ACSH Explains: What's The Story On Cyclic Aliphatic Bromides Cluster (HBCD)?

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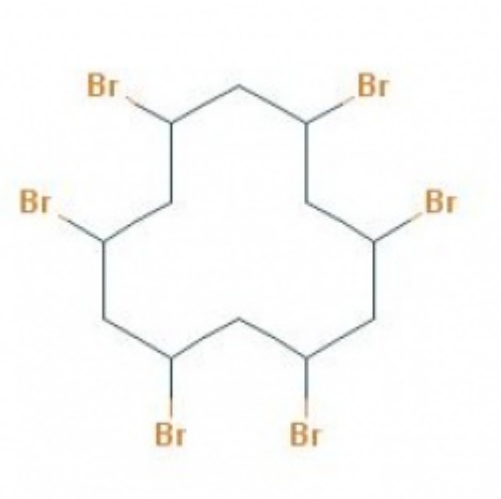
By Michael Dourson — August 14, 2018



Credit: PubChem Open Chemistry Database [1]

The Frank R. Lautenberg Chemical Safety for the 21st Century Act amends the Toxic Substances Control Act (TSCA) [2] and was signed into law June 22, 2016. It created a mandatory requirement for EPA to evaluate existing chemicals with clear and enforceable deadlines, to do so in a transparent fashion, and to do so using risk-based chemical assessments rather than rely on simple epidemiological correlations.

EPA selected the first 10 chemicals to undergo risk evaluation under the amended TSCA and to make those understandable for the public, the American Council on Science and Health is producing risk-based evaluations of each, which will then be compiled into a free downloadable book for consumers and policy makers.

What is Cyclic Aliphatic Bromides Cluster?

Cyclic aliphatic bromides cluster, also known as hexabromocyclodecanes (or HBCD), are polybrominated flame retardants. They consist of three chemicals with similar characteristics: hexabromocyclododecane; 1,2,5,6,9,10-hexabromocyclododecane; and 1,2,5,6-tetrabromocyclooctane. Since uses for 1,2,5,6-tetrabromocyclooctane have not been identified (EPA, 2017), the current commentary on HBCD is limited to either hexabromocyclododecane and/or 1,2,5,6,9,10-hexabromocyclododecane.

HBCD is a white, odorless solid with a chemical structure of $C_{12}H_{18}Br_6$, as shown in the US National Library of Medicine's Toxnet database (NLM, 2018). HBCD comes in either technical or

commercial grade, neither of which vaporizes easily, but both of which are slightly soluble in water. Technical HBCD is often described as a mixture of the three main chemicals listed above, which differ only in the way that the atoms are arranged or spaced within the molecule. Commercial-grade HBCD may contain some impurities, such as tetrabromocyclododecene or other isomers (an isomer of a molecule has the same number of atoms of each element but has a different arrangement of the atoms) of HBCD.

The primary use of HBCD is as a flame retardant in expanded polystyrene (EPS) foam and extruded polystyrene (XPS) foam in the building and construction industry for thermal insulation boards and foam insulation panels. HBCD also has limited use in replacement parts for automobiles. Past uses of HBCD included use in high impact polystyrene for electrical and electronic appliances, such as audio-visual equipment, refrigerator lining, some wire and cable applications, and in the back coating of textiles.

HBCD is expected to be persistent, bioaccumulative, and toxic at low levels, and is therefore listed as a persistent organic pollutant under the Stockholm Convention in 2013 (EPA, 2018). According to EPA, this listing has resulted in industry phasing out manufacture and use of HBCD.

In recent years, domestic manufacture of HBCD has ceased, although a small amount of import of HBCD may be ongoing.

Exposure To HBCD

Potential exposures to HBCD may result from suspended particles in the air, and from exposure to levels found in sediment, soil and indoor dust by either direct contact or incidental ingestion. However, inhalation exposure to particulates and dermal exposure, including skin contact with particulates are likely to be the predominant route of exposure for workers and the public. This exposure comes from import, processing, distribution, repackaging and recycling of industrial, commercial, and consumer uses of HBCD and subsequent releases into the air, water or land. In indoor environments, there may also be exposures resulting from legacy uses of HBCD in articles (textiles, electronics and electrical products) containing HBCD. These exposures are expected to decline over time as use of these articles is phased out (EPA, 2018).

As described in a number of EPA documents (EPA 2014, 2015, 2016, 2017, 2018), HBCD is expected to take months or greater for half of the amount released into the environment to break down. Moreover, HBCD is expected to bind to particulates and sediments and not to readily move through the soil. Thus, it is expected to remain largely immobile in landfills. It is also not expected to escape into the atmosphere from soils and water surfaces.

