

# Flame Retardants and Firefighter Exposure and Health

REPORT TO THE MINNESOTA STATE LEGISLATURE



## Flame Retardants and Firefighter Exposure and Health

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As requested by Minnesota Statute 3.197: This report cost approximately \$22,640 in staff time to prepare.

Language in Minnesota's 2015 Firefighter and Children Health Protection Act instructed the Minnesota Department of Health to work in consultation with the State Fire Marshal on this report. The State Fire Marshal appointed St. Paul Fire Captain Chris Parsons. Captain Parsons contributed to this report by providing industry knowledge and expertise, and acting as a subject matter expert. MDH did not solicit stakeholder input or peer review.

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January 2016



# Contents

Executive Summary .....	v
Abbreviations and Acronyms.....	vii
Abbreviations .....	vii
Glossary of Chemicals .....	viii
Flame Retardants and Firefighter Exposure and Health .....	1
Introduction.....	1
History.....	2
Scope of this report.....	3
Part 1: Laws, Regulations, and Safety Standards.....	5
1.1 Background .....	5
1.2 Regulations at the State Level .....	5
1.3 Regulations at the Federal Level .....	8
1.4 Regulations at the International Level .....	8
1.5 Fire Safety Standards and Practices .....	9
Part 2: Exposure .....	11
2.1 Introduction .....	11
2.2 Chemistry of Combusted Flame Retardants.....	12
2.3 Biomonitoring Findings.....	13
2.4 General Population Exposure.....	17
2.5 Firefighter Exposure.....	21
Part 3: Health Findings.....	23
3.1 Introduction .....	23
3.2 Relevant Toxicity Findings .....	24
3.3 Relevant Epidemiological Findings.....	33
Part 4: Risk Characterization Needs .....	36
4.1 Research Needs.....	36
4.2 Ongoing Research .....	38
4.3 Risk Characterization .....	39

Summary.....	40
References .....	42
Appendices .....	1
Appendix A. Complete Text of Flame Retardant Bill .....	2
Appendix B: Laws and Regulations.....	4
Appendix C. PBDE Biomonitoring Comparison Plots.....	9
Appendix D. Summary of Published Biomonitoring Equivalents .....	18

# Executive Summary

Minnesota legislators passed into law the “Firefighter and Children Health Protection Act” (Minn. Stat. 2015 325F.071) during the 2015 Minnesota legislative session. The session law required the Minnesota Department of Health (MDH), in consultation with the State Fire Marshal, to report to the Legislature on two general areas regarding flame retardant chemicals. MDH was asked to report on laws and regulations regarding relevant fire safety standards and flame retardant chemicals in upholstered furniture, mattresses, and carpet pads. MDH was also asked to report on the status of research about flame retardant chemicals and health and safety effects of exposures, particularly in firefighting settings.

MDH found that Minnesota is among many states that have been taking action on or researching concerns about flame retardants, exposure, and health. Multiple states have imposed bans on manufacturing certain flame retardants and placed restrictions on selling and purchasing particular products containing these chemicals. However, the bans and restrictions vary as states have targeted different consumer products and classes of flame retardants. The states of New York, Washington, and California have been particularly active in regulating manufacturing and researching health concerns around flame retardants. Restrictions on brominated and other flame retardant chemicals have been increasing nationally, with a focus on children (a life stage sensitive to health effects) and firefighters (a highly exposed occupation).

MDH found that research on firefighter exposure to flame retardants and health is in a formative stage. There are a growing number of studies that are focused on understanding firefighters’ exposures to flame retardants and other chemical hazards released by fires. While cancer is a well-known occupational hazard of firefighters, research has not yet indicated whether increased risk of cancer is due to exposure to flame retardants, and to what degree. Biomonitoring studies show that firefighters, compared to the general population, have more of certain flame retardants in their bodies. There are a wide variety of firefighting activities that result in exposure, and one key finding is that there is a high level of flame retardants in dust measured in fire stations compared to homes. We were not able to find information on flame retardants in the air that firefighters breathe during or after a fire, or flame retardants that may be absorbed through the skin.

MDH reviewed toxicity data from animal experiments and human health data from epidemiology studies. When tested in animal studies, flame retardants have a harmful effect on early development, reproduction, and hormone systems. Some flame retardants cause cancer. With additional work, these data could be used to estimate dust and air contamination levels of concern. However, we did not find data we need to use this information to calculate the amount of flame retardants in people’s bodies that does or does not pose a health risk. We found that studies of the adult general population are generally limited to only one class of flame retardants, the polybrominated diphenyl ethers. Findings in epidemiology studies are consistent with findings in animal studies. The data show there may be an association between exposure and thyroid hormone alterations and reproductive effects. The studies we reviewed

do not address the unique exposures and health effects that may result from the combustion of flame retardants in firefighting settings or in firefighters.

In summary, research shows that firefighters have a greater exposure to some flame retardants than the general population. We are concerned that there is a lack of information on cumulative risk from mixtures of chemicals and combustion by-products. MDH cannot, at this time, determine if firefighters' exposures exceed the levels that are associated with health risks studied in animals and humans. Further work is needed to either develop guidance for firefighters on levels of concern for flame retardants in air and dust, or to assess harmful levels of flame retardants in blood. MDH concludes that reducing the levels of flame retardants in dust and in air in the settings in which firefighters live and work will likely reduce firefighters' exposures to these chemicals.

# Abbreviations and Acronyms

## Abbreviations

ATSDR	Agency for Toxic Substances and Disease Registry
BMDL	benchmark dose level
CAS	Chemical Abstract Service
C.F.R.	Code of Federal Regulations
CPSC	Consumer Product Safety Commission
ECHA	European Chemicals Agency
EPA	U.S. Environmental Protection Agency
EU	European Union
FOX	Firefighter Occupational Exposure Study
IARC	International Agency for Research on Cancer
LOAEC	lowest-observed adverse effect concentration
LOAEL	lowest-observed adverse effect level
LOD	limit of detection
MDH	Minnesota Department of Health
mg/kg-d	milligram per kilogram per day
mg/m <sup>3</sup>	milligram per cubic meter
NIOSH	National Institute for Occupational Safety and Health
ng/kg-d	nanograms per kilogram of body weight per day
NOAEC	no-observed adverse effect concentration
NOAEL	no-observed adverse effect level
NSRL	no significant risk Level
NTP	National Toxicology Program
PBT	persistent, bioaccumulative, and toxic chemicals
pg/m <sup>3</sup>	picograms per cubic meter
POPS	persistent organic pollutants
REACH	Registration, Evaluation, Authorisation, and Restriction of Chemicals
RfD	reference Dose
RoHS	Restriction of Hazardous Substances
SNUR	Significant New Use Rule
SVHC	substances of very high concern
TB 117	State of California Technical Bulletin 117
U.S.	United States
µg/kg-d	microgram per kilogram of body weight per day
WTC	World Trade Center

## Glossary of Chemicals

Chemical Class	Abbreviation	Full Chemical Name	CAS Number
PBDEs		Polybrominated diphenyl ethers	
	TriBDE	Tribromodiphenyl ether (congeners: 16-39)	49690-94-0
	BDE-17	2,2',4'-tribromodiphenyl ether	147217-75-2
	BDE-28	2,4,4'-tribromodiphenyl ether	41318-75-6
	BDE-33	2',3,4-tribromodiphenyl ether	N/A
	TetraBDE	Tetrabromodiphenyl ether (congeners: 40-81)	40088-47-9
	BDE-47	2,2',4,4'-tetrabromodiphenyl ether	5436-43-1
	BDE-49	2,2',4,5'-tetrabromodiphenyl ether	243982-82-3
	BDE-66	2,3',4,4'-tetrabromodiphenyl ether	189084-61-5
	BDE-71	2,3',4',6-tetrabromodiphenyl ether	189084-62-6
	BDE-75	2,4,4',6-tetrabromodiphenyl ether	189084-63-7
	BDE-77	3,3',4,4'-tetrabromodiphenyl ether	93703-48-1
	PentaBDE	Pentabromodiphenyl ether (congeners: 82-127)	32534-81-9
	BDE-85	2,2',3,4,4'-pentabromodiphenyl ether	182346-21-0
	BDE-99	2,2',4,4',5-pentabromodiphenyl ether	60328-60-9
	BDE-100	2,2',4,4',6-pentabromodiphenyl ether	189084-64-8
	BDE-118	2,3',4,4',5-pentabromodiphenyl ether	446254-80-4
	BDE-119	2,3',4,4',6-pentabromodiphenyl ether	189084-66-0
	HexaBDE	Hexabromodiphenyl ether (congeners: 128-169)	36483-60-0
	BDE-138	2,2',3,4,4',5'-hexabromodiphenyl ether	182677-30-1
	BDE-153	2,2',4,4',5,5'-hexabromodiphenyl ether	68631-49-2
	BDE-154	2,2',4,4',5,6'-hexabromodiphenyl ether	207122-15-4
	BDE-155	2,2',4,4',6,6'-hexabromodiphenyl ether	35854-94-5
	HeptaBDE	Heptabromodiphenyl ether (congeners: 170-193)	68928-80-3
	BDE-183	2,2',3,4,4',5',6-heptabromodiphenyl ether	207122-16-5
	OctaBDE	Octabromodiphenyl ether (congeners: 194-205)	32536-52-0
	BDE-196	2,2',3,3',4,4',5,6'-octabromodiphenyl ether	446255-39-6
	BDE-197	2,2',3,3',4,4',6,6'-octabromodiphenyl ether	117964-21-3
	BDE-201	2,2',3,3',4,5',6,6'-octabromodiphenyl ether	446255-50-1
	BDE-202	2,2',3,3',5,5',6,6'-octabromodiphenyl ether	67797-09-5
	BDE-203	2,2',3,4,4',5,5',6-octabromodiphenyl ether	337513-72-1



FLAME RETARDANTS AND FIREFIGHTER EXPOSURE AND HEALTH

Chemical Class	Abbreviation	Full Chemical Name	CAS Number
	NonaBDE	Nonabromodiphenyl ether (congeners: 206-208)	63936-56-1
	BDE-206	2,2',3,3',4,4',5,5',6-nonabromodiphenyl ether	36687-28-0
	BDE-207	2,2',3,3',4,4',5,6,6'-nonabromodiphenyl ether	437701-79-6
	BDE-208	2,2',3,3',4,5,5',6,6'-nonabromodiphenyl ether	N/A
	DecaBDE	Decabromodiphenyl ether (congener: 209)	1163-19-5
	BDE-209	2,2',3,3',4,4',5,5',6,6'-decabromodiphenyl ether	1163-19-5
Other polybrominated or polychlorinated flame retardants			
	HBCD	Hexabromocyclododecane	25637-99-4
	PBB	Polybrominated biphenyl	67774-32-7
	SCCPs	Short-chained chlorinated paraffins	63449-39-8; 85535-84-8
	TBB	2-Ethylhexyltetrabromobenzoate	183658-27-7
	TBBPA	Tetrabromobisphenol A	79-94-7
	TBPH	Bis(2-ethylhexyl)tetrabromophthalate	26040-51-7
	TCEP	Tris(2-chloroethyl)phosphate	115-96-8
	TCPP	Tris(1-chloro-2-propyl)phosphate	13674-84-5
	TDBPP	Tris(2,3-dibromo-1-propyl)phosphate	126-72-7
	TDCPP	Tris(1,3-dichloro-2-propyl)phosphate	13674-87-8
		Trixylyl Phosphate	25155-23-1
Antimony and Antimony Compounds			
	ATO	Antimony trioxide	1309-64-4
Other chemicals			
	PAH	Polycyclic aromatic hydrocarbons	130498-29-2
	PCB	Polychlorinated biphenyl	1336-36-3

# Flame Retardants and Firefighter Exposure and Health

## Introduction

Minnesota legislators passed into law the “Firefighter and Children Health Protection Act” ([Minn. Stat. 2015 325F.071](#)) during the 2015 Minnesota legislative session. This legislation prohibits the sale and distribution of children’s products and upholstered residential furniture that contain more than a certain amount of one or more flame retardant chemicals named within the bill.

The statute states (see Appendix A for the complete text of the session law) that “On and after July 1, 2018, no manufacturer or wholesaler may manufacture, sell, offer for sale, distribute for sale, or distribute for use in this state a children’s product or upholstered residential furniture containing, in amounts greater than 1,000 parts per million in any product component, the following flame-retardants:

- Tris(1,3-dichloro-2-propyl)phosphate (TDCPP), Chemical Abstracts Service number 13674-87-8;
- Decabromodiphenyl ether (decaBDE), Chemical Abstracts Service number 1163-19-5;
- Hexabromocyclododecane (HBCD), Chemical Abstracts Service number 25637-99-4; and
- Tris(2-chloroethyl)phosphate (TCEP), Chemical Abstracts Service number 115-96-8.”

The statute also applies to retailers, stating “On and after July 1, 2019, no retailer may sell or offer for sale or use in this state a children’s product or upholstered residential furniture containing in amounts greater than 1,000 parts per million in any product component the flame retardant chemicals listed [as prohibited].” Manufacturers are also prohibited from replacing any of the four flame retardants with chemicals that harm development or reproduction; cause systemic toxicity; cause cancer or genetic damage, or disrupt hormone systems.

Finally, the session law required the Minnesota Department of Health (MDH), in consultation with the State Fire Marshal, to report to the Legislature regarding:

- “the status of federal, international, and other states’ laws and regulations in identifying, prioritizing, evaluating, and regulating the use of flame retardants in upholstered furniture, mattresses, and carpet pads;
- the status of relevant fire safety standards and practices for residential settings for products including mattresses, upholstered furniture, and carpet pads;
- the status of and any authoritative findings from studies and reports on a direct link to meaningful negative health and safety effects and impacts on firefighters of flame retardants covered by this section, particularly as it relates to the combustion of flame retardants in articles in actual firefighting settings relative to overall smoke hazards and combustion byproducts;

- in developing the report, the agency may consult with stakeholders, including representatives of state agencies, product manufacturers, chemical manufacturers, firefighters, public health experts, and independent scientists. The report must include information on any stakeholder process consulted with or used in developing the report.”

As required, MDH consulted with the State Fire Marshal in developing the content for the report. MDH contacted the National Institute for Occupational Safety and Health (NIOSH) as recommended by the State Fire Marshal. MDH also contacted the State of California for clarification of research conducted by Biomonitoring California. Due to time and staff constraints and because this report was limited to the status of research and regulations rather than policy recommendations or a risk assessment, MDH did not solicit stakeholder input or conduct a scientific peer review of the material in this report.

MDH submits this report to the Legislature to fulfill the reporting requirement.

## History

The title of the legislation, “Firefighter and Children Health Protection Act”, reflects the concern among citizen and firefighter groups that flame retardants may present an exposure and health concern to certain populations and stages of life. When the bill was introduced, legislators were asked to consider ten flame retardants of concern, take actions to reduce children’s exposures to flame retardants, and to consider information on exposure and health that was unique to firefighters. Minnesota legislators heard from concerned groups of citizens and from firefighters that firefighters are likely exposed to toxic substances from their work. Data were presented to legislators that showed that firefighters may have an increased risk of developing certain cancers. Information was presented on the flame retardants present in buildings and the toxic by-products that form when flame retardants are burned. The Legislature heard questions about whether exposure to flame retardants contribute to elevated rates of cancer or other diseases that may affect firefighters. As a result of that testimony and interest, and because questions remained about links between exposure to flame retardants and specific health risks that firefighters experience, MDH was tasked with summarizing and analyzing findings on exposure and health concerns for firefighters.

Firefighters may be exposed to flame retardants to a greater extent and in different ways than the general population. Firefighters may be exposed to chemicals, including flame retardants and combustion by-products, during a fire, during overhaul (searching for fire extending into building spaces), or cleaning firefighting equipment. Firefighters may be exposed through contact with contaminated vehicles, clothing and equipment, and firehouses. Firefighters may also bring contaminants into their homes when their work shifts end. Research has been started in a few areas of the United States to determine if firefighters have more exposure to flame retardants than the general public.

Higher rates of cancer among firefighters have been established, but the specific types and levels of exposure to constituents of smoke and the potential resulting causes of cancer are not understood. The International Agency for Research on Cancer (IARC) classified firefighting as a

possible cause of cancer (IARC 2010) based on limited evidence of cancer from occupational exposures. Multiple toxic combustion by-products, including possible and known carcinogens, are released in fires and have been described by IARC. However, flame retardants were not included in IARC's work.

In recent years, regulatory and scientific communities have been asked by the public to become more involved in understanding the public health consequences of flame retardants. One reason for interest in the issue is media coverage questioning the benefits and efficacy of flame retardants (Callahan and Roe 2012). A more compelling reason for the rising concern over exposure to flame retardants is that these chemicals are detected in the bodies of people who participate in biomonitoring studies. An obvious question is whether firefighters have higher than average levels of flame retardants in their bodies, and whether that leads to greater health risks.

## Scope of this report

In preparing this report, MDH considered the ten flame retardants that appeared in the original bill (see table below), flame retardants that were addressed in legislation elsewhere in the United States, flame retardants found in people's bodies, scientific literature on the toxicity and epidemiology of flame retardant chemicals, and occurrence and exposure studies of flame retardants. As required, MDH also consulted with the State Fire Marshal in considering which chemicals to include. MDH cast a wide net in order to understand as much as possible about the potential flame retardants of interest and relevance to the requested report on laws, regulations, exposure, and health. Once a few key flame retardants were researched, MDH found other chemicals that may co-occur, are closely related, or could degrade to similar chemicals either in the environment or in the body.

Staff found that each area of research (regulation, toxicology, epidemiology, and exposure) focused on a different suite of flame retardants of interest or concern. However, there was significant overlap as well. The table below shows the flame retardants that have been studied or addressed in the various areas of research and regulation that MDH reviewed. The Glossary of this report includes a full list of the flame retardant chemicals discussed in this report, along with their Chemical Abstract Service (CAS) identification numbers when available.

### CHEMICALS DISCUSSED BY TOPIC

Flame Retardant Chemical <sup>1</sup>	Regulations	Toxicity	Epidemiology/ Biomonitoring <sup>2</sup>	Exposure
TriBDE			X	X
TetraBDE	X	X	X	X
PentaBDE	X	X	X	X
HexaBDE		X	X	X
HeptaBDE			X	X
OctaBDE	X	X	X	X

Flame Retardant Chemical <sup>1</sup>	Regulations	Toxicity	Epidemiology/ Biomonitoring <sup>2</sup>	Exposure
NonaBDE			X	X
DecaBDE*	X	X	X	X
TDCPP*	X	X		
TCEP*	X	X		
TCPP*	X	X		
TDBPP	X			
TBPH*		X		
TBB*		X		
TBBPA*	X	X		X
Trixylyl Phosphate	X			
HBCD*	X	X	X	X
PBBs	X			
Antimony* and Antimony Compounds	X	X	X	
Short-Chained Chlorinated Paraffins*		X		

<sup>1</sup> See the Glossary for full chemical names

<sup>2</sup> Chemicals measured in biomonitoring studies of firefighters

\*Flame retardant chemical identified in the introduced bill

The nomenclature of various flame retardant chemicals may vary across publications and other reports. This is especially true for PBDEs as 209 chemical configurations (congeners) are included in this group of chemicals. For this report MDH used abbreviations, such as pentaBDE (pentabromodiphenyl ether), when referring to a group of PBDE congeners with the same number of bromines and used BDE-# (for example, BDE-47) when referring to specific PBDE congeners. This nomenclature for PBDEs as groups and as congeners is commonly used in scientific publications. Commercial mixtures of PBDEs contain a variety of congeners. The mixtures are named for the greatest average number of attached bromines present. For example, the commercial mixture of pentaBDE will mostly consist of PBDE congeners with five bromines, but it will also contain a smaller percentage of congeners with four, six and seven bromines in the mixture. For this reason, studies looking into pentaBDE exposure may find exposures to other PBDE congeners as well.

As MDH identified specific flame retardants, health effects, and exposures to include in this report, we found we were unable to address all of the questions of potential interest to Minnesotans. MDH determined that there were insufficient time and staff capacity to evaluate the relationship between chemical combustion, exposure, and health. We were not able to compile information on the harmful constituents of smoke (particulates in soot, for example) or the extent to which exposure to smoke adds to or exacerbates the health impacts from exposures to other chemicals. MDH recognizes that the heating or combustion of flame

retardants will causes the chemicals to change, including the potential to degrade into dioxins and dioxin-like compounds (Babrauskas 2015). However, understanding the extent to which combustion alters flame retardants, exposures, and cumulative health risks is beyond the scope of this report.

# Part 1: Laws, Regulations, and Safety Standards

## 1.1 Background

In this section of the report we discuss the laws, regulations, and fire safety standards that surround the use of flame retardant chemicals at the state, federal, and international levels. We have focused on regulations and standards for upholstered furniture, mattresses, and carpet pads as directed by the Minnesota Legislature. Some regulations and fire safety standards not related to the above product types are included when it seemed appropriate to do so.

Flame retardant chemicals have been manufactured in the United States since about the 1960s and their increases and decreases in use have coincided with a handful of state and national level standards and regulations (Cordner 2013). These chemicals have a wide use in product types such as electronics, textiles, furniture, building materials, resins, carpets, and car interiors with an intended purpose to slow combustion (Cordner 2013; Fromme et al. 2015).

Starting in the early 2000s the United States began to see an increasing number of policy advances related to flame retardant chemicals. These policy advances are probably due to a combination of many factors including a growing body of scientific research on flame retardant chemicals and a concern about the effectiveness and potential health effects of the chemicals (Cordner 2013). Other contributors may be the increasing advocacy group work focused on reducing flame retardant chemical use and media attention such as the *Chicago Tribune's* investigative series, "Playing with Fire", which was published in 2012 (Callahan and Roe 2012). Nationally there has also been a surge in the green chemistry movement to use more benign chemicals in consumer products. All or some of these factors have probably played a role in establishing the regulatory and fire safety standards seen at state, federal, and international levels. The two main classes of flame retardant chemicals that have gathered the most attention, and are discussed in the following section, are polybrominated diphenyl ethers (PBDEs) and other halogenated chemicals, such as halogenated phosphate esters.

## 1.2 Regulations at the State Level

Most of the regulatory action taken towards flame retardant chemicals in the United States has happened at the state level and has mainly taken place since about the year 2000. State level regulations can be found in 12 states (including Minnesota) and the District of Columbia (see the table States Prohibiting PBDE Use, below). As stated above, there are two main chemical

classes that the majority of the regulations seek to control, PBDEs and other halogenated chemicals (usually containing chlorine or bromine). Most of the state level regulations are restrictive in nature however in the past seven years chemical reporting and disclosure laws have been passed in several of the 12 states. For brief summaries, including links to the full text of the acts and regulations discussed in this section of the report, see Appendix B.

### 1.2.1 Polybrominated Diphenyl Ethers

Each of the 12 states and the District of Columbia have a regulation restricting or prohibiting the use of PBDEs. This is largely due to an increased concern about the safety of PBDEs coupled with biomonitoring research in the early 2000s showing an accumulation of PBDEs in breast milk (Cordner 2013). Minnesota enacted a law in 2007 that prohibits the manufacturing, processing or distribution of products containing more than one-tenth of one percent of pentaBDE and octabromodiphenyl ether (octaBDE) and authorized a study of the health and environmental effects of decaBDE (MPCA 2008). Many of the bills passed in other states have very similar language to that found in Minnesota's law. States mainly varied on the prohibited PBDEs being octaBDE and pentaBDE or being octaBDE, pentaBDE, and decaBDE. Many of the states, such as Minnesota, that only prohibited octaBDE and pentaBDE did include studies of the health and environmental effects of decaBDE. The octaBDE and pentaBDE restrictions for each state and the District of Columbia covered all product types and those entities that included restrictions for decaBDE (D.C., ME, MD, OR, VT, WA) typically included mattresses, mattress pads, and/or upholstered furniture among the restricted products. Minnesota's 2015 Firefighter and Children Health Protection Act now restricts the use of decaBDE in children's products and residential upholstered furniture.

Oregon, Vermont, and Washington have chemical disclosure laws that require manufacturers to report to the state if their children's products contain certain listed chemicals by each state. All three of these states include decaBDE on their lists of reportable chemicals. In 2009, Minnesota passed the Toxic Free Kids Act, which instructed the state to list, for information purposes, chemicals that posed potential health risks to children and/or pregnant women. DecaBDE is listed on Minnesota's Priority Chemicals list.

Compared with other classes of flame retardant chemicals, PBDEs have garnered the most regulatory attention. This may be because they are one of the more thoroughly studied classes of flame retardants (data are available on toxicity, biomonitoring, and use) and they previously had a very widespread use in a number of different product types.

#### STATES PROHIBITING PBDE USE

States with Regulations	PBDEs Regulated
CA, HI, IL, MI, NY, RI	PentaBDE & OctaBDE
D.C., ME, MD, MN, OR, VT, WA	PentaBDE, OctaBDE, & DecaBDE

### 1.2.2 Other Halogenated Flame Retardants

At the state level PBDEs were the first class of flame retardant chemical subject to widespread regulatory attention. As PBDE use began to decline, research and regulatory attention has turned towards other flame retardant chemicals, especially a class of halogenated phosphates which, among other uses, were being used as replacement chemicals for PBDEs. In this section we refer to flame retardants in this class and related classes as ‘other halogenated flame retardants’.

One of these chemicals that has garnered regulatory attention is TDCPP. This regulatory attention includes bans and disclosure. Vermont prohibits the sale of residential upholstered furniture, children’s products, and certain electronic devices containing TDCPP or related chemical TCEP. Maryland and New York prohibit the sale of children’s products containing TDCPP and TCEP.

California’s recently enacted Safer Consumer Products program targets chemical uses in specific products for alternatives assessments and chemical substitutions. One of the first three initial product/chemical combinations named by this program is TDCPP in children’s foam-padded sleeping products. California also lists TCEP, TDCPP, and tris(2,3-dibromo-1-propyl)phosphate (TDBPP) under their Proposition 65 law which requires businesses operating in California to notify citizens of potential exposures from products to chemicals known to the State of California to cause cancer, birth defects, or other reproductive harm.

Oregon, Vermont, and Washington, which have the chemical disclosure laws mentioned in the PBDEs section, also list some of these other halogenated flame retardants under their reporting requirements. All three states require reporting for children’s products containing TDCPP and TCEP. These state chemical disclosure laws also include reporting of two other halogenated flame retardant chemicals: HBCD and tetrabromobisphenol A (TBBPA).

Other than the 2015 Firefighter and Children Health Protection Act, which restricts TDCPP, TCEP, and HBCD, Minnesota does not have any other regulations concerning this class of flame retardant chemicals. The brominated flame retardant HBCD is listed as a Minnesota Priority Chemical in the Toxic Free Kids program and TDCPP is a candidate for the list. However, as previously mentioned, this is informational and there is currently no regulatory component associated with being named to this list.

#### STATES WITH CHEMICAL DISCLOSURE LAWS THAT INCLUDE FLAME RETARDANT CHEMICALS

States	Flame Retardants Listed in each State
Oregon	Antimony and Antimony Compounds, DecaBDE, HBCD, TBBPA, TDCPP, TCEP
Vermont	
Washington	



## 1.3 Regulations at the Federal Level

While there have been more recent pushes for regulatory action on flame retardant chemicals since the early 2000s, the first regulatory action happened in 1977 at the federal level when research showed that the flame retardant TDBPP, which was used in children's sleepwear at the time, was mutagenic (Blum 1977). This information combined with other research findings and a growing health concern lead to the Consumer Product Safety Commission (CPSC) banning TDBPP for use in children's sleepwear. This ban was overturned the same year but TDBPP was later restricted through a Significant New Use Rule (SNUR) under the Toxic Substance Control Act (Cordner 2013).

This initial effort to ban TDBPP is the only evidence of strong regulatory action at the federal level taken towards flame retardant chemicals. Instead of bans and restrictions being placed manufacturers have instead entered into agreements to voluntarily withdraw the uses of a number of flame retardant chemicals. This includes voluntary agreements to stop the use of TDCPP in children's sleepwear (initially used as a replacement for TDBPP), and to voluntarily end the uses of pentaBDE, octaBDE, and decaBDE. The voluntary agreement reached between the United States Environmental Protection Agency (EPA) and manufacturers of pentaBDE and octaBDE was to stop producing these two PBDEs by the end of 2004. In 2009 the EPA reached an agreement with manufacturers of decaBDE to cease sales by the end of 2013 (USEPA 2009c).

Other than relying on the voluntary phase outs of flame retardant chemicals the EPA has also issued SNURs to prevent certain flame retardants from new uses. In 1987 the EPA issued a SNUR for TDBPP (USEPA 2015e). In 2006 a SNUR was issued for pentaBDE and octaBDE and in 2012 the SNUR was amended to include decaBDE (USEPA 2012b). The most recent flame retardant chemical to have a SNUR issued is HBCD, which was finalized in September 2015 (USEPA 2015f).

### FEDERAL REGULATIONS

Action	Flame Retardants
Voluntary Phase out	PentaBDE, OctaBDE, DecaBDE, TDCPP*
EPA Issued SNUR	PentaBDE, OctaBDE, DecaBDE, TDBPP, HBCD

\*phased out in children's sleepwear

## 1.4 Regulations at the International Level

The European Union's (EU) Registration, Evaluation, Authorisation, and Restriction of Chemicals (REACH) is their chemical management legislation used to evaluate chemical data, make decisions on the acceptable uses of specific chemicals, and to help ensure a high level of protection for human health and the environment. To assist in this effort REACH has established a list of substances of very high concern (SVHC) that contain chemicals consisting of: persistent, bioaccumulative, and toxic chemicals (PBT); very persistent and very bioaccumulative toxic chemicals; carcinogenic, mutagenic, and reproductive toxicants; and

endocrine active chemicals. The SVHC list is the first step of the authorization process that controls the use of chemicals and may lead to a chemical being restricted (ECHA-a). As of June 15, 2015, the SVHC list contains 163 chemicals including at least four as flame retardants (decaBDE, HBCD, TCEP, and trixylyl phosphate). Of these four flame retardants HBCD and TCEP are on the authorization list, which means that as of August 2015 they can only be used in products if authorized to do so by the European Chemicals Agency (ECHA) (ECHA-b). A restriction proposal for decaBDE was issued in 2014 (ECHA 2014).

Along with REACH, the EU has restrictions for flame retardant chemicals through two other directives, however these directives do not affect upholstered furniture, mattresses, or carpet pads. The first directive, called the Restriction of Hazardous Substances (RoHS), restricts the use of certain chemicals in electrical and electronic equipment including flame retardant PBDEs and polybrominated biphenyls (PBBs) and requires them to be substituted by safer alternatives (EC 2011). The second, under the EU's toy safety directive, restricts the use of TCEP, TDCCP, and tris(1-chloro-2-propyl)phosphate (TCPP) in children's toys above the amount of 5 mg/kg (EC 2014).

The Stockholm Convention on Persistent Organic Pollutants (POPS, also known as PBTs) is an international treaty that calls for the phase out of an agreed upon list of POP chemicals. At the convention's fourth meeting in 2009, tetrabromodiphenyl ether (tetraBDE) and pentaBDE were amended to the list and at the sixth meeting in 2013 HBCD was added to the list (Stockholm Convention-a). DecaBDE is currently proposed for listing by the Convention (Stockholm Convention-b). The United States has not ratified the Stockholm Convention.

A second international treaty called the Rotterdam Convention requires prior informed consent and information exchange for the importation and exportation of certain pesticides and industrial chemicals deemed to be particularly harmful to the environment and/or to human health (Rotterdam Convention-a). Chemicals included in this convention are then subject to import bans or restrictions by those countries who have ratified the treaty. The flame retardant chemicals included in the Rotterdam Convention are octaBDE, pentaBDE, and TDBPP (Rotterdam Convention-b). The United States has not ratified the Rotterdam Convention.

## INTERNATIONAL REGULATIONS

Regulatory Action	Flame Retardant Chemicals
European Union (SVHC, RoHS, Toy Safety)	DecaBDE, HBCD, trixylyl phosphate, TCEP, TDCPP, TCPP, PBBs, PBDEs
Stockholm Convention	TetraBDE, PentaBDE, HBCD
Rotterdam Convention	PentaBDE, OctaBDE, TDBPP

## 1.5 Fire Safety Standards and Practices

Fire safety standards and practices play a significant role in the use of flame retardant chemicals. The standards set at federal and state levels contribute to the widespread use of

flame retardant chemicals in a range of product types because use of these chemicals is one method for meeting fire safety standards. The bill language for this report instructed MDH to provide information on fire safety standards and practices that relate to residential settings for products including mattresses, carpet pads, and upholstered furniture. As a result, the following information will focus on these three product types even though there are other fire safety standards and regulations that affect other product types and settings such as standards for clothing, building insulation, and public occupancies to name a few.

### 1.5.1 Mattresses

Mattresses used in a residential setting, including mattresses used for children and crib mattresses, must meet two federal flammability standards that are part of the Flammable Fabrics Act (16 C.F.R. §1602-1633) that is administered by the Consumer Product Safety Commission (CPSC). The CPSC is a federal agency charged with protecting the public from unreasonable risk associated with the use of a wide range of consumer products. The first flammability standard that mattresses must meet before sale or introduction into commerce, is a test to determine the ignition resistance when the mattress is exposed to a lighted cigarette (16 C.F.R. §1632). Mattresses pass or fail this test based on a measured char length of two inches or less. Multiple locations on the mattress are tested and each location must pass this test (USGPO 2012). The second flammability standard mattresses must meet before sale or introduction into commerce is a test that measures heat release when mattresses are exposed to an open flame (16 C.F.R. §1633). Under controlled conditions samples from a mattress are exposed to specified flaming ignition sources for specified amounts of time while a determination is made as to the heat release rate of the samples, thus quantifying the energy generated by the fire (USGPO 2012). Neither of these standards regulate the use of flame retardant chemicals to pass the required tests. The standards are performance based tests and do not require or prohibit the use of any specific materials or chemicals in order to meet these flammability standards. The use of flame retardant chemicals is one method manufacturers could choose in order to meet these mattress flammability standards. A more common way to meet these standards today is through the use of specific outer fabric or fiber barriers that are intended to prevent ignition of the more flammable internal materials of a mattress.

### 1.5.2 Carpet Pads

Carpet pads do not appear to be subject to flammability standards. The various materials used for carpet padding will confer varying levels of potential flammability, but MDH did not find specific flammability standards for carpet pads. The CPSC administers a flammability standard for carpets and rugs under the Flammable Fabrics Act, 16 C.F.R. §1630 (1967), and it is very similar to the ignition resistance test required for mattresses in §1632 of the Flammable Fabrics Act (USGPO 2012).

### 1.5.3 Upholstered Furniture

Currently there are no federal level flammability standards for upholstered furniture. However the CPSC had proposed rulemaking that would add flammability standards for residential

upholstered furniture under the Flammable Fabrics Act. The standard would require upholstered furniture to meet cigarette ignition and open flame tests similar to those required for mattresses (NIST 2013). This rule, however, has not yet been enacted and information as to its current status was not available for this report. While no federal flammability standard applies to upholstered furniture there are state level standards as well as voluntary industry standards that do apply.

In 1975 California passed Technical Bulletin 117 (TB 117), which set a flammability standard for the filling materials used in upholstered furniture. TB 117 required that the fill material/paddings withstand 12 seconds of an open flame without spreading the flame (State of California 2000). California is still the only state to pass a fire safety regulation for upholstered furniture. As a result of this, as well as the large market share of California compared to other states in the United States, many upholstered furniture products sold across the United States are designed to comply with this California standard. The most common method to assure compliance was to add flame retardant chemicals, initially PBDEs (NFPA 2013). In 2013 California updated TB 117 (now referred to as TB 117-2013), moving away from the open flame test of the filling material to a lighted cigarette (smolder) test to be performed on the cover material (State of California 2013). In theory this could allow for less use of flame retardant chemicals as a smolder test could be passed using other methods of flame resistance (for example, use of flame resistant fabrics). California has another upholstered furniture standard which applies only to furniture in public occupancies referred to as Technical Bulletin 133. This standard requires that upholstered furniture in public places meet certain thresholds for heat release (State of California 1991).

A voluntary smolder test for residential upholstered furniture has existed in the United States since 1979 and has been updated through the years. This standard, which is very similar to the new California TB 117-2013 standard, is followed by manufacturers who are members of the Upholstered Furniture Action Council and as of November 2015 this organization consists of 91 manufacturing companies (UFAC 2015).

## Part 2: Exposure

### 2.1 Introduction

Exposure to flame retardants is common among the general population of the United States. Over time, measurements of flame retardant exposure have reflected changes in fire safety standards and the introduction and removal of individual flame retardants from common use. Changes in the use of flame retardants can take a long time to affect human exposure levels because many products containing flame retardants are kept in the home for many years. This may be especially true for older homes and households of low socio-economic status, which leads to concerns about disparities in exposures.

During the performance of his or her duties, a firefighter has the potential to be exposed at a much higher level than the general population. Exposure through lungs, mouth, and skin may occur during contact with smoke and soot. Fumes, gases, and small inhaled particles reach deep into the lungs where flame retardants may be absorbed into blood. Some chemicals may move through layers of skin when soot is deposited on exposed skin.

Exposure assessment encompasses an understanding of sources and pathways of exposure, and the resulting amount that may enter the body. Exposures to specific populations, such as nursing infants, adults, or firefighters, may be studied. Exposure may be estimated by measuring chemicals in the environment (including air, food, house dust, or other sources of exposure) and in occupational settings (such as factory settings). Amounts of a chemical that have entered (or are likely to enter) the bodies of individuals may be estimated. Exposures to chemicals may also be measured through biomonitoring, that is, the measurement of a chemical or its breakdown products in an individual's body fluids or tissues (including blood, urine, breast milk, and hair).

## 2.2 Chemistry of Combusted Flame Retardants

Most of the study of flame retardant chemicals has been done on the chemical in its original form. Exposures to the general population are likely to be to the original form of a flame retardant chemical due to leaching from products. However, firefighters are exposed to the combustion products of flame retardant chemicals as well as the original forms of the chemicals. Of great concern is that dioxin and furan compounds can be produced during the heating and combustion of halogenated flame retardant chemicals (Shaw 2010; Ortuno 2014). Dioxin and furans are toxic chemicals that can lead to liver problems and elevated blood lipid levels, and are considered to be reproductive toxins as well as carcinogens (ATSDR 1998; Health Canada 2005; CDC 2009). While the combustion of halogenated flame retardant chemicals is certainly not the only source of dioxins and furans, an increased exposure to these harmful chemicals could result from the presence of flame retardant chemicals in a fire. In a review of halogenated flame retardant chemicals in residential settings, Babrauskas reported that laboratory tests have shown that the production of dioxins will peak in the range of 700 to 900 degrees Celsius, which is also the range for flashover in house fires (Babrauskas 2015). Babrauskas also described research comparing fires with and without brominated flame retardants present. Most fires produce polycyclic aromatic hydrocarbons (PAHs), a class of chemicals that includes carcinogens and reproductive toxicants. However, the fires with flame retardants produced tenfold greater amounts of PAHs, and more of the more toxic PAHs, than fires without these flame retardants (Babrauskas 2015). So the combustion of products that contain halogenated flame retardant chemicals is likely increasing the exposure potential not only of these flame retardant chemicals, but of two other classes of chemicals (dioxins/furans and PAHs) with reproductive toxicity and carcinogenic properties as well.

Another area of concern associated with the combustion of chemically flame retarded materials is the production of carbon monoxide, smoke, and soot. Carbon monoxide and smoke are considered major contributors to death from a fire and high levels of soot will decrease visibility in a fire (Einhorn 1975). Chandrasiri Jayakody et al. found an increased production of all three

elements, carbon monoxide, smoke and soot, during combustion of polyurethane foams that had been treated with flame retardant chemicals (such as decaBDE and TDCPP) compared to foam that had not been treated (Jayakody 2000). Polyurethane foam is commonly used as the padding material in upholstered furniture, mattress pads, and other consumer products. An increased production of these three elements in a fire could contribute to an increased potential of harm or even death from a fire.

## 2.3 Biomonitoring Findings

Biomonitoring is the measurement of chemicals in the tissues or fluids of the body. Blood, hair, urine, and breast milk are commonly tested. Biomonitoring results tell us that exposure has occurred to a chemical, but not the pathway by which the chemical entered the body (food, air, water or through the skin). In most cases, biomonitoring alone cannot tell us if there are health risks associated with the exposure.

MDH found that two biomonitoring studies of flame retardants in firefighters have been published in the literature: Biomonitoring California's<sup>1</sup> Firefighter Occupational Exposure (FOX) Study of firefighters in Southern California (Park et al. 2015); and a pilot study of twelve firefighters in San Francisco (Shaw et al. 2013). Since these two studies only measured PBDEs in firefighters, other classes of flame retardants cannot be assessed for comparison purposes. However, there is some information on antimony in World Trade Center (WTC) responders that will be discussed later in this section.

FOX study participants worked as full-time firefighters in Southern California for a minimum of one year prior to sampling. Blood samples from the 101 firefighters were collected in 2010-11. Participants in the 2009 San Francisco pilot study worked as firefighters for a minimum of the previous five years. Blood samples from the 12 firefighters were collected within 12 hours of fighting a fire. The San Francisco pilot study is severely limited by sample size but is included here due to the paucity of flame retardant biomonitoring studies of firefighters.

Comparing biomonitoring results from studies of firefighters to comparison groups is useful for establishing whether flame retardant exposures in firefighters differ from the general population. In selecting studies of comparison groups, MDH considered the location of studies, the years during which the populations were studied, and the demographics of the populations studied.

Both of the firefighter studies were conducted in California. California residence is associated with significantly higher PBDE serum levels compared to U.S. residents outside California (Eskenazi et al. 2011; Rose et al. 2010; Windham et al. 2010; Zota et al. 2008). The higher body burden of Californians is thought to be a result of the state's stringent furniture flammability standard (Technical bulletin 117, see State of California 2000). Further, U.S. residents tend to

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<sup>1</sup>Biomonitoring California (also known as The California Environmental Contaminant Biomonitoring Program), is a legislatively mandated, state-funded biomonitoring program created in 2006. It is a joint program of the CA Department of Public Health, the Department of Toxic Substances Control, and the Office of Environmental Health Hazard Assessment.

have substantially higher body burdens of flame retardants than those who live in other parts of the world. As a result, there are major limitations to comparing California firefighters to non-firefighter populations residing in other areas of the U.S. or outside of the U.S. Even so, a comparison between PBDE serum concentrations in FOX firefighters in 2010-11 and adult men in the general U.S. population in 2003-04 (as measured in the U.S. Center for Disease Control and Prevention's National Health and Nutrition Examination Survey) was recently published (Park et al. 2015). Levels of PBDEs in the firefighters were elevated compared to national levels, even though California's ban of pentaBDE and octaBDE, effective in 2006, could be expected to have resulted in decreased body burden of PBDEs over this timeframe. The contribution of occupational exposure to this difference, versus dissimilarities in geography, demographics, or other factors is unknown. However, the fact that Park and colleagues found an association between lower levels of serum PBDEs in the FOX study and optimal practices for cleaning and storing clothing and equipment after fires is consistent with higher exposure due to occupational factors.

It is possible to compare PBDE levels in FOX firefighters to other California residents since the Biomonitoring California program has released results from several recent studies. The studies are of California adults; but the summary results currently available from Biomonitoring California could not be further stratified by age group, ethnicity or gender. These factors may influence serum levels of PBDEs. An analysis of PBDE serum levels in the general U.S. population (12 years of age and older) found only slight differences by gender and race/ethnicity; and a decrease in serum levels with increasing age until around age 60, after which a slight increase was noted (Sjodin et al. 2008 cited in CDC 2013). In the FOX study, the firefighters were predominately male (98 percent) and non-Hispanic white (77 percent), with an average age of 43 years. Other factors that may influence PBDE serum levels, such as income, occupation, years living in the U.S. or geographic region of California, also differ among the California studies. A study of PBDE house dust levels in two regions of California found regional differences, with some intra-regional variability related to race/ethnicity and income (Whitehead et al. 2013).

The firefighter and other California studies span several years, from 2006 to 2013, and may be influenced by changes in flame retardant use. California's ban of pentaBDE and octaBDE likely resulted in decreased body burden of PBDEs over this timeframe. A decline in BDE congeners - 47, -99, -100 and -153 was reported in a small study of pregnant Californians between 2008-09 and 2011-12 (Zota et al. 2013). The major congener found in octaBDE is BDE-183 with minor contributions from BDE-203 and several octa- and nonabromodiphenyl ethers (nonaBDE). EPA announced a voluntary agreement with the three largest PBDE manufacturers to discontinue the manufacture of decaBDE at the end of 2013. DecaBDE contains mostly BDE-209.

Differing analytical methods and variation in the serum volumes collected can result in different laboratory limits of detection (LODs) across studies. To lessen the impact of differing LODs, we limited our comparisons to median and upper percentile serum concentrations.

A brief description of the selected non-firefighter comparison studies follows. Additional information about the CA Biomonitoring studies can be found at:

<http://biomonitoring.ca.gov/projects/current>

**California Childhood Leukemia Study:** Results are from 48 mothers of children with and without childhood leukemia in Northern California and the Central Valley of California (Whitehead et al. 2015). Blood samples were collected in 2006-07. The authors consider this to be “the period of peak exposure to pentaBDE in California.” In the table below, this study is labeled “**2006-07 CA mothers**”.

**Study of Use of Products and Exposure-Related Behavior (SUPERB) Study:** This study included 90 parents of young children from northern California and 59 older adults (≥55 years old) from California’s Central Valley (Wu et al. 2015). Blood samples were collected in 2008-09. In the table below, results from this study are labeled “**2008-09 CA parents**” and “**2008-09 CA older adults**”.

**California Teachers Study:** A state-wide study of current and former female professional school employees with and without breast cancer. Blood samples were collected in 2011-12. In the table below, this study is labeled “**2011-12 CA teachers**” and the results are based on 1,279 participants.

**Pilot and Expanded Biomonitoring Exposures Study (“BEST”)<sup>2</sup>:** A study of adults in California’s Central Valley, randomly selected across gender, age, race/ethnicity, and location. Pilot BEST samples were collected in 2011-2012 and Expanded BEST in 2013. Pilot BEST results are based on 110 participants. Expanded BEST results are based on more participants (217) and diverse populations, which was achieved by oversampling Asian Pacific Islanders and Hispanics. In the table below, this study is labeled “**2011-12 and 2013 Central CA adults**”.

The following table shows the BDE congeners for which summary results were available by study.

#### PBDE CONGENERS REPORTED IN CALIFORNIA STUDIES

Study	Congeners						
	17	28	47, 99, 100, 153	66, 85, 183	154	197, 206, 207, 208	209
<b>2010-11 FOX firefighters</b>	X	X	X	X	X	X	X
<b>2009 San Francisco firefighters</b>		X	X				X
2006-07 CA mothers			X		X		
2008-09 CA older adults	X	X	X	X	X		X

<sup>2</sup> BEST percentile concentrations and the 95<sup>th</sup> percentile concentration from the CA Childhood Leukemia Study were not available on the Biomonitoring California website at the time this report was written. These data were provided to MDH by Nerissa Wu, Chief, Chemical Exposure Investigations Unit at the CA Department of Public Health on 12/11/2015.



Study	Congeners						
2008-09 CA parents	X	X	X	X	X		X
2011-12 CA teachers	X	X	X	X	X	X	X
2011-12 and 2013 Central CA adults		X	X				

In general, BDE-47 (a tetraBDE present in commercial pentaBDE mixtures) is the congener reported at the highest concentrations in human tissues (CDC 2013). Commercial pentaBDE-associated congeners, BDE-99, -100, and -153, have also been detected at higher levels than other PBDE congeners in the general population. Only recently has BDE-209, the congener of decaBDE, been routinely included in biomonitoring studies, mainly because it was not suspected to build up in human tissues and it can be difficult to measure. However, it became the most used PBDE product after penta- and octaBDE were banned.

MDH compared the results of the firefighter studies to the other California studies. The study comparisons are shown in Appendix C as plots of biomonitoring results, by individual congener, from each study. In general, PBDE congener concentrations were higher in the earliest available study (2006-07 CA Childhood Leukemia Study), the two firefighter studies, and the BEST studies in 2011-12 and 2013<sup>3</sup>. The results suggest higher than expected PBDE concentrations in firefighters, particularly for BDE-209. Firefighters also had higher levels of BDE-197, -206, -207, and -208. However, only one non-firefighter study was available for comparison. The results for BDE-47, -99, -100, and -153 suggest higher levels in firefighters, but the differences, due to a large amount of variability in the comparison group results, are not definitive.

In conclusion, a comparison of California firefighters to adult men in the general U.S. population finds elevated PBDE concentrations among firefighters. Further, a comparison of PBDE serum concentrations in firefighter and non-firefighter studies in California suggest exposures to several congeners are higher among firefighters. However, in some of the comparisons the differences were small and we could not account for demographic and socio-economic differences between studies. A non-firefighter California reference population with comparable demographics is needed to properly interpret FOX results.

In addition to PBDEs, there is also some evidence of higher antimony concentrations in firefighters as a result of their duties. One study examined firefighters who worked as rescue and recovery workers at the WTC site (Edelman et al. 2003). Firefighters present at the collapse had urinary antimony levels that were statistically higher than those of firefighters arriving one to two days post-collapse or of firefighters who did not work at or near the WTC because of assignment to office duties. The authors suggest that combustion of plastics from the WTC collapse (which may have 7 to 30 percent antimony by weight for use as a flame retardant) likely explains this increase in exposed firefighters. Similarly, Julander (Julander et al. 2014)

<sup>3</sup> A California Biomonitoring study of 300 Northern California women conducted in 2012-2013 found PBDE levels comparable to those in BEST (personal communication with Nerissa Wu, CA Department of Public Health 1/8/16). Results from this study have not been published as of the writing of this report and were not provided to MDH.

reported positive linear relationships between antimony concentrations in air and antimony concentrations in the urine and blood of e-waste recycling workers. One study assessed firefighter exposure to antimony from use of antimony-treated uniforms (de Perio et al. 2010). Uniform pants made from FireWear® fabric are widely worn by firefighters across the United States. Urine antimony levels were not significantly different between firefighters who wore antimony-containing pants compared to those who did not. The authors concluded that no significant dermal exposure occurs in firefighters who wear pants containing antimony.

## 2.4 General Population Exposure

MDH considered how firefighters' occupational exposures might differ from the pathways and sources of exposure that affect the general population. MDH staff reviewed studies of flame retardants in air, dust, and diet, and found estimates for the general population of total exposure at different stage of life.

### 2.4.1 Air

Flame retardants are common contaminants in indoor air. Electronics, upholstery, fabrics, and other consumer products all contribute to the contamination. The relative abundance of individual flame retardants is highly dependent on location due to differences in the types of products found in the home, as well as differences in flammability standards and regulatory restrictions on individual flame retardants. In three studies of indoor air in the United States, mean total PBDE concentrations in air, including both the vapor phase and particulate matter, ranged from 452 to 3730 picograms per cubic meter (pg/m<sup>3</sup>). The congeners examined in each study were not identical; see table below. The predominant congeners common to all three indoor air studies are BDE-47, BDE-99, and BDE-100. In the Batterman study (Batterman et al. 2009), BDE-17 and -28 are also major contributors to the total; in the Allen study (Allen et al. 2007) study, BDE-209 and BDE-28/33 are major contributors. In the Johnson-Restrepo study (Johnson-Restrepo et al. 2009) study, BDE-66 and BDE-28 are major contributors.

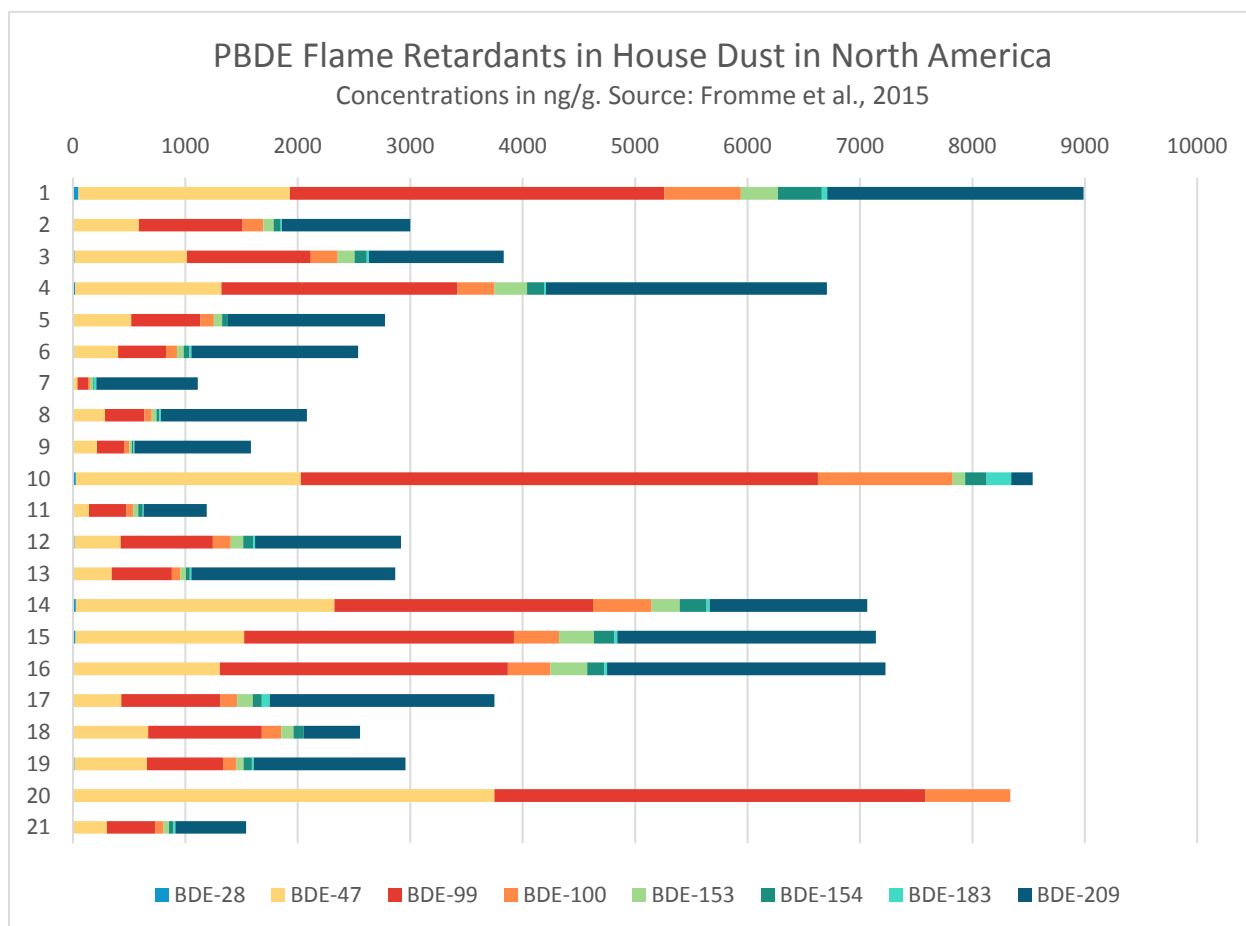
#### PBDE CONGENER DETECTIONS IN AIR

Study	Congeners	Sample location	Sample Type	Mean concentration, sum of all congeners (pg/m <sup>3</sup> )
Batterman et al. 2009	12 congeners	Indoor air, house	Vapor	4500
			Particulate	1200
Johnson-Restrepo et al. 2009	15 congeners	Indoor air, house	Vapor + Particulate	1260

Study	Congeners	Sample location	Sample Type	Mean concentration, sum of all congeners (pg/m <sup>3</sup> )
Allen et al. 2007	11 congeners	Personal air	Vapor + Particulate	765.7
		Indoor air, bedroom	Vapor + Particulate	460.4
		Indoor air, main living area	Vapor + Particulate	452.8
Batterman et al. 2009	12 congeners	Outdoor air	Vapor	710
			Particulate	480

### 2.4.2 Dust

As with indoor air, the concentrations of individual PBDEs in house dust vary with location. Fromme (Fromme et al. 2015) summarizes the results of 21 studies of PBDE congeners in house dust in North America (18 in the United States and three in Canada); see figure below. In 15 of these studies, BDE-209 has the highest median concentration; in five studies, BDE-99 has the highest median concentration; in one study, BDE-99 and BDE-47 have the highest concentrations.



### 2.4.3 Diet

Fromme (Fromme et al. 2015) summarize the results of several studies of dietary PBDE intake from around the world. Globally, the combined mean or median dietary intake for all PBDEs ranged from 0.14 to 2.22 nanograms per kilogram of body weight per day (ng/kg-d). For the three U.S.-based studies, the range was 0.28 to 1.17 ng/kg-d. There was no clear difference in intakes between men and women, but most of the studies indicated that intake declines with advancing age; toddlers had the highest intake levels.

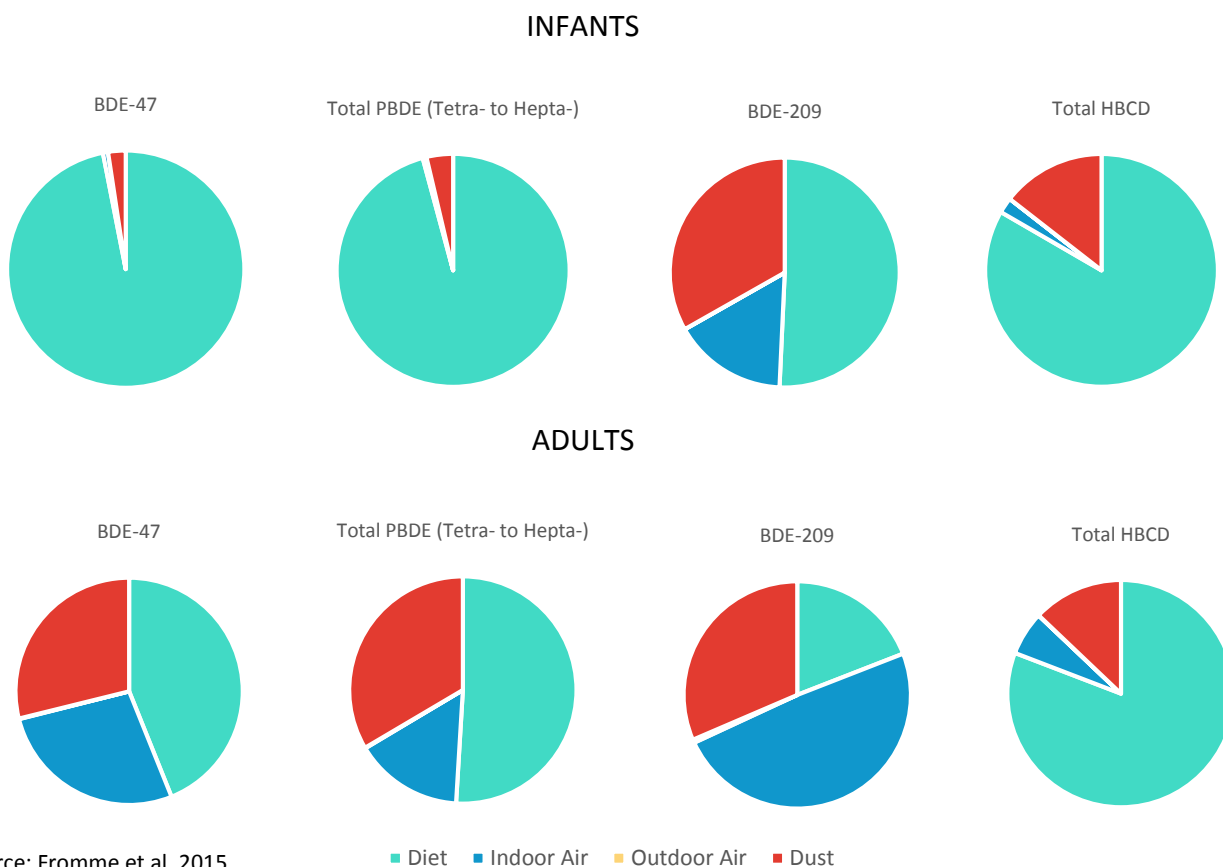
In the U.S., meat and dairy products are the predominant source of dietary PBDEs (Schecter et al. 2010). DecaBDE (BDE-209) accounted for about 63 percent of total PBDE intake, followed by tetraBDE (BDE-47, -49, and -66) and pentaBDE (BDE-85, -99, -100, and -119) each accounting for about 12 percent of total PBDE intake, nonaBDE (BDE-206 and -207) accounting for about 8 percent, and other PBDEs (tri-, hexa-, hepta-, and octa-BDE) making up the remainder. For most PBDE congeners, especially those that contribute significantly to the total, dairy and eggs are the predominant source, followed by meat.

In the same study, Schecter (Schecter et al. 2010) estimated dietary intake of HBCD. Intake was about one-third of the total PBDE intake. Meat was the predominant source of HBCD in food, and HBCD was not detected in dairy and egg samples.

### 2.4.4 Exposure Assessment: General Population

By combining the available data on flame retardant levels in food, air, and dust with established rates of human intake of these media, it is possible to estimate flame retardant exposure among the general population. Using data from EPA's Exposure Factors Handbook (U.S. EPA, 2011) and other sources, Fromme (Fromme et al. 2015) estimated flame retardant exposures for infants and adults, taking into account the bioavailability of each compound; see charts below.

#### Relative Contributions of Diet, Air, and Dust to PBDE and HBCD Exposure for Infants and Adults



Source: Fromme et al. 2015

The most striking aspect of these estimates is the large contribution of diet to flame retardant exposure in infants. For PBDEs other than decaBDE, diet contributes 95 percent or more of the total estimated exposure for infants. For decaBDE, diet contributes about half of the estimated infant exposure, and for total HBCD, diet contributes 83 percent of the estimated infant exposure. The median estimate of infant dietary exposure to BDE-47 (173  $\mu\text{g}/\text{kg-d}$ ) exceeds the EPA's toxicological reference dose (RfD) of 100  $\mu\text{g}/\text{kg-d}$  (EPA IRIS, 2008). Using 95th percentile intake rates, the infant exposure is 1,984  $\mu\text{g}/\text{kg-d}$ , exceeding the EPA RfD by a factor of nearly 20. Median and 95th percentile intakes estimated for other age groups do not exceed the EPA RfD.

## 2.5 Firefighter Exposure

In contrast to the exposures of the general population (exposures from dust and air of buildings and diet), firefighters have unique occupational exposures to chemicals that are emitted from materials as they burn. A few studies have been conducted that show exposures associated with firefighting are greater than exposures to the general population. Studies have shown that contaminated dust in fire stations is a large contributor to exposure, and potentially greatly exceeds the general population's exposure to flame retardants in dust.

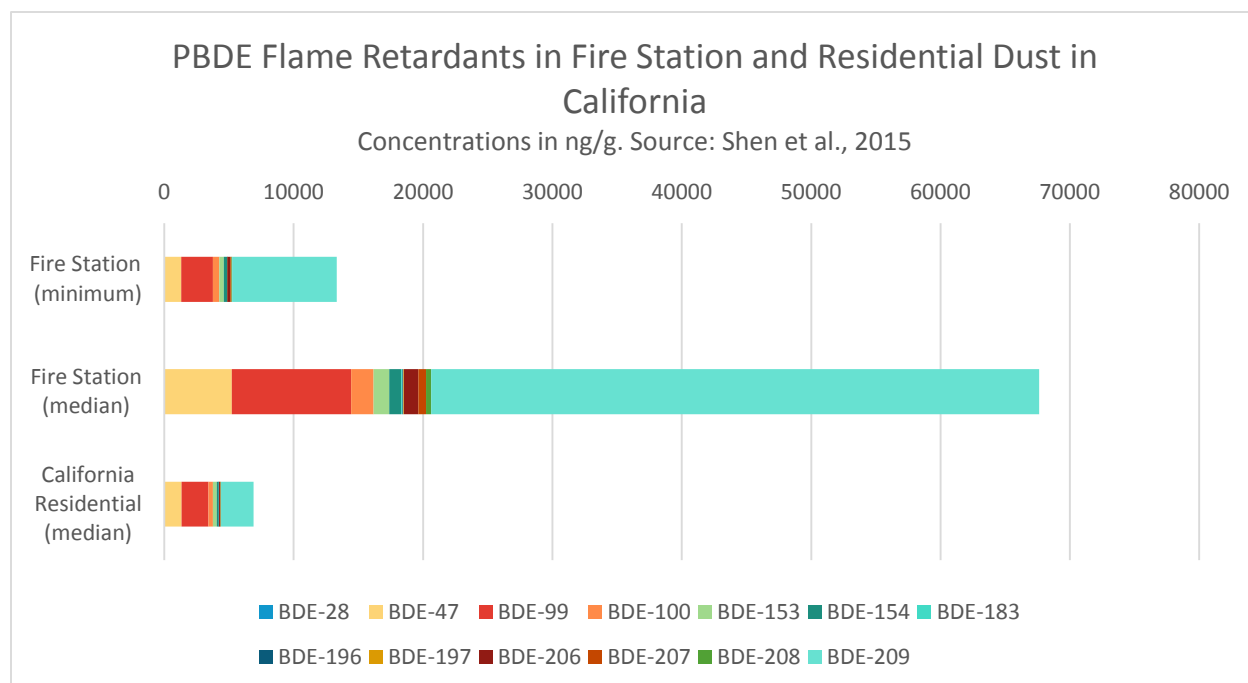
### 2.5.1 Exposures During Response Calls

During fire suppression activities, inhalation, dermal absorption, and ingestion of flame retardants may occur. The level of contact is highly dependent on the degree of protection provided by the firefighter's equipment, and the firefighter's use of protective equipment. Chemical residues from soot, including some flame retardants, have been detected on firefighting equipment (Shen et al. 2015; Hsu et al. 2011).

Overhauling is a careful inspection of the fire site that occurs at the end of the fire suppression process and is intended to reveal and control any remaining combustion sources that may re-ignite the fire. Shaw reported in a presentation to the League of Minnesota Cities (Shaw 2015) that concentrations of air contaminants during the overhaul phase can exceed occupational exposure limits.

### 2.5.2 Exposures at the Fire Station

As part of the FOX study, Shen (Shen et al. 2015) analyzed dust samples collected from vacuum cleaner bags at 20 California fire stations. Samples were analyzed for 22 PBDE congeners, and results reported for 13 PBDE congeners (-28, -47, -99, -100, -153, -154, -183, -196, -197, -206, -207, -208, and -209). All 13 of these PBDE congeners were detected at all of the stations. Ten PAHs and eight polychlorinated biphenyls (PCBs) were also detected at all of the stations. Because some stations used two vacuum cleaners and provided two bags, the total number of dust samples was 27. For 23 of the 27 samples, BDE-209 had the highest concentration, and for 20 of the samples, BDE-209 constituted at least 50 percent of the total of the 22 PBDE congeners. Ninety percent or more of the total PBDE concentration consisted of five congeners: BDE-209, BDE-153, BDE-100, BDE-99, and BDE-47; see figure below.



Dust levels of BDE-209 in this study are among the highest ever reported, far exceeding occupational levels from around the world and residential levels observed in the United States. The median BDE-209 concentrations in the fire stations were 20 times higher than those reported in California residences by Whitehead (Whitehead et al. 2013). The maximum detected concentrations of each congener (data not shown) were typically 5 to 20 times higher than the median value, but for BDE-153, the maximum exceeded the median by a factor of 190. Concentrations of BDE-47 and BDE-99 were positively correlated with the age of the fire station. There was no such correlation with BDE-209. Similarly, no correlation was found between BDE-209 concentrations and the number of fire incident responses at each station. This indicates that ash and other residues carried back to the station from the fire site may not be the principal source of PBDEs in the station dust.

Brown (Brown et al. 2014) reported on non-PBDE flame retardants in dust collected in the FOX study and in multiple residential studies, including California residences. The predominant chemicals measured in fire station dust were TBB and TBPH. As with the PBDEs, non-PBDE flame retardant concentrations in fire station dust far exceeded residential levels, indicating a potential for unusually high exposures among firefighters residing at the station.

### 2.5.3 Exposure Assessment: Firefighters

As discussed in the previous section, residential dust contributes significantly to the total general population exposure to PBDE flame retardants, constituting about a third of overall exposure for adults. For infants, the relative contribution of dust is smaller, due to the much larger dietary exposure at this stage of life. To the extent that a fire station functions as a residence, fire station dust will contribute to firefighter exposure as residential dust contributes to general population exposure. Median concentrations of PBDE congeners in fire station dust

exceed median residential concentrations by factors ranging from 2 (BDE-28) to 18.8 (BDE-209). Maximum detected concentrations in fire station dust may be 5 to 20 times higher than the median values.

Considering the median dust concentrations in the FOX study, a dust ingestion rate of 30 mg/day (USEPA, 2011), and a body weight of 70 kg, exposure to the 13 PBDE congeners in the FOX study would range from 0.017 to 20.1 ng/kg-d; see table below.

#### ESTIMATED PBDE INTAKES\* BASED ON FOX STUDY DUST SAMPLING

	BDE-28	BDE-47	BDE-99	BDE-100	BDE-153	BDE-154	BDE-183	BDE-196	BDE-197	BDE-206	BDE-207	BDE-208	BDE-209
Fire Station Dust, ng/g (median)	40.3	5170	9240	1720	1220	919	77.9	76.6	51.1	1130	592	379	47000
Intake from Dust, ng/kg-d	0.017	2.22	3.96	0.74	0.52	0.39	0.033	0.033	0.022	0.48	0.25	0.16	20.1

\*Assumes dust intake rate of 30 mg/day and a body weight of 70 kg. Source: Shen et al. 2015

### 2.5.4 Exposure Assessment: Secondary Effects

It is possible for the exposure situations encountered by firefighters to have secondary impacts on non-firefighters. As discussed above, fire station dust contains PBDEs at levels that far exceed ordinary residential dust, and also exceed most occupational levels. Non-firefighters working at a fire station (emergency medical technicians, administrative and support staff, maintenance workers, and others) are potentially exposed during work hours. The mechanism of transport of house dust in and around firefighters, their workspaces, and their equipment has not been extensively studied. The potential exists for flame retardants to migrate into the private residences of firefighters, just as pesticides can be tracked into the homes of agricultural workers. This could potentially expose family members and other household contacts to flame retardants. To our knowledge, studies of these potential exposures have not been reported in the literature.

Nursing infants are another potentially exposed non-firefighter population group. Considering the levels of infant exposure to some PBDEs via breastfeeding among the general population, it is reasonable to hypothesize that even higher levels of PBDE exposure, and possibly exposure to other flame retardants, would be found in the nursing infant children of female firefighters. No studies of this exposed population group were found in the literature.

## Part 3: Health Findings

### 3.1 Introduction

Information on human health effects of flame retardants are derived from experimental and observational studies. The purpose these studies is to estimate the likelihood that exposures



will harm humans. An example of an experimental study is a toxicity study in which animals are exposed to a chemical under controlled conditions (such as multiple dose levels) and the resulting health effects are measured. Such studies are conducted with the assumption that humans will be similarly affected. Another type of experimental study is *in vitro* toxicity testing in which components of cells or tissues that have been isolated from humans or animals are exposed to a chemical under controlled conditions. We assume that the effects from *in vitro* exposures are relevant to exposures to animals or humans. There are instances when groups of people have been accidentally or inadvertently exposed to potentially harmful chemicals. Scientists study the resulting effects of such exposures using epidemiology, a type of observational research. In epidemiology, data on exposures (for example, the concentration of a flame retardant in people's bodies or in environmental media) and health effects are collected and then a determination is made about whether a statistical association exists between the two. Since epidemiological research is not conducted under controlled conditions, a single study cannot directly establish a cause-effect relationship. Therefore, a judgment on causality is made based on the "weight of evidence", which involves evaluating the consistency, reproducibility, and biologic plausibility of results of multiple epidemiology and experimental studies.

## 3.2 Relevant Toxicity Findings

### 3.2.1 Background

This section summarizes key toxicity information available from laboratory animal studies for selected flame retardants. Relevant toxicity values for oral, dermal and inhalation exposures for both cancer and non-cancer effects were obtained from published risk assessments and reports. MDH has not presented a comprehensive toxicological review of all possible effects for each chemical. Instead, the focus is primarily on identifying toxicity information to compare to available human exposure data.

The main toxicity concerns for flame retardants that we researched include effects on the endocrine system (testosterone and thyroid hormones), neurobehavioral developmental effects, and cancer.

The agency IARC identified the firefighting occupation as "possibly carcinogenic to humans" (Group 2B) based on limited evidence in humans (IARC 2010). In addition to the cancer classification for the occupation of firefighting, some of the individual flame retardant chemicals are also classified as carcinogens by various organizations (NIEHS 2015, IARC 2015, OEHHA 2015, and USEPA 2008b). Some carcinogenic flame retardant chemicals include commercial grade pentaBDE mixture, decaBDE, TDCPP, TCEP, antimony trioxide (ATO), and short-chained chlorinated paraffins (SCCPs). It is well-recognized that firefighters may be exposed to a multitude of chemical carcinogens present in smoke or soot and that the types of chemicals released in a fire can vary greatly in different circumstances. Over 30 carcinogenic chemicals or chemical groups that have been detected in smoke during firefighting operations, not including flame retardants (IARC 2015). While it is beyond the scope of this report to discuss the multiple non-flame retardant carcinogenic chemicals, it is important to recognize

that firefighters may have an elevated cancer risk from smoke or soot exposure regardless of whether flame retardants are present or not.

The preferred type of toxicity value to use for comparing toxicity to exposure is a reference value (a dose in the body or concentration in the air), which is considered to be protective for human health. MDH lists and describes below reference doses derived by recognized national or international authorities in published sources or values that were previously published by MDH. However, when a reference value was not available, MDH lists either the no observed adverse effect level or concentration (NOAEL or NOAEC), benchmark dose level (BMDL), or a lowest observed adverse effect level or concentration (LOAEL or LOAEC) from a relevant animal study. Relevant dermal toxicity values were not found for any of the flame retardant chemicals; however, the percentage absorbed through the skin into the body was included, if available. Dermal absorption of chemicals can vary widely depending on many factors, including the amount and nature of the chemical, the location on the body, the surface area exposed, length of time on the skin, presence of moisture, temperature, and the degree that the skin is tightly covered by clothing or bandages. The relevance of skin absorption information obtained from animal or tissue studies to firefighters' exposure conditions is unknown.

The flame retardants reviewed in this section include PBDEs, polybrominated non-PBDEs, chlorinated phosphate esters, ATO, and SCCPs. Toxicity values presented in this report are based on chemicals studied individually, except for one study that evaluated DE-71, a mixture of BDE-47, -99, and -153. However, these chemicals can be present in smoke or soot as complex and variable mixtures and can include thermal degradation products. The toxicity of individual chemicals may be influenced by other chemicals in a mixture in an additive, less-than-additive, or more-than-additive way.

### 3.2.2 Toxicity Findings for PBDEs

For PBDEs, endocrine and metabolic effects in adult rodents are the basis for derivation of the reference doses and appear to be the most sensitive endpoint based on a review of various published risk assessments (ATSDR 2015). Neurobehavioral developmental effects in offspring exposed during pregnancy and early life are also a major toxicological concern for PBDEs. However, the reference doses based on exposure to adult rats with effects on testosterone and serum glucose are much lower, and therefore more protective, than reference doses based on developmental neurological effects.

#### Oral

DecaBDE, a "higher-brominated" PBDE, is generally considered less toxic than the "lower-brominated" PBDEs (ATSDR 2015). The lower-brominated PBDEs are more likely to be absorbed from the lungs or the intestines and also tend to stay in the body for a much longer time. The lower-brominated PBDEs have a very low oral reference dose of 0.000003 mg/kg-d which is considered protective for effects on serum testosterone, thyroid hormones and neurobehavioral developmental effects (ATSDR 2015). This reference dose is derived based on a study of BDE-47, but is considered by ATSDR (2015) to be applicable for other non-decaPBDEs

either in the absence of suitable data for the other PBDEs or because it is more conservative than other published values and, therefore, more health protective.

The National Toxicology Program (NTP) recently completed a chronic study in rats and mice for a technical-grade mixture of pentaBDE, called DE-71, consisting of 36 percent tetraBDE, 54 percent pentaBDE and 7 percent hexabromodiphenyl ether (hexaBDE) (NTP 2015c). Non-cancer effects included reduced thyroid hormone (T4), liver hypertrophy, thyroid follicular cell hypertrophy, and lesions in the kidneys, prostate gland, uterus, testes, and adrenal cortex. The time-adjusted NOAEL of 0.0071 mg/kg-d was based on reduced T4 and liver hypertrophy in rats after subchronic exposure. Measurements of tissue levels suggested that there might be a higher bioaccumulation potential for BDE-153, a hexaBDE congener.

In contrast to the lower-brominated BDEs, the oral reference value for decaBDE is 0.0002 mg/kg-d for protection from metabolic changes (serum glucose) and neurobehavioral developmental effects in offspring from exposure during pregnancy (ATSDR 2015).

## Inhalation

Inhalation of PBDEs can result in absorption from the lungs to cause effects elsewhere in the body. An inhalation reference concentration of 0.006 mg/m<sup>3</sup> can be applied to protect from effects on thyroid hormones based on a study of BDE-197 (ATSDR 2015). Other than BDE-197, no chemical-specific inhalation values were found in the literature for the other PBDE congeners. However, ATSDR (2015) considered the inhalation value for BDE-197 to be applicable for all lower-brominated BDEs. Absorption into the body from inhalation of decaBDE is assumed to be negligible (ECHA 2015), but overall, systemic absorption after inhalation is unknown for decaBDE (USEPA 2014c).

## Dermal

Relevant dermal toxicity studies are not available and very little information on skin absorption is available for most of the PBDEs. Up to 62 percent of BDE-47 is reported to be absorbed through the skin (USEPA 2008a), although other PBDE congeners (for example, BDE-153, BDE-197 and BDE-209) appear to be absorbed to a lesser degree ( $\leq 4.5$  percent) (ATSDR 2015, EC 2003). No dermal absorption information was found for BDE-99. Laboratory studies include patch testing in rodents, *in vitro* tests in rodent and/or human skin, and an estimate based on physical-chemical properties and structural analogy to PCBs. The applicability of dermal absorption data from these various types of studies to firefighters' exposure conditions is unknown.

## Cancer

Although cancer is identified as a concern for PBDEs, the only available oral cancer value for PBDEs is based on liver tumors in a rodent study for decaBDE (BDE-209). NTP (2015c) concluded that a commercial grade pentaBDE mixture called DE-71 (containing 36 percent tetraBDE, 54 percent pentaBDE and 7 percent hexaBDE) clearly causes liver cancer and may cause precancerous lesions in the liver and thyroid in rats and mice (NIEHS 2015), but published

cancer risk values are not yet available. No cancer information is available for other lower-brominated PBDEs. Based on the cancer value of 0.0143 mg/kg-d for decaBDE derived from an EPA cancer slope factor of 0.0007 (mg/kg-d)<sup>-1</sup> (USEPA 2008b), the non-cancer toxicity value appears to be protective for cancer. It is not known whether or not the other PBDEs may cause cancer or if the cancer value for decaBDE would be protective for other PBDEs.

### TOXICITY VALUES FOR PBDE CONGENERS

Toxicity Value	BDE-47	BDE-99	BDE-153	Technical-Grade Mixture, DE-71 (BDE-47, -99, -153)	BDE-197	BDE-209 (decaBDE)
Oral* (mg/kg-d)	0.000003 (MRL)	0.000003 (MRL)	0.000003 (MRL)	0.0071 (NOAEL <sub>adj</sub> )	0.000003 (MRL)	0.0002 (MRL)
Inhalation (mg/m <sup>3</sup> )	0.006	0.006	0.006	Not available	0.006	Not available
Dermal (%) absorbed	62	Not found	1.88	Not available	4.5	0.34
Cancer (mg/kg-d)	Not Available	Not Available	Not Available	Not Available (liver, thyroid)	Not Available	0.0143 (liver)

\*MRL is a "Minimal Risk Level" derived from a NOAEL divided by various risk assessment uncertainty factors. A NOAEL<sub>adj</sub> is the NOAEL adjusted to account for dosing for only five days per week.

### 3.2.3 Toxicity Findings for Brominated Phthalates, Phenols and Aliphatic Bromides/Cyclododecanes

In addition to the PBDEs described above, data for four other polybrominated flame retardants are summarized, including TBBPA, bis(2-ethylhexyl)tetrabromophthalate (TBPH), 2-ethylhexyltetrabromobenzoate (TBB), and HBCD. Thyroid hormone effects appear to be the most sensitive endpoint for most of these chemicals. Doses causing thyroid changes are lower than the doses that caused developmental effects in offspring. However, the most sensitive health endpoint for exposure to HBCD was neurotoxicity after exposure early in development (pre-conception through weaning). Cancer was the most sensitive health endpoint for exposure to TBBPA.

The toxicity values are summarized in the table below. No oral reference doses were found for this group of chemicals. Therefore, the oral toxicity values presented below are based on NOAELs or BMDLs.

#### Oral

The major health concerns for this group of chemicals include effects on thyroid hormones and developmental effects. The oral NOAEL for TBBPA was 10 mg/kg-d based on effects on thyroid hormones (T4) in adult offspring exposed from gestation through adulthood (EFSA 2013). The

oral NOAELs for TBPH and TBB were 50 mg/kg-d for each chemical (USEPA 2015a). Reduced body weights in fetuses, offspring and adults were reported at higher doses. For HBCD, the oral BMDL was 0.2 mg/kg-d with neurodevelopmental effects on hearing impairment at a higher dose (USEPA 2014a).

## Inhalation

Inhalation toxicity information was limited to TBBPA with a NOAEC of 2,000 mg/m<sup>3</sup> (2 mg/L) of air breathed in a 14-day whole body inhalation study in rats. Effects reported at a higher air concentration (18,000 mg/m<sup>3</sup>) included salivation, nasal discharge and watery eyes (USEPA 2015c). No toxicity was reported elsewhere in the body. Longer duration inhalation studies were not found for TBBPA. The EU (EU 2006, as cited by USEPA 2015d) estimated that only a small amount of TBBPA will reach deep into the lung with only about 5 percent absorption from the lung into the body. The EU estimated about 70 percent will deposit in the upper respiratory tract where it will either be exhaled or swallowed. In the absence of suitable inhalation studies for HBCD, the EU (2008c) assumed that 100 percent of all particle sizes less than 100 µM was absorbed into the body after inhalation for risk assessment purposes. Once HBCD is absorbed into the body from the lungs, similar toxicity can be expected as for ingestion.

## Dermal

Dermal absorption was not very extensive and ranged from less than 1 percent for TBBPA to 4 percent for HBCD fine particles (USEPA 2015c; EU 2008c). No dermal absorption or toxicity information was found for TBPH or TBB. Laboratory studies consisted of *in vitro* dermal absorption tests. Additionally, no systemic toxicity was found when rabbits were dermally exposed to TBBPA for 21 days. The applicability of dermal absorption data from *in vitro* studies to firefighters' exposure conditions is unknown.

## Cancer

The only available oral cancer value for this group of non-PBDE brominated flame retardants is based on clear evidence for uterine tumors in a rat study for TBBPA (NTP 2014). The cancer value for TBBPA of 0.0030 mg/kg-d is derived from a cancer slope factor of 0.00329 (mg/kg-d)<sup>-1</sup> based on uterine cancer (USEPA 2015d). No cancer information was available for TBPH, TBB, or HBCD.

## TOXICITY VALUES FOR BROMINATED PHTHALATES, PHENOLS AND ALIPHATIC BROMIDES/CYCLODODECANES

Toxicity Value	TBBPA	TBPH	TBB	HBCD
Oral (mg/kg-d)	10	50	50	0.2
Inhalation (mg/m <sup>3</sup> )	2,000	Not Available	Not Available	Not Available

Toxicity Value	TBBPA	TBPH	TBB	HBCD
Dermal Absorption (%)	0.73	Not Available	Not Available	4 (fine particles); 2 (granular particles)
Cancer (mg/kg-d)	0.0030 (uterine tumors)	Not Available	Not Available	Not Available

### 3.2.4 Toxicity Findings for Halogenated Phosphate Ester Flame Retardants

Data for three halogenated phosphate esters, TDCPP, TCEP, and TCPP, are summarized below. The major health concerns for this group of chemicals include effects on cancer, kidneys, liver, male reproductive system, and endocrine system. There are also concerns about developmental toxicity and nervous system effects. Cancer appears to be the most sensitive endpoint for the chlorinated phosphate esters with cancers reported in kidney, thyroid, liver and testes of laboratory animals.

#### Oral

The oral reference dose for TDCPP was 0.0019 mg/kg-d based on non-cancer effects on kidneys and male reproductive system (seminal vesicle atrophy) at higher doses (MDH 2013a). The oral reference dose for TCEP was 0.067 mg/kg-d (MDH 2013b) with kidney effects reported at higher doses. For TCPP, ATSDR (2012) concluded that there were insufficient studies available to identify sensitive health endpoints or to derive toxicity values. New subchronic, chronic, and gestational developmental studies for TCPP have been conducted in rodents, but reports and conclusions are not yet available at the time of publication of this MDH Flame Retardant report (NTP 2015a, USEPA 2015b). The EPA reported a screening-level value of 0.014 mg/kg-d (USEPA 2012a) from NTP's unpublished subchronic mouse study based on BMDL of 138 mg/kg-d for liver hypertrophy. Thyroid effects occurred in another study at much higher doses. The oral reference values for these chlorinated phosphate esters may also be protective for reproductive and developmental effects from exposure during pregnancy. Developmental effects reported in a few limited studies decreased number of male pups per litter (TCEP; MDH 2013b), increased number of runts (TCPP; EU 2008b), missing fetal ribs (TCPP; USEPA 2012a), and increased fetal death (TDCPP; EU 2008a).

#### Inhalation

Inhalation toxicity information was limited to TCEP with a recommended workplace exposure limit in air of  $\leq 0.2$  mg/m<sup>3</sup> to protect from cancer (EU 2009). In the absence of suitable inhalation studies for TDCPP and TCPP, the EU (EU 2008a, 2008b) assumed that 100 percent of all particle sizes less than 100  $\mu$ M was absorbed into the body after inhalation for risk assessment purposes. Once the chemical is absorbed into the body from the lungs, similar toxicity can be expected as for ingestion.

## Dermal

The chlorinated phosphate esters are readily absorbed into the body from the skin. Dermal absorption was significant in rats for TDCPP and *in vitro* human skin for TCPP (USEPA 2015b). The EU assumed that a worst-case dermal absorption was 30 percent for TDCPP and 40 percent for TCPP based on results from human skin tested *in vitro* (EU 2008a, 2008b). In the absence of specific dermal absorption data for TCEP, the EU (2009) assumed 100 percent dermal absorption. Additionally, the EU (2009) recommended that dermal exposure to TCEP be controlled to levels less than 2 mg per person per day, or 0.029 mg/kg-d for a 70-kg person, to protect from cancer.

## Cancer

The cancer value for TDCPP was based on an OEHHA-derived cancer slope factor of  $0.13 \text{ (mg/kg-d)}^{-1}$  and a No Significant Risk Level (NSRL) of  $5.4 \text{ }\mu\text{g/day}$  or  $0.000077 \text{ mg/kg-d}$  for a 70-kg person (OEHHA 2013). The cancer value for TCEP was based on an EPA-derived cancer slope factor of  $0.02 \text{ (mg/kg-d)}^{-1}$  (USEPA 2009a) which results in a cancer value of  $35 \text{ }\mu\text{g/day}$  or  $0.0005 \text{ mg/kg-d}$  for a 70-kg person. A new cancer bioassay in rodents for TCPP has recently been completed by NTP; however, the report is not yet available (NTP 2015a, USEPA 2015b). In the absence of cancer data for TCPP, the EU (2008b) considered structural similarity to TDCPP and TCEP and attempted a “read-across” alternative approach to estimating cancer risk for TCPP. However, the EU concluded that this alternative approach based on structural similarity was not appropriate for a quantitative risk assessment due to substantial differences in metabolism, target organs, severity of effects, and potency.

## TOXICITY VALUES FOR HALOGENATED PHOSPHATE ESTERS

Toxicity Value	TDCPP	TCEP	TCPP
Oral (mg/kg-d)	0.0019	0.067	0.014
Inhalation (mg/m <sup>3</sup> )	Not Available, assume 100% absorption from lungs	$\leq 0.2$	Not Available, assume 100% absorption from lungs
Dermal Absorption (%)	30	100	40
Cancer (mg/kg-d)	0.000077 (liver, kidney, testes)	0.0005 (kidney)	Not Available*

\* A new oral cancer bioassay in rats and mice has recently been completed, the report is not yet available NTP (2015a)

### 3.2.5 Toxicity Findings for Other Flame Retardants – Antimony Trioxide and Chlorinated Paraffins:

Toxicity values for two structurally unrelated chemicals found in flame retardant products, ATO and SCCPs, are summarized in the table below. The toxicity values for antimony are based on ATO because it is the primary form commonly used together with brominated and chlorinated flame retardants. The health effect from antimony is primarily lung damage from inhalation, with cancer of the lung a possible concern at higher exposures. The health effect of concern from SCCPs is primarily cancer from oral exposure, and at higher levels, harm to the liver, kidney, and thyroid.

#### Oral – Antimony Trioxide

ATO is not highly toxic after ingestion, probably due to relatively poor absorption from the intestines; however, minor effects on the liver were reported in a laboratory animal study. The oral reference dose selected at the representative toxicity value for ATO is 0.5 mg/kg-d based on effects on triglycerides, liver enzymes, and liver weight in laboratory animals (USEPA 2008c). No oral developmental studies were found for ATO, but due to poor intestinal absorption, developmental effects are not expected to be a sensitive effect for ingestion of ATO (see inhalation discussion below). Antimony compounds have been associated with cardiac toxicity in exposed workers and in laboratory animals (USEPA 2008d), but the associated compound (antimony trisulfide) is more soluble and easily absorbed into the body than ATO. Reports of cardiac toxicity for ATO were not found in humans or laboratory animals; however, antimony was found in heart tissue after oral exposure to ATO in rats (EU 2008d).

#### Inhalation – Antimony Trioxide

Lung effects are considered to be the major health concern from inhalation of ATO, primarily because it is not easily absorbed into the body and tends to stay in the lungs for a long time (USEPA 2009b, USEPA 2014b). Inhalation of ATO has resulted in lung fibrosis, inflammation and pneumoconiosis with effects on macrophages in the lungs as the most sensitive effect (USEPA 2009b). No developmental effects were found when rats were exposed to ATO via inhalation during pregnancy (USEPA 2014b).

The American Council of Governmental Industrial Hygienists (ACGIH) and the U.S. Occupational Safety and Health Administration (OSHA) have set a time-weighted average (TWA) occupational exposure limit of 0.5 mg/m<sup>3</sup> for antimony compounds to protect workers from respiratory tract irritation, chronic lung effects, functional disorders of the heart, and degeneration of heart muscle (OSHA 2012). The EU identified a NOAEC of 0.51 mg/m<sup>3</sup> from 1-year rat study for risk assessment for lung inflammation (EU 2008d). A much lower inhalation toxicity reference value of 0.0002 mg/m<sup>3</sup> was developed by USEPA (1995) based on lung toxicity in rats at 1.1 mg/m<sup>3</sup>, with no effects at 0.25 mg/m<sup>3</sup> exposed for 6 hours per day for 5 days per week. The EPA inhalation value for ATO, however, is not relevant for firefighter exposures because it was adjusted to make it relevant to the general population who might be exposed to environmental sources for a lifetime for 24 hours per day and every day of the week.



## Dermal – Antimony Trioxide

Dermal absorption was reported to be poor for ATO, with only about 0.26 percent absorbed through the skin (ECHA 2009).

## Cancer – Antimony Trioxide

At the present time there is considerable uncertainty regarding the inhalation cancer potency for ATO due to some controversies and inconsistencies regarding the results of previous animal studies. The mechanism of cancer is unclear, but until recently it was thought that cancer is most likely related to particle overload in the lungs, followed by impaired clearance and inflammation leading to fibrosis and lung tumors in rats (EU 2008d). Therefore, the EU considered ATO to be a threshold carcinogen so that the NOAEC of 0.51 mg/m<sup>3</sup> for non-cancer lung effects can also be considered protective for carcinogenicity (EU 2008d). A better understanding of the cancer risks for ATO, including the mechanism of action, may be evident once the review for new chronic inhalation carcinogenicity studies in rats and mice has been completed (NTP 2015b). The new studies suggest a non-threshold mechanism for cancer, in which case, it is possible that the non-cancer, no-effect level may not be sufficiently protective for cancer. At the time of this writing, the NTP Expert Panel Peer Review of the new cancer study is scheduled for February 16, 2016 (NTP 2016). The peer review will consider evidence of tumors in rats and mice and the mechanism by which ATO causes cancer.

## Oral – Short-Chained Chlorinated Paraffins

The oral toxicity reference value for SCCPs is 0.01 mg/kg-d for effects on the liver, kidney, and thyroid in laboratory animal studies with a NOAEL of 10 mg/kg-d and a LOAEL of 100 mg/kg-d (Health Canada 1996). There was no evidence of developmental toxicity in laboratory animals (USEPA 2009b).

## Inhalation - Short-Chained Chlorinated Paraffins

No inhalation information was found for SCCPs, but absorption into the body after inhalation was assumed to be 100 percent for risk assessment purposes (ECHA 1999) with potential effects similar to ingestion.

## Dermal - Short-Chained Chlorinated Paraffins

Dermal absorption was reported to be poor for SCCPs, with less than 1 percent absorbed through the skin (ECHA 1999).

## Cancer - Short-Chained Chlorinated Paraffins

The cancer value for SCCPs is based on liver tumors in mice and a cancer slope factor of 0.089 (mg/kg-d)<sup>-1</sup> which results in a NSRL of 8 µg/d or 0.00011 mg/kg-d for a 70-kg person (OEHHA 1992).

**TOXICITY VALUES FOR OTHER FLAME RETARDANTS**

Toxicity Value	ATO	SCCPs
Oral (mg/kg-d)	0.5	0.01
Inhalation (mg/m <sup>3</sup> )	0.5 (8-hr OSHA/ACGIH TWA, workers)  0.51 (NOAEC)	Not Available, assume 100% absorption from lungs
Dermal Absorption (%)	0.26	≤ 1
Cancer	0.51 mg/m <sup>3</sup> (inhalation exposure, lung*)	0.00011 mg/kg-d (oral exposure, liver)

\* 2-year inhalation cancer bioassay in rats and mice is completed, and the report is scheduled for NTP Peer Review in February 2016 NTP (2015b)

### 3.3 Relevant Epidemiological Findings

#### 3.3.1 Introduction

A large body of literature has examined potential links between working as a firefighter and adverse health outcomes. The majority of research has focused on cancer using several methodological approaches (for example, Tsai et al. 2015; Daniels et al. 2014, Pukkala et al. 2014; Kang et al. 2008; review and meta-analysis in LeMasters et al. 2006). Studies find that firefighting is significantly associated with an increased risk for developing many types of cancer (recently reviewed in Tsai et al. 2015), although there are inconsistencies in findings between studies. A smaller subset of studies have focused on non-cancer outcomes, mainly cardiovascular and respiratory disease (reviewed in Crawford and Graveling 2012); or both cancer and non-cancer outcomes (Baris et al. 2001; Daniels et al. 2015). One concern is that many of the cancer studies reflect exposures that occurred prior to advances in building and consumer product materials that have introduced firefighters to new chemical carcinogens (Tsai et al. 2015).

Cancer risks to firefighters were assessed by the World Health Organization's International Agency for Research on Cancer in 2010 (IARC 2010). The IARC review encompassed several types of epidemiological study designs along with other relevant data. Based on meta-analysis, IARC identified three types of cancer that showed significant increases in summary risk estimates in firefighters: testicular cancer, prostate cancer, and non-Hodgkin lymphoma. As a result, IARC classified working as a firefighter as "possibly carcinogenic to humans" based on limited evidence in humans. The studies reviewed by IARC, as well as other epidemiological studies in the literature, generally do not distinguish between different types of exposure or firefighter tasks when linking firefighter occupation to adverse health outcomes.

In this report, MDH is tasked with reporting findings from studies that examine adverse health outcomes in firefighters specifically from exposure to flame retardants. Because of the number of toxic components in smoke and the variety of other exposures and tasks related to firefighting, studies relating working as a firefighter and health outcomes are of limited use to meeting this goal. Unfortunately, no epidemiological studies specifically address flame retardant exposures in firefighters and health effects. Therefore, the remainder of this section summarizes the main findings from the epidemiological literature on flame retardants conducted within the general population, other types of occupational workers, and sensitive subgroups. There are some limitations to this review. Since the majority of flame retardant epidemiological studies measure PBDEs only, MDH could not address health outcomes associated with exposures to other types of flame retardants. Also, MDH could not address potential health effects related to dermal/inhalation exposures (from the combustion of flame retardants), as studies have been mainly limited to associations between PBDE exposure and health effects in the general public, for which the main exposure route is oral.

### 3.3.2 Adverse Effects of PBDEs in Adults

The main PBDE target of concern in adults is the endocrine system. The weight-of-the-evidence is lacking for other endpoints such as cancer and reproductive effects. However, this is a very active area of research and many epidemiological investigations are currently underway (as described in ATSDR 2015).

The chemical structures of PBDEs are similar to that of thyroid hormones; and as described in the Toxicity Findings section, PBDEs have been shown to affect thyroid regulation in laboratory animal studies. Based on this toxicological evidence, numerous epidemiological studies have examined the relationship between thyroid hormone status and serum PBDE levels in pregnant and non-pregnant adults (Abdelouahab et al. 2011, 2013; Bloom et al. 2008; Chevrier et al. 2010; Dallaire et al. 2009; Hagmar et al. 2001; Huang et al. 2014; Julander et al. 2005; Kim et al. 2013; Mazdai et al. 2003; Meeker et al. 2009; Stapleton et al. 2011; Turyk et al. 2008; Wang et al. 2010; Yuan et al. 2008; Zota et al. 2011). The majority of these epidemiological studies report associations between exposure to PBDEs and altered thyroid hormone regulation. However, the specific findings have been inconsistent, with positive, negative, and null associations reported between certain PBDE congeners and various thyroid hormone levels; even when restricting to similar subpopulations such as adult men. For example, studies have shown both increases and declines in thyroid hormone levels (thyroid stimulating hormone and triiodothyronine) in relation to PBDE exposure. In sum, the majority of epidemiology studies have demonstrated that PBDEs can interact with the human endocrine system to affect thyroid hormone levels; however, a clear pattern in the findings has not emerged across studies. A recent meta-analysis of sixteen studies was conducted to determine the association between PBDE exposure and thyroid function (Zhao et al. 2015). The results indicate that the conflicting direction of effects of PBDEs on thyroid function may be due to differences in PBDE serum levels between studies, coupled with a non-monotonic dose-response relationship. Future epidemiology studies may help clarify how PBDEs affect thyroid hormones in adults.

Compared to thyroid effects, there is more limited information on which to assess reproductive effects of PBDEs in adults. These studies are difficult to interpret as a whole due to lack of uniformity in health endpoints (such as fecundity, hormone levels, and menstruation characteristics) between available studies and discordance in findings on the same endpoints. Strong inverse correlations between serum BDE-153 concentration and sperm concentration and testes size were found in a very small pilot study of ten fertile men (Akutsu et al. 2008). No relationship was observed with the 13 other PBDE congeners measured in the study. Researchers found semen mobility was negatively related to BDE-47, BDE-100 and total BDE (but not BDE-153) in a small study of 52 men recruited in a fertility clinic (Abdelouahab et al. 2011). No relationships were observed with other semen parameters. In a study of serum PBDE and hormone levels in male Great Lakes fish consumers, a significant positive relationship was found for BDE-47 (but not other congeners) and serum testosterone levels (Turyk et al. 2008). Researchers reported associations between sex hormone levels in men and concentrations of flame retardants in house dust (Johnson et al. 2013). Both positive and negative associations were found between sex hormone levels and penta-, octa-, and decaBDE. Although the sample size was relatively small and the reliability of house dust as a surrogate for internal exposure is highly uncertain, this study is of interest for its inclusion of alternative brominated flame retardants in addition to PBDEs. For example, HBCD was associated with decreased sex hormone-binding globulin and increased free androgen index. For adult women, studies are sparser and have mainly focused on effects of PBDEs on fertility/fecundity and menstrual cycle length with mixed results (Buck Louis et al. 2013; Chao et al. 2007 and 2010; Harley et al. 2010; Johnson et al. 2013). In sum, there are fewer human studies on reproductive effects in adults compared to the thyroid; and as a whole, the current evidence for reproductive effects in humans is insufficient at this time. However, some studies have found results suggestive of reproductive effects, and reproductive effects are documented in animal studies.

### 3.3.3 Adverse Effects of PBDEs in Children

A review of flame retardant epidemiological studies focusing on flame retardant exposures and health effects in children is considered outside the scope of this report. However, there are epidemiological findings that are relevant to firefighters who are pregnant or may become pregnant. PBDEs can be transferred to the fetus across the placenta and to nursing infants via breast milk. Numerous human and animal studies suggest that exposure to PBDEs *in utero* and/or in early childhood can result in thyroid hormone alterations and effects on the developing nervous system. In fact, ATSDR has identified the developing thyroid and nervous system as “targets of concern” for PBDEs (ATSDR 2015). Some epidemiological studies have evaluated potential associations between concentrations of PBDEs in maternal or cord blood samples and other developmental effects and birth outcomes, but the findings have been null, mixed, or suggestive but in need of further replication. To date, the strongest evidence of developmental effects from human studies (and animal studies) suggest that PBDE exposure may affect the developing thyroid and neurodevelopment (ATSDR 2015).

### 3.3.4 Adverse Effects of Occupational Exposure to Antimony

In addition to PBDEs, there is sufficient evidence in the epidemiological literature linking exposure to antimony in occupational settings (for example, smelting plants) and adverse health outcomes. The human health effects of antimony are summarized in Cooper and Harrison 2009 and ATSDR's Toxicological Profile for Antimony (ATSDR 1992). According to ATSDR, "the toxicological effects of antimony in humans following inhalation or oral exposure are pneumoconiosis, altered EKG readings, increased blood pressure, abdominal distress, ulcers, dermatosis, and ocular irritation." The relevance of these findings to firefighters is unclear, as exposure to antimony in the studied occupational cohorts was generally high and occurred over a 40-hour work week. It is unknown whether any effects may occur at the intermittent levels to which firefighters may be exposed.

In sum, epidemiological studies of flame retardant exposures and health effects in firefighters are lacking. Therefore, we must base our understanding of potential health effects on epidemiological studies of the general population or other occupational cohorts. Epidemiology studies in the adult general population are generally limited to PBDEs. These studies currently suggest thyroid hormone alterations and possibly reproductive effects as the main targets of concern. Two factors increase our confidence that a relationship may exist between PBDE exposure and these health endpoints in adults. First, there are consistent findings in experimental animal studies and *in vitro* studies, which help us understand why PBDEs cause damage in animal's organs and cells and the relationship between animal and human health. Second, perturbations of the thyroid have been reported in a variety of human studies. However, there are also study limitations to consider. Many of the studies measured exposure to PBDEs and the health outcomes at the same point in time. This gives no indication of the sequence of events (whether exposure occurred before, after or during the onset of the health effect), making it difficult to infer causality. Further, the designs of the studies ranged in how well co-exposures and confounders that may be correlated with PBDE exposure and/or the health outcome were measured and considered. This increases uncertainty in the results. Finally, the studies do not address the unique exposures and health effects that may result from the combustion of flame retardants in firefighting settings.

## Part 4: Risk Characterization Needs

### 4.1 Research Needs

While we did not conduct a definitive analysis of the literature on flame retardants, MDH staff reviewed a sufficient number of studies to evaluate whether information was available to assess exposure and toxicity for the purpose of characterizing health risks for firefighters. There are many gaps in the available data, in particular, the paucity of suitable exposure and health studies of firefighters and reference populations, and the fact that the studies that are relevant have focused on different classes of flame retardants. As a result there are gaps in understanding one or more aspects of risk (exposure, toxicity, or epidemiology) that may be

essential for characterizing health risks to firefighters or the general public. Other issues that could be addressed in the future as additional research is conducted include cumulative risk from exposure to flame retardants, potentiation of risk from constituents of smoke other than flame retardants, risks from combustion by-products, and extrapolation from animal studies to human health.

#### 4.1.1 Biomonitoring and Biomonitoring Equivalents

Biomonitoring studies continue to be conducted and the suite of chemicals analyzed will continue to change. Laboratory methods are still being developed and implemented that will likely yield more information over time. We lack a consistent set of flame retardants that are routinely analyzed, but as more risk characterization is conducted, greater priority will likely be given to the more toxic as well as the more prevalent flame retardants that can be measured in the body.

Interpreting biomonitoring data on flame retardants from a health risk standpoint is challenging. For certain substances, such as lead and mercury, biomonitoring data from definitive epidemiology studies have been used to develop estimates of the risk associated with an amount of chemical in the body. This approach has not yet been developed for flame retardants.

Another approach to using human biomonitoring data in risk assessment is to compare the levels of a chemical in people to levels in test animals that have been studied for toxic effects. Biomonitoring equivalents are then calculated to extrapolate between animals and humans, describing the pharmacokinetic relationship between toxicity from an administered dose in an animal study (amount of chemical ingested in the diet, for example) and the internal dose (levels of chemical in the body) for both animals and people. The differences in how animals and humans absorb and retain chemical is critical to understanding this relationship. MDH would need to know the animal's blood level that is associated with a harmful effect (such as the lowest observable adverse effect level (LOAEL)) in a study in which a known amount of flame retardant is given to the animal (such as in the diet). MDH would need to understand the animal and human differences in absorption and retention of chemicals to determine what level of chemical in the blood of humans would cause toxicity. We would use that human biomonitoring equivalent to interpret risks for data found in biomonitoring studies. MDH found only a few human biomonitoring equivalents have been published for flame retardants (Appendix D). In reviewing the literature, staff found that only a few animal studies of flame retardants have measured internal doses. In addition, the studies from which these data were developed may not have targeted appropriate health effects for firefighters, sometimes the units of analysis (biomarker metric) were not appropriate, and appropriate pharmacokinetic models are rarely available to relate animal data to humans (Appendix D).

#### 4.1.2 Cumulative Risks From Mixtures of Chemicals

The health effects from exposures to mixtures of PBDE congeners, which each vary in toxicity, may be greater or less than the toxicity of the individual congeners. The effects of mixtures is difficult to estimate without studies of chemical and biological interactions at the cellular level

or toxicity or epidemiology studies that compare the harm from doses or exposures of individual congeners versus mixtures. Instead, risk can be very simplistically (and likely inaccurately) added together. However, this requires MDH to determine safe levels in media (air, dust, skin) and have corresponding measured levels of exposure. MDH has only developed media-specific values for a few flame retardants, and only for oral exposure through drinking water (MDH 2015).

Staff did not locate exposure or health information for complex questions related to combustion of flame retardants. For example, it is possible that flame retardants increase exposure to smoke/soot, and that this exposure adds to the health effects from flame retardants. In addition, combustion will change a portion of the chemicals present, and there is evidence that fires transform flame retardants into more toxic by-products, such as dioxins. But that change has not been carefully studied to be useful in characterizing health risks.

#### 4.1.3 Attention to Replacement Chemicals

Staff are concerned that if specific flame retardants are replaced in manufacturing products, we will have less information about the hazards of the replacement flame retardants. Our review of the epidemiology literature found few studies on potential human health effects of PBDE replacement compounds. This is a growing concern since people's levels of non-PBDE chemicals are increasing in response to the PBDE bans.

## 4.2 Ongoing Research

### 4.2.1 Biomonitoring and Epidemiology

PBDEs remain an active area of epidemiological research and there are several ongoing investigations evaluating potential associations between PBDEs in human biospecimens and a variety of health outcomes. Ongoing studies are described in the Draft Toxicological Profile for Polybrominated Diphenyl Ethers (Section 3.12.3, ATSDR 2015). The ongoing research will both add to the weight-of-evidence for PBDE health effects described in the current literature as well as explore the potential for other health effects for which research is currently lacking.

Additional flame retardant biomonitoring studies in firefighters are underway, including a biomonitoring study of female firefighters with the San Francisco Fire Department ("The Women Firefighters Biomonitoring Collaborative Study"). According to the study website, firefighter blood and urine is being tested for "a wide variety of flame retardants" among other chemicals<sup>4</sup>. The study will also include some indicators of physiological changes including thyroid hormone levels and telomere length, an indication of cellular aging. Approximately 80 female San Francisco firefighters will be included, along with 80 female city office workers who will serve as the comparison group.

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<sup>4</sup> The Women Firefighters Biomonitoring Collaborative Study, <http://womenfirefighterstudy.com/>



The California Biomonitoring Program has non-firefighter biomonitoring studies underway that include PBDEs and results will be available in the future. Further, the program plans to analyze archived samples from the FOX firefighter study for non-PBDE flame retardants, including TDCPP and TCEP.<sup>5</sup>

#### 4.2.2 Exposure

Ongoing exposure assessment work by NIOSH, led by the Health Hazard Evaluation Program, is focused on the flame retardants that are released into the air and onto surfaces during residential fires. The NIOSH program is studying contamination of firefighters' gear and field-based decontamination. The group is continuing to study the pathways (via the lungs or skin) by which flame retardants enter the body. NIOSH scientists are analyzing environmental and biological samples for PBDEs, other brominated flame retardants (TBB, TBPH, TBBPA), and chlorinated or phosphorylated flame retardants (TPP, TCP, TDCPP). Analytical results will not be available until after mid-2016<sup>6</sup>.

#### 4.2.3 Toxicology

In addition to the pending NTP toxicology study reports and NTP peer reviews for TCPP and ATO mentioned in Section 3.2, there are several areas of active research in animals, tissues, and cells to better understand the toxicity of flame retardant chemicals. NTP selected several flame retardants for special studies related to gene and protein activity within cells or tissues (toxicogenomics) including BDE-47, BDE-99, BDE-153, BDE-209, TBBPA, TBPH, TBB, and HBCD (NTP 2015d, NTP 2015e). Some of the planned studies include evaluations of pregnant rats and their offspring as well as oral studies in rats and mice. In addition to evaluating individual chemicals, NTP is also evaluating some BDE mixtures including DE-71 (a mixture of BDE-47, -99, and -153), Firemaster 680, and Firemaster 550 in several toxicogenomic studies (NTP 2015d, NTP 2015e).

Ongoing animal studies are also presented in the Draft Toxicological Profile for PBDEs (Section 3.12.3, ATDSR 2015). Areas of particular focus include neurobehavioral changes as they might apply to attention-deficit disorders, immune system effects relevant to autism and autoimmune diseases, and effects on the brain and complex social behaviors. There are also studies to better understand the mechanisms of toxicity and how the chemicals are absorbed, metabolized, distributed and eliminated from the body.

### 4.3 Risk Characterization

MDH has determined that with more time and resources, it would be possible to develop a risk assessment for firefighter's health risks from exposure to flame retardants. Staff would model such a risk assessment on the work conducted by Fromme (Fromme et al. 2015). MDH would use the most relevant toxicity and exposure data for adult occupational exposure to

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<sup>5</sup> Nerissa Wu, California Department of Public Health, personal communication, 11/23/2015

<sup>6</sup> Personal communication with K. Fent, 10/9/2015



characterize risk. Selecting the most appropriate data for firefighters may be challenging due to the lack of definitive studies on firefighter exposures. The most robust set of data for risk assessment would be drawn from animal studies rather than epidemiology studies. Staff conclude that a characterization of risks to firefighters will have flaws. The greatest issue is that exposure to flame retardants also includes exposures to combustion by-products, including particulates. Much of the cancer risk that is associated with the occupational risk of cancer for firefighters is assumed to be due to chemical and particulate exposure other than flame retardants. In addition, MDH is not yet able to describe the transformation of flame retardants to dioxins and furans, and the resulting magnitude of exposure and risk. However, staff are concerned that additional exposures to dioxins and furans will increase cancer risks, perhaps significantly.

Decisions to protect public health do not need to be based on a definitive risk characterization. A precautionary approach that has already been taken by NIOSH scientists evaluating chemical exposures from fires is to recommend full protective gear and take additional precautions in removing, transporting, cleaning, and storing equipment so that exposures are minimized (NIOSH 2013). The State of Wisconsin has developed recommendations on reducing firefighters' occupational exposures through adherence to occupational hygiene recommendations (WDSPS 2015). These steps, aimed at reducing PAHs, particulates, and volatile organic compounds, will likely reduce exposures to flame retardants as well. Until more definitive research is available, NIOSH and research partners are articulating both the potential concern about flame retardants and the precautions firefighters can take to reduce exposure (Fent et al. 2015).

## Summary

Minnesota is among many states that have been taking action on or researching concerns about flame retardants, exposure, and health. New York has focused on flame retardants in homes and businesses (New York 2013), Washington has focused on exposure and harm early in life (Washington 2015), and California, like Minnesota, has included firefighters in their focus (Biomonitoring California 2015). Much of this work is associated with state legislative activity on regulating flame retardants in certain consumer products. Bans on manufacturing, selling, and purchasing vary across the states and across the classes of flame retardant chemicals.

Little of this work has focused on firefighters and occupational health. However, there are a growing number of studies, some currently in progress in Maine and California that are focused on understanding firefighters' potential exposures to flame retardants released by fires. It is well recognized that firefighters have an occupational hazard of increased cancer. What is not known is whether exposure to flame retardants contributes to that increased harm, and if so, to what degree.

MDH reviewed biomonitoring studies that show that firefighters are absorbing flame retardants into their bodies. We found that when the levels of PBDE flame retardants in Californians were compared to the levels in California firefighters, it is apparent that firefighters are exposed to

higher levels of some PBDE flame retardants. What cannot be known from this work is whether the predominant source of exposure is swallowing dust, breathing in air, or absorption from the skin. In addition, we do not know the extent to which certain activities (such as fighting fires, cleaning equipment, or working inside fire stations) lead to increased exposure. This knowledge would be useful to understand how to better protect firefighters from exposures.

MDH reviewed exposure data and found sufficient information to estimate levels of flame retardants in dust of fire stations. However, we found that it is not fully understood how the contaminated dust is generated or how it is transported to the fire station. The limited set of fire station data from California suggest that certain flame retardants in fire station dust (TBB, TBPH, and PBDEs) greatly exceed the levels commonly found in homes. We did not find sufficient information to estimate levels of flame retardants in the air that firefighters breathe during or after a fire. While it is assumed that exposure through inhalation is a major route of exposure, and there is a growing concern about absorption through the skin, MDH does not have data that demonstrate the amount that each route of exposure make to total exposure. Such information will be important in developing interventions to reduce overall exposure.

MDH reviewed toxicity data from animal experiments and found sufficient information to estimate exposures that would be protective (cause no harm to health) from direct ingestion, such as swallowing contaminated dust. Some information was also available concerning breathing in contaminated air. With additional work, these data could be used to estimate the levels of concern in dust and air. However, we lack data necessary to fully understand if or how doses from animal studies might be translated or used to interpret the body burden of flame retardants found in people. In particular, MDH did not find pharmacokinetic studies to evaluate the amount of flame retardant in a firefighter's body that poses a risk to health.

Epidemiological studies of flame retardant exposures and health effects in the adult general population are generally limited to PBDEs and focus primarily on thyroid hormone alterations and reproductive effects. The studies indicate that there may be an association between exposure and adverse effects for these two health endpoints. These studies do not address the unique exposures and health effects that may result from the combustion of flame retardants in firefighting settings or in firefighters. The majority of work on general population and firefighter exposure to flame retardants has been conducted in California. Due to past regulations, Californians have greater exposure to flame retardants than residents of other states. However, there is no reason to believe that firefighters' exposure to flame retardants relative to the general population is any different in Minnesota.

MDH concludes that firefighters have a greater exposure to some flame retardants than the general population. MDH cannot, at this time, determine if those exposures exceed the levels that are associated with health risks that have been studied animals and humans. Further work will be needed to either develop guidance for firefighters on levels of concern for flame retardants in air and dust, or to assess harmful levels of flame retardants in blood.

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# Appendices

Appendix A. Complete Text of Flame Retardant Bill

Appendix B: Laws and Regulations

Appendix C. PBDE Biomonitoring Comparison Plots

Appendix D. Summary of Published Biomonitoring Equivalents

## Appendix A. Complete Text of Flame Retardant Bill

Current 2015 Minnesota Statutes are available through the Minnesota Legislature and the Office of the Revisor of Statutes ([www.revisor.mn.gov](http://www.revisor.mn.gov)). A search of chapter 325.071 will display the current statute. The requirement to report to the Legislature is not included in the current statutes, but was passed as Minnesota Session Law of the 2015 regular session, chapter 62. That bill is reproduced below:

### CHAPTER 62--S.F.No. 1215

*An act relating to health; prohibiting the use of certain flame-retardant chemicals in certain products; requiring a report; proposing coding for new law in Minnesota Statutes, chapter 325F.*

BE IT ENACTED BY THE LEGISLATURE OF THE STATE OF MINNESOTA:

Section 1. [325F.071] FLAME-RETARDANT CHEMICALS; PROHIBITION.

Subdivision 1. Definitions.

- (a) For the purposes of this section, the following terms have the meanings given.
- (b) "Child" means a person under 12 years of age.
- (c) "Children's product" means a product primarily designed or intended by a manufacturer to be used by or for a child, including any article used as a component of such a product, but excluding a food, beverage, dietary supplement, pharmaceutical product or biologic, children's toys that are subject to the most recent version of the American Society for Testing and Materials F963, Standard Consumer Safety Specification for Toy Safety, a medical device as defined in the Federal Food, Drug, and Cosmetic Act, United States Code, title 21, section 321(h), products listed under section 116.9405, clauses (10) and (11), and products listed under sections 325F.03 and 325F.04.
- (d) "Upholstered residential furniture" means furniture with padding, coverings, and cushions intended and sold for use in the home or places of lodging.

Subd. 2. Flame-retardant chemicals; prohibition.

- (a) On and after July 1, 2018, no manufacturer or wholesaler may manufacture, sell, offer for sale, distribute for sale, or distribute for use in this state a children's product or upholstered residential furniture containing, in amounts greater than 1,000 parts per million in any product component, the following flame-retardants:
  - (1) TDCPP (tris(1,3-dichloro-2-propyl)phosphate), Chemical Abstracts Service number 13674-87-8;
  - (2) decabromodiphenyl ether, Chemical Abstracts Service number 1163-19-5;
  - (3) hexabromocyclododecane, Chemical Abstracts Service number 25637-99-4; and
  - (4) TCEP (tris(2-chloroethyl)phosphate), Chemical Abstracts Service number 115-96-8.
- (b) On and after July 1, 2019, no retailer may sell or offer for sale or use in this state a children's product or upholstered residential furniture containing in amounts greater than 1,000 parts per million in any product component the flame retardant chemicals listed in paragraph (a).

(c) The sale or offer for sale of any previously owned product containing a chemical restricted under this section is exempt from the provisions of this section.

Subd. 3. Flame-retardant chemicals; replacement chemicals.

A manufacturer shall not replace a chemical whose use is prohibited under this section with a chemical identified on the basis of credible scientific evidence by a state, federal, or international agency as being known or suspected with a high degree of probability to:

- (1) harm the normal development of a fetus or child or cause other developmental toxicity;
- (2) cause cancer, genetic damage, or reproductive harm;
- (3) disrupt the endocrine or hormone system; or
- (4) damage the nervous system, immune system, or organs, or cause other systemic toxicity.

Sec. 2. FLAME RETARDANT REPORTS.

By January 15, 2016, the commissioner of health, in consultation with the state fire marshal, shall report to the chairs and ranking minority members of the senate and house of representatives committees with primary jurisdiction over environment and natural resources policy, commerce, health, and public safety regarding:

- (1) the status of federal, international, and other states' laws and regulations in identifying, prioritizing, evaluating, and regulating the use of flame retardants in upholstered furniture, mattresses, and carpet pads;
- (2) the status of relevant fire safety standards and practices for residential settings for products including mattresses, upholstered furniture, and carpet pads;
- (3) the status of and any authoritative findings from studies and reports on a direct link to meaningful negative health and safety effects and impacts on firefighters of flame retardants covered by this section, particularly as it relates to the combustion of flame retardants in articles in actual firefighting settings relative to overall smoke hazards and combustion byproducts;
- (4) in developing the report, the agency may consult with stakeholders, including representatives of state agencies, product manufacturers, chemical manufacturers, firefighters, public health experts, and independent scientists. The report must include information on any stakeholder process consulted with or used in developing the report.

Presented to the governor May 18, 2015

Signed by the governor May 19, 2015, 4:04 p.m.

## Appendix B: Laws and Regulations

### STATES LAWS/REGULATIONS AFFECTING FLAME RETARDANT CHEMICALS IN UPHOLSTERED FURNITURE, MATTRESSES, AND CARPET PADS

State	Citation	Summary <sub>1</sub>	Flame Retardant(s) Regulated/Effectuated
California	<a href="#">CA Health and Safety Code § 108920 to 108923</a>	Prohibits manufacturing, processing or distributing a product, or a flame- retarded part of a product, containing more than one-tenth of 1 percent of pentaBDE or octaBDE, except for products containing small quantities of PBDEs that are produced or used for scientific research on the health or environmental effects of PBDEs.	PentaBDE, OctaBDE
	<a href="#">CA Code of Regulations Ch.55 § 69501 - 69510</a>	California's Safer Consumer Products Act identifies Candidate Chemicals that exhibit at least one hazard trait that can harm people or the environment. From this list, Priority Products are then named which are specific chemicals paired with specific products. Priority Products containing the Candidate Chemical can be subject to regulation and manufacturers will need to perform an alternatives analysis to determine whether the chemical is needed or can be replaced with a safer chemical. One of the three initial Priority Products proposed is Children's foam-padded sleeping products with TDCPP.	TDCPP
	<a href="#">California Proposition-65</a>	Proposition 65 was enacted in 1986 and requires California to publish a list of chemicals known to cause cancer or birth defects or other reproductive harm. The list currently includes around 800 chemicals including flame retardant chemicals ATO, TDCPP, TCEP, and TDBPP (other flame retardant chemicals may also be on the list). Business are required to provide "clear and reasonable" warning before knowingly and intentionally exposing anyone to a chemical listed under Prop 65. This often takes the form of a product label but can also be in the form of posting signs at the workplace, distributing notices at a rental housing complex, or publishing notices in a newspaper.	TDBPP, TDCPP, TCEP, ATO
	<a href="#">CA Business &amp; Professions Code § 19094 (2014)</a>	Certain upholstered furniture is required to contain a specific label stating that the product meets existing state smoldering ignition standards (TB117-2013). The standard provides methods for smolder resistance of cover fabrics, barrier materials, resilient filling materials, and decking materials for use in upholstered furniture. This bill requires manufacturers to indicate on the product label whether or not the product contains added flame retardant chemicals by including a specified statement on that label.	Any Flame Retardant Chemical

FLAME RETARDANTS AND FIREFIGHTER EXPOSURE AND HEALTH

State	Citation	Summary <sub>1</sub>	Flame Retardant(s) Regulated/Effectuated
District of Columbia	<a href="#">DC Statute § 8-108.02</a>	Prohibits manufacturing, selling or distributing any product containing pentaBDE or octaBDE except certain vehicle parts. Prohibits manufacture, sale or distribution of certain products containing decaBDE by 2014. Mattresses, upholstered furniture and television or computer monitors containing decaBDE are prohibit beginning in 2013. Exempts certain vehicle parts, recycling activities, and existing retailer inventory.	PentaBDE, OctaBDE, DecaBDE
Hawaii	<a href="#">HI Rev Stat § 332D-1 to 332D-3 (2004)</a>	Prohibits manufacturing, processing or distributing a product, or a flame-retarded part of a product, containing more than one-tenth of one per cent, by mass, of pentaBDE, octaBDE, or any other chemical formulation that is part of these classifications. This prohibition does not apply to the processing of metallic recyclables containing pentaBDE or octaBDE.	PentaBDE, OctaBDE
	<a href="#">HI House Concurrent Resolution No. 235 (2010)</a>	Hawaii Legislature supports the phase out of production and importation of decaBDE and all other PBDEs in the United States. Major producers and importers of decaBDE had committed to end production, importation, and sales of decaBDE for most uses in the United States by December 31, 2012 and to end all uses by the end of 2013.	DecaBDE
Illinois	<a href="#">410 ILCS 48/1 to 48/99</a>	Prohibits manufacturing, processing or distributing a product, or a flame- retarded part of a product, containing more than one-tenth of 1 percent of pentaBDE or octaBDE. Exempts used products and the processing of recyclable material containing pentaBDE or octaBDE. Authorizes a study of the health and environmental effects of decaBDE.	PentaBDE, OctaBDE, DecaBDE
Maine	<a href="#">38 M.R.S.A § 1609</a>	Prohibits selling or distributing a product containing more than 0.1% of pentaBDE or octaBDE mixtures. Prohibits manufacturing, selling or distributing certain products containing the decaBDE mixture. These products include mattresses, mattress pads, upholstered furniture, shipping pallets, televisions, and computers. Exempts transportation vehicles and parts, parts and equipment used in industrial manufacturing, and electronic cable and wiring used in power transmission. Requires manufacturers of products containing PBDE to notify retailers of prohibitions.	PentaBDE, OctaBDE, DecaBDE
	<a href="#">Governor of Maine Executive Order (2006)</a>	Among other priorities listed in the executive order (An Order Promoting Safer Chemicals in Consumer Products and Services) was that of a report to be issued by the DEP on emerging information related to the alternatives to decaBDE and to re-	DecaBDE

FLAME RETARDANTS AND FIREFIGHTER EXPOSURE AND HEALTH

State	Citation	Summary <sub>1</sub>	Flame Retardant(s) Regulated/Effectuated
		examine the department's preliminary conclusion that safer alternatives are nationally available.	
Maryland	<a href="#">MD Code, Environment, § 6-1201 to -1205</a>	Prohibits manufacturing, processing or distributing a product, or a flame- retarded part of a product, containing more than one-tenth of 1 percent of pentaBDE or octaBDE. Prohibits the manufacture, lease, sale or distribution of mattresses, upholstered furniture (residential use), and electrical or electronic equipment containing decaBDE. Makes certain exemptions.	PentaBDE, OctaBDE, DecaBDE
Michigan	<a href="#">MI C.L. § 324.14721 to .14725</a>	Prohibits the manufacturing, processing or distribution of products or materials containing than 1/10 of 1% of pentaBDE or octaBDE. Authorizes PBDE advisory committee to study human health and environmental risks of PBDEs.	PentaBDE, OctaBDE
Minnesota	<a href="#">Minn. Stat. § 325E.385 to .388</a>	Prohibits manufacturing, processing or distributing a product or flame-retardant part of a product containing more than one-tenth of one percent of pentaBDE or octaBDE by mass. Makes certain exemptions. Authorizes a study of the health and environmental effects of decaBDE. Commissioner of administration makes available for purchase and use by the state equipment, supplies, and other products that do not contain PBDEs.	PentaBDE, OctaBDE, DecaBDE
	<a href="#">Minn. Stat. § 116.9401 to .9407</a>	Minnesota's Toxic Free Kids Act requires the state to create and maintain two chemical lists that contain chemicals of potential health concern, focusing on children and women who are pregnant or may become pregnant. The two lists are tiered with the Chemicals of High Concern being the larger, first tier list, and the Priority Chemicals list being built from the CHC list. Currently, no regulatory action is required as a result of a chemical being named to either lists. Lists are simply maintained by MDH and made publicly available. The Priority Chemical list contains two flame retardant chemicals, HBCD and decaBDE. The CHC list contains 41 chemicals that list "flame retardant" as part of its use example or class.	DecaBDE, HBCD

## FLAME RETARDANTS AND FIREFIGHTER EXPOSURE AND HEALTH

State	Citation	Summary <sub>1</sub>	Flame Retardant(s) Regulated/Effectuated
New York	<a href="#">NY Env. Cons. L. § 37-0111</a>	Prohibits manufacturing, processing or distributing a product, or a flame-retardant part of a product, containing more than one-tenth of one percent of pentaBDE or octaBDE, by mass. Makes certain exemptions.	PentaBDE, OctaBDE
Oregon	<a href="#">ORS § 453.005-7e</a>	Lists pentaBDE, octaBDE and decaBDE as hazardous substances and therefore subject to labeling and product restrictions under O.R.S. §§ 453.005 to 435.185.	PentaBDE, OctaBDE, DecaBDE
	<a href="#">Toxic-Free Kids Act-78th Oregon Legislative Assembly</a>	Oregon's Toxic Free Kids Act requires manufacturers and retailers to report to the state if any of their children's products contain one or more of 67 chemicals listed on the High Priority Chemicals of Concern to Children list. The initial starting point for this list is Washington State's CHCC list. Flame retardant chemicals on the list include antimony and antimony compounds, decaBDE, HBCD, TBBPA, TCEP, and TDCPP. One possible product covered under the "children's products" definition could be mattresses (intended for sale to children). This regulation is effective beginning in 2016.	Antimony, DecaBDE, HBCD, TBBPA, TCEP, TDCPP
Rhode Island	<a href="#">RI Gen.L. § 23-13.4-1 to 13.4-6</a>	Codifies legislative finding that the state should develop a precautionary approach regarding the production, use, storage, and disposal of products containing brominated fire retardants. Prohibits manufacturing, processing or distributing a product or a flame-retardant part of a product containing more than one-tenth (1/10 %) of one percent (1%) of pentaBDE or octaBDE. Makes certain exemptions. Authorizes a study of the health and environmental effects of decaBDE.	PentaBDE, OctaBDE, DecaBDE
Vermont	<a href="#">9 V.S.A. § 2972 to 2980</a>	Prohibits manufacturing, processing or distributing a product, or a flame-retarded part of a product, containing greater than 0.1 percent of pentaBDE or octaBDE by weight. Prohibits manufacturing, selling or distributing certain products containing greater than 0.1 percent decaBDE. These products include mattresses, mattress pads, upholstered furniture, televisions, computers, and shipping pallets. Prohibits sale of residential upholstered furniture, children's products, or certain electronic devices containing greater than 0.1 percent	TCEP, TDCPP, TCPP, DecaBDE, OctaBDE, PentaBDE

## FLAME RETARDANTS AND FIREFIGHTER EXPOSURE AND HEALTH

State	Citation	Summary <sup>1</sup>	Flame Retardant(s) Regulated/Effectuated
		of TCEP or TDCPP. Requires manufacturers of products containing decaBDE, TCEP, and TDCPP to notify retailers of prohibitions. Requires decaBDE, TCEP, and TDCPP be replaced with safer alternatives. Allows for Vermont Dept. of Health to adopt a rule prohibiting manufacture, sale, or distribution of children's products and residential upholstered furniture containing TCPP if Department finds TCPP poses significant risk to public health.	
Vermont	<a href="#">18 V.S.A. chapter 38A § 1771 - 1775</a>	Vermont's Chemical Disclosure Program for Children's Products requires manufacturers and retailers to report to the state if any of their children's products contain one or more of 67 chemicals listed on the Chemicals of High Concern to Children list. Flame retardant chemicals on the CHCC list include antimony and antimony compounds, decaBDE, HBCD, TBBPA, TCEP, and TDCPP. One possible product covered under the "children's products" definition could be mattresses (intended for sale to children). First reports to Vermont due by July 1, 2016.	Antimony & Antimony Compounds, DecaBDE, HBCD, TBBPA, TCEP, TDCPP
Washington	<a href="#">RCW § 70.76.005 to .110</a>	Prohibits manufacturing, selling or distributing noncombustible products containing PBDEs but in particular pentaBDE, octaBDE, and decaBDE. Makes certain exemptions. Prohibits manufacturing, selling or distributing mattresses containing decaBDE. This prohibition extends to upholstered furniture, televisions, and computers if the state, in consultation with a fire safety committee, finds that a safer and technically feasible alternative to decaBDE is available. Requires manufacturers of products containing PBDEs to notify retailers of the prohibitions.	PentaBDE, OctaBDE, DecaBDE
	<a href="#">RCW § 70.240.010 - .060</a>	Washington's Children's Safe Products Act requires manufacturers and retailers to report to the state if any of their children's products contain one or more of 67 chemicals listed on the Chemicals of High Concern to Children list. Flame retardant chemicals on the CHCC list include antimony and antimony compounds, decaBDE, HBCD, TBBPA, TCEP, and TDCPP. One possible product covered under the "children's products" definition could be mattresses (intended for sale to children).	Antimony & Antimony Compounds, DecaBDE, HBCD, TBBPA, TCEP, TDCPP

1. Summaries on PBDE regulations taken/paraphrased from the National Conference of State Legislatures website. Accessed in October/November 2015. Available at: <http://www.ncsl.org/research/environment-and-natural-resources/flame-retardants-in-consumer-products.aspx>



## Appendix C. PBDE Biomonitoring Comparison Plots

PBDE serum concentration plots in California firefighters and other California residents are shown in the bar charts below. Interpretative language is provided with each plot. The “2010-2011 CA firefighters” results in the bar charts are from the FOX study. **See section 2.3 for a description of all of the firefighter and non-firefighter studies used to create these bar charts.**

The following should be noted:

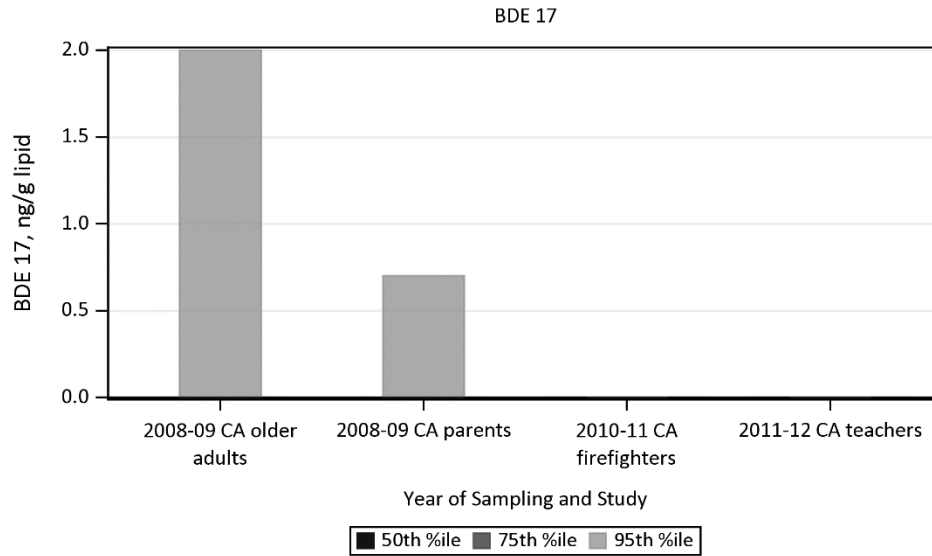
- Only studies that included a particular PBDE congener are shown in the congener-specific plots (the number of studies per plot ranges from two to seven).
- Since the “2009 San Francisco firefighters” study only included 12 individuals, we chose to only present the median in the plots. Apart from this caveat, **if no bar is shown for a study listed on the x-axis, this means the percentile concentration was less than the limit of detection (LOD)**<sup>7</sup>. This is because percentile concentrations below the LOD were set to zero in the figures. No plots are shown for the following PBDE congeners because all percentiles were below the LODs: BDE-196; -201; -202; and -203.
- Studies are shown in ascending order by year of sample collection. The anticipated decline in certain PBDE congener serum concentrations from 2006 to 2013 limits our ability to make direct comparisons across populations, particularly for studies farther apart in time. In plots showing a decline in penta- and octaBDE congener levels over time, comparing the firefighter and non-firefighter studies requires knowing whether the decline is more or less than what we’d expect based on the overall downwards trend.
- Differences between the California studies (e.g., demographics, region) limits our ability to compare the firefighters and non-firefighters. Information on these factors is not currently available from CA Biomonitoring.
- For studies with smaller sample sizes (see Section 2.3 for study descriptions), the 95<sup>th</sup> percentile is less stable and should be viewed with caution.

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<sup>7</sup> For example, if less than 50% of participants had a result above the limit of detection, the median concentration is <LOD and it is assigned a zero value in the plot.

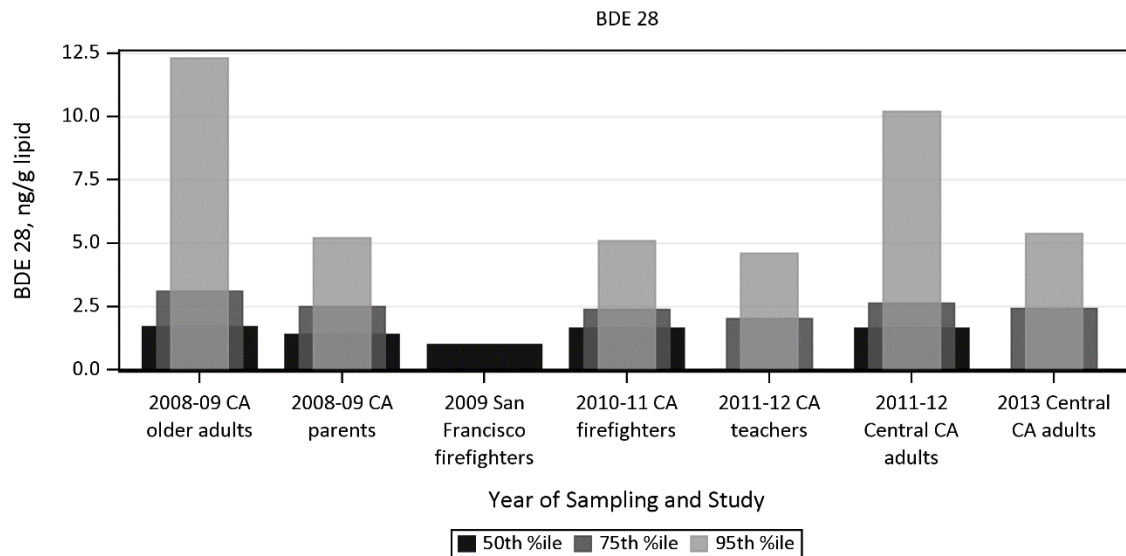
## Comparison Graph of BDE-17

Four studies analyzed for BDE-17. The two earlier studies had detectable results at the 95<sup>th</sup> percentile. There is no indication that FOX firefighters are more highly exposed.



## Comparison Graph of BDE-28

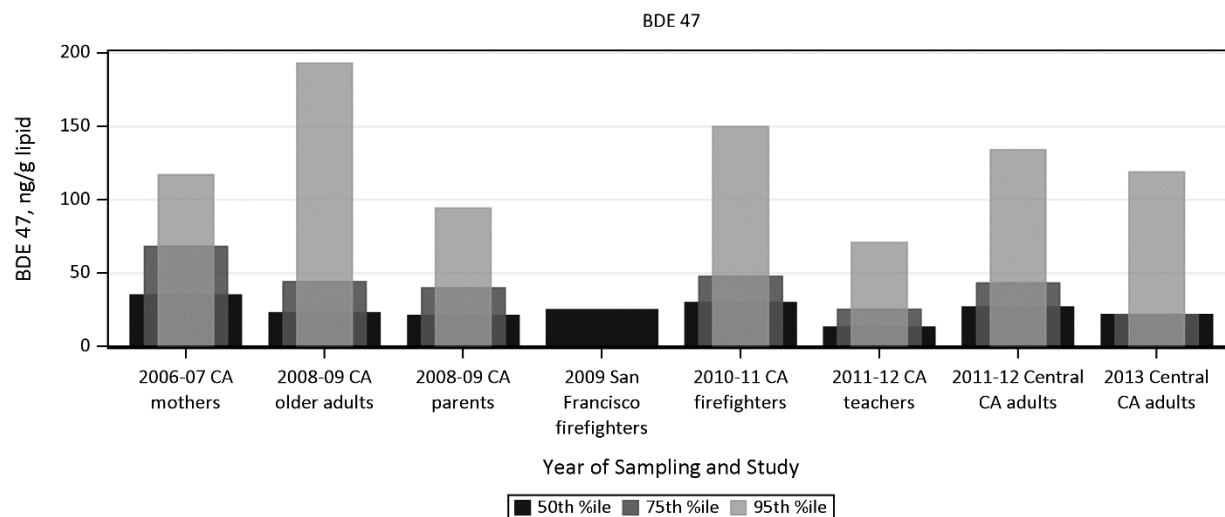
BDE-28 was commonly detected across studies. Variability in the concentrations over time and across studies makes any differences between firefighter and non-firefighter populations unclear.



Due to small sample size, only the median is shown for 2009 San Francisco firefighters.

## Comparison Graph of BDE-47

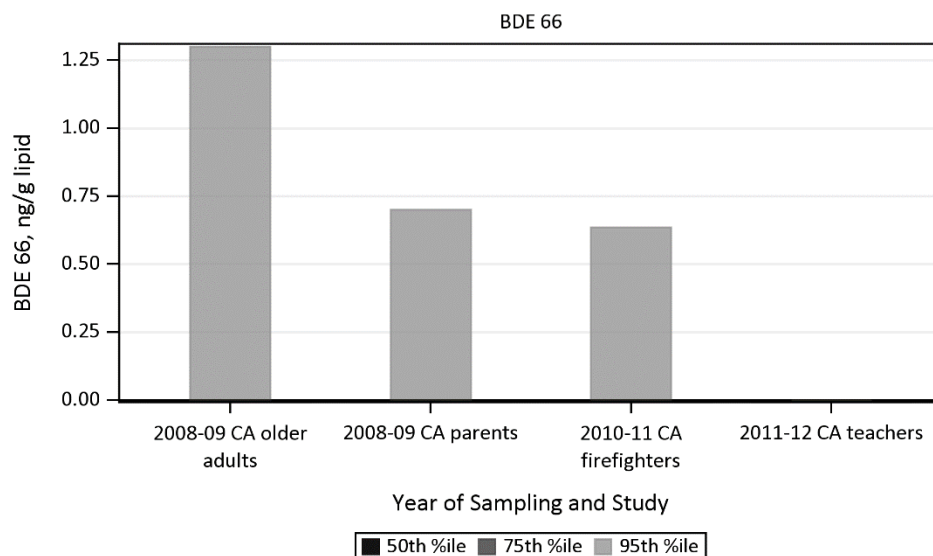
BDE-47, a component of pentaBDE, was commonly detected across populations and found at higher concentrations compared to other congeners. A decreasing trend in non-firefighter population concentrations over time is seen at the 50<sup>th</sup> and 75th percentiles from 2006-2013, with the exception of the Central CA adult studies. FOX firefighters had slightly higher percentile concentrations of BDE-47 compared to most of the comparison studies.



Due to small sample size, only the median is shown for 2009 San Francisco firefighters.

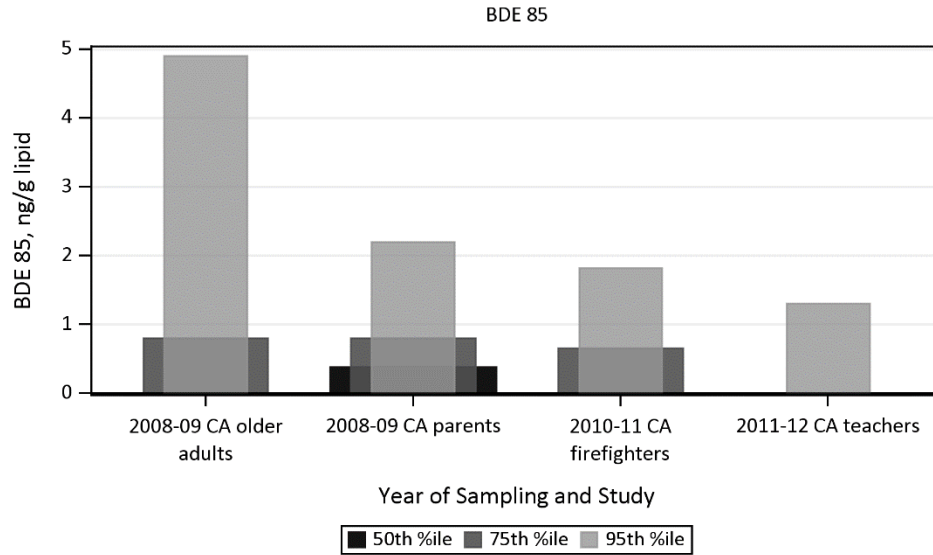
## Comparison Graph of BDE-66

Very low levels of BDE-66 were found in three of the four studies at the 95<sup>th</sup> percentile. .



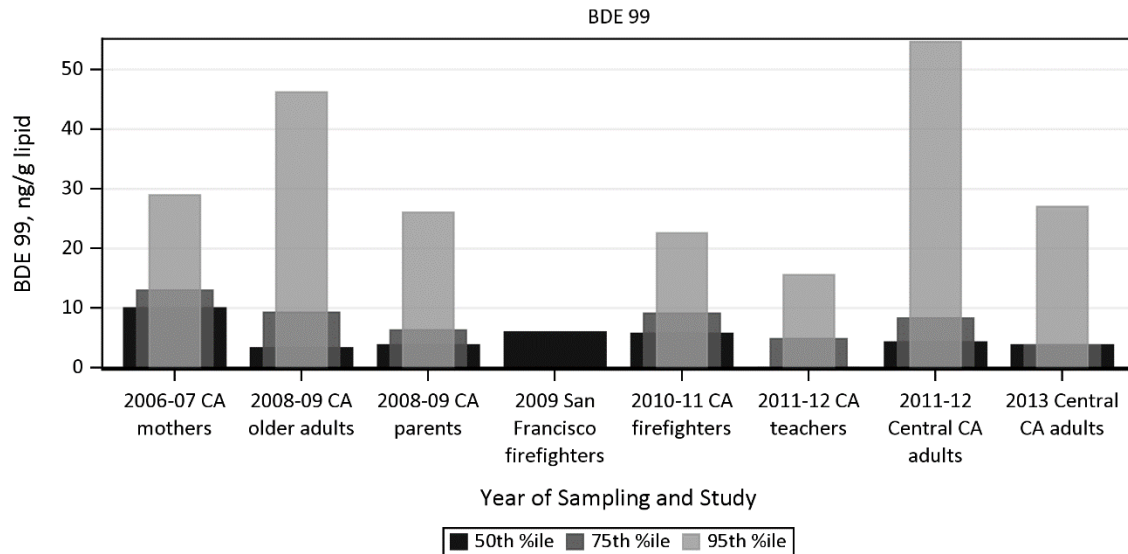
## Comparison Graph of BDE-85

BDE-85 results appear to decrease over time. There is no clear indication that FOX firefighters are more highly exposed.



## Comparison Graph of BDE-99

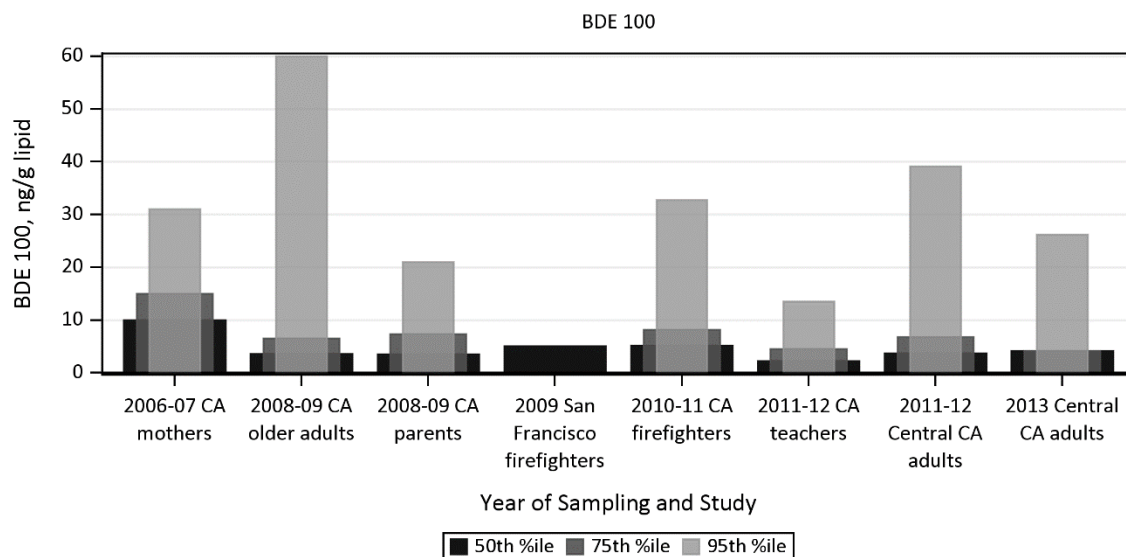
BDE-99 was commonly found across studies. Median concentrations were higher in the firefighter studies with the exception of the earliest study in 2006-07.



Due to small sample size, only the median is shown for 2009 San Francisco firefighters.

### Comparison Graph of BDE-100

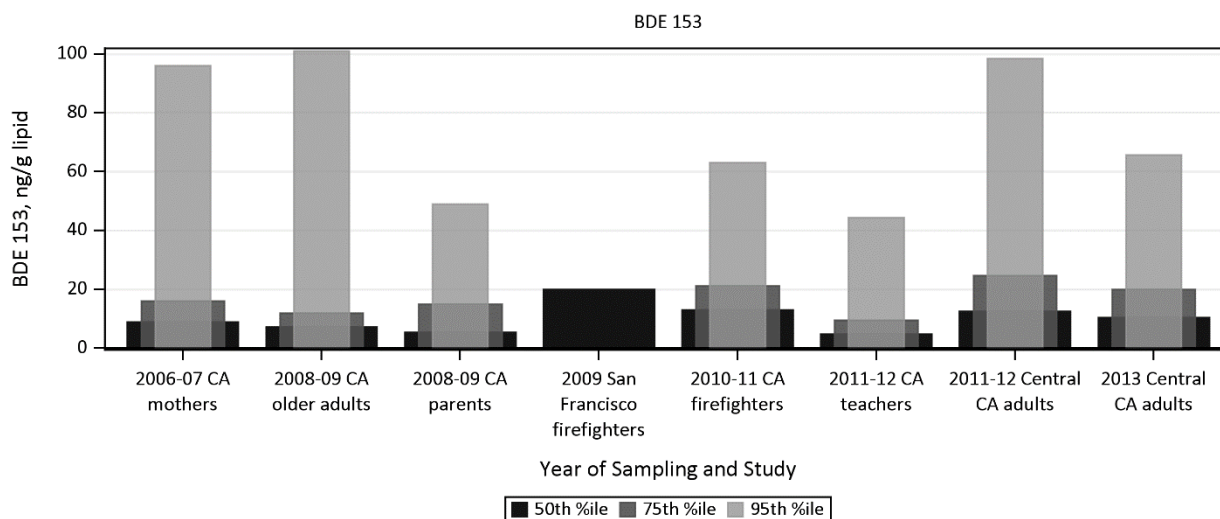
BDE-100 was commonly found across studies. BDE-100 50<sup>th</sup> and 75<sup>th</sup> percentile concentrations are slightly higher in the firefighter studies compared to the non-firefighter populations with the exception of the earliest study.



Due to small sample size, only the median is shown for 2009 San Francisco firefighters.

### Comparison Graph of BDE-153

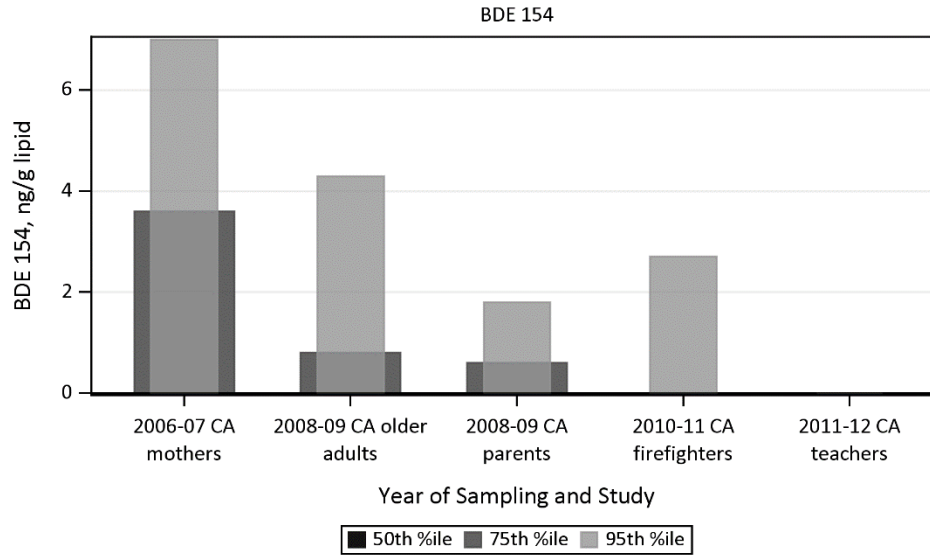
BDE-153 was commonly found across studies. A general decline in BDE-153 median concentrations over time is seen in the non-firefighter studies with the exception of the Central CA adult studies and the firefighter studies. Median concentrations are highest in the firefighter studies. There is variability in the upper percentiles across populations.



Due to small sample size, only the median is shown for 2009 San Francisco firefighters.

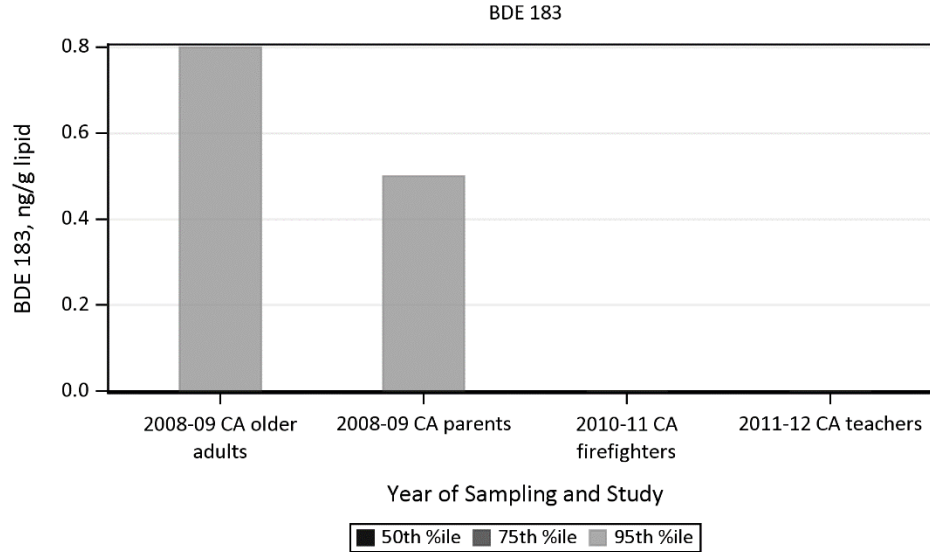
### Comparison Graph of BDE-154

All BDE-154 median concentrations were less than the LOD. 75<sup>th</sup> percentile concentrations decrease over time to less than the LOD. There is no clear evidence that FOX firefighters are more highly exposed.



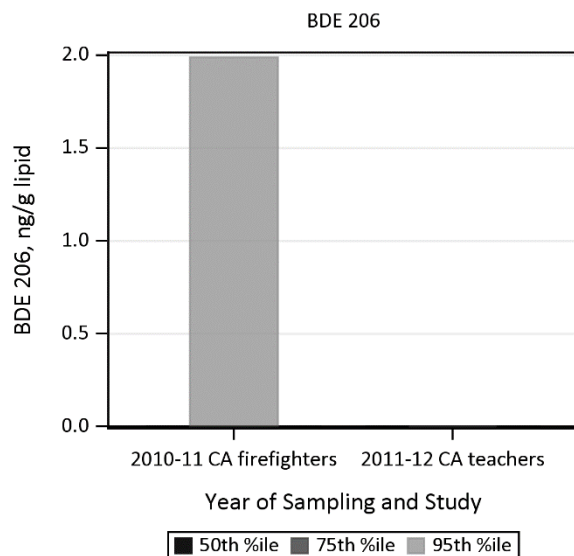
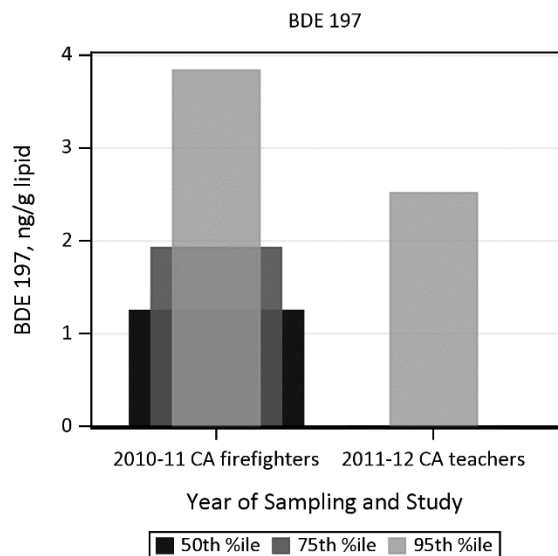
### Comparison Graph of BDE-183

BDE-183 is rarely found. There is no indication that FOX firefighters are more highly exposed.

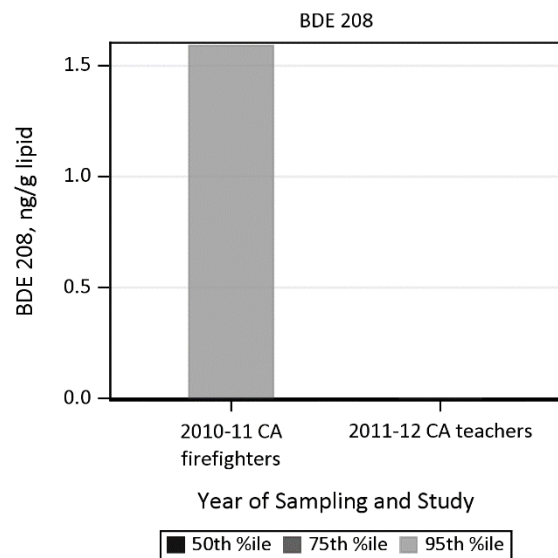
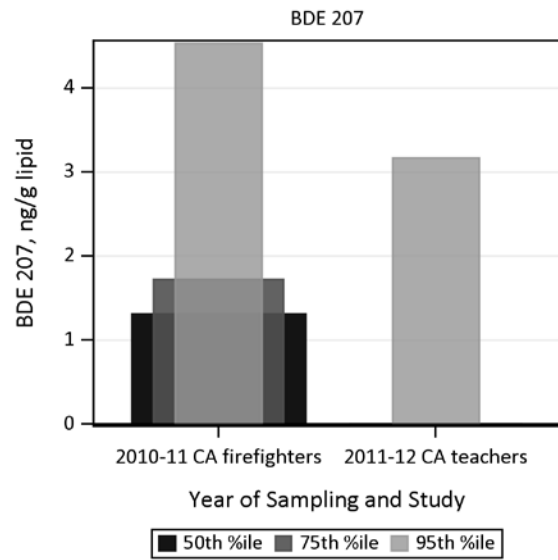


### Comparison Graphs of BDE-197, -206, -207, and -208

The following four PBDE congeners (-197, -206, -207, -208) were only analyzed in two studies: The FOX firefighter study and the CA Teachers Study. Higher percentile concentrations are consistently seen in FOX firefighters. However, lower levels of PBDEs overall are found in the CA Teachers Study compared to the other non-firefighter studies. The inclusion of additional, relevant comparison studies would aid interpretation.



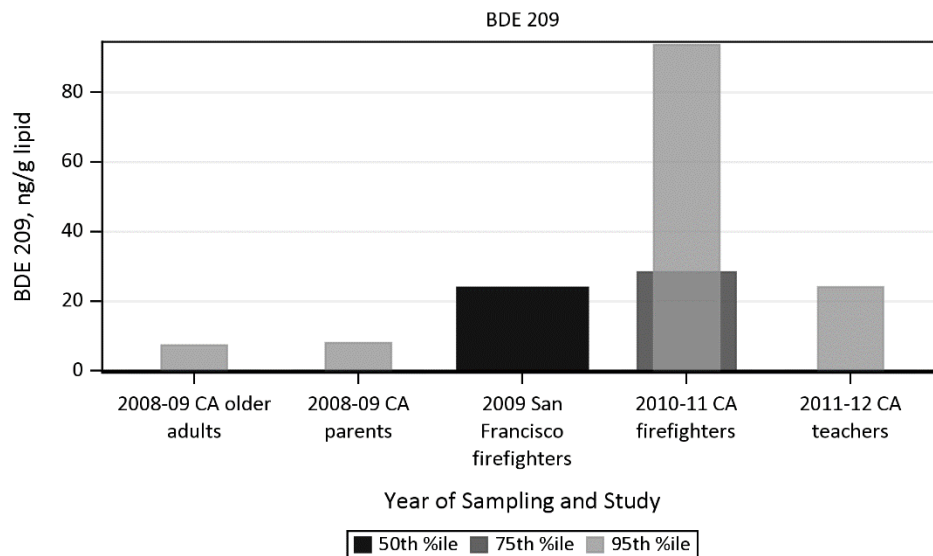
# FLAME RETARDANTS AND FIREFIGHTER EXPOSURE AND HEALTH





### Comparison Graph of BDE-209

BDE-209 is the only congener of decaBDE. Higher concentrations are seen in both firefighter studies. The elevated median result for the San Francisco firefighters is not unexpected since the participants fought fires in the past 12 hours and therefore should have retained relatively high proportions of the shorter-lived higher brominated congeners.



Due to small sample size, only the median is shown for 2009 San Francisco firefighters.

## Appendix D. Summary of Published Biomonitoring Equivalents

### Summary of Published Biomonitoring Equivalents

Chemical	Lab Animal Internal Dose at the Selected Toxicity Value	Toxicity Value (type)	Effect	Biomarker Metric	Human Biomonitoring Equivalent (BE)	PBPK Model Available <sup>4</sup>	Data Gaps & Uncertainties
BDE-47	Not available	0.000003 mg/kg-d (RfD)	Reduction in serum testosterone	ng/g lipid	Not available	Yes, for rats <sup>4</sup>	PBPK model to extrapolate to humans <sup>4</sup>
BDE-99	51.6 mg/kg lipid Calculated estimate <sup>1</sup>	0.0001 mg/kg-d (RfD)	Decrease in rearing habituation (neuro-behavioral development; direct dosing to neonates on day 10 after birth)	ng/g lipid	520 ng/g lipid <sup>1</sup>	Not available	Not based on the most conservative toxicity value; direct dosing to neonates does not represent firefighters
BDE-99	Not available	0.000003 mg/kg-d (RfD, based on BDE-47)	Reduced serum testosterone	ng/g lipid	Not available	Not available	Measure or estimate of internal doses in rodents at RfD and/or suitable toxicity value; PBPK model
pentaBDE technical-grade mixture, DE-71 (BDE-47, -99, -153)	As µg/g of rat plasma (not lipid-adjusted)  BDE-47: 0.44-0.73  BDE-99: 0.22-0.40  BDE-153: 0.20-0.44	2.1 mg/kg-d of mixture (LOAEL <sub>adj</sub> )  Estimated amount in mixture at LOAEL: BDE-47: 0.77 mg/kg-d BDE-99: 0.90 mg/kg-d BDE-153: 0.071 mg/kg-d	Liver hypertrophy, thyroid hypertrophy	ng/g lipid	Not available	Not available	Appropriate dose metrics (plasma vs. serum vs. lipid; lipid-adjusted or not), PBPK model
HBCD	121,000 ng/g lipid <sup>2</sup>	10 mg/kg-d (NOAEL)	Fertility & developmental	ng/g lipid	10,000 ng/g lipid <sup>2</sup>	Not available	Not based on the most conservative toxicity value
HBCD	192,000 ng/g lipid <sup>2</sup>	22.9 mg/kg-d (NOAEL)	Liver weight	ng/g lipid	20,000 ng/g lipid <sup>2</sup>	Not available	Not based on the most conservative toxicity value
HBCD	Not available	0.2 mg/kg-d (BMDL)	Developmental (hearing impairment)	ng/g lipid	Not available	Not available	Measure or estimate of Internal doses in rodents at RfD and/or suitable toxicity value; PBPK model

Chemical	Lab Animal Internal Dose at the Selected Toxicity Value	Toxicity Value (type)	Effect	Biomarker Metric	Human Biomonitoring Equivalent (BE)	PBPK Model Available <sup>4</sup>	Data Gaps & Uncertainties
ATO	3.078 to 3.275 µg antimony per gram red blood cells in pregnant rats <sup>3</sup>	2.6 mg/m <sup>3</sup> (LOAEC)	Maternal lung toxicity	Not known	Not available	Not available	Appropriate biomarker(s) (blood or urine); PBPK model; Risk assessment to convert rat internal doses to human equivalent doses
ATO	5.591 µg antimony per gram red blood cells in pregnant rats <sup>3</sup>	≥ 6.3 mg/m <sup>3</sup> (NOAEC)	Developmental endpoints, no effects at highest dose tested	Not known	Not available	Not available	Appropriate biomarker(s) (blood or urine); PBPK model; Risk assessment to convert rat internal doses to human equivalent doses

<sup>1</sup> An internal dose estimate for BDE-99 was calculated based on an equation that considered dose, body weight, estimated absorption fraction, estimated volume of distribution in the body, and a chemical-specific elimination constant. Blood or tissue levels were not measured. From: Krishnan, K., et al. 2011. Biomonitoring equivalents for 2,2',4,4',5-pentabromodiphenylether (PBDE-99). *Regulatory Toxicology and Pharmacology*, 60:165-171.

<sup>2</sup> A measured internal dose for HBCD was based on concentrations of lipid-adjusted HBCD concentrations in rat livers at the end of a 28-day study. The estimate in serum lipids is based on the amount measured in liver lipid with an assumption that HBCD distributes equally in lipids throughout the body. From: Aylward, L.L., Hays, S.M. 2011. Biomonitoring-based risk assessment for hexabromocyclododecane (HBCD). *International Journal of Hygiene and Environmental Health*, 214:179-187.

<sup>3</sup> ATO internal doses were measured during an inhalation developmental toxicity study in rats. The antimony levels in red blood cells of pregnant rats were statistically higher than controls: 0.128 ± 0.0286, 3.275 ± 1.0391, 3.078 ± 0.5624 and 5.591 ± 1.3248 µg/g for the dose groups 0, 2.6, 4.4, 6.3 mg/m<sup>3</sup>, respectively. From: EU (European Union) 2008d. Risk Assessment Report Diantimony Trioxide.

<sup>4</sup> Physiologically based pharmacokinetic (PBPK) models are available for rats (developmental exposure) and mice (for elimination) for BDE-47. The model was first developed for BDE-47 in rats with the goal of expanding the model to simulate BDE-47 toxicokinetics across species (mice) and then extrapolating to humans. After models for mouse and humans are developed, there are plans to evaluate additional PBDEs, as well as mixtures. However, at the time of this report, these additional models to extrapolate to humans and other PBDEs were not available. From: (1) Emond, C., et al. 2010. A physiologically based pharmacokinetic model for developmental exposure to BDE-47 in rats. *Toxicology and Applied Pharmacology*, 242:290-298; and (2) Emond, C., et al. 2013. Proposed mechanistic description of dose-dependent BDE-47 urinary elimination in mice using a physiologically based pharmacokinetic model. *Toxicology and Applied Pharmacology*, 273:335-344.