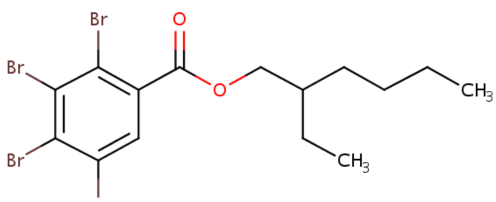
CAS RN 183658-27-7

Substance Name 2-ethylhexyl 2,3,4,5-tetrabromobenzoate (TBB, also EH-TBB)



Source: EPA Chemistry Dashboard

Uses

TBB is an ingredient in common market replacements for PBDEs in flexible polyurethane foam [1]. Approximately 50% of the Firemaster® 550 mixture is TBB and TBPH at a ratio of 4:1 by mass [2, 3]. TBB treated foams have been used in many everyday products such as couches, chairs, other upholstered furniture, children's furniture, baby products, office furniture, foam used in gymnastic facilities, and automotive cushions. TBB may also be present in products made from recycled foam such as carpet backings and pads [2, 4, 5].

Uses reported recently to U.S. Environmental Protection Agency (EPA) include industrial use as a flame retardant in furniture and related product manufacturing and commercial use as a flame retardant in foam seating and bedding. The maximum concentration in foam was reported as 30% by weight. Some consumer products containing TBB are reported to be intended for children[6].

Manufacturers and U.S. Production

Past and current national production volume of TBB is withheld as confidential business information. One U.S. manufacturing site, not in Washington State, was reported[1] to EPA in 2016 [2, 6].

Toxicity

EPA classified TBB as a moderate hazard for reproductive, developmental, neurological and repeated dose toxicities [3]. There is very little data on TBB individually. EPA's rating was based on the observed toxicity of a closely related confidential analog, and studies of commercial mixtures, which contain TBB as a major component. EPA could not release the name or chemical structure of the confidential analog but reported that the lowest observed adverse effect level for a rodent study of this compound was 25 mg/kg-d for reproductive toxicity [3]. In addition, EPA reviewed three unpublished toxicity studies provided by manufacturers on a commercial mixture, Firemaster® BZ-54, which contains 70% TBB and 30% TBPH. In a prenatal developmental toxicity study of Firemaster® BZ-54 in rats, maternal and fetal weight were reduced at 100 mg/kg-day and abnormal bone formation in vertebrae and in the skull were

[1] Manufacturers of chemicals listed on the Toxic Substances Control Act (TSCA) Inventory were required to report to EPA in 2016 if they produced or imported the chemical in volumes ≥25,000 pounds at a US site during any of the calendar years 2012, 2013, 2014, or 2015. https://www.epa.gov/chemical-data-reporting/2016-chemical-data-reporting-results#overview

observed at 300/mg/kg-d. The no observed adverse effect level (NOAEL) for maternal and developmental toxicity was 50 mg/kg-d [7]. A two-generation reproductive toxicity study with the same mixture observed reduced body weights and spleen weight in offspring at 165 mg/kg-d. The NOAEL was 50 mg/kg-d [7].

Firemaster® 550, is another commercial mixture that contains TBB along with TBPH and two organophosphate flame retardants. Pregnant rats exposed orally to Firemaster® 550 during gestation and lactation had altered thyroid function and produced offspring that were 30–60% heavier by weaning, an effect that persisted into adulthood [8]. Female offspring of treated rats entered puberty sooner and had glucose intolerance and elevated anxiety behaviors in maze testing. These developmental effects were observed at 1 mg/kg-d, the lowest dose tested [8]. There is some *in vitro* evidence that the other ingredients in Firemaster®550 activate peroxisome proliferator-activated receptor gamma (PPARγ) and may be responsible for lipid accumulation following Firemaster®550 exposure [9]. Neither TBB nor its metabolite 2,3,4,5- tetrabromobenzoic acid (TBBA) showed marked activity on PPARα or PPARγ *in vitro* [10].

TBB is extensively metabolized to TBBA within several hours in rats [11]. TBB but not TBBA showed anti-glucocorticoid activity in a reporter gene assay (IC_{50} were 1.9 nM, 37.5 nM, respectively) [12]. The glucocorticoid receptor plays key roles in the immune system, metabolism and fetal development. Both the parent compound and TBBA were potent agonists of the pregane X receptor (PXR) and induced transcription of gene products (CYP3A4 mRNA) *in vitro* [10]. Activation of PXR helps detoxify xenobiotics but can also cause endocrine disruption through enhanced metabolism of endogenous hormones. Smythe et al. 2017, reported that TBB did not alter the activity of two enzymes that regulate intercellular thyroid hormone levels (thyroid hormone deiodinase and sulfotransferase) in human liver microsomal and cytosolic bioassays [13].

