CPSC Staff Statement on the
Toxicology Excellence for Risk Assessment Report,
"Environmental Concentrations and Consumer Exposure Data for Selected Flame Retardants (TBB, TBPH, TBBPA, ATO)"
August 13, 2015

The report, *Environmental Concentrations and Consumer Exposure Data for Selected Flame Retardants (TBB, TBPH, TBBPA, ATO),* presents the findings of research conducted by Toxicology Excellence for Risk Assessment (TERA) under a contract[1] with the U.S. Consumer Product Safety Commission (CPSC). TERA performed this work to compile human exposure information for four selected flame-retardant chemicals.

The selected flame retardants are:

- 2-Ethylhexyl 2,3,4,5-tetrabromobenzoate (TBB)
- Di(2-ethylhexyl) tetrabromophthalate (TBPH)
- Tetrabromobisphenol A (TBBPA)
- Antimony trioxide (ATO)

TERA reviewed available information related to human exposure to the selected flame retardants, including published scientific literature and data from U.S. government agencies and other authoritative bodies. The research focused on indoor air and dust, drinking water, and consumer products (including children's products, upholstered furniture, mattresses, apparel, household products, building materials, and electronics), and included biomonitoring studies and exposure estimates, where available.

This research was completed in support of CPSC staff's work on flame-retardant chemicals to assess potential for exposure from household products, and to prioritize work on specific products and chemicals.

This report will be posted on CPSC's website to keep stakeholders informed of the progress of technical research related to the agency's regulatory activities. A portion of the work presented in the contractor report includes information relevant to staff's ongoing work to understand consumer exposures to certain organohalogen flame retardant chemicals from consumer products, including furniture, mattresses, and electronic products.

[1] Task order 0010 under contract No. CPSC-D-12-0001, awarded 8/13/2014.

TERA

Environmental Concentrations and Consumer Exposure Data for Selected Flame Retardants (TBB, TBPH, TBBPA, ATO)

Task Order 10
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Abbreviations and Acronyms

µg/L	microgram(s) per liter
µg/g	microgram(s) per gram
ABS	Acrylonitrile-Butadiene-Styrene
AC	Activity coefficient
ADME	Absorption, Distribution, Metabolism, and Excretion
ATO	Antimony trioxide
ATSDR	Agency for Toxic Substances and Disease Registry
BSEF	Bromine Science and Environmental Forum
CalEPA	California Environmental Protection Agency
CEPA	Canadian Environmental Protection Act
CPSC	U.S. Consumer Product Safety Commission
ECHA	European Chemicals Agency
EFSA	European Food Safety Authority
EURAR	European Union Risk Assessment Report
FSA	Food Standards Agency
FM550	Firemaster 550
FR	Flame retardant
g/mL	gram(s) per milliliter(s)
g/mol	gram(s) per mole
HIPS	High Impact Polystyrene
HSDB	Hazardous Substance Database
IARC	International Agency for Research on Cancer
ICRP	International Commission on Radiological Protection
IPCS	International Programme on Chemical Safety
K_{oc}	Soil organic carbon-water partition coefficient
K_{ow}	Octanol-water partition coefficient
kPa	kilopascal
LOD	Level of Detection
log K_{ow}	Logarithmic octanol-water partition coefficient
m	meter
max	Maximum
mg/kg	milligram(s) per kilogram(s)
mg/kg/day	milligram(s) per kilogram(s) per day
mg/L	milligram (s) per liter
Min	minimum
mm Hg	millimeter of mercury
ng	nanogram(s)
ng/mL	nanogram(s) per milliliter(s)

NRC	National Research Council
PC	Personal computer
PBDE	Polybrominated diphenyl ether
PU	Polyurethane
PUF	Polyurethane foam
PVC	Polyvinylchloride
SC	Stratum corneum
SVOCs	Semi-Volatile Organic Compounds
T3	Triiodothyronine
TBB	2-Ethylhexyl 2,3,4,5-tetrabromobenzoate
TBBA	2,3,4,5-Tetrabromobenzoic acid
TBBPA	Tetrabromobisphenol A
TBMEHP	Mono(2- ethylhexyl) tetrabromophthalate
TBPH	Di(2-ethylhexyl) tetrabromophthlate
TERA	Toxicology Excellence for Risk Assessment
TV	Television
U.S.	United States
U.S. EPA	U.S. Environmental Protection Agency
USGS	U.S. Geological Survey
VP	Vapor pressure
XFR	X-ray fluorescence

1 Introduction

This document compiles available human exposure information on the following four flame retardants:

- 2-Ethylhexyl 2,3,4,5-tetrabromobenzoate (TBB)
- Di(2-ethylhexyl) tetrabromophthalate (TBPH)
- Tetrabromobisphenol A (TBBPA)
- Antimony trioxide (ATO)

Flame retardant chemicals are added to materials to increase a product's resistance to ignition or to decrease the spread of flames. They are used in many different types of consumer products, including upholstery and mattresses, toys, children's products, electrical devices, appliances, building materials, and apparel. Various flame retardants or their metabolites have been detected in human fluids or tissues, indicating human exposure and absorption of at least some of these chemicals.

Toxicology Excellence for Risk Assessment (TERA) reviewed available literature and data relating to human exposure of the selected flame retardants. Data were obtained from assessments of the flame retardants prepared by United States (U.S.) government agencies and other authoritative bodies. We also searched the scientific literature for available data on human exposures and environmental measurements of flame retardants. In particular, data on concentrations in indoor air and dust, potential drinking water, and in consumer products (including children's products, upholstered furniture, mattresses, apparel, household products, building materials, and electronics) were sought. The information is compiled by "media" with data on measured concentrations identified in ambient air, indoor air, household dust, drinking water (and surface and groundwater), and food presented in tables. Available measurements of concentrations in consumer products, such as electronics, furniture, mattresses, toys, and building materials, are also presented. Results of available biomonitoring studies and exposure estimates, if any, are also included. Appendix A includes a description of the literature search strategy, key words, and databases searched.

It should be noted that this report compiles data from a variety of sources. We have not evaluated the quality of the studies and their results; rather we included all the relevant data we found. The estimates described in the exposure assessment sections are presented "as is" without a detailed analysis or critique of the methodology, assumptions, or underlying data quality. Further review on the quality and representativeness of these studies would be needed before using these data to estimate human exposures.

In reviewing the results and compilation of the available literature, it is apparent that there is a dearth of quality exposure information for these flame retardants to quantify human exposure. We observed several common elements from our review.

There is a basic lack of monitoring data in environmental media for these chemicals.

The U.S. Geological Survey (USGS) has conducted sampling for some of the flame retardants in drinking water and U.S. waters, but there is no systematic or routine monitoring in place by the federal government. Most of the studies we identified focused on measurements in heavily industrialized rivers where, presumably, contamination was suspected due to manufacturing. Several studies noted the ability of treatment to remove particular flame retardants from drinking water influent or manufacturing effluent. For some flame retardants, treatment reduced concentrations and in other cases, it did not.

Much of the available information is from studies outside of the U.S.

We found limited U.S. data for these flame retardants. Data from other countries may introduce uncertainty into exposure estimates because particular flame retardant levels in other countries may not be representative of products, flame retardants, and building parameters found in the U.S. Within the U.S., California has traditionally had more stringent flame retardant regulations, and as a result, levels of flame retardants in dust in California may be higher than in other parts of the country.

Limited data on emission or migration rates from products and materials containing the flame retardant chemicals.

Unlike concentrations in environmental media (e.g., air, water, dust), flame retardant concentrations measured in consumer products and building materials cannot be used directly as a proxy for concentration levels to which consumers are exposed. Any product that contains a flame retardant has the potential to contribute to household dust levels. To develop realistic consumer exposure concentrations, the flame retardant levels in these products would need to be paired with experimental or monitoring results that reflect the availability of the specific compound to leave these products and be available to enter the body. These data are not generally available. Alternatively, emission or migration rates could be used to model or estimate exposures for:

- Near-field exposure for persons proximate to the product
- Far-field exposure in the room and building
- Long term rate of flame retardant input to the space

For example, the work of Fromme et al. (2014) detecting and measuring TBB and TBPH in house dust could be used to estimate exposure. Another example is the work of Harrad et al.

(2010) measuring the concentrations of TBBPA in the dust found in day cares and primary classrooms.

Without the data to make the link between concentrations and exposure levels, the data on flame retardant content in a product provides only a qualitative indication of the ultimate availability of that flame retardant to be released into the indoor environment, into either the air or dust. The rate of release will depend upon the individual products, their physical and chemical properties, and how they are used.

Flame retardants used in many products come in contact with people's skin, but there is uncertainty associated with percutaneous exposure due to a lack of testing.

An area of uncertainty is exposure potential from dermal contact with or without ingestion from mouthing of objects containing a flame retardant. The general mechanism for diffusion out of treated plastics and into dust is relatively well understood based on first principle models (e.g., http://www.epa.gov/nrmrl/appcd/mmd/i-sovc.html). Similarly, the potential for hand-to-mouth transfer of dust is understood and established. This is not the case for dermal or mouthing transfer of flame retardants from contact with treated objects. The potential dermal or mouth exposure to a flame retardant as it is diffusing and being "expressed" from the treated plastic is not well understood or documented. The flame retardant molecules will have some rate of dermal penetration if they are in contact with the skin. This exposure route may be particularly important for children's items, such as changing table pads, infant sleep positioners, portable crib mattresses, and nursing pillows, as well as clothing. Transfer and ingestion via child-mouthing of these items, toys, and treated furniture in general is another area of uncertainty.

Changes in usage of particular flame retardants as manufacturers and government agencies identify potential problems and substitute alternative flame retardants.

As government agencies, manufacturers, and consumers are more aware of flame retardant usage and potential exposures, usage patterns change, with new chemicals substituting for old or different concentrations and chemicals used in new products. Past measurements may not be representative of current conditions, with changing product content or usage patterns. Also, the time frame of these exposure events suggests that the exposure potential could continue to grow for months or years after the initial use and placement of treated objects indoors.

Both dust and vapors may contribute to total concentrations in indoor air.

Depending upon the flame retardant's properties, a particular flame retardant may or may not be anticipated to become airborne as a vapor out of organic substrates indoors. However, particulates, such as dust, are quite mobile and can become airborne. The flame retardant could be distributed within the indoor environment in dust on surfaces with a lesser amount of the

flame retardant containing dust being airborne. An exception to this rule of low airborne levels would be relatively “dusty” rooms where the dust has been allowed to accumulate and/or activities occurs that tend to continually entrain the dust into the air. In these indoor environments, relatively high levels of airborne flame retardant (dissolved in dust) may be found. This, as well as computer equipment and furniture, may explain some rare reports of relatively high levels of flame retardant in the indoor air of an office or house (see for example, Johnson et al. 2013; Ni and Zeng, 2013).

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

2.1 TBB Chemical and Physical Properties

2-Ethylhexyl-2,3,4,5-tetrabromobenzoate (TBB) is a widely used flame retardant that exists as a liquid in its pure form. The water solubility value of 1.144×10^{-5} mg/L at 25°C indicates that TBB has very low solubility in water but would be expected to be soluble in most solvents (U.S. EPA, 2008). It will adsorb to solids and sediments in water based on an estimated Log(K_{ow}) value of 8.75 (U.S. EPA, 2008). The estimated room temperature vapor pressure values for TBB is $<10^{-8}$ mmHg. These values indicate that TBB will exist predominantly in the particulate phase in the atmosphere. Significant volatilization from water surfaces is not expected based on its anticipated low volatility as a vapor.

TBB is an additive flame retardant and one of the alternative replacements for the polybrominated diphenyl ether (PBDE) flame retardants in polyurethane foam (Stapleton et al., 2008). TBB and bis(2-ethylhexyl) tetrabromophthalate (TBPH) (CAS No. 26040-51-7) are components of several Firemaster® commercial flame retardant mixtures (Roberts et al., 2012). Both TBB and TBPH are listed as high production volume chemicals by the U.S. EPA (U.S. EPA, 2009a as cited in Springer et al., 2012).

Figure 2-1. Molecular Structure of TBB (ChemIDPlus, 2014)

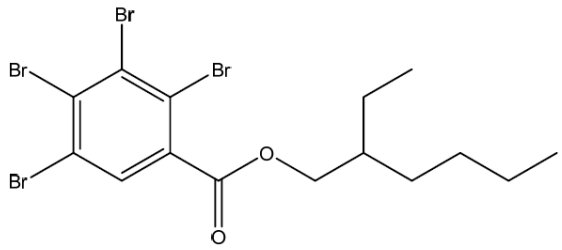

Table 2-1. CAS Registry Number and Synonyms for TBB (ChemIDPlus, 2014; CalEPA, 2008)

CAS registry/RN	183658-27-7
Synonyms	2-Ethylhexyl-2,3,4,5-tetrabromobenzoate; TBB

Table 2-2. Physical and Chemical Properties of TBB (ChemIDPlus, 2014; HSDB, 2013a; Santa Cruz Biotechnology, 2015; U.S. EPA, 2008, 2014)

Molecular Formula	$C_{15}H_{18}Br_4O_2$
Molecular Weight	549.9212
Melting Point	No data located
Boiling Point	~477.5 °C at 760 mmHg (predicted, Santa Cruz Biotechnology, 2015)
Density	~1.8 g/mL (predicted, Santa Cruz Biotechnology, 2015)
Solubility (in water)	1.144×10^{-5} mg/L at 25°C (predicted, U.S. EPA, 2008)
Log K_{ow}	8.75 (predicted, U.S. EPA, 2008)
Vapor Pressure	$<10^{-8}$ mmHg (estimated, HSDB, 2013a)
Henry's Law Constant	No data located

Semi-Volatile Organic Compounds (SVOCs), such as TBB, are typically characterized by relatively high molecular weight, low vapor pressure/volatility, low or moderate solubility in water and a high octanol-water partition coefficient. To a significant degree, these properties determine the fate of TBB in the environment, which impacts the potential for human exposure. The high octanol-water partition coefficient means it will be lipophilic or "fat loving," that is, it will partition into any sediment layers in an environmental water column. In the indoor environment, it will not be highly present in the air as a vapor but will readily partition into (and be present in) available organic rich substrates like house dust.

The vapor pressure (VP) of pure TBB indicates that it cannot exist in ambient air at significant concentrations as a vapor:

$(<10^{-8}$ torr/760 torr) (1,000,000) (549.9/24.4) = $<3 \times 10^{-4}$ mg/m^3

This is approximately <0.3 µg/m^3.

In reality, TBB would never be expected to exist as a pure material indoors. Initially, it is in the polymer matrix and after it diffuses out of the matrix, it comes to the surface and then is associated with house dust that is primarily composed of human skin cells, which have been shed in a process known as desquamation. As such, house dust is essentially an organic substrate. In this case, the 0.01 torr VP at 30°C (86°F) of pure TBB is highly attenuated via what is known as Raoult's Law:

(VP of Pure TBB)(Mole Fraction of TBB in substrate) = VP over the substrate

This is for “ideal mixtures” of TBB in various substrates (e.g., polyurethane foam or typical house dust, which is made of skin cells which are continuously shed by the occupants). For real world mixtures, a thermodynamic activity coefficient (AC) is added.

(VP of Pure TBB)(Mole Fraction of TBB in substrate)(AC) = VP over the substrate

Given this reality, one might expect indoor vapor concentrations in the nanogram/m^3 realm or lower. This seems to be confirmed by measured values of TBB indoor in which the majority of these concentrations are probably associated with airborne particulate (i.e., dust).

2.2 TBB Uses

TBB is an additive flame retardant. It is a major brominated component in the flame retardant mixture Firemaster® 550 (FM550) (along with TBPH), which is the primary replacement for PBDEs in polyurethane foam used in furniture and baby products (Stapleton et al., 2009, 2011). The approximate ratio of TBB to TBPH in FM550 was reported to be 4:1 by Stapleton et al. (2008) and 2.5:1 by Bearr et al. (2010).

Historically, large volumes of brominated flame retardants have been used in furniture and electronics (Stapleton et al., 2008), and their use in furniture foam may be increasing (Stapleton et al., 2009).

2.3 TBB Human Exposure

TBB has been found in various environmental media including indoor air and ambient air. It was also found to a limited extent in a single study of food in Eastern China. It has also been measured or detected in or on consumer products, including child-specific products, furniture, and, to a small extent, in electronics. TBB has been measured in dust of many indoor environments, including homes, offices, automobiles, daycare centers, gyms, childcare centers, and an airplane. Stapleton et al. (2008) analyzed paired dust samples from different rooms in homes and found that levels of TBB (and TBPH) were higher in main living areas than bedrooms.

TBB in polyurethane foam or any polymer matrix is not chemically bound to the polymer. TBB can become available in contaminated house dust as products containing the TBB release the chemical over time. The primary route of human exposure would likely be through ingestion or inhalation of contaminated dust. Recent studies indicate that gymnasts may be exposed to TBB due to the presence of the chemical in foam matting (Carignan et al., 2013), and exposure to firefighters has been studied (Brown et al., 2014).

Davis et al. (2012) detected TBB in biosolid samples from waste water treatment plants in North Carolina and California and suggested that TBB and other PBDE replacement chemicals may be migrating out of consumer products into the ambient environment.

The available literature on concentrations of TBB in relevant environmental media and consumer products is heavily focused on concentrations in dust, reflecting what is reasonably considered to be perhaps the most important exposure pathway of concern for children and others. Children's overall exposure to flame retardants will be influenced by their hand-to-mouth behavior and subsequent ingestion of TBB containing material, and particularly dust. Frequent hand washing is associated with lower flame retardant levels on the hands (Stapleton et al. 2014). In addition, children could also receive exposure to TBB via dermal contact with foam surfaces or surfaces proximate to the foam, such as covers for foam. See the discussion below on dermal absorptions and exposure potential of an applied exposure to TBB (Section 2.3.5).

2.3.1 TBB in Indoor and Ambient Air

TBB has been measured in indoor and ambient air (Table 2-3). Indoors, TBB has been measured in houses, gyms, a daycare center, and indoor ventilation air. The concentrations of TBB measured in indoor air ranged from <0.330-143 ng/m^3 (La Guardia et al., 2015; Bradman et al., 2014; Carignan et al., 2013; Newton et al., 2015). As mentioned above, the vast majority of this exposure is expected to be from particulates and not vapors.

Table 2-3. TBB Concentrations in Indoor Air

Country	Location	Media	TBB Concentrations[1]	Reference	Notes
United States	Seattle, Washington	House	Mean: 6.93 ng/m^3	La Guardia et al., 2015	8-hour samples of <4 µm particulates (AirChek 2000 pump). 4 samples for each location.
		Gym	Mean: 5.41 ng/m^3		
		House	Mean: 22.0 ng/m^3		
		Gym	Mean: 143 ng/m^3		
	California	Daycare centers (n=40)	Median: <MDL Max: 16.23 ng/m^3	Bradman et al., 2014	Single rotary vane pump, 6-10 hours, MDL not specified
	Eastern U.S.	Gym, within 30 cm of the loose foam in the pit	26.1 ng/m^3	Carignan et al., 2013	Stationary air sampling pumps collected samples over a continuous 75 hour period

Country	Location	Media	TBB Concentrations[1]	Reference	Notes
United States		Gym, opposite side of gym away from the pit	5.01 ng/m^3		
Sweden	Stockholm	Indoor Ventilation air (n=12)	Median: <0.330 ng/m^3 (<330 pg/m^3) Range: <0.330-9.2 ng/m^3 (<330-9,200 pg/m^3)	Newton et al., 2015	Sampler configuration consisting of four sampling trains, each containing a GFF and two PUFs for collecting particle phase and gas phase contaminants

[1]For ease of comparison, all units are converted to ng equivalent. Original study units, if different, are shown in parentheses.
Max – maximum; MDL – maximum detection limit; GFF – glass fiber filters, PUF – polyurethane foam

TBB was measured in ambient air at concentrations much lower than those seen in indoor environments (Table 2-4). TBB was measured in multiple locations in the Great Lakes area with concentrations ranging from <0.000029-0.055 ng/m^3 (Ma et al., 2012). Newton et al. (2015) measured concentrations up to 0.00047 ng/m^3 in Stockholm, Sweden.

Table 2-4. TBB Concentrations in Ambient Air

Country	Location	Media	TBB Concentrations[1]	Reference	Notes
United States	Chicago, Illinois (n=86)	Ambient Air	Mean: 0.0048 ng/m^3 (4.8 pg/m^3) Range: 0.0005-0.019 ng/m^3 (0.5-19 pg/m^3)	Ma et al., 2012	24 hour samples every 12 days from 1 January 2005 to 31 December 2011 using high-volume air samplers. XAD-2 resin to trap vapor phase chemicals, quartz fiber filter to collect particles.
	Cleveland, Ohio (n=76)		Mean: 0.0057 ng/m^3 (5.7 pg/m^3) Range: 0.0005-0.055 ng/m^3 (0.5-55 pg/m^3)		
	Sturgeon Point, New York (n=95)		Mean: 0.00072 ng/m^3 (0.72 pg/m^3) Range: 0.00011-0.041 ng/m^3 (0.11-41 pg/m^3)		

Country	Location	Media	TBB Concentrations[1]	Reference	Notes
United States	Eagle Harbor, Michigan (n=100)	Ambient Air	Mean: 0.00057 ng/m^3 (0.57 pg/m^3) Range: 0.00005-0.0066 ng/m^3 (0.050-6.6 pg/m^3)	Ma et al., 2012	24 hour samples every 12 days from 1 January 2005 to 31 December 2011 using high-volume air samplers. XAD-2 resin to trap vapor phase chemicals, quartz fiber filter to collect particles.
	Sleeping Bear, Michigan (n=100)		Mean: 0.00097 ng/m^3 (0.97 pg/m^3) Range: 0.000086-0.0075 ng/m^3 (0.086-7.5 pg/m^3)		
Canada	Point Petre, Ontario (n=45)		Mean: 0.00031 ng/m^3 (0.31 pg/m^3) Range: 0.000074-0.00082 ng/m^3 (0.074-0.82 pg/m^3)		
Sweden	Stockholm	Outdoor air	Median: 0.00013 ng/m^3 (0.13 pg/m^3) Range: <0.000029-0.00047 ng/m^3 (<0.029-0.47 pg/m^3)	Newton et al., 2015	48-hour samples taken from April 30 to June 4, 2012 at seven locations using a high volume air pump, connected to a sampling head containing a GFF and two PUFs (samples are PUFs and GFFs combined). DF=75%

[1]For ease of comparison, all units are converted to ng equivalent. Original study units, if different, are shown in parentheses.
Max – maximum; GFF – glass fiber filters, PUF – polyurethane foam, DF – detection frequency

2.3.2 TBB in Water

No data were identified on TBB concentrations in drinking or other waters.

2.3.3 TBB in Food

One study was located with data on TBB concentrations in foods, comparing foods from towns directly impacted with electronic-waste (e-waste) facilities to foods from towns not involved with e-waste facilities (i.e., controls) (Labunska et al., 2015) (Table 2-5). Samples of foods from Eastern China included vegetable oil; fish; chicken, shrimp, duck, and pork muscles; chicken and

duck livers; and, chicken and duck eggs. Concentrations of TBB from the e-waste area ranged from <3.09 to 62.2 ng/g lipid weight, which were greater than that measured in the control foods (<0.20 to 11.7 ng/g lipid weight) (Labunska et al., 2015).

As noted in Section 2.3, Davis et al. (2012) detected TBB in biosolids (i.e., treated sewage sludge) from waste water treatment plants. Biosolids are applied to croplands and used as fertilizer in the U.S. (U.S. EPA, 2012), which might result in uptake of these chemicals by food crops and into human food.

Table 2-5. TBB Concentrations in Food

Country	Location	Media/ Area	TBB Concentrations	Reference	Notes
China	Eastern China	Foods from control town	Range: <0.20-11.7 ng/g lipid weight	Labunska et al., 2015	Foods included: vegetable oil; fish; chicken, shrimp, duck, and pork muscles; chicken and duck livers; and, chicken and duck eggs.
		Foods acquired near e-waste facilities	Range: <3.09-62.2 ng/g lipid weight		

2.3.4 TBB in Dust

Given the properties of TBB and the quantity of data found on dust and air levels, it would appear that dust ingestion is one of the primary sources of human exposure to TBB, and to a lesser extent, inhalation of TBB-contaminated house dust. TBB has been measured in dust in a variety of indoor settings in the U.S. (Table 2-6). TBB was reported in dust of homes at a wide range of concentrations from as low as <0.64 ng/g to as high as 75,000 ng/g (La Guardia et al., 2015; Shreder and La Guardia et al., 2014; Dodson et al., 2012; Hoffman et al., 2014; Stapleton et al., 2008; Brown et al., 2014; Johnson et al., 2013; Stapleton et al., 2009). Other tested areas (gyms, daycare centers, airplanes, universities, and fire station living quarters) also had a similar range of concentrations from <0.64 to 85,600 ng/g (La Guardia et al., 2015; Carignan et al., 2013; Bradman et al., 2014; Allen et al., 2013; Brown et al., 2014). Stapleton et al. (2014) and Hoffman et al. (2014) also measured dust on participants' hands (see Section 2.3.5).

In Canada, TBB was measured in household dust ranging from <0.30-22,251 ng/g (Shoeib et al., 2012, as cited by Brown et al.; Peng et al., 2015). The range of TBB concentrations reported in other countries (Belgium, Egypt, Germany, New Zealand, Pakistan, and Sweden) was significantly lower with 2,285 ng/g measured on living room floors in New Zealand as the highest concentration reported (Ali et al., 2012a).

Table 2-6. TBB Concentrations in Dust

Country	Location	Media/ Area	TBB Concentrations[1]		Reference	Notes
United States	Seattle, Washington	House (n=4)	Mean: 2,580 ng/g (2.58 µg/g)	Range: 500-7,100 ng/g (0.5-7.1 µg/g)	La Guardia et al., 2015	Settled dust samples (~1 g) were collected from SGA gymnasium floors (bare floor and carpet) at each of the four training facilities and residences of the four coaches.
		Gym (n=4)	Mean: 40,800 ng/g (40.8 µg/g)	Range: 12,300-73,500 ng/g (12.3-73.5 µg/g)		
	Eastern U.S.	Gym 1 (n=5)	Median: 28,900 ng/g (28.9 µg/g)	Range: 20,800-85,600 ng/g (20.8-85.6 µg/g)	Carignan et al., 2013	Gym 1- 1 dust sample from each of the women's gymnastics apparatus (vault, bars, beam, and floor) and 1 from within the loose foam pit. Collected in a cellulose extraction thimble inserted into the crevice tool of a Eureka Mighty-Mite canister vacuum cleaner.
		Gym 2 (n=3)	Median: 10 ng/g (0.01 µg/g)	Range: <1-320 ng/g (<0.001-0.35 µg/g)		Vacuumed dust from two locations: (1) within the loose foam pit and (2) from the surface of a landing mat that covered a small portion of the pit. Vacuum cleaner bag also collected from the gym's vacuum cleaner.

Country	Location	Media/ Area	TBB Concentrations[1]		Reference	Notes
United States	California	Early Childhood Education Center (n=39)	Median: 362.4 ng/g	Max: 14,812 ng/g	Bradman et al., 2014	High voltage surface sampler, ASTM D 5438-05
	Boston	House (n=20)	Median: 190 ng/g	Max: 1430 ng/g	Shreder and La Guardia et al., 2014	No range reported
	Airplane	Floor (n=19)	Median: 350 ng/g	Range: 200-3,000 ng/g	Allen et al., 2013	300 mg dust samples were collected and quantified using GC/EIMS by ion fragments
		Vent (n=19)	Median: 740 ng/g	Range: 300-5,000 ng/g		
	San Francisco Bay Area, California	Homes (2006) (n=16)	Median: 48 ng/g	Range: 4-740 ng/g	Dodson et al., 2012	
		Homes (2011) (n=16)	Median: 100 ng/g	Range: 45-5,900 ng/g		
	North Carolina	House (n=53)	Geo mean: 315.1 ng/g	No other values reported	Hoffman et al., 2014	Nylon thimble in hose attachment of home vacuum – 2 minutes.
	Boston, Massachusetts	House, main living area (n=16)	Geo mean: 322 ng/g	Range: <6.6-15,030 ng/g	Stapleton et al., 2008	Dust collected using Eureka Mighty-Mite Vacuum
		Bedroom (n=14)	Geo mean: 90.4 ng/g	Range: <10.6-378 ng/g		
		House (n=7)	Geo mean: 91.1 ng/g	Range: 35.7-669 ng/g		Dust collected using home vacuum cleaner
		House (n=30)	Geo mean: 97 ng/g	Range: 6.0-2,430 ng/g		Dust collected on hardwood and carpeted floors using a vacuum cleaner with a cellulous thimble

Country	Location	Media/ Area	TBB Concentrations[1]		Reference	Notes
United States	Northern California	Homes (n=59)	Geo mean: 310 ng/g	Range: <0.64-19,198 ng/g	Brown et al., 2014	2010 Childhood leukemia study; dust samples collected from vacuum cleaners
		Fire station living quarters (n=27)	Geo mean: 1,400 ng/g	Range: <0.64-29,007 ng/g		2010-2011 Firefighter occupational exposure study; dust samples collected from vacuum cleaners
	Massachusetts	House (n=38)	Geo mean: 409 ng/g	Max: 72,460 ng/g	Johnson et al., 2013	Detected in 47% of home vacuum samples
	Boston, Massachusetts	House (n=50)	Geo mean: 840 ng/g	Range: <450-75,000 ng/g	Stapleton et al., 2009	Household vacuum cleaner bag collection
Canada	Vancouver, BC	Homes (n=116)	Median: 120 ng/g	Range: <0.30-18,000 ng/g	Shoeib et al., 2012, as cited by Brown et al., 2012	
	Saskatoon, Saskatchewan	House (n=23)	Geo mean: 734 ng/g	15-22,251 ng/g	Peng et al., 2015	
Belgium		House	Median: 1 ng/g	(<2-436 ng/g)	Ali et al., 2011a	Dust samples collected by brushing 4 m^2 of floor surface. Samples were sieved through a 500 µm mesh sieve.
Egypt	Cairo	Homes (n=17)	Median: 0.8 ng/g	Range: 0.2-500 ng/g	Hassan and Shoeib 2015	Dust sampled from vacuum cleaner contents; ranges estimated from graph
		Work-places (n=14)	Median: 7.1 ng/g	Range: 0.7-200 ng/g		
		Cars (n=5)	Median: 5.81 ng/g	Range: 0.4-90 ng/g		

Country	Location	Media/ Area	TBB Concentrations[1]		Reference	Notes
Germany	Southern Germany and Munich	House (n=20)	Mean: 4.2 ng/g Median: <3.0 ng/g	Range: 3.0-13.6 ng/g	Fromme et al., 2014	8 samples above LOQ, LOQ=3.0 ng/g. household vacuum cleaner bags
New Zealand	Wellington, Wairarapa Christchurch and North Canterbury	Living Room Floors (n= 34)	Mean: 4 ng/g Median: 2 ng/g	Range: 2-2,285 ng/g	Ali et al., 2012a	Nilfisk Sprint Plus 1600W vacuum cleaner used on bare floors, rugs, and carpet.
Pakistan	Gujrat	Home (n=31)	Mean: 0.37 ng/g Median[2]: 0.03 ng/g	Range: <0.2-4.50 ng/g	Ali et al., 2012b	Dust samples collected with brush over 4 m^2 floor surface; sieved through a 500 µm mesh sieve; LOD not reported.
		Mosques (n=12)	Median: 0.03 ng/g	Range: 0.2-3 ng/g (estimated from graph)		
	Faisalabad	University (n=16)	Mean: 2 ng/g Median: 1.3 ng/g	Range: <0.2-16	Ali et al., 2014	Dust samples collected by brushing 4 m^2 of floor surface. Samples were sieved through a 500 µm mesh sieve.
		clothing (n= 15)	Mean: 0.6 ng/g Median: 0.7 ng/g	Range: <0.2-1.2 ng/g		
		Electronic (n=30) stores	Mean: 3 ng/g Median: 1 ng/g	Range: 0.2-15 ng/g		
Sweden	Stockholm	Various (homes, offices, schools, public spaces) (n=27)	Median: 9.1 ng/g	Range: <2.5-65 ng/g	Newton et al., 2015	Dust samples were collected immediately after a 24 hour air sampling period. Settled dust was collected from surfaces at least one meter above the floor.

Country	Location	Media/ Area	TBB Concentrations[1]		Reference	Notes
Thailand	Ayutthaya and Nonthaburi Provinces	E-waste storage facility (n=21)	Mean: 18 ng/g SD: 14	Range: <2-59 ng/g	Ali et al., 2011b	Dust samples were collected using 25-µm pore size nylon sampling socks inserted in the nozzle of a vacuum cleaner

[1]For ease of comparison, all units are converted to ng equivalent. Original study units, if different, are shown in parentheses.
[2]Ali et al., 2012b did not explain why the median reported is outside of the range of all values.
Max – maximum; Geo mean – geometric mean; LOQ – limit of quantification ; LOD – limit of detection; SD – standard deviation

2.3.5 TBB on Skin

The potential for dermal TBB exposure has been investigated in several studies that measured TBB on the hands of residents (<0.60-154 ng/g) (Hoffman et al., 2014; Stapleton et al., 2014) and gymnasts (8.05-770 ng/wipe) (Carignan et al., 2013) (Table 2-7).

Table 2-7. Concentrations of TBB Measured on Skin

Country	Location	Media/ Area	TBB Concentrations	Reference	Notes
United States	North Carolina	Hands (n=43)	Geo mean: 4.1 ng Range: <0.60-154 ng	Stapleton et al., 2014	Hands wiped with sterile gauze wipe soaked in isopropyl alcohol
		Hands (n=53)	Geo mean: 31.4 ng/g	Hoffman et al., 2014	Hands wiped with sterile gauze wipe soaked in isopropyl alcohol; no range given
	Eastern U.S.	Hands before practice (n=11)	Median: 60.8 ng/wipe Range: 8.05-651 ng/wipe	Carignan et al., 2013	Analyzed hand wipes from gymnasts before and after 2.5 hour practice; 100% detection frequency. Median increase from before to after: 152 ng/wipe; 100% detection frequency
		Hands after practice (n=11)	Median: 22 ng/wipe Range: 34.9-770 ng/wipe		

Geo – geometric

2.3.6 TBB in Consumer Products

Only a few studies were located that tested for TBB in consumer products, but a variety of products have been tested (Table 2-8). TBB has been found in a variety of baby products (Stapleton et al., 2011), furniture (Stapleton et al., 2009; Stapleton et al., 2012), mattresses (Ali et al., 2012a), electronics and household appliances (Ali et al., 2011b), and foam used in gymnastic pits (La Guardia et al., 2015). Primary exposure routes for TBB in consumer products would be oral ingestion (e.g., children's mouthing of materials or products, incidental ingestion of house dust) and potentially dermal exposure. See the discussion below on dermal absorptions and exposure potential of an applied exposure to TBB (Section 2.6). Off-gassing of TBB as a vapor will not occur to any reasonable extent because of its very low vapor pressure; however, inhalation of re-suspended TBB-contaminated house dust could provide a source of exposure, especially in dusty homes.

2.3.6.1 TBB in Children and Baby Products

TBB was found in polyurethane (PU) foam samples from baby products, including car seats, changing table pads, mattresses, baby carriers, and rocking chairs. Stapleton and colleagues (2011) reported levels of TBPH and TBB (measured together) ranging from 5.85×10^6 ng/g to 4.25×10^7 in 17 of 101 PU foam samples tested.

2.3.6.2 TBB in Furniture and Bedding

Stapleton et al. (2012) detected TBB in PU foam samples from furniture; the sum of TPP, TBB, and TBPH ranged from 5.18×10^6 ng/g to 36.85×10^6 in 13 of 102 PU foam samples. Ali et al. (2012a) vacuumed dust from mattresses in New Zealand, and the median concentration of TBB was 3 ng/g. These represent the single largest concentration of TBB found in residences. Stapleton et al. (2009) detected TBB in 1 of 26 consumer products (mostly furniture items) purchased between 2003 and 2009; TBB and TBPH were measured together (4.2% by weight) in a couch purchased in 2007.

2.3.6.3 TBB in Electronic Products

TBB was measured in a number of electronic waste products at an e-waste facility in Thailand, including PCs, printers, TVs, and other appliances. Concentrations ranged from <2 ng/g to 59 mg/g, with a median of 13 ng/g (Ali et al., 2011b).

Table 2-8. TBB Concentrations in Consumer Products

Country	Item	Type	TBB Concentrations[1]	Reference	Notes
United States	Couch	PU foam	4.2% by weight (TBB and TBPH together)	Stapleton et al., 2009	One couch tested, purchased in 2007
	Gymnastic pit foam block	Foam (n=6)	Range: 1,400,000-13,700,000 ng/g) (1,400-13,700 µg/g)	La Guardia et al., 2015	4 foam blocks from Gym #4 pit, 1 from Gym #2 pit, 1 new block from Gym #4 storage
	Baby products, donated used and purchased new	PU foam from car seats, changing table pads, mattresses, rocking chairs (n=101)	Mean: 18,510,000 ng/g (18.51 mg/g) Range: 5,850,000-42,500,000 ng/g (5.85-42.5 mg/g) (TBB/TBPH measured together)	Stapleton et al., 2011	TBB/TBPH was found in 17 of 101 baby products sampled. TBB/TBPH comprise 50% of the overall mixture of FM 550
	Furniture	PU foam (n=102)	Mean: 19,760,000 ng/g (19.76 mg/g) Range: 5,180,000-36,850,000 ng/g (5.18 - 36.85 mg/g) Sum of TPP, TBB, and TBPH	Stapleton et al., 2012	Donated PU foam samples from numerous cities in U.S. Measured as FM 550; found in 13 of 102 samples.
New Zealand	Mattress	Mattress (n=16)	Median: 3 ng/g (no range provided)	Ali et al., 2012a	Any mattress covers and under sheets were left on and mattress vacuumed evenly and thoroughly for dust collection

Country	Item	Type	TBB Concentrations[1]	Reference	Notes
Thailand	E-waste Storage Facility	PC + Printer (n=12)	Range: 4-59 ng/g	Ali et al., 2011b	Dust samples were collected using 25 µm pore size nylon sampling socks inserted in the nozzle of a vacuum cleaner in a room containing the products listed under type.
		TV (n=2)	Range: <2 -9 ng/g		
		PC + TV (n=1)	11 ng/g		
		Fridge + Washing Machine (n=1)	10 ng/g		
		TV + Video Recorder (n=1)	36 ng/g		
		TV + Fan (n=1)	5 ng/g		
		TV + Fan + Microwave (n=1)	8 ng/g		
		Rice cooker + Photocopier (n=1)	13 ng/g		
		Typewriter + Video Recorder (n=1)	26 ng/g		

[1]For ease of comparison, all units are converted to ng equivalent. Original study units, if different, are in shown in parentheses.
ND – not detected; PU – polyurethane foam

2.4 TBB ADME and Biomonitoring Studies

Absorption. Little is known about the toxicokinetics of TBB. Limited evidence indicates that it is absorbed following oral exposure. Hoffman et al. (2014) administered a single oral dose of TBB to rats as Firemaster® 550 solution (~3.5 mg/kg) in a food treat pellet. Systemic bioavailability of TBB was demonstrated by urinary elimination of the TBB metabolite 2,3,4,5-tetrabromobenzoic acid (TBBA) (Hoffman, 2014).

Distribution. The TBB content of 102 human female serum samples and 105 breast milk samples was evaluated in a cross-sectional study. Samples were randomly selected from the biobank of a cohort study of nursing women in Sherbrooke, Québec, Canada; no exposure cohorts were designated. TBB was detected in 56.9% of serum samples and 78.1% of breast milk samples. Based on the information provided in the study, it is not possible to determine if a correlation exists between TBB serum levels and breast milk levels (Zhou et al., 2014). Metabolites of TBB in the samples were not evaluated.

Metabolism. Human liver microsomes rapidly metabolized TBB to TBBA via cleavage of the 2-ethylhexyl chain without requiring any added cofactors. TBB was also metabolized to TBBA by purified porcine carboxylesterase at a rate (6.29 ± 0.58 nmol/min/mg protein) that was much greater than that catalyzed by microsomes. The estimated K_m and V_{max} for TBB metabolism by human microsomes were 11.1 ± 3.9 μM and 0.644 ± 0.144 nmol/min/mg protein, respectively. A similar K_m of 9.3 ± 2.2 μM was calculated for porcine carboxylesterase, indicating similar enzyme specificity. Mass balance analysis suggested that TBBA formation appeared to account for approximately 30% of TBB metabolized by liver microsomes, suggesting the likely presence of other uncharacterized metabolites. It should be noted that previous studies have shown that human and porcine carboxylesterases catalyze similar metabolic reactions with differences only in the observed reaction rates (Roberts, 2012). In studies comparing the capacity of human and rat tissues to metabolize TBB, human liver microsomes were determined to metabolize TBB at a rate approximately 60% of that observed for rats (Roberts, 2012), and so it appears there is similarity in the metabolism of TBB by rats, pigs and humans.

It is expected that rapid metabolism of TBB will reduce its bioaccumulation potential; however, the kinetic disposition of TBBA is unknown. Although Roberts et al. (2012) did not identify phase II metabolites of TBBA, other products of TBB metabolism have not been investigated.

A limited *in vivo* study conducted in rats further supports the biotransformation of TBB to TBBA. Following a single oral dose of TBB (as Firemaster® 550, ~3.5 mg/kg), elevated levels of TBBA were detected in urine over a 24 hour period (Hoffman, 2014). The possibility that other metabolites were produced was not evaluated. Further support is provided by a cross-sectional study where TBBA was detected in the urine of 27% of adults and 70% of children (Butt, 2014).

Elimination. *In vitro* evidence indicates that TBB is metabolized to TBBA. TBBA was detected in the urine of rats given a single oral dose of Firemaster® 550. Maximum mean urinary concentrations occurred within 2 to 3 hours following exposure. This was followed by a rapid decrease in concentration, which leveled off around 6 to 8 hours post-exposure. The study did not provide information on either cumulative excretion or volume of urine collected; therefore, it is not possible to determine the fraction of the administered dose renally eliminated during the collection period (24 hours). At the end of the collection period, the mean urinary concentration was in the range of 60% of the maximum urinary concentration, indicating that dose elimination continued well beyond the end of the urinary collection period. No information on systemic kinetics (plasma area under the curve, maximum plasma concentration, serum half-life, etc.) was provided. Together these data indicate that TBB is orally bioavailable and is metabolized to TBBA, which is eliminated in the urine to an unknown extent. Urinary elimination of TBB was not evaluated (Hoffman et al., 2014). Likewise, in a human study, TBBA was identified in

72.4% of urine samples collected from 64 adult subjects. Unfortunately, the study authors were not able to determine the route of exposure (Hoffman et al., 2014).

Biomonitoring: Several biomonitoring studies have been conducted in the U.S. and Canada (Table 2-9). Hoffman et al. (2014) measured urinary metabolite levels of TBBA and used TBBA as a biomarker for TBPH and TBB exposure. The authors measured household dust levels and took hand wipe and urine samples from adults in North Carolina. Approximately seventy-two percent (72.4%) were found to have TBBA in their urine at levels of up to 340 ng/g, with a geometric mean of 5.6 ng/g. Levels of TBB (and TBPH) in dust were positively correlated with corresponding levels of each in the hand wipes; TBB in hand wipes was positively correlated with the urinary TBBA levels.

Butt et al. (2014) measured TBBA in urine collected from 21 mother-child pairs (most sampled one child per pair; five pairs sampled two children each; one mother did not provide one child's urine; total of 22 mothers and 26 children) in a U.S. pediatric clinic in Princeton, NJ. Participants were recruited between August 2013 and January 2014, and children were between 1 and 5 years of age. Due to insufficient urine volume in three samples, there were only 23 samples tested for TBBA. TBBA was detected in urine of 27% of the mothers (<3.0-62.2 ng/mL) and 70% of children (<3.0-84.9 ng/mL).

In Canada, Zhou et al. (2014) recorded levels in human serum and breast milk collected in 2008-2009. TBB was found in 56.9% of 102 serum samples, with levels ranging from below detection (LOD =0.38 ng/g) to 68 ng/g lipid weight, with a geometric mean of 1.3 ng/g lipid weight. TBB was found in 78.1% of the 105 milk samples with a geometric mean of 1.3 ng/g lipid weight, and levels ranging from below level of detection (LOD=0.03 ng/g) to 24 ng/g lipid weight.

Johnson et al. (2013) measured serum hormone levels and estimated corresponding exposure by measuring concentrations of TBPH and TBB in house dust. Serum hormone data were from 62 men recruited through a U.S. infertility clinic from 2002 to 2003 and household dust was sampled from donated existing vacuum bags for a subset (n=38). TBPH and TBB were detected in 63% (geometric mean 377 ng/g) and 47% (409 ng/g), respectively, of dust samples. TBPH exposure (as estimated from dust samples) was positively associated with total T3 (triiodothyronine).

Table 2-9. TBB Biomonitoring Data

Country	Tissue/fluid	TBB Concentrations		Reference	Notes
United States	Urine (TBBA) (n=53)	Geo mean: 5.6 pg/mL TBBA	Max: 340 ng/g	Hoffman et al., 2014	Hand wipe and urine samples from adults in North Carolina. 76.9% had TBBA levels detected. Levels of TBB in hand wipes positively correlated with urinary TBBA. 1 urine sample had insufficient volume.
	Urine (TBBA) (n=22 mother; n=23 children)	Geo mean: Mother - not available (detection frequency < 50%) Child - 7.4 ng/mL	Mother: Range: <3.0-62.2 ng/mL Child Range: <3.0-84.9 ng/mL	Butt, 2014	MDL = 3.0 ng/mL; 21 mother/toddler pairs (some mothers had 2 children) recruited between August 2013 and January 2014. TBBA detected in 27% of adults and 70% of children.
United States	Serum hormone, T3 (n=38)	T3 concentrations not provided		Johnson et al., 2013	62 men, aged 18-54 years recruited from couples seeking infertility treatment; TBPH (but not TBB) exposure (estimated from home vacuum bag dust) positively associated with T3 for subset of 38 men. TBB was detected in 47% (409 ng/g) of dust samples.
Canada (Sherbrooke, Quebec)	Maternal serum (n=100)	Median: 1.6 ng/g lw Mean: 5.4 ng/g lw	Range: <0.38 -68 ng/g lw	Zhou et al., 2014	100 paired samples from nursing women. TBB detected in 56.9% of serum samples; 78.1% of breast milk samples.
	Breast milk (n=100)	Median: 0.41 ng/g lw Mean: 1.3 ng/g lw	<0.03-24 ng/g lw		

ND – not detected; Max – maximum; Geo – geometric; TBBA – 2,3,4,5- tetrabromobenzoic acid,; lw – lipid weight; T3 – Triiodothyronine

2.5 TBB Exposure Assessments and Estimates

We did not locate any authoritative reviews on TBB that estimated intakes or exposure. Fromme et al. (2014) calculated the daily intake via dust consumption for adults and toddlers for TBB based upon their measurements of TBB in dust in German homes. The "average" adult intake was estimated at 1 pg/kg bw/day (5 pg/kg bw/day for the 95th percentile intake) and 8 pg/kg bw/day average (63 pg/kg bw/day 95th percentile) for toddlers.

Higher estimates could be made for children by using the highest levels of TBB in contaminated dust with a dust ingestion rate of 100 mg/day for a 15 kg child.

2.6 TBB Discussion

TBB is a widely used flame retardant in the U.S. and has been measured in consumer products, dust, and air. Concentrations of TBB are highest in the dust of indoor environments, and contact with dust appears to be the main source of exposure for consumers to TBB. The highest dust concentrations of TBB were measured in indoor rooms that were presumably proximate to TBB-treated foam. Normal hand-to- mouth activity is a primary known or established route of exposure for semi-volatile compounds that partition to dust. Incidental hand-to-mouth activity occurs over a person's entire lifetime, but it occurs most often and most significantly in children, and therefore, children may have greater exposures than adults. The U.S. EPA estimates daily dust/dirt ingestion rates for children in the range of 50 to 100 mg per day, and a significantly lower rate for adults of 30 mg per day (central tendency) in the general population (U.S. EPA, 2011a).

An area of uncertainty is the percutaneous exposure potential from dermal contact with or ingestion from mouthing of objects containing TBB. The general mechanism for TBB diffusion out of treated plastics including foam and into dust is relatively well understood. Similarly, the potential for hand-to-mouth transfer of dust is understood and established. This is not the case for dermal or direct mouthing transfer of this flame retardant from contact with treated objects. The potential dermal or direct oral (mouthing) exposure to TBB as it is diffusing and being "expressed" from the treated foam is not well understood or documented. Most foam is covered, and the manner and degree of transfer from the foam to the cover's surface for potential mouthing or dermal exposure is another source of uncertainty.

The very high pK_{ow} of TBB would be predicted to limit its rate of dermal absorption because water in the viable dermis will restrict the rate of absorption to the systemic circulation. Also, molecules of TBB in contact with the skin would be expected to have a reasonable rate of penetration into the stratum corneum (SC) or the very top layer of dead and dry skin cells. If left undisturbed, the TBB molecules would be expected ultimately to diffuse into the viable dermis where they would slowly be absorbed. Working against this eventuality is the dynamic

mechanism of desquamation or human skin shedding. This continuous loss of skin cells occurs at a rate that might be expected basically to eliminate the initially absorbed TBB in the SC as these skin layers turn-over or shed completely, approximately every two weeks (IPCS, 2006; U.S. EPA, 2004). The applied dermal dose of TBB could be particularly important with regard to children's items, such as changing table pads, mattresses, and car seats.

Availability, transfer, and ingestion via child-mouthing of these items and treated furniture in general are areas of significant uncertainty.

It should be noted that this report compiles data from a variety of sources. We have not evaluated the quality of the studies and their results; rather we included all the relevant data we found. The estimates described in the exposure assessments are presented "as is" without a detailed analysis or critique of the methodology, assumptions, or underlying data quality.

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

3.1 TBPH Chemical and Physical Properties

Bis(2-ethylhexyl) tetrabromophthalate (TBPH) is a flame retardant being used as one of the replacements for PBDE flame retardants. It is a solid with a melting point of 229.2°C. Its water solubility value of 1.98 x 10^{-11} mg/L (estimated from logK_{ow}) indicates that it has very low solubility in water, but it is expected to be soluble in most solvents and adsorb to solids (like house dust) and sediments in water, based on an estimated logK_{ow} value of 11.95. The estimated vapor pressure value for TBPH is very low at 1.71 x 10^{-11} mg Hg at 25ºC. These properties indicate that TBPH will exist primarily in particulate phases in the atmosphere.

Limited volatilization from water surfaces is expected based on an estimated Henry's Law constant of 3.1 x 10^{-7} atm-cu m/mole (estimated at 25°C). Any release to natural water systems would be expected to partition into sediment where it would be anticipated to remain pending possible long-term degradation.

TBPH is an additive flame retardant and one of the alternative replacements for the PBDE flame retardants used in polyurethane foam (Stapleton et al., 2008). TBPH and 2-Ethylhexyl-2,3,4,5-tetrabromobenzoate (TBB) (CAS No. 183658-27-7) are components of several Firemaster® commercial flame retardant mixtures (Roberts et al., 2012). Both TBPH and TBB are listed as high production volume chemicals by the U.S. EPA (U.S. EPA, 2009a as cited in Springer et al., 2012).

Figure 3-1. Molecular Structure of TBPH (ChemIDPlus, 2014)

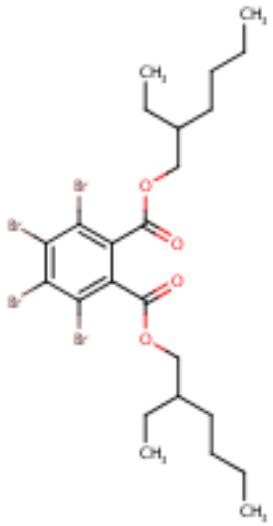

Table 3-1. CAS Registry Number and Synonyms for TBPH (ChemIDPlus, 2014; CalEPA, 208)

CAS registry/RN	26040-51-7
Synonyms	Bis(2-ethylhexyl) tetrabromophthalate, TBPH, BEH-TBP, BEH-TEBP, EINECS 247-426-5, Phthalic acid, tetrabromo-, di(2-ethylhexyl) ester; bis(2-ethylhexyl)-3,4,5,6-tetrabromophthalate

Table 3-2. Physical and Chemical Properties of TBPH (ChemIDPlus, 2014; HSDB, 2013b; ChemNet, 2015; Health and Environmental Horizons, 2003; PubChem, 2015)

Molecular Formula	C24-H34-Br4-O4
Molecular Weight	706.1446
Melting Point	229.2 C (Health and Environmental Horizons, 2003)
Boiling Point	584.8C (ChemNet, 2015)
Density	1.529 g/cm^3 (ChemNet, 2015)
Solubility (in water)	1.98 x10^{-11} mg/L (estimated, from LogKow)
Log K_{ow}	11.95 (predicted, U.S. EPA, 2008)
Vapor Pressure	1.71 x 10^{-11} mg Hg at 25ºC
Henry's Law Constant	3.1X10-7 atm-cu m/mole (estimated, PubChem, 2015)

Semi-Volatile Organic Compounds (SVOCs), such as TBPH, are characterized by relatively high molecular weight, low vapor pressure/volatility, low solubility in water and a high octanol-water partition coefficient. To a significant degree, these properties determine the fate of TBPH in the environment, which impacts the potential for human exposure. The high octanol-water partition coefficient means it will be lipophilic or "fat loving," and will partition into any sediment layers in an environmental water column. In the indoor environment, it will essentially not be present in the air as a vapor but will readily partition into (and be present in) available organic rich substrates like house dust.

Because of its properties and fate in the indoor environment, the vapor pressure (VP) of pure TBPH indicates that it cannot exist in ambient air at significant concentrations as a vapor:

(1.7 x 10^{-11} torr/760 torr) (1,000,000) (706.1/24.4) = 6.5 x 10^{-7} mg/m^3

This is approximately 0.7 ng/m^3.

The above model estimates the maximum level of airborne contamination possible over at large surface area of pure TBPH. In reality, TBPH would never be expected to exist as a pure material indoors. Initially, it is in the polymer matrix, and, after it diffuses out of the matrix, it is

associated with house dust that is primarily composed of human skin cells, which have been shed in a process known as desquamation. As such, house dust can be thought of as an organic substrate and the primary route for the accumulation of and exposure to TBPH.

3.2 TBPH Uses

TBPH is an additive flame retardant. It is a major brominated component in the flame retardant mixture Firemaster® 550 (FM550) (along with TBB), which is the primary replacement for pentaBDEs in polyurethane foam used in furniture and baby products (Stapleton et al., 2009, 2011). The approximate ratio of TBB to TBPH in FM550 was reported to be 4:1 by Stapleton et al. (2008) and 2.5:1 by Bearr et al. (2010). TBPH is also present in the commercial mixture DP-45, which is used as a flame retardant plasticizer for polyvinylchloride (PVC) applications (Chemtura, 2007a, as cited in Davis et al., 2012). Additional uses for flame retardants containing TBPH include PVC, neoprene, wire insulation, carpet backing, coated fabrics, and wall coverings (Covaci et al., 2011, as cited in Springer, 2012)

Historically, large volumes of brominated flame retardants have been used in furniture and electronics (Stapleton et al., 2008), and their use in furniture foam may be increasing (Stapleton et al., 2009).

3.3 TBPH Human Exposure

TBPH has been found in various media including indoor and ambient air, and, to a limited extent, food, and water. It has also been measured or detected in consumer products, including child-specific products, furniture, and electronics. TBPH has been measured in dust samples from many types of indoor environments, including homes, gyms, childcare centers, and an airplane, as well as in indoor air in homes, gyms, and a daycare center. Stapleton et al. (2008) analyzed paired dust samples from different rooms in homes and found levels of TBPH (and TBB) were higher in main living areas than bedrooms.

TBPH in polyurethane foam or any polymer matrix is not chemically bound to the polymer. TBPH can become available in air and dust as it diffuses out of products or the plastic degrades to dust over time. The primary route of human exposure would likely be through ingestion or inhalation of contaminated dust. Because the room temperature vapor pressure of TBPH is low, significant exposure to TBPH vapor is not expected. Recent studies indicate that gymnasts may be exposed to TBPH due to the presence of the chemical in foam matting (Carignan et al., 2013), and exposure of firefighters has been studied (Brown et al., 2014).

TBPH was detected in sewage sludge from wastewater treatment plants that discharge effluent into the San Francisco Bay (Betts, 2008; CalEPA 2008). Davis et al. (2012) detected TBPH in biosolid samples from waste water treatment plants in North Carolina and California and

suggested that TBPH and other PBDE replacement chemicals may be migrating out of consumer products into the ambient environment.

The available literature on concentrations of TBPH in relevant environmental media and consumer products is heavily focused on concentrations in dust and air. Dust may reasonably be considered to be the most important exposure pathways of concern for children and others. Children's overall exposure to flame retardants will be influenced by their hand-to-mouth behavior and subsequent ingestion of TBPH-containing materials, particularly dust. Frequent hand washing is associated with lower flame retardant levels on the hands (Stapleton et al., 2014). In addition, children can also receive exposure to TBPH via dermal contact with polymer surfaces.

3.3.1 TBPH in Indoor and Ambient Air

TBPH air concentrations have been measured in daycares, gyms, and other indoor air (Table 3-3). In the U.S., the concentrations of TBPH measured in indoor air ranged from less than the method detection limit to as high as 34.3 ng/m^3 (Bradman et al., 2014; Carignan et al., 2013; La Guardia et al., 2015). In Sweden, indoor air measurements of TBPH ranged from <0.035-0.150 ng/m^3 (Newton et al., 2015) As noted above, the vapor pressure of TBPH is very low, thus any measured concentration in air is likely associated with particulates, perhaps re-suspended contaminated dust.

Table 3-3. TBPH Concentrations in Indoor Air

Country	Location	Media	TBPH Concentrations[1]	Reference	Notes
United States	Seattle, Washington	House	Mean: 21.4 ng/m^3	La Guardia et al., 2015	8-hour samples of <4 µm particulates (AirChek 2000 pump); 4 samples for each location.
		Gym	Mean: 11.4 ng/m^3		
		House	Mean: 8.61 ng/m^3		
		Gym	Mean: 34.3 ng/m^3		
	California	Daycare centers (n=40)	Median: <MDL Max: 5.39 ng/ m^3	Bradman et al., 2014	Single rotary vane pump, 6-10 hours, MDL not specified

Country	Location	Media	TBPH Concentrations[1]	Reference	Notes
United States	Eastern U.S.	Gym, within 30 cm of the loose foam in the pit	16.9 ng/m^3	Carignan et al., 2013	Stationary air sampling pumps collected samples over a continuous 75 hour period beginning prior to practice and ending after practice.
	Eastern U.S.	Gym, opposite side of gym away from the pit	2.66 ng/m^3		
Sweden	Stockholm	Indoor air (n=12)	Median:<0.035 ng/m^3 (<35 pg/m^3) Range: <0.035-0.150 ng/m^3 (<35 150 pg/m^3)	Newton et al., 2015	Sampler configuration consisting of four sampling trains, each containing a GFF and two PUFs for collecting particle phase and gas phase contaminants

[1]For ease of comparison, all units are converted to ng equivalent. Original study units, if different, are shown in parentheses.
Max – maximum; MDL – Method Detection Limit; GFF – Glass Fiber Filters; PUF – Polyurethane Foam

Limited data are available regarding TBPH concentrations in ambient air, with concentrations generally lower overall than what was found in indoor air. TBPH was measured in multiple locations in the Great Lakes area with concentrations ranging from 0.00011 to 0.290 ng/m^3 (Ma et al., 2012). See Table 3-4 below for TBPH concentrations in ambient air.

Table 3-4. TBPH Concentrations in Ambient Air

Country	Location	Media	TBPH Concentrations[1]	Reference	Notes
United States	Chicago, Illinois (n=86)	Ambient Air	Mean: 0.0062 ng/m^3 (6.2 pg/m^3) Range: 0.00036-0.076 ng/m^3 (0.36-76 pg/m^3)	Ma et al., 2012	24 hour samples every 12 days from January 1, 2005 to December 31, 2011 using high-volume air samplers: XAD-2 resin to trap vapor phase chemicals, quartz fiber filter to collect particles
	Cleveland, Ohio (n=76)		Mean: 0.014 ng/m^3 mean (14 pg/m^3 Range: 0.00047-0.290 ng/m^3 (0.47-290 pg/m^3)		24 hour samples every 12 days from January 1, 2005 to December 31, 2011 using high-volume air samplers: XAD-2 resin to trap vapor phase chemicals, quartz fiber filter to collect particles
	Sturgeon Point, New York (n=95)		Mean: 0.0009 ng/m^3 (0.9 pg/m^3) Range: 0.00014-0.017 ng/m^3 (0.14-17 pg/m^3)		
	Eagle Harbor, Michigan (n=100)		Mean: 0.0011 ng/m^3 (1.1 pg/m^3) Range: 0.00013-0.032 ng/m^3 (0.13-32 pg/m^3)		
	Sleeping Bear, Michigan (n=100)		Mean: 0.0011 ng/m^3 (1.1 pg/m^3) Range: 0.00011-0.016 ng/m^3 (0.11-16 pg/m^3)		
Canada	Point Petre, Ontario (n=45)		Mean: 0.00079 ng/m^3 (0.79 pg/m^3) Range: 0.00018-0.0037 ng/m^3 (0.18-3.7 pg/m^3)		

[1]For ease of comparison, all units are converted to ng equivalent. Original study units, if different, are shown in parentheses.

3.3.2 TBPH in Water

TBPH concentrations in drinking water were not located. However, one study was available measuring TBPH concentrations in a few water bodies in Spain. Average concentrations reported ranged from 1.3 to 2.2 ng/L (Valls-Cantenys et al., 2013). See Table 3-5 below.

Table 3-5. TBPH Concentrations in Water

Country	Location	Media	TBPH Concentrations	Reference	Notes
Spain	Western Coast	Sea	Mean: 2.1 ng/L	Valls-Cantenys et al., 2013	"Several" samples taken
		River	Mean: 2.2 ng/L		
		Ria (an inlet)	Mean: 1.3 ng/L		

3.3.3 TBPH in Food

One study was located with data on TBPH concentrations in foods comparing foods from towns directly impacted with electronic-waste (e-waste) facilities to towns not involved with e-waste facilities (i.e., controls) (Labunska et al., 2015) (Table 3-6). Samples of foods from Eastern China included vegetable oil; fish; chicken, shrimp, duck, and pork muscles; chicken and duck livers; and, chicken and duck eggs. Concentrations of TBB from foods in areas where e-waste occurs ranged from 0.81 to 16.3 ng/g lipid weight, which are greater than the control foods (ranged from <0.25 to 9.32 ng/g lipid weight) (Labunska et al., 2015).

As noted in Section 2.3, Davis et al. (2012) detected TBB in biosolids (i.e., treated sewage sludge) from waste water treatment plants. Biosolids are applied to croplands and used as fertilizer in the U.S. (U.S. EPA, 2012), which might result in uptake of these chemicals by food crops and into human food.

Table 3-6: TBPH Concentrations in Food

Country	Location	Media/ Area	TBPH Concentrations	Reference	Notes
China	Eastern China	Foods from control town	Range: <0.25-9.32 ng/g lw	Labunska et al., 2015	Foods included: vegetable oil; fish; chicken, shrimp, duck, and pork muscles; chicken and duck livers; and, chicken and duck eggs.
		Foods acquired near e-waste facilities	Range: 0.81-16.3 ng/g lw		

lw – lipid weight

3.3.4 TBPH in Dust

Given the properties of TBPH and the quantity of data found on dust, it would appear that dust ingestion is one of the primary sources of human exposure to TBPH.

TBPH has been measured in dust in a variety of indoor settings in the U.S. and other countries (Table 3-7). In the U.S., TBPH was reported in dust of homes at a wide range of concentrations from <0.64 ng/g to 47,110 ng/g (La Guardia et al., 2015; Shreder and La Guardia et al., 2014; Springer et al., 2012; Stapleton et al., 2014; Stapleton et al., 2008; Dodson et al., 2012; Brown et al., 2014; Hoffman et al., 2014; Johnson et al., 2013; Stapleton et al., 2009). Stapleton et al. (2014) and Hoffman et al. (2014) also measured dust on participants' hands. Other tested areas (gyms, offices, cars, daycare centers, airplanes, and fire station living quarters) had a similar range of concentrations from <0.64 to 44,900 ng/g (La Guardia et al., 2015; Carignan et al., 2013; Bradman et al., 2014; Allen et al., 2013; Springer et al., 2012; Brown et al., 2014).

In Canada, TBPH was measured in household dust ranging from 10 to 22,251 ng/g (Shoeib et al., 2012, as cited by Brown et al., 2012; Peng et al., 2015). A lower range of concentrations (0.05-2,274 ng/g) were measured in dust in a number of other countries (Belgium, Egypt, Germany, New Zealand, Pakistan, and Sweden) (Hassan and Shoeib 2015; Ali et al., 2014; Ali et al., 2012a; Fromme et al., 2014; Ali et al., 2012b; Newton et al., 2015; Ali et al., 2011b).

Table 3-7. TBPH Concentrations in Dust

Country	Location	Media/ Area	TBPH Concentrations[1]		Reference	Notes
United States	Seattle, Washington	Gym (n=4)	Mean: 24,300 ng/g (24.3 µg/g)	Range: 4,800-44,900 ng/g (4.8-44.9 µg/g)	La Guardia et al., 2015	Settled dust samples (~1 g) were collected from SGA gymnasium floors (bare floor and carpet) at each of four training facilities and residences of the four coaches.
		House (n=4)	Mean: 1,850 ng/g (1.85 µg/g)	Range: 700-3,100 ng/g (0.7-3.1 µg/g)		
United States	Eastern U.S.	Gym 1 (spring 2012) (n=5)	Median: 30,000 ng/g (30.0 µg/g)	Range: 17,300-44,900 ng/g (17.3-44.9 µg/g)	Carignan et al., 2013	Gym 1- 1 dust sample from each of the women's gymnastics apparatus (vault, bars, beam, and floor) and 1 from within the loose foam pit. Collected in a cellulose extraction thimble inserted into the crevice tool of a Eureka Mighty-Mite canister vacuum cleaner.

Country	Location	Media/ Area	TBPH Concentrations[1]		Reference	Notes
United States	Eastern U.S.	Gym 2 (fall 2010) (n=3)	Median: 60 ng/g (0.06 µg/g)	Range: <1-210 ng/g (<0.001-0.21 µg/g)	Carignan et al., 2013	Vacuumed dust from two locations: (1) within the loose foam pit and (2) from the surface of a landing mat that covered a small portion of the pit. Collected the gym vacuum cleaner bag that had been used in all areas of the gym including the office and lobby
	California	Early Childhood Education Center dust (n=39)	Median: 132.9 ng/g	Max: 7,489.7 ng/g	Bradman et al., 2014	High voltage surface sampler, ASTM D 5438-05
	Boston, Massachusetts	House (n=20)	Median: 115 ng/g	Max: 435 ng/g	Shreder and La Guardia et al., 2014	No range provided
	Airplane	Floor (n=19)	Median: 640 ng/g	Range: 400-1,600 ng/g	Allen et al., 2013	300 mg dust samples were collected and quantified using GC/EIMS by ion fragments
		Vent (n=19)	Median: 1200 ng/g	Range: 350-3,600 ng/g		
	Boston, Massachusetts	Office (n=31)	Median: 410 ng/g	Range: 95-15,500 ng/g Range	Springer et al., 2012	
		Homes (n=31)	Median: 150 ng/g	Range: <4-12,400 ng/g range		

Country	Location	Media/ Area	TBPH Concentrations[1]		Reference	Notes
United States	Boston, Massachusetts	Car (n=20)	Median: 400 ng/g	Range: <36–4,830 ng/g range	Springer et al., 2012	
	North Carolina	Household (n=30)	Geo mean: 604 ng/g	Range: 82.9-20,960 ng/g	Stapleton et al., 2014	Dust collected on hardwood and carpeted floors using a vacuum cleaner with a cellulous thimble
	Boston, Massachusetts	House – main living area (n=16)	Geo mean: 234 ng/g	Range: 3.0-10,630 ng/g	Stapleton et al., 2008	Dust collected using Eureka Mighty-Mite Vacuum
		Bedroom (n=14)	Geo mean: 105 ng/g	Range: 1.5-763 ng/g		
		Home (n=7)	Geo mean: 65.8 ng/g	Range: 24.3-111 ng/g		Dust collected using home vacuum cleaner
	San Francisco Bay Area, California	Homes (2006) (n=16)	Median: 140 ng/g	Range: 36-1,900 ng/g	Dodson et al., 2012	
		Homes (2011) (n=16)	Median: 260 ng/g	Range: <2-3,800 ng/g		
	Northern California	Homes (n=59)	Geo mean: 144 ng/g	Range: <0.64-3,483 ng/g	Brown et al., 2014	2010 Childhood leukemia study; dust samples collected from vacuum cleaners

Country	Location	Media/ Area	TBPH Concentrations[1]		Reference	Notes
United States	Northern California	Fire station living quarters (n=27)	Geo mean: 1096 ng/g	Range: <0.64-11,422 ng/g	Brown et al., 2014	2010-2011 Firefighter occupational exposure study; samples were collected from vacuum cleaners
	North Carolina	House (main living areas) (n=53)	Geo mean: 364.7 ng/g	No range provided	Hoffman et al., 2014	Nylon thimble in hose attachment of home vacuum – 2 minutes.
	Massachusetts	House (n=38)	Geo mean: 377 ng/g	Max: 47,110 ng/g	Johnson et al., 2013	TBPH detected in 63% of home vacuum samples
	Boston, Massachusetts	House (n=50)	Geo mean: 650 ng/g	Range: <300-47,110 ng/g	Stapleton et al., 2009	Household vacuum cleaner bag collection; collected between 2002-2007; 60% detection
Canada	Vancouver, British Columbia	Homes (n=116)	Median: 99 ng/g	Range: 10-6,400 ng/g	Shoeib et al., 2012, as cited by Brown et al., 2012	

Country	Location	Media/ Area	TBPH Concentrations[1]		Reference	Notes
Canada	Saskatoon Saskatchewan (SK),	House (n=23)	Geo mean: 734 ng/g, dry mass	Range: 15-22,251 ng/g, dry mass	Peng et al., 2015	Dust samples were collected from 8 houses (2-3 dust samples per house) using a Eureka Mighty-Mite vacuum cleaner with cellulose extraction thimble; 100% detection frequency
Egypt	Cairo	Homes (n=17)	Median: 0.1 ng/g	Range: 0.06-1.3 ng/g	Hassan and Shoeib 2015	Dust sampled from vacuum cleaner contents. Values estimated from graph.
		Workplace (n=5)	Median: 0.09 ng/g	Range: 0.05-0.4 ng/g		
		Cars (n=9)	Median: 0.6 ng/g	Range: 0.5-9 ng/g		
Pakistan	Faisalabad	University (n=16)	Mean: 35 ng/g Median: 19 ng/g	Range: 3-225 ng/g	Ali et al., 2014	Dust samples collected by brushing 4 m^2 of the floor surface. Samples were sieved through a 500 µm mesh sieve.
		Clothing Store (n=15)	Mean: 11 ng/g Median: 9 ng/g	Range: <0.2-35 ng/g		
		Electronic Store (n =30)	Mean: 100 ng/g Median: 20 ng/g	Range: 0.6-950 ng/g		
	Gujrat	Home (n=31)	Mean: 7.3 ng/g Median: 3.5 ng/g	Range: <0.2-141 ng/g	Ali et al., 2012b	Dust samples collected with brush over 4 m^2 floor surface; sieved through a 500 µm mesh sieve; level of detection not reported.

Country	Location	Media/ Area	TBPH Concentrations[1]		Reference	Notes
Pakistan	Gujrat	Mosques (n=12)	Median: 8 ng/g (estimated from graph)	Range: 1.0-10.0 ng/g (estimated from graph)	Ali et al., 2012b	Dust samples collected with brush over 4 m^2 floor surface; sieved through a 500 µm mesh sieve; level of detection not reported.
New Zealand	Wellington, Wairarapa Christ-church and North Canterbury	Living Room Floors (n= 34)	Median: 12 ng/g	Range: <2-640 ng/g	Ali et al., 2012a	Nilfisk Sprint Plus 1600W vacuum cleaner used on bare floors, rugs, and carpet.
Germany		House (n=20)	Median: 343 ng/g	Range: 25-2,274 ng/g	Fromme et al., 2014	All samples above LOQ (1.5 ng/g); household vacuum cleaner bags
Sweden	Stockholm	Various (homes, offices, schools, public spaces) (n=27)	Median: 140 ng/g	Range: <33-1,500 ng/g	Newton et al., 2015	Dust samples were collected immediately after a 24 hour air sampling period. Settled dust was collected from surfaces at least one meter above the floor
Thailand	Ayutthaya and Nonthaburi Province	E-waste storage facility (n=21)	Mean: 270 ng/g StDev: 265	Range: 79-1,300 ng/g	Ali et al., 2011b	Dust samples were collected using 25-µm pore size nylon sampling socks inserted in the nozzle of a vacuum cleaner

[1]For ease of comparison, all units are converted to ng equivalent. Original study units, if different, are shown in parentheses.
Max – maximum; Geo – geometric; LOQ – Limit of quantification; StDev – Standard deviation

3.3.5 TBPH on Skin

The potential for dermal TBPH exposure has been investigated in several studies that measured TBPH on hands of residents (<0.70 - 116 ng) (Hoffman et al., 2014; Stapleton et al., 2014) and gymnasts (<3.19 - 416 ng/wipe) (Carignan et al., 2013) (Table 3-8).

Table 3-8. Concentrations of TBPH Measured on Skin

Country	Location	Media/ Area	TBPH Concentrations	Reference	Notes
United States	North Carolina	Hands (n=43)	Geo mean: 2.5 ng Range: <0.70-116 ng	Stapleton et al., 2014	Hands wiped with sterile gauze soaked in isopropyl alcohol
		Hands (n=53)	Geo mean: 23.4 ng/wipe Range: 9.9 ng/wipe(25^{th}) – 655.1 ng/wipe (max)	Hoffman et al., 2014	Hands wiped with sterile gauze soaked in isopropyl alcohol
	Eastern U.S.	Hands before practice (n=11)	Median: 27.9 ng/wipe Range: <3.19-264 ng/wipe	Carignan et al., 2013	Analyzed hand wipes from gymnasts before and after 2.5 hour practice; 91% detection frequency
		Hands after practice (n=11)	Median: 96.4 ng/wipe Range: 15.5-416 ng/wipe		Median increase from before to after: 70.8 ng/wipe; 100% detection frequency

Geo – geometric

3.3.6 TBPH in Consumer Products

Only a few studies were located that tested for TBPH in consumer products, but a variety of products were tested (Table 3-9). TBPH has been found in PU foam from a variety of baby products (Stapleton et al., 2011), furniture (Stapleton et al., 2011), and a gymnastic pit (La Guardia et al., 2015), in dust from mattresses (Ali et al., 2012a), and in electronics and household appliances at an e-waste facility (Ali et al., 2011b). Significant potential exposure routes for TBPH from consumer products would be oral ingestion (e.g., children's mouthing of materials or products or incidental ingestion of dust) and potentially dermal exposure from furniture and other treated objects indoors. Off-gassing of TBPH as a vapor will not occur to any reasonable extent because of its very low vapor pressure; however, inhalation of re-suspended TBPH-contaminated house dust could provide a source of exposure especially in dusty homes.

3.3.6.1 TBPH in Children and Baby Products

TBPH was found in PU foam samples from baby products, including car seats, changing table pads, mattresses, baby carriers, and rocking chairs. Stapleton and colleagues (2011) reported levels of TBPH and TBB (measured together) ranging from $5.85x10^6$ ng/g to $4.25x10^7$ ng/g in 17 of 101 PU foam samples tested (Stapleton et al., 2011).

3.3.6.2 TBPH in Furniture

Stapleton et al. (2012) detected TBPH (as the sum of TPP, TBB, and TBPH) in 13 of 102 PU foam samples from furniture ranging from 5.18×10^6 ng/g to 36.85×10^6 ng/g . Ali et al. (2012a) vacuumed dust from mattresses in New Zealand, and the median concentration of TBPH was 1 ng/g. Stapleton et al. (2009) detected TBPH in 1 of 26 consumer products (mostly furniture) purchased between 2003 and 2009; TBB and TBPH were measured together (4.2% by weight) in a couch purchased in 2007.

3.3.6.3 TBPH in Electronic Products

TBPH was measured in an e-waste facility in a number of electronic waste products including PCs, printers, TVs, and other appliances. Concentrations reported ranged from 79 to 1,300 ng/g, with a median of 180 ng/g (Ali et al., 2011b).

Table 3-9. TBB Concentrations in Consumer Products

Country	Item	Type	TBPH Concentrations[1]	Reference	Notes
United States	Couch	PU foam	4.2% by weight (TBB and TBPH together)	Stapleton et al., 2009	One couch tested, purchased in 2007
	Gymnastic pit foam block	Foam (n=6)	Range: 225,000-5,710,000 ng/g (225-5,710 µg/g)	La Guardia et al., 2015	4 foam blocks from Gym #4 pit, 1 from Gym #2 pit, 1 new block from Gym #4 storage

Country	Item	Type	TBPH Concentrations[1]	Reference	Notes
United States	Baby products, donated used and purchased new	PU foam from car seats, changing table pads, mattresses, rocking chairs	Mean: 18,510,000 ng/g (18.51 mg/g) Range: 5,850,000 ng/g to 42,500,000 ng/g (5.85-42.5 mg/g) (TBB/TBPH measured together)	Stapleton et al., 2011	TBB/TBPH was found in 17 of 101 baby products sampled. TBB/TBPH comprise 50% of the overall mixture of FM 550
	Furniture	PU foam	Mean: 19,760,000 ng/g (19.76 mg/g) Range: 5,180,000-36,850,000 ng/g (5.18-36.85 mg/g of foam). (Sum of TPP, TBB, and TBPH levels)	Stapleton et al., 2012	Donated PU foam samples from numerous cities in U.S. Measured as FM 550; found in 13 of 102 PU foam samples.
New Zealand	Mattress (n=16)	Dust	Median: 1 ng/g (no range provided)	Ali et al., 2012a	Any mattress covers and under sheets were left on and mattress vacuumed evenly and thoroughly
Thailand	e-waste Storage Facility	PC + Printer (n=12)	Range: 110-1,300 ng/g	Ali et al., 2011b	Dust samples were collected using 25 µm pore size nylon sampling socks inserted in the nozzle of a vacuum cleaner in a room containing the products listed under type.
		TV (n=2)	Range: 144-181 ng/g		
		PC + TV (n=1)	122 ng/g		
		Fridge + Washing Machine (n=1)	98 ng/g		
		TV + Video Recorder (n=1)	132 ng/g		

Country	Item	Type	TBPH Concentrations[1]	Reference	Notes
Thailand	e-waste Storage Facility	TV + Fan (n=1)	79 ng/g	Ali et al., 2011b	Dust samples were collected using 25 µm pore size nylon sampling socks inserted in the nozzle of a vacuum cleaner in a room containing the products listed under type.
		TV + Fan + Microwave (n=1)	151 ng/g		
		Rice cooker +Photo-copier (n=1)	145 ng/g		
		Typewriter + Video Recorder (n=1)	419 ng/g		

[1]For ease of comparison, all units are converted to ng equivalent. Original study units, if different, are in shown in parentheses.
PU – polyurethane foam; TPP –triphenyl phosphate

3.4 TBPH ADME and Biomonitoring Studies

Absorption. Little is known about the toxicokinetics of TBPH. No evidence was identified to permit evaluation of the systemic bioavailability of TBPH by any route. TBB, a close structural analog of TBPH, has been shown to possess oral bioavailability; however, the rate and extent of TBB bioavailability was not established (Hoffman, 2014).

Distribution. The TBPH content of 102 human female serum samples and 105 breast milk samples was evaluated in a cross-sectional study (Zhou et al., 2014). Samples were randomly selected from the biobank of a cohort study on nursing women in Sherbrooke, Québec, Canada; no exposure cohorts were designated. TBPH was detected in 16.7% and 32.4% of serum and milk samples, respectively. In general, levels of TBPH were found to be lower than TBB levels except for the serum samples containing TBPH at the 95th percentile and maximum concentration samples. Based on the information provided by the published study, it is not possible to say, if there was any correlation between TBPH serum and breast milk levels (Zhou et al., 2014).