HBCD has been detected in the dust of residences, commercial buildings, automobiles, and airplanes in the U.S. When detected in the dust, concentrations are generally reported in the parts per billion (ppb) or parts per million (ppm) range. Studies of surface water in the U.S. are limited to a study of suspended sediment from the Detroit River, a highly industrialized area (EPA, 2015). In this study, the maximum measured concentration in sediment suspended in water was 3.7 ppb. However, greater than 300 ppb was found in sediment at the Yadkin River at the outfall downstream from a textile facility in North Carolina, U.S.

Approximately 20 ppb HBCD was measured in sludge samples analyzed from the EPA 2001 National Sewage Sludge Survey (EPA, 2015). Unfortunately, other measured concentrations of HBCD in wastewater or in soils in the U.S. are not available.

Health Effects Of Hexabromocyclododecanes

According to both EPA (2014, 2015, 2016, 2018) and the European Chemicals Agency (EChA, 2008), humans may be exposed to HBCD thorough oral, inhalation, and dermal routes. Information is lacking in humans on the potential of HBCD to be absorbed, metabolized, distributed and eliminated following exposure. In experimental animals, HBCD can be absorbed following oral exposure, but absorption through the skin is poor. No information exists on absorption after inhalation. Following oral absorption in animals, HBCD is preferentially distributed to fat, where it can accumulate. It is distributed to a lesser extent to other organs and tissues including the liver, skin, muscles, blood, heart, lungs, gonads, uterus, spleen, kidneys, and the brain. Absorbed HBCD is eliminated mostly in the feces as an unchanged parent compound, but is also eliminated in the urine as breakdown products.

Like exposure to any chemical, toxicity of HBCD depends on the level to which one is exposed and the length of time of exposure. Both EPA (2014, 2015, 2016) and EChA (2008) have health effects information on HBCD. Limited available human studies have reported potential effects of HBCD on thyroid hormones. In experimental animals, exposure to single, oral high doses of HBCD may result in death, while high inhalation exposures may cause eye squint, slight difficulty in breathing, salivation, lacrimation, and nasal discharge. Short- and long-term oral exposures may cause an increase in thyroid weight, changes in the level of thyroid hormones, and changes in the structure of the thyroid gland showing disease; and may also cause increases in liver weight with changes in the liver that show disease.

However, the effects on the liver are inconsistent across the available experimental animal studies, and EPA noted that it is not clear if the observed effects are treatment-related. According to EPA (2018), animal studies provide stronger evidence of changes in the thyroid associated with HBCD exposure than in humans.

In addition, while the potential for HBCD to affect the female reproductive system has not been investigated in humans, experimental animal studies provide some evidence that HBCD exposure may alter fertility and pregnancy outcomes. For male reproductive effects, epidemiological studies provide some support for an association between HBCD exposure and changes in the levels of serum testosterone and the sex hormone binding globulin. **(1)** However, animal studies did not report any effects on male reproductive organ weights, reproductive development, hormone concentrations or spermatogenic measures.

Epidemiological data provided mixed results on the developmental toxicity of HBCD. However, in animal studies, exposure to high doses of HBCD early in life may cause developmental toxicity, including reduced offspring viability, reduced pup weight, and changes in eye opening. Based on the available studies for HBCD, EPA concludes that there is sufficient evidence to support a concern for moderately to high toxicity from exposure to HBCD based on its potential developmental and reproductive effects.

In similar fashion, epidemiological data do not suggest a strong association between HBCD exposure and developmental neurotoxicity, where potential effects include alteration of physical or behavioral signs of development in infants and children and changes in muscular activity and thinking that persist into adulthood. However, experimental animal studies provide evidence that HBCD exposure around the time of birth may cause developmental neurotoxicity (EPA, 2018). For example, HBCD exposure appears to affect changes in hearing, brain weight, and function in multiple studies. Effects on nervous system development were observed in both sexes and across a wide range of doses and exposure durations. There is also some evidence that hearing impairment is another effect, however it is difficult to determine if the effect is due to fetal exposure to HBCD, or is a result of repeated-dose exposure, or results from a combination of these two exposures (EPA, 2018). Neurotoxicity appears to be the most sensitive endpoint studied, and, therefore, a concern exists for exposure to HBCD during pre-conception through weaning.

No studies that adequately evaluated the carcinogenic potential of HBCD in humans or experimental animals were found in the available literature (EPA, 2015, 2016); however, based on the available genotoxicity data and one limited carcinogenicity study, existing assessments have concluded that HBCD is not carcinogenic (EPA, 2018).

HBCD Safe or Virtually Safe Levels

The federal and state governments develop regulations and recommendations to protect public health. Regulations and recommendations are often expressed as a safe or virtually safe level, that is, a level of a substance in air, water, soil, or food that is not expected to cause any adverse health effect, even in people who are sensitive to the chemical’s effects.

These safe levels are usually based on information from experiments with animals (usually rodents) at much higher levels of the chemicals than humans would typically encounter. The higher animal exposures are used to see what the adverse health effects could be. The scientists then conjecture what the adverse effects could possibly be in humans at a lower level of exposure. Scientists can then estimate the level that will most likely protect humans, including sensitive humans.

Sometimes these safe levels differ among federal and state organizations because they used different assumptions for human exposure, different animal studies, or employ methods that differ slightly. Other times, these recommendations differ because new science develops that suggests different levels are toxic or safe. Recommendations and regulations are also updated periodically as more information becomes available.

For HBCD, no safe or virtually safe concentrations/doses have been developed by any authoritative body. However, EPA (2014), conducted a benchmark dose (BMD) modeling to

predict at which dose the effects caused by HBCD could occur, including impaired hearing, pup mortality, and thyroid effects. EPA (2014) derived an oral BMDL of 0.2 mg/kg/day based on hearing impairment. BMDL = 95% lower confidence limit on the benchmark dose (BMD). A BMD modeling is used to estimate the dose or exposure of a chemical or chemical mixture associated with a given response level, to facilitate hazardous pollutant risk assessments.

No toxicity values are available for the inhalation or dermal route. No oral cancer slope factor or inhalation unit risk has been developed for HBCD.

Why Is EPA Looking At This Under The Lautenberg Chemical Safety Act?

EPA (2018) is currently looking at the likely routes of exposure to HBCD in the environment and will be further developing exposure scenarios, or pathways, of how the public comes into contact with HBCD. These exposure pathways will then be studied by EPA scientists by comparing the amount of HBCD exposure in the pathway to its safe or virtually safe level.

If human exposure in the pathway is at or below this safe or virtually safe level, then HBCD exposure from the pathway is not considered to be a human health concern. If exposure is above this safe or virtually safe level, then the pathway might be considered as a possible health concern; **(2)** also, several pathways may be added together to suggest a health concern.

In either event, regulations might be developed to lessen the exposure of HBCD from this pathway(s). See EPA (2018) for additional information related to the assessment of HBCD under the new Lautenberg Chemical Safety Act (LCSA).

Controversy Over HBCD

EPA (2018) interprets the mandates within the LCSA to conduct risk evaluations on current and prospective uses of hexabromocyclodecanes for which manufacturing, processing, or distribution in commerce “is intended, known or reasonably foreseen.”

Thus, EPA is excluding from its problem formulation conditions of the use of HBCD that are not intended, known, or reasonably foreseen. Since domestic manufacture of HBCD has ceased, prior domestic uses of HBCD are excluded. This excluded list includes uses in expanded polystyrene resin and extruded polystyrene masterbatch, the use of HBCD in high impact polystyrene (HIPS) in electronic components, and legacy uses of HBCD including adhesives, textiles (including upholstery fabric, floor mats and headliners in automobiles, and commercial uses), electronics and electrical products, and other uses (e.g., toys and games, car seats, toys, and toy vehicles). However, HBCD has a number of other uses, for example, within the automotive and building industries, and these categories of use are included within the current scope of EPA’s evaluation. See EPA (2018) for a much more complete description of included and excluded uses.

The fact that studies in both humans and animals have identified neurotoxicity to be the most sensitive endpoint for hexabromocyclodecanes is not controversial. Many flame retardants, including the best known and used flame retardant - water - are known to be neurotoxic at a high dose. Controversy does exist, however, regarding the usefulness of flame retardants in preventing injury and death. We have covered the benefits of flame retardants for human safety extensively [3]

, including in a white paper: Brominated Flame Retardants: A Burning Issue [4].

Given the available data on risk and bioaccumulation and the availability and affordability of polymeric flame retardant as a replacement, it is reasonable for EPA to further limit this similar to what other countries have done even though the harms are only found in animal models.

NOTES:

(1) Sex hormone-binding globulin is a glycoprotein that binds to the two sex hormones: androgen and estrogen. A glycoprotein, also called glycopeptide, is any of a class of proteins that have carbohydrate groups attached to the polypeptide chain.

(2) Small excesses of the safe or virtually safe dose are seldom cause for concern since these safety levels are developed from conservative assumptions, including the use of safety factors that tend to exaggerate risk and exposure pathways that tend to exaggerate exposure.

More analyses in **our series on the Lautenberg Chemical Safety Act compounds**:

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ACSH Explains: What's The Story On Methylene Chloride (DCM)? [9]

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Links

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[2] https://www.epa.gov/laws-regulations/summary-toxic-substances-control-act
[3] https://www.google.com/search?q=%22flame+retardants%22+site%3Aacsh.org&rlz=1C1CHBF_enUS710US710&8
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