Exposure

TBB is used as an additive flame retardant and can escape treated materials in everyday products and furniture over time. TBB has been measured with high frequency in residential indoor dust in studies in the U.S. [14-19] and Canada [20]. Mean levels from these studies ranged from 310 – 1,062 ng/g in indoor dust. Maximum level reported was 75,000 ng/g dust. Hammel et al. 2017, looked at the contribution of household sofas to house dust concentrations of flame retardants in the same room [18]. Geometric mean levels of TBB in house dust were four times higher when the sofa contained Firemaster®550 compared to sofas without this flame retardant in its foam cushions. This study suggests that furniture foam is a major source for TBB in house dust [18]. In a study of North Carolina adults, levels of TBB in hand wipes correlated positively with TBBA metabolite in urine suggesting that dermal contact with dust or treated surfaces was linked to overall exposure [11]. Hand wipes between mothers and their three year old children were highly correlated in samples collected from New York City participants in 2012-13. Median concentration of TBB +TBPH on toddler's hands (0.86 ng/cm^2) was nearly twice as high as the median concentrations measured on mother's hands (0.48 ng/cm^2) [21].

TBB has also been measured in indoor air. Venier et al. 2016, collected air samples in 64 homes in Indiana and Toronto in 2013. TBB was detected in 100% of home air samples, the mean concentration in air was 23 picograms per cubic meter (pg/m^3) in U.S. homes and 32 pg/m^3 in Canadian homes, and the maximum concentration reported was of 291 pg/m^3 [19]. Two smaller studies collected indoor air samples in the Seattle area [5, 22]. Mean concentration of TBB in inhalable particulate (>4 µm) was 143 ng/m^3 in gymnastic facilities, 22.0 ng/m^3 in gym coaches homes, and 3.23 ng/m^3 in other homes and offices. Mean concentration of TBB associated with smaller respirable particles (<4 µm) was 11.4, 21.4, and 2.99 ng/m^3 for gyms, coaches homes, and other homes and offices, respectively [23].

TBB was commonly detected in urban air samples collected regularly over a two year period (2008-10) in the Great Lakes region. Concentrations ranged from 0.5-55 pg/m^{3}in the Chicago and Cleveland areas and 0.05-7.5 pg/m^3 in more remote areas [24].

TBB has also been found in other environments where children spend time. It was found in 100% of indoor dust samples from 39 childcare centers in Northern California [25]. TBB was recently measured in a study of flame retardants in car interiors in Greece that included American-made cars. TBB was detected in 100% of samples with a median of 15.2 ng/g dust and a maximum detection of 244 ng/g dust [26]. Children also spend time in gymnastic facilities where flame retardants are commonly in the foam of blocks and mats that cushion landings. There is some evidence that levels of TBB in settled dust and air at gyms may be higher than in the homes[5]. Studies in collegiate gymnasts have demonstrated that transfer to skin occurs in gyms, median concentrations of TBB and TBPH in paired hand wipe samples were 2–3 times higher after gymnastics practice compared to before practice [27].

TBB was absorbed into the skin, and slowly penetrated into systemic circulation in rats exposed dermally. Excretion occurred primarily as the TBBA metabolite in urine although a lesser amount (about 1/6) was recovered in feces [28]. In *in vitro* studies, human skin was less permeable than rat skin leading the National Toxicology Program authors to conservatively predict that approximately 10±3% of TBB may be absorbed into human skin *in vivo*, with 0.8±0.6% reaching systemic circulation after 24 hours of continuous exposure, likely in the form of TBBA [28]. Young children also frequently mouth and suck on their hands so an ingestion of residue on hands is probably significant for this life stage. Fang et al. 2014, used simulated digestive fluids to estimate a 49% bioavailability of TBB in ingested indoor dust [29].

The TBBA metabolite was detected in urine of 45-70% of toddlers and 27-36% of their mothers in New Jersey and California studies [30, 31]. Levels measured in children tended to be higher than their mothers in both studies. The maximum concentration reported was 62.2 ng/ml in maternal urine and 225 ng/mL in children's urine across both studies. The U.S. Centers for Disease Control recently analyzed urine samples collected in 2013-14 for the TBBA metabolite in a representative sample of the U.S. population. TBBA was only detected above the study detection limit (0.05 ng/ml) in 5% of all participants. In the youngest children tested (6-11 years old) the 95th percentile was 0.07 ng/ml. The maximum value was 1.14 ng/ml [32, 33].