Metabolism. Incubation of TBPH with human liver microsomes resulted in no loss of TBPH and no formation of metabolites. This is unlike other analogs of TBPH, including TBB and DEHP, which were readily metabolized in parallel experiments (Roberts, 2012). However, a metabolic product of TBPH, mono(2-ethylhexyl) tetrabromophthalate (TBMEHP) was formed when TBPH was incubated in the presence of purified porcine carboxylesterase. The rate of formation was approximately 1.08 pmol/min/mg protein, which was determined to be approximately 1/600th the

rate at which TBBA is formed by human microsomes (Roberts, 2012). The slow metabolism of TBPH to form TBMEHP may have implications on the toxicity of TBPH as it may not be rapid enough to affect the bioaccumulation of TBPH. No Phase II metabolites of TBMEHP were observed.

In a separate investigation, the formation of TBMEHP from TBPH was catalyzed *in vitro* by porcine esterases. A high concentration of TBPH (5.6 µM) was used to maximize detection of potential metabolites. At this concentration of TBPH, the rate of TBMEHP formation was 89 pmol/hr/mg esterase. Lower concentrations of TBPH were evaluated under similar reaction conditions, but no TBMEHP formation was detected.

Elimination: No studies were located that have evaluated the elimination of TBPH. TBPH is highly lipophilic with an estimated log octanol:water partition coefficient of ~12. Consequently, TBPH as a parent molecule is unlikely to be efficiently eliminated by the renal route, and it is likely highly bound to plasma proteins. For this reason, efficient systemic elimination likely requires biotransformation to a more polar form.

In studies using liver microsomes and cytosolic fractions, it appears that TBPH is very poorly metabolized (Roberts et al., 2012). Consequently, TBPH may have a long biological systemic half-life. In one study analyzing marine mammals from the Pearl River Delta, China, mean concentrations of TBB (a structural analog of TBPH) were 5.6 ± 17 ng/g lipid, whereas concentrations of TBPH were 342 ± 883 ng/g lipid. This ~60-fold ratio is despite the fact that the commercial mixture of Firemaster® 550 is 4:1.6 (Roberts et al., 2012).

Biomonitoring: Several biomonitoring studies have been conducted in the U.S. Canada, Pakistan, and China (Table 3-10). Hoffman et al. (2014) measured urinary metabolite levels of tetrabromobenzoic acid (TBBA), a urinary metabolite of TBB, and used TBBA as a biomarker for TBPH and TBB exposure. The authors measured household dust levels and took hand wipe samples from adults in North Carolina. TBBA was found in 72.4% of urine samples at levels of up to 340 ng/g, with a geometric mean of 5.6 ng/g. The geometric mean of hand wipe samples was 23.4 ng/wipe. Levels of TBPH (and TBB) in dust were positively correlated with corresponding levels of each in the hand wipe samples.

In Canada, Zhou et al. (2014) recorded levels of TBPH in maternal serum and breast milk collected from 2008-2009. TBPH was found in 16.7% of 102 serum samples, with levels ranging from below detection (LOD =7.3 ng/g) to 164 ng/g (no mean calculated). TBPH was found in 78.1% of 105 breast milk samples with levels ranging from below detection (LOD=0.15 ng/g) to 6.6 ng/g.

Johnson et al. (2013) measured serum hormone levels and estimated corresponding exposure by measuring concentrations of TBPH and TBB in house dust. Serum hormone data were from 62 men recruited through a U.S. infertility clinic from 2002 to 2003, and household dust was sampled from donated existing vacuum bags for a subset (n=38). TBPH and TBB were detected in 63% (geometric mean 377 ng/g) and 47% (409 ng/g), respectively, of dust samples. TBPH exposure (as estimated from dust samples) was positively associated with total T3.

Ali et al. (2014) collected paired dust and serum samples from 61 people in Faisalabad, Pakistan in December 2011. The mean and median TBPH concentrations in the serum of subjects working in clothing stores or at a university were less than 1 ng/g lipid weight. The mean concentration for those working in electronic stores was 1.5 (±8) ng/g lipid weight, the median was <1 ng/g lipid weight, and the range was 1-18 ng/g lipid weight.

He et al. (2013) measured concentrations of flame retardants, including TBPH, in serum from 305 residents of Laizhou Bay, China in 2011. A TBPH concentration of 260 ng/g lipid weight was measured in a pooled sample from females aged 30-39. TBPH was not detected in stored mixed serum samples from an earlier study in 2007.

Table 3-10. TBPH Biomonitoring Data

Country	Tissue/fluid	TBPH Concentrations[1]		Reference	Notes
United States	Urine (TBBA) (n=53)	Geo mean: 5.6 pg/mL TBBA	Max: 340 ng/g	Hoffman et al., 2014	Hand wipe and urine samples from adults in North Carolina. 76.9% had TBBA levels detected. 1 urine sample had insufficient volume.
	Serum hormone, T3 (n=38)	T3 concentrations not provided		Johnson et al., 2013	62 men, aged 18-54 years recruited from couples seeking infertility treatment; TBPH exposure (estimated from home vacuum bag dust) positively associated with T3 for subset of 38 men. TBPH was detected in 63% (geometric mean 377 ng/g) of dust samples.

Country	Tissue/fluid	TBPH Concentrations[1]		Reference	Notes
Canada	Serum (n=102)	No mean	Range: ND-164 ng/g lw	Zhou et al., 2014	LOD=7.3 ng/g, TBPH detected in 16.7% of samples
	Breast milk (n=105)	No mean	Range: ND-6.6 ng/g lw		LOD=0.15 ng/g, TBPH detected in 32.4% of samples
China	Serum	260 ng/g lw		He et al., 2013	TBPH detected in 30-39 year old female group only (pooled sample)
Pakistan	Serum	Mean and median: <1 ng/g lw		Ali et al., 2014	Clothing store and university employees
		1.5 ng/g lw	Range: 1-18 ng/g lw		Electronic store employees

[1]For ease of comparison, all units are converted to ng equivalent. Original study units, if different, are shown in parentheses.
ND – not detected; Max – maximum; Geo – geometric; LOD – limit of detection, TBBA – Tetrabromobenzoic Acid; lw – lipid weight; T3 – Triiodothyronine

3.5 TBPH Exposure Assessments and Estimates

We did not locate any authoritative reviews on TBPH that estimated intakes or exposure. Fromme et al. (2014) calculated the daily intake via dust consumption for adults and toddlers for TBPH based upon their measurements of TBPH in dust in German homes. The "average" adult intake was estimated at 147 pg/kg bw/day (348 pg/kg bw/day for the 95th percentile intake) and 1715 pg/kg bw/day average (4055 pg/kg bw/day 95th percentile) for toddlers.

3.6 TBPH Discussion

TBPH is a widely used flame retardant in the U.S. and has been measured in water, dust, consumer products, and air. Concentrations of TBPH are highest in dust of indoor environments, and contact with dust appears to be a significant route of exposure for consumers. The highest TBPH dust concentrations were measured in indoor rooms that were presumably proximate to the TBPH-treated polymers. Normal hand-to- mouth activity is the primary known or established route of exposure. Incidental hand- to-mouth activity occurs over a person's entire life, but it occurs most often and most significantly in children, and therefore, children may have greater exposures than adults. The U.S. EPA estimates daily dust/dirt ingestion rates for children in the

range of 50 to 100 mg per day, and a significantly lower rate for adults of 30 mg per day (central tendency) in the general population (U.S. EPA, 2011a).

An area of uncertainty is the exposure potential from dermal contact with, or ingestion from, mouthing of objects containing TBPH. The general mechanism for TBPH diffusion out of treated plastics, including foam, and into dust is relatively well understood. Similarly, the potential for hand-to-mouth transfer of dust is understood and established. The potential dermal or direct oral (mouthing) exposure to TBPH as it is diffusing and being "expressed" from the treated foam is not well understood or documented. Most foam is covered, and the manner and degree of transfer from the foam to the cover's surface for potential mouthing or dermal exposure is another source of uncertainty.

The very high pK_{ow} of TBPH would be predicted to limit its rate of dermal absorption because water in the viable dermis will restrict the rate of absorption to the systemic circulation. Also, molecules of TBPH in contact with the skin would be expected to have a reasonable rate of penetration into the stratum corneum (SC) or the very top layer of dead and dry skin cells. If left undisturbed, the TBPH molecules would be expected ultimately to diffuse into the viable dermis where they would slowly be absorbed.. Working against this eventuality is the dynamic mechanism of desquamation, or human skin shedding. This continuous loss of skin cells occurs at a rate that might be expected basically to eliminate the initially absorbed TBPH in the SC as these skin layers turn-over or shed completely approximately every two weeks (IPCS, 2006; U.S. EPA, 2004). Experimental work is needed to confirm this expectation. The applied dermal dose of TBPH could be particularly important for children's items, such as changing table pads, mattresses, and car seats. Availability, transfer, and ingestion of TBPH via child-mouthing of these items and treated furniture in general are areas of significant uncertainty.

It should be noted that this report compiles data from a variety of sources. We have not evaluated the quality of the studies and their results; rather we included all the relevant data we found. The estimates described in the exposure assessments are presented "as is" without a detailed analysis or critique of the methodology, assumptions, or underlying data quality.

4 Tetrabromobisphenol A (TBBPA) (CAS 79-94-7; 121839-52-9)

4.1 TBBPA Chemical and Physical Properties

Tetrabromobisphenol A (TBBPA) is a widely used flame retardant and is a white crystalline powder (EURAR, 2006). The water solubility of TBBPA increases with increasing pH, which can be seen in the range of solubility from 0.148 mg/L at 25°C and pH 5, to 2.34 mg/L at 25°C and pH 9. This indicates that TBBPA has low solubility in water, but it is soluble in most solvents and will adsorb to solids and sediments in water based on estimated soil-water coefficient (K_{oc}) values of 49,726; 700,000; and 1,000,000 (EURAR, 2006, HSDB, 2013; Bbzblog, 2014). Estimated vapor pressure values for TBBPA range from 4.68 x 10^{-8} torr to 1.76 x 10^{-11} at 25°C. These values indicate that TBBPA will exist in both the vapor and particulate phases in the atmosphere (EURAR, 2006). Significant volatilization from water surfaces is not expected based on an estimated Henry's Law constant of 7.05 x 10^{-11} atm-m^3/mol at 25°C (ECHA, 2008).

Figure 4-1. Molecular Structure of TBBPA (ChemIDPlus, 2014)

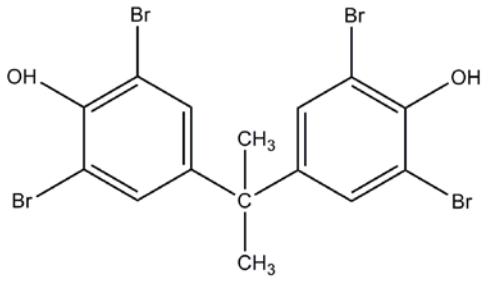

Table 4-1. CAS Registry Number and Synonyms for TBBPA (ChemIDPlus, 2014; EURAR, 2006)

CAS registry/RN	
Synonyms	2,2',6,6'-Tetrabromobisphenol A; TBBPA; 2,2-Bis(3,5-dibromo-4-hydroxyphenyl)propane; 2,2-Bis(4-hydroxy-3,5-dibromophenyl)propane; 3,3',5,5'-Tetrabromobisphenol A; 3,5,3',5'-Tetrabromobisphenol A; 4,4'-(1-Methylethylidene)bis(2,6-dibromophenol); 4,4'-Isopropylidenebis(2,6-dibromophenol); 4,4'-Isopropylylidenebis(2,6-dibromophenol); Bromdian; EC 201-236-9; Great Lakes BA-59P; Phenol, 4,4'-(1-methylethylidene)bis(2,6-dibromo-); Phenol, 4,4'-isopropylidenebis(2,6-dibromo-); Saytex RB 100PC; Tetrabromo-4,4'-isopropylidenediphenol; Tetrabromodian; Tetrabromodiphenylopropane; tetrabromodihydroxy diphenylpropane; Fire Guard 2000; FG 2000; F-2016; F-2400; F-2400E; FR-1524; Firemaster® BP 4A

Table 4-2. Physical and Chemical Properties of TBBPA (ChemIDPlus, 2014; HSDB, 2013c; ECHA, 2008)

Molecular Formula	$C_{15}H_{12}Br_4O_2$
Molecular Weight	543.87 g/mol
Melting Point	178-182°C
Boiling Point	~316°C
Density	2 kg/L at 4°C
Solubility (in water) (range of values)	pH 5 - 0.148 mg/l at 25°C pH 7 - 1.26 mg/l at 25°C pH 9 - 2.34 mg/l at 25°C pure water - 0.063 mg/l at 21°C and 0.24 mg/l at 25°C
Log K_{ow}	5.90
Vapor Pressure (range of values)	1.76×10^{-11} torr at 25°C (estimated) $< 8.9 \times 10^{-8}$ torr at 20°C (measured below limit of quantification) 4.68×10^{-8} torr at 25°C (measured)
Henry's Law Constant	7.05×10^{-11} atm-m^3/mole at 25°C

Semi-Volatile Organic Compounds (SVOCs), such as TBBPA, are typically characterized by a relatively high molecular weight, low vapor pressure/volatility, low or moderate solubility in water and a high octanol-water partition coefficient. To a significant degree, these properties determine the fate of TBBPA in the environment, which impacts the potential for human exposure. The high octanol-water partition coefficient means it will be lipophilic or "fat loving," and will partition into any sediment layers in an environmental water column. Unless there are large areas of volatilizing surface in the indoor environment, it will not be highly present in the air as a vapor but will ultimately partition out of treated objects and into (and be present in) available organic rich substrates like house dust. Contaminated dust could then be ingested by individuals within the residence. Dermal and hand-to-mouth or direct mouthing exposure to TBBPA "bloomed" onto plastic surfaces is also a possibility. If associated with food packaging, it could partition into the food.

Because of its properties and fate in the indoor environment, the vapor pressure (VP) of pure TBBPA can be misleading in estimating its potential to become airborne as a vapor. Using the measured vapor pressure at typical room temperature of 25°C (73°F) results in the following estimation of a maximum or saturated airborne concentration:

(4.7E-08 torr/760 torr) (1,000,000) (543.9/24.4) = 1.400 ng/m^3

All organic monomers (including monomeric flame retardants like TBBPA) embedded within polymer matrices will move out of that matrix into surrounding media (e.g., air or water)

following classic laws of diffusion. Given a timeframe of years, a significant portion of the monomer will diffuse out of the polymer and into the residential environment. In reality, TBBPA would never be expected to exist as a pure material indoors. Initially, it is in the polymer matrix and, after it diffuses out of the matrix, it comes to the surface and then is associated with house dust that is primarily composed of human skin cells, which have been shed in a process known as desquamation. As such, house dust is essentially an organic substrate. In this case, an estimated 4.7E-08 mmHg VP at 25°C (73°F) of pure TBBPA is highly attenuated via what is known as Raoult's Law:

(VP of Pure TBBPA)(Mole Fraction of TBBPA in substrate) = VP over the substrate

This is for "ideal mixtures" of TBBPA in various substrates including house dust. For real world mixtures a thermodynamic activity coefficient (AC typically <1) is added.

(VP of Pure TBBPA)(Mole Fraction of TBBPA in substrate)(AC) = VP over the substrate

Thus, one would not expect but a small portion of the above saturation airborne vapor concentration to occur in indoor air. The measured indoor air values presented below agree with this expectation. Some or most of these concentrations would be expected to be from re-suspended dust containing TBBPA rather than pure TBBPA vapor.

4.2 TBBPA Uses

TBBPA is a high production volume chemical and the most widely used flame retardant with 170,000 tons produced in the global market in 2004 (BSEF, 2007 as cited in Makinen et al., 2009; EFSA, 2011). TBBPA is used mostly as a reactive brominated flame retardant but is also used as an additive flame retardant. It is primarily used as a reactive flame retardant in the production of epoxy resin printed electronic circuit boards by covalently binding to epoxy and polycarbonate resins, and therefore, it no longer exists as a separate chemical entity (Abb et al., 2011; ACC, 2001, BSEF, 2012). TBBPA is used as an additive flame retardant in the production of acrylonitrile-butadiene-styrene (ABS) resins used in electronic enclosures and electronic consumer products with an outer plastic casing (ACC, 2001, BSEF, 2012). TBBPA is found in 95% of printed circuit boards worldwide (BSEF, 2012). Examples of consumer products that use a printed circuit boards are: TVs, vacuum cleaners, washing machines, refrigerators, microwaves, copiers, computers, printers, fax machines, radios, entertainment equipment, and automotive and aviation equipment. TBBPA is also used as a flame retardant for plastics, paper and textiles, and is applied to office furniture and carpet (HSDB, 2013). It is also a plasticizer in adhesives and coatings, used in high impact polystyrene (HIPS) and phenolic resins, and as a chemical intermediate in the synthesis of other flame retardants (ACC, 2001; BSEF, 2012; Deng et al., 2014; EFSA, 2011; HSDB, 2013). When used as a reactive flame retardant, the free residual monomer is very low, and TBBPA is not available for release into the environment.

However, when it is used as an additive flame retardant, TBBPA can migrate out of the product and into the environment (HSDB, 2013; EFSA, 2011; ECHA, 2006).

4.3 TBBPA Human Exposure

TBBPA is found throughout the environment in various media including indoor and ambient air and water. It is also found in dust, food, consumer products, child-specific products, furniture, and electronics. Work performed in China indicates that the diet in that country is believed to be a major route of exposure for the general population (EFSA, 2011; Shi et al., 2009). Work in other countries did not confirm this (Driffield et al., 2008; EFSA, 2011; Fernandes et al., 2008). People can also be exposed to TBBPA through inhalation or dermal exposure to dust from products containing TBBPA (Makinen et al., 2009). Production of TBBPA and recycling of electronic products containing TBBPA are believed to be the major routes of occupational exposure (Deng et al., 2014).

When used as an unreacted flame retardant in a polymer matrix, TBBPA is not chemically bound to the polymer. Thus, it will continually diffuse out of the polymer, such as plastic, and into indoor environmental media, such as into dust. Due to its ubiquitous presence in, and release from, plastic products used indoors, TBBPA has been detected in dust in homes, offices, automobiles, classrooms, and some monitored workplaces at various locations throughout the world. Concentrations of TBBPA in various media and a summary of exposure assessments and estimates found in the literature are presented below.

The available literature on concentrations of TBBPA in relevant environmental media show potentially significant concentrations in a workplace processing circuit boards, but relatively little information is available on indoor air levels in homes. Except for a study in China, levels measured in food appear to be relatively low, as are the rare reports of TBBPA in surface water. Relative to residences, the available data appear to be focused on concentrations in dust, reflecting what might reasonably be anticipated to be the most important exposure pathway of concern for children and others. The result of these studies show relatively low concentrations of TBBPA in dust compared to other flame retardants.

Assuming relatively high levels of TBBPA in contaminated dust are possible; children's overall exposure to this flame retardant will be influenced by their hand-to-mouth behavior and subsequent ingestion of TBBPA containing material, particularly dust.

4.3.1 TBBPA in Indoor Air

No studies were located reporting air measurements in homes, but one study reported personal air concentrations measured in workshops, electronic dismantling facilities, and offices in Finland for both particles and gases (Table 4-3). Makinen et al. (2009) measured exposures in

workers using personal air samplers and patch tests. The concentrations of TBBPA measured in indoor air ranged from less than 3 ng/m^3 to as high as 180 ng/m^3 (Makinen et al., 2009).

Table 4-3. TBBPA Concentrations in Indoor Air

Country	Location	Media	TBBPA Concentrations[1]	Reference	Notes
Finland	Circuit board factory	Indoor air	Geo mean: <3 ng/m^3	Makinen et al., 2009	Two samplers: a glass fiber filter placed in an IOM sampler collected the inhalable fraction of particles; an OVS sampler containing a filter collected particles. XAD resin and PU foam were used for the sampling of compounds present in the gas phase. In the analysis, the gas and particle phases were not separated.
	Furniture workshop	Indoor air	Geo mean: 6 ng/m^3		
	Electronics dismantling facility I	Indoor air	Geo mean: 100 ng/m^3 Range: 60-180 ng/m^3		
	Electronics dismantling facility II	Indoor air	Geo mean: 60 ng/m^3 Range: 20-170 ng/m^3		
	Computer classroom	Indoor air	Geo mean: <6 ng/m^3		
	Offices and social premises of factory and workshops	Indoor air	Geo mean: <6 ng/m^3		

[1]For ease of comparison, all units are converted to ng equivalent. Original study units, if different, are shown in parentheses.
Geo – geometric; PU – polyurethane; IOM – Institute of Occupational Medicine; OVS – OSHA Versatile Tubes

4.3.2 TBBPA in Water

TBBPA concentrations in drinking water were not available. However, studies reported concentrations in freshwater lakes in the United Kingdom and China. Concentrations reported ranged from 0.14 to 4.87 ng/L (Harrad et al., 2009; Yang et al., 2012) (Table 4-4).

Table 4-4. TBBPA Concentrations in Water

Country	Location	Media	TBBPA Concentrations[1]	Reference	Notes
United Kingdom	England	Freshwater lake	Range: 0.14-3.2 ng/L (140-3200 pg/L)	Harrad et al., 2009	3 samples taken from each of 7 lakes
China	Lake Chaohu	Freshwater lake	Max: 4.87 µg/L	Yang et al., 2012	7 lakes sampled in July, September, November

[1]For ease of comparison, all units are converted to ng equivalent. Original study units, if different, are shown in parentheses.
Max – maximum

4.3.3 TBBPA in Food

Several studies have reported TBBPA concentrations in a wide range of foods across several countries but not in the U.S. (Table 4-5). Concentrations in all but one study were less than 1 ng/g, and concentrations for many foods were not greater than the limits of quantification. The highest concentrations reported were by Yang et al. (2012) in fish in China; the range of concentrations was 28.5 to 39.4 ng/g (Harrad et al., 2009; Driffield et al., 2008; EFSA, 2011; Fernandes et al., 2008; Shi et al., 2009; Yang et al., 2012; Papke et al., 2010 as cited in EFSA 2011; Morris et al., 2004; Van Leeuwen, 2009 as cited in EFSA 2011; Schlabach et al., 2004 as cited in EFSA 2011; Ashizuka et al., 2008; Thomsen et al., 2002b).

Table 4-5. TBBPA Concentrations in Food

Country	Location	Food	TBBPA Concentrations[1]	Reference	Notes
United Kingdom	9 English lakes	Freshwater fish	Range: <LOQ-1.7 ng/g lw	Harrad et al., 2009	LOQ=0.29 ng/g lw
	Not specified	Oils and fats, nuts, eggs, other vegetables, milk	<LOD	Driffield et al., 2008	LOD=0.11-0.19 ng/g (0.11-.19 µg/kg)
	Not specified	Canned vegetables, potatoes, fresh fruit, sugars and preserves	<LOD		LOD=0.017-0.036 ng/g (0.017-0.036 µg/kg)

Country	Location	Food	TBBPA Concentrations[1]	Reference	Notes
United Kingdom	Not specified	Fruit, meat and dairy products, green vegetables, carcass meat, offal, fish, poultry, bread, miscellaneous cereals	<LOD	Driffield et al., 2008	LOD=0.043-0.084 ng/g (0.043-0.084 µg/kg)
	Scotland	Oysters (n=5 locations, 1 value per location)	<LOD		LOD=<0.020-<0.050 ng/g (<0.020-<0.050 µg/kg). Samples from 5 different locations were below the LOD for each location. Multiple samples from each location were homogenized together for one value per location.
		Mussels (n=10 locations, 1 value per location)	<LOD		LOD=<0.010-<0.12 ng/g (<0.010-<0.12 µg/kg). Multiple samples from each location were homogenized together for one value per location.

Country	Location	Food	TBBPA Concentrations[1]	Reference	Notes
United Kingdom	Scotland	Scallops (n=20 locations, 1 value per location)	<LOD	Driffield et al., 2008	LOD=<0.010-<0.35 ng/g (<0.010-<0.35 µg/kg). Multiple samples from each location were homogenized together for one value per location.
	7 locations around Scotland	Mussels, oysters and scallops (n=35 pooled)	ND	Fernandes et al., 2008	LOD=0.01 ng/g (0.01 µg/kg)
European Countries (Ireland, Norway, Spain and the United Kingdom)	Not specified	Fish and other seafood (including amphibians, reptiles, snails and insects) (n=465)	<LOQ	EFSA, 2011	LOQ=1.00 ng/g
	Not specified	Meat and meat products (including edible offal) (n=49)	<LOQ		LOQ=0.14 ng/g
	Not specified	Milk and dairy products (n=40)	<LOQ		LOQ=0.65 ng/g
	Not specified	Animal and vegetable fats and oils (n=41)	<LOQ		LOQ=4.99 ng/g
	Not specified	Products for special nutritional use (n=10)	<LOQ		LOQ=0.34 ng/g
	Not specified	Snacks, desserts, and other foods, eggs and egg products (n=30)	<LOQ		LOQ=0.08-0.10 ng/g

Country	Location	Food	TBBPA Concentrations[1]	Reference	Notes
European Countries (Ireland, Norway, Spain and the United Kingdom)	Not specified	Fruit and fruit products, grains and grain-based products, vegetables and vegetable products (including fungi), starchy roots and tubers (n=17)	<LOQ	EFSA, 2011	LOQ=0.01-0.02 ng/g
Europe	Not specified	Milk	Mean: <0.005 ng/g ww Range: <0.005-0.006 ng/g ww	Papke et al., 2010 as cited in EFSA 2011	
	Not specified	Fish, shellfish and crustacean	Range: <0.005-<0.26 ng/g ww		
Netherlands	Not specified	Fish, shellfish and crustacean	Range: <0.1-245 ng/g lw	Morris et al., 2004	
	Not specified	Fish, shellfish and crustacean	Range: <0.1-5.3 ng/g ww	Van Leeuwen, 2009 as cited in EFSA 2011	
Norway	Not specified	Fish, shellfish and crustacean	Range: 1.0-13.7 ng/g lw	Schlabach et al., 2004 as cited in EFSA 2011	
	Not specified	Milk	0.013 ng/g lw (13 pg/g lw)	Thomsen et al., 2002b	Lipid content was 3.9%, equivalent to a whole milk concentration of $5.1x10^{-4}$ ng/g ($5.1x10^{-4}$ µg/kg)
China	Guangdong Province in southern China	Meat	Mean: 0.263 ng/g lw (263 pg/g lw) Range: <LOD-1.386 ng/g lw (<LOD-1,386 pg/g lw)	Shi et al., 2009	LOD[2] = 0.07 ng/g ww (70 pg/g ww)

Country	Location	Food	TBBPA Concentrations[1]	Reference	Notes
China	Guangdong Province in southern China	Aquatic food group	Mean: 0.738 ng/g lw (738 pg/g lw) Range: <LOD-2.044 ng/g lw (<LOD-2,044 pg/g lw)	Shi et al., 2009	LOD = 0.1 ng/g ww (100 pg/g ww)
	Not specified	Eggs	Mean: 0.194 ng/g lw (197 pg/g lw) Range: <LOD-0.692 ng/g lw (<LOD-692 pg/g lw)		LOD=0.06 ng/g (60 pg/g ww)
		Milk	Mean: 0.211 ng/g lw (211 pg/g lw) Range: <LOD-0.848 ng/g lw (<LOD-848 pg/g lw)		LOD=0.05 ng/g (50 pg/g ww)
	Anhui Province in Eastern China	Four fish species (*Culter alburnus, Cyprinus carpio, Carassius auratus, and Silurus asotus*)	Means: 28.5-39.4 ng/g	Yang et al., 2012	
Japan	Nagoya (N) Seto Inland Sea(S) Kyushu (K)	Fish	N region Mean: 0.01 ng/g S region Mean: 0.01 ng/g K region Mean: 0.02 ng/g Range: 0.01-0.11 ng/g ww	Ashizuka et al., 2008	Detected in 29 fish samples from Japanese food markets in 3 different regions, 2004-2005

[1]For ease of comparison, all units are converted to ng equivalent. Original study units, if different, are shown in parentheses.
[2] Shi et al., 2009 do not explain why the concentration values are reported in lipid weight and the LOD in wet weight
LOQ – limit of quantification; LOD – limit of detection; ND – not detected; lw – lipid weight; ww – wet weight

4.3.4 TBBPA in Dust

TBBPA has been measured in the dust in a variety of indoor settings, mostly outside the U.S. (Table 4-6). TBBPA was reported in the dust of homes in the U.S., Germany, the UK, Belgium, Australia, Portugal, and Japan, with concentrations ranging from not detected to 1,480 ng/g (Abb et al., 2011; Fromme et al., 2014; Wanner et al., 2008, as cited in Abb et al., 2011; Abdallah et al., 2008a, as cited in Abb et al., 2011; Toms et al., 2009 as cited in Abb et al., 2011; D'Hollander et al., 2010; Greens et al., 2009; Cunha et al., 2010 as cited in Abb et al., 2011; Takigami et al., 2009; Deng et al., 2014). These concentrations are significantly lower than are those reported for other brominated flame retardants, such as TBB and TBPH (see Tables 2.6 and 3.7 above). Other tested areas (offices, cars, classrooms, and workshops) had a wide range of concentrations from 2 ng/g in a car in the UK (Abdallah et al., 2008a, as cited in Abb et al., 2011) to 59,140 ng/g in an office in China (Ni and Zheng, 2013).

Table 4-6. TBBPA Concentrations in Dust

Country	Location	Media/ Area	TBBPA Concentrations[1]	Reference	Notes
U.S. and Germany	Various	House (U.S. n=2; Germany n=24)	Median: 48 ng/g Avg: 86 ng/g Max: 470 ng/g	Abb et al., 2011	Household vacuum cleaner bag collection; detected in 20 of 26 samples
Germany	Munich	House (n=20)	Mean: 44.1 ng/g Median: 28.0 ng/g 95th percentile: 105 ng/g Range: 2.9-233 ng/g	Fromme et al., 2014	Household vacuum cleaner bag collection
	Not specified	House (n=34)	ND	Wanner et al., 2008, as cited in Abb et al., 2011	Detection level not reported
United Kingdom	Birming-ham, England	House (n=45)	Median: 62 ng/g Avg: 87 ng/g	Abdallah et al., 2008a, as cited in Abb et al., 2011	Samples collected using nylon sample socks (25 μm pore size) that were mounted in the furniture attachment tube of vacuum cleaner.
		Office (n=28)	Median: 36 ng/g		
		Car (n=20)	Median: 2 ng/g		

Country	Location	Media/ Area	TBBPA Concentrations[1]	Reference	Notes
United Kingdom	West Midlands	Daycare centers and primary schools classrooms (n= 43)	Mean: 200 ng/g Median: 110 ng/g Range: 17-1,400 ng/g	Harrad et al., 2010	Portable vacuum cleaners with 25 ug mesh sock, entire floor surface
Australia	Not specified	House (n=10)	ND	Toms et al., 2009 as cited in Abb et al., 2011	Detection level and method not reported
Belgium	Flanders	House (n= 45)	Median: 11.7 ng/g dw 95th Percentile: 141 ng/g dw	D'Hollander et al., 2010	Samples collected with a vacuum using a nylon sock mounted in the furniture attachment
		Office (n=10)	Median: 70.4 ng/g dw 95th Percentile: 212 ng/g dw Range: <3-419 ng/g dw		
		House (n=18)	Median: 10 ng/g Range: 1-1,480 ng/g	Greens et al., 2009	Collected using a vacuum cleaner
		Office (n=2)	Median: 75 ng/g Range: 45-100 ng/g		
Portugal	Not specified	House (n=10)	ND	Cunha et al., 2010 as cited in Abb et al., 2011	Detection level not reported
Japan	Not specified	House (n=2)	Median: 520 ng/g Avg: 490 ng/g	Takigami et al., 2009	Owners' vacuum cleaners
China	Not specified	Dismantling and sorting workshop (n=12)	Range: 206-950 ng/g	Deng et al., 2014	Waste electrical and electronic equipment recycling plant; handheld vacuum cleaner collection
		Printed circuit board recycling workshop (n=15)	Range: 189-961 ng/g		

Country	Location	Media/ Area	TBBPA Concentrations[1]	Reference	Notes
China	Not specified	Wire recycling workshop (n=3)	80.4 ng/g	Deng et al., 2014	
	Shenzhen	Office (n=56)	Geo Mean: 949 ng/g Arithmetic Mean: 3,382 ng/g Median: 975 ng/g Range: 30-59,140 ng/g	Ni and Zeng, 2013	Central air conditioner filter dusts were collected as Particulate Phase of Indoor Air samples

[1]For ease of comparison, all units are converted to ng equivalent. Original study units, if different, are shown in parentheses.
ND – not detected; dw – dry weight; Avg – average; Max – maximum; Geo – geometric

4.3.5 TBBPA Potential for Dermal Exposure

Several studies were located that contained information that may be useful for evaluating dermal exposures to TBBPA. Makinen et al. (2009) measured exposures in workers using personal air samplers (Table 4-3), but also measured dermal exposure through patch tests affixed to workers and from hand washing (Table 4-7). The concentrations of TBBPA measured in the patch tests worn by workers ranged from <0.09 to 63 ng/cm^2 (Makinen et al., 2009). These results demonstrate that there is a potential for people to be exposed dermally to TBBPA, but one would need to investigate further the conditions of exposure in the work places to determine the relevance of this exposure for the general population.

Gallen et al. (2014) conducted wipe testing of plastic surfaces of a variety of consumer products in Australia. Excluding the sampled baby accessories, for which no TBBPA was detected, these researchers found a range of detection from 22% to 67% and a range of concentrations from 2.7 ng/wipe to 160,000 ng/wipe (Table 4-8). The authors concluded that this demonstrates the ability of TBBPA (and other brominated flame retardants) to migrate easily from the product surfaces, suggesting that dermal contact is a potential route of exposure.

Table 4-7. TBBPA Data on Dermal Exposure

Country	Location	Media/ Area	TBPH Concentrations	Reference	Notes
Finland	Circuit board factory	Patch test (n=3; chest, arm, thigh)	Geo mean: <0.09 ng/cm^2	Makinen et al., 2009	Patch test: Absorbent patches affixed to worker clothing for 6 hours. Hand wash: workers rubbed hands while ethanol poured over for 30 seconds.
		Hand wash (n=2)	Geo mean: <0.09 ng/two hands		
	Furniture workshop	Patch test (n=1; chest)	Geo mean: <0.09 ng/cm^2		
		Hand wash (n=2)	Geo mean: <0.09 ng/two hands		
	Electronics dismantling facility I	Patch test (n=3; chest, arm, thigh)	Geo mean: 2.0 ng/cm^2 Range: 0.4-17 ng/cm2		
	Electronics dismantling facility II	Patch test (n=3; chest, arm, thigh)	Geo mean: 6.7 ng/cm^2 Range: <0.09-63 ng/cm^2		

Geo – geometric

4.3.6 TBBPA in Consumer Products

Several studies were located that measured TBBPA in or on consumer products or plastics/materials used for consumer products (Table 4-8). TBBPA has been measured in the product itself through destructive chemical analysis, from wipe samples of product surfaces, and in material vacuumed from the inside of televisions (Napoli-Davis and Owens, 2013; Gallen et al., 2014; Choi et al., 2009; Takigami et al., 2008; Deng et al., 2014). Products tested include electronics, wiring, toys, and household appliances. Concentrations measured from destructive testing ranged from 12,000 ng/g to 150,000,000 ng/g (Gallen et al., 2014) and Choi et al. (2009) measured 8,100 ng/g TBBPA in the raw material used for TV housing. In addition, Rani et al. (2014) measured concentrations in food packaging and containers (below detection to 545 ng/g), and Samsonek et al. (2013) measured concentrations of TBBPA in thermal cup lids (26,000-300,000 ng/g). Some of these products contain TBBPA for flame retardant purposes, such as the electronics. However, for other products, such as food packaging, it is not likely that the TBBPA is present for flame retardant purposes. Takigami et al. (2008) measured concentrations of TBBPA up to 97,000,000 ng/g in material vacuumed from the inside of TV sets.

Two studies investigated the use of surface wipe testing for TBBPA in consumer products. Napoli-Davis and Owens (2013) conducted wipe testing to collect TBBPA on plastic surfaces of

electronics. Gallen and colleagues investigated a three-tier testing strategy for identifying brominated flame retardant-containing plastics using X-ray fluorescence (XRF), surface wipe testing, and destructive chemical analysis (Gallen et al., 2014). They tested 1714 largely plastic products (wide variety of product types including computers, televisions, children's toys, and power tools) for the presence of bromine during October 2012 using a handheld XRF device. Products with a high concentration of bromine measured by XRF were chosen for surface wipe testing along with additional products to provide a broad range of product types. Destructive chemical analysis was conducted on samples from 48 products selected from a range of products types. Results of wipe tests found an overall detection rate of 47% (across product types, with detection for specific product types from zero to 58%). Concentrations for all detects ranged from 2.7 ng/wipe to 160,000 ng/wipe. Destructive analysis detection ranged from 50-100%, with concentrations from (12,000-164,000,000 ng/g). The authors concluded that a combination of XRF and surface wipe tests is predictive of the presence or absence of TBBPA (>81% accuracy), despite limitations in the individual methods. The authors concluded that their results demonstrate the ability of TBBPA (and other brominated flame retardants) to easily migrate from the product surfaces, suggesting that dermal contact is a potential route of exposure (Gallen et al., 2014).

4.3.6.1 TBBPA in Children's Products

TBBPA was not detected in surface wipe samples of three baby accessories (not specified) tested (Gallen et al.. 2014). Gallen et al. (2014) measured 20,000 ng TBBPA per wipe on the plastic surface of one of three toys tested and also measured 59,000,000-164,000,000 ng/g in destructive chemical analysis of samples from two plastic toys.

4.3.6.2 TBBPA in Electronic and Household Products

TBBPA was measured in a number of electronic products including computers, circuit boards, wires, copiers, printers, TVs, microwaves, and other appliances (Table 4-8). In the one study from the U.S., mean concentrations from wipe samples ranged from below the limit of quantification to 4.18 ng/100 cm^3 (Napoli-Davis and Owens, 2013). Using destructive testing, Gallen et al. (2014) measured TBBPA in various electronic and household products. Concentrations of TBBPA in these products ranged from 26,000 to 164,000,000 ng/g.

Takagami et al. (2008) vacuumed the inside of TV sets and measured concentrations of TBBPA ranging from 120- 97,000,000 ng/g. Deng et al. (2014) measured concentrations in electronics at a recycling center up to 18,500,000 ng/g.

The available data indicate that the likely important exposure routes for TBBPA from consumer products would be oral ingestion (e.g., children's mouthing of materials or products and

incidental hand-to-mouth ingestion of dust associated with these products) and dermal exposure (Table 4-8).

Table 4-8. TBBPA Concentrations in Consumer Products

Country	Item	Media	TBBPA Concentrations[1]	Reference	Notes
United States	Copier	Electronic surfaces	Mean: <LOQ	Napoli-Davis and Owens, 2013	LOQ not reported. Wipe samples using Kimwipe misted with methanol/acetone mixture. Five 100 cm^2 areas were surveyed on each plastic-surface component of the electronics.
	Computer towers	Electronic surfaces	Mean: <LOQ		
	Microwave	Electronic surfaces	Mean: 1.65 ng/100 cm^2		
	Refrigerator	Electronic surfaces	Mean: 1.55 ng/100 cm^2		
	Computer monitors	Electronic surfaces	Mean: 4.18 ng/100 cm^2		
	Printers	Electronic surfaces	Mean: 1.46 ng/100 cm^2		
Australia	Electronic TV (n=20)	Plastic surfaces	Range: 75-160,000 ng/wipe	Gallen et al., 2014	55% detects, wipe samples: 90 mm glass filter paper wetted with isopropanol firmly wiped over a 100 cm^2 area
	Electronic small household appliances (n=75)	Plastic surfaces	Range: 2.7-20,000 ng/wipe		47% detects, wipe samples: 90 mm glass filter paper wetted with isopropanol firmly wiped over a 100 cm^2 area

Country	Item	Media	TBBPA Concentrations[1]	Reference	Notes
Australia	Electronic large household appliances (n=9)	Plastic surfaces	Range: 4.7-220 ng/wipe	Gallen et al., 2014	22% detects, wipe samples: 90 mm glass filter paper wetted with isopropanol firmly wiped over a 100 cm^2 area
	Electronic other (n=19)	Plastic surfaces	Range: 6.1-22,000 ng/wipe		58% detects, wipe samples: 90 mm glass filter paper wetted with isopropanol firmly wiped over a 100 cm^2 area
	Toys plastic (n=3)	Plastic surfaces	20,000 ng/wipe		33% detects, wipe samples: 90 mm glass filter paper wetted with isopropanol firmly wiped over a 100 cm^2 area
	Plastic other (n=5)	Plastic surfaces	Range: 3.9-2,600 ng/wipe		67% detects, wipe samples: 90 mm glass filter paper wetted with isopropanol firmly wiped over a 100 cm^2 area
	Baby accessories (n=3)	Plastic surfaces	Not detected		0% detects, wipe samples: 90 mm glass filter paper wetted with isopropanol firmly wiped over a 100 cm^2 area

Country	Item	Media	TBBPA Concentrations[1]	Reference	Notes
Australia	Electronic computer (n=3)	Plastic surfaces	75 ng/wipe	Gallen et al., 2014	33% detects, wipe samples: 90 mm glass filter paper wetted with isopropanol firmly wiped over a 100 cm^2 area
	Electronic TV (n=12)	Plastic	Range: 110,000-150,000,000 ng/g (110-150,000 µg/g)		83% detects, destructive chemical analysis with GC-MS
	Electronic small household appliances (n=17)	Plastic	Range: 26,000-160,000,000 ng/g (26-160,000 µg/g)		59% detects, destructive chemical analysis with GC-MS
	Electronic large household appliances (n=4)	Plastic	Range: 12,000-110,000 ng/g (12-110 µg/g)		50% detects, destructive chemical analysis with GC-MS
	Electronic other (n=10)	Plastic	Range: 59,000,000-164,000,000 ng/g (59,000-164,000 µg/g)		70% detects, destructive chemical analysis with GC-MS
	Toys plastic (n=2)	Plastic	Range: 150,000-143,000,000 ng/g (150-143,000 µg/g)		100% detects[2], destructive chemical analysis with GC-MS
	Plastic other (n=1)	Plastic	2,700,000 ng/g (2,700 µg/g)		100% detects, destructive chemical analysis
	Electronic computer (n=2)	Plastic	150,000 ng/g (150 µg/g)		50% detects, destructive chemical analysis with GC-MS

Country	Item	Media	TBBPA Concentrations[1]	Reference	Notes
Japan	TV housing	Premolded plastic	8,100 ng/g	Choi et al., 2009	Raw material for TV housing from a TV manufactured in 2002
	TV (n=5)	Circuit board	Mean: 280,000 ng/g (280 µg/g) Range: 7,900-1,300,000 ng/g (7.9–1300 µg/g)	Takigami et al., 2008	Collected by vacuuming the inside of each TV set until sufficient mass (>200 mg) was collected on a glass fiber filter.
	TV (n=5)	Front cabinet	Mean: 20,000 ng/g (20 µg/g) Range: 240-67,000 ng/g (0.24–67 µg/g)		
	TV (n=5)	Rear cabinet	Mean: 19,000,000 ng/g (19,000 µg/g) Range: 120- 97,000,000 ng/g (0.12–97,000 µg/g)		
	TV set (n=5)	Dust	Mean: 240,000 ng/g (240 µg/g) Range: 5,500-680,000 ng/g (5.5-680 µg/g)		Collected by vacuuming the inside of each TV set until sufficient mass (>200 mg) was collected on a glass fiber filter.
China	TV housing (n=12)	Premolded plastic	Mean: 18,500,000 ng/g	Deng et al., 2014	Waste electrical and electronic equipment recycling center
	Printed circuit board (n=10)	Electronic board	Mean: 20,500 ng/g		
	Wires (n=6)	Insulated wire	Mean: 7,450 ng/g		

Country	Item	Media	TBBPA Concentrations[1]	Reference	Notes
Korea	Polystyrene products (PS) (n=34)	Packaging material, food containers, insulation, buoys	Range: ND-545 ng/g	Rani et al., 2014	3 types of PS: expanded PS, extruded PS and extruded PS foam; detected in 7 of 34 samples; detection level not reported
Slovakia/ Bratislava	Thermo cup (travel mug)	Plastic sliding stopper	Range: 26,000-300,000 ng/g (26-300 mg/kg)	Samsonek et al., 2013	TBBPA was also found in combination with other FRs but are not reported here because the value reported was for the mixture of FRs.
Belgium/ Brussels	Thermo cup (travel mug)	Plastic sliding stopper	44,000 ng/g (44 mg/kg)		TBBPA-BDBPE was detected.

[1]For ease of comparison, all units are converted to ng equivalent. Original study units, if different, are in shown in parentheses.
[2]Gallen et al. (2014) Table 3 indicates 50% detects but it appears to be a typographical error and we believe it is 100% detects (2 out of 2).
LOQ – limit of quantification; ND – not detected; PS – polystyrene; FR – flame retardants; TBBPA-BDBPE – tetrabromobisphenol A bis(2,3-dibromopropyl) ether; GC-MS gas chromatography combined with mass spectrometry

4.4 TBBPA ADME and Biomonitoring Studies

In experimental animals, toxicokinetic data are available in the rat only. As the available data described below indicate, the toxicokinetics behavior of TBBPA in humans and rats is generally quite similar.

Absorption
Inhalation: It is estimated that approximately 75% of TBBPA particles will be absorbed following inhalation exposure, but the majority (70%) of absorption will occur through the gastrointestinal tract. The particle size of TBBPA indicates that very little will be respirable. Only 4% of TBBPA particles have an aerodynamic diameter of < 15 µm (Inveresk, 2002 as cited in EURAR 2006). The respirable range of particles is generally considered to be < 10 µm (CEN, 1993 as cited in EURAR 2006), with an optimum size for particle deposition in the alveolar

region of rat lungs in the range of 1-2 μm (Morrow et al., 1964). Hence, the majority of particles (in the range of approximately 70%) can be expected to deposit in the nasopharyngeal region of the respiratory tract, where they are swallowed, with only a small fraction (< 4%) being absorbed through the lungs. The remaining fraction of inhaled TBBPA is likely exhaled. Therefore, data from oral exposure studies are important for understanding potential health hazards following inhalation exposure.

Dermal: The low water solubility, high octanol/water partition coefficient (5.9), and the high molecular weight (>500) of TBBPA, suggests that systemic exposure via the dermal route should be low (EURAR 2006).

Oral: In rats, TBBPA undergoes extensive, nearly complete (100%), absorption from the gastrointestinal tract. In rats, a peak plasma concentration (C_{max}) is reached within three hours of orally administering a 300 mg/kg dose (Schauer et al., 2006). At a lower dose (20 mg/kg) the oral C_{max} occurred more quickly, by about 30 minutes. Although rapidly absorbed, systemic bioavailability of TBBPA is very low (~1.6 % based on AUC) (Kuester et al., 2007). The low systemic bioavailability is primarily a consequence of rapid liver conjugation with glucuronic acid and elimination in the bile. In this regard, approximately 50% of a 20 mg/kg dose of TBBPA was recovered in the bile within two hours of oral administration, primarily as glucuronide conjugates (Kuester et al., 2007). This indicates rapid oral absorption and substantial first pass metabolism. In human subjects, Schauer et al. (2006) was unable to detect any parent compound in plasma samples following administration of a single low oral dose of TBBPA (0.1 mg/kg). In this study, TBBPA-glucuronide was detected in all blood samples taken up to 72 hours after administration of TBBPA, with peak metabolite concentrations observed at two and six hours after TBBPA administration. This study indicates that metabolism is also very rapid in humans.

Distribution

The volume of distribution at steady-state was determined to be approximately 0.7 L/kg following IV administration of a 20 mg/kg dose (126 ml for male Fisher rats weighing 161 – 190 g). The tissue distribution of ^{14}C labeled TBBPA was evaluated in rats 72 hours after administration of a single radio labeled oral 200 mg/kg dose. Together, the total fraction of the radio labeled dose retained in tissues was only 0.4% of the administered dose (Kuester et al., 2007). Likewise, following 10 days of repeated daily administration, the percent of dose remaining in all tissues 24 hours after the last dose remained was less than 1%. The vast majority of TBBPA remaining in any tissue was located in the cecum tissue itself and in the contents of the intestines and cecum (Kuester et al., 2007).

In earlier studies, the distribution ^{14}C-TBBPA was evaluated in female Sprague-Dawley rats gavaged with a single 7 mg/kg dose. Animals were sacrificed at 8, 24 and 72 hours post dosing

and liver, kidney, brain, muscle, fat, spleen, skin and gonads were excised for assessment of radioactive TBBPA and its metabolites (intestines were either not evaluated or reported). Analysis of these tissues at eight hours following administration accounted for only 0.725% of the administered dose with the highest levels found in the liver (0.4%), muscle (0.12%), skin (0.12%) and fat (0.7%). At 24 hours post-administration, tissues accounted for approximately 0.85% of the dose, and at 72 hours, approximately 0.2% of the dose. The distribution of radiolabel was similar across all time points. Thus, distribution to the selected tissues accounted for less than 1% of the administered radioactivity irrespective of time following dosing (Velsicol Chemical Corporation, 1978).

The thyroid gland and the kidneys are two tissues that have been reported to be biologically affected by high dose TBBPA exposure (Fukuda et al., 2004; Meerts et al., 1999 as cited in Keuster et al., 2007). Minimal levels of TBBPA or its metabolites were observed in these tissues at 24 hours after oral dose administration following either a single dose or after 10 consecutive days of dosing.

One toxicokinetic study, (Meerts et al. 1999 as cited in Keuster et al., 2007), orally exposed pregnant rats to 5 mg [14C]-TBBPA per kg body weight from day 10 to day 16 of gestation and demonstrated no significant trans-placental transfer of TBBPA or its metabolites to the fetus (EURAR, 2006). There is evidence that once absorbed, TBBPA and/or its metabolites can be excreted via breast milk (EURAR part II 2006).

Metabolism

In rats and humans, the major TBBPA metabolites are mono and a diglucuronide conjugates of TBBPA (Keuster et al., 2007; Hakk et al., 2000; Schauer et al., 2006). Glucuronidation is the key process for TBBPA elimination via biliary excretion, which explains its very limited oral systemic bioavailability (Keuster et al., 2007; Hakk et al., 2000; Schauer et al., 2006). In humans, the maximum plasma concentrations of TBBPA-glucuronide(s) were observed within four hours of oral administration (Schauer et al., 2006). TBBPA-glucuronide was observed in all human subjects, whereas low level TBBPA-sulfate was only detected in the blood from two human subjects. In rats, other minor metabolites have been identified including tribromobisphenol, TBBPA glucuronide-sulfate conjugate and a glucuronide metabolite of tribromobisphenol A (Hakk et al., 2000; Schauer et al., 2006). With the data currently available, it is not possible to determine if all the minor metabolites identified in rats are also formed in humans or if their production in rats is due to differences in metabolic pathways or to higher doses administered.

Keuster et al. (2007) reported that elimination of TBBPA-glucuronide in the feces appeared slowest at the highest dose of TBBPA (200 mg/kg). It was speculated that this likely represents increasing saturation of metabolic and/or transport processes in the liver (Keuster et al., 2007).

Elimination

TBBPA has little potential to bioaccumulate. Of a 20 mg/kg oral dose administered to male Fisher rats (equivalent to a 1.2 g dose in a 60 kg human adult), only 1.6% of the dose was bioavailable (Keuster et al., 2007). Mass balance studies have shown that approximately 90-95% of TBBPA is eliminated within 72 hours of administration (Hakk et al., 2000; Keuster et al., 2007). Keuster et al. (2007) showed that greater than 80% of a TBBPA dose was eliminated in the feces between 12 and 24 hours after administration. This is somewhat more rapid than reported by Hakk et al. (2000), where the peak fecal excretion (with 66% of the administered dose) was between 24-48 hours after oral administration. The rapid elimination of TBBPA in humans is supported by single oral dose studies conducted in human volunteers where the parent molecule was undetectable in plasma at all time points (1-178 hours). Urinary elimination of TBBPA is minimal, with less than 1% eliminated regardless of the dose (Schaure et al., 2006)

The elimination half-life in rats was determined by Keuster et al. (2007) to be 82 minutes following intravenous administration and 95 minutes following oral administration. This is significantly shorter than the half-life determined by Schauer et al. (2006), which was approximately 13 hours. The difference between these two half-life determinations likely reflect dramatic differences in dosing (20 mg versus 300 mg/kg), the portion of the curve determined to represent the terminal elimination phase, and application of the Pharsight WinNonlin compartmental PBPK modeling software used by Kuester et al. (2007) compared to Excel spreadsheet analysis used by Schauer et al. (2006).

Analysis of biliary excreta in bile duct cannulated rats suggests biliary elimination is the major route of elimination. Keuster et al. (2007) observed that approximately 50% of a 20 mg/kg dose administered to rats was excreted in the bile within two hours of administration. These results are in the range reported by Hakk et al. (2000) during the first 24 hours after oral administration, also in rats.

Biomonitoring

Biomonitoring studies have measured TBBPA in breast milk, adipose tissue, blood and umbilical cord serum, blood plasma, and urine (Table 4-9). In the U.S., Carignan et al. (2012) detected TBBPA in breast milk of 35% of 34 first time mothers (0.03 - 0.55 ng/g lipid weight). Studies in other countries reported breast milk concentrations ranging from 0.034 ng/g to 688 ng/g lipid weight (Lankova et al., 2013; Agdallah and Harrad, 2011; Cariou et al., 2008; Antignac et al., 2008; Thomsen et al., 2002b; Thomsen et al., 2003; Pratt et al., 2013; Shi et al., 2009; Kemmlein, 2000, as cited in EURAR, 2006). In a study of human adipose tissue in the U.S., the average concentration was reported at 0.048 ng/g lipid weight (Johnson-Restrepo et al., 2008 as cited in Abdallah and Harrad, 2011), while in the UK and Japan, TBBPA was not detected in human adipose tissue (Criou et al., 2008; Watanabe and Tatsukawa, 1989 as cited in EURAR, 2006).

Outside of the U.S., TBBPA has been measured in blood, serum, or plasma in studies from multiple countries, but study authors differed in components tested and the units used to report concentrations, making it difficult to compare findings across studies (Cariou et al., 2008; Antignac et al., 2008; Hagmar et al, 2000a as cited in EURAR, 2006; Hagmar and Bermgan, 2001 as cited in EURAR, 2006; Thomsen et al.. 2001a,b,c, as cited in EURAR, 2006; Thomsen et al., 2002a as cited in EURAR, 2006; Dirtu et al., 2008; Dirtu et al., 2010; Kicinski et al., 2012; Nagayama et al., 2001 as cited in EURAR, 2006; Nagayama et al., 2000 as cited in EURAR, 2006; Fujii et al., 2014a; Fujii et al., 2014b; Kim et al., 2014). TBBPA has been measured in umbilical cord serum in France; Cariou et al. (2008) reported a range of 2.09-649.45 ng/g lipid weight and Antignac et al. (2008) reported a range of 0.002-1.012 ng/g fresh weight. In the only study of urine, Yang et al. (2014) did not detect TBBPA in urine (LOD 0.04 ng/ml) in China.

Table 4-9. TBBPA Biomonitoring Data

Country	Tissue/fluid	TBBPA Concentrations[1]	Reference	Notes
United States	Breast milk	Range: 0.03-0.55 ng/g lw (<30-550 pg/g lw)	Carignan et al., 2012	34 first time mothers in Boston, MA; detected in 35% of samples
	Human adipose tissue	Avg: 0.048 ng/g lw	Johnson-Restrepo et al., 2008 as cited in Abdallah and Harrad, 2011	Number of samples not reported
United Kingdom	Breast milk	Median: <0.04 ng/g lw Avg: 0.06 ng/g lw Range: <0.04-0.65 ng/g lw	Abdallah and Harrad, 2011	Birmingham; detected in 36% of 34 samples
France, Toulouse	Breast milk	Mean: 4.11 Median: 0.48 ng/g lw Range: 0.06-37.34 ng/g lw	Cariou et al., 2008	Detected in 56% of 77 samples
	Human adipose tissue	ND		Detection limit not reported. n=44
	Maternal serum	Mean: 19.87 ng/g lw Median: 16.14 ng/g lw Range: 0.23-93.22 ng/g lw		Detected in 32% of the 91 samples
	Umbilical cord serum	Mean: 103.52 ng/g lw Median: (54.76 ng/g lw Range: 2.09-649.45 ng/g lw		Detected in 30% of the 90 samples

Country	Tissue/fluid	TBBPA Concentrations[1]	Reference	Notes
France, Toulouse	Breast milk (n=23)	Median: 0.172 ng/g lw (172 pg/g lw) Range: 0.034-9.4 ng/g lw (34-9,400 pg/g lw)	Antignac et al., 2008	Samples obtained from volunteer women during caesarean deliveries; 26 mother/newborn pairs
	Maternal serum (n=26)	Median: 0.007 ng/g fw (7 pg/g fw) Avg: 0.054 ng/g fw (54 pg/g fw) Range: 0.002-0.783 ng/g fw (2-783 pg/g fw)		
	Umbilical cord serum (n=26)	Median: 0.01 ng/g fw (10 pg/g fw) Avg: 0.152 ng/g fw (152 pg/g fw) Range: 0.002-1.012 ng/g fw (2-1,012 pg/g fw)		
Sweden	Blood serum	Range: <0.5-1.8 ng/g lw (<0.5-1.8 µg/kg lw)	Hagmar et al., 2000a as cited in EURAR, 2006	Detected in 4 of 19 samples of computer technicians
	Blood serum (n=4)	Range: 1.1-3.8 ng/g lw (1.1-3.8 µg/kg lw)	Hagmar et al., 2000b as cited in EURAR, 2006	Concentrations measured in electronic equipment dismantling workers decreased during vacation. Half-life of 2.2 days in blood serum.
	Blood plasma	0.76 ng/g lw (0.76 µg/kg lw)	Hagmar and Bergman, 2001 as cited in EURAR, 2006	Detected in only 1 of 9 samples from smelter workers
	Blood plasma	Median: <0.54 ng/g lw (<0.54 µg/kg lw) Range : <0.54-1.8 ng/g lw (<0.54-1.8 µg/kg lw)	Jakobsson et al., 2002 as cited in EURAR, 2006	LOQ=0.54 ng/g lw; detected in 8 of 10 samples; above LOQ in only 4 samples

Country	Tissue/fluid	TBBPA Concentrations[1]	Reference	Notes
Norway	Blood plasma	Mean: 1.3 ng/g lw (1.3 µg/kg lw) Range: 0.64-1.8 ng/g lw (0.64-1.8 µg/kg lw)	Thomsen et al., 2001a,c as cited in EURAR, 2006	Electronic equipment dismantlers, LOQ=400 ng/g
		Mean: 0.54 ng/g/lw (0.54 µg/kg/lw) Range: ND-0.80 ng/g lw (ND-0.80 µg/kg/lw)		Circuit board producers, LOQ=400 ng/g
		Mean: 0.34 ng/g/lw (0.34 µg/kg/lw) Range: ND-0.52 ng/g/lw (ND-0.52 µg/kg/lw)		Laboratory personnel, LOQ=400 ng/g
	Blood plasma	400 ng/g plasma (0.4 ng/kg plasma)	Thomsen et al., 2001b as cited in EURAR, 2006	
	Blood serum, 1977 and 1981 (n=5 pools of 10-14 individuals)	ND	Thomsen et al., 2002a as cited in EURAR, 2006	LOQ=400-1600 ng/g serum. Archived samples of males aged 40-50 years old were analyzed.
	Blood serum 1986 and 1999 (n=5 pools of 10-14 individuals)	1986: 0.44 ng/g lw (0.44 µg/kg lw) 1999: 0.65 ng/g lw (0.65 µg/kg lw)		1986 and 1999
	Blood serum 1998 (n=8 pools of 10-14 individuals)	Range : 0.31-0.71 ng/g lw (0.34-0.71 µg/kg lw)		Archived samples of all age groups. Highest levels found in the 0-4 year old group.
	Breast milk	0.067 ng/g lw (67 pg/g lw)	Thomsen et al., 2002b	Lipid content was 2.6%, equivalent to a whole milk concentration of 0.0017 ng/g (0.0017 µg/kg)
	Breast milk, Dimethyl-TBBPA (n=3 pools of 10-12 individuals)	Range: ~0.010-0.10 ng/g lw (~10-100 pg/g/lw)	Thomsen et al., 2003	One sample from each of 3 different geographic areas was collected in 2001.

Country	Tissue/fluid	TBBPA Concentrations[1]	Reference	Notes
Belgium	Blood (n=7 individual)	Median: 0.08 ng/mL	Dirtu et al., 2008	
	Blood (n=24 pooled)	Median: 0.096 ng/mL		
	Blood (n=20)	Median: <LOQ Range: <LOQ-0.0025 ng/mL (<LOQ-2.5 pg/mL)	Dirtu et al., 2010	LOQ= 0.002 ng/mL (2 pg/mL). n= 20
	Serum (n=515)	Median: <LOQ 95th percentile: 22 ng/L Max: 186 ng/L	Kicinski et al., 2012	LOQ=15 ng/L Cross-sectional data on 515 adolescents (13.6-17 yrs, mean of 14.9 yrs) were used for analysis. Neurobehavioral test found no significant association between TBBPA level and the finger tapping test.
Ireland	Breast milk (n=11 pools of 10-11 individuals	Mean: 0.05-0.33 ng/g Range UB: <0.29-0.17 ng/g	Pratt et al., 2013	11 pooled breast milk samples were collected from 109 first-time mothers at four centers across Ireland
Romania	Blood (n=53)	Median: <LOQ Range: <LOQ-0.013 ng/mL (<LOQ-13 pg/mL)	Dirtu et al., 2010	LOQ=0.002 ng/mL (2 pg/mL). n=53
China	Breast milk (n=12)	Means: 0.933-0.961 ng/g lw (933-961 pg/g lw) Range: ND-5.124 ng/g lw (ND-5124 pg/g lw)	Shi et al., 2009	1,237 individual samples were collected from 12 different locations in 2007. Individual samples from each area were pooled into one sample for analysis.

Country	Tissue/fluid	TBBPA Concentrations[1]	Reference	Notes
China	Urine	ND	Yang et al., 2014	LOD=0.04 ng/ mL; spot urine samples collected from 94 individuals living near a Bisphenol AF manufacturing plant; 50 females (aged 26–79 years) and 44 males (aged 26–84 years
Japan	Blood (n=54)	Median: 2.4 ng/g lw (2.4 µg/kg lw) Max: 12.0 ng/g lw (12.0 µg/kg lw)	Nagayama et al., 2001 as cited in EURAR, 2006	54 volunteers (27 males and 27 females) in the age range 37 to 49 years old in 1998
	Blood (n=14)	Mean: 1.35 ng/g (1.35 µg/kg)	Nagayama et al., 2000, as cited in EURAR, 2006	
	Human adipose, Dimethylated TBBPA (n=5)	ND	Watanabe and Tatsukawa, 1989 as cited in EURAR, 2006	LOD: 20 ng/g fat (20 µg/kg fat)
Japan, Kyoto	Blood, 1989 (n=20)	Mean: NR Range: <LOQ-0.94 ng/g ww (<LOQ-940 pg/g/ww)	Fujii et al., 2014a	LOQ= 0.05 pg/g ww); NR=not reported due to low detection frequency
	Blood, 1999 (n=20)	Mean: NR Range: <LOQ-0.95 ng/g ww (<LOQ-950 pg/g ww)		
	Blood, 2010 (n=20)	Mean: NR Range: <LOQ-0.42 ng/g ww (<LOQ-420 pg/g ww)		
	Blood (no year specified), 20 yr olds (n=30)	Mean: NR Range: <LOQ-0.95 ng/g ww (<LOQ-950 pg/g ww)		
	Blood (no year specified), >50 yr olds (n=30)	Mean: NR Range: <LOQ-0.42 ng/g ww (<LOQ-420 pg/g ww)		

Country	Tissue/fluid	TBBPA Concentrations[1]	Reference	Notes
Japan, Okinawa	Breast milk (no year specified), (n=9)	Median: 0.72 ng/g lw Mean: 1.04 ng/g lw Range: 0.39-2.22 ng/g lw	Fujii et al., 2014b	
	Blood (no year specified), (n=3)	Median: 1.0 ng/g ww Mean: 40.5 ng/g ww Range: <LOQ-238 ng/g ww		LOQ not reported
Korea	Blood Serum Mother/infant pairs (n=12; controls)	*Mothers* Mean: 10.93 ng/g lipid Range: <MDL-73.96 ng/g lipid *Infants* Mean: 77.65 ng/g lipid Range: <MDL-457.4 ng/g lipid	Kim et al., 2014	MDL=0.072 ng/g Study also sampled blood serum from 26 mother/infant pairs of infants with congenital hypothyroidism
Germany, West Berlin,	Breast milk	0.29-0.94 ng/g lw (0.29-0.94 µg/kg lw)	Kemmlein, 2000, as cited in EURAR, 2006	Detected in 2 of 4 samples (25-37 year old); 1998/1999
Faroe Islands	Breast milk	11.0 ng/g lw (11.0 µg/kg lw)	Kemmlein, 2000, as cited in EURAR, 2006	
Czech Republic	Breast milk	Range: <2-688 ng/g lw	Lankova et al., 2013	LOQ=2 ng/g lw. 50 mothers from 20-43 years. TBBPA detected above LOQ in less than 30% of samples. Mean and median levels were not calculated because less than 30% of samples were above the LOQ.

[1]For ease of comparison, all units are converted to ng equivalent. Original study units, if different, are shown in parentheses.

ND – Not Detected; lw – lipid weight; fw – fresh weight; ww – wet weight; LOQ – limit of quantification; LOD – limit of detection; NR – not reported; SPE – Solid Phase Extraction; MDL – Method Detection Limit; UB- upper – bound

4.5 TBBPA Exposure Assessments and Estimates

A few governmental agencies estimated worst case daily intakes for TBBPA for higher exposed subpopulations, but limited available data precluded them from more robust estimates of general population exposures (ECHA, 2006; EFSA, 2011). Several publications were reviewed where the authors estimated exposure levels for specific media (e.g., fish, human milk), generally based upon the results of their particular studies (e.g., Abb et al., 2011; Abdallah and Harrad, 2011, Ashizuka et al., 2008, Driffield et al., 2008; Fujii et al., 2014b; Shi et al., 2009; Greens et al., 2009).

ECHA (2006) estimated a "highest predicted local[1] human intake" of 0.19 mg/kg bw/day for people exposed indirectly from the environment to TBBPA used as an additive flame retardant in ABS resins during production. They predicted a "regional[2]" human intake of 7.8×10^{-5} mg/kg bw/day.

EFSA (2011) assessed exposure to TBBPA and its derivatives in food for the Panel on Contaminants in the Food Chain (CONTAM Panel). They reported on data submitted on 652 food samples from four European countries that covered a period from 2003 to 2010. All samples were less than the limit of quantification (LOQ), and EFSA concluded that a meaningful exposure assessment for the general population was not possible (EFSA, 2011). However, EFSA reports on a worst case intake estimate made by the CONTAM Panel for high intake adult fish consumers and for high cow's milk consuming toddlers. CONTAM substituted the maximum LOQ reported for the respective food group resulting in an "upper bound" intake estimate of 2.6 ng/kg bw/day from adult fish consumption and 55.7 ng/kg bw/day from toddler cow's milk consumption (EFSA, 2011). EFSA calculated TBBPA intake for infants from human milk (concentrations ranging from 0.06 to 37.3 ng/g fat) ranging from 0.28 to 171 ng/kg bw/day for average consumption rate (800 ml/day) and 0.41 to 257 ng/kg bw/day for high consumption rate (1200 mL/day).

The Food Standards Agency (FSA, 2007d, as cited by Driffield et al., 2008) estimated upper bound adult dietary intakes of TBBPA using data from dietary surveys. Values ranged from 0.05 ng/kg bw/day for nuts to 2 ng/mg bw/day for green vegetables. Harrad et al. (2010) reported concentrations of TBBPA in indoor samples from 43 day care centers and primary school classrooms in West Midlands, United Kingdom from the winter of 2007 to the spring of 2008. They estimated dust ingestion for children for low, medium, and high exposure scenarios using data from classroom concentrations in their study and home and car data from other studies in the UK. Their estimates ranged from 0.05 to 2.3 ng/kg bw/day for the three scenarios (Harrad et

[1] Local reflects the largest local site.

[2] Regional refers to semi-industrialized European Union geographic area with a surface area of 40,000 km^2 and a population of 20 million people.

al., 2010), which the authors noted is far below the tolerable daily intake of 1,000,000 ng/kg bw/day derived by the UK Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT, 2004, as cited by Harrad et al., 2010).

4.6 TBBPA Discussion

Even though the available data are quite sparse, purely from consideration of the physical properties of TBBPA, it does not appear that inhalation of ambient or indoor air presents a significant route of exposure.

TBBPA is slightly soluble in water, and the data on the concentration of TBBPA in potable water are essentially non-existent; thus, its exposure potential via this route remains an area of uncertainty. If sources of public water supplies are contaminated with TBBPA at levels seen in fresh water lakes in the UK and China, then drinking water could be a significant source of exposure, assuming standard treatment methods do not remove it.

As noted above, the levels of TBBPA in dust reported in this report are significantly lower than those found for other flame retardants of the same general type. This fact notwithstanding, exposure from dust appears to remain a primary mode of human exposure from treated products. Indeed, the concentrations of TBBPA in the dust of tested indoor environments and contact with dust appears to be a significant if not the main source of exposures for consumers to TBBPA. The highest dust concentrations of TBBPA were measured in indoor rooms that were presumably proximate to consumer products treated with TBBPA. Normal hand-to- mouth activity is the primary known or established route of exposure for house dust. Incidental hand-to-mouth activity occurs over a person's entire life, but it occurs most often and most significantly in children. Therefore, children may have greater exposures than adults may. The U.S. EPA estimates daily dust/dirt ingestion rates for children in the range of 50 to 100 mg per day, and a significantly lower rate for adults of 30 mg per day (central tendency) in the general population (U.S. EPA, 2011a).

Another potentially important source of human exposure to TBBPA is via breast milk. This is based on measured concentrations reported in one study (Lankova et al., 2013) and an infant's estimated daily ingestion of 750 grams per day of breast milk with 4% lipid content (Enig, 2001; Bonyata, 2011).

An area of uncertainty is the exposure potential from dermal contact with or ingestion from mouthing of objects containing TBBPA. The general mechanism for TBBPA diffusion out of treated plastics has been anticipated, tested, and modeled in the past (U.S. EPA, 2011b). Similarly, the potential for hand-to-mouth transfer of dust is understood and established (U.S. EPA, 2011a) The potential for dermal or direct oral (mouthing) exposure to TBBPA as it is diffusing and being "expressed" from the treated polymer is not well understood or documented.

TBBPA's logK_{ow} value of 5.9 would be predicted to optimize its rate of dermal absorption because it resides between logKow >1 and < 8. LogK_{ow}s in this range are high enough to facilitate diffusion through the lipophilic SC top skin layer while retaining enough water solubility to allow a reasonable rate of absorption to the systemic circulation after crossing the SC. If the rate of transfer to the systemic circulation is rapid enough then the dynamic mechanism of desquamation or human skin shedding will have little effect in reducing the amount absorbed through the skin. That is, this continuous upwelling or loss of skin cells occurs at a rate that would be too slow to eject and eliminate the initially absorbed TBBPA in the SC. The SC skin cell layers turn-over or shed completely approximately every two weeks (IPCS, 2006; U.S. EPA, 2004).

It should be noted that this report compiles data from a variety of sources. We have not evaluated the quality of the studies and their results; rather we included all the relevant data we found. The estimates described in the exposure assessments are presented "as is" without a detailed analysis or critique of the methodology, assumptions, or underlying data quality.

5 Antimony Trioxide (ATO) (CAS 1309-64-4)

5.1 ATO Chemical and Physical Properties

Antimony trioxide (ATO) is a flame retardant synergist and a metal-containing inorganic substance that is a white solid crystalline and odorless powder (HSDB, 2015). Because ATO is a metal-containing compound, fate and transport and some other physical and chemical properties of antimony metal ions are relevant to ATO. Therefore, data on antimony chemical and physical properties are also included when applicable.

The reported water solubility values for ATO are variable and depend on the environmental properties of the receiving waters, but, in general, ATO is only slightly water soluble (Health Canada, 2010; HSDB, 2015). ATO is soluble in dilute acids, alkali hydroxides (it is amphoteric), organic solvents, and sulfides (HSDB, 2015; EPA, 2012). Once dissolved in water, a variety of transformation products occur in combination with the parent compound, which, depend on pH, oxygen level, and available ligands for binding (HC, 2010). The calcium concentration will also impact antimony speciation once dissolved in water due to potential precipitation of calcium antimonite (HC, 2010). Antimony ions are released during dissolution, and they have a tendency to adsorb to suspended particles in the aquatic and terrestrial environments, such as soils, sediments, and other organic matter (HC, 2010; Butterman and Carlin, 2004).

ATO exerts zero partial pressure in the air and is considered non-volatile (estimated vapor pressure of $<1x10^{-6}$ torr at 25°C). This means that it is released into the environment principally as fine particulate matter (EPA, 2014; HC, 2010). ATO is considered persistent for all environmental media given that the antimony ions are not degraded, and these ions tend to reversibly interchange between different oxidation/speciation forms (pentavalent and trivalent) in soil, water, and air (HC, 2010; ECHA, 2008).

Typically, antimony is released into the atmosphere as an aerosol where it can be oxidized to ATO or other trivalent forms (ATSDR, 1992). These ATO particles are not expected to react further, and atmospheric half-lives were estimated at 1.9 days for antimony and 3.2 days for ATO (Mueller, 1985, as cited in ATSDR, 1992).

Soils and sediments have been noted as a sink for environmental metals, and metals are typically classified as persistent because they do not break down over time (HC, 2010; ECHA, 2008). However, antimony is not anticipated to bioconcentrate (Butterman and Carlin, 2004). ATO released to dry soil will remain intact or adsorb to soil until a wetting/precipitation event (HC, 2010). Combining this information with measured levels of antimony in dust indicates that house or indoor dust is an important media for exposure.

ATO is unlike SVOC flame retardants. When used within plastic matrices, SVOCs will slowly but readily diffuse from the polymer to the surface where they typically become associated with and adsorbed to house dust because of their high degree of lipophilicity. It is uncertain whether ATO, as a non-volatile species with in-determinant lipophilicity, will have the same tendency and rate of migration from a plastic matrix. There is one report of antimony migrating from PET food trays into food products at levels that exceeded regulatory limits (Haldimann et al., 2007). The mechanism for this transfer is uncertain and may reflect a relatively high level of antimony on the surface of the trays. Even though these uncertainties exist when ATO is used in polymer products, it may become available for human exposure. The mechanism may be a combination of diffusion and physical breakdown of the products to antimony-containing particulate during use. Another, more plausible explanation is that a majority of antimony measured in indoor dust comes from ambient $PM_{2.5}$ particulates containing this element entering the home. See discussion below.

Figure 5-1. Molecular Structure of ATO (Health Canada, 2010)

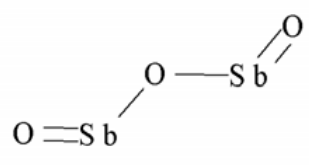

Table 5-1. CAS Registry Number and Synonyms for ATO (ChemIDPlus, 2015; HSDB, 2013; HC, 2010)

CAS registry/RN	1309-64-4
Synonyms and Trade Names	Antimonius oxide; antimony oxide, diantimony trioxide, flowers of antimony; antimony sesquioxide; senarmontite; valentinite; antimony white; antimony peroxide; timothox; exitelite; HP; LP; KR; White Star; White Star M; KR-LTS; Thermoguard S; Thermoguard L; Senarmontite3; H grade; L Grade; Fire Shield H; Fire Shield L; Montana Brand 100A; A 120; A 120 (corrosion inhibitor); A 1582; ACC-BS; AN 800; Antimony Bloom 100A; Antimony Bloom 500AAntox; AO 3; AO 5; AP 50; AP 50 (metal oxide); AT 3; AT 3B; Atox 3CN; Atox B; Atox F; Atox R; Atox S; Bluestar RG; Bluestar Z; C.I. 77052; C.I. Pigment White 11; Chemetron Fire Shield; Dechlorane A-O; F 45; F 45 (oxide); FCP 100; Fire Cut AT 3; Fireshield FSPO 405; FireShield H; FireShield LS-FR; Flame Cut 610; Flame Cut 610R; Flameguard VF 59; FSPO 405; HM 203P; LSB 80; LS-FR; MIC 3; Microfine AO 3; Microfine AO 5; MSA; MSA (flame retardant);MSF; Nyacol A 1510LP; Nyacol A 1530; Octoguard FR 10; P 3; Patox A; Patox C; Patox CF; Patox H; Patox HS; Patox L; Patox M; Patox MK; Patox P; Patox-P; Patox S; Patox U; Performax 401; Poliflam HT 3; Polysafe 60; Polysafe 100T; Pyroguard AN 700; Pyroguard AN 800; Pyroguard AN 800T; Pyroguard AN 900; RAC 1; Sanka Anchimonzol C; SHLB 80; Stibiox MS; Stibital; Stox W 60; Thermoguard B; Timonox Red Star; Timonox RT; Timonox White Star; TMS; TMS (flame retardant); Trutin 40; TT 88; UF; UF (oxide); Ultrafine II; UN 1549; Valentinite1; White Star N

Table 5-2. Physical and Chemical Properties of ATO (HSDB, 2013; U.S. EPA, 2014; Health Canada, 2010)

Molecular Formula	O_3-Sb_2
Molecular Weight	291.52
Melting Point	655°C
Boiling Point	1425°C
Density	5.2 - 5.9 g/cm^3
Solubility (in water)	19.7 mg/L at pH 5 and 20°C 25.6 mg/L at pH 7 and 20°C 28.7 mg/L at pH 9 and 20°C
Log K_{ow}	Not available*
Vapor Pressure (range of values)	1 mm Hg at 574°C <1x10^{-6} torr at 25°C (estimated; U.S. EPA, 2014)
Henry's Law Constant	Likely negligible

* Having some degree of solubility in water and reportedly being soluble in organic solvents, ATO should, under certain conditions, have a measureable partitioning coefficient between water and octanol. For example, the ATO could be first dissolved in octanol, then mixed with water, and then have both phases analyzed for antimony. We could not find a literature value for K_{ow}, however.

ATO, the trivalent form of antimony, occurs naturally in the environment and is also released into the environment from human activities and products. Environmental exposures to antimony occur due to its natural presence, which may result in antimony being found in air, soil, and some food and drinking water (ECHA, 2008). Anthropogenic sources of antimony include air releases from smelters, incinerators, and combustion of gas and coal, and aquatic releases into effluents and wastewater (Carex Canada; ECHA, 2008). There are few studies that report concentrations of the trivalent form in the literature (Health Canada, 2010). ATO and other forms of antimony are measured as the ionic form, as opposed to bonded antimony (including the ATO speciation). For this report, we conservatively assumed that the presence of the antimony ion may be an indication of the presence of ATO, and therefore, include reports of antimony concentrations in any form measured in environmental media, dust, food, and consumer products. However, because the purpose of this report is to identify potential human exposure to ATO from its use as a flame retardant, we do not report on potential sources of antimony or ATO exposure that are not related to ATO use for flame retardancy.

ATO is used as a synergist to enhance flame retardancy of brominated flame retardants where it will not be covalently bound to a product. According to the HSDB and U.S. EPA, ATO and antimony ions are expected to continually diffuse out of materials and products over time and with aging (HSDB, 2013; U.S. EPA, 2014). This judgment is at odds with the following statement from the ATSDR:

> "The antimony oxide that is added to many materials for fire protection is very tightly attached to these materials and does not expose people to antimony." (ATSDR, 1992, page 3)

We believe the uncertainty around the critical properties of ATO that might drive the diffusion of ATO out of treated matrices is most likely responsible for the above disagreement in predicted behavior. As discussed above, we do not know whether inorganic ATO readily diffuses from plastics similar to SVOC flame retardants. We do know that antimony, possibly from ATO, is present in house dust as a primary source for human exposure. However, antimony measured in house dust may not be predominantly from its use as a flame retardant in products but, rather, from $PM_{2.5}$ ambient particulates containing this element in the ambient environment being brought into the indoor environment. See discussion below in Section 5.6.

5.2 ATO Uses

ATO is a flame retardant synergist, which, when used in combination with brominated flame retardants (such as decabromodiphenyl oxide), increases flame retardancy for textiles and plastics (U.S. EPA, 2014; Babich, 2005). The addition of ATO into the product reduces the amount of halogenated flame retardant needed (U.S. EPA, 2014). ATO is used as a flame retardant in plastics, paints, textiles, adhesives, and rubbers (Anderson et al., 2012; Tristar Primer, 2012). ATO has uses as a flame retardant in consumer products, such as furniture, carpets, and mattress covers (U.S. EPA, 2014; RIVM, 2011). Tristar Primer (2012) reports that about 10% is used in coated fabrics, furniture upholstery, and bedding, while the rest is used in electronics and plastics.

ATO is also used as an opacifier, an additive in semi-conductors, and as a coating; in alloy metal products (lead batteries, sheet metal, cable coverings); in non-metal products (ceramics, glass, plastic manufacture, pigments); and has other manufacturing uses (HSDB, 2013; Snedeker et al., 2014). ATO is used as a catalyst in the production of polyethylene terephthalate (PET), which is a thermoplastic polymer resin used in bottles, films, and other food contact items (U.S. EPA, 2014). Note that this report focuses on ATO flame retardant uses only.

ATO accounts for roughly 80% of global antimony consumption (U.S. EPA, 2014). In the U.S., nearly 60% of antimony is used in flame retardants as ATO (72% in Europe, 50% in China) (Tristar Primer, 2012). ECHA reports the distribution of ATO used as a flame retardant in 2005 in the European Union (EU) was 38% in plastics, 36% in PVC, 9% in rubber, and 7% in textiles. The remaining 10% of ATO was in non-flame retardant uses (ECHA, 2008). The U.S. EPA reports that the typical ATO concentration is 25-33% by weight when used as a flame retardant in plastics, with end concentrations in the product ranging from 1.5-12% (U.S. EPA, 2014).

Mansson et al. (2009) reported that ATO accounts for 3-4% of the product by weight when applied as a flame retardant.

5.3 ATO Human Exposure

As mentioned in Section 5.2, ATO is used in the manufacture of a number of materials and products, only some of which include ATO for flame retardancy purposes. ATO is widely used in consumer products including toys, furniture upholstery, textiles, electrical wiring and equipment, clothing, and furnishings (Babich, 2005; ECHA, 2008). Health Canada determined that primary consumer exposure pathways for ATO come from use in furniture upholstery, mattress covers, and polyester fabrics in children's toys (Health Canada, 2010). Exposure to ATO occurs when products begin to break down from use, and ATO is released as particulates into the air and dust leading to dermal and inhalation exposure (ECHA, 2008). Another potential exposure route is oral ingestion that results from the hand-to-mouth behavior of children or from sucking on products containing ATO, such as toys (ECHA, 2008). However, the presence of antimony in any of these matrices does not necessarily mean that the source of the antimony was from ATO used as a flame retardant (ECHA, 2008). For example, ATO is used as a catalyst to make PET, which is used for beverage containers; however, the ATO is not included in PET for flame retardancy purposes.

When identifying and reporting ATO concentrations in different media, it is important to note that many analytical methods do not distinguish between the different forms of antimony. Therefore, they likely overestimate the potential exposure specifically attributed to ATO, as compared to other antimony forms (ATSDR, 1992).General population exposure to antimony (including ATO) from all routes of exposure is expected to be low (U.S. EPA, 2012). The majority of *antimony* exposure is expected to be in the pentavalent form with greatest exposure from food and water sources (U.S. EPA, 2012). The majority of exposure to *ATO* specifically is expected to come from consumer products (Health Canada, 2010).

5.3.1 ATO in Indoor and Ambient Air

ATO is typically not measured directly in air; rather, air samples measure the antimony ion. Antimony concentrations in ambient air reflect the total of natural and anthropological sources, which may or may not include antimony from flame retardant uses. Health Canada (2010) reported that studies in the U.S. and Canada indicate detectable levels of antimony in ambient air, ranging from 0.0005 to 0.055 $\mu g/m^3$. Whether any of the antimony found in ambient air if from uses of ATO as a flame retardant is not known. This is important information that will be used below in an analysis of the contribution of ambient $PM_{2.5}$ containing antimony to indoor dust levels. It should be noted that a conversion factor of 1.2 is needed when concentrations or levels are reported as antimony in order to convert this value to ATO, assuming the measured antimony came from ATO.

ATO is used in products and materials that may be found in indoor environments, but it is not known whether antimony found in indoor air concentrations are from ATO used as a flame retardant, ATO from other uses, or other sources of antimony. For this report, we have included all indoor (non-occupational) air measurements found, assuming that they might be from ATO use as a flame retardant. Health Canada (2010) reported no data were located on indoor air concentrations from non-occupation settings. We located three studies on antimony measurements in indoor air that were published after the Health Canada assessment (Table 5-3).

In the U.S., Majestic et al. (2012) reported a mean indoor air concentration of 17±7 ng/m^3 of antimony (in PM_1) in the air of an elementary school in Arizona. The authors attributed the increased indoor antimony air concentrations in this size fraction (with an indoor PM_1 mass 86 times greater than the outdoor PM_1 mass) to emission and re-suspension of antimony from ATO used in the carpet as a flame retardant. Rivas et al. (2014) measured concentration of antimony (in $PM_{2.5}$) ranging from 0.13 to 1.6 ng/m^3 inside a school in Spain, but the authors suggest the antimony is related to traffic pollution exposures and not from flame-retardants. Huang et al. (2014) reported a mean concentration of 29.78 ng antimony/m^3 (in $PM_{2.5}$) in seven homes in urban areas of China. The authors did not attribute the antimony concentration to a specific source, nor did they mention flame retardants as a potential source.

Table 5-3. ATO Concentrations Indoor Air

Country	Location	Media/ Area	Antimony Concentrations[1]	Reference	Notes
United States	Flagstaff, Arizona	Indoor elementary school, PM_1	Mean: 17 ng/m^3 StD: 7 ng/m^3 Only mean reported	Majestic et al., 2012	2 MOUDI samplers used to sample PM_1 from approximately 8 am to 6 pm; Antimony measured using HR-ICP-MS.
Spain	Barcelona	Indoor school air, $PM_{2.5}$ (n=77)	Mean 0.83 ng/m^3 StD: 0.35 ng/m^3 Range 0.13-1.6 ng/m^3	Rivas et al., 2014	$PM_{2.5}$ samples obtained with high volume sampler MCV CAV-A/mb using an inlet with a nozzle plate for $PM_{2.5}$ (MCV), and then collected on Pallflex quartz fiber filters; Antimony measured using ICP-AES

Country	Location	Media/ Area	Antimony Concentrations[1]	Reference	Notes
China	Guangzhou	Household, $PM_{2.5}$ (n=7)	Mean: 29.78 ng/m^3 (2.79 mg/kg) Median: 25.4 ng/m^3 (2.35 mg/kg) No range reported	Huang et al., 2014	Sampled in urban areas. Active SLC $PM_{2.5}$/PM_{10} sampler and $PM_{2.5}$ air monitoring membrane; Antimony quantified using ICP-MS

[1]For ease of comparison, all units are converted to ng equivalent. Original study units, if different, are shown in parentheses.
StD – standard deviation; MOUDI - multiple orifice uniform distribution impactor; PM_1 – a particulate matter (≤1 µ diameter); $PM_{2.5}$ – a particulate matter (2.5 µ diameter); PM_{10} – a particulate matter (10 µ diameter); HR-ICP-MS – high resolution magnetic sector inductively coupled plasma-mass spectrometry; ICP-AES – inductively Coupled Plasma-Atomic Emission Spectrometry; ICP-MS – inductively coupled plasma-mass spectrometry

5.3.2 ATO in Water

Antimony is an element that occurs naturally in the environment, and there are multiple anthropogenic sources of environmental antimony. We did not locate any concentrations of ATO or antimony in water attributed to ATO's use as a flame retardant. U.S. EPA (2014) reports that antimony concentrations in natural waters are typically reported at or below 1 ppb. In their 2010 Antimony assessment, Health Canada reported no exceedances of antimony above the maximum acceptable concentration of 6 µg/L, and they concluded that drinking water was not a major source of consumer exposure to antimony (Health Canada, 2010).

5.3.3 ATO in Food

We did not identify any reports of ATO in food, and only scant data were available on antimony concentrations in food (HC, 2010). None of the studies identified ATO use as a flame retardant as the source of antimony. Because there are so many natural and anthropogenic sources of antimony, and naturally occurring antimony can be taken up from the soil into food crops, it is not reasonable to use general antimony concentrations in food as a surrogate for ATO concentrations in food.

Haldimann and colleagues found that antimony migrated from PET food trays into food products at levels that exceeded regulatory limits (Haldimann et al., 2007). While ATO in this case was not present due to flame retardant purposes, it is likely that ATO used as a catalyst or thermal stabilizer in food tray production was the source of antimony exposure (Snedeker et al., 2014).

5.3.4 ATO in Dust

Dust is a potential pathway for human exposure to ATO from its use as a flame retardant in household and consumer products. As the materials and products are worn or abraded, they break down into small particles, and ATO (and antimony ions) along with these particles will adhere to household dust (ECHA, 2008). As discussed above, ATO may also diffuse from treated plastics and adsorb onto house dust. A third mechanism for ATO residing in household dust is through ambient $PM_{2.5}$ particulates with antimony entering the indoors. Exposure to dust may result in uptake by dermal or inhalation routes for adults and children, and, for children exposure, could also include ingestion due to typical child hand-to-mouth behaviors (ECHA, 2008). Health Canada (2010) considered the inhalation exposure route for antimony in dust to be negligible, but they estimated exposure to antimony particulates from sitting on furniture and considered dermal exposure from house dusts (see Section 5.5 on exposure estimates).

Available studies measuring antimony concentrations in dust are described in Table 5-4 below. When available, the speciation and/or source of the antimony is noted. Our intention was to report only antimony concentrations in dust that could be attributed to flame retardant uses; however, many studies did not identify the source of antimony. Therefore, we included all of the studies on antimony in dust that were found. Some studies attributed antimony concentrations to local soil concentrations (Fergusson et al., 1986) or proximity to anthropogenic sources (Davis and Gulson, 2005; Fonturbel et al., 2011). We did not locate any studies that identified ATO used as a flame retardant as the source of antimony found in the dust.

Variable units, collection methods, and analytical techniques make it difficult to compare across studies. In some instances, antimony was quantified as µg per sample (Gonzales et al., 2004) or in terms of surface area as $\mu g/m^2$ (Glorennec et al., 2012; McDonald et al., 2010). However, there were a number of other studies that reported dust concentrations as a per gram unit (Fergusson et al., 1986; Davis and Gulson, 2005; Rasmussen et al., 2001; Barbieri et al., 2014; Fontúrbel et al., 2011; Turner and Hefzi, 2010; Yoshinaga et al., 2014; Bi et al., 2011). Reported concentrations in dust from the studies listed ranged from below the level of quantification (800 ng/m^2) (Glorennec et al., 2012) to as high as 439,000 ng/g in vacuum cleaner dust (Yoshinaga et al., 2014). We include data from the control areas, as available, as these data may aid in understanding "background" levels of antimony in indoor dust and assist in estimating human exposure to ATO from flame retardant use.

Table 5-4. Antimony Concentrations in Dust (Antimony sources not always specified)

Country	Location	Media/ Area	Antimony Concentrations[1]	Reference	Notes
United States	New Mexico, Zuni reservation	Indoor surface dust, control homes (n=8)	Geo mean: 7 ng/ sample (0.007 µg/sample) Range: 5-9 ng/sample (0.005-0.009 µg/sample)	Gonzales et al., 2004	Study looked at concentrations of surface-dust metals in Native American jewelry making homes. Data reported here are from non-jewelry making control homes; surface dust samples were collected by wiping Whatman 41 70-mm filter paper on 715 cm^2 surface areas; Antimony measured using ICP-MS and AAS.
New Zealand	Christchurch	House dust (n=11)	Mean: 10 ng/g (10 µg/kg) StD: 9.64 ng/g (9.64 µg/kg) Range: 1.83-30.6 ng/g (1.83-30.6 µg/kg) No median reported	Fergusson et al., 1986	Samples were taken from the carpet in the main living area using a small diaphragm vacuum pump from a 0.25 m^2 area of carpet onto a 37 mm filter; authors suggested concentrations similar to that in local soils
Australia	Sydney	Ceiling dust/attic dust in homes not near industry (n=10)	Mean: 7,000 ng/g (7.0 mg/kg) StD: 4,600 ng/g (4.6 mg/kg) Median: 6,800 ng/g (6.8 mg/kg) Geo mean: 5,500 ng/g (5.5 mg/kg) Range: 2,000-14,700 ng/g (2.0-14.7 mg/kg)	Davis and Gulson, 2005	Sampling was performed by brushing a measured area of dust (100 cm^2 if possible) into polyethylene containers. The authors suggest potential contributions from vehicular traffic, combustion, chemical oxidation, building and construction material, and probably the dispersion of particulates carried by winds

Country	Location	Media/ Area	Antimony Concentrations[1]	Reference	Notes
Canada	Ottawa, Ontario	Homes (n=48)	Mean: 7,280 ng/g (7.28 mg/kg) Range: 1,160-57,410 ng/g (1.16-57.41 mg/kg) 95th percentile: 15,380 ng/g (15.38 mg/kg)	Rasmussen et al., 2001	Residents collected indoor dust by vacuuming; antimony measured with ICP-MS. Authors note that mean concentration in dust was greater than concentration in soil from same houses, suggesting there could be additional sources of antimony in the homes.
	Ontario, Barrie, Greater Sudbury, Thunder Bay	Household wipe samples; entry area of homes (n=208)	50th percentile: 500 ng/m^2 (0.5 µg/m^2) 95th percentile: 4,800 ng/m^2 (4.8 µg/m^2) Max: 23,000 ng/m^2 (23 µg/m^2)	McDonald et al., 2010	Wipe samples collected from January to March 2008. Samples taken with Ghost Wipes™ brand within a 30 cm^2 plastic template area (ASTM E 1728 protocol; measured antimony using ICP-MS. No minimum or mean reported. Entry areas 57% < LOQ; interior areas 74% < LOQ; LOQ – 0.60 µ/m^2
		Household wipe samples; interior areas of homes (498 samples from 228 homes)	50th percentile: 200 ng/m^2 (0.2 µg/m^2) 95th percentile: 2,700 ng/m^2 (2.7 µg/m^2) Max: 18,000 ng/m^2 (18 µg/m^2)		
Bolivia	Oruro, suburban non-mining district	House dust (n=41)	Median: 33,960 ng/g (33.96 ppm) Range: (5-95th %s): 23,470-84,310 ng/g (23.47-84.31 ppm)	Barbieri et al., 2014	Roughly 1 g dust collected from the top surfaces of furniture or windowsills using a 1.5 inch brush.

Country	Location	Media/ Area	Antimony Concentrations[1]	Reference	Notes
Bolivia	Oruro, peripheral district, 3.5 km from mine	House dust (n=41)	Arithmetic mean: 46,430 ng/g (46.43 ppm) StD: 5,930 ng/g (5.93 ppm) Geo mean: 39,230 ng/g (39.23 ppm) Range: 18,110-203,650 ng/g (18.11-203.65 ppm)	Fontúrbel et al., 2011	Roughly 1 g dust collected from the top surfaces of furniture or windowsills using a 1.5 inch brush. The authors suggest that exposure is related to proximity to the mine.
France	Various areas	House dust (n=473)	Majority of samples and median value <LOQ Range: <LOQ-8,600 ng/m^2 (<LOQ-8.6 µg/m²)	Glorennec et al., 2012	A floor area of 0.1 m² was sampled with a moist lead-free wipe. LOQ=800 ng/m^2 (0.8 µg/m²)
Saudi Arabia	Dhahran	House (n=9)	Geo mean: 5,450 ng/g (5.45 µg/g) StD: 2,650 ng/g (2.65 µg/g) Arithmetic mean: 5,860 ng/g (5.86 µg/g) Range: not reported	Turner and Hefzi, 2010	Dust collected by vacuuming entire accessible floor space using an upright, bagless vacuum cleaner and passed through 63 µm Nylon mesh; Antimony measured using ICP-MS
Japan	Several regions	House (n=100)	Mean: 10,100 ng/g (10.1 mg/kg) StD: 2,060 ng/g (2.06 mg/kg) Range; 1,930-439,000 ng/g (1.93-439 mg/kg)	Yoshinaga et al., 2014	Study investigating source of lead from house dust measured other elements, including Antimony. Volunteered samples from 100 residences collected 2006-2012; vacuum cleaner dust passed through 250 µm –mesh; Antimony measured using ICP-MS.
China	Guiyu town in Shantou, Guangdong province	House Dust, control (n=5)	Range: 660-2,450 ng/g (0.66-2.45 mg/kg)	Bi et al., 2011	5 control sites and 5 non-e-waste; dust samples were collected inside from the floor using a brush and plastic spatula

Country	Location	Media/ Area	Antimony Concentrations[1]	Reference	Notes
China	Guiyu town in Shantou, Guangdong province	House Dust, non-e-waste (n=5)	Range: 6,100-9,200 ng/g (6.1-9.2 mg/kg)	Bi et al., 2011	5 control sites and 5 non-e-waste; dust samples were collected inside from the floor using a brush and plastic spatula

[1]For ease of comparison, all units are converted to ng equivalent when possible. Original study units, if different, are shown in parentheses. See text for explanation.
Geo – geometric; StD – standard deviation; LOQ – limit of quantification; ICP-MS – inductively coupled plasma-mass spectrometry

5.3.5 ATO in Consumer Products

As reported above, ATO has many non-flame retardant uses. Because of this, there are data reporting ATO concentrations in products and materials not related to use as a flame retardant. ATO has been found in a number of consumer products for non-flame retardant purposes, including children's toys (Korfali et al., 2013; Guney and Zagury, 2013), children's jewelry (Guney and Zagury, 2013), and a number of PET product types (food trays, water bottles, etc.) (Dutra et al., 2014; Halidmann et al., 2007). These exposures are not relevant for the current assessment, and concentrations of antimony in these materials were not investigated further. Only those data on ATO (or antimony, as a presumed or possible surrogate for ATO) related to flame retardant use in consumer products are presented in this report.

Overall, there is little information available regarding consumer exposure to ATO from flame retardant uses (Snedeker et al., 2014). A number of studies detected antimony in electronic waste materials (Lincoln et al., 2007; Morf et al., 2005; Schlummer et al., 2007). Even though waste products are a post-consumer exposure scenario, available information from these studies are noted here because they may provide some information to help inform on the concentrations of antimony present in electronics where ATO may be present for flame retardancy purposes.

Release of antimony gas from PVC cot (crib) mattresses following microbial degradation from mattress bacteria has been postulated to cause Sudden Infant Death Syndrome (SIDS) in children (Cooper and Harrison, 2009). Available data suggest that antimony concentrations released from this pathway do not correlate with the occurrence of SIDS and suggests that antimony concentrations are not high enough to be toxicologically relevant (Cooper and Harrison, 2009; Shyam and Jaya 2010; Jenkins et al., 1998; Snedeker et al., 2014).

We located limited additional information on measurements of ATO (antimony) in consumer products for flame retardant purposes. For those studies and reports that explicitly mention flame retardant use, we report information in Table 5-5 (Lincoln et al., 2007; CPSC, 2006a; Majestic et al., 2012; EURAR, 2008 as cited by Health Canada, 2010; Jenkins et al., 1998; Jenkins et al.,

2000; Morf et al., 2005; Schlummer et al., 2007). Some of the studies and reports do not specify ATO use for flame retardancy, and it is not clear whether the ATO presence reflects this use; we have captured information from those studies and reports in Table 5-6 (Butterman and Carlin, 2004; HealthyStuff.org, 2014; EURAR, 2008 as cited in Health Canada, 2010; Vasile, 2000 as cited in Health Canada, 2010; HealthyStuff, 2009 as cited in Sørensen et al., 2005; CPSC, 2006a; Mansson et al., 2009; Huisman et al., 2007 as cited in Chancerel et al., 2013; Sorensen et al., 2005; Isama et al., 2011; Kawamura et al., 2006).

Table 5-5. Antimony Concentrations in Consumer Products (FR use specified or presumed)

Country	Item	Media	Antimony Concentrations[1]	Reference	Notes
United States	Cell phones	Shredded and digested samples	Mean: 1,023,000 ng/g (1,023 mg/kg) Range: 860,000-1,290,000 ng/g (860-1,290 mg/kg)	Lincoln et al., 2007	Brominated FR were absent as reported by authors. This may be suggestive that ATO was not used as a FR synergist.
	Mattress barriers/fabric	Cotton batting	Mean: 2.4%	CPSC, 2006a	FR use, as reported by authors
	Mattress barriers/fabric	Nonwoven modacrylic /Visil	Mean: 3.8%		
	Mattress barriers/fabric	Modacrylic knit	Mean: 4.5%		
	Mattress barriers/fabric	Coated foam/ melamine	Mean: 4.1×10^7 ng/g (41,000 mg/kg or 4.1%)		
	Mattress barriers/fabric	Coated poly-cotton ticking/ melamine	Mean: 2.7%		
	Mattress barriers/fabric	Coated poly-cotton/ melamine	Mean: 3.1%		
	Mattress barriers/fabric	Coated knit/ melamine	Mean: 4.4%		

Country	Item	Media	Antimony Concentrations[1]	Reference	Notes
United States	Carpet in elementary school	Carpet	6,000 ng/g (6.0 µg/g)	Majestic et al., 2012	The authors correlate school air Antimony concentrations with emission and/or resuspension from carpet (FR use)
Canada	Fabrics		Range: 2,000,000-60,000,000 ng/g (2,000-60,000 mg/kg)	EURAR, 2008 as cited by Health Canada, 2010	FR use, as reported by Health Canada
United Kingdom	Bedding	PVC cot (crib) mattress covers	Range: 230,000 - 310,500,000 ng/g (0.23-31.05 mg/g)	Jenkins et al., 1998	FR use, as reported by authors
	Bedding	Cot (crib) mattress covers	Range: <200-220,600 ng/g (<0.2 - 220.6 µg/g)	Jenkins et al., 2000	FR use, as reported by authors
	Bedding	PU foam samples	Range: <200- > 3,300 ng/g <0.2->3.3 µg/g)		FR use, as reported by authors
Switzerland	Small electrical and electronic equipment waste materials	Printed circuit boards	Mean: 2,100,000 ng/g StD: 100,000 ng/g (2,100 ± 100 mg/kg)	Morf et al., 2005	Materials from an e-waste recycling plant; some FR use expected, as reported by authors
		TV housings (wood)	Mean: 57,000 ng/g StD: 1,000 ng/g (57 ± 1 mg/kg)		
		TV/PC housings (plastic)	Mean: 16,000,000 StD: 5,000,000 ng/g (16,000 ± 5000 mg/kg)		

Country	Item	Media	Antimony Concentrations[1]	Reference	Notes
Germany	Housing shredder residues	From TV sets and monitors	Range: 0.2-1.8% (only % reported)	Schlummer et al., 2007	Authors suggest concentrations due to FR use; samples from e-waste recycling
	Mixed WEEE shredder residues	Residues from WEEE recycling plants processing unsorted WEEE	4,000,000 ng/g (~4,000 mg/kg) (~4,000 ppm) (estimated from graph)		
	Single housing Samples	Single TV set and monitor housings	3,000,000 ng/g (~3,000 mg/kg (~3,000 ppm) (estimated from graph)		

[1]For ease of comparison, all units are converted to ng equivalent when possible. Original study units, if different, are shown in parentheses. See text for explanation.
StD – standard deviation; FR – flame retardant; WEEE – waste from electrical and electronic equipment

Table 5-6. Antimony Concentrations in Consumer Products (FR use not specified, or not certain)

Country	Item	Media	Antimony Concentrations[1]	Reference	Notes
United States	Flexible PVC, polyolefins, polystyrene, PET, acrylonitrile-butadiene-styrene (ABS), and polyurethanes	Not specified	1.5-12%	Butterman and Carlin, 2004	
	Rubber and other elastomers	Not specified	5-30%		
	PVC insulation on electrical wires and cables	Not specified	3%		

Country	Item	Media	Antimony Concentrations[1]	Reference	Notes
United States	Canvas, carpets, carpet padding, drapes, tenting, and other (usually heavier) textiles	Not specified	7%	Butterman and Carlin, 2004	
	Paper	Not specified	5-25%		
	Consumer products, fabrics, foams, holiday decorations		Range: 15,000-12,714,000 ng/g (15-12,714 ppm)	HealthyStuff.org, 2014	FR use not specified; consumer products from U.S. stores
Canada	Plastics	Polymers	Range: <80,000,000-250,000,000 ng/g (<80,000-250,000 g/kg)	EURAR, 2008 as cited in Health Canada, 2010	FR use not specified
		PET	Range: 180,000-200,000 ng/g (180-200 mg/kg)		
		PP	20,000,000 ng/g (20,000 mg/kg)	Vasile, 2000 as cited in Health Canada, 2010	
		HDPE	Range: 35,000,000-100,000,000 ng/g (35,000 -100,000 mg/kg)		
	Fabrics	Polyester	Range: >600-700,000 ng/g (>0.6-700 mg/kg)	HealthyStuff, 2009 as cited in Sørensen et al., 2005	FR use not specified
		Poly-cotton blend fabrics	Range: 27,000,000-38,000,000 ng/g (27,000-38,000 mg/kg)	CPSC, 2006a	
	Not specified	Coated foam	41,000,000 ng/g 41,000 mg/kg		

Country	Item	Media	Antimony Concentrations[1]	Reference	Notes
Sweden	Not specified	Packaging	Avg: 287,000 ng/g StD: 27,000 ng/g (287 mg/kg ± 27 mg/kg)	Mansson et al., 2009	FR use not specified
	Not specified?	Textiles	Avg: 134,000 ng/g StD: 29,000 ng/g (134 mg/kg ± 29 mg/kg)		FR use not specified
Germany	Electrical and electronic equipment	PCBS of information and communications technology equipment	Range: 0.04-0.35%	Huisman et al., 2007 as cited in Chancerel et al., 2013	Tested ATO in PCBs
Netherlands	Toys	Not specified	Range: 400-47,000 ng/g (0.4-47 ppm)	Sorensen et al., 2005	Not clear as to FR use
Japan	Household products made of synthetic resin that infants may swallow	Decorations part – acrylic	ND	Isama et al., 2011	Japanese article with only abstract and tables available in English; not clear if FR use. Only single values reported; ND level not specified
		PVC strap – orange	389 ng/g (0.389 mg/kg)		
		PVC strap – yellow	722 ng/g (0.722 mg/kg)		
	Tested PVC toys	Orange animal toy	Mean of 2 trials: 5,300 ng/g (5.3 mg/kg)	Kawamura et al., 2006	Japanese article with only abstract and tables available in English; not clear if FR use

[1]For ease of comparison, all units are converted to mg equivalent. Original study units, if different, are in shown in parentheses.

Avg – average; StD – standard deviation; FR – flame retardant; HDPE – high-density polyethylene; PET – polyethylene terephthalate; PP – polypropylene; PVC – polyvinyl chloride; WEEE – waste from electrical and electronic equipment; PCBs – poly chlorinated biphenyls; ND – not detected

5.4 ATO ADME and Biomonitoring Studies

Absorption: ATO has been shown to be poorly absorbed following oral administration in animal studies (ECHA, 2008; De Bie and Salmon-te Rietstap, 2005; Felicetti et al., 1974 as cited in

ECHA 2008). Human clinical studies of antimonial compounds administered for the treatment of parasitic diseases indicate that oral bioavailability in humans is poor (WHO, 2003 as cited in U.S. EPA, 2014). Based on results reported by the International Commission on Radiological Protection (ICRP), a systemic absorption in the range of ~1% may be assumed when estimating ATO uptake from the gastrointestinal tract (as cited in EURAR, 2008). This bioavailability has been cited by multiple assessments (Health Canada, 2010; ECHA, 2008; U.S. EPA, 2014) and is based on studies of various organic and inorganic antimony compounds, including ATO. It is notable that the toxicity of ATO is greater following exposure when dissolved in citric acid than when dissolved in water, suggesting that solubility can affect antimony absorption (Fleming, 1938 as cited in NRC, 2000).

Studies have consistently shown that animals and humans accumulate antimony in lung tissues following repeated inhalation exposures to ATO (McCallum et al., 1970; Gerhardsson et al., 1982; Leffler et al., 1984; Newton et al., 1994; Garg et al., 2003 as cited in Health Canada, 2010). Studies in retired workers suggest that inhaled antimony is retained in the lungs for several years following exposure (IPCS INTOX Databank, 2005; Gerhardsson et al., 1982). Evidence indicates that some fraction of inhaled ATO is bioavailable via the pulmonary route; however, the extent of systemic ATO bioavailability in humans has not been determined (Kim et al., 1997 as cited in NRC, 2000). Systemic absorption of antimony compounds following inhalation exposure is mainly influenced by chemical form, particle size, and solubility. It has been suggested that at least a portion of systemic absorption following inhalation exposure is due to the clearance of large particles (via mucociliary transport) and subsequent uptake *via* the gastrointestinal tract (Brain et al., 1994 as cited in U.S. EPA, 2014). Using modeled and predicted deposition patterns for inhaled ATO particles (4 μm), the total systemic absorption (reflecting combined uptake in the lungs and gastrointestinal tract) was estimated at approximately 7% (EURAR, 2008; U.S. EPA, 2014; Health Canada, 2010; ECHA, 2008).

Based on an *in vitro* human skin percutaneous study, dermal absorption of ATO is considered negligible at approximately 0.26% (Roper and Stupart, 2006 as cited in U.S. EPA, 2014; ECHA, 2008). EURAR (2008) has proposed this absorption rate of 0.26% be used for human skin (Health Canada, 2010).

Distribution: No information was found on the tissue distribution of antimony in humans following oral exposure (NRC, 2000). Studies in laboratory animals suggest systemic antimony binds to red blood cells and distributes widely to most tissues and organs, including bone marrow, thyroid, liver, spleen, kidney, heart, lungs, and hair (Gross et al., 1955a as cited in Health Canada, 2010; NRC, 2000; Sunagawa, 1981; Hiraoka, 1986 as cited in Health Canada, 2010). In humans, repeated ATO inhalation exposures result in lung accumulation and prolonged retention of antimony in the lungs. Among the retired workers evaluated by Gerhardsson et al. (1982), antimony concentrations measured in organs other than the lungs (e.g., liver and kidney)

were comparable to control levels measured in unexposed individuals, indicative of either a short biological (systemic) half-life of inhaled antimony or insignificant systemic distribution to these tissues (Gerhardsson et al., 1982 as cited in U.S. EPA, 2014). Additional data indicate that systemic antimony can be distributed to the fetus and excreted in breast milk to nursing infants; thus, when maternal systemic levels are elevated, increased exposures may occur both *in utero* and during breast-feeding (ECHA, 2008; Belyaeva, 1967 [Article in Russian] as cited in NRC, 2000; Clemente et al., 1982; Iyengar et al., 1982; Shand et al., 1985 as cited in Health Canada, 2010; Wappelhorst et al., 2002 as cited in Health Canada, 2010). No studies were identified on the tissue distribution of antimony trioxide following dermal exposure (NRC, 2000).

Metabolism: Because antimony is a metallic element, it is not expected to be metabolized or broken down systemically and may only change valence or form. Intraperitoneal injection of rats with 800 μg trivalent antimony chloride/kg did not result in detectable levels of any organic form of antimony in the bile or urine, indicating that trivalent antimony is not methylated *in vivo* and is excreted in the inorganic form in urine. Antimony can form a complex with glutathione *in vivo* (Bailly et al., 1991 as cited in IARC, 1989).

Excretion: Toxicokinetic studies in animals have shown that the primary route of excretion for orally administered trivalent antimony (Sb(III)) is primarily in the feces and, to a much lesser extent, the urine (Gross et al., 1955a; TNO, 2005, as cited in Health Canada, 2010; ECHA, 2014). The large amount of antimony excreted in the feces soon after exposure suggests that a substantial portion of the compound is excreted without being absorbed systemically. This is consistent with the assumed oral absorption rate of ~1% (ICRP, 1981, as cited by NRC, 2000).

Once systemically available, antimony compounds are eliminated mainly in the urine, with small amounts appearing in feces *via* bile excretion after conjugation with glutathione. Since antimony has been measured in blood and urine in workers with pulmonary ATO exposures (Bailly et al., 1991, as cited in U.S. EPA, 2014), it appears that systemic elimination exceeds pulmonary absorption, which would explain why Gerhardsson et al. (1982 as cited in U.S. EPA, 2014) did not observed tissue accumulation in occupationally exposed individuals. A significant amount of antimony excreted in bile undergoes enterohepatic circulation (Bailly et al., 1991, as cited in Harrison et al., 1998). This is indicative of a slow release and renal elimination of antimony from uncharacterized tissue storage depot(s). This is supported by an evaluation of the plasma elimination of pentavalent antimony following intramuscular injection that demonstrated a two-compartment pharmacokinetic disposition. These results are consistent with a renal elimination half-life of four days estimated in 21 employees of a starter battery manufacturing plant who were exposed to ATO via inhalation (Kentner et al., 1995, as cited in U.S. EPA, 2014; Harrison et al., 1998; Kentner et al., 1995, as cited in U.S. EPA, 2014).

Elimination of ATO from the lungs following inhalation is slow relative to oral exposure. In humans, antimony may be retained in the lungs for long periods following inhalation exposure. Lung retention times measured in seven male workers accidentally exposed to radiolabeled aerosols of ATO (^{125}Sb) showed that most of the radio labeled material was confined to the lungs with negligible amounts detected in other parts of the body. As with systemically bioavailable ATO following oral administration, McCallum (1963) reported that urinary excretion from occupational inhalation exposure also occurs in humans and that inhalation exposures are also systemically available.

Biomonitoring: Biomonitoring data are available for worker exposure to ATO (Clemente et al., 1982 as cited in Snedeker et al., 2014; Barbieri et al., 2014; Barbieri et al., 2011; Schulz et al., 2009, as cited in Snedeker et al., 2014; Gebel et al., 1998; Nordic Council of Ministers, 1998; CDC, 2015; Cooper and Harrison, 2009; Shyam and Jaya, 2010; ICRP, 1981, as cited in ATSDR, 1992; and as cited in ATSDR, 1992: Sumino et al., 1975; Muramatsu and Parr, 1988; Takagi et al., 1986; Mansour et al., 1967; Olmez et al., 1978) (Table 5-7). Overall, data suggest that in the general population antimony concentrations in urine have been decreasing over time, as evidenced by reviews of the NHANES urinary antimony concentrations over time (Snedeker et al., 2014; CDC, 2015).

Firefighters' exposure to antimony (exposure via flame-retardant-treated uniforms) was tested with urine samples (de Perio et al., 2010). Shyam and Jaya (2010) report that the CDC recommends urine testing as the most accurate, reliable, and valid test for measuring antimony. Two other studies were identified that linked antimony concentrations in workers to ATO exposure (Kim et al., 1999; Iavicoli et al., 2002). There may be additional worker biomonitoring studies, but since the focus of this report was not on occupational exposure, we may not have captured all occupational exposure data here. ATSDR (1992) noted that antimony may be released during fires and cited a study by Willetts et al. (1982) that analyzed the presence of antimony in soot and in tracheal specimens of 18 fire victims. The study showed that 50% of tracheal antimony concentrations exceeded the normal range of 0.1-124.0 ppm.

Table 5-7. Antimony Biomonitoring Data

Country	Tissue/fluid	Antimony Concentrations[1]	Reference	Notes
United States	Urine	Geo mean: 56 ng/L (0.056 µg/L) Range: 53-59 ng/L (0.053-0.059 µg/L)	CDC, 2015	NHANES Survey: 1999-2010

Country	Tissue/fluid	Antimony Concentrations[1]	Reference	Notes
United States	Urine (n=148)	Range: <20-500 ng/L (<0.02-0.5 µg/L) in 97.5% of samples; Range: >1000 ng/L (1 µg/L) in 3.5%	Cooper and Harrison, 2009	Children from pre-term infants until 2 years of age, part of cot (crib) study; 122 term and 26 pre-term infants; LOD=20 ng/L
	Urine	Range: 120-364 ng/g (0.120-0.364 µg/g) creatinine	Shyam and Jaya, 2010	Ranges for urinary antimony levels in the general population
	Total body burden	7,900,000 ng (7.9 mg)	ICRP, 1981, as cited in ATSDR, 1992	
Various	Skin	96 ng/g (0.096 µg/g)	Sumino et al., 1975; Muramatsu and Parr, 1988; Takagi et al., 1986; Mansour et al., 1967; Olmez et al., 1978; as cited in ATSDR, 1992	Autopsy data from unexposed Japanese and Swedish adults; hair samples from North America (USA, Canada), Europe (Poland), and Asia (Japan and India). Detection limit not reported. Not clear whether the reported single values are one measurement or an average.
	Hair	Range: 96-120 ng/g (0.096-0.12 µg/g)		
	Adrenal gland	73 ng/g (0.073 µg/g)		
	Lung	62 ng/g (0.062 µg/g)		
	Large intestine	47 ng/g (0.047 µg/g)		
	Trachea	45 ng/g (0.045 µg/g)		
	Cerebellum	30 ng/g (0.030 µg/g)		
	Kidney	ND-43 ng/g (ND-0.043 µg/g)		
	Small intestine	39 ng/g (0.039 µg/g)		
	Heart	32 ng/g (0.032 µg/g)		
	Pancreas	30 ng/g (0.030 µg/g)		
	Spleen	29 ng/g (0.029 µg/g)		
	Liver	ND-23 ng/g (ND-0.023 µg/g)		
	Ovary	21 ng/g (0.021 µg/g)		
	Testicle	17 ng/g (0.017 µg/g)		
	Cerebrum	16 ng/g (0.016 µg/g)		

Country	Tissue/fluid	Antimony Concentrations[1]	Reference	Notes
Various	Blood	0.016-0.34 (no units reported)	Sumino et al., 1975; Muramatsu and Parr, 1988; Takagi et al., 1986; Mansour et al., 1967; Olmez et al., 1978; as cited in ATSDR, 1992	
	Saliva	0.003 (no units reported)		
	Mean body burden	700 ng/g (0.7 mg/kg)		
Nordic Countries	Blood	Mean: 700-85,000 ng/L (0.7-85 µg/L) Range: ND-33,000,000 ng/L (ND-33,000 µg/L)	Nordic Council of Ministers, 1998	Background levels in human biological material (wet weight) from non-occupationally exposed. Detection level not specified.
	Urine	Mean: <1000-6,200 ng/L (<1.0-6.2 µg/L) Range: ND-11,000 ng/L (ND-11 µg/L)		
	Serum	Mean: <600-5,200 ng/L (<0.6-5.2 µg/L) Range: ND-15,000 ng/L (ND-15 µg/L)		
	Liver	Mean: 6-23 ng/g (0.006-0.023 mg/kg) Range: <10-70 ng/g (<0.01-0.07 mg/kg)		
	Lung	Mean: 17-95 ng/g 0.017-0.095 mg/kg Range: <10-200 ng/g (<0.01-0.20 mg/kg)		
	Hair	Mean: 41 ng/g (0.041 mg/kg) Range: ND-2,640 ng/g (ND-2.64 mg/kg)		
	Teeth	Range: 5-670 ng/g (0.005-0.67 mg/kg)		

Country	Tissue/fluid	Antimony Concentrations[1]	Reference	Notes
Nordic Countries	Bone	Median: 7 ng/g (0.007 ppm) Range: 7-100 ng/g (0.007-0.1) ppm)	Nordic Council of Ministers, 1998	
Italy	Breast milk	Range: <1.0-49.6 ng/g	Clemente et al., 1982 as cited in Snedeker et al., 2014	
Germany	Urine	300 ng/L (0.3 µg/L)	Schulz et al., 2009, as cited in Snedeker et al., 2014	Children aged 3 to 14 years old
	Urine	Mean: 1,530 ng/24 hrs (1.53 µg/24 hrs) Range: < 500-4,740 ng/hrs (<0.5-4.74 µg/24 hrs)	Gebel et al., 1998 (Also stratified by exposed and reference groups)	Males
	Urine	Mean: 980 ng/24hrs (0.98 µg/24 hrs) Range: 500-5,350 ng/24hrs (<0.5-5.35 µg/24 hrs)		Females
	Blood	Mean: 970 ng/L (0.97 µg/L) Max: 7,540 ng/L (7.54 µg/L)		Males
	Blood	Mean: 700 ng/L (0.70 µg/L) Max: 3,580 ng/L (3.58 µg/L)		Females
	Scalp hair	Mean: 47 ng/g (0.047 µg/g) Range: 5-140 ng/g (<0.005-0.14 µg/g)		Males
	Scalp hair	Mean: 51 ng/g (0.051 µg/g) Range: <5-840 ng/g (<0.005-0.84 µg/g)		Females

[1]For ease of comparison, all units are converted to ng equivalent. Original study units, if different, are shown in parentheses.
ND – not detected; Max – maximum; Geo – geometric; ATO – antimony trioxide; StD – standard deviation; FR – flame retardant; ICP-MS – inductively coupled plasma-mass spectrometry; SF-ICP-MS – sector field inductively coupled plasma-mass spectrometry

5.5 ATO Exposure Assessments and Estimates

Several authoritative agencies have estimated exposure to ATO for adults and children (Health Canada, 2010; ECHA, 2008; Babich. 2006; NRC, 2000). Not all of the exposure estimates differentiate ATO exposures from flame retardant uses, other uses, or all uses.

It should be noted that multiple approaches exist to calculate the average daily intake, each utilizing different values, institutional practices and accepted assumptions about many factors (e.g., safety factors, using high end, or average values for intake estimates, assumptions about food intake, derivation of those values for subpopulations, such as children, toddlers). In an exposure assessment, choices for those values and the assumptions and approaches should be discussed and defended.

Health Canada (2010) conducted a screening assessment of antimony trioxide (CAS RN 1309-64-4) under Section 74 of the Canadian Environmental Protection Act (CEPA) Challenge Program. They concluded that the general population is expected to be primarily exposed to antimony trioxide from use of household products containing flame retardants, but the total anticipated exposure is low (Health Canada, 2010).

Health Canada estimated upper bound daily intake of antimony for infants, children and adults (non-occupational exposure in Canada) (Health Canada, 2010). Intakes included exposure via air, drinking water, food and beverages, and soil. Antimony intake levels were converted to antimony trioxide using a molar ratio of 1.2. The upper bound estimates for antimony trioxide ranged from a low of 0.4 µg/kw bw/day for breast milk fed infants (no antimony or ATO detected in breast milk, this value represents intake from soil) to a high of 4.5 µg/kw bw/day for "not formula fed" infants. The next highest intake level was 3.89 µg/kw bw/day for a child aged 0.5 to 4 years with food accounting for almost all of the estimated exposure (Health Canada, 2010). Even though antimony can be found in dust, Health Canada considered the inhalation exposure route for antimony in house dust to be negligible (Health Canada, 2010). They estimated an upper bound estimate of dermal exposure to antimony trioxide from house dust using methods described by Environ (Environ, 2003a, b) and data from Rasmussen et al. (2001). Estimates ranged from 0.37 ng/mg bw/day (children aged 5-11) to 0.54 ng/kg bw/day (infant up to six months).

For consumer products, Health Canada calculated upper bound estimates of potential daily exposure from ATO for several exposure scenarios and presented the worst-case scenario estimates in Appendix 5 of the Health Canada screening assessment (Health Canada, 2010).

- 0.03 mg/kg bw/day (as antimony trioxide) - dermal exposure of a child (0.5 to 4 years) sitting on a couch, using scenario from NRC (2000) and assumptions from EURAR (2008), Health Canada (1995), NRC (2000), and Health Canada (1998).
- 45 µg/kg bw/day (as antimony trioxide) - dermal exposure of infant (0-6 months) lying on a mattress cover (sweat mediated), using scenario and default assumptions for antimony trioxide from CPSC (2006b) and additional assumptions from Health Canada (1995), Howard and Wong (2001), and Health Canada (1998).
- 2.2 µg/kg bw/day (as antimony trioxide) - dermal exposure of a child (0.5 to 4 years) lying on a mattress cover (urine mediated), using scenario and default assumptions from CPSC (2006b) and additional assumptions from Health Canada (1995), Howard and Wong (2001), and Health Canada (1998).
- 0.24 µg/m^3/day (as antimony trioxide) – inhalation of particulates (all ages) from sitting on upholstery, using scenario and default values from NRC (2000).
- 0.7 µg/kg bw/day (as antimony trioxide) – oral ingestion of infants (0 to 6 months) mouthing polyester fabric of plush toys and upholstery, using scenario and default values from NRC (2000) and additional assumptions from Health Canada (1998).
- 0.2 µg/kg bw/day (as antimony trioxide) – oral ingestion of infants (0 to 6 months) mouthing mattress cover, using scenario and default values from NRC (2000) and additional assumptions from Environ (2003)

ECHA has evaluated ATO and prepared a summary risk assessment report (2008) that estimates exposure to ATO from the general environment and from consumer products. ECHA (2008) concluded that consumer exposure may occur from articles containing ATO through inhalation, ingestion, and dermal contact with household dust.

ECHA (2008) estimated reasonable worst-case exposures to ATO for a number of consumer scenarios based on measured data (measured concentrations of antimony were adjusted by 1.2 molar fraction to correct for molecular weight and calculate the concentration of ATO):

- 1.8 µg/kg bw/day (ATO particles) - dermal exposure for an adult sitting on upholstery fabric
- 0.25 µg/kg bw/day[3] - oral exposure of children from sucking on cuddly toys
- 3.15×10^{-6} mg/m^3 - inhalation exposure from indoor air. The relevant exposure pathway includes ATO released as inhalable particles from consumer products
- 0.60 µg/kg bw/day - oral exposure of children from ingestion of dust
- 0.035 µg/kg bw/day[1] (adjusted to ATO) – oral exposure of adults from drinking from a PET bottle.

[3] The measured concentrations of antimony are adjusted by a factor of 1.2 (to correct for molecular weight) to calculate the concentration of ATO.

ECHA (2008) estimated reasonable worst-case daily intakes to ATO in the general environment for four regional[4] scenarios (based on measured data):

- Food – oral exposure via food is 0.096 μg/kg bw/day for adults
- Breast milk: oral exposure via breast milk is 0.087 μg/kg bw/day for infants during the first 0-3 months
- Drinking water - oral exposure via drinking water is estimated to 0.029 μg/kg bw/day.
- Outdoor air - 3.12 ng/m^3

ECHA also estimated a maximum local[5] exposure via water ingestion of 2.8 μg/kg/day. They cautioned that this is based on untreated surface water concentrations, which are not representative of drinking water in the EU, and therefore, this intake should be considered a gross overestimate.

The U.S. CPSC staff assessed human health risks from exposure to a number of flame retardant chemicals, including ATO, in residential upholstered furniture (Babich and Thomas, 2001). U.S. CPSC calculated an average daily dose (ADD) for ATO of 4.9×10^{-4} for adults and 6.9×10^{-4} for children for a combination of scenarios that included oral, inhalation and dermal exposure. U.S. CPSC concluded that oral and dermal exposures to ATO were below a level of concern, but inhalation of particles was near the level of concern for both cancer and non-cancer effects (Babich and Thomas, 2001).

The National Research Council (NRC, 2000) conducted an upper bound worst-case screening assessment of the risk and exposure of several flame retardants including ATO in a project for U.S. CPSC. NRC developed risk values for oral and inhalation routes of exposure and compared these with exposure estimates to calculate hazard indices that provide an indication of potential risk.

For dermal exposure, NRC estimated a level of 2.0×10^{-2} mg/kg/day based upon an exposure scenario of adults sitting for 25% of their time on furniture upholstery treated with ATO. When divided by the NRC-developed oral reference dose (RfD) of 0.2 mg/kg/day, the result is a hazard index of 0.1, indicating that ATO used as a flame retardant in upholstery fabric is not expected to present a non-cancer hazard for dermal exposure in worst-case scenarios (NRC, 2000).

For inhalation exposure, NRC (2000) used a scenario assuming a quarter of one's lifetime spent in a 30 m^3 room with a low air-change rate, ATO-treated upholstery fabric (2.5 mg/cm^2) gradually worn over 15 years of product lifetime reducing the initial quantity of ATO by half,

[4] Regional refers to semi-industrialized European Union geographic area with a surface area of 40,000 km^2 and a population of 20 million people.

[5] Local reflects the largest local site.

and an estimated release rate of 2.3 x 10^{-7} per day. This resulted in an inhalation time-average exposure ATO concentration of 0.24 μg/m^3 for adult exposure to particles. NRC divided this by the NRC-developed inhalation reference concentration of 0.0002 mg/m^3 resulting in a hazard index of 1.2, indicating that inhalation of ATO particles may possibly pose a non-cancer risk under a worst-case exposure scenario (NRC, 2000).

For oral exposure, NRC (2000) used a scenario of a child sucking on 50 cm^2 of fabric back-coated with ATO daily for two years. Using the highest expected application rate of 2.5 mg/cm^2 and a fractional release rate of 0.001/day, they estimated an average oral dose rate of 0.00052 mg/kg/day. Considering the NRC-derived RfD of 0.2 mg/kg/day, a hazard index of 0.0026 would results from this use of worst-case exposure assumptions; therefore, ATO would not pose a non-cancer risk by the oral route.

5.6 ATO Discussion

The above data compilation and data represent a best effort to render useful information that was responsive to the task. The lack of basic data has significantly hindered this effort. This analysis of environmental concentrations and consumer exposure to ATO was very challenging because it is fraught with uncertainty due to a lack of basic experimental data and inconsistency relative to the reporting of available information.

We could find little or no data directly related to the availability of ATO associated with treated objects regarding direct human exposure potential. The most important and consistent data available provides information on the concentration of antimony (presumably from ATO) in house dust. Unfortunately, even in this area there is little information as to whether the antimony in dust came from diffusion from flame retardant containing or treated objects or the physical breakup of the treated product leading to antimony-containing dust.

In doing this work, a third possibility occurred to us regarding the presence of antimony (or ATO) in house dust; namely, antimony-containing ambient $PM_{2.5}$ particulates entering the indoor environment.

The ambient levels of antimony in ambient air in the U.S. and Canada have been reported to range from 0.5 to 55 ng/m^3 (Health Canada, 2010). We will assume a median of 5 ng/m^3 for this analysis. Studies in urban and suburban areas in the U.S. in the 1990s indicated an annual average concentration of $PM_{2.5}$ of approximately 15,000 ng/m^3 in ambient air (Chuersuwan et al., 2000). Assuming that the ambient 15,000 ng/m^3 $PM_{2.5}$ contains 5 ng/m^3 antimony, the following is an estimated average concentration of antimony in the ambient $PM_{2.5}$ particulate:

5 ng/m^3 / 15,000 ng/m^3 = 330,000 ng/g

Exposure research has shown that a majority of the ambient atmospheric $PM_{2.5}$ concentrations can enter the indoor environment (Joseph et al., 2010; Sarnat et al., 2006)**.** These particles containing antimony, once indoors, could settle and comingle with dust within the residence and this could easily lead to some and perhaps most of the measured antimony-in-dust concentrations reported above. Also, tracking in of dirt containing antimony from settled $PM_{2.5}$ would contribute to this exposure potential. The mean of 17 ng/m^3 measured by Majestic et al. (2012) in an Arizona school falls within the range of 5 to 55 ng/m^3 cited by Health Canada (2010) for ambient air. Ambient air will always be present indoors while the particles are slowly settling. Given the large fraction of indoor dust that likely transfers from ambient air and the limited available measurement data, it is not clear that any significant ATO exposure comes from the use of ATO as a flame retardant.

As such, despite best efforts, product-related human exposure potential to ATO has not been shown. Well-designed and focused experiment data and evidence will be required to reasonably confirm or deny any product/ATO exposure connection. There is simply too much uncertainty in the currently available data to make a determination.

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Appendix A – Flame Retardant Exposure Literature Search Strategy

TERA conducted a thorough literature search that included: Pubmed, Google Scholar, Science Direct, TOXNET (including Toxline), CAB abstracts databases and a general web search. The search terms that were used are listed below.

Search terms

Chemical name OR CAS number AND exposure
Chemical name OR CAS number AND human
Chemical name OR CAS number AND children
Chemical name OR CAS number AND consumer
Chemical name OR CAS number AND consumers
Chemical name OR CAS number AND residential
Chemical name OR CAS number AND residential AND children
Chemical name OR CAS number AND residential AND consumers
Chemical name OR CAS number AND dust
Chemical name OR CAS number AND "hand to mouth"
Chemical name OR CAS number AND mouthing
Chemical name OR CAS number AND dislodgeable residue
Chemical name OR CAS number AND dermal
Chemical name OR CAS number AND oral
Chemical name OR CAS number AND inhalation
Chemical name OR CAS number AND ingestion
Chemical name OR CAS number AND indoor air
Chemical name OR CAS number AND products
Chemical name OR CAS number AND toys
Chemical name OR CAS number AND pillows
Chemical name OR CAS number AND baby carriers
Chemical name OR CAS number AND baby products
Chemical name OR CAS number AND human exposure assessment
Chemical name OR CAS number AND human risk assessment
Chemical name OR CAS number AND migration
Chemical name OR CAS number AND electronics
Chemical name OR CAS number AND plastic
Chemical name OR CAS number AND food
Chemical name OR CAS number AND air
Chemical name OR CAS number AND soil
Chemical name OR CAS number AND water
Chemical name OR CAS number AND bedding
Chemical name OR CAS number AND mattress

Chemical name OR CAS number AND foam
Chemical name OR CAS number AND carpet
Chemical name OR CAS number AND furniture
Chemical name OR CAS number AND biomonitoring
Chemical name OR CAS number AND breast milk

Inclusion criteria

According to the SOW, exposure should be human with an emphasis on residential or consumer exposures. Therefore, preference will be given to those articles that describe residential or consumer exposures. Articles will be included if human exposures or children's exposures to other sources are included. Articles will also be included if they describe levels in the environment and /or other media because they represent potential sources of exposure. If found, biomonitoring data will be included as they are represented of an exposed population. Also to be included is "grey" literature, such as white papers, poster, or presentations. More focus will be placed on references published two to three years prior to and after the publication of any identified major secondary references (i.e., ATSDR, EPA) for flame retardants because it is assumed that they did a thorough literature search. We will not apply any time exclusions.