March 25, 2013

Chief Tonya Blood
Bureau of Electronic and Appliance Repair, Home Furnishings and Thermal Insulation
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Via email to TB117comments@dca.ca.gov and diana.godines@dca.ca.gov

Re: Support for Proposed Amendments to California Furniture Flammability Standard

Dear Chief Blood:

Earthjustice submits these comments on behalf of Center for Environmental Health,\(^1\) Friends of the Earth\(^2\), Green Science Policy Institute\(^3\) and Physicians for Social Responsibility – Los Angeles\(^4\) in support of the proposal of the Bureau of Electronic and Appliance Repair, Home Furnishings and Thermal Insulation of the California Department of Consumer Affairs (the “Bureau”) to amend sections 1101, 1126, 1370, 1373.2, 1374, 1374.1, 1374.2, 1374.3 and 1383.2 of Title 4 of the California Code of Regulations (the “furniture flammability regulations”), and to replace Technical Bulletin (“TB”) 117\(^5\) with TB 117-2013.\(^6\) Amending the furniture

\(^1\) Center for Environmental Health (“CEH”) works to hold corporations accountable for their use of toxic

\(^2\) The mission of Friends of the Earth (“FoE”), a membership organization with over 150,000 members, is to defend the environment and champion a healthy and just world. FoE relies on sound science and uses the law to create and advocate for innovative strategies to protect public health and the environment.

\(^3\) Green Science Policy Institute provides unbiased scientific data to government, industry, and non-governmental organizations to facilitate more informed decision-making about chemicals used in consumer products in order to protect health and environment world-wide.

\(^4\) Physicians for Social Responsibility – Los Angeles (“PSR-LA”) is a physician membership organization working towards system and policy changes to protect public health from environmental degradation. Representing over 5,000 physicians, health professionals, and concerned residents in California, PSR-LA informs the medical community and policymakers about toxic threats, teaches them about safer practices, builds coalitions with state-wide and national organizations, and strengthens local community organizations to engage in meaningful public health and environmental advocacy.

flammability regulations and adopting TB 117-2013 will significantly improve fire safety in the state because TB 117-2013, unlike TB 117, is tailored to address smoldering fires from smoking materials, which are the overwhelmingly most common type of fire involving upholstered furniture. We especially applaud the Bureau’s decision to omit the seriously flawed “open flame” flammability standard in TB 117, given the strong evidence that this test does not enhance fire safety because it does not reflect real-life fire scenarios, and endangers humans and the environment by creating exposures to toxic chemicals. We also strongly support the Bureau’s decision to rely on the existing furniture flammability standard developed by ASTM International (“ASTM”) as the starting point for its new standard. California law and regulations rely extensively on ASTM technical standards, including in the area of fire safety. Given the deficiencies in the current flammability standard, there is no reason for the Bureau to create an entirely new flammability standard when the ASTM standard is known to be effective and is already in wide use. For the reasons below, and in the Bureau’s Initial Statement of Reasons and supporting attachments, we urge the Bureau to finalize the amended regulations, including TB 117-2013, as soon as possible.

1. The Outdated TB 117 Standard Must Be Changed Because It Does Not Ensure Furniture is “Fire Retardant”

Section 19161 of the California Business and Professional Code requires “all seating furniture sold or offered for sale … in this state … [to] be fire retardant.” California regulations implement Section 19161 by requiring all filling materials contained in any article of upholstered or reupholstered furniture to meet the flammability standards in TB 117. The primary way that TB 117 ensures that furniture meets the statutory “fire retardant” requirement is the requirement that fill material in seating furniture withstand a small open flame for at least twelve seconds.

The Bureau has correctly identified the four main flaws with the flammability standard in TB 117: 1) fires involving furniture made with TB 117 compliant foam are no less severe than

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7 CAL. BUS. & PROF. CODE § 19161(c). The Bureau may exempt items of furniture that in its discretion it “deem[s] not to pose a serious fire hazard.” Id. § 19161.5.

8 CAL. CODE REGS. tit. 4, § 1374(a).

9 TB 117, supra note 5, at 2-4.
fires involving furniture manufactured with untreated foam;\textsuperscript{10} 2) TB 117 is not designed to address the most common type of upholstered furniture fire, namely fires ignited by smoking materials. These fires, which result in a disproportionately high number of residential fire injuries and fatalities, start off with a smoldering fire characterized by a slow, low temperature form of combustion, not an open flame. Yet because TB 117 is designed to inhibit “small open flames” applied directly to foam, it does not inhibit smoldering fires\textsuperscript{11}; 3) when foam treated with flame retardants is exposed to a smoldering ignition source, the foam burns more than untreated foam\textsuperscript{12}; and 4) TB 117 is not designed to retard or reduce the severity of a fire involving upholstered furniture because it does not adequately take into account the flammability of the outer cover fabric and the fact that if the combustion of the outer fabric results in a flaming fire, the fire would rapidly spread across the fabric resulting in a large open flame, even if the ignition source is a small open flame.\textsuperscript{13}

Given these serious deficiencies in TB 117, the Bureau is not merely wise to amend the furniture flammability regulations and TB 117, it has no choice but to do so. It is doubtful the current standard meets the statutory “fire retardant” requirement.

2. The Bureau Is Correct to Adopt A Furniture Flammability Standard That Does Not Rely on Chemical Flame Retardants

To comply with the ineffective small open flame standard required by TB 117, furniture manufacturers have added chemical flame retardants to sofas, chairs and certain juvenile

\textsuperscript{10} Vytenis Babrauskas, \textit{Upholstered Furniture Heat Release Rates: Measurements and Estimation}, 1 J. FIRE SCIENCES 9, 31 (1983) (study compared the peak heat release rate of identically-constructed furniture where one piece of furniture was made with TB 117-compliant foam and the other was made with untreated foam. No difference was found between the two types of furniture in peak heat release rate, the generally accepted main measure of a fire’s severity, or in visual fire development); Memorandum from Ronald L. Medford, Assistant Exec. Dir. for Hazard Identification & Reduction, and Dale R. Ray, Project Manager, to U.S. Consumer Prod. Safety Comm’n (Oct. 24, 1997), \textit{available at} http://legacy.library.ucsf.edu/tid/akc76c00;\textsuperscript{11} Vytenis Babrauskas et al., \textit{Flame Retardants in Furniture Foam: Benefits and Risks}. 10 FIRE SAFETY SCIENCE 265, 265-278 (2011). 10.3801/IAFSS.FSS.10-265 at 3. A copy of this article is submitted herewith as Exhibit 1.

\textsuperscript{11} Memorandum from Weiying Tao, Textile Technologist, Div. of Elec. & Flammability Eng’g, to Dale Ray, Project Manager, CPSC (May 12, 2005), \textit{available at} www.cpsc.gov/PageFiles/103632/uff2.pdf; Memorandum from Linda Fansler and Lisa L. Scott, Div. of Elec. & Flammability Eng’g, to Dale Ray, CPSC (May 16, 2005).

\textsuperscript{13} Babrauskas et al., \textit{supra} note 11, at 2-3.
products. The chemicals are not sealed into the consumer products, and migrate from them to the larger environment. Flame retardant chemicals are found in household dust and indoor air; and wastewater transports these chemicals into the outdoor environment where they have been detected in California’s surface waters, sediments and wildlife. Californians have significantly higher body burden levels of flame retardants than a representative sample of people in other states, as well as compared to people in Canada and Western Europe. Exposures are the highest in children, most likely because of their hand to mouth behaviors. Exposures are also disproportionately high in low-income communities.

Until 2004, furniture manufacturers complied with TB 117’s open-flame requirement primarily by adding the chemical pentabromodiphenyl ether (“pentaBDE”) to the foam fill material in seating furniture. However, due to mounting health concerns about pentaBDE, and increased state legislative efforts to ban the chemical, the sole U.S. manufacturer voluntarily ceased production in 2004. Since then, TDCPP, one of three chemicals known as chlorinated


15 In July 2011, the Office of Environmental Health Hazard Assessment (OEHHA) of California’s Environmental Protection Agency published its assessment of the carcinogenicity of the chemical TDCPP (sometimes referred to as TDCP). This report stated that “TDCPP has been detected in both indoor and outdoor environments in the U.S. and abroad. It has been measured in household and office dust, indoor air, and in streams, sewage influents, effluents, and sludge.” JOHN B. FAUST AND LAURA MEEHAN AUGUST, CAL. ENVTL. PROT. AGENCY, EVIDENCE ON THE CARCINOGENICITY OF TRIS (1,3-DISCHLORO-2-PROPYL) PHOSPHATE 1 (2011) (hereinafter the “OEHHA Tris Carcinogenicity Report”). A copy of this Report is submitted herewith as Exhibit 3.

16 Ami R. Zota et al., Elevated House Dust and Serum Concentrations of PBDEs in California: Untended Consequences of Furniture Flammability Standards?, 42 ENVTL. SCI. & TECH. 8158, 8160 & Table 1 (2008). A copy of this article is submitted herewith as Exhibit 4.

17 Stapleton et al., supra note 14, at 7494 & Figure 2 (average estimated cumulative exposure to flame retardants from dust for children is calculated to be about 1600 ng/day, whereas for an adult it is about 325 ng/day).

18 Zota et al., supra note 16, at 8161-62.

19 Babrauskas et al., supra note 11, at 3.

20 California banned pentaBDE in 2003; eight other states and the European Union followed suit. Shortly thereafter, the United States Environmental Protection Agency (“EPA”) adopted a rule, applicable to all polybrominated diphenyl ethers (“PBDEs”), including pentaBDE, that would make it very difficult for production to resume, citing its “concerns regarding the environmental fate and the exposure pathways that lead to PBDE presence in wildlife and people, and the persistence, bioaccumulation, and toxicity (PBT) potential” of these chemicals. Certain Polybrominated Diphenylethers; Significant New Use Rule, 71 Fed. Reg. 34,015, 34,017 (June 13, 2006). More recently, EPA has expressed concern that human exposure to PBDEs could cause liver toxicity, thyroid toxicity, developmental toxicity, and developmental neurotoxicity. See EPA, POLYBROMINATED DIPHENYL ETHERS (PBDES) ACTION Plan 5
tris, and Firemaster 550 have been the primary chemicals used by furniture manufacturers to comply with TB 117. TDCPP was also recently found to be prevalent in a wide variety of children’s products, such as nursing pillows, changing pads, and car seats.

Both TDCPP and Firemaster 550 raise serious health concerns. TDCPP was briefly used as a flame retardant in children’s pajamas, but manufacturers voluntarily stopped this practice after a published report indicated that chlorinated tris is a mutagen. In 2005, the EPA concluded that TDCPP presents a cancer hazard and may cause non-cancer human health effects as well. In addition, when the CPSC looked at the safety of flame retardants in upholstered furniture, it concluded that:

TDCCP may be considered probably toxic in humans, based on sufficient evidence of chronic toxicity in animals. TDCCP exposure also induced tumors at multiple doses in the kidneys and liver of both male and female rats. Therefore, TDCCP may be considered a probable human carcinogen based on sufficient evidence in animals (Ferrante 1999b; Bittner et al. 2001). This conclusion is further supported by structural similarity to another animal carcinogen, [brominated] TRIS.

In addition, the OEHHA Tris Carcinogenicity Report concluded that “[e]xposure to TDCPP in male and female rats resulted in statistically significant increases in tumors at multiple sites.”


21 In a recent study of foam samples taken from 102 couches across the United States, 93% of the foam samples from sofas purchased between 2005 and 2010, after the PBDE phaseout, contained high levels of flame retardants, and the two most common flame retardants in these relatively new couches were TDCPP and Firemaster 550. One of these two chemicals was present in 74% of the couches bought in this country since 2005. Heather M. Stapleton, et al., Novel and High Volume Use Flame Retardants in US Couches Reflective of the 2005 PentaBDE Phase Out, 46 ENVTL. SCI & TECH. 13,432, 13,438 (2012). A copy of this study is submitted herewith as Exhibit 5.

22 Heather M. Stapleton et al., Identification of Flame Retardants in Polyurethane Foam Collected from Baby Products, 45 ENVTL. SCI & TECH. 5323, 5327 (2011). A copy of this study is submitted herewith as Exhibit 6.

23 Marian D. Gold et al., Another Flame Retardant, Tris-(1,3-Dichloro-2-Propyl)-Phosphate, and Its Expected Metabolites Are Mutagens, 200 SCIENCE 785, 785-87 (1978).


While Firemaster 550 has been less studied than TDCPP, the combination of the lack of studies and the fact that Firemaster 550 appears to be bioaccumulative is very concerning. According to a review of the manufacturer’s own health studies conducted by The Chicago Tribune, exposing rats to Firemaster 550 lowered birth weight, altered female genitalia and caused skeletal malformations.\textsuperscript{27} A 2013 study found that Firemaster 550 is an endocrine disruptor that caused weight gain, early onset of puberty, and cardiovascular effects in rats.\textsuperscript{28}

Although few human studies have been conducted on the health effects of chlorinated tris and/or Firemaster 550, the studies that have been done raise serious concerns.\textsuperscript{29} For example, a recent study showed that men living in homes with high amounts of TDCPP and TPP (another flame retardant and an ingredient in Firemaster 550) in household dust had reduced sperm counts and altered levels of hormones related to fertility and thyroid function.\textsuperscript{30} High levels of chlorinated tris in dust are associated with an increase in the hormone prolactin (considered to be a marker of decreased neuroendocrine/dopamine activity; prolactin may also be associated with erectile dysfunction), and a decline in free thyroid hormone levels. In general, human studies have shown associations between increased pentaBDE flame retardant body levels and reduced IQ in children, reduced fertility, endocrine and thyroid disruption, and changes in male hormone levels.\textsuperscript{31}

Not only do the primary flame retardants currently used in furniture fill materials present serious human health risks, there is sound reason to conclude that any chemical that might be chosen to replace TDCPP and Firemaster 550 will pose health risks, just as these chemicals, which replaced the phased-out, toxic penta-BDE, have been shown to do. This cycle of replacing toxic flame retardants with a new generation of toxic and/or untested flame retardants was described in a recent study that looked at dust samples from 16 homes in California both in


\textsuperscript{29} The inhalation and ingestion of contaminated dust has been shown to be a major route of human exposure, especially for children. Stapleton et al., supra note 14, at 7494. According to the OEHHA Tris Carcinogenicity Report, “[i]n humans, TDCPP has been measured in adipose tissue, seminal plasma and breast milk.” OEHHA Tris Carcinogenicity Report, supra note 15, at 1.


2006 and 2011 to assess how levels of flame retardants in house dust had changed since the phase out of penta-BDE. The study found that after the PBDE phase-out, “other [flame retardants] with considerable evidence of toxicity appear to remain at high or increasing levels of use. Some [flame retardants] appear to be replaced by less-studied chemicals whose health implications are unknown.”

It is virtually inevitable that if California retains a chemical-based flammability standard, TDCPP and Firemaster 550 would eventually be phased out due to persistent questions about their safety. But it is equally inevitable that any flame retardant that might replace TDCPP and Firemaster 550 would present hazards. This risk is underscored by a comprehensive health and environmental hazard screening conducted for nearly 100 organohalogen flame retardant chemicals by toxicologists at the University of California Riverside. Using publicly available information and giving priority consideration to human health hazards, the researchers assigned a concern level to each hazard category to predict hazard potential for each of 91 organohalogen flame retardants. Where no data was available, structure activity relationship models were used to predict hazard potential. After assigning concern levels for each priority health effect, every chemical received a score, similar to a report card. The majority of the screened chemicals received either a D or F grade due to empirical data suggesting high hazard, structure activity relationship model predictions, and/or excessive data gaps. Based on this assessment, any argument that the chemicals used to comply with TB 117 can be improved and made safer than the chemicals used to date (penta-BDE, TDCPP, Firemaster 550) is not credible.

In sum, there can be little doubt that chemical flame retardants, which are in the bodies of nearly all North Americans—with the highest levels in young children and Californians—have the potential to harm human health and the environment. The Bureau is required by California law to make “[p]rotection of the public” its “highest priority.” Given the serious risks posed by continued reliance on chemical flame retardants and the Bureau’s obligation to protect the public, the Bureau’s decision to adopt a furniture flammability standard that does not require the use of chemicals was plainly the right decision.

32 Robin E. Dodson et al., After the PBDE Phase-Out: A Broad Suite of Flame Retardants in Repeat House Dust Samples From California, 46 ENVTL. SCI. & TECH. 13,056, 13,064 (2012). A copy of this study is submitted herewith as Exhibit 7.

33 David A. Eastmond et al., A Screening Level Assessment of Health and Environmental Hazards of Organohalogen Flame Retardants (2012) (poster attached hereto as Exhibit 8).

34 CAL. BUS. & PROF. CODE § 19004.1.
3. The Bureau Is Correct to Rely on the ASTM Standard As the Starting Point for Its Revised Furniture Flammability Standard

Finally, we also strongly endorse the Bureau’s decision to use ASTM’s Standard Test Methods for Cigarette Ignition Resistance of Components of Upholstered Furniture, which, unlike TB 117, test the fire resistance of all components of upholstered furniture, as the starting point for its revised furniture flammability standard. This ASTM standard is recognized as accurate and reproducible, and is already widely used by furniture manufacturers. Relying on consensus standards like the ASTM standard as the starting point for a new flammability standard, rather than starting from scratch to develop a new scientific standard, is prudent and efficient. Indeed, a range of existing California statutes and regulations involving safety and scientific matters already incorporate or reference ASTM standards.35 Most significantly, the California Legislature mandates use of ASTM standards in a variety of contexts involving fire safety. For example, state law requires reliance on an ASTM standard for testing the ignition strength of cigarettes to ensure compliance with fire-safe cigarette standards,36 and for the design and construction of portable gasoline containers.37 It therefore stands to reason that the ASTM flammability standard that is already in wide use should underlie any new California furniture flammability standard.

In sum, the proposed rulemaking will be a significant public health advance in two respects: it will bring the state’s furniture flammability standards into compliance with California law requiring that furniture be “fire retardant,”38 a criterion that likely is not met by TB 117, and it will fulfill the Bureau’s obligation to make “[p]rotection of the public” its “highest priority,”39 by allowing furniture manufacturers to cease using flame retardant

35 See, e.g., CAL. HEALTH & SAFETY CODE § 24502(b) (cribs are presumed unsafe unless they comply with ASTM standards); CAL. CODE REGS. tit. 8, § 3195.1(b) (incorporating by reference into the California Code of Regulations seven ASTM standards governing amusement rides and devices); CAL. CODE REGS. tit. 22, § 66261.21(a)(1) and (a)(3)(A) (requiring the use of ASTM standards for determining if a liquid waste exhibits the characteristic of ignitability and if a mixture is a “compressed gas”); CAL. CODE REGS. tit. 13, §2292.6 (using ASTM test methods to establish specifications for liquefied petroleum gas); CAL. CODE REGS. tit. 13, §2292.1 (using ASTM test methods to establish specifications for M100 fuel methanol); CAL. CODE REGS. tit. 8, § 5607(b) (requiring malleable iron castings in materials for pipe fittings to conform to ASTM standard); CAL. CODE REGS. tit. 4, § 4148 (biodiesel fuel blends must meet ASTM standards).

36 CAL. HEALTH & SAFETY CODE § 14952(a)(1) (“Testing of cigarettes shall be conducted in accordance with the American Society of Testing and Materials (ASTM) Standard E2187-04....”).

37 CAL. HEALTH & SAFETY CODE § 13139(a) (the State Fire Marshal shall approve and list portable gasoline containers that are designed according to either the ASTM standard or a standard approved by another national testing laboratory recognized by the State Fire Marshal).

38 CAL. BUS. & PROF. CODE § 19161.

39 CAL. BUS. & PROF. CODE § 19004.1.
chemicals that endanger humans and the environment. Given the significant benefits of TB 117-2013, we urge the Bureau to finalize the amended regulations, without delay. When it does so, we ask the Bureau to make clear that manufacturers are permitted to come into compliance with TB 117-2013 even before the mandatory compliance date of July 1, 2014. Finally, we urge the Bureau to limit to one year the time period after July 1, 2014, in which retailers may continue to sell inventory that was manufactured to meet the TB 117 standard. The risks to consumers from the continued sale of products made to comply with TB 117—both in terms of diminished fire safety and resulting exposures to toxic chemicals—are simply too great for the state to allow their sale to continue indefinitely.

Sincerely,

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Exhibit 1
Flame Retardants in Furniture Foam: Benefits and Risks

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ABSTRACT

The extensive use of chemical flame retardants to meet the California Furniture Flammability Standard Technical Bulletin 117 (TB 117) [1] provides an example of the need for consideration of environmental impacts of fire safety interventions before they are implemented. Flame retardants are currently being used in products with high levels of human exposure without adequate toxicological testing. For example, flame retardants commercially used to meet TB117 have been found to have negative impacts upon human, animal, and environmental health [2] and notably, the TB117 standard has not been shown to have a measurable fire safety benefit. Both the unintended adverse impacts and the lack of fire safety benefits of California TB117 are discussed in detail.

KEYWORDS: flame retardants, halogens, PBDE, flammability.