TBB was also commonly detected in serum (n=102) and breast milk (n=105) collected in a 2008-2009 study in nursing women living in Québec Canada [34]. TBB was detected in 57% of serum, with a mean level of 5.4 ng/g lipid weight, and a 95th percentile of 22 ng/g lipid. TBB was detected in 78% of milk samples, mean concentration was 1.3 ng/g lipid and the 95th percentile was 24 ng/g lipid [34]. Lower levels have been reported in Europe. TBB was detected in 69% of breast milk samples collected in the Netherlands in 2011-14. Median concentration of TBB in breast milk was about 3 times lower than in the Canadian study: 0.13 vs 0.41 ng/g lipid. Exposure to 2-3 month old nursing infants was estimated to be 0.45 ng/kg-day [35]. TBB was detected in 9 out of 10 breast milk samples collected in the UK in 2014-15. The mean level was 0.21 ng/g lipid and the maximum detection was 0.48 ng/g lipid. The estimated daily exposure to a one-month old infant from breast milk based on that mean was 1.2 ng/kg-day [36].

Environmental Fate and Transport

TBB was classified by EPA as high hazard for persistence and bioaccumulation [3]. A joint evaluation by Health Canada and Environment Canada in 2016 agreed that TBB is expected to be persistent in water, soil, and sediment. However, Canadian risk evaluators did not agree that TBB was likely to be highly bioaccumulative, due in part to poor bioavailability, evidence of metabolic biotransformation and absence of increased concentrations in predator-prey relationships in biomonitoring biota [37].

Summary from 2016 Review by Environment Canada/Health Canada [37]

If released to air	• TBB declines rapidly in gas phase of air (predicted half-life 11.8 hours) but may persist in the air compartment via sorption to fine particulates. • TBB has been frequently detected in ambient air at low pg/m^3 concentrations. Ma et al. 2012, provided evidence that airborne TBB in the Great Lakes area was rapidly increasing overtime [24]. • TBB is detected in remote environments, likely due to long-range transport on airborne particulate.
If released to soil	• TBB has very low water solubility, very low vapor pressure, and a high to very high octanol-water partition coefficient. TBB is expected to strongly sorb to solid phases in various media (e.g., biosolids, sediments, soil). • TBB is expected to be persistent. Biodegradation of TBB in a TBB/ TBPH mixture was reported to be 6% after 28 days in inoculated mineral media. • No biodegradation of TBB was observed in 21 days in a simulation of waste water treatment activated sludge solids.
If released into water	• It is expected to partition to sediments, with a modest fraction remaining in water. TBB has been measured in Great Lakes water and sediment.

	• In a study of environmental fate in shallow test ponds, TBB was detected in suspended solids with a dissipation half-life of 9 days. It was not detected in sediments [38]. • A study of a TBB/TBPH mixture found degradation half-lives of 3.5 days and 8.5 days in active water and active sediment.
Bioconcentration and bioaccumulation	• TBB has been measured in a number of bird species, fish, and mammals with highest levels in polar bears and marine mammal blubber. • While physical properties of TBB suggest a high potential for bioconcentration and bioaccumulation, it appears that TBB is metabolized in biota. Specific metabolites identified for TBB include 2,3,4,5-tetrabromobenzoic acid (TBBA), which may further be metabolized to methyl 2,3,4,5-tetrabromobenzoate, and 2-ethylhexyl 3,4-dibromobenzoate. • Empirical data suggest a limited potential for bioaccumulation of TBB in the tissues of biota.

Physical-Chemical Properties for TBB from EPA Chemistry Dashboard

Property	Predicted Average	Predicted Median	Predicted Range	Unit
LogP: Octanol-Water	9.64 (5)	9.47	7.57 to 12.0	-
Water Solubility	1.54e-08 (4)	1.73e-08	2.81e-15 to 2.73e-08	mol/L
Density	1.76 (2)	1.76	1.53 to 2.00	g/cm^3
Flash Point	283 (2)	283	259 to 307	°C
Melting Point	113 (4)	83.9	55.0 to 229	°C
Boiling Point	492 (5)	513	393 to 585	°C
Surface Tension	41.3 (1)	-	-	dyn/cm
Thermal Conductivity	127 (1)	-	-	mW/(m*K)
Vapor Pressure	4.37e-09 (4)	1.26e-09	1.16e-13 to 1.50e-08	mmHg
LogKoa: Octanol-Air	11.7 (1)	-	-	-
Henry's Law	8.92e-07 (1)	-	-	atm-m^3/mole
Index of Refraction	1.54 (1)	-	-	-
Molar Refractivity	145 (1)	-	-	cm^3
Molar Volume	462 (1)	-	-	cm^3
Polarizability	57.6 (1)	-	-	Å^3

Numbers in parentheses indicate the number of different measurements or model predictions considered by EPA.

Regulatory

In 1998, EPA placed limitations on the manufacturing, processing, or use of this chemical through a Consent Order under TSCA §5(e). Use of the chemical in a manner inconsistent with the Consent Order is a Significant New Use. Manufacturers and processors must notify EPA before the new use begins through submission of a Significant New Use Notice (SNUN) so that EPA has the opportunity to review and, if necessary, place restrictions on the new use (40 CFR 721.2925). EPA's concern was about aquatic and terrestrial toxicity and new uses that would release this substance into surface water.

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