain). In contrast, reactive flame retardants are chemically bound to material in the product. The bound chemicals are not released from products, but residual, unreacted flame retardant present in the product can be released and lead to human exposure.

In California, all upholstered furniture manufactured or sold in the State has to meet flammability standards specified in Technical Bulletin No. 117, promulgated by the Bureau of Home Furnishings and Thermal Insulation. California is the only state that has such a requirement. This regulation has resulted in extensive use of additive chemical flame retardants, particularly BFRs and CFRs, in furniture sold in California for over 25 years. To avoid the expense of having a separate product line for California and to voluntarily comply with the most stringent flammability requirements in the U.S., many large manufacturers and distributors of furniture or furniture components have had flame retardants added to their products sold in other states as well.

Prior to 2006, polybrominated diphenyl ethers (PBDEs) were the primary additive flame retardants in furniture foam. These additive BFRs migrated from furniture into indoor and outdoor environments. Some of the highest PBDE concentrations in the world have been found in California homes and residents. Effective 2006, California became the first state in the nation to ban two PBDE mixtures, pentaBDEs and octaBDEs, because of concerns about the buildup of PBDEs in the bodies of Californians and their possible health effects. Commercial decaBDE which contains approximately three percent of nonaBDE, is banned in the European Union (EU) and in Washington and Maine.

Many of the BFRs and CFRs included in this document are marketed as substitutes for the banned PBDEs. Some of these substitute chemicals have already been found in house dust, indicating that they are being released from products. These chemicals persist in the

Brominated and Chlorinated Flame Retardants

environment and many have been found to be bioaccumulative. In addition to the PBDE replacements, other BFRs and CFRs that are used as flame retardants in a wide of variety of products.

This document provides a brief overview of the following BFRs and CFRs (listed in alphabetical order):

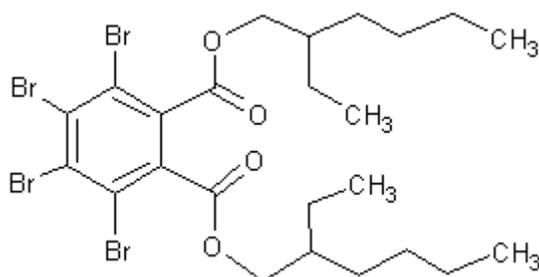
- Bis(2-ethylhexyl) tetrabromophthalate
- Bis(hexachlorocyclopentadieno)cyclooctane
- 1,2-Bis(2,4,6-tribromophenoxy)ethane
- Decabromodiphenylethane
- 1,2-Dibromo-4-(1,2-dibromoethyl)cyclohexane
- 2-Ethylhexyl-2,3,4,5-tetrabromobenzoate
- Hexabromocyclododecane
- Hexachlorocyclopentadienyl-dibromocyclooctane
- Pentabromoethylbenzene
- Short-chain chlorinated paraffins
- Tetrabromobisphenol A
- Tris(1,3-dichloro-2-propyl)phosphate
- Tris(2-chloroethyl)phosphate

A list of some other BFRs and CFRs is given at the end of the document.

Need to assess efficacy of public health actions:

The State of California banned two commercial mixtures of PBDEs, effective in 2006, because of concerns about high exposures in California and the potential human health effects of such exposures. Biomonitoring flame retardants will help the State to assess whether the new “alternatives” or other flame retardants are also accumulating in California residents and presenting a threat to public health.

Bis(2-ethylhexyl) tetrabromophthalate (TBPH) [CAS No. 26040-51-7]



Exposure or potential exposure to the public or specific subgroups:

TBPH is an additive flame retardant and one of two brominated chemicals in Firemaster 550, the primary replacement for pentaBDEs in polyurethane foam. In addition to its uses as a flame retardant, TBPH is also marketed as a plasticizer for flexible polyvinylchloride and for use in wire and cable insulation, film and sheeting, carpet backing, coated fabrics, wall coverings and adhesives. Annual U.S. production/imports were 1-10 million pounds for the reporting years 1990, 1994, 1998 and 2002 (U.S. EPA, 2002). TBPH has recently been identified in house dust at levels ranging from 1.5 – 10,630 nanograms/gram (ng/g), with a median value of 142 ng/g (Stapleton et al., 2008). It was recently detected in sewage sludge from wastewater treatment plants that discharge effluent into the San Francisco Bay (Betts, 2008).

Known or suspected health effects:

TBPH has not been adequately studied for potential human health effects. Health effects are suspected because TBPH is a brominated analogue of di(ethylhexyl)phthalate (DEHP), which is listed under Proposition 65 as known to cause cancer and reproductive and developmental toxicity.

Potential to biomonitor:

Physical and chemical properties¹:

Vapor pressure: 1.71×10^{-11} mg Hg at 25°C

Water solubility: 1.98×10^{-11} mg/L (estimated, from LogK_{ow})

Octanol/water partition coefficient: LogK_{ow} = 11.95 (estimated)

Bioaccumulation: Bioconcentration factor (BCF) 3.2 (predicted, PBT Profiler).

Persistence: Not readily biodegradable, based on 28-day closed bottle test;

Half-life in soil 120 d; in sediment 540 d (predicted, PBT Profiler)

Past biomonitoring studies: None identified.

Availability of analytical methods: GC-MS methods are being developed. A labeled standard is available from Wellington Isotope Laboratories. New methods would be required to analyze metabolites.

¹ Data for this section have been taken from various sources. See references for individual flame retardants.

Brominated and Chlorinated Flame Retardants

Availability of adequate biospecimens: Serum or breast milk. Urine may be suitable for metabolite analysis.

Incremental analytical cost: Analysis for the parent compound may be bundled with PBDEs or other BFRs.

References:

Betts K (2008). New flame retardants detected in indoor and outdoor environments. *Environ Sci Technol* 42(18):677808.

High Production Volume (HPV) Challenge Program (2004). Test Plan for Phthalic acid Tetrabromo Bis-2(ethylhexyl) ester. Prepared by Health & Environment Horizons, Ltd. For Brominated Phthalate Ester Panel. July 1, 2004. Available at: <http://www.epa.gov/HPV/pubs/summaries/phthacid/c15484tp.pdf>

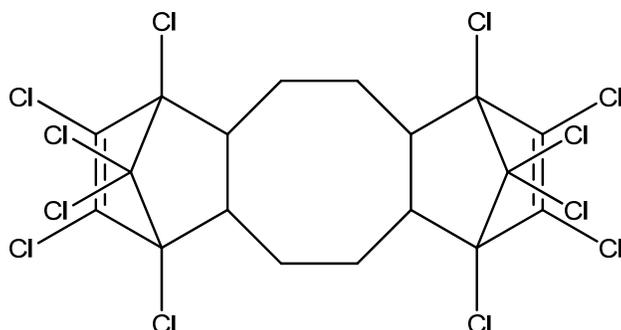
Muir D and Howard P (2007). Developing analytical methodology for PB&T substances – a systematic process for identification of important chemicals. Report to U.S. EPA Great Lakes National Program Office, Chicago IL. September 11, 2007. Environment Canada. Unpublished Report.

PBT Profiler. Developed by Environmental Science Center for the Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency. Available at: <http://www.pbtprofiler.net/>

Stapleton et al. (2008). Alternate and new brominated flame retardants detected in U.S. house dust. *Environ Sci Technol* 42(18):6910-6.

U.S. Environmental Protection Agency (U.S. EPA, 2002). Non-Confidential Inventory Update Reporting Production Volume Information. Toxic Substances Control Act (TSCA) Inventory. Available at: <http://www.epa.gov/oppt/iur/tools/data/2002-vol.htm>

**Bis(hexachlorocyclopentadieno)cyclooctane [CAS No. 13560-89-9]
Dechlorane Plus (DP)**



Exposure or potential exposure to the public or specific subgroups:

Dechlorane Plus (DP) is an additive chlorinated flame retardant. DP was introduced in the 1960s as a substitute for Dechlorane (Mirex) which was banned because of toxicity to marine invertebrates. Uses include electrical wires and cables, connectors for computers and plastic roofing material. The sole U.S. producer of DP is located in Niagara Falls, New York. DP has been detected in at least three of the Great Lakes. Studies of DP in sediment cores suggest that there was a relatively large input of the chemical into the Great Lakes, starting around 1970 and peaking 5-10 years later. Concentrations in the surface sediment suggest that the input of DP is now about half of what it was at its peak. U.S. production/import volume was reported as 1-10 million pounds for 1986 and each year since then (U.S. EPA, 2002). The extent to which DP may be used as a substitute for banned or phased out PBDEs is unknown. DP has recently been found in air, fish and sediment samples in the Great Lakes Region (Hoh et al., 2006) and in Herring Gull eggs (Gauthier et al., 2007). DP has also been detected in tree bark in the northeastern United States, with higher levels near the U.S. manufacturing source in Niagara Falls, New York. DP has also been detected at relatively high concentrations in bark samples from Korea and China, suggesting manufacturing in Asia (Qiu et al., 2008). DP has been found in house dust in Ottawa, Canada (Zhu et al., 2007).

Known or suspected health effects:

Although DP has been in use for over 40 years, toxicological data could not be located. DP shares a structural feature, the chlorinated norbornene moiety, with a number of chemicals listed under Proposition 65. The chemicals (and their Proposition 65 designation) are as follows: the flame retardant chlorendic acid (cancer) and organochlorine pesticides dieldrin (cancer), chlordane (cancer), heptachlor (cancer and developmental toxicity), and endrin (developmental toxicity). The organochlorine pesticide endosulfan also has this structural feature. DP has a larger molecular size than the above chemicals which may hinder its bioavailability.

Potential to biomonitor:

Physical and chemical properties

Vapor pressure: 7.1×10^{-10} mm Hg at 25°C (predicted)

Water solubility: 4.4×10^{-8} mg/L

Octanol/water partition coefficient: Log K_{ow} 11.6 (predicted)

Brominated and Chlorinated Flame Retardants

Bioaccumulation: BCF 3.2 (predicted, PBT Profiler)

Persistence: Half-life in soil 360 d; in sediment 1600 d (predicted, PBT Profiler)

Stereoisomers: Syn- and anti-isomers of DP appear to bioaccumulate differently.

Past biomonitoring studies: None identified.

Availability of analytical methods: GC-MS methods are available. Unlabelled standards are available from Cambridge Isotope Laboratories.

Availability of adequate biospecimens: Serum or breast milk.

Incremental analytical cost: Analysis can be bundled with current PBDE or POP methods. Costs for separation of stereoisomers will be greater.

References:

Betts K (2008). New data on widely used flame retardant. *Environ Sci Technol* 42:5-6.

Gauthier et al. (2007). Current-use flame retardants in the eggs of herring gulls (*Larus argentatus*) from the Laurentian Great Lakes. *Environ Sci Technol* 41:4561-4567.

Hoh et al. (2006). Dechlorane Plus, a chlorinated flame retardant, in the Great Lakes. *Environ Sci Technol* 40:1184-1189.

HSDB (Hazardous Substances Data Bank). Available at <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB>

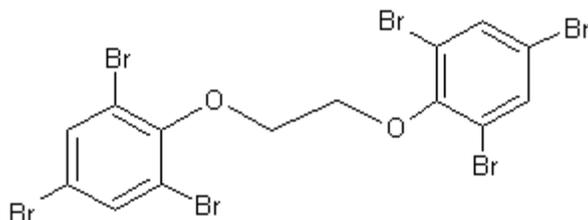
Qiu et al. (2008). Dechlorane Plus: a review with new data. *Organohalogen Compounds* 70:216-219.

U.S. Environmental Protection Agency (U.S. EPA, 2002). Non-Confidential Inventory Update Reporting Production Volume Information. Toxic Substances Control Act (TSCA) Inventory. Available at: <http://www.epa.gov/oppt/iur/tools/data/2002-vol.htm>

Zhu et al. (2007). Detection of dechlorane plus in residential indoor dust in the city of Ottawa, Canada. *Environ Sci Technol* 41:7694-8.

Zhu et al. (2008). Identification and determination of hexachlorocyclopentadienyl-dibromocyclooctane (HCDBCO) in residential indoor air and dust: a previously unreported halogenated flame retardant in the environment. *Environ Sci Technol* 42:386-91.

1,2-Bis(2,4,6-tribromophenoxy)ethane (BTBPE) [CAS No. 37853-59-1]



Exposure or potential exposure to the public or specific subgroups:

BTBPE is an additive flame retardant in thermoplastic and thermosetting plastics systems and may be used as a replacement for octaBDE mixtures. Annual U.S. production/imports were 10-50 million pounds for the reporting years 1986, 1990 and 1994, but decreased to 1-10 million pounds in 1998 and 2002 (U.S. EPA, 2002). Information on current use and production volume, which might indicate increasing use as a PBDE replacement, is unavailable. Recent studies report detection of BTBPE in ambient air samples collected from several sites around the U.S. and also in sediment samples from Lake Michigan (Hoh et al., 2005). BTBPE has been detected in Northern Fulmar eggs from the Faroe Islands (Karlsson et al., 2006), in Herring Gull eggs in the Great Lakes basin (Gauthier et al., 2007), in Glaucous Gull eggs from the Norwegian Arctic (Verreault et al., 2007) and in the Lake Winnipeg (Canada) food web. BTBPE has been recently found in house dust from the United States, with levels ranging from 1.6 to 789 ng/g (Stapleton et al., 2008).

Known or suspected health effects:

BTBPE is structurally similar to DBDPE and decaBDE (see discussion of toxicity for DBDPE). One identified metabolite of BTBPE is the flame retardant 2,4,6-tribromophenol. Research findings indicate that 2,4,6-tribromophenol is a thyroid hormone disrupting chemical (Hamers et al., 2006; Suzuki et al., 2008). A Japanese study found 2,4,6-tribromophenol in umbilical cord and umbilical cord blood samples (Kawashiro et al., 2008).

Potential to biomonitor:

Physical and chemical properties:

Vapor pressure: 2.3×10^{-1} mm Hg (estimated)

Water solubility: 0.2 mg/L

Octanol/water partition coefficient: LogK_{ow} 9.15 (estimated)

Bioaccumulation: BCF 8.7-27.1 (measured in *Cyprinus carpio* in the Great Lakes)

Persistence: Half-life in soil 360 d; in sediment, 1600 d (predicted, PBT Profiler)

Pharmacokinetics and metabolism: Dietary studies in animals suggest minimal gastrointestinal absorption. One study found that after dietary administration, the great majority of BTBPE was excreted unchanged in the feces. However, metabolites have been identified and characterized (Hakk et al., 2004). Metabolites include 2,4,6-tribromophenol and hydroxylated-BTBPE products, suggesting cytochrome P-450 mediated biotransformation. Although inhalation may be the predominant route of human exposure, no studies of inhalation exposure were found.

Past biomonitoring studies: None identified.

Brominated and Chlorinated Flame Retardants

Availability of analytical methods: GC-MS methods for environmental analysis exist. Isotope labeled standards are available from Cambridge Isotope Laboratories ($^{13}\text{C}_{12}$).

Availability of adequate biospecimens: Breast milk and serum samples for parent compound; serum or urine for metabolites.

Incremental analytical cost: Analysis of the parent compound may be bundled with other BFRs using current PBDE or POPs methods; costs for metabolite analysis may be greater.

References:

Gauthier et al. (2007). Current-use flame retardants in the eggs of herring gulls (*Larus argentatus*) from the Laurentian Great Lakes. *Environ Sci Technol* 41:4561-4567.

Hakk et al. (2004). Metabolism, tissue disposition and excretion of 1,2-bis(2,4,6-tribromophenoxy)ethane (BTBPE) in male Sprague-Dawley rats. *Chemosphere* 54: 1367-1374.

Hakk H and Letcher RJ (2003). Metabolism in the toxicokinetics and fate of brominated flame retardants – a review. *Environ Intl* 29:801-828.

Hamers et al. (2006). *In vitro* profiling of the endocrine-disrupting potency of brominated flame retardants *Toxicol Sci* 92:157-173.

Hoh E et al. (2005). Novel flame retardants, 1,2-bis(2,4,6-tribromophenoxy)-ethane and 2,3,4,5,6-pentabromoethylbenzene, in the United States' Environmental Samples. *Environ Sci Technol* 39:2472-2477.

Kawashiro et al. (2008). Perinatal exposure to brominated flame retardants and polychlorinated biphenyls in Japan. *Endocr J* August 22, 2008. [Epub ahead of print].

Karlsson et al. (2006). Levels of brominated flame retardants in Northern Fulmar (*Fulmaris glacialis*) eggs from the Faroe Islands. *Sci Total Environ* 367:840-846.

Lyubimov et al. (1998). Developmental neurotoxicity and immunotoxicity in Wistar rats. *Neurotoxicology* 19:303-12.

Law et al. (2006). Bioaccumulation and trophic transfer of some brominated flame retardants in a Lake Winnipeg (Canada) food web. *Environ Toxicol Chem* 25:2177-2186.

Muir D and Howard P (2007). Developing analytical methodology for PB&T substances – a systematic process for identification of important chemicals. Report to U.S. EPA Great Lakes National Program Office, Chicago IL. September 11, 2007. Environment Canada. Unpublished Report.

PBT Profiler. Developed by Environmental Science Center for the Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency. Available at: <http://www.pbtprofiler.net/>

Stapleton et al. (2008). Alternate and new brominated flame retardants detected in U.S. house dust, *Environ Sci Technol* 42(18):6910-6.

Suzuki et al. (2008). Identification of brominated and chlorinated phenols as potential thyroid-disrupting compounds in indoor dusts. *Environ Sci Technol* 42:1974-1800.

Brominated and Chlorinated Flame Retardants

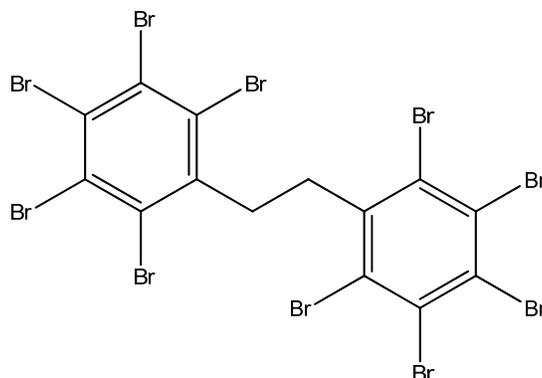
Syracuse Research Corporation (SRC). PhysProp Database. Available at:
<http://www.syrres.com/esc/physdemo.htm>

Tomy et al. (2007). Dietary exposure of juvenile rainbow trout (*Oncorhynchus mykiss*) to 1,2-bis(2,4,6-tribromophenoxy)ethane: Bioaccumulation parameters, biochemical effects and metabolism. *Environ Sci Technol* 41:4913-4918.

U.S. Environmental Protection Agency (U.S. EPA, 2002). Non-Confidential Inventory Update Reporting Production Volume Information. Toxic Substances Control Act (TSCA) Inventory. Available at:
<http://www.epa.gov/oppt/iur/tools/data/2002-vol.htm>

Verreault et al. (2007). Brominated flame retardants in glaucous gulls from the Norwegian Arctic: More than just an issue of polybrominated diphenyl ethers. *Environ Sci Technol* 41:4925-2931.

Decabromodiphenylethane (DBDPE) [CAS No. 84852-53-9]



Exposure or potential exposure to the public or specific subgroups:

DBDPE is an additive flame retardant that has similar applications to those of decaBDE (e.g., in both acrylonitrile-butadiene-styrene (ABS) and high impact polystyrene (HIPS) plastics as well as textile backcoating) and has been marketed as general purpose substitute for decaBDE. Information on trends in use and production volume, which might suggest the use of DBDPE as a PBDE replacement, is unavailable. DBDPE was recently detected in fish in Lake Winnipeg, Canada (Law et al., 2006) and found in house dust from the United States, with levels ranging from <10 ng/g to 11,070 ng/g (Stapleton et al., 2008).

Known or suspected health effects:

DBDPE is structurally similar to decaBDE, the PBDE mixture still in commercial use in California. Research findings indicate that, like exposures to the other PBDE mixtures, decaBDE exposures to neonatal animals cause changes in learning and behavior in adult animals (Viberg et al., 2003). Viberg et al. (2007) found that neonatal exposure to decaBDE resulted in an altered response to nicotine, indicating a change in the brain cholinergic system.

Potential to biomonitor:

Physical and chemical properties:

Vapor pressure: $\sim 1 \times 10^{-6}$ Pa at 25 °C (assumed, Dungey and Akintoye, 2007)

Water solubility: ~ 0.72 $\mu\text{g/L}$ at 25 °C (measured, Dungey and Akintoye, 2007)

Octanol/water partition coefficient: $\text{LogK}_{\text{ow}} = 3.55$ (measured, but considered an estimate due to analytical uncertainties); other estimates: 7-10 (Dungey and Akintoye, 2007).

Bioaccumulation: BCF 3.2 (predicted, PBT Profiler).

Persistence: Half-life in soil 360 d; 1600 d in sediment (predicted, PBT Profiler)

Past biomonitoring studies: None identified

Availability of analytical methods: GC-MS methods exist for environmental analysis of DBDPE; a standard is available from Wellington Isotope Laboratories. Analytical challenges similar to those with decaBDE exist, due to the number of bromine atoms in the molecule.

Brominated and Chlorinated Flame Retardants

Availability of adequate biospecimens: Plasma or serum. Human levels of DBDPE will likely be low due to its high molecular weight (similar to decaBDE). Required sample volume may be 2-5 mL.

Incremental analytical cost: Analysis can be bundled with PBDEs or other BFRs.

References:

Dungey S and Akintoye L. (2007). Environmental risk evaluation report: 1,1'-(Ethane-1,2-diyl)bis[penta-bromobenzene] CAS: 84852-53-9. Product Code: SCHO0507BMOR-E-P. Environment Agency for England and Wales. Available at: www.environment-agency.gov.uk

Law et al. (2006) Bioaccumulation and trophic transfer of some brominated flame retardants in a Lake Winnipeg (Canada) food web *Environ Toxicol Chem* 25:2177-2186.

Pakalan et al. (2007). Review on production processes of decabromodiphenyl ether (decaBDE) used in polymeric applications in electrical and electronic equipment, and assessment of the availability of potential alternatives to decaBDE. European Chemicals Bureau. European Commission. January 2007. Available at: http://ecb.jrc.it/documents/Existing-Chemicals/Review_on_production_process_of_decaBDE.pdf

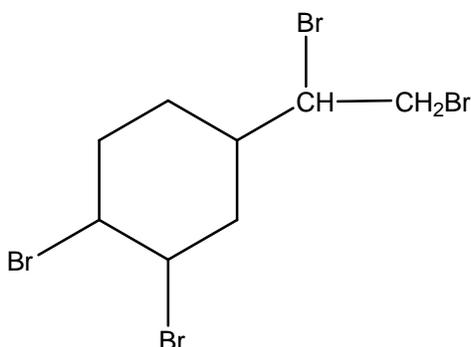
PBT Profiler. Developed by Environmental Science Center for the Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency. Available at: <http://www.pbtprofiler.net/>

Stapleton et al. (2008). Alternate and new brominated flame retardants detected in U.S. house dust, *Environ Sci Technol* 42(18):6910-6.

Viberg et al. (2007). Changes in spontaneous behaviour and altered response to nicotine in the adult rat, after neonatal exposure to the brominated flame retardant, decabrominated diphenyl ether (PBDE 209). *Neurotoxicolog.* 28:136-42.

Viberg et al. (2003). Neurobehavioral derangements in adult mice receiving decabrominated diphenyl ether (PBDE 209) during a defined period of neonatal brain development. *Toxicol Sci* 76:112-120.

**1,2-Dibromo-4-(1,2-dibromoethyl)cyclohexane [CAS No. 3322-93-8]
Tetrabromoethylcyclohexane [TBECH]**



Exposure or potential exposure to the public or specific subgroups:

TBECH is an additive flame retardant used primarily in expandable polystyrene beads (used for thermal insulation in housing). It is also used as a flame retardant for extruded polystyrene foam and for adhesives in fabric and vinyl lamination, electrical cable coatings, high-impact plastic parts of appliances and some construction materials (U.S. EPA, 1984). Annual U.S. production/imports were 10,000-500,000 pounds for the reporting years 1986, 1990, 1994, 1998 and 2002 (U.S. EPA, 2002). TBECH was recently identified in blubber of Beluga whales from the Canadian Arctic (Tomy et al., 2008).

Known or suspected health effects:

Findings from a recent *in vitro* study suggest that TBECH is a strong androgen agonist (Larsson et al., 2006). TBECH was shown to bind to and activate the human androgen receptor in human liver cells. Further, co-exposure to the androgen dihydrotestosterone and TBECH resulted in additive androgen activity. TBECH was found to be mutagenic in an *in vitro* study in mammalian cells (McGregor et al., 1991).

Potential to biomonitor:

Physical and chemical properties:

Vapor pressure: 1.05×10^{-4} mm Hg (estimated, SRC, 2000)

Water solubility: 0.0692 mg/L (estimated, SRC, 2000)

Octanol/water partition coefficient: $\log K_{ow} = 5.24$ (estimated, SRC, 2000)

Bioaccumulation: BCF 2000 (predicted, FR, 1984)

Persistence: Half life in soil: 75 days (predicted PBT profiler).

Stereoisomers: The technical mixture of TBECH consists primarily of a 1:1 mixture of α -TBECH and β -TBECH, two of four diastereomers. The other two diastereomers, γ -TBECH and δ -TBECH, can be formed by interconversion at high temperatures. Although not present in the technical mixture, they may be relevant environmental contaminants because of the high temperatures used in manufacturing processes.

Past biomonitoring studies: None identified.

Availability of analytical methods: GC-MS methods have been developed.

Brominated and Chlorinated Flame Retardants

Availability of adequate biospecimens: Serum or breast milk.

Incremental analytical cost: Analysis can be bundled with PBDEs or other BFRs.

References:

Arsenault et al. (2008). Structure characterization and thermal stabilities of the isomers of the brominated flame retardant 1,2-dibromo-4-(1,2-dibromoethyl)cyclohexane. *Chemosphere* 72:1163-117-

Larsson et al. (2006). Identification of the brominated flame retardant 1,2-dibromo-4-(1,2-dibromoethyl)cyclohexane as an androgen agonist. *J Med Chem* 49:7366-7372.

McGregor et al. (1991). Responses to the L5178Y Mouse Lymphoma Forward Mutation Assay. V: 27 coded Chemicals. *Environ Mol Mutagen* 17:196-219.

PBT Profiler. Developed by Environmental Science Center for the Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency. Available at: <http://www.pbtprofiler.net/>

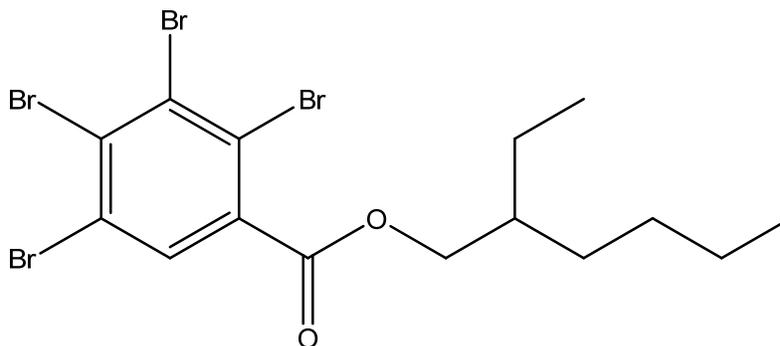
Syracuse Research Corporation (SRC). PhysProp Database. Available at: <http://esc.syrres.com/interkow/physdemo.htm>.

Tomy et al. (2008) Identification of the novel cycloaliphatic brominated flame retardant 1,2-dibromo-4-(1,2-dibromoethyl)cyclohexane in Canadian Arctic Beluga (*Delphinapterus leucas*). *Environ Sci Technol* 42:543-549.

U.S. EPA (1984). Fourteenth Report of the Interagency Testing Committee to the Administrator; receipt of report and request for comments regarding priority list of chemicals. *Federal Register* 49:22389-22401. May 29, 1984.

U.S. Environmental Protection Agency (U.S. EPA, 2002). Non-Confidential Inventory Update Reporting Production Volume Information. Toxic Substances Control Act (TSCA) Inventory. Available at: <http://www.epa.gov/oppt/iur/tools/data/2002-vol.htm>

2-Ethylhexyl-2,3,4,5-tetrabromobenzoate (TBB) [CAS No. 183658-27-7]



Exposure or potential exposure to the public or specific subgroups:

TBB is an additive flame retardant. It is the major brominated component in the flame retardant mixture Firemaster 550 (FM550), the primary replacement for pentaBDEs in polyurethane foam. The other brominated chemical in Firemaster 550 is bis(2-ethylhexyl) tetrabromophthalate (TBPH). The approximate ratio of TBB/TBPH in FM550 is 4:1. TBB has recently been identified in house dust at levels ranging from <6/6 – 15,030 ng/g (Stapleton et al., 2008). TBB was recently detected in sewage sludge from wastewater treatment plants that discharge effluent into the San Francisco Bay (Betts, 2008).

Known or suspected health effects:

Toxicological data on TBB could not be located. However, TBB is structurally similar to TBPH, lacking only the second ester group. Health effects are suspected for TBPH, a brominated analogue of di(ethylhexyl)phthalate (DEHP) which is listed under Proposition 65 as known to cause cancer and reproductive and developmental toxicity.

Potential to biomonitor:

Physical and chemical properties:

Vapor pressure: Not identified.

Water solubility: 1.144×10^{-5} mg/L at 25°C (predicted, U.S. EPA, 2008)

Octanol/water partition coefficient: $\text{Log}K_{ow} = 8.75$ (predicted, U.S. EPA, 2008)

Bioaccumulation: BCF 260 (predicted, PBT Profiler)

Persistence: Half-life in soil 120 d; in sediment 540 d (predicted, PBT Profiler)

Past biomonitoring studies: None identified.

Availability of analytical methods: GC-MS methods have been developed. New methods will be required to analyze metabolites.

Biospecimen availability: Serum or breast milk. Urine may be suitable for metabolite analysis.

Incremental analytical cost: Analysis of the parent compound can be bundled with PBDEs or other BFRs.

Brominated and Chlorinated Flame Retardants

References:

Betts K (2008). New flame retardants detected in indoor and outdoor environments. *Environ Sci Technol* 42(18):6778.

Stapleton et al. (2008). Alternate and new brominated flame retardants detected in U.S. house dust. *Environ Sci Technol* 42(18):6910-6.

PBT Profiler. Developed by Environmental Science Center for the Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency. Available at: <http://www.pbtprofiler.net/>

US EPA (2008). Estimation Programs Interface Suite™ for Microsoft® Windows, v 3.20. United States Environmental Protection Agency, Washington, DC, USA. Available at: <http://www.epa.gov/oppt/exposure/pubs/episuite.htm>

Hexabromocyclododecane (HBCD)

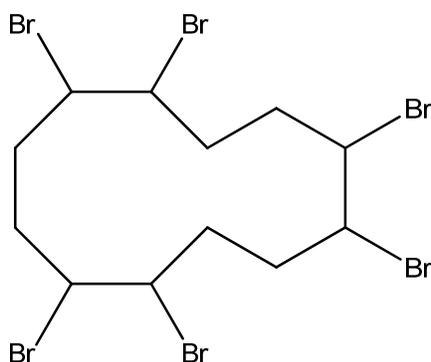
α -HBCD CAS No. 34237-50-6

β -HBCD CAS No. 34237-51-7

γ -HBCD CAS No. 134237-52-8

Mixed isomers (α -, β -, γ -) CAS No. 3194-55-6

Stereochemistry unspecified CAS No. 25637-99-4



Exposure or potential exposure to the public or specific subgroups:

HBCD is an additive flame retardant used in polystyrene insulation boards, in building constructions (e.g., house walls, indoor ceilings); in HIPS plastic for electrical and electronic parts (e.g., housings for VCRs, video cassette housings); as a textile coating agent (e.g., upholstery fabric, bed mattress ticking, upholstery seating in transportation, draperies and wall coverings). Annual U.S. production/import volume was 10-50 million pounds for the reporting years 1994, 1998 and 2002 (U.S. EPA, 2002). Although use in North America has been historically much less than that in Europe, HBCD may be used increasingly as a substitute for PBDEs. Long-range atmospheric transport and biomagnification in top predators, including marine mammals and birds of prey have been documented. Analysis of HBCD in tissues of harbor porpoises from the United Kingdom from 1994-2003 indicated a sharp increase in HBCD concentrations from about 2001 onward (Law et al., 2006). In California, levels of HBCD in sea lions increased from 0.7 to 12 ng/g wet weight between 1993 and 2003 (Stapleton et al., 2006). HBCD has been recently found in house dust from the United States, Canada and the United Kingdom (Abdallah et al., 2008). In a recent study in the U.S., HBCD levels in house dust ranged from <4.5 ng/g and 130,200 ng/g (Stapleton et al., 2008).

γ -HBCD is the predominant stereoisomer in commercial HBCD mixtures (75-89%); however, rearrangement of the configuration of HBCDs can occur at the high temperatures required to incorporate HBCD into products such as extruded polystyrene. α -HBCD has been found to be the predominant stereoisomer in marine fish, birds, mammals and humans in most studies. Levels of α -HBCD in indoor dust average 32% of total HBCDs (range, 14-67%).

Known or suspected health effects:

Developmental and reproductive toxicity studies have found decreased fertility (Ema et al., 2008) and after neonatal exposure to HBCD, significant changes in spontaneous behavior, learning and memory (Eriksson et al., 2006). Other effects include interference with thyroid

Brominated and Chlorinated Flame Retardants

hormone homeostasis, cytochrome P450 induction (van der Ven et al., 2006) and inhibition of neurotransmitter uptake (Mariussen and Fonnum, 2003).

Potential to biomonitor:

Physical and chemical properties:

Vapor pressure: 4.7×10^{-7} mm Hg at 21°C

Water solubility (µg/L): α -HBCD 48.8±1.9, β -HBCD 14.7±0.5, γ -HBCD 2.1±0.2.

Octanol/water partition coefficient: $\text{LogK}_{ow} = 5.625$ technical mixture; individual stereoisomers:
 α -HBCD 5.07 ± 0.09 , β -HBCD 5.12 ± 0.09 , γ -HBCD 5.47 ± 0.10

Bioaccumulation: BCF > 6000

Persistence: Half-life in aerobic soil is > 120 d.

Past biomonitoring studies:

Antignac et al. (2008) studied 26 mother-infant pairs in France and found α -HBCD in 50% of samples of maternal adipose tissue (levels ranging from 1 – 12 ng/g lw). α -HBCD was found in 7 of 26 breast milk samples (levels ranging from 2.5 – 5 ng/g lw). HBCD was not found in maternal or infant serum samples, which the authors attributed to both a very restricted sample amount and the LC-MS/MS equipment used. Weiss et al. (2004) found HBCD in both maternal and cord blood in the Netherlands. HBCD in maternal blood was measured during weeks 20 and 35 of pregnancy (n=78) and averaged 1.1 ng/g lw with a range of <0.16-7.0 ng/g lw. The mean in cord blood (n=12) was 1.7 ng/g lw with a range of <0.16-4.2 ng/g lw. Guerra et al. (2008) found HBCD in 13 of 15 breast milk samples with levels ranging from 7.9 to 188 ng/g lw. Unlike other studies, this Spanish study found markedly higher levels of γ -HBCD compared to levels of α -HBCD.

Availability of analytical methods: Reliable methods for the analysis have been established and are readily available for GC-MS or LC-MS/MS analysis. Isotope labeled standards ($^{13}\text{C}_{12}$) are available from Cambridge Isotope Laboratories and Wellington Laboratories.

Availability of adequate biospecimens: HBCD can be detected in serum or breast milk.

Incremental analytical cost: LC-MS/MS can be used for analysis; however, new method development will be required. Sample extraction and clean-up can possibly be bundled with methods for other BFRs. Samples could also be analyzed with current GC-MS based methods and bundled with other BFRs for analysis.

References:

Abdallah et al. (2008). Hexabromocyclododecanes in indoor dust from Canada, the United Kingdom and the United States. *Environ Sci Technol* 42:459-464.

Antignac, JR, Cariou R, Maume D et al (2008). Exposure assessment of fetus and newborn to brominated flame retardants in France: preliminary data. *Mol Nutr Food Res* 52:258-265.

Covaci et al. (2006). Hexabromocyclododecanes (HBCDs) in the Environment and Humans: A Review. *Environ Sci Technol* 40:3679-3688.

Brominated and Chlorinated Flame Retardants

Ema M, Fujii, S, Hirata-Koizumi M, Matsumoto M (2008). Two-generation reproductive toxicity study of the flame retardant hexabromocyclododecane in rats. *Reprod Toxicol* 25:335-51.

Eriksson P et al. (2002). A comparison on developmental neurotoxic effects of hexabromocyclododecane, 2,2',4,4',5,5'-hexabromodiphenylether (PBDE153) and 2,2',4,4',5,5',-hexachlorobiphenyl (PCB 153) *Organohalogen Compd* 57:389-392.

European Union (2008). Annex XV dossier. Proposal for identification of a substance as a CMR, CAT 1 or 2, PBT, vPvB or a substance of an equivalent level of concern. Proposal for identification of hexabromocyclododecane as a SVHC. Identification of SVHC CAS NO: 25637-99-4

Guerra et al. (2008). Hexabromocyclododecane in human breast milk: levels and enantiomeric patterns. *Organohalogen Compounds* 70:309-312.

Johnson-Restrepo et al. (2008). Tetrabromobisphenol A (TBBPA) and hexabromocyclododecanes (HBCDs) in tissues of humans, dolphins, and sharks from the United States. *Chemosphere* 70:1935-1944.

Law et al. (2006). Levels of the flame retardants hexabromocyclododecane and tetrabromobisphenol A in the blubber of harbor porpoises (*Phocoena phocoena*) stranded or caught in the U.K., with evidence for an increase in HBCD concentrations in recent years. *Environ Sci Technol* 40:2177-2183.

Mariussen E and Fonnum F (2003). The effect of brominated flame retardants on neurotransmitter uptake into rat brain synaptosomes and vesicles. *Neurochem Int* 43:533-42.

PBT Profiler. Developed by Environmental Science Center for the Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency. Available at: <http://www.pbtprofiler.net/>

Stapleton et al. (2006). Determination of HBCD, PBDEs and MeO-BDEs in California sea lions (*Zalophus californianus*) stranded between 1993 and 2003. *Mar Pollut Bull* 52:522-31.

Stapleton et al. (2008). Alternate and new brominated flame retardants detected in U.S. house dust. *Environ Sci Technol* 42(18):6910-6.

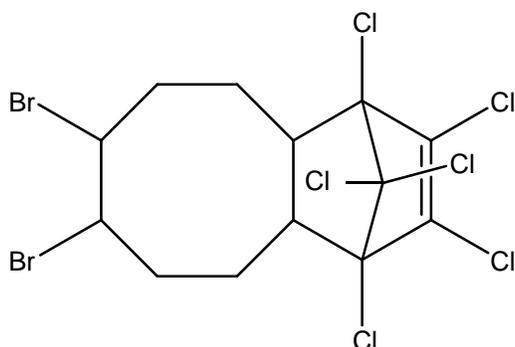
Syracuse Research Corporation (SRC). PhysProp Database. Available at: <http://esc.syrres.com/interkow/physdemo.htm>.

U.S. Environmental Protection Agency (U.S. EPA, 2002). Non-Confidential Inventory Update Reporting Production Volume Information. Toxic Substances Control Act (TSCA) Inventory. Available at: <http://www.epa.gov/oppt/iur/tools/data/2002-vol.htm>

Van der Ven et al. (2006). A 28-day oral dose toxicity study enhanced to detect endocrine effects of hexabromocyclododecane in Wistar rats. *Toxicol Sci* 94: 281-292.

Weiss J et al. (2004). PBDE and HBCDD levels in blood from Dutch mothers and infants- Analysis of a Dutch Groningen Infant Cohort. *Organohalogen Compd* 66: 2677-2682.

Hexachlorocyclopentadienyl-dibromocyclooctane (HCDBCO)
[CAS No. 51936-55-1]



Exposure or potential exposure to the public or specific subgroups: HCDBCO is a flame retardant that shares a structural feature with Dechlorane Plus (i.e., the chlorinated norbornene moiety). HCDBCO is unusual among flame retardants in that it contains both chlorine and bromine atoms. Its use as a flame retardant is reportedly in “styrenic polymers” (IPCS, 1997). No information was found on the U.S. production/imports volume for this chemical. HCDBCO has been found in house dust in Ottawa, Canada at levels ranging from less than 0.24 ng/g to 93,000 ng/g, with a median level of 2.0 ng/g (n=69). HCDBCO was also found in indoor air samples at levels that were higher than those of the major PBDE congeners (Zhu et al., 2008).

Known or suspected health effects:

There is little information on the toxicity of HCDBCO. HCDBCO, like Dechlorane Plus, has a structural similarity to several chemicals listed under Proposition 65. These chemicals share the same chlorinated norbornene moiety. The chemicals (and their Proposition 65 designation) are as follows: the flame retardant chlorendic acid (cancer), the organochlorine pesticides dieldrin (cancer), chlordane (cancer), heptachlor (cancer and developmental toxicity), and endrin (developmental toxicity). The organochlorine pesticide endosulfan also has this structural feature.

Potential to biomonitor:

Physical and chemical properties

Vapor pressure: Not identified.

Water solubility: 6.84×10^{-5} (predicted, U.S. EPA, 2008)

Octanol/water partition coefficient: $\text{Log } K_{ow} 7.91$

Bioaccumulation: BCF 3600 (predicted, PBT Profiler)

Persistence: Half-life in soil 360 d; in sediment 1600 d (predicted, PBT Profiler)

Past biomonitoring studies: None identified.

Availability of analytical methods: GC-MS.

Availability of adequate biospecimens: Serum or plasma.

Brominated and Chlorinated Flame Retardants

Incremental analytical cost: New analytic methods may need to be developed. HCDBCO can possibly be bundled with PBDEs and/or other BFRs using current PBDE and other POP methods.

References:

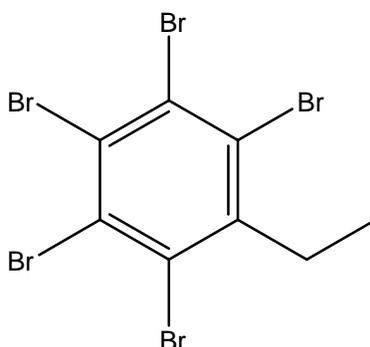
IPCS (1997). Flame Retardants: A General Introduction. Environmental Health Criteria 192. International Program of Chemical Safety. World Health Organization. Available at:
<http://www.inchem.org/documents/ehc/ehc/ehc192.htm>.

PBT Profiler. Developed by Environmental Science Center for the Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency. Available at: <http://www.pbtprofiler.net/>

U.S. EPA (2008). Estimation Programs Interface Suite™ for Microsoft® Windows, v 3.20. United States Environmental Protection Agency, Washington, DC, USA. Available at:
<http://www.epa.gov/oppt/exposure/pubs/episuite.htm>

Zhu et al. (2008). Identification and determination of hexachlorocyclopentadienyl-dibromocyclooctane (HCDBCO) in residential indoor air and dust: a previously unreported halogenated flame retardant in the environment. *Environ Sci Technol* 42:386-91.

Pentabromoethylbenzene (PBEB) [CAS No. 85-22-3]



Use and extent of exposure:

PBEB is an additive flame retardant that was used in thermoset polyester resins (circuit boards, textiles, adhesives, wire and cable coatings, polyurethanes) and thermoplastic resins in the 1970's and 1980's. Production was reported to have declined after the U.S. Environmental Protection Agency (EPA) proposed that the manufacturer test for environmental fate and effects in 1985. U.S. production/import volume was listed as 10,000-500,000 pounds for 1986, but no information is available beyond that time (U.S. EPA, 2002). U.S. EPA withdrew its proposed rule for testing in 1988 as at that time it found no intended manufacturing or processing of the chemical (Hoh et al., 2005). However, relatively high concentrations of PBEB were recently detected in Chicago air samples (Hoh et al., 2005). PBEB has been detected in pooled samples of Herring Gull eggs in the Great Lakes basin (Gauthier et al., 2007) and in egg yolk samples of Glaucous Gulls from the Norwegian Arctic (Verreault et al., 2007).

Known or suspected health effects:

Toxicological data on PBEB could not be located. Health effects are suspected because PBEB is a brominated analogue of ethylbenzene, which is listed as known to cause cancer under Proposition 65.

Potential to biomonitor:

Physical and chemical properties:

Vapor pressure: 4.69×10^{-6} mm Hg (estimated, SRC 2000)

Water solubility: 0.0467 mg/L at 25°C (estimated, SRC 2000)

Octanol/water partition coefficient: $\text{Log } K_{ow} = 7.48$ (estimated, SRC 2000)

Bioaccumulation: BCF 14000 (predicted, PBT Profiler)

Persistence: Half-life in soil 360 d; in sediment 1600 d (predicted, PBT Profiler)

Past biomonitoring studies: None identified.

Availability of analytical methods: GC-MS methods have been developed.

Availability of adequate biospecimens: Serum or breast milk.

Brominated and Chlorinated Flame Retardants

Incremental analytical cost: Analysis can be bundled with PBDE or other BFRs.

References:

Gauthier et al. (2007). Current-use flame retardants in the eggs of herring gulls (*Larus argentatus*) from the Laurentian Great Lakes. *Environ Sci Technol* 41:4561-4567.

Hoh et al. (2005). Novel flame retardants, 1,2-bis(2,4,6-tribromophenoxy)-ethane and 2,3,4,5,6-pentabromoethylbenzene, in United States' environmental samples. *Environ Sci Technol* 39:2472-2477.

PBT Profiler. Developed by Environmental Science Center for the Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency. Available at: <http://www.pbtprofiler.net/>

Syracuse Research Corporation (SRC). PhysProp Database. Available at: <http://www.syrres.com/esc/physdemo.htm>

U.S. Environmental Protection Agency (U.S. EPA, 2002). Non-Confidential Inventory Update Reporting Production Volume Information. Toxic Substances Control Act (TSCA) Inventory. Available at: <http://www.epa.gov/oppt/iur/tools/data/2002-vol.htm>

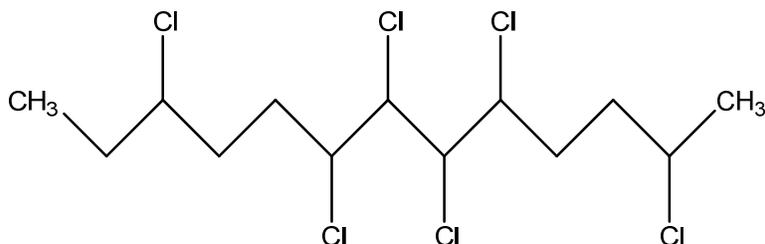
Verreault et al. (2007). Brominated flame retardants in glaucous gulls from the Norwegian Arctic: More than just an issue of polybrominated diphenyl ethers. *Environ Sci Technol* 41:4925-2931.

Short-chain chlorinated paraffins

Chain length C₁₀ – C₁₃

[CAS No. 85535-84-8 and 71011-12-6]

Example structure: C₁₃H₂₂Cl₆



Exposure or potential exposure to the public or specific subgroups:

There are three categories of chlorinated paraffins: Short-chain chlorinated paraffins (SCCPs), medium-chain chlorinated paraffins (MCCPs) and long-chain chlorinated paraffins (LCCPs). SCCPs are discussed here because of their known toxicological effects. SCCPs are used primarily as in metal-working fluids but they are also used as flame retardants (as well as plasticizers and in paints and sealants). SCCPs have been found in water and sediments in the Great Lakes and elsewhere worldwide. Houde et al. (2008) found high levels of SCCPs in food webs from Lake Ontario and Lake Michigan. Chlorinated paraffins have been found in Canadian Arctic biota (Environment Canada, 2004).

Known or suspected health effects:

Chlorinated paraffins (average chain length, C₁₂; approximately 60 percent chlorine by weight) (i.e., SCCPs) are listed as causing cancer under Proposition 65.

Potential to biomonitor:

Physical and chemical properties:

Vapor pressure: 0.0213 Pa (Australian Government, 2004)

Water solubility: 150-470 µg/L was reported for C₁₁; 59% Cl. (IPCS, 1996)

Octanol/water partition coefficient: Log K_{ow} 4.39-8.01 (IPCS, 1996)

Bioaccumulation: BCFs 5,785-138,000 wet wt, measured in mussels (Environment Canada, 2004); BCFs 1,000 to 50,000 reported in freshwater and marine organisms (whole body) (Australian Government, 2004).

Persistence: Residues in Canadian lake sediments, dating back over 25 years, suggest that the half-life in sediment is greater than 1 year (Environment Canada, 2004).

Past biomonitoring studies: Short-chain chlorinated paraffins were analyzed in breast milk of 18 individuals (25 total samples) in both urban and rural areas of the United Kingdom. The median concentration was found to be 180 ng/g fat (range of 49 to 820 ng/g fat), with no differences found between individuals living in urban and rural areas (Thomas et al., 2006).

Availability of analytical methods: GC-MS or GC-ECD methods are available.

Brominated and Chlorinated Flame Retardants

Availability of adequate biospecimens: Serum and breast milk.

Incremental analytical cost: New analytic methods may need to be developed. SCCPs can possibly be bundled with other chlorinated compounds.

References:

Australian Government (2004). Environmental Exposure Assessment of Short Chain Chlorinated Paraffins (SCCPs) in Australia. National Industrial Chemicals Notification and Assessment Scheme (NICNAS). Department of Health and Aging. Available at:

http://www.nicnas.gov.au/Publications/CAR/Other/SCCP_Environ_Exposure_Assessment_PDF.pdf.

Bayen et al. (2006). Chlorinated paraffins: A review of analysis and environmental occurrence. *Environment International* 32: 915-929.

Environment Canada (2004). Follow-up Report on a PSL1 Substance: Chlorinated Paraffins. Available at:

http://www.ec.gc.ca/substances/ese/eng/psap/PSL1_chlorinated_paraffins.cfm.

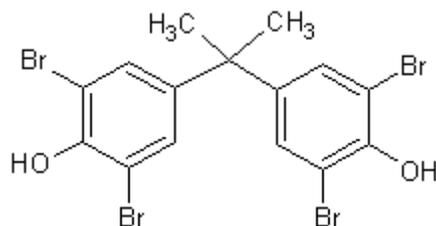
IPCS (1996). Chlorinated Paraffins. Environmental Health Criteria 181. International Program of Chemical Safety. World Health Organization. Available at:

<http://www.inchem.org/documents/ehc/ehc/ehc181.htm#SectionNumber:2.2>.

Houde et al. (2008). Bioaccumulation and trophic magnification of short- and medium-chain chlorinated paraffins in food webs from Lake Ontario and Lake Michigan.

Thomas et al. (2006). Short and medium chain length chlorinated paraffins in UK human milk fat. *Environ Int* 32:34-40.

Tetrabromobisphenol A (TBBPA) [CAS No. 79-94-7]



Exposure or potential exposure to the public or specific subgroups:

TBBPA is the most widely used brominated flame retardant worldwide; it is used primarily (approximately 90 percent) as a *reactive* flame retardant in printed circuit boards. Alternatives to TBBPA have been developed and are increasingly being used for this application. TBBPA is also used as an additive flame retardant in plastics and resins. TBBPA incorporated into printed circuit boards would not be expected to be released into the environment. However, printed circuit boards may contain unreacted TBBPA: one study found approximately ~4 mg free TBBPA per gram of TBBPA used (referenced in NTP, 2002). Annual U.S. production/imports were 100-500 million pounds for the reporting years 1994, 1998 and 2002 (U.S. EPA, 2002). TBBPA was found in air particulate samples in rooms containing computers and other electrical equipment (referenced in NTP, 2002). TBBPA has been detected in soils and sediments, fish, marine mammals and predatory bird eggs (Berger et al., 2004; Johnson-Restrepo et al., 2008; NTP, 2002).

Known or suspected health effects:

TBBPA is structurally similar to thyroxine and exhibits thyroid hormone activity *in vivo* and *in vitro* (Van der Ven et al., 2008). TBBPA has also been found to have estrogenic activity in experimental animals (Kitamura et al., 2005). Van der Ven et al. (2008) found that TBBPA-exposed animals had decreased serum thyroxine and increased weight of testes and pituitary in male offspring. In neurotoxicity studies, TBBPA was found to inhibit neurotransmitter uptake, affecting dopamine, GABA and glutamate uptake (Mariussen and Fonnum, 2003).

Potential to biomonitor:

Physical and chemical properties:

Vapor pressure: $<8.9 \times 10^{-8}$ mm Hg

Water solubility: 1.2 $\mu\text{g/L}$ (estimated)

Octanol/water partition coefficient: $\text{LogK}_{\text{ow}} = 4.5 - 5.3; 5.90$

Bioaccumulation: Maximum BCF 1000 in three different fish species;

BCF ranging from 20 to 3200 in aquatic organisms (NTP, 2002).

Persistence: Half-lives ranging from 44-179 days in soil, 48-84 days in water, and 1-9 days in air (from U.S. EPA, as cited by NTP, 2002).

Pharmacokinetics and metabolism: TBBPA is absorbed from the gastrointestinal tract and extensively metabolized to glucuronide and sulfate conjugates.

Brominated and Chlorinated Flame Retardants

Past biomonitoring studies:

Antignac et al. (2008), studying 26 mother-infant pairs in France, found TBBPA in breast milk at levels ranging from 34 to 9400 pg/g lw (median, 172 pg/g lw). TBBPA was measured in maternal serum at levels ranging from 2 to 783 pg/g (median, 7 pg/g lw; average, 54 pg/g lw); TBBPA was found in cord serum at concentrations ranging from 2 to 1012 pg/g lw (median 10 pg/g lw; average 152 pg/g lw). TBBPA has also been detected in blood and adipose tissue (Jakobsson et al., 2002; Johnson-Restrepo et al., 2008).

Availability of analytical methods: Deconjugation with enzymatic hydrolysis (beta-glucuronidase from *H. Pomatia* purified juice). Diazomethane derivatization coupled with GC-MS or SPE sample clean up and LC-MS/MS determination; requires new method development; LOD is in high ppt range. Isotope labeled standards ($^{13}\text{C}_{12}$) are available from Cambridge Isotope Laboratories.

Availability of adequate biospecimens: TBBPA can be detected in plasma or serum. Required sample volume may be 2-5 mL.

Incremental analytical cost: Analysis can be bundled with hydroxy-PCB or PCP methods.

References:

Antignac, JR, Cariou R, Maume D et al (2008). Exposure assessment of fetus and newborn to brominated flame retardants in France: preliminary data. *Mol Nutr Food Res* 52:258-265.

Berger et al. (2004). Two trace analytical methods for determination of hydroxylated PCBs and other halogenated phenolic compounds in eggs from Norwegian birds of prey. *Anal Chem* 76:441-452.

Jakobsson K et al. (2002). Exposure to polybrominated diphenyl ethers and tetrabromobisphenol A among computer technicians. *Chemosphere* 46:709-716.

Johnson-Restrepo et al. (2008). Tetrabromobisphenol A (TBBPA) and hexabromocyclododecanes (HBCDs) in tissues of humans, dolphins, and sharks from the United States. *Chemosphere* 70:1935-1944.

Kitamura et al. (2005). Comparative study of the endocrine-disrupting activity of Bisphenol A and 19 related compounds. *Toxicol Sci* 84:2005.

Mariussen E and Fonnum F (2003). The effect of brominated flame retardants on neurotransmitter uptake into rat brain synaptosomes and vesicles. *Neurochem Int* 43:533-42.

NTP (2002). Tetrabromobisphenol A [79-94-7]. Review of Toxicological Literature. Prepared by Integrated Laboratory Systems, Research Triangle Park, NC for the National Institute of Environmental Health Sciences, Research Triangle Park, NC. Contract No. N01-ES-65402. Available at:
http://ntp.niehs.nih.gov/ntp/htdocs/Chem_Background/ExSumPdf/tetrabromobisphenola.pdf

Pakalin S et al. (2007). Review on production processes of decabromodiphenyl ether (decaBDE) used in polymeric applications in electrical and electronic equipment, and assessment of the availability of potential alternatives to decaBDE. European Chemicals Bureau. European Commission. EUR 22693 EN. January 2007. Available at:
http://ecb.jrc.it/documents/Existing-Chemicals/Review_on_production_process_of_decaBDE.pdf

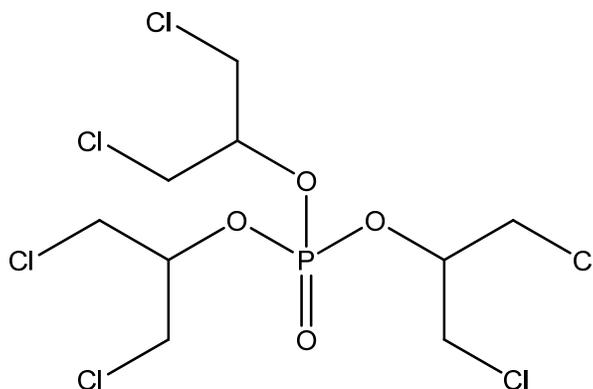
Tada et al. (2006). Effects of tetrabromobisphenol A, brominated flame retardant in ICR mice after prenatal and postnatal exposure. *Food Chem Toxicol* 44:1408-1413.

Brominated and Chlorinated Flame Retardants

U.S. Environmental Protection Agency (U.S. EPA, 2002). Non-Confidential Inventory Update Reporting Production Volume Information. Toxic Substances Control Act (TSCA) Inventory. Available at: <http://www.epa.gov/oppt/iur/tools/data/2002-vol.htm>

Van der Ven et al. (2008). Endocrine effects of tetrabromobisphenol A (TBBPA) in Wistar rats as tested in a one-generation reproductive study and a subacute toxicity study. *Toxicology* 245:76-89.

Tris(1,3-dichloro-2-propyl)phosphate (TDCPP) [CAS No. 13674-87-8]



Exposure or potential exposure to the public or specific subgroups:

TDCPP is an additive flame retardant used widely in polyurethane foam. Other reported uses are in plastics and resins and in fabric backcoating. It is currently one of the primary flame retardants replacing pentaBDEs in polyurethane foam. In the 1970s, TDCPP was briefly used in children's sleepwear after tris(2,3-dibromopropyl)phosphate (TRIS) was banned. The use of TDCPP in sleepwear was withdrawn in 1977. Annual U.S. production/import volume was 10-50 million pounds for the reporting years 1994, 1998 and 2002 (U.S. EPA, 2002). TDCPP was detected in a study of water samples from 139 streams across the United States (Kolpin et al., 2002).

Known or suspected health effects:

The U.S. Consumer Product Safety Commission (2006) concluded that TDCPP is a probable human carcinogen based on sufficient evidence in animals. TDCPP is structurally similar to TRIS and tris(2-chloroethyl)phosphate, which are both listed as causing cancer under Proposition 65. TDCPP is being tracked as a candidate for possible listing as causing cancer under Proposition 65.

Potential to biomonitor:

Physical and chemical properties:

Vapor pressure: 7.36×10^{-8} mm Hg (estimated)

Water solubility: 7 mg/L

Octanol/water partition coefficient: $\text{LogK}_{\text{ow}} = 3.65$

Bioaccumulation: BCF 21 (predicted, PBT Profiler);

Persistence: Not readily degradable in sewage sludge (IPCS, 1998);

half-life in soil 360 d; in sediment 1600 d (predicted, PBT Profiler)

Pharmacokinetics and metabolism: Animal studies found TDCPP is readily absorbed from the skin and gastrointestinal tract and is rapidly distributed. It is extensively metabolized. The major metabolite in rats, bis(1,3-dichloro-2-propyl)phosphate, is excreted primarily in urine. After an i.v. dose, greater than 80% of TDCPP was excreted in the first 24 hours (Lynn et al., 1981; Nomeir et al., 1981).

Brominated and Chlorinated Flame Retardants

Past biomonitoring studies: Studies in the 1980s found TDCPP in human adipose autopsy samples, with levels ranging from 0.5-276 ng/g (LeBel and Williams, 1986) and in seminal fluid (34 of 123 tested individuals had levels ranging from 5-50 ppb) (Hudec et al., 1981).

Availability of analytical methods: GC-MS or –NPD methods are available. An analytical standard can be obtained from Sigma-Aldrich.

Availability of adequate biospecimens: Serum or urine.

Incremental analytical cost: Current CECBP equipment can be used for analysis. New methods development may be required.

References:

Hudec et al. (1981). Tris(dichloropropyl)phosphate, a mutagenic flame retardant: frequent occurrence in human seminal plasma. *Science* 211:951-952.

IPCS (1998). Flame retardants: tris(chloropropyl) phosphate and tris(2-chloroethyl) phosphate. Environmental Health Criteria 209. International Program of Chemical Safety, World Health Organization. Available at: <http://www.inchem.org/documents/ehc/ehc/ehc209.htm#SectionNumber:1.2>

LeBel and Williams (1986). Levels of triaryl/alkyl phosphates in human adipose tissue from Eastern Ontario. *Bull Environ Contam Toxicol* 37:41-46.

Lynn et al. (1981). Disposition of the flame retardant, tris(1,3-dichloro-2-propyl)phosphate, in the rat. *Drug Metab Dispos* 9:434-441.

Kolpin et al. (2002). Pharmaceuticals, hormones, and other organic wastewater contaminants in US streams, 1999-2000: A national reconnaissance. *Environ Sci Technol* 36:1202-1211.

Nomeir et al. (1981). The metabolism and disposition of tris(1,3-dichloro-2-propyl)phosphate (Fyrol FR-2) in the rat. *Toxicol Appl Pharm* 57:401-413.

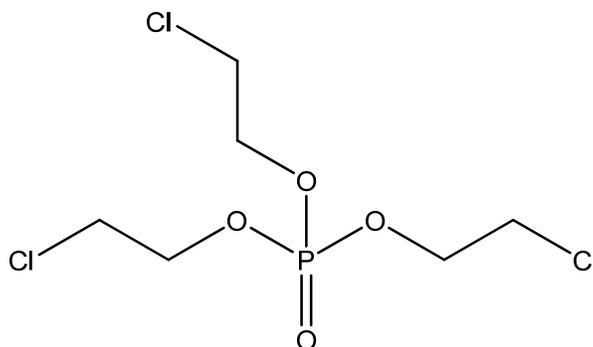
PBT Profiler. Developed by Environmental Science Center for the Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency. Available at: <http://www.pbtprofiler.net/>

Syracuse Research Corporation (SRC). SRC PhysProp Database. Available at: <http://esc.syrres.com/interkow/physdemo.htm>

U.S. Consumer Product Safety Commission (2006). CPSC Staff Preliminary Risk Assessment of Flame Retardant (FR) Chemicals in Upholstered Furniture Foam. December 21, 2006.

U.S. Environmental Protection Agency (U.S. EPA, 2002). Non-Confidential Inventory Update Reporting Production Volume Information. Toxic Substances Control Act (TSCA) Inventory. Available at: <http://www.epa.gov/oppt/iur/tools/data/2002-vol.htm>

Tris(2-chloroethyl)phosphate(TCEP) [CAS No. 115-96-8]



Exposure or potential exposure to the public or specific subgroups:

TCEP is an additive flame retardant and plasticizer used in flexible and rigid polyurethane foams, plastics, carpet backing, and textile backcoating. A German study found TCEP present in 85 percent of 983 house dust samples (Ingerowski et al., 2001). TCEP was one of the most frequently detected organic environmental contaminants in a study of water samples from 139 streams in the United States (Kolpin et al., 2002). In a study designed to assess the effectiveness of removal of contaminants by drinking water treatment processes, TCEP was poorly removed by both ozone and chlorine processes (Westerhoff et al., 2005). Annual U.S. production/import volume was 1-10 million pounds for the reporting years 1986, 1990, 1994, 1998 and 2002 (U.S. EPA, 2002). TCEP is currently not produced in the EU and is being replaced there by a similar chlorinated organophosphate, tris(1-chloro-2-propyl)phosphate (TCPP).

Known or suspected health effects:

TCEP is listed as causing cancer under Proposition 65. Adverse reproductive outcomes have also been reported (NTP, 1997).

Potential to biomonitor:

Physical and chemical properties:

Vapor pressure: 0.0613 mm Hg (SRC)

Water solubility: 7000 mg/L (SRC)

Octanol/water partition coefficient: $\text{LogK}_{ow} = 1.44$ (SRC)

Bioaccumulation: BCF 1-2 (IPCS, 1998); 0.43 (predicted, PBT Profiler)

Persistence: Half-life in soil 120 d; in sediment 540 d (predicted, PBT Profiler)

Pharmacokinetics and metabolism: In animal studies, there was greater than 75% urinary elimination within 24 hours of oral administration. The major metabolite was identified as bis(2-chloroethyl)carboxymethyl phosphate (Burka et al., 1991).

Past biomonitoring studies: None identified.

Availability of analytical methods: GC-MS or -FPD.

Brominated and Chlorinated Flame Retardants

Availability of adequate biospecimens: Serum or urine.

Incremental analytical cost: Analysis can be bundled with TDCPP analysis. New methods development may be required.

References:

Burka et al. (1991). Metabolism of tris(2-chloroethyl)phosphate in rats and mice. *Drug Metab Dispos* 19:443-447.

Kolpin et al. (2002). Pharmaceuticals, hormones, and other organic wastewater contaminants in US streams, 1999-2000: A national reconnaissance. *Environ Sci Technol* 36:1202-1211.

Ingerowski et al. (2001). Chlorinated ethyl and isopropyl phosphoric trimesters in the indoor environment – an inter-laboratory exposure study. *Indoor Air* 11:145-149.

IPCS (1998). Flame retardants: tris(chloropropyl) phosphate and tris(2-chloroethyl) phosphate. Environmental Health Criteria 209. International Program of Chemical Safety, World Health Organization. Available at: <http://www.inchem.org/documents/ehc/ehc/ehc209.htm#SectionNumber:1.2>

NTP (1997). Tris(2-chloroethyl)phosphate. *Environ Health Perspect* 105 Suppl 1:365-6.

PBT Profiler. Developed by Environmental Science Center for the Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency. Available at: <http://www.pbtprofiler.net/>

Shah et al. (2006). Determination of phosphoric acid trimesters in human plasma using solid-phase microextraction and gas chromatography coupled to inductively coupled plasma mass spectrometry. *J Chromatography* 1103:329-336.

Syracuse Research Corporation (SRC). SRC PhysProp Database. Available at: <http://esc.syrres.com/interkow/physdemo.htm>.

U.S. Environmental Protection Agency (U.S. EPA, 2002). Non-Confidential Inventory Update Reporting Production Volume Information. Toxic Substances Control Act (TSCA) Inventory. Available at: <http://www.epa.gov/oppt/iur/tools/data/2002-vol.htm>

Westerhoff et al. (2005). Fate of endocrine disruptor, pharmaceutical and personal care product chemicals during simulated drinking water treatment processes. *Environ Sci Technol* 39:6649-6663.

Brominated and Chlorinated
Flame Retardants

*List of Some Other Brominated and Chlorinated Organic Chemical Compounds
used as Flame Retardants*

2,2-Bis(bromomethyl)-1,3-propanediol [CAS No. 3296-90-0]

2,2-Bis(chloromethyl)trimethylene bis[bis(2-chloroethyl)phosphate]
[CAS No. 38051-10-4]

Bis(2-hydroxyethyl ether) TBBPA [CAS No. 4162-45-2]

Chlorendic acid [CAS No. 115-28-6]

2,3-Dibromopropyl-2,4,6-tribromophenyl ether [35109-60-5]

N-N-Ethylene-bis(tetrabromophthalimide) [CAS No. 32588-76-4]

2-Ethylhexyl 2,3,4,5-tetrabromobenzoate [CAS No. 183658-27-7]

Hexabromobenzene [CAS No. 87-82-1]

Hexachlorocyclopentadienyl-dibromocyclooctane [CAS No. 51936-55-1]

Pentabromotoluene [CAS No. 87-83-2]

Tetrabromobisphenol A bis(2,3)dibromopropyl ether [CAS No. 21850-44-2]

Tetrabromophthalic anhydride [CAS No. 632-79-1]

Tetrakis(2-chloroethyl)dichloroisopentyldiphosphate [CAS No. 38051-10-4]

2, 4, 6-Tribromophenol [CAS No 118-79-6]

Tris(1-chloro-2-propyl)phosphate [CAS No. 13674-84-5]

Tris(2,3-dichloro-1-propyl)phosphate [CAS No. 66108-37-0]