INTRODUCTION

Flame retardant (FR) additives are commonly used to meet regulatory requirements mandating certain levels of fire safety performance. Even though a wide variety of FR additives have been developed, for most man-made polymers halogenated FR chemicals have been the most frequently used. This is due to their cost, availability, and extensive industry experience with this class of additives. Until recent years, only the potential benefits of their usage have been considered by regulatory bodies and not the potential drawbacks. For example, after decades of use and hundreds of studies detecting adverse health and environmental consequences, two polybrominated diphenyl ether (PBDE) commercial mixtures—PentaBDE and OctaBDE—were banned in 2003 in California and in 2004 in the European Union [3] and voluntarily withdrawn from production by the sole US manufacturer [3]. These two PBDE mixtures were subsequently listed as persistent organic pollutants (POPs) by the Stockholm Convention [4]. The cause for concern with these and other PBDEs, their replacements, and other currently used halogenated replacement chemicals is now well recognized [5].

The assumption held by much of the public, industry and scientists, is that any hazardous FR additives would be restricted from use in consumer products. However, in the United States, only chemicals in foods, drugs, and pesticides are regulated prior to reaching the marketplace. There is no requirement for health data nor sufficient authority to regulate other chemicals [6]. When a number of halogenated flame retardants received detailed study, they were found to be persistent when introduced into the environment and to have serious adverse health consequences [2]. In light of these findings, it seems necessary to consider the net outcome associated with the use of FR agents, instead of only evaluating their effects on the improvement of fire safety. This could require a complex weighing of alternatives which lack a common basis for comparison, e.g., death or injury due to fire, versus damage to the environment or long-term health effects associated with direct ingestion, consumption of contaminated foodstuffs, and other modes of transfer. In some cases, however, such a complex assessment may not be needed. One example would be if there were no fire safety benefits associated with a particular usage. The use of organohalogen FRs to meet California Furniture Flammability Standard Technical Bulletin 117 (TB 117) is examined here as an example of such a case.
BENEFITS OF CALIFORNIA FURNITURE FLAMMABILITY STANDARD TB117

The California Furniture Flammability Standard TB117 was implemented in 1975 by the California Bureau of Electronic and Appliance Repair, Home Furnishings and Thermal Insulation (the Bureau). Its avowed purpose is to reduce fire deaths and injuries associated with upholstered furniture. The standard is a small-flame ignition standard which requires polyurethane foam in juvenile products and upholstered furniture to withstand exposure to a small open flame for 12 s [7]. The standard also regulates smolder behavior of foams and provides fire tests for other, non-foam components. But these aspects are not of relevance to the present paper, since chemical fire retardants are not added to foams to pass the smolder test, while other components are either in very limited use or require no treatment, or both. Compliance with the standard is mandatory for all products sold in California, irrespective of where they are manufactured. Of the 50 US States, California is the only state which has such a standard. Increasingly many national furniture manufacturers are using this standard for all of their furniture sold across North America to avoid maintaining a double inventory and for defense against fire liability claims. Thus TB117 is becoming a de facto national standard, with the organohalogen flame retardants typically used to meet it being found in most furniture and baby products containing polyurethane foam sold in the US and Canada. A small-flame fire standard such as TB117 would have a fire safety benefit if a positive answer could be obtained to at least one of the two questions posed below.

Do TB117 Compliant Materials Significantly Reduce the Severity of the Fire?

The severity of a particular fuel package is quantified by its peak heat release rate (peak HRR), measured in kilowatt units [8]. Babrauskas [9] studied furniture where the peak HRR of identically-constructed furniture passing TB117 was compared to furniture made with non-fire-retardant (non-FR) foam. The differences observed between the furniture with non-FR foam and furniture made with foam complying with TB117 were within the normal data scatter from this type of test. In addition, visually the fire development over the furniture was seen to be identical. Schuhmann and Hartzell [10] also found use of TB117 foam did not reduce the peak HRR compared to non-FR foam in normal residential furniture construction. On the other hand, they found advanced foams (of much higher density and with much higher levels of flame retardants than required by TB117) did show a peak HRR about 42% lower than for TB117 foams. Similarly Babrauskas et al. [11] later also compared furniture made with non-FR foam and advanced foam, but not with TB117 foam. The advanced foam contained three different FR additives and had a density 2.5 times greater than the non-FR foam. A chair that showed 1200 kW peak HRR when made with non-FR foam showed a peak HRR value of approximately 50 kW when made with advanced FR foam. The advanced foam used was costly and not found in residential furniture, but was used to illustrate the performance achievable by incorporating state-of-the-art technology. The study concluded: “The average available escape time was more than 15-fold greater for the FR products in the room burn tests,” compared to the non-FR products (113 s versus 1789 s) [12]. This statement has been distorted and improperly cited to imply that use of TB117 foams can create such a difference [12]. This is incorrect, in that the study did not examine any TB117 foams but only a costly, state-of-the-art formulation not used in residential furniture. Furthermore, the tests were carried out in fully-furnished rooms where numerous combustibles were burned and were not tests of upholstered furniture items alone. Finally, while peak HRR is the primary metric of fire hazard, time to reach peak HRR can be a useful supplemental variable, since it may reflect on the escape time available. The earlier study by Babrauskas [9] presented data showing the time-to-peak for non-FR and TB117 foams were identical, to within the data scatter of the apparatus. Thus, the answer to the first question, “Is the severity of the fire significantly reduced by the use of TB117 foam?” is clearly No.

Does TB117 Foam Serve to Prevent Ignitions from Small Flame Sources?

A severe fault of the TB117 test is that the foam alone is exposed to a small burner flame, rather than the composite piece of furniture. Under such conditions, TB117 foam with 3 to 5% of FR additive can resist a small open flame. But actual upholstered furniture always consists of a composite of at least two layers, with a fabric cover on top of foam. Furthermore, fabrics are thin membranes of about 1 mm that do not serve as a barrier to the flow of heat from the outside to the foam and it is common for the upholstery fabric itself to ignite from small flame sources such as a candle or a lighter. Once the fabric is burning, the foam is presented with a flame challenge which is many times larger than the cigarette lighter flame which may have originally ignited the fabric. (Note that TB117 does not consider protection from ignition by large flame sources and that it is well-established that targets which might resist a smaller flame attack may be
unable to resist one from a larger flame [13,14]). It must additionally be noted that (a) the TB117 standard contains a separate test provision for fabrics. But this is a moot test since the procedure is the same as mandated in the Federal CS 191-53 test [15], which all fabrics sold in the US are already required to meet by the Federal government. (b) While an ostensible, but moot fabric test exists within TB117, the standard never assesses the behavior of an actual composite, i.e., a fabric on top of a layer of foam. However, the latter question has been experimentally investigated by two groups. Talley [16] tested 15 different upholstery fabrics, each over non-FR and TB117 foams of matched density (24 kg·m⁻²). All specimens ignited except those using one of the 15 fabrics, and for that fabric neither of the foams used led to ignition. Talley also visually observed flame spread behavior of the specimens that did ignite, and his conclusion was that “The TB117 foam made no significant, consistent difference in either ignition or flame spread.” Talley also ran additional tests which showed that TB117 foams did not offer any benefit in regards to resisting smoldering ignition from cigarettes. In addition, the US Consumer Product Safety Commission (CPSC) conducted laboratory research on actual chairs and also found the test to be ineffective [17]. More broadly, as part of their regulatory mission, they undertook to determine if adopting of the TB117 standard would likely reduce deaths and injuries due to fire and concluded that “TB117 component results were not predictive of full scale performance” and that “TB117…would not, if federally mandated, ensure a substantial reduction in the risk of small open flame ignition of finished articles of furniture.” Thus, the answer to the question “Does TB117 foam serve to prevent ignitions from small flame sources?” is also No.

It is important to emphasize that the above findings have not been disputed. There are no published research studies where the answer to either of the two questions is “Yes.” Thus, the evaluation of the fire safety benefits of TB117 foams is simple—there are no benefits—and a public policy judgment weighing fire safety gains against health and environmental drawbacks (discussed below) is not required.

**HOW HAS CALIFORNIA FURNITURE FLAMMABILITY STANDARD TB117 BEEN MET?**

From its implementation in the late 1970s until 2004, TB117 was primarily met with the addition of three to five percent pentabromodiphenyl ether (pentaBDE) to the foam in furniture and juvenile products (nursing pillows, strollers, baby carriers, etc.). PentaBDE is a commercial mixture of several congeners of polybrominated diphenyl ethers (PBDE). Due to its persistence and tendency to bioaccumulate, pentaBDE has become a global contaminant and the most well studied of the brominated flame retardants.

PentaBDE and the other PBDEs are structurally similar to known human toxicants PBBs, PCBs, dioxins and furans. In addition to having similar mechanisms of toxicity in animal studies [18], PBDEs similarly persist and bioaccumulate in humans and animals [19]. In 1999 and 2001, 98% [20] and 95% [21], respectively, of the usage of pentaBDE, was in North America, in large part to meet TB117. PentaBDE was banned in California in 2003 due to its persistence and toxicity; eight other states and the European Union (EU) followed suit. In 2004, Chemtura, (previously Great Lakes Chemical), the sole US manufacturer, voluntarily ceased production. In 2009 pentaBDE was listed as a persistent organic pollutant under the Stockholm Convention [22]. However pentaBDE continues to be a global pollutant, moving from reservoirs in furniture and other products into the biota.

**HEALTH EFFECTS OF PENTABDE**

Halogenated flame retardants, including PBDEs, have been associated with cancer, immune and endocrine disruption, and reproductive and neurodevelopmental effects in humans and a variety of animal species [2].

**Effects of PentaBDE on Laboratory Animals**

A large body of experimental data, both *in vivo* and *in vitro*, shows that pentaBDE can disrupt the endocrine system in mammals, birds, and fish, resulting in effects on thyroid, ovarian, and androgen function [23,24]. PentaBDE also disrupts thyroid hormone homeostasis which can cause neurologic impairments, including a reduction in the IQ of offspring [25,26].

Many of these effects result from exposure during prenatal or neonatal development [25,27]. Such effects include impacts on gene expression of liver enzymes [28,29] endocrine disruption (altered thyroid hormone levels) [30], reproductive damage [31–33], immunotoxicity [34,35], and neurotoxic effects [36]. Experiments conducted by Eriksson and co-workers in mice developmentally exposed either to penta- or higher BDEs [37–40] during the period of rapid brain growth have shown neurotoxic effects, including impair-
ment of spontaneous behavior, cholinergic transmitter susceptibility, and habituation capability. The deficits in learning and memory were observed to persist into adulthood and worsen with age. The developmental effects of PBDEs are exacerbated by co-exposure to PCBs in rats [41].

As an endocrine disruptor, pentaBDE exposure results in increased lypolysis and reduced insulin-stimulated metabolism in rat adipocytes [42], effects which have been associated with obesity, insulin resistance, and Type 2 diabetes. PentaBDE is also anti-androgenic [43,44].

Exposure and Health Impacts of PentaBDE on Humans

A wide range of adverse effects in humans associated with pentaBDE exposure include developmental, endocrine, thyroid, reproductive and neurological effects, as well as diabetes [25,45,46].

Exposure

Halogenated flame retardants such as pentaBDE and its replacements are a predominant class of toxic chemicals found in human biomonitoring studies [47]. The importance of house dust as a major exposure route for pentaBDE in humans has been studied [49,51]. Human external exposure from dust, diet, and air and the resulting internal exposure to pentaBDE has been recently reviewed [48,49]. About 20% of exposure to PBDEs in Americans is currently estimated to derive from diet, with the highest exposure from butter, seafood, and meat [50]. The remaining 80% of exposure is assumed to come mainly from the ingestion and inhalation of PBDE-contaminated dust [51].

The PBDE concentrations in the North American general population are 10 to 40-times higher than the concentrations reported for populations in Europe and other parts of the world [52–55]. A positive correlation between pentaBDE concentrations in house dust and breast milk has been shown [56]. In California, populations have been shown to be disproportionately exposed to pentaBDE, likely due to the state’s fire regulation TB117 that has led to high usage of halogenated flame retardants in furniture and baby products [47]. A recent study found that body burden levels in California children are two to nine times higher than in similar-aged children across the US, and four to nine times higher than children in Mexico, and up to one hundred times higher than those in children of similar ages in Europe and Mexico [57].

Developmental Effects

Exposure to pentaBDE in umbilical cord blood is associated with adverse neurodevelopmental effects in children [58]. Children in the highest 20% of the exposure distribution showed lower IQ performance scores (ranging from 5 to 8 points lower) at all ages [58]. In the Netherlands, prenatal exposure to pentaBDE was associated with significant adverse effects on motor, cognitive, and behavioral outcomes in the children [59]. PentaBDE congeners appear to affect the development of fetal human neural progenitor cells via endocrine disruption of cellular thyroid hormone signaling [60]. These studies are the first to suggest a biological mechanism for in vivo studies reporting behavioral and IQ effects after developmental exposures.

In addition to their prenatal exposures, after birth young children are exposed at higher levels than adults from breast milk and ingestion of dust due to hand-to-mouth contact [61,62]. It has been estimated that a breastfed infant in the US would be exposed to 1500 ng/day of PBDEs [63]. Accordingly, the highest serum levels of PBDEs are found in infants and toddlers, most vulnerable to developmental toxins [64,65].

Reproductive Effects

Harley et al. reported an association between pentaBDE exposure and reduced fertility in women from a predominantly Mexican-immigrant community in California [46]. Increasing serum levels of pentaBDE were significantly associated with longer time to pregnancy. Prenatal exposure of the infants of these women was associated with low birth weight, altered cognitive behavior, and significantly reduced plasma levels of thyroid stimulating hormone (TSH) [46]. Another study reported that elevated levels of pentaBDE in breast milk of pregnant Taiwanese women were associated with adverse birth outcomes including decreased weight, length, and chest circumference of their infants [66]. The effects were observed at levels lower than the average pentaBDE levels in the adult US population.

Elevated pentaBDE levels in breast milk were correlated with cryptorchidism (undescended testicles) in the sons of mother-son pairs studied in Denmark and Finland [67]. The levels associated with cryptorchidism were also positively correlated with serum lutenizing hormone (LH) concentrations in the infants, which
suggested a possible compensatory mechanism to achieve normal testosterone levels. This observation is consistent with the anti-androgenic effects of PBDEs observed in experimental animals. A pilot study conducted by Japanese researchers reported that elevated blood levels of BDE-153 were correlated with decreased sperm count and decreased testes size [68].

A recent study in the US reported a relationship between altered hormone levels in men and pentaBDE levels in house dust [69]. The findings included significant inverse associations between PBDEs in house dust and serum concentrations of the free androgen index, LH, and follicle-stimulating hormone (FSH) and positive associations between pentaBDE and sex-hormone binding globulin (SHBG) and free T₄.

**Thyroid Effects**

Turyk et al. reported an association between pentaBDE and elevated T₄ levels and thyroglobulin antibodies in the blood of adult male consumers of Great Lakes sport fish [70]. The effects were observed at pentaBDE levels comparable to those found in the general US population and were independent of PCB exposure and sport fish consumption. A recent study of Inuit adults [71] reported that plasma concentrations of BDE-47 were related to increasing total T₃ levels.

**Endocrine Disruption**

As endocrine-disruptors, some PBDEs are reported to cause disturbances in glucose and lipid metabolism in rat adipose tissue, which is characteristic of metabolic obesity and Type 2 diabetes [42], but few studies have examined the relationships between PBDEs and diabetes in humans. Turyk et al. reported a non-significant association between PBDE exposure and diabetes in Great Lakes sport fish consumers with hypothyroid disease [72,70]. A recent study in US adults examined the association between diabetes and PBDEs [73]. The serum concentrations of the hexa-BDE congener -153 were significantly related to metabolic syndrome and diabetes prevalence at background concentrations, suggesting that PBDEs may contribute to diabetes in the general population.

**Carcinogenic Effects**

The carcinogenic potential of PBDEs has not yet been adequately addressed in animal or human studies. Part of the observed increase in thyroid cancer rates in the U.S. is hypothesized to be related to the increasing population exposure to pentaBDE and other thyroid hormone disrupting compounds [28]. A study by Hardell et al. [74] reported an association between BDE-47 concentrations and an increased risk for non-Hodgkin’s lymphoma (NHL). In the highest risk/highest exposure group, BDE-47 was significantly correlated with elevated titers to Epstein Barr IgG, a herpes virus that associated with certain subgroups of NHL.

**Effects of PentaBDE on Wildlife**

Because of the usage of pentaBDE in North America to comply with TB117, the levels found in wildlife are increasing in a variety of species of fish, birds, and marine mammals as well as humans [75–78].

**Fish**

Recent studies have shown that PBDE exposure may affect thyroid hormone homeostasis, sperm production, disease resistance and neurodevelopment in fish [34,79]. Plasma T₄ levels were significantly reduced in juvenile lake trout exposed to 13 PBDE congeners at levels somewhat higher than those found in the environment [80]. In male fathead minnows, repeated oral exposure to BDE-47 reduced sperm production [81]. Low-dose embryonic exposure of killifish to a pentaBDE mixture resulted in neuro-behavioral effects and a subtle developmental asymmetry with respect to tail curvature direction, with a J-shaped dose-response curve suggestive of thyroid hormone disruption [82]. Similarly, exposure of zebrafish embryos to high doses of BDE-47 resulted in developmental effects, including morphological, cardiac, and neural deficits that impaired later survivorship in the fish larvae [83]. Chronic exposure of juvenile zebrafish to ecologically relevant levels of BDE-47 resulted in altered locomotion behavior [79]. A recent study showed that dietary exposure of juvenile Chinook salmon to environmentally relevant concentrations of PBDEs increased susceptibility to pathogenic micro-organisms [34].

**Birds**

PBDEs are detected at high concentrations in birds of prey, such as peregrine falcons and common kestrels. Recent studies have shown PBDE-related endocrine-disrupting and reproductive effects at environmentally
relevant concentrations. In captive American kestrels, Fernie et al. [84] reported decreased plasma T\textsubscript{4} and vitamin A levels, as well as indications of oxidative stress in kestrels dosed with environmentally relevant levels of the pentaBDE mixture DE-71. DE-71 exposure also had a negative impact on the timing and frequency of courtship [85]. Exposure to DE-71 resulted in delayed egg laying, reduced egg size, eggshell thinning, and reduced fertility and reproductive success in kestrels and falcons [86,87]. Fernie et al. [86] concluded that these changes in the reproductive success of captive kestrels, particularly eggshell thinning, may partially explain the decline of American kestrels across North America. McKernan et al. [88] reported decreased piping and hatching success in American kestrel embryos following the air cell injection of DE-71. Similarly, Johansson et al. [86] reported a negative relationship between PBDEs and reproductive success in peregrine falcons from Sweden. PBDE concentrations in eggs were negatively related to the average number of young produced from individual breeding females over a 2–7 year period. Van den Steen et al. [89] observed negative effects of PBDEs on reproductive performance in European starlings. A field study in the US [90] reported a negative relationship between reproductive performance and PBDEs in eggs of wild ospreys at two locations in the highly contaminated Columbia River valley of Oregon and Washington. North American osprey populations may be at risk for contaminant-induced reproductive impairment.

**Marine mammals**

Marine mammals accumulate extremely high concentrations of pentaBDE and other persistent organic pollutants through feeding on contaminated prey. Adult animals are exposed through the consumption of contaminated fish and young animals are exposed to PBDEs *in utero* and in breast milk. Marine mammals from the California coast contain the highest reported pentaBDE levels on record. These include adult male sea lions [91] and transient killer whales off the California coast, as well as in resident killer whales from the Puget Sound–Strait of Georgia Basin [92,93]. Along the US Atlantic coast, relatively high pentaBDE concentrations were reported in young harbor seals [94] and in juvenile bottlenose dolphins [95].

Studies have shown that co-exposure to pentaBDE and PCBs is associated with thyroid hormone alterations in gray seals [96] and harbor seals [97], and with thymic atrophy and splenic depletion in harbor porpoises from the North and Baltic Seas [98]. A study of infectious diseases in California sea otters co-exposed to PCBs and pentaBDE also suggested possible synergistic interactions between these contaminant groups [99]. However, a recent study reported that in grey seals, levels of PBDEs alone significantly reduced the probability of first year survival [100].

**CHEMICAL REPLACEMENTS FOR PENTABDE**

After pentaBDE was phased out in 2004, a major replacement used for TB117 compliance was Firemaster 550, also produced by Chemtura, a mixture of four flame retardant chemicals whose composition was a trade secret. In 2004, the EPA Design for the Environment predicted reproductive, neurological, and developmental toxicity and persistent degradation products for the brominated components of Firemaster 550 [101]. In 2005, Chemtura agreed to conduct reproductive and developmental toxicity and migration studies by January 2009. Data provided by Chemtura in November 2008 have recently been evaluated by the EPA. Firemaster 550 components include: (1) triphenyl phosphate which is known to be eco-toxic, (2) Triaryl phosphate isopropylated which is a probable reproductive toxin, (3) Bis (2-ethylhexyl) tetrabromophthalate, and (4) 2-ethylhexyl-2,3,4,5-tetrabromobenzoate [102]. The brominated components have been found in dust [102], sewage sludge [103], marine mammals [104], and seven species in the Arctic [105]. Firemaster 600, described by Chemtura as having a trade-secret composition, is another pentaBDE replacement.

TDCPP or chlorinated tris is also a widely used replacement flame retardant for pentaBDE in polyurethane foam. It is produced by Israeli Chemicals, Limited (ICL) under the trade name Pyrol and by Albermarle under the trade name Antibilaze. Recent studies show TDCPP, like pentaBDE and Firemaster 550 components, can migrate from foam products into indoor house dust [106]. These semi-volatile compounds can form thin films on walls and windows [107]. The inhalation and ingestion of contaminated dust has been shown to be a major route of human exposure, especially for children [106].

**EXPOSURE AND HEALTH EFFECTS OF PENTABDE REPLACEMENTS**

Few studies have been conducted on the health effects of these replacement chemicals in animals or humans. The brominated Firemaster 550 components TBB and TBPH are genotoxic in fish, causing increased DNA strand breaks in orally exposed fish [108]. Triphenyl phosphate (TPP) is toxic to aquatic organisms including
Daphnia [109], rainbow trout, and fathead minnows [110]. Triaryl phosphate isopropylated is a reproductive/developmental toxin at mid- to high doses in rats [101,110]. Histopathologic changes were observed in female reproductive organs and adrenals at all doses.

TDCPP, or chlorinated Tris, was removed from use in children’s pajamas in 1978 due to its mutagenicity and has subsequently been found to be a probable human carcinogen in a study at the US Consumer Product Safety Commission (CPSC) [111]. The CPSC report estimates the lifetime cancer risk from tris-treated furniture foam is up to 300 cancer cases/million and their chronic hazard guidelines define a substance as hazardous if lifetime cancer risk exceeds one in a million. TDCPP is also absorbed by humans [112]. The US EPA considers TDCPP a moderate hazard for cancer and reproductive/developmental effects [113].

A recent study showed that men living in homes with high amounts of the organophosphate flame retardants TPP and TDCPP in house-hold dust had reduced sperm counts and altered levels of hormones related to fertility and thyroid function [114]. High levels of TPP in dust were associated with a substantial reduction of sperm concentrations and an increase in prolactin levels. Increased prolactin is considered a marker of decreased neuroendocrine/dopamine activity and also may be associated with erectile dysfunction [115]. High levels of TDCPP in dust were associated with a 17% increase in prolactin and a 3% decline in free thyroid hormone levels. The possible synergistic or additive effects of the numerous flame retardant chemicals in use have not been studied in animals or humans.

CONCLUSIONS

Since 1975, hundreds of millions of kilograms of pentaBDE and its replacements which include TDCPP and Firemaster 500 have been used to meet California TB117. A fire safety benefit has not been established. Research suggests that this standard should be reevaluated in light of the fire science and health information discussed above. Prior to implementing new flammability standards, decision makers should evaluate the potential fire safety benefit as well as the health and environmental impacts of the chemicals, materials, or technologies likely to be used. Special scrutiny should be given to small open-flame standards that are likely to be met by adding organohalogen flame retardants to foam or plastic in consumer products.

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Exhibit 2
Detection of Organophosphate Flame Retardants in Furniture Foam and U.S. House Dust

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Restrictions on the use of polybrominated diphenyl ethers (PBDEs) have resulted in the increased use of alternate flame retardant chemicals to meet flammability standards. However, it has been difficult to determine which chemical formulations are currently being used in high volumes to meet flammability standards since the use of flame retardant formulations in consumer products is not transparent (i.e., not provided to customers). To investigate chemicals being used as replacements for PentaBDE in polyurethane foam, we analyzed foam samples from 26 different pieces of furniture purchased in the United States primarily between 2003 and 2009. Samples included foam from couches, chairs, mattress pads, pillows, and, in one case, foam from a sound-proofing system of a sound-proofing system. We included foam from couches, chairs, mattress pads, pillows, and, in one case, foam from a sound-proofing system of a sound-proofing system.

Prior to 2004, polybrominated diphenyl ethers (PBDEs) were one of the most common flame retardant mixtures used in furniture and electronic products. PBDEs were sold commercially as different formulations referred to as PentaBDE, OctaBDE, and DecaBDE, each having different applications. However, due to their persistence, bioaccumulation, and potential health effects, PentaBDE and OctaBDE were banned or voluntarily phased out from use beginning in 2002 in many regions of the world, and will soon be added to the list of banned chemicals included in the Stockholm Convention on Persistent Organic Pollutants (8). PentaBDE was historically used in the highest volumes in North America (primarily U.S. and Canada) to treat polyurethane foam in furniture (9). The higher use of PentaBDE in North America led to elevated levels of the PentaBDE congeners in the U.S. population relative to European and Asian populations, likely due to a higher exposure from house dust (10–17). Several studies have recently found associations between human body burdens of PBDEs (primarily PentaBDE) and health effects such as thyroid hormone and androgen abnormalities, cryptorchidism, and low birth weights (18–21).

The phase-out of PentaBDE has led to the development of alternate flame retardant formulations and the increased use of existing flame retardant chemicals to meet flammability standards for polyurethane foam (22). We recently identified the brominated components of a PentaBDE replacement mixture suspected of high volume use in polyurethane foam (23); however, for many flame retardants, basic information such as chemical identity and their consumer product applications is typically not available. Lack of information significantly restricts environmental and human health assessments for these chemicals, which is of considerable concern, particularly since the PentaBDE replacement chemicals recently identified were also detected in U.S. house dust (23). Occurrence in house dust suggests that human exposure to these flame retardants will also occur, and raises concerns regarding the potential for exposure to other PBDE replacements that have yet to be identified. Though several studies have reported the environmental fate

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and effects of PBDEs, very little information on the occurrence, fate, and toxicity of their replacement chemicals exists. In our previous study, we identified two brominated compounds in a flame retardant mixture (Firemaster 550) now being used as a replacement for PentaBDE in polyurethane foam (23). However, it has been suggested that organophosphate compounds, some chlorinated, are also currently used or have historically been used as flame retardant chemicals in high volumes (24). Tris (1,3-dichloro-2-propyl) phosphate (TDCPP) and triaryl phosphates such as triphenyl phosphate (TPP) have been used for decades as flame retardants and plasticizers in a wide variety of applications, resulting in widespread environmental contamination (25, 26). Production and use of these flame retardants in furniture foam may have increased due to the phase-out of PBDEs.

Based on this information, we designed this study to identify potential organophosphate flame retardant chemicals currently being used in polyurethane foam in residential and office furniture purchased in the United States. To do this we specifically targeted furniture items produced by a major furniture retailer in the U.S. which claimed to have phased-out the use of brominated flame retardants. A second objective was to determine whether these alternative flame retardants were accumulating in house dust. Fifty house dust samples collected between 2002 and 2007 in Boston, MA, which were initially analyzed for PBDEs and other brominated flame retardants, were screened for organophosphate flame retardants identified in the foam. Lastly, we estimated the cumulative exposure to a suite of flame retardant chemicals now being detected in house dust to adults and children.

Materials and Methods

Materials. Internal and recovery standards used in this study were purchased from Chiron (Trondheim, Norway) and Wellington Laboratories (Guelph, Ontario). PBDE quantification standards were purchased from Accusstandard (New Haven, CT). The 2-ethylhexyl-2,3,4,5-tetrabromobenzoate (TBB) and bis (2-ethylhexyl) tetrabromophthalate (TBPB) standards were purchased from Wellington Laboratories. Tris (1-chloro-2-propyl) phosphate (TCPH) and tri (1,3-dichloro-2-propyl) phosphate (TDCPP) were purchased from Pfaltz & Bauer (Waterbury, CT) and Chem Service (West Chester, PA), respectively. Triphenyl phosphate (TPP, 99% pure) was purchased from Sigma-Aldrich (St. Louis, MO). All solvents used throughout this study were HPLC grade.

Sample Collection. Foam samples were donated by friends, family, and colleagues of the authors residing in the Boston, MA area between 2002 and 2007; the samples were not collected from the same locations as the foam samples. Details on collection, treatment, and storage of the dust samples are provided elsewhere (20).

Sample Extraction. Our method for the analysis of the brominated flame retardants measured in this study is reported in Stapleton et al. (23). The analysis of the foam and dust samples for the organophosphate compounds is briefly outlined here. Approximately 0.3–0.5 g of sieved dust was accurately weighed, spiked with 50–100 ng of two internal quantification standards ([4]trfluoro-2,3,4,6-tetrabromodiphenyl ether (F-BDE 69) and [13C]-labeled decabromodiphenyl ether ([13C] BDE 209)), and extracted in stainless steel cells using pressurized fluid extraction (ASE 300, Dionex Inc.).

Cells were extracted three times with 50:50 dichloromethane/hexane at a temperature of 100 °C and at 1500 psi. Foam samples of approximately 0.2–0.3 g in weight were also extracted using the same solvents on the ASE system but no internal standards were spiked into the ASE cell. Final extracts were reduced in volume to approximately 1.0 mL using an automated nitrogen evaporation system (Turbo Vap II, Zymark Inc.). Foam sample extracts of approximately 3.5 mL were then accurately weighed in a 4 mL amber vial and a 50 μL aliquot was transferred to an autosampler vial, spiked with 100 ng of a carbon-labeled chlorinated diphenyl ether ([13C]CDE 141), and prepared for gas chromatography mass spectrometry (GC/MS) analysis. Dust extracts were purified by elution through a glass column containing 4.0 g of 6% deactivated alumina. All analytes were eluted with 50 mL of a 50:50 mixture of dichloromethane/hexane. The final extract was then reduced in volume to 0.5 mL, and 50 ng of the recovery standard, [13C] CDE 141, was added prior to GC/MS analysis. For the foam extracts, an aliquot of the extract was transferred to an autosampler vial and spiked with the recovery standard and analyzed by GC/MS.

Sample Analysis. All samples were analyzed using an Agilent (Wilmington, DE) gas chromatograph (model 6890N) mass spectrometer (model 5975). Foam extracts were scanned in both electron impact (EI) and electron capture negative ionization mode (GC/ECNI-MS) over a scan range of 50–1050 amu and EI spectra were compared to the NIST mass spectral database (2005). Dust sample extracts were analyzed in electron impact mode (GC/EI-MS) for the detection of TCPP and TPP, or by GC/ECNI-MS for TDCPP and the brominated flame retardants. A 0.25 mm (i.d.) × 15 m fused silica capillary column coated with 5% phenyl methylpolysiloxane (J&W Scientific, 0.25 μm film thickness) was used for separation of the analytes. Pressurized temperature vaporization (PTV) injection was employed in the GC. The inlet was set to a temperature of 80 °C for 0.3 min and then a 600 °C/min ramp to 275 °C was employed to efficiently transfer the samples to the head of the GC column. The oven temperature program was held at 40 °C for 1 min followed by a temperature ramp of 18 °C/min to 250 °C, followed by a temperature ramp of 1.5 °C/min to a temperature of 260 °C, followed by a final temperature ramp of 25 °C/min to 300 °C which was held for an additional 20 min. The transfer line temperature was maintained at 300 °C and the ion source temperature was held at 200 °C. PBDEs were quantified by monitoring bromide ions (m/z 79 and 81). [13C] BDE-209 was quantified by monitoring m/z 494.6 and 496.6, TDCPP was quantified by monitoring m/z 319 and 317, TCPP was quantified by monitoring m/z 277 and 201, and TPP was quantified by monitoring m/z 326 and 325.

Quality Assurance. As part of our data quality assurance we examined levels of these specific analytes in laboratory blanks (n = 4), replicate samples (n = 3), and matrix spikes (n = 3). Sample measurements were blank-corrected by subtracting the average mass measured in the laboratory blanks. Laboratory blank masses for TCPP, TDCPP, and TPP were 16.7 ± 8.5, 11.7 ± 6.6, and 15.7 ± 11.9 ng, respectively. Method detection limits equaled the average plus three times the standard deviation of the blank levels. Matrix spikes were prepared by adding 25–100 ng of TCPP, TDCPP and TPP to ASE cells filled with sodium sulfate powder. Matrix spikes were extracted using the same method used for dust and examined for percent recovery using 50 ng of [13C] CDE 141 as an internal standard. Recoveries averaged 76 ± 20, 86 ± 7, and 89 ± 2% for TCPP, TDCPP, and TPP, respectively.

Results and Discussion

Foam Analysis. Foam samples were collected from 26 pieces of furniture that included chairs, couches, futons, ottomans, pillows, a baby stroller, and in one case, foam insulation.
from a piece of laboratory equipment, a dust sieve shaker unit. A small piece of each foam sample (approximately 1 cm³) was first screened for chemical additives by extracting the foam and analyzing the extract in scan mode on a gas chromatograph equipped with a mass spectrometer (GC/MS). Extracts were scanned in both electron impact mode (GC/EI-MS) and negative chemical ionization mode (GC/ECNI-MS). Chromatograms generated for each foam sample were examined and all significant peaks were compared to the NIST mass spectral database (2005) for identification. Figure S1 displays a chromatogram collected from a foam sample which was found to have a positive match for TDCPP in the NIST database. Foam extracts were also examined for the presence of bromine in GC/ECNI-MS mode, as bromine-containing compounds generally generate a strong bromide signal (e.g., m/z 79 and 81). The primary chemical additives detected in each foam sample are presented in Table 1. Positive identification of all compounds was made by comparison to authentic standards.

Of the 26 extracts scanned, only two generated a strong bromine signal after analysis in GC/ECNI-MS mode. One contained PBDE congeners 47, 99, 100, 153, and 154 in ratios identical to those reported for PentaBDE commercial mixture (27). This sample was collected from a futon purchased secondhand in the U.S., thus the manufacture date is unknown. The presence of PentaBDE indicates that it was likely produced prior to the 2004 phase-out and ban of PentaBDE. The second sample was from a couch purchased in 2007 in California and contained two brominated components found in a new formulation called Firemaster 550 (FM 550): 2-ethylhexyl 2,3,4,5-tetrabromobenzoate (TBB) and bis(2-ethylhexyl) tetrabromophthalate (TBPH). Concentrations by weight of these compounds are reported in Table 1.

Among the remaining 24 samples, 15 contained tris(1,3-dichloro-2-propyl)phosphate (TDCPP; CAS 13674-87-8) and 4 contained tris(1-chloro-2-propyl) phosphate (TCP; CAS 13674-84-5). Structures for these two phosphate compounds are presented in Figure 1. Two samples produced strong responses for two different unknown chemicals which appeared in the GC/MS chromatograms. These may be unknown flame retardants; no bromine signals (m/z 79/81) were detected. In three samples no trace of any flame retardant could be observed in the GC/MS chromatograms (i.e., no peaks observed). Using authentic TDCPP and TCP standards, the flame retardant concentration in the foam samples was measured. Concentrations of TDCPP and TCP varied from 1 to 5% and 0.5 to 2.2% by weight of the foam, respectively (Table 1). This is similar to reported concentrations of PentaBDE measured previously in polyurethane foam (5).

Based on these results it appears that TDCPP and TCP are common replacements for PentaBDE in polyurethane foam.

**Table 1. Characteristics of the Polyurethane Foam Samples Analyzed in This Study**

<table>
<thead>
<tr>
<th>sample ID</th>
<th>source</th>
<th>year purchased</th>
<th>flame retardant detected</th>
<th>% by weight of flame retardant</th>
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<td>2004</td>
<td>unidentified</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>mattress pad</td>
<td>2009</td>
<td>N/D</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>leather couch</td>
<td>2005</td>
<td>unidentified</td>
<td></td>
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<td>4</td>
<td>sofa bed</td>
<td>2008</td>
<td>TDCPP</td>
<td>1.3</td>
</tr>
<tr>
<td>5</td>
<td>chair</td>
<td>2008</td>
<td>N/D</td>
<td></td>
</tr>
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<td>chair</td>
<td>2006</td>
<td>TDCPP</td>
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<td>chair</td>
<td>2007</td>
<td>TDCPP</td>
<td>3.8</td>
</tr>
<tr>
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<td>chair</td>
<td>2005</td>
<td>TDCPP</td>
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<td>2007</td>
<td>TDCPP</td>
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<td></td>
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<td>2008</td>
<td>TDCPP</td>
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<td>2009</td>
<td>TDCPP</td>
<td>2.9</td>
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<tr>
<td>24</td>
<td>foam insulation from sieve/shaker</td>
<td>2008</td>
<td>TDCPP</td>
<td>2.2</td>
</tr>
<tr>
<td>25</td>
<td>baby stroller</td>
<td>2009</td>
<td>TDCPP</td>
<td>NM</td>
</tr>
<tr>
<td>26</td>
<td>couch</td>
<td>2007</td>
<td>TBB, TBPH</td>
<td>4.2</td>
</tr>
</tbody>
</table>

* N/A - Not available. N/D - Not detected. NM - not measured due to low mass of foam available. TDCPP - Tris-(1,3-dichloro-2-propyl)phosphate. TCP - Tris(1-chloro-2-propyl)phosphate. PentaBDE - Pentabromodiphenyl ether commercial mixture. TBB - ethylhexyl 2,3,4,5-tetrabromobenzoate. TBPH - bis(2-ethylhexyl) tetrabromophthalate.
foam. TDCPP is a chlorinated phosphate flame retardant additive that was previously used in children’s pajamas in the 1970s and early 1980s but was phased out of use in this application after a study suggested it was a weak mutagen (28). TDCPP replaced the structurally similar tris(2,3-dibromopropyl) phosphate (Tris-BP) which was banned from use in children’s sleepwear in 1977 after studies documented it was mutagenic, carcinoenic, and absorbed by children wearing the tris-BP treated sleepwear (2, 3, 28). However, unlike tris-BP, use of TDCPP continued. In addition to polyurethane foam, other reported applications for TDCPP include plastics, resins, textiles, and polyisocyanurate foams (29). TDCPP has been sold by several chemical companies under trade names such as Firefly FLR2, Firemaster T33P, and Antiflame 111 and is marketed for use in polyester, polyether, and polyurethane foams. The U.S. EPA Inventory Update Reporting (US EPA IUR) regulation requires manufacturers and importers of certain chemical substances included on the TSCA Chemical Substance Inventory to report site and manufacturing information for chemicals manufactured (including imported) in amounts of 25,000 pounds or greater at a single site (http://www.epa.gov/iur/). In reporting years 1986 and 1990, between 1 and 10 million pounds of TDCPP was produced, but in reporting years 1994, 1998, 2002, and 2006, production increased to between 10 and 50 million pounds.

TDCPP has been in use since the mid-1960s and was used as a replacement for tris(chloroethyl) phosphate (TCEP) (29). TCEP is structurally similar to TCEP, which has been identified as a carcinogen by the World Health Organization (30) and the State of California (http://www.oehha.ca.gov/prop65.html). In the 1986 reporting of the US EPA IUR, between 1 and 10 million pounds of TDCPP was produced, but in reporting years 1990, 1994, 1998, 2002, and 2006, production increased to between 10 and 50 million pounds.

We had limited detection of new or alternate types of halogenated flame retardants (e.g., FM 550, hexabromocyclododecane (HBCD), dibromobis(2-fluorobutyethyl) phosphate (BTBPE), hexabromobenzene (HBB), or 1,2-dibromo-4-(1,2-dibromo-ethyl)cyclohexane (TBECH)). FM 550 is a new flame retardant mixture marketed as a replacement for PentaBDE in polyurethane foam and contains both TBB and TBPH. Our research group recently identified TBB and TBPH in house dust samples. However, detection of FM 550 in only one sample may be explained by the fact that most of the foam samples analyzed in this study were manufactured outside of the United States. FM 550 may be used primarily in foam products manufactured in the United States. Since our study design did not include random sampling, these samples may not represent the prevalence of alternative flame retardants currently found in the US market.

**Dust Concentrations.** The use of TCPP and TDCPP as chemical additives in furniture foam suggests that they may leach out over time, accumulate in indoor environments, and lead to human exposure, similar to the fate of other additive flame retardants (e.g., PBDEs). Because few data are available on the levels of these organophosphate compounds in house dust samples from the U.S., we analyzed 50 dust samples collected from the Boston, MA area between 2002 and 2007 for TCPP and TDCPP. In addition, we included triphenylphosphate (TPP) in our analysis since it is a major component of FM 550.

All three organophosphate compounds were detected in house dust samples (see Supporting Information for Dust Chromatograms). The detection frequency of TCPP and TDCPP was 96%, while the detection frequency of TCPP was only 24%. However, it is possible that the low detection frequency for TCPP in the dust samples was a result of a coelution problem. TCPP was monitored in GC/El-MS mode by tracking ions 277 and 201. The expected ratio of these two ions was 65 ± 20% based on responses from the authentic standard. In a majority of the dust samples, ion 277 [M – CH3Cl]+ and 201 [M – CH2H3Cl]+ were observed at the correct GC retention time; however, the area of ion 277 was very high in many samples, resulting in a quant/qual ion ratio ranging from 90 to 400%. Thus coelution of a compound producing a signal for m/z 201 may have interfered with our ability to adequately quantify TCPP. Improvements in our method development are needed to overcome this potential challenge.

Concentrations of TCPP, TDCPP, and TBB ranged from <MDL to 1,800,000 ng/g, <MDL to 5490 ng/g, and from <MDL to 56,090 ng/g, respectively. Geometric mean values were 7360, 572, and 1890 ng/g, respectively. TTP and TDCPP were log-normally distributed, similar to the distribution of PBDEs in these samples, and similar to previous reports for the distribution of PBDEs and other alternate brominated flame retardants in dust samples (14, 23). The organophosphate chemical concentrations are in the same range as the PBDE concentrations measured in these dust samples (Table 2) and in house dust from both the U.S. and Canada measured in previous studies (11, 14, 31). In fact, higher concentrations of TTP were measured in these dust samples compared to PBDEs.

Several Swedish studies found high concentrations of TTP on computer wipes (3300–4000 μg/g), in several public and residential dust samples (25), and have identified video display units as an emission source of TTP (32). TTP is used as both a plasticizer and flame retardant in a variety of applications (plastics, resins, rubber); thus the high levels detected here could have resulted from its use in either application. TDCPP dust concentrations measured here are similar to concentrations recently reported for dust collected in hotels in Japan (33). This same study also measured TTP in eight dust samples and found concentrations ranging from 110 to 2600 ng/g, lower than concentrations measured in these U.S. house dust samples. TTP, TCPP, and TDCPP were detected in air samples collected from residential and public areas in Sweden with concentrations ranging from <0.3 to 570 ng/m3 (34, 35), concentrations that are much higher than PBDE levels measured in indoor environments in the U.S. (36).

The dust samples in this study were collected from home vacuum cleaners and were previously analyzed for PBDEs and several alternate halogenated flame retardants (HBCD, BTBPE, TBB, TBPH, and Dechlorane Plus; data not yet published). No significant correlations were found between...

**TABLE 2. Concentration (ng/g) and Detection Frequencies for the Flame Retardants Detected in House Dust Samples (n = 50)**

<table>
<thead>
<tr>
<th>flame retardant</th>
<th>% detection</th>
<th>minimum</th>
<th>maximum</th>
<th>geometric mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCPP</td>
<td>24</td>
<td>140</td>
<td>5490</td>
<td>572</td>
</tr>
<tr>
<td>TDCPP</td>
<td>96</td>
<td>&lt;90</td>
<td>56,090</td>
<td>1890</td>
</tr>
<tr>
<td>total PBDEs</td>
<td>100</td>
<td>90</td>
<td>44,550</td>
<td>4740</td>
</tr>
<tr>
<td>BTBPE</td>
<td>100</td>
<td>1.4</td>
<td>950</td>
<td>21</td>
</tr>
<tr>
<td>HBCD</td>
<td>92</td>
<td>&lt;2</td>
<td>2,750</td>
<td>166</td>
</tr>
<tr>
<td>TBB</td>
<td>44</td>
<td>&lt;450</td>
<td>75,000</td>
<td>840</td>
</tr>
<tr>
<td>TBPH</td>
<td>60</td>
<td>&lt;300</td>
<td>47,110</td>
<td>650</td>
</tr>
</tbody>
</table>

1 TTP - triphenyl phosphate; TCPP - tris(1-chloro-2-propyl) phosphate; TDCPP - tris(1,3-dichloro-2-propyl) phosphate; Total PBDEs: Sum of PBDEs: 30, 17, 25, 28/33, 75, 49, 71, 47, 66, 100, 119, 98, 116, 85/155, 154, 153, 138, 156, 183, 191, 181, 190, 205, 206, 207, 206, 209; BTBPE - dibromophenoxymethane; HBCD - total hexabromocyclododecane; TBB - ethylhexyl 2,3,4,5-tetrabromobenzzoate; TBPH - bis(2-ethylhexyl) tetrabromophthalate.
the levels of organophosphate flame retardants and PBDEs. However, there was a moderate correlation (Spearman \( r = 0.4 \)) between TPP, TBB, and TBPH in the dust, which are all components of FM 550, a PentaBDE replacement mixture designed for use in polyurethane foam.

**Significance for Human Exposure.** The presence of these organophosphate flame retardants in house dust suggests that people, and especially children, are being exposed to these compounds from dust, presumably in a manner similar to what has been reported for PBDEs (12, 13, 37, 38). Exposure estimates for house dust often rely upon uncertain estimates of dust ingestion for different age classes. The U.S. EPA estimates that children ages 1–5 ingest on average approximately 100–200 mg dust/day, whereas adults ingest about 20–50 mg dust/day (13, 39, 40). Using the lower bound dust ingestion estimates and the geometric mean concentrations of each flame retardant measured in these dust samples, we calculated the cumulative average exposure for U.S. children and adults for the summation of nine types of flame retardant chemicals (Figure 2). The average estimated cumulative exposure to flame retardants from dust for children is calculated to be about 1600 ng/day, whereas for an adult it is about 325 ng/day, a factor 3 times higher than recently reported for exposure to PBDEs alone in Canada and the U.S. (13, 14). A majority of this exposure is due to exposure from PBDEs, TPP, and TDCPP.

It is also interesting to note that the distributions of these flame retardants are quite different among the dust samples (see Table S1). The sum total of the nine flame retardants measured in this study for each dust sample ranged from 3680 to 1,857,000 ng/g. The 95th percentile of this sum is 77,000 ng of flame retardants/g dust. If we assume that these dust samples from Boston, MA are representative of the U.S., approximately 5% of homes could have very high levels of flame retardants in the house dust, and any children living in these homes may be exposed to as much as 77,000 ng of flame retardants/day. Given this, it may be important for scientists to start evaluating potential health effects from exposure to mixtures of these compounds. Currently no data are available to indicate if exposure to these mixtures would be additive, antagonistic, or perhaps synergistic, and thus risk evaluations that routinely consider exposure on a chemical specific basis may underestimate potential risk.

For comparison purposes we calculated the potential inhalation exposure to the organophosphate compounds based on measurements in indoor air recently reported in Finland, Sweden, and Japan (41–43). Assuming an inhalation rate of 15 m³/day for an average adult, inhalation exposure to TPP in certain occupational settings could be high (750 to 12,800 ng/day, depending on the work environment e.g., circuit board factory, electronics dismantling facility), compared to our estimated median exposure from inadvertent dust ingestion in homes (147 ng/day). The estimated occupational exposure to TDCPP from inhalation would be in the range of <900–1350 ng/day compared to our estimates of dust ingestion of 38–189 ng/day for adults and children in homes, respectively. Little data is available on the levels of these organophosphate flame retardants in indoor air from homes; however, Staal and Ostman et al. (41) and Saito et al. (43) reported concentrations ranging from <DL to 17 and <DL to 8.7 ng/m³ in home and office air for TPP and TDCPP, respectively, in Sweden and Japan. This suggests that inhalation exposure to these compounds may be comparable to dust ingestion in some indoor environments; however, further studies are needed to evaluate the levels of these flame retardants in indoor air in the U.S.

Our data suggest that levels of these organophosphate flame retardants in indoor dust are comparable to, or in some cases greater than, levels of PBDEs in dust. Studies have reported that TDCPP is mutagenic (22, 28) and carcinogenic in rats (29); it is also absorbed by humans (30). The U.S. Consumer Product Safety Commission considers TDCPP a probable human carcinogen (22) while the U.S. EPA considers it a moderate cancer hazard (24). The U.S. EPA also considers TDCPP to be a moderate hazard for reproductive and developmental effects (24). Given the high prevalence of these flame retardants in indoor dust and the high concentrations of all flame retardants measured in dust (e.g., as high as 1.8 mg/g), further studies are warranted to evaluate health effects from exposure to these organophosphate flame retardants in dust and from exposure to mixtures of these flame retardants, particularly for children.

**Acknowledgments**

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**Supporting Information Available**

This material is available free of charge via the Internet at http://pubs.acs.org.

**Literature Cited**


(4) Alaee, M.; Arias, P.; Sjödin, A.; Bergman, A. An overview of commercially used brominated flame retardants, their applications, their use patterns in different countries/regions and possible modes of release. Environ. Int. 2003, 29 (6), 683–689.

Exhibit 3
EVIDENCE ON THE CARCINOGENICITY OF TRIS(1,3-DICHLORO-2-PROPYL) PHOSPHATE

July 2011
The Office of Environmental Health Hazard Assessment’s (OEHHA) Reproductive and Cancer Hazard Assessment Branch was responsible for the preparation of this document.

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PREFACE

Proposition 65 requires the publication of a list of chemicals “known to the state” to cause cancer or reproductive toxicity.¹ It specifies that “a chemical is known to the state to cause cancer … if in the opinion of the state’s qualified experts the chemical has been clearly shown through scientifically valid testing according to generally accepted principles to cause cancer …” The “state’s qualified experts” regarding findings of carcinogenicity are the members of the Carcinogen Identification Committee (CIC) of the OEHHA Science Advisory Board.²

The lead agency for implementing Proposition 65 is the Office of Environmental Health Hazard Assessment (OEHHA) of the California Environmental Protection Agency. OEHHA selected tris(1,3-dichloro-2-propyl) phosphate (TDCPP) for preparation of hazard identification materials. Upon selection, the public was given the opportunity to submit information relevant to the assessment of the evidence on the carcinogenicity of TDCPP. OEHHA reviewed and considered those submissions in preparing this document.

OEHHA developed this document to provide the CIC with comprehensive information on TDCPP’s carcinogenicity for use in its deliberations on whether or not the chemical should be listed under Proposition 65.

¹ The Safe Drinking Water and Toxic Enforcement Act of 1986 (California Health and Safety Code 25249.5 et seq.)
² Title 27 Cal. Code of Regs. §25302
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1 EXECUTIVE SUMMARY

The halogenated phosphate triester tris(1,3-dichloro-2-propyl) phosphate (TDCPP) is a high-production volume chemical used primarily as an additive flame retardant in flexible polyurethane foams. It is also used as a flame retardant and plasticizer in rigid polyurethane foams, resins, plastics, textile coatings, and rubber.

TDCPP has been detected in both indoor and outdoor environments in the U.S. and abroad. It has been measured in household and office dust, indoor air, and in streams, sewage influents, effluents, and sludge. In humans, TDCPP has been measured in adipose tissue, seminal plasma and breast milk.

TDCPP has been tested for carcinogenicity in two-year studies in male and female Sprague-Dawley rats. Statistically significant increases in the incidence of benign and malignant tumors were observed in both male and female rats:

- In both sexes, the incidences of benign, malignant, and combined malignant and benign liver tumors were significantly increased among TDCPP treated animals.
- Benign kidney tumors were significantly increased in both sexes.
- In males, benign interstitial tumors of the testes were significantly increased.

TDCPP is genotoxic in multiple in vitro studies of bacterial and mammalian cells. It induced mutations in Salmonella and mouse lymphoma cells, induced chromosomal aberrations in mouse lymphoma and Chinese hamster fibroblast cells, and induced sister chromatid exchange (SCE) in mouse lymphoma cells. There is also evidence for DNA binding in mouse kidney, liver and muscle following in vivo exposure.

TDCPP induced malignant cell transformation of Syrian hamster embryo cells in culture.

TDCPP is metabolized to several chemicals identified as carcinogenic by IARC and listed under Proposition 65, namely 1,3-dichloro-2-propanol (1,3-DCP), 3-monochloropropane-1,2-diol (3-MCPD), epichlorohydrin and glycidol. TDCPP is structurally similar to two halogenated phosphate triester carcinogens identified under Proposition 65, tris(2,3-dibromopropyl) phosphate (TDBPP or Tris) and tris(2-chloroethyl) phosphate (TCEP).

Some of these metabolites and structurally similar compounds induce tumors at the same sites as TDCPP – liver, kidney, testes. 1,3-DCP induces liver tumors in rats; glycidol and TDBPP induce liver tumors in mice. 1,3-DCP, 3-MCPD, TDBPP and TCEP induce kidney tumors in rats; TDBPP and TCEP induce kidney tumors in mice. 3-MCPD induces interstitial cell tumors of the testes in rats.
2 INTRODUCTION

2.1 Identity of Tris(1,3-dichloro-2-propyl) phosphate (TDCPP)

Tris(1,3-dichloro-2-propyl) phosphate (TDCPP) is a viscous, colorless liquid at temperatures greater than 27°C. It is soluble in water and most organic solvents (IPCS, 1998). Its structure is given in Figure 1 and physical and chemical characteristics are given below.

![Figure 1. Chemical Structure of TDCPP.](image)

**Molecular Formula:** C$_9$H$_{15}$Cl$_6$O$_4$P  
**Molecular Weight:** 430.91  
**CAS Registry Number:** 13674-87-8  
**IUPAC Systematic Name:** 2-Propanol, 1,3-dichloro-, phosphate (3:1)  
**Synonyms:** TDCPP; TDCP; chlorinated Tris; 2-Propanol, 1,3-dichloro-, phosphate (3:1); Fyrol FR-2; Antiblaze 195®, Tris[2-chloro-1-(chloromethyl)ethyl]phosphate; Tris(1,3-dichloroisopropyl)phosphate  
**Chemical Class:** Phosphate ester  
**Chemical Appearance:** Colorless  
**Melting Point:** 27°C  
**Boiling point:** 236-237°C (at 5 mmHg)  
**Water Solubility:** 7 mg/L (at 24°C)  
**Vapor pressure:** 0.01 mmHg at 30°C  
**Octanol-water coefficient:** LogK$_{OW}$ = 3.65

2.2 Occurrence and Use

TDCPP is produced by the epoxide opening of epichlorohydrin in the presence of phosphorus oxychloride (HSDB, 2001). It is a high production volume chemical, primarily used as an organophosphate flame retardant in flexible polyurethane foams (U.S. EPA, 2006; European Commission, 2009; Levchik and Weil, 2004). Other reported uses are as flame retardants and plasticizers in rigid polyurethane foams,
resins, plastics, textile coatings, and rubber for use in the U.S. and Europe (IPCS, 1998; NRC, 2000). As a flame retardant, TDCPP is an additive, meaning it is not chemically reacted but physically combined with the material being treated.

Most of TDCPP’s current use can be attributed to flexible polyurethane foams for upholstered furniture and automotive products such as seat cushions and headrests (European Commission, 2009). TDCPP was commonly used in children’s sleepwear in the 1970s until manufacturers voluntarily withdrew it in 1977 due to concerns regarding its mutagenicity (CPSC, 1977; IPCS, 1998). More recently, in order to meet California’s upholstered furniture flammability standard, Technical Bulletin 117 (California Bureau of Home Furnishings and Thermal Insulation, 2000), TDCPP has been used as a replacement for the flame retardant pentabromodiphenyl ether (pentaBDE), which was banned in 2006 (California Health and Safety Code, Section 108922). A 2011 study identified TDCPP in more than a third of the 101 baby products analyzed (e.g., car seats, changing table pads) (Stapleton et al., 2011).

The use of TDCPP as an additive flame retardant suggests it may be released from the treated product throughout the product life cycle into the indoor environment (e.g., in dust), leading to human exposure (Marklund et al., 2003; U.S. EPA, 2005; Stapleton et al., 2009). Indeed, TDCPP has been detected in household dust in the U.S. and abroad (Stapleton et al., 2009, Takigami et al., 2009; Marklund et al., 2003; Meeker and Stapleton, 2010).

In a study of 50 homes in Boston, Massachusetts, concentrations of TDCPP in dust were comparable to, and in some cases higher than, concentrations of polybrominated diphenyl ethers, with a geometric mean of 1.89 micrograms per gram (µg/g) of dust (maximum: 56.08 µg/g) (Stapleton et al., 2009). TDCPP was detected in both dust and air samples in a variety of indoor environments such as homes, day care centers, hospital wards and offices in Sweden (Marklund et al., 2003).

TDCPP’s use as a flame retardant and plasticizer for many decades has resulted in widespread distribution in the environment. In a study of 139 streams across the U.S., including California, TDCPP was detected in over half (Kolpin et al., 2002). An analysis of Swedish sewage treatment facilities found detectable concentrations of TDCPP in the influents, effluents and sludge from each of the plants studied (Marklund et al., 2005).

Biomonitoring studies have detected TDCPP in human tissues. In the 1980s, levels were measured in human adipose tissue (maximum of 260 nanograms (ng)/g) (LeBel and Williams, 1983; LeBel et al., 1989) and in human seminal plasma (Hudec et al., 1981). More recently, TDCPP was detected in the lipids of human milk with a median level of 4.3 ng/g and a maximum level of 5.3 ng/g (Sundkvist et al., 2010).

3 DATA ON CARCINOGENICITY

3.1 Carcinogenicity Studies in Humans

An unpublished retrospective cohort cancer mortality study of workers employed at a TDCPP manufacturing plant for the years 1956 to 1980 was conducted by Stauffer
Chemical Company (Stauffer Chemical Company, 1983b, as described by the European Commission, 2009, and ATSDR, 2009). The cohort consisted of 289 workers. Ten deaths were reported in the cohort over the course of the study period. Three deaths due to lung cancer were observed among the ten deaths (deaths from other malignant cancers were observed by the study authors, but not described in the European Commission, 2009, and ATSDR, 2009 reports). When the observed deaths from the study were compared to a similar population of U.S. males, standard mortality ratios (SMR) were higher than expected for all cancers and lung cancer, although p-values were not calculated due to small sample size. The average time-weighted concentration of TDCPP in air within the work environment was assessed at the end of the study period and described as very low (0.4–0.5 μg/m³). The authors concluded that although the SMR from lung cancer was higher than expected, overall there was no evidence linking the lung cancers to TDCPP exposure because all three cases with lung cancer were heavy to moderate cigarette smokers. Small sample size and the inability to account for confounding factors make it difficult to draw conclusions from this study.

3.2 Carcinogenicity Studies in Animals

A review of the scientific literature regarding the carcinogenicity of TDCPP in experimental animals identified one set of studies conducted in rats. Male and female Sprague-Dawley CD rats (60/sex/group) were fed a diet containing TDCPP at concentrations intended to achieve dose rates of 0, 5, 20, or 80 mg TDCPP/kg-day (Bio/dynamics, 1981; Freudenthal and Henrich, 2000). Ten male and female rats from each group were sacrificed after 12 months on the diet for interim evaluation. At 24 months, all remaining surviving animals were sacrificed. At both 12 and 24 months, control and high-dose animals were examined microscopically for lesions in a broad suite of tissues. However, for animals in the low- and mid-dose groups only the liver, kidneys, testes, and adrenal glands were examined microscopically at the 12- and 24-month sacrifices.

Survival among male rats in the high-dose group (80 mg/kg-day) was significantly lower compared to control male rats. Among high-dose male rats, body weights were 20% lower than control animals at the end of the study. Body weights of high-dose male rats were significantly lower than control rats throughout the study. Survival was not significantly affected by TDCPP treatment in female rats at any dose. Body weights of high-dose female rats were also significantly lower that control rats throughout the study, with a similar 20% decrease in body weight observed by the end of the study. Food intake was not affected by treatment in either male or female rats.

Among male rats treated with TDCPP, benign and malignant tumors were seen (see Table 1 below for all tumor incidence data). Statistically significant increases were observed in the high-dose group for hepatocellular adenoma (p < 0.01), hepatocellular carcinoma (p < 0.05), and combined hepatocellular adenoma and carcinoma (p < 0.01) by pairwise comparison with the control group. The incidences across dose groups showed statistically significant positive trends with dose for adenomas (p < 0.001), carcinomas (p < 0.01), and combined adenomas and carcinomas (p < 0.001). Three hepatocellular adenomas were also observed in high-dose male rats at the 12-month interim sacrifice.
Also among male rats treated with TDCPP, statistically significant increases in renal cortical adenomas were increased in both the mid- (p < 0.05) and high-dose groups (p < 0.01) by pairwise comparison with the control group. The incidences across all groups showed a statistically significant positive trend with dose (p < 0.001).

In addition, statistically significant increases in benign interstitial (Leydig) cell tumors of the testes were observed in both the mid- and high-dose male rats by pairwise comparison with the control (p < 0.01). The incidence across all groups showed a statistically significant positive trend with dose (p < 0.001). Three interstitial cell tumors were observed in each of the mid- and high-dose groups at the 12-month interim sacrifice.

Among female rats in the high-dose group treated with TDCPP, statistically significant increases in hepatocellular adenomas (p < 0.05) and combined hepatocellular adenomas and carcinomas (p < 0.01) were observed. The incidences across dose groups showed a statistically significant positive trend with dose for hepatocellular adenomas (p < 0.005), carcinomas (p < 0.05), and combined adenomas and carcinomas (p < 0.001). One hepatocellular adenoma was also observed in high-dose female rats at the 12-month interim sacrifice.

Also among female rats treated with TDCPP, statistically significant increases in renal cortical adenomas were observed in both the mid- and high-dose groups by pairwise comparison with the control group (p < 0.01). The incidences across all groups showed a statistically significant positive trend with dose (p < 0.001).

In addition, statistically significant increases in cortical adenomas of the adrenal gland were observed in high-dose female rats by pairwise comparison with the control group (p < 0.05). The incidences across all groups showed a statistically significant positive trend with dose (p < 0.001). Two malignant adrenal cortical carcinomas were found in the control group and one in the mid-dose group. No treatment related increase in adrenal cortical carcinomas was observed. An increased incidence of combined cortical adenomas and carcinomas was observed in the high dose by pairwise comparison (p < 0.05) and by trend (p < 0.01).

At the 12-month interim sacrifice, five animals with adrenal cortical adenomas were observed in the control group and one in the high dose group of female rats. The presence of animals with tumors in the control group at the interim sacrifice warranted further analysis. If all animals are considered together (i.e., interim, unscheduled, and terminal deaths), the incidence of adrenal cortical adenomas in the high-dose group does not show a statistically significant increase above controls by pairwise comparison, but still shows a statistically significant positive trend with dose (p < 0.01; data not shown). Similarly, combined incidence of adrenal cortical adenomas and carcinomas among all animals (interim, unscheduled, and terminal deaths) are not significantly increased by pairwise comparison, but there is a significant positive trend with dose.

In summary, exposure to TDCPP in male and female rats caused statistically significant increases in tumors at multiple sites. Treatment-related increases in combined benign and malignant liver tumors were observed in both male and female rats. Increased incidences of benign tumors of the kidneys were also observed in both male and female rats. Interstitial cell tumors of the testes were increased in male rats. An increased
Table 1. Tumor Incidences in Male and Female Sprague-Dawley Rats Treated with TCDPP.

<table>
<thead>
<tr>
<th>Organ</th>
<th>Tumor a</th>
<th>Dose group (mg/kg/day)</th>
<th>Trend test (p-value)b</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td><strong>Male rats</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>Hepatocellular adenoma (Interim)a</td>
<td>2/45</td>
<td>7/48</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Hepatocellular carcinoma (Interim)a</td>
<td>1/45</td>
<td>2/48</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Combined hepatocellular adenoma and carcinoma</td>
<td>3/45</td>
<td>9/48</td>
</tr>
<tr>
<td>Kidney</td>
<td>Renal cortical adenoma (Interim)a</td>
<td>1/45</td>
<td>3/49</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Testes</td>
<td>Interstitial cell tumor (Interim)a</td>
<td>7/43</td>
<td>8/48</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Female rats</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>Hepatocellular adenomas (Interim)a</td>
<td>1/49</td>
<td>1/47</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Hepatocellular carcinoma (Interim)a</td>
<td>0/49</td>
<td>2/47</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Combined hepatocellular adenoma and carcinoma</td>
<td>1/49</td>
<td>2/47</td>
</tr>
<tr>
<td>Kidney</td>
<td>Renal cortical adenoma (Interim)a</td>
<td>0/49</td>
<td>1/48</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Adrenal gland</td>
<td>Cortical adenoma (Interim)a</td>
<td>8/48</td>
<td>5/48</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Cortical carcinoma (Interim)a</td>
<td>2/48</td>
<td>0/48</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Combined cortical adenoma and carcinoma</td>
<td>9/48</td>
<td>5/48</td>
</tr>
</tbody>
</table>

a Incidences presented next to tumor types represent the combined incidences from all unscheduled deaths plus the terminal sacrifice at two years (Bio/dynamics, 1981). The 12-month interim sacrifice tumor incidences are not included in the statistical analyses.
b Exact test for linear trend.
c Statistically significant increase in incidence compared to control (p < 0.01, by Fisher’s exact test).
d Statistically significant increase in incidence compared to control (p < 0.05, by Fisher’s exact test).
e Numbers of animals with tumors in the 12-month interim sacrifice groups were calculated by OEHHA by subtracting the combined terminal and unscheduled incidences from the combined terminal, unscheduled, and interim incidences that were presented in Bio/dynamics (1981).
f No statistically significant pairwise comparisons between dosed and control animals were found for adrenal tumors when the incidences from interim sacrifice were combined with the unscheduled and terminal sacrifice incidences; however, the trends for adenomas and combined adenomas and carcinomas were still significant.
incidence of adrenal gland tumors in female rats among terminal and unscheduled deaths was tempered by a finding of these tumors in control animals at the one-year interim sacrifice.

**Non-neoplastic findings**

In addition to the body weight (males and females) and survival (males only) effects noted above, there were several other signs of toxicity from treatment of the rats observed in the TDCPP studies.

Potentially pre-neoplastic lesions were observed in some organs in which tumors occurred. The incidence of altered hepatocellular foci was significantly increased in high-dose female rats following long-term treatment (Bio/dynamics, 1981; p < 0.05, by Fisher's exact test). In high dose male rats they were increased and of borderline statistical significance (p = 0.07). Significant increases in the incidences of hyperplasia of the convoluted tubules of the kidney were observed in both male and female rats (p < 0.05).

TDCPP treatment resulted in significant decreases in the hemoglobin, hematocrit, and total erythrocyte counts among high dose male and female rats (Freudenthal and Henrich, 2000). High dose male and female animals also showed lower serum alkaline phosphatase levels than the control groups. Absolute liver and kidney weights were significantly higher among both mid-and high-dose male rats. Relative weights of kidney, brain, and thyroid were increased among mid- and high-dose male rats and relative liver weight was increased among high-dose male rats. Absolute kidney weights were significantly higher among female rats in the mid- and high-dose groups, while the high-dose group of female rats also showed significant increases in relative weights of liver, brain, and thyroid. Freudenthal and Henrich (2000) also reported the animals showed “a variety of abnormalities in the livers, kidneys, and testes of the treated animals, including discoloration, masses, nodules, and cysts” and that “mid- and high-dose male animals exhibited a higher incidence of small seminal vesicles and testicular enlargement, as compared to control males.”

### 3.3 Other Relevant Data

#### 3.3.1 Genotoxicity

Multiple *in vitro* and *in vivo* studies have investigated the genotoxicity of TDCPP. The findings are presented in Tables 2, 3, and 4 below.

TDCPP’s ability to induce reverse mutations was examined across various strains of *Salmonella typhimurium* and in the yeast *Saccharomyces cerevisiae* in the presence and absence of metabolic activation systems (S9 fraction of rodent liver microsomes). Results are summarized in Table 2. Studies in *Salmonella* strains sensitive in detecting frameshift mutations (TA 97, TA 98, TA 1537, and TA 1538) indicate that TDCPP induces frameshift mutations with or without metabolic activation. TDCPP treatment of *Salmonella* strains TA 100 and TA 1535, sensitive to base-pair substitution mutations, produced mutations with and without S9 metabolic activation. Discrepancies in results between studies of the same strain may be due to the method of metabolic activation.
(Babich, 2006; Gold et al., 1978). Overall, TDCPP induced mutations with and without S9 activation across multiple *Salmonella* strains. TDCPP did not induce mutations in *Saccharomyces cerevisiae*.

In *in vitro* mammalian cell assays for gene mutation, TDCPP gave both positive and negative results (Table 3). TDCPP induced gene mutations in one study in L5178Y mouse lymphoma cells (Inveresk Research International, 1985) and not in another (Brusick et al., 1980). TDCPP was negative for gene mutations in V79 Chinese hamster cells (Soderlund et al., 1985).

TDCPP caused an increase in chromosomal aberrations *in vitro* in mouse lymphoma and Chinese hamster fibroblast cells (Brusick et al., 1980; Ishidate, 1983), but not in Chinese hamster ovary cells (Covance Laboratories Inc., 2004). TDCPP weakly induced sister chromatid exchanges (SCE) in mouse lymphoma cells using two methods of metabolic activation in one set of experiments (Brusick et al., 1980), but not in another (Stauffer Chemical Company, 1977). TDCPP induced a weakly positive response in the *in vitro* rat hepatocyte DNA synthesis (UDS) assay, in the absence, but not in the presence, of phenobarbital induction (Soderlund et al., 1985).

For the most part, *in vivo* genotoxicity assays of TDCPP have been negative (Table 4). Studies in *Drosophila melanogaster* did not result in an increase of sex-linked recessive lethal (SLRL) mutations (Stauffer Chemical Company, 1978). TDCPP did not induce chromosome aberrations in mouse bone marrow or chick embryos, or micronuclei in mouse bone marrow erythrocytes (Brusick et al., 1980; Bloom, 1984, Thomas and Collier, 1985). *In vivo* exposure of rats to TDCPP did not induce UDS in hepatocytes (Cifone, 2005).

In an *in vivo* study designed to evaluate covalent binding, TDCPP readily bound to DNA and proteins in liver, kidney and muscle in mice intravenously treated with TDCPP and sacrificed 6 hours later (Morales and Matthews, 1980).
Table 2. *In Vitro* Genotoxicity Studies in Non-Mammalian Species.

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Strain</th>
<th>Concentrations Tested</th>
<th>Results</th>
<th>Activation System</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Reverse</td>
<td>TA 97</td>
<td>Variable: Upper limit of 10 mg/plate</td>
<td>+</td>
<td>+</td>
<td>Mortelmans <em>et al</em>., 1986</td>
</tr>
<tr>
<td>mutations (Salmonella typhimurium)</td>
<td>TA 98</td>
<td>50–1000 µg/plate</td>
<td>+</td>
<td>NT</td>
<td>Ishidate, 1983*</td>
</tr>
<tr>
<td></td>
<td>TA 98</td>
<td>Variable: Upper limit of 10 mg/plate</td>
<td>+</td>
<td>+</td>
<td>Mortelmans <em>et al</em>., 1986</td>
</tr>
<tr>
<td></td>
<td>TA 98</td>
<td>20–15200 µg/plate</td>
<td>−</td>
<td>−</td>
<td>Safepharm Laboratories Ltd., 1984*; Safepharm Laboratories Ltd., 1985*</td>
</tr>
<tr>
<td></td>
<td>TA 1537</td>
<td>50–1000 µg/plate</td>
<td>+</td>
<td>NT</td>
<td>Ishidate, 1983*</td>
</tr>
<tr>
<td></td>
<td>TA 1537</td>
<td>Variable: Upper limit of 10 mg/plate</td>
<td>+</td>
<td>+</td>
<td>Mortelmans <em>et al</em>., 1986</td>
</tr>
<tr>
<td></td>
<td>TA 1537</td>
<td>20–15200 µg/plate</td>
<td>−</td>
<td>−</td>
<td>Safepharm Laboratories Ltd., 1984*; Safepharm Laboratories Ltd., 1985*</td>
</tr>
<tr>
<td></td>
<td>TA 1538</td>
<td>0, 1, 10 µl/plate</td>
<td>−</td>
<td>−</td>
<td>Prival <em>et al</em>., 1977</td>
</tr>
<tr>
<td></td>
<td>TA 1538</td>
<td>20–15200 µg/plate</td>
<td>−</td>
<td>−</td>
<td>Safepharm Laboratories Ltd., 1984*; Safepharm Laboratories Ltd., 1985*</td>
</tr>
<tr>
<td></td>
<td>TA 100</td>
<td>50-250 µg/plate</td>
<td>+</td>
<td>NT</td>
<td>Brusick <em>et al</em>., 1980</td>
</tr>
<tr>
<td></td>
<td>TA 100</td>
<td>0-1000 µg/plate</td>
<td>−</td>
<td>NT</td>
<td>Brusick <em>et al</em>., 1980</td>
</tr>
<tr>
<td></td>
<td>TA 100</td>
<td>50-250 µg/plate</td>
<td>+</td>
<td>NT</td>
<td>Gold <em>et al</em>., 1978</td>
</tr>
<tr>
<td></td>
<td>TA 100</td>
<td>20-50 µg/plate</td>
<td>±</td>
<td>NT</td>
<td>Ishidate, 1983*</td>
</tr>
<tr>
<td>Endpoint</td>
<td>Strain</td>
<td>Concentrations Tested</td>
<td>Results</td>
<td>Activation System</td>
<td>References</td>
</tr>
<tr>
<td>--------------------------</td>
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<td>---------</td>
<td>-----------------------------------------</td>
<td>---------------------------------------------------------------------------</td>
</tr>
<tr>
<td></td>
<td>TA 100</td>
<td>0, 50, 125, 500, 750, 1000 µg/plate</td>
<td>±</td>
<td>PB-induced mouse S9</td>
<td>Lynn et al., 1981</td>
</tr>
<tr>
<td></td>
<td>TA 100</td>
<td>High dose: 500 µg/plate</td>
<td>±</td>
<td>PB-induced rat S9 or PB-induced mouse S9</td>
<td>Majeska and Matheson, 1983</td>
</tr>
<tr>
<td></td>
<td>TA 100</td>
<td>Variable: Upper limit of 10 mg/plate</td>
<td>+</td>
<td>Not described</td>
<td>Mortelmans et al., 1986</td>
</tr>
<tr>
<td></td>
<td>TA 100</td>
<td>0-300 µmole/plate</td>
<td>+</td>
<td>PCB-induced rat S9</td>
<td>Nakamura et al., 1979</td>
</tr>
<tr>
<td></td>
<td>TA 100</td>
<td>20 – 15200 µg/plate</td>
<td>−</td>
<td>Not described</td>
<td>Safepharm Laboratories Ltd., 1984*; Safepharm Laboratories Ltd., 1985*</td>
</tr>
<tr>
<td></td>
<td>TA 100</td>
<td>50, 250, 500, 1000 µg/plate</td>
<td>+</td>
<td>PB-induced rat S9</td>
<td>Soderlund et al., 1985</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>−</td>
<td>PB-induced rat hepatocyte monolayer activation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TA100</td>
<td>0.98 – 500 µg/plate</td>
<td>±</td>
<td>PCB- induced rat S9</td>
<td>Stauffer Chemical Company, 1983a*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>±</td>
<td>PB- induced mouse S9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TA 1535</td>
<td>0 – 50 µg/plate</td>
<td>−</td>
<td>PCB-induced rat S9</td>
<td>Brusick et al., 1980</td>
</tr>
<tr>
<td></td>
<td>TA 1535</td>
<td>50– 1000 µg/plate</td>
<td>+</td>
<td>Not described</td>
<td>Ishidate, 1983*</td>
</tr>
<tr>
<td></td>
<td>TA 1535</td>
<td>0-300 µmole/plate</td>
<td>+</td>
<td>PCB-induced rat S9</td>
<td>Nakamura et al., 1979</td>
</tr>
<tr>
<td></td>
<td>TA 1535</td>
<td>Variable: Upper limit of 10 mg/plate</td>
<td>+</td>
<td>PCB-induced rat S9</td>
<td>Mortelmans et al., 1986</td>
</tr>
<tr>
<td></td>
<td>TA 1535</td>
<td>20 – 15200 µg/plate</td>
<td>−</td>
<td>Not described</td>
<td>Safepharm Laboratories Ltd., 1984*; Safepharm Laboratories Ltd., 1985*</td>
</tr>
<tr>
<td>Reverse mutations (Saccharomyces cerevisiae)</td>
<td>Strain S4</td>
<td>1.5 – 7565 µg/plate</td>
<td>−</td>
<td>Not described</td>
<td>Stauffer Chemical Company, 1976*; Stauffer Chemical Company, 1977*</td>
</tr>
</tbody>
</table>

+ = positive result; − = negative result; ± = weakly positive result
NT= not tested; S9= supernatant fraction from liver homogenate; PB = phenobarbital; PCB = polychlorinated biphenyls
* As reported in European Commission (2009).
Table 3. In Vitro Genotoxicity Studies in Mammalian Species.

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Assay System</th>
<th>Conc. Tested</th>
<th>Results</th>
<th>Activation System</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gene mutations</strong></td>
<td>L5178Y mouse lymphoma cells (forward mutation at Tk locus)</td>
<td>0 – 0.07 µl/ml</td>
<td>−</td>
<td>−</td>
<td>Brusick et al., 1980</td>
</tr>
<tr>
<td></td>
<td>L5178Y mouse lymphoma cells (forward mutation at Tk locus)</td>
<td>1.25 – 60 µg/ml; 10 – 120 µg/ml</td>
<td>+</td>
<td>−</td>
<td>Inveresk Research International, 1985*</td>
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<td></td>
<td>V79 Chinese hamster cells (point mutation)</td>
<td>0.02 mM high dose</td>
<td>−</td>
<td>NT</td>
<td>Soderlund et al., 1985</td>
</tr>
<tr>
<td><strong>Chromosomal aberrations</strong></td>
<td>L5178Y mouse lymphoma cells</td>
<td>0.05 – 0.1 µl/ml</td>
<td>+ ±</td>
<td>PCB-induced mouse S9</td>
<td>Brusick et al., 1980</td>
</tr>
<tr>
<td></td>
<td>Chinese hamster fibroblast cells</td>
<td>Not reported</td>
<td>+</td>
<td>NT</td>
<td>Not described</td>
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<tr>
<td></td>
<td>Chinese hamster ovary cells</td>
<td>6.78 – 1000 µg/ml</td>
<td>−</td>
<td>−</td>
<td>Covance Laboratories Inc., 2004*</td>
</tr>
<tr>
<td><strong>Sister chromatid exchanges (SCE)</strong></td>
<td>L5178Y mouse lymphoma cells</td>
<td>0.004 – 0.072 µg/ml</td>
<td>± ±</td>
<td>PCB-induced mouse S9</td>
<td>Brusick et al., 1980</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>± ±</td>
<td>PB-induced mouse S9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>L5178Y mouse lymphoma cells</td>
<td>0.0047 – 0.072 µl/ml</td>
<td>−</td>
<td>NT</td>
<td>Stauffer Chemical Company, 1977*</td>
</tr>
<tr>
<td><strong>Unscheduled DNA synthesis</strong></td>
<td>Rat hepatocytes</td>
<td>0.025, 0.05, 0.10 mM</td>
<td>−</td>
<td>±</td>
<td>Soderlund et al., 1985</td>
</tr>
</tbody>
</table>

+= positive result; − = negative result; ± = weakly positive result
NT = not tested; S9 = supernatant fraction from liver homogenate; PB = phenobarbital; PCB = polychlorinated biphenyls
*As reported in European Commission (2009).
Table 4. *In Vivo* Genotoxicity Studies.

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Assay System</th>
<th>Conc. Tested</th>
<th>Results</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex-linked recessive lethal (SLRL) mutations</td>
<td><em>Drosophila melanogaster</em></td>
<td>2.5%, 25% TDCPP</td>
<td>−</td>
<td>Stauffer Chemical Company, 1978*</td>
</tr>
<tr>
<td>Chromosomal aberrations</td>
<td>CD-1 mouse bone marrow</td>
<td>0.05, 0.17, or 0.5 mL/kg for 1 or 5 days</td>
<td>−</td>
<td>Brusick <em>et al.</em>, 1980</td>
</tr>
<tr>
<td></td>
<td>Chick embryo/neonate</td>
<td>50 – 100 µl/embryo</td>
<td>−</td>
<td>Bloom, 1984</td>
</tr>
<tr>
<td>Micronuclei</td>
<td>CFLP mouse bone marrow erythocytes</td>
<td>200, 630, 2000 mg/kg</td>
<td>−</td>
<td>Thomas and Collier, 1985**</td>
</tr>
<tr>
<td>Unscheduled DNA synthesis</td>
<td>Rat hepatocytes</td>
<td>500, 1000, 2000 mg/kg</td>
<td>−</td>
<td>Cifone, 2005**</td>
</tr>
<tr>
<td>DNA binding assay</td>
<td>CD-1 mouse liver, kidney and muscle</td>
<td>94.4 µmol/kg</td>
<td>+</td>
<td>Morales and Matthews, 1980</td>
</tr>
</tbody>
</table>

+ = positive result; − = negative result; ± = weakly positive result

* As reported in European Commission (2009).
** As reported in Babich (2006).

### 3.3.2 In Vitro Transformation Studies

TDCPP was tested in *in vitro* cell transformation assays using BALB/c 3T3 cells and Syrian hamster embryo (SHE) cells (see Table 5 below). These assays are designed to detect a change in growth pattern of fibroblasts that is indicative of loss of contact inhibition, a phenotype that is characteristic of cancer cells.

TDCPP did not induce transformed foci in the BALB/c 3T3 cells (Brusick *et al.*, 1980), but was positive in SHE cells in two separate experiments (Soderlund *et al.*, 1985). In the first SHE cell experiment, 20 µM TDCPP resulted in a transformation frequency of 1.85%. In the second experiment, 30 µM TDCPP induced a transformation frequency of 1.35%. A transformation frequency greater than one percent was considered by the authors to be a positive response.
### Table 5. *In Vitro* Cell Transformation Assays.

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Assay System</th>
<th>Conc. Tested</th>
<th>Results</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphological transformation</td>
<td>BALB/c 3T3 cells</td>
<td>0.02 – 0.312 µl/ml</td>
<td>−</td>
<td>Brusick <em>et al.</em>, 1980</td>
</tr>
<tr>
<td></td>
<td>Syrian hamster embryo cells</td>
<td>Control, 20 µM</td>
<td>+</td>
<td>Soderlund <em>et al.</em>, 1985</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Control, 10 µM, 30 µM</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

+ = positive result; − = negative result; ± = weakly positive result

### 3.3.3 Pharmacokinetics and Metabolism

TDCPP is readily absorbed following dermal application and oral administration of $^{14}$C-labeled compound to Sprague-Dawley rats (Nomeir *et al.*, 1981). More than 90% of an oral dose of TDCPP was absorbed within 24 hours of administration to rats. Oral dosing or dermal application of TDCPP resulted in rapid distribution through the blood and to the liver, lung, kidney, adipose tissue and muscle. The half-life for clearance from various tissues ranged from 1.5 to 5.4 hours. TDCPP is also reported to be well absorbed from dermal application to rabbit skin (Ulsamer *et al.*, 1980). Rabbit liver and kidney were also reported to accumulate the highest levels of radiolabeled TDCPP.

The elimination of TDCPP from Sprague-Dawley rats administered propyl-$^{1,3}$-14C-labeled TDCPP has also been reported in several studies. Within 10 days, 47% of radioactivity from an applied dose of TDCPP was found in the urine, with less than half that amount found in feces (−21%) (Nomeir *et al.*, 1981). The finding of substantial levels of radiolabeled compound in bile relative to feces (~27% within four hours), suggests that a portion of that present in bile was subsequently reabsorbed from the gastrointestinal tract. Approximately 20% of the applied intravenous dose was eliminated as carbon dioxide in exhaled air (Nomeir *et al.*, 1981). In other studies, approximately 98% of an oral dose of $^{14}$C-labeled TDCPP administered to Wistar rats was eliminated after seven days, with radioactivity appearing in urine (~43%), feces (~39%), and expired air (~16%) (Minegishi *et al.*, 1988). Similarly, Lynn *et al.* (1981) report that 92% of an intravenous dose of propyl-$^{1,3}$-14C-labeled TDCPP administered to Sprague-Dawley rats was excreted within five days in urine (~54%), feces (~16%), and expired air (22%).

In the Nomeir *et al.* studies, less than one percent of the applied intravenous dose was eliminated intact as TDCPP after 24 hours. Isolation and identification of urinary metabolites was carried out by acidification, drying, then reaction with diazomethane, followed by thin-layer chromatography (isolation), then extraction and high-performance liquid chromatography (HPLC) analysis (identification). Analysis of urine collected from rats up to 120 hours following treatment showed the diester, bis(1,3-dichloro-2-propyl) phosphate (BDCPP), to be the primary metabolite (67%), with much of the balance an unidentified polar metabolite (see Figure 2) (Nomeir *et al.*, 1981). Trace amounts of the monoester, 1,3-dichloro-2-propyl phosphate, and unmetabolized TDCPP were also found in the urine (0.29 and 0.45%, respectively).
In the Lynn et al. (1981) studies, urine from rats administered TDCPP intravenously was analyzed for metabolites by gas chromatographic-electron impact-mass spectroscopy. Briefly, urine samples were extracted with ether, acidified, and re-extracted. The aqueous residue was dissolved in pyridine and N,O-bis-(trimethylsilyl) trifluoroacetamide with trimethylchlorosilane to produce derivatives of the possible metabolites. The monotrimethylsilyl derivative of BDCPP was identified, accounting for 63% of the radioactivity present in the urine (Lynn et al., 1981).

Lynn et al. also evaluated metabolites of rats treated either intraperitoneally or intravenously with TDCPP, creating both trimethylsilyl and methylation derivatives for analysis by HPLC and gas chromatography mass spectrometry (GC/MS) following extraction (Lynn et al., 1981). BDCPP was identified in the urine from the i.p. studies, as well as in urine, feces, and bile from the i.v. administration studies. A methylated derivative of the monoester, 1,3-dichloro-2-propyl phosphate (MDCPP), was also identified in urine and bile. 1,3-Dichloro-2-propanol (1,3-DCP) was also identified as a urinary metabolite by chloroform extraction of urine followed by GC/MS analysis (no derivatization step).

Ulsamer et al. reported 1,3-DCP as the only metabolite detected in the urine of TDCPP-treated animals (rats and rabbits; Ulsamer et al., 1980). Experimental details were not provided.

In vitro studies by Nomeir et al. (1981) examined the ability of various rat liver fractions and rat blood plasma to metabolize TDCPP. Soluble liver fractions (both 10,000g and 100,000g supernatants) were able to metabolize TDCPP, and this was true to a lesser extent for microsomal and mitochondrial fractions. Rat blood plasma had relatively weak ability to metabolize TDCPP. Metabolism by liver fractions was enhanced by the addition of either glutathione or NADPH. In microsomal fractions, NADPH substantially increased the metabolism of TDCPP. Microsomal metabolism was decreased by the addition of SKF 525A, an inhibitor of cytochrome P450 mixed function oxidase activity.

Several products of metabolism were identified by in vitro reaction of TDCPP with microsomal fractions of male rat liver (Nomeir et al., 1981). Metabolites were isolated using silica gel plates that were then identified using HPLC. The primary metabolites identified from this in vitro system were 1,3-DCP, 3-MCPD [3-chloro-1,2-propanediol], and BDCPP, as well as unknown metabolites. 3-MCPD were identified by chromatography, while 1,3-DCP was identified following methylation or acetylation, then thin-layer chromatography and HPLC. BDCPP, 3-MCPD, and the unknown metabolites increased over time in this system, though levels of 1,3-DCP remained somewhat steady. The authors hypothesized that this was due to the conversion of 1,3-DCP to 3-MCPD. Neither 3-MCPD nor 1,3-DCP was detected in the urine of TDCPP-exposed rats in the in vivo Nomeir et al. studies. The authors hypothesized that these metabolites identified in the in vitro studies were further metabolized and released (or reincorporated by other metabolic processes) as carbon dioxide before they could be excreted in vivo.
Soluble fraction metabolism in vitro was increased by the addition of glutathione. The one major metabolite from this reaction was tentatively identified as glutathione-conjugated TDCPP. This was based on evidence that this metabolite was ninhydrin-positive, indicating the presence of an unprotected amine-containing group, and heating the metabolite produced two breakdown products, BDCPP, and another ninhydrin-positive product.

The metabolism of two TDCPP metabolites, 1,3-DCP and 3-MCPD, was recently characterized (see Figure 3 below) (OEHHA, 2010a; OEHHA, 2010b). 1,3-DCP can be metabolized by two main pathways, one leading directly to the formation of 1,3-dichloroacetone, a mutagen and skin tumor initiator. The other pathway leads to the formation of epichlorohydrin, a genotoxic carcinogen. Epichlorohydrin can either be conjugated with glutathione then further converted to a mercapturic acid or it can be metabolized to 3-MCPD. 3-MCPD can be metabolized to glycidol, another genotoxic carcinogen, or to β-chlorolactaldehyde. β-Chlorolactaldehyde can form either 1,2-propanediol or oxalic acid. Glycidol can either be conjugated with glutathione then further converted to a mercapturic acid or it can be metabolized to glycerol.

Diester phosphate formation in urine has been found to occur in rats from metabolism of another halogenated phosphotriester compound, tris(2,3-dibromopropyl) phosphate (Lynn et al., 1980). Early studies of the urine of rats and mice administered tri-alkyl phosphate compounds with simple alkyl groups, such as trimethyl-, triethyl-, tri-n-propyl-, tri-isopropyl-, and tri-n-butylphosphate, identified the presence of diesters (Jones, 1970). Little mono-ester was observed in the urine in the Jones study. Diester
phosphate compounds including bis(2-chloroethyl)-, diphenyl-, di-\textit{m}-cresyl-, and di-\textit{p}-cresyl-, bis(2-chloropropyl)-, and di-\textit{n}-butyl phosphate have been detected in human urine (Schindler et al., 2009a; Schindler et al., 2009b). These are likely metabolites resulting from exposure to the corresponding phosphotriester flame retardants.

**Figure 3. Metabolism of 1,3-DCP and 3-MCPD.**

In an early publication that addressed the subject of TDCPP’s metabolism, Gold et al. (1978), hypothesized several possible metabolites and mechanisms based on the similarities to other phosphotriester compounds. Oxidative dealkylation was proposed to produce 1,3-dichloropropanone [1,3-dichloroacetone] with subsequent 1,3-DCP formation. Phosphotriester hydrolase acting on TDCPP was proposed to produce 1,3-DCP directly. Glutathione S-transferases were proposed to result in the formation of glutathione chloro-thio-ethers. Lynn et al. (1980) hypothesized that three enzyme systems are capable of cleaving ester bonds of organophosphorus alkyl triesters: mixed function oxidase, hydrolase, and glutathione-S-alkyl transferase.
The overall evidence from *in vitro* and *in vivo* studies, along with similarities to evidence from related compounds, suggests that multiple metabolic systems may play a role in the metabolism of TDCPP. The phosphodiester metabolite is the most prevalent urinary metabolite, though 1,3-DCP and the monoester have also been detected in rats and rabbits (1,3-DCP only). *In vitro* studies report production of 1,3-DCP and 3-MCPD from liver homogenate fractions. Differences in experimental methods of detection or rapid metabolism to further breakdown products may explain the lack of detection of products of the moiety cleaved from the phosphotriester in *in vivo* systems.

### 3.3.4 Animal Tumor Pathology

TDCPP significantly increased the incidence of combined benign and malignant liver tumors in male and female rats, benign renal tumors in male and female rats, and testicular interstitial cell tumors in male rats. An increase in benign adrenal tumors was observed in female rats, but this increase was not statistically significant by pairwise comparison when tumors observed at the 12-month sacrifice were included (Bio/dynamics, 1981; Freudenthal and Henrich, 2000).

The liver tumors observed in treated male and female rats were identified as neoplastic nodules and hepatocellular carcinomas in the original report (Bio/dynamics, 1981). The more recent publication of these studies' results in the open literature refers to the nodules as hepatocellular adenomas (Freudenthal and Henrich, 2000), consistent with current pathology nomenclature. Hepatocellular adenomas and carcinomas arise from the same cell type, and adenomas can progress to carcinomas. For this reason, these two tumor phenotypes are aggregated when evaluating study results (IARC, 2006; McConnell *et al.*, 1986).

The benign kidney tumors observed in treated male and female rats were identified as “renal cortical tumors” in the original report (Bio/dynamics, 1981), and as “renal cortical adenomas” in the more recent publication of these studies' results (Freudenthal and Henrich, 2000). These proliferative lesions of the renal cortex tend to be characterized currently as renal cell adenomas. While no malignant renal cell carcinomas were observed in these studies, renal cell adenomas are known to progress to carcinomas.

Testicular interstitial cell tumors, also referred to as Leydig cell tumors, were observed in male Sprague-Dawley rats. Leydig cells are located in the interstitium of the testis, between the seminiferous tubules. There is a continuum of Leydig cell proliferative response, ranging from hyperplasia to adenomas and carcinomas (Boorman *et al.*, 1990). Differential diagnosis is based on size of the lesion. Leydig cell adenomas and carcinomas are aggregated for carcinogen identification (IARC, 2006; McConnell *et al.*, 1986). In Sprague-Dawley rats, the spontaneous incidence of Leydig cell tumors is generally low (~1% incidence).

The benign adrenal gland tumors observed in treated female rats were identified as “adrenal cortical adenomas” by Freudenthal and Henrich (2000). While no increases in malignant adrenal cortical tumors were observed in the female rats, the adenomas are considered to have the potential to progress from benign to malignant phenotypes (Duprat *et al.*, 1990).
3.3.5 Structure-Activity Comparisons

TDCPP is a halogenated phosphate triester that shares structural similarity with several other compounds. TDCPP’s metabolites also present concerns for potential carcinogenicity.

TDCPP Metabolites

Several compounds that are potential products of the metabolism of TDCPP are known to cause cancer (see Figure 3 and Table 6).

1,3-DCP, a metabolite of TDCPP detected in rat and rabbit urine, is a chlorinated three-carbon alcohol that is further metabolized to 3-MCPD via the formation of epichlorohydrin. 1,3-DCP induced tumors in male and female rats (kidney, liver, tongue, thyroid) and is genotoxic in \textit{in vitro}, but not \textit{in vivo} assays (OEHHA, 2010a).

3-MCPD, a metabolite of 1,3-DCP, and therefore also a metabolite of TDCPP\textsuperscript{3}, is a chlorinated three-carbon alcohol (OEHHA, 2010b). 3-MCPD induced tumors in male and female rats (kidney, Leydig cell tumors of testes, mammary gland), and is genotoxic in \textit{in vitro}, but not \textit{in vivo} assays.

Epichlorohydrin is a chlorinated three-carbon epoxide compound that is a direct metabolite of 1,3-DCP and an intermediate in the formation of 3-MCPD. Epichlorohydrin is carcinogenic in male and female rats (foregut, nasal cavity) and male mice (lung) and is genotoxic \textit{in vitro} without metabolic activation and in several \textit{in vivo} assays (ILS, 2005; IARC, 1999).

Another direct metabolite of 1,3-DCP is 1,3-dichloroacetone (1,3-DCA). 1,3-DCA has not been tested in long-term carcinogenesis studies, but it has been shown to be a skin tumor initiator in SENCAR mice and is positive in a wide range of \textit{in vitro} and \textit{in vivo} genotoxicity assays. These include observations of induction of mutations in \textit{S. typhimurium}, with and without S9 metabolic activation, and production of micronuclei in peripheral erythrocytes of the newt, \textit{Pleurodeles waltl} (IARC, 1995).

Glycidol is a three-carbon epoxide compound that is a metabolite of 1,3-DCP, epichlorohydrin, and 3-MCPD. Glycidol is carcinogenic in both sexes of rats and mice, inducing tumors at multiple sites, and is genotoxic \textit{in vitro} without metabolic activation and \textit{in vivo} (IARC, 2000).

The primary metabolite of TDCPP found in the urine of exposed animals is the diester BDCPP. This compound has not been tested for carcinogenicity in experimental animals. Limited testing in \textit{S. typhimurium in vitro} has provided no evidence for mutagenicity.

Chemicals Structurally-Related to TDCPP

Tris(2,3-dibromopropyl) phosphate (TDBPP; Tris), a brominated analogue of TDCPP, is a phosphate triester that is halogenated with bromine instead of chlorine (see Table 6 below). TDBPP is carcinogenic in both sexes of rats and mice, inducing tumors at multiple sites in mice, and is genotoxic \textit{in vitro} and \textit{in vivo} (IARC, 1999).

\textsuperscript{3} Detected following \textit{in vitro} incubation of rat liver homogenate fractions with TDCPP (Nomeir \textit{et al.}, 1981).
Tris(2-chloroethyl) phosphate (TCEP) is a chlorinated phosphate triester. TCEP induces tumors in both sexes of rats and mice, inducing tumors at multiple sites in rats, and is genotoxic in vitro and in vivo (IARC, 1999).

Tris(1-chloro-2-propyl) phosphate (TCPP) is another chlorinated phosphate triester. TCPP has not been tested in long-term studies for carcinogenicity in experimental animals. TCPP is genotoxic in in vitro, but not in vivo assays (European Commission, 2008).

Structure-Activity Summary

The compounds discussed here are metabolites of TDCPP or are structurally similar to TDCPP. Several of the compounds included in Table 6 have positive carcinogenicity data in rodent studies and are listed under Proposition 65 as causing cancer and/or are classified by IARC as Group 2A or Group 2B carcinogens (i.e., 1,3-DCP, 3-MCPD, epichlorohydrin, glycidol, TDBPP, TCEP). Most of the compounds included in Table 6 induce tumors at multiple sites, and in most cases in more than one sex/species. Liver and/or kidney tumors were induced by TDCPP and several TDCPP metabolites (i.e., 1,3-DCP, 3-MCPD, glycidol) and structurally similar halogenated phosphate triesters (i.e., TDBPP, TCEP). Interstitial cell tumors of the testes were induced by TDCPP and 3-MCPD. All of the compounds in Table 6, except BDCPP, have positive results in genotoxicity assays performed in vitro. Of the compounds in Table 6 tested for in vivo genotoxicity, all but three, 1,3-DCP, 3-MCPD, and TCPP, have some positive results.
Table 6. Structure-Activity Comparisons for TDCPP and its Metabolites.

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Target Tumor Sites</th>
<th>Genotoxicity</th>
<th>Cancer Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chemical</strong></td>
<td><strong>Mice</strong></td>
<td><strong>Rats</strong></td>
<td><strong>In vitro</strong></td>
</tr>
<tr>
<td>TDCPP</td>
<td>Not tested</td>
<td>Males: Liver, kidney, testes Females: Liver, kidney, adrenal gland</td>
<td><strong>In vitro</strong>: positive In vivo: positive (mouse kidney, liver and muscle DNA binding) and negative (Drosophila SLRL, mouse bone marrow and chick embryo CA, mouse MN, rat UDS)</td>
</tr>
<tr>
<td>Metabolized to: BDCPP, 1,3-DCP, and 3-MCPD, among others</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metabolites of TDCPP</td>
<td>Bis(1,3-dichloro-2-propyl)phosphate (BDCPP)¹</td>
<td>Not tested</td>
<td>Not tested</td>
</tr>
<tr>
<td>Metabolite of: TDCPP</td>
<td>¹Metabolite of: TDCPP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1,3-DCP²</td>
<td>Not tested</td>
<td>Males: liver, kidney, tongue, thyroid Females: liver, tongue, thyroid</td>
<td><strong>In vitro</strong>: positive In vivo: negative (Drosophila wing spot mutation, rat bone marrow MN, rat UDS)</td>
</tr>
<tr>
<td>Metabolized to: 1,3-dichloroacetone; epichlorohydrin; 3-MCPD; glycidol; among others</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemical</td>
<td>Target Tumor Sites</td>
<td>Genotoxicity</td>
<td>Cancer Classification</td>
</tr>
<tr>
<td>-------------------</td>
<td>-------------------</td>
<td>------------------------------------------------------------------------------</td>
<td>-----------------------</td>
</tr>
</tbody>
</table>
| **3-MCPD**<sup>2</sup> |                   | **Males**: kidney, testes, mammary  
**Females**: kidney | Listed  
(2B (Grosse et al., 2011)) |
| ![3-MCPD](image) |                   | *In vitro*: positive  
*In vivo*: negative (*Drosophila* wing spot mutation assay, dominant lethal assay in mice and rats, bone marrow MN in mice and rats, UDS in rats, DNA damage (comet assay) in rats) |                       |
| Metabolite of: 1,3-DCP & epichlorohydrin  
Metabolized to: glycidol; among others |                   | **Males**: forestomach, nasal cavity  
**Females**: forestomach |                       |
| **Epichlorohydrin**<sup>2</sup> |                   | **Males**: liver, lung, mammary, skin, thyroid, subcutis, Harderian gland, forestomach  
**Females**: mammary, subcutis, Harderian gland, uterus | Listed  
(Group 2A<sup>4</sup> (1999)) |
| ![Epichlorohydrin](image) |                   | **Males**: thyroid, mammary, tunica vaginalis, brain, forestomach, intestine, skin, Zymbal’s gland  
**Females**: mouth/tongue, mammary, brain, forestomach, leukemia, clitoral gland |                       |
| Metabolite of: 1,3-DCP  
Metabolized to: 3-MCPD; among others |                   | **Males**: lung  
**Females**: forestomach |                       |
| **Glycidol**<sup>2</sup> |                   | **Males**: lung  
**Females**: mammary, subcutis, Harderian gland, uterus | Listed  
(Group 2A (2000)) |
| ![Glycidol](image) |                   | **Males**: liver, lung, mammary, skin, thyroid, subcutis, Harderian gland, forestomach  
**Females**: mammary, subcutis, Harderian gland, uterus |                       |
<table>
<thead>
<tr>
<th>Chemical</th>
<th>Target Tumor Sites</th>
<th>Genotoxicity</th>
<th>Cancer Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,3-Dichloroacetone (1,3-DCA; 1,3-Dichloropropanone)⁵</td>
<td>Mice: Not tested</td>
<td>Not tested</td>
<td>Prop. 65</td>
</tr>
<tr>
<td></td>
<td>Rats: Not tested</td>
<td>In vitro: positive (newt MN)</td>
<td>Not evaluated</td>
</tr>
<tr>
<td></td>
<td>Metabolite of: 1,3-DCP</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Skin tumor initiator</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1,3-Dichloroacetone (1,3-DCA; 1,3-Dichloropropanone)⁵</td>
<td>In vitro: positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>In vivo: positive (newt MN)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Chemicals Structurally-Related to TDCPP**

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Target Tumor Sites</th>
<th>Genotoxicity</th>
<th>Cancer Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tris(2,3-dibromopropyl) phosphate (TDBPP, Tris)</td>
<td>Males: kidney, lung, forestomach</td>
<td>In vitro: positive (Salmonella mutations, V79 Chinese hamster lung cell mutations, Chinese hamster lung cells SCE, rat liver and testicular cell DNA strand breaks, rat kidney and liver DNA binding, SHE and C3H mouse cell transformation)</td>
<td>Listed</td>
</tr>
<tr>
<td></td>
<td>Females: liver, lung, forestomach, skin, oral cavity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tris(2,3-dibromopropyl) phosphate (TDBPP, Tris)</td>
<td>Males: kidney, thyroid, leukemia, brain</td>
<td>In vitro: positive (Salmonella mutations, Chinese hamster lung V79 cells SCE, SHE and C3H mouse cell transformation)</td>
<td>Listed</td>
</tr>
<tr>
<td></td>
<td>Females: kidney, thyroid, brain</td>
<td>In vivo: positive (rat dominant lethal)</td>
<td></td>
</tr>
</tbody>
</table>

Tris(2-chloroethyl) phosphate (TCEP)⁶

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Target Tumor Sites</th>
<th>Genotoxicity</th>
<th>Cancer Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tris(2-chloroethyl) phosphate (TCEP)⁶</td>
<td>Males: kidney (marginal increase)</td>
<td>In vitro: positive (Salmonella mutations, Chinese hamster lung V79 cells SCE, SHE and C3H mouse cell transformation)</td>
<td>Listed</td>
</tr>
<tr>
<td></td>
<td>Females: Harderian gland (marginal increase)</td>
<td>In vivo: positive (rat dominant lethal)</td>
<td></td>
</tr>
<tr>
<td>Tris(2-chloroethyl) phosphate (TCEP)⁶</td>
<td>Males: kidney, thyroid, brain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chemical</td>
<td>Target Tumor Sites</td>
<td>Genotoxicity</td>
<td>Cancer Classification</td>
</tr>
<tr>
<td>----------</td>
<td>-------------------</td>
<td>--------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>Tris(1-chloro-2-propyl) phosphate (TCPP; Tris(2-chloro-1-methylethyl) phosphate)</td>
<td></td>
<td></td>
<td>Prop. 65</td>
</tr>
<tr>
<td></td>
<td>Not tested</td>
<td>Not tested</td>
<td>In vitro: positive (<em>Salmonella</em> and mouse lymphoma cell mutations, mouse BALB/c 3T3 cell transformation)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>In vivo: negative (mouse MN, rat bone marrow CA, UDS, DNA damage [comet assay] in rat liver)</td>
</tr>
</tbody>
</table>

CA = chromosomal aberrations; MN = micronuclei; SCE = sister chromatid exchange; SLRL = sex-linked recessive lethal; UDS = unscheduled DNA synthesis.

1 Lynn *et al.*, 1981
2 As reviewed in OEHHA (2010a)
3 IARC Group 2B: Possibly carcinogenic to humans
4 IARC Group 2A: Probably carcinogenic to humans
5 As reported in the IARC review of 1,2,3-trichloropropane (IARC, 1995)
7 IARC Group 3: Not classifiable as to its carcinogenicity to humans
8 As reviewed by European Commission (2008)
4 MECHANISMS

TDCPP induced benign and malignant tumors in the liver and benign tumors of the kidney and testes in Sprague-Dawley rats, with evidence of a positive trend in benign tumors of the adrenal gland in females. The mechanism by which TDCPP induces tumors at these various tissues is unknown. However, a body of evidence suggests that TDCPP is likely to be carcinogenic by a genotoxic mechanism or mechanisms.

TDCPP tested positive in a variety of genotoxicity assays (described in Section 3.3.1 Genotoxicity above). Evidence for genotoxicity includes positive tests for mutagenicity in multiple strains of *Salmonella* and in mouse lymphoma cells, chromosomal aberrations in mouse lymphoma and hamster fibroblast cells, SCE in mouse lymphoma cells, and UDS in rat hepatocytes exposed *in vitro*. There is also evidence for DNA binding in mouse liver, kidney and muscle following *in vivo* exposure. Further, TDCPP is metabolized to several genotoxic and carcinogenic metabolites, including 1,3-DCF, epichlorohydrin, 3-MCPD, and glycidol (see Section 3.3.3 Pharmacokinetics and Metabolism above).

Potentially pre-neoplastic lesions were observed in some organs in which tumors occurred. The incidence of altered hepatocellular foci was significantly increased in high-dose female rats (*p* < 0.05, by Fisher’s exact test) (Bio/dynamics, 1981), while altered foci were only slightly increased in male rats in the high-dose group (*p* = 0.07). Significant increases in the incidences of hyperplasia of the convoluted tubules of the kidney were observed in both male and female rats (*p* < 0.05). The triggers for these proliferative responses and their relationship to the development of tumors in the liver or kidney are unknown. It is possible that TDCPP causes tumors by more than one mechanism, and different mechanisms may be responsible for the tumors observed in the different tissues.

In summary, while the mechanism(s) of carcinogenic action of TDCPP remain unknown, the available evidence suggests that genotoxicity is involved. Evidence for TDCPP’s genotoxic action includes evidence from a number of *in vitro* test systems, *in vivo* DNA binding studies, metabolism to genotoxic carcinogens, and similarity to two other genotoxic and carcinogenic halogenated phosphate triesters. Other mechanisms, yet to be elucidated, may also be operative.

5 REVIEWS BY OTHER AGENCIES

TDCPP has not been classified as to its potential carcinogenicity by the U.S. EPA, IARC, the U.S. Food and Drug Administration, the National Toxicology Program, or the National Institute for Occupational Safety and Health.

The data relating to the carcinogenicity of TDCPP has, however, been reviewed by several other agencies or organizations:

- The National Research Council, in a report prepared for the Consumer Product Safety Commission, concluded that “[t]he available animal data on TDCPP provide sufficient evidence of carcinogenicity in rats following chronic oral exposure” (NRC, 2000).
A preliminary staff report prepared by the U.S. Consumer Product Safety Commission concluded: “[TDCPP] exposure also induced tumors at multiple doses in the kidneys and liver of both male and female rats. Therefore, TDCP [TDCPP] may be considered a probable human carcinogen based on sufficient evidence in animals … This conclusion is further supported by structural similarity to another animal carcinogen, TRIS. TDCP [TDCPP] and its metabolites were genotoxic in some assays, although the majority of tests were negative.” (Babich, 2006)

A report from the European Union prepared by Rapporteur Member States Ireland and the United Kingdom classified TDCPP as Carcinogen Category 3 (R40), “limited evidence of a carcinogenic effect” (European Commission, 2009).

6 SUMMARY AND CONCLUSIONS

6.1 Summary of Evidence

Chronic exposure to TDCPP significantly increased the incidence of combined benign and malignant liver tumors, and benign tumors of the kidney and testes in two-year dietary studies conducted in male and female Sprague-Dawley CD rats. A positive trend with dose in combined benign and malignant adrenal gland tumors was also observed in female rats.

The following increases in tumors were observed:

Liver tumors
- In male rats, TDCPP significantly increased the incidence of hepatocellular adenomas, hepatocellular carcinomas, and combined adenomas and carcinomas in the high-dose group as compared with the control group.
- In female rats, TDCPP significantly increased the incidence of hepatocellular adenomas and combined adenomas and carcinomas in the high-dose group as compared with the control group.

Kidney tumors
- In male rats, TDCPP significantly increased the incidence of renal cortical adenomas in the mid- and high-dose groups as compared with the control group.
- In female rats, TDCPP significantly increased the incidence of renal cortical adenomas in the mid- and high-dose groups as compared with the control group.

Testicular tumors
- Interstitial cell tumors of the testes were significantly increased among male rats treated with TDCPP (mid- and high-dose groups compared to the control group).

Adrenal gland tumors
- Cortical tumors of the adrenal gland were significantly increased by trend test among female rats treated with TDCPP, including when tumors observed at the 12-month interim sacrifice were included in the analysis. No positive trends in malignant cortical tumors of the adrenal gland were observed, however.
Evidence of TDCPP’s genotoxicity comes from the following non-mammalian and mammalian test systems:

*In vitro:*

- TDCPP induced both base-pair substitution and frameshift mutations in *Salmonella typhimurium* in the presence or absence of exogenous metabolic activation.
- TDCPP induced forward mutations in mouse lymphoma cells.
- TDCPP induced chromosomal aberrations in mouse lymphoma and Chinese hamster fibroblast cells.
- TDCPP induced SCEs in mouse lymphoma cells.
- TDCPP induced unscheduled DNA synthesis in rat hepatocytes.

*In vivo:*

- TDCPP bound to DNA and proteins in mouse liver, kidney and muscle cells.

TDCPP induced malignant transformation of SHE cells in culture.

Metabolites of TDCPP and structurally similar halogenated phosphate triesters present concern regarding the carcinogenicity of TDCPP:

- Multiple metabolites of TDCPP are carcinogens identified by IARC and listed under Proposition 65: 1,3-DCP, 3-MCPD, epichlorohydrin and glycidol. Each are genotoxic *in vitro*. Epichlorohydrin and glycidol are genotoxic *in vivo*.
- TDCPP is structurally similar to the halogenated phosphate triesters TDBPP, TCEP and TCP. TDBPP and TCEP are listed under Proposition 65 as carcinogens and are genotoxic *in vitro* and *in vivo*. TDBPP has been identified by IARC as a carcinogen.
- Several TDCPP metabolites and structurally similar halogenated phosphate triesters induce tumors at the same sites as TDCPP (liver, kidney, testes):
  - 1,3-DCP induces liver tumors in rats; glycidol and TDBPP induce liver tumors in mice
  - 1,3-DCP, 3-MCPD, TDBPP and TCEP induce kidney tumors in rats; TDBPP and TCEP induce kidney tumors in mice
  - 3-MCPD induces testes (interstitial cell) tumors in rats.

### 6.2 Conclusions

Evidence for carcinogenicity of TDCPP comes primarily from two-year diet studies conducted in both sexes of Sprague-Dawley rats. Exposure to TDCPP in male and female rats resulted in statistically significant increases in tumors at multiple sites. In male rats, an increased incidence of benign, malignant and combined benign and malignant liver tumors was observed. Increases in benign tumors of the kidneys and testes were also found in male rats. The incidence of benign and combined malignant
and benign liver tumors was significantly increased in female rats. Benign kidney tumors were also significantly increased in female rats.

Positive findings in multiple in vitro genotoxicity test systems indicate that TDCPP may be carcinogenic through a genotoxic mechanism. TDCPP induced mutations in multiple strains of Salmonella typhimurium and in mouse lymphoma cells. It induced chromosomal aberrations in mouse lymphoma and hamster fibroblast cells, increased the formation of SCE in mouse lymphoma cells, and induced unscheduled DNA synthesis in rat hepatocytes. In an in vivo study, TDCPP bound to DNA and proteins in mouse liver, kidney and muscle. TDCPP also induced malignant transformation of SHE cells in culture.

TDCPP is structurally similar to two halogenated phosphate triester carcinogens identified under Proposition 65 (TDBPP, TCEP) and is metabolized to several chemicals identified as carcinogenic by IARC and listed under Proposition 65 (1,3-DCP, 3-MCPD, epichlorohydrin, glycidol).
7 REFERENCES


Covance Laboratories Inc. (2004). Chromosomal aberrations in chinese hamster ovary (CHO) cells (Unpublished report) [as described by European Commission, 2009].


Exhibit 4
Elevated House Dust and Serum Concentrations of PBDEs in California: Unintended Consequences of Furniture Flammability Standards?

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Studies show higher house dust and body burden levels of PBDE flame retardants in North America than Europe; but little is known about exposure variation within North America, where California’s furniture flammability standard affects PBDE use. We compared dust samples from 49 homes in two California communities with 120 Massachusetts homes and with other published studies. Dust concentrations [median (range)] ng/g] in California homes of BDE-47, -99, and -100 were 2700 (112-107 000), 3800 (102-170 000), and 684 (<MRL-30 900), respectively, and were 4-10 times higher than previously reported in North America. Maximum concentrations were the highest ever reported in indoor dust. We then investigated whether human serum PBDE levels were also higher in California compared to other North American regions by analyzing the 2003–2004 National Health and Nutrition Examination Survey (NHANES), the only data set available with serum from a representative sample of the U.S. population (n = 2040). California residence was significantly associated with nearly 2-fold higher \( \Sigma \)PBDE serum levels [least square geometric mean (LSGM) ng/g lipid, 73.0 vs 38.5 (\( p = 0.002 \))]. Elevated PBDE exposures in California may result from the state’s furniture flammability standards; our results suggest the need for further research in a larger representative sample.

Introduction

Polybrominated diphenyl ethers (PBDEs) are widely used as flame retardants in upholstered furniture and electronics and are released in indoor environments via volatilization or as dust particles (1). PBDEs are ubiquitous globally and have been detected in human blood and tissue, marine mammals, sediments, and virtually any matrix taken from anywhere on the planet (2). Concentrations in environmental and human samples vary internationally, with much higher serum, breast milk, and house dust levels reported in the U.S. compared with Europe (3, 4). Regional variation within the U.S. may result from more stringent furniture flammability standards in California than in other states; however, this possibility has not been evaluated.

Three major PBDE commercial mixtures have been commonly used in consumer products: deca-BDE, octa-BDE, and penta-BDE (5). Penta-BDE has been most often mixed into polyurethane foam (PUF) used in furniture, while octa- and deca-BDE are used in electronics and other plastic products (6). Penta-BDE is typically about 3-5% by weight in treated foam, and is easily liberated into dust because it is not chemically bound to the foam product. Penta-BDE has been used almost exclusively in the U.S (6) and mostly in furniture for sale in California in order to comply with Technical Bulletin 117 (TB117), the state’s 1975 performance-based furniture flammability standard (5, 7). Regional differences may be somewhat lessened, however, because some TB-117-compliant products are distributed nationwide (8), and not all furniture sold in California has complied with the standard (9).

Although the effect of California’s furniture flammability standard on regional variations in PBDE exposures has not been systematically examined, a few studies have reported serum levels in California, and these results may be compared with serum PBDE levels measured in the National Health and Nutrition Examination Survey (NHANES), a cross-sectional sample representative of the U.S. population. Serum PBDE levels in one California family exceeded the 95th percentile for NHANES (10, 11). Separate studies in two groups of California immigrant women—Laotian and Mexican—found serum levels similar to or lower than those of U.S. women in NHANES (11–13).

House dust has been identified as the primary route of exposure for PBDEs (1, 3). An EPA review concluded that 82% of exposure is from incidental ingestion and dermal contact with house dust (3). Wu and colleagues (14) reported that breast milk PBDE levels in 11 women were correlated with their house dust concentrations. While diet may also contribute to human exposure (14), it does not appear to be the major route either in the general population (15) or in high fish-consuming subpopulations (16). Concern about human exposure stems from animal studies that consistently show thyroid disruption and adverse neurodevelopmental and reproductive effects following in utero exposures of PBDEs (17, 18). In addition, structural and mechanistic similarities with PCBs (18, 19), for which extensive human data demonstrate effects on neurodevelopment and other end points (20, 21), suggest the relevance of these endpoints to PBDEs. To date, there are few human health studies of PBDEs, and results are limited and inconsistent (22, 23).

While questions remain about the health effects, the toxicology database has been strong enough that use of penta-BDEs and octa-BDEs was banned by the European Union in 2003; and in 2004, U.S. manufacturers discontinued production of these compounds (24). Currently, 11 states, including California, have banned the use of penta-BDE and octa-BDE; however, the ubiquity of these chemicals combined with the slow replacement time for products previously manufactured with penta- and octa-BDE suggests that a long-term, substantial exposure reservoir will remain for some time despite PBDE phase-outs (25).

In order to investigate whether California flammability standards may result in higher exposures there, we used two distinct data sets to compare penta-BDE concentrations in house dust and in serum in California with the rest of the
U.S. First, we compared new data on house dust concentrations in 49 California homes with concentrations we previously reported for 120 Massachusetts homes (4) and several studies reporting house dust PBDE concentrations in various North American regions. Second, we used data from NHANES to compare serum PBDE levels in California participants and those from other U.S. locations. Currently, no single data set allows for both dust and serum PBDE exposure comparisons on such a large geographic scale. Therefore, we report these findings together because the serum data are most relevant to potential human health outcomes, and the dust data highlight sources of exposure that may contribute to any observed regional differences in serum levels. To our knowledge these regional comparisons provide the first assessment of how California’s unique furniture flammability standard may affect regional differences in PBDE exposures within the United States.

**Experimental Section**

**PBDE Dust Measurements.** As part of the California Household Dust Exposure Study, dust samples were collected from 49 nonsmoking homes in two Northern California communities: Richmond and Bolinas. The research protocol was approved by Brown University’s Institutional Review Board. Richmond is a predominately low income, urban, minority community near transportation corridors and numerous industries including two oil refineries. Bolinas is a rural community north of San Francisco. Sampling protocols and analytical methods have been described in detail elsewhere (4). Briefly, dust samples were collected using a Eureka Mighty-Mite vacuum cleaner attached to a Teflon crevice tool, modified to collect dust into a cellulose thimble (Whatman Inc., Clifton, NJ). Samples were collected by vacuuming the surface of rugs, upholstery, wood floors, windowsills, ceiling fans, and furniture in the primary living areas of the home. BDE-47, -99, and -100 were analyzed using gas chromatography/mass spectrometry in selected ion monitoring mode with a method reporting limit (MRL) of 42.0 ng/g. Additional information on analytical methods and QA/QC is provided in the Supporting Information. Three BDE-100 concentrations below the MRL were replaced by one-half the MRL. Differences in dust concentrations between Richmond and Bolinas were assessed using the Wilcoxon rank-sum test.

**PBDE Serum Measurements.** NHANES uses a complex, multistage sampling framework to produce a sample representative of the noninstitutionalized, civilian U.S. population. As part of the 2003–2004 NHANES survey, a random one-third subset of the participants (n = 2305) aged 12 years and above were chosen for PBDE serum analysis. From this subsample, PBDEs were successfully measured in 2040 serum samples. Concentrations for the following 10 PBDE congeners were determined by gas chromatography isotope dilution high resolution mass spectrometry: BDE-17, -28, -47, -66, -95, -99, -100, -153, -154, and -183 (National Center for Environmental Health, CDC, Atlanta, GA). Distributions and percents detected for these congeners have been reported elsewhere (11). For this analysis, we selected the six congeners (BDE-28, -47, -99, -100, -153, and -154) that had at least 50% of samples above the LOD. Concentrations below the LOD were substituted by the CDC with a value equal to the congener-specific LOD divided by the square root of two. Since congeners 47, 99, 100, 153, and 154 are the major components of the penta-BDE formulation, with BDEs 47 and 99 accounting for approximately 75% of the total mass, and BDE-28 is a minor component of penta-BDE (17, 26), we summed the six congeners to create a summary metric for the penta-BDE formulation (ΣPBD). If data for one or more congeners was not reported by the CDC, the participant was coded as missing for ΣPBD. Total PBDE concentrations were calculated for 1942 participants and are expressed as ng PBDE per gram serum lipid. Serum PBDE concentrations approximated a log-normal distribution and were log-transformed prior to statistical analyses.

Information pertaining to NHANES participants’ county, state, and region of residence (West, Midwest, South, and Northeast) were obtained through the Research Data Center (RDC) (National Center for Health Statistics, Hyattsville, MD). Participants with PBDE serum measurements resided in 29 U.S. counties; four of which were located in California. For confidentiality reasons, the actual survey locations are not disclosed.

Participants from California counties were assigned a “yes” for a binary measure indicating residence in California, versus “no” for participants from counties in other U.S. states. Publicly accessible NHANES data files provide masked variance units (MVUs) to estimate sampling error and to comply with disclosure agreements that prohibit the release of the primary sampling units (PSUs) (27). We obtained the true PSUs and stratum information through the RDC and used this information to construct our main variable of interest, residence in California, and to calculate standard errors for all estimates.

We also included these covariates in the serum analysis: age (12–19, 20–39, 40–59, and ≥60 years), sex (male or female), education (≥18 years and not completed high school versus completed high school or <18 years), annual household income (more or less than $20,000), race (non-Hispanic white, non-Hispanic black, Mexican American, or other), and country of origin. (U.S.-born or foreign-born.)

All analyses were conducted in SUDAAN 9.0 (Research Triangle Institute, Cary, NC) and SAS 9.1 (SAS Institute Inc., Cary, NC). SUDAAN calculates variance estimates after incorporating the nonrandom sampling design and the oversampling of certain subgroups. For univariate analyses, geometric means and percentile estimates were calculated with PROC DESCRIPT. Boxplots were constructed using weighted percentile estimates. Differences across groups for categorical data were evaluated using the chi square test. The least-square geometric means (LSGM), which provide geometric mean estimates for a variable after adjustment for other model covariates, were calculated from multivariate regression models.

To obtain the final model, we used backward elimination with a threshold p < 0.05 for retaining the variable in the model. We assessed confounding by adding each of the excluded variables back into the model and determining whether the beta coefficient for the main effect changed by >10%. If so, we retained the nonsignificant confounding variable in the model. Participants who were classified in a race/ethnicity category other than Mexican American, non-Hispanic black, or non-Hispanic white (n = 149) were included in the descriptive statistics but not in regression analyses. Country of origin and race/ethnicity were not modeled together in multivariate regression models due to the small number of foreign-born non-Hispanic blacks and non-Hispanic whites among California NHANES participants. Alternatively, a four category race/ethnicity variable that distinguished between U.S.-born and foreign-born Mexican Americans was created and used in sensitivity analyses. Results from regression models with ΣPBD as the outcome are presented below. Similar models with BDE-47 serum levels as the outcome were constructed and are briefly discussed in the results.

**Results**

**Household Dust.** PBDE household dust concentrations in Richmond and Bolinas, California, are presented in Table 1. Median concentrations of BDE-47, -99, and -100 across all
homes \((n = 49)\) were 2700, 3800, and 684 ng/g, respectively. Concentrations were higher in Richmond \((n = 39)\) than Bolinas \((n = 10)\), but these differences were not statistically significant. California PBDE concentrations were also compared with summary measures from previously published studies. Characteristics for our study and comparison studies, including year and location of sampling, sample size, and median dust levels of BDE-47, -99, and -100, are presented in Figure 1. PBDE dust levels in California were markedly higher than previously reported in Europe and North America for all three penta-BDE congeners. Median house dust levels in California were 200 times higher than those reported from Germany \((28)\) and United Kingdom \((29)\), and 4–10 times higher than levels in Ottawa, Canada \((1)\), Cape Cod, MA \((4)\), Boston, MA \((4)\), Washington, DC \((30)\), and Texas \((29)\). Maximum dust concentrations (Table 1) in our California study homes were higher than any we were able to identify in the peer-reviewed literature.

**Serum.** Regional PBDE serum levels were compared across the NHANES sample. Individual BDE congeners and \(\Sigma PBDEs\) varied by U.S. region \((p < 0.05)\) with highest levels occurring in the Western region (which includes California) and lowest in the Northeast (Figure 2). The unadjusted medians for the West and California are very similar, with the 95th percentile being highest in California. In adjusted models (described below), the LSGM is slightly higher for California than the West; and the pattern across the four U.S. regions remains the same (results not shown).

Personal characteristics and PBDE serum concentrations of participants living in California versus the rest of the country are presented in Table 2. Of the 2040 NHANES participants, 276 (14%) were from California. California participants were similar to others in the U.S. in age, sex, and income. However, compared to the rest of the U.S., California participants were similar to others in the U.S. in age, sex, and income. However, compared to the rest of the U.S., California had lower percentages of non-Hispanic whites and non-Hispanic blacks but a higher percentage of Mexican Americans. California also had higher percentages of foreign-born individuals and those not completing high school.

Four BDE congeners and \(\Sigma PBDEs\) were significantly higher in California residents \((p < 0.01)\). BDEs 153 and 154 were also higher in California residents, although these differences were not statistically significant. Levels of BDE-47, the

### Table 1. PBDE House Dust Concentrations in Two California Communities (\(n = 49\))

<table>
<thead>
<tr>
<th></th>
<th>Richmond ((n = 39))</th>
<th>Bolinas ((n = 10))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% &gt; MRL(^a)</td>
<td>Median (ng/g)</td>
</tr>
<tr>
<td>BDE-47</td>
<td>100</td>
<td>3750</td>
</tr>
<tr>
<td>BDE-99</td>
<td>100</td>
<td>3830</td>
</tr>
<tr>
<td>BDE-100(^b)</td>
<td>92.3</td>
<td>756</td>
</tr>
</tbody>
</table>

\(^a\) Method reporting limit (MRL) = 42 ng/g.  
\(^b\) Values below the MRL were substituted with \(0.5 \times MRL\).  
\(^c\) Differences between groups tested using the Wilcoxon rank-sum test.

![Figure 1](https://example.com/figure1.png)  
**Figure 1.** Median concentrations (ng/g) of BDE-47, -99, -100 in household dust from different locations. Data from Cape Cod, MA (Rudel et al. 2003, ref 4) and California collected by the same research group using similar methodology. Data for Germany from Knob et al. (2002, ref 28), UK and Texas from Harrad et al. (2008, ref 29), Canada from Wilford et al. (2005, ref 1), Boston, MA from Wu et al. (2007, ref 14), and Washington DC, from Stapleton et al. (2005, ref 30). Study location, sample size and year of sample collection are also shown. Adjusted geometric mean estimates, calculated using maximum likelihood estimation for data below the reporting limit, are shown for Cape Cod, MA.
Our analysis is also one of the first studies to examine associations between socioeconomic status (SES) and PBDE exposure. Our results suggest that lower household income is associated with increased serum PBDE exposures. The physical weathering and crumbling of PBDE-treated foam in older furniture, often found in lower income homes, may contribute to elevated PBDE levels in these environments. Additionally, lower household income was positively associated with living in California, highlighting the importance of considering regional variations in PBDE exposure.

In conclusion, our study provides valuable insights into regional variations in PBDE exposure and highlights the need for targeted public health interventions to reduce exposures, particularly in lower income and foreign-born populations. Further research is needed to better understand the underlying factors contributing to these differences and to develop effective strategies for mitigation and prevention.
TABLE 2. Personal Characteristics and Serum PBDE Levels for NHANES Participants Living in California vs Other U.S. States (n=2040)

<table>
<thead>
<tr>
<th>Personal Characteristics</th>
<th>California (n = 276)</th>
<th>frequency (%)</th>
<th>95% CI</th>
<th>other U.S. states (n = 1764)</th>
<th>frequency (%)</th>
<th>95% CI</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12–19</td>
<td>15.8</td>
<td>9.7–24.6</td>
<td></td>
<td>13.7</td>
<td>12.0–15.6</td>
<td></td>
<td>0.12</td>
</tr>
<tr>
<td>20–39</td>
<td>40.1</td>
<td>29.8–51.4</td>
<td></td>
<td>32.7</td>
<td>28.8–36.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40–59</td>
<td>28.3</td>
<td>16.9–43.3</td>
<td></td>
<td>33.7</td>
<td>30.6–36.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥60</td>
<td>15.9</td>
<td>11.2–22.0</td>
<td></td>
<td>19.9</td>
<td>17.3–22.8</td>
<td></td>
<td>0.31</td>
</tr>
<tr>
<td>sex</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>male</td>
<td>53.5</td>
<td>46.1–61.8</td>
<td></td>
<td>47.8</td>
<td>44.7–51.0</td>
<td></td>
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<tr>
<td>less than high school education</td>
<td>22.9</td>
<td>17.0–28.8</td>
<td></td>
<td>14.9</td>
<td>13.0–16.8</td>
<td></td>
<td>0.01</td>
</tr>
<tr>
<td>household income &lt;$20000</td>
<td>26.7</td>
<td>15.2–42.6</td>
<td></td>
<td>25.1</td>
<td>20.8–30.0</td>
<td></td>
<td>0.82</td>
</tr>
<tr>
<td>race/ethnicity</td>
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<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>non-Hispanic white</td>
<td>46.6</td>
<td>33.6–60.1</td>
<td></td>
<td>73.3</td>
<td>64.7–80.6</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>non-Hispanic black</td>
<td>4.7</td>
<td>1.9–11.0</td>
<td></td>
<td>12.5</td>
<td>9.1–16.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mexican American</td>
<td>28.0</td>
<td>18.6–39.7</td>
<td></td>
<td>6.1</td>
<td>2.8–12.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>other</td>
<td>20.8</td>
<td>12.7–32.1</td>
<td></td>
<td>8.0</td>
<td>5.7–11.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>country of origin</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>United States</td>
<td>61.2</td>
<td>51.1–70.4</td>
<td></td>
<td>88.2</td>
<td>82.8–92.0</td>
<td></td>
<td>0.002</td>
</tr>
<tr>
<td>Mexico</td>
<td>17.2</td>
<td>11.5–24.9</td>
<td></td>
<td>2.9</td>
<td>1.5–5.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>other</td>
<td>21.6</td>
<td>14.7–30.6</td>
<td></td>
<td>8.9</td>
<td>6.1–12.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PBDE Serum Measures</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>BDE-28</td>
<td>2.1</td>
<td>1.5–2.7</td>
<td></td>
<td>1.1</td>
<td>0.9–1.3</td>
<td></td>
<td>0.003</td>
</tr>
<tr>
<td>BDE-47</td>
<td>36.2</td>
<td>25.0–47.4</td>
<td></td>
<td>19.5</td>
<td>16.6–22.4</td>
<td></td>
<td>0.003</td>
</tr>
<tr>
<td>BDE-99</td>
<td>7.4</td>
<td>5.2–9.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.01</td>
</tr>
<tr>
<td>BDE-100</td>
<td>6.0</td>
<td>4.2–7.8</td>
<td></td>
<td>3.8</td>
<td>3.2–4.4</td>
<td></td>
<td>0.01</td>
</tr>
<tr>
<td>BDE-153</td>
<td>6.8</td>
<td>5.2–8.4</td>
<td></td>
<td>5.6</td>
<td>4.8–6.4</td>
<td></td>
<td>0.18</td>
</tr>
<tr>
<td>BDE-154</td>
<td>0.8</td>
<td>0.6–1.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.05</td>
</tr>
<tr>
<td>ΣPBDEs</td>
<td>62.0</td>
<td>44.6–79.4</td>
<td></td>
<td>38.6</td>
<td>33.5–43.7</td>
<td></td>
<td>0.009</td>
</tr>
</tbody>
</table>

* Estimates are adjusted for survey design and sample weight. 
Significant (p < 0.05) differences between CA and other U.S. states are bolded. 
Data were missing for education (n = 3) and income (n = 38). 
Geomean is the geometric mean concentration. 
Data were missing for BDE-28 (n = 53), BDE-47 (n = 24), BDE-99 (n = 55), BDE-153 (n = 1), BDE-154 (n = 26), and ΣPBDEs (n = 98). 
Geometric mean is below the highest limit of detection for individual samples. 
ΣPBDEs equal to the sum of BDE-28, BDE-47, BDE-99, BDE-100, BDE-153, and BDE-154.

TABLE 3. Adjusted Least Square Geometric Mean (LSGM) Concentrations of ΣPBDE Serum Concentrations (ng/g lipid) by Geographic Location and Other Personal Characteristics (n=1771)

<table>
<thead>
<tr>
<th>variable</th>
<th>LSGM (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>geographic location</td>
<td></td>
</tr>
<tr>
<td>California</td>
<td>73.0 (70.7–75.2)</td>
</tr>
<tr>
<td>other U.S. states</td>
<td>38.5 (36.4–40.5)</td>
</tr>
<tr>
<td>age</td>
<td></td>
</tr>
<tr>
<td>12–19 years</td>
<td>50.9 (48.8–53.0)</td>
</tr>
<tr>
<td>20–39 years</td>
<td>43.4 (41.3–45.5)</td>
</tr>
<tr>
<td>40–59 years</td>
<td>34.8 (32.7–37.0)</td>
</tr>
<tr>
<td>≥60 years</td>
<td>40.4 (35.2–39.4)</td>
</tr>
<tr>
<td>sex</td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>44.3 (42.2–46.4)</td>
</tr>
<tr>
<td>female</td>
<td>37.3 (35.2–39.4)</td>
</tr>
<tr>
<td>household income</td>
<td></td>
</tr>
<tr>
<td>≤$20000</td>
<td>50.4 (48.3–52.5)</td>
</tr>
<tr>
<td>&gt;$20000</td>
<td>37.7 (35.6–39.8)</td>
</tr>
<tr>
<td>country of origin</td>
<td></td>
</tr>
<tr>
<td>U.S.-born</td>
<td>42.1 (40.0–44.2)</td>
</tr>
<tr>
<td>foreign-born</td>
<td>27.9 (25.8–30.0)</td>
</tr>
</tbody>
</table>

LSGM estimates are from multivariate regression models adjusted for survey design and sample weights. 
Referent group. 
p < 0.05. 
p < 0.01.

Manufactured in ways that release these chemicals in greater amounts. Our dust findings were consistent with the observation of higher serum PBDE in lower SES groups since we observed higher PBDE dust levels in Richmond (a lower SES community) than Bolinas, although this difference was not statistically significant, possibly due to our small sample size.

Our analysis of the NHANES serum PBDE levels contrasted in some respects from the results of Sjodin and colleagues (11). Although we found similar patterns in PBDE levels for sex and age, we found different effects for country of origin and race. After controlling for geographic location, serum PBDE levels of Mexican Americans were not higher than non-Hispanic whites. In fact, foreign-born Mexican Americans had significantly lower serum PBDE levels compared to U.S.-born Mexican Americans and non-Hispanic whites. Sjodin’s finding of higher PBDE levels in Mexican Americans may result from the large proportion of Mexican Americans from California surveyed in NHANES. Similarly, his lack of association between country of origin and BDE-47 may be due to the high proportion of foreign-born participants from California in NHANES. Future research should further examine how exposure patterns among foreign-born immigrants change with length of residence in the U.S.

There are several limitations to our study. While NHANES is designed to be a representative sample of the U.S. population, the individuals sampled in California are not intended to be representative of California’s population and are sampled from just four of California’s 58 counties. Similarly, our dust samples from Richmond and Bolinas in Northern California may not be representative of the entire state. Furthermore, while we build on studies that point to dust as the primary source of human exposure (1, 3), we...
were not able to examine direct associations between PBDEs in household dust and body burden in this study. However, the data sources used in this analysis currently provide the most viable way to examine regional variation in PBDE exposure within the U.S.; and the consistent geographic differences we report in PBDE levels in both dust and serum compel additional research in a larger representative population where dust and blood samples can be analyzed from the same cohort. Lastly, while our analysis identified several important predictors of PBDE exposure, most of the variation was unexplained, implying that other unmeasured factors contribute and that determinants of exposure should be further investigated.

Given that PBDEs are ubiquitous and exposures differ among subpopulations, it is necessary to evaluate the impact of these exposures on human health endpoints such as thyroid hormone disruption. In an analysis of NHANES data, higher serum levels of PCBs, which share structural and mechanistic similarities with PBDEs, were associated with significant changes in thyroid hormone levels in the general U.S. population (21). Additionally, an increased prevalence of feline hyperthyroidism, which may, in part, be a result of PBDE exposures, has been observed in California cats (33). Unfortunately, thyroid hormone levels were measured in previous NHANES cohorts but not in 2003–2004 when PBDE levels were available. Concurrent measurements of PBDE biomarkers and thyroid levels should be a priority in future NHANES cycles.

Our regional analysis of PBDE serum levels adds to prior NHANES analyses that have considered the impacts of public health regulations and policies on population exposure. Prior studies in this vein include an evaluation of urine cotinine, a marker of tobacco smoke exposure, in relation to local regulations about smoking in public places (34), and an assessment of blood lead reductions due to the phasing out of lead in gasoline and household paint (35). Future studies should continue to monitor penta-BDE body burden, while also tracking exposures to replacement compounds.

Our findings show significantly elevated penta-BDE exposure in house dust and serum in California, which may reflect the unintended consequences of the state’s stringent furniture flammability standards (7). There may be other explanations for elevated PBDE levels in California. For example, there could be regional differences in diet; however, diet is not considered to be the major source of PBDE exposures (3), and dietary differences would not explain the regional differences observed in house dust. These findings raise concern about pending regulations and performance standards that encourage the widespread use of chemical flame retardants, which are toxic or whose safety is uncharacterized. For example, the California agency that promulgated TB117 is on the verge of extending flammability requirements to bed clothing (36); and in the past two years, several state and federal initiatives have proposed adopting California’s TB117 for furniture flammability (19). Although use of penta-BDE has been phased out, new chemicals have been substituted without assessment of their safety or environmental impact, and our findings may foreshadow exposure patterns to be anticipated from these substitutes. Taken together with existing research documenting the distribution of penta-BDEs internationally, these findings suggest the need for more anticipatory assessments of the environmental health impacts of consumer product decisions prior to their implementation.

Acknowledgments
We thank Carla Pérez, Jessica Tovar, Andrea Samulon, Amanda Keller at Communities for a Better Environment for sample collection and collaboration throughout this research; Elizabeth Newton for statistical consultation; and Susan Schober for RDC proposal consultation. This work was supported by the New York Community Trust and National Institute of Environmental Health Sciences (5R25ES13258-4).

Supporting Information Available
Dust analytical methods and QA/QC; regression models for ΣPBDEs and pairwise comparisons of ΣPBDEs by race/ethnicity (Tables S1–S2 and Figure S1) This material is available free of charge via the Internet at http://pubs.acs.org.

Literature Cited

ES801792Z.
Exhibit 5
Novel and High Volume Use Flame Retardants in US Couches Reflective of the 2005 PentaBDE Phase Out

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§Department of Chemistry, University of California, and Green Science Policy Institute, Berkeley, California, United States

ABSTRACT: California’s furniture flammability standard Technical Bulletin 117 (TB 117) is believed to be a major driver of chemical flame retardant (FR) use in residential furniture in the United States. With the phase-out of the polybrominated diphenyl ether (PBDE) FR mixture PentaBDE in 2005, alternative FRs are increasingly being used to meet TB 117; however, it was unclear which chemicals were being used and how frequently. To address this data gap, we collected and analyzed 102 samples of polyurethane foam from residential couches purchased in the United States from 1985 to 2010. Overall, we detected chemical flame retardants in 85% of the couches. In samples purchased prior to 2005 (n = 41) PBDEs associated with the PentaBDE mixture including BDEs 47, 99, and 100 (PentaBDE) were the most common FR detected (39%), followed by tris(1,3-dichloroisopropyl) phosphate (TDCPP; 24%), which is a suspected human carcinogen. In samples purchased in 2005 or later (n = 61) the most common FRs detected were TDCPP (52%) and components associated with the Firemaster550 (FM 550) mixture (18%). Since the 2005 phase-out of PentaBDE, the use of TDCPP increased significantly. In addition, a mixture of nonhalogenated organophosphate FRs that included triphenyl phosphate (TPP), tris(4-butylphenyl) phosphate (TBPP), and a mix of butylphenyl phosphate isomers were observed in 13% of the couch samples purchased in 2005 or later. Overall the prevalence of flame retardants (and PentaBDE) was higher in couches bought in California compared to elsewhere, although the difference was not quite significant (p = 0.054 for PentaBDE). The difference was greater before 2005 than after, suggesting that TB 117 is becoming a de facto standard across the U.S. We determined that the presence of a TB 117 label did predict the presence of a FR; however, lack of a label did not predict the absence of a flame retardant. Following the PentaBDE phase out, we also found an increased number of flame retardants on the market. Given these results, and the potential for human exposure to FRs, health studies should be conducted on the types of FRs identified here.

INTRODUCTION

In the United States, a major driver of flame retardant (FR) use in residential furniture appears to be the California flammability standard, Technical Bulletin 117 (TB 117). This standard requires that polyurethane foam used in furniture withstand a 12 s open flame test with minimal loss of foam and no sustained ignition after the flame is removed. TB 117 was instituted in 1975 primarily to protect against home fires started by small open flames, such as candles, matches, and lighters.¹

To meet this standard, a variety of flame retardant chemicals have historically been used, but due to the proprietary nature of some FRs and the lack of a labeling requirement, it is very difficult to determine their presence or identity in products. It has been suggested that TB117 was primarily met by treating foam with PentaBDE prior to the 2005 phase-out, after which time TDCPP and FM 550 were primarily used. However, this is anecdotal, and no previous studies have investigated which FRs were historically used in furniture, nor have they identified which FRs are now in common use.

Numerous studies dating back to the 1970s have raised concerns about the exposure and health effects from both TDCPP and PentaBDE. TDCPP was found to be a mutagen more than three decades ago²³ and was recently determined to be potentially neurotoxic.⁴ Based on its carcinogenicity, it was added to California’s Proposition 65 List of Potential Carcinogens in 2011. In 2006, the Consumer Product Safety Commission conducted a risk assessment for several FRs used in upholstered furniture and specifically evaluated adult and children’s exposure to TDCPP.⁵ While
their report was limited to the use of modeled exposure data, their estimates suggested that both adults and children are receiving exposures that are 2 and 5 times higher, respectively, than the acceptable daily dose for noncancer end points. For cancer end points, they estimated that an adults lifetime individual cancer risk was 300 per million, based on a lifetime exposure to TDCPP treated furniture. Estimated cancer risks in children from two years of exposure to TDCPP treated furniture was 20 per million. The CPSC states that cancer risks greater than one in a million are considered relevant for regulatory consideration under the chronic hazard guidelines.

In the 1990s, several studies demonstrated that polybrominated diphenyl ethers (PBDEs) present in PentaBDE were biomagnifying in food webs and increasing in concentration in human tissues and the environment.\(^8\) Given the similarity in structure between PBDEs and thyroid hormones, a number of exposure studies with rodents, fish, and birds were conducted. Significant effects of PBDEs on thyroid hormone regulation and neurodevelopment were observed in these studies.\(^9 - 12\) By 2004 both the state of California and the European Union had banned the use of PentaBDE and another PBDE mixture, OctaBDE, from use in consumer products.\(^13\) These bans and banned the use of PentaBDE and another PBDE mixture, OctaBDE components.\(^15\) The lack of labeling, and information on flame retardant use in consumer products, has hampered research investigating sources of human exposure to PBDEs and their replacements. Several US studies have found significant associations between PBDE body burdens, dietary sources,\(^16,17\) and house dust,\(^18,19\) suggesting both are significant sources of exposure. More recently, several of our authors demonstrated that PBDE residues on hands were strong predictors of serum PBDE levels in children\(^20\) and in adults,\(^21\) suggesting hand to mouth contact is a significant source of exposure to these chemicals.

In 2011 we investigated the use of FR chemicals in foam from baby products such as nursing pillows, strollers, high chairs, and baby carriers.\(^22\) Such products are considered juvenile furniture and are required to meet the TB 117 standard. We found that 80% of the 101 products tested contained a FR, and all but one was halogenated.\(^22\) This was an important finding as there were no data available on the prevalence, identity, or levels of FRs in children’s products containing foam. As a follow-up to that study, we are now investigating the use of FR in residential furniture purchased in the United States. One primary objective was to identify the types of FR chemicals commonly used in residential couches before and after the PentaBDE phase-out in 2005 as well as their concentrations in the foam. A second objective was to compare FR use in products sold within and outside of California (but all within the US). Studies have found higher levels of PBDEs in California house dust and residents, which may be due to TB 117.\(^23\)

**Materials and Methods**

**Materials.** The internal standard used for PBDE, TBB, and TBPH analysis, 4-fluoro-2,3,4,6-tetrabromodiphenylether (FBDE 69), was purchased from Chiron (Trondheim, Norway). Deuterated triphenyl phosphate (TPP) was purchased from Sigma Aldrich (St. Louis, MI), while deuterated tris(2-chloroethyl) phosphate (TCEP) and tris(1,3-dichloroisopropyl) phosphate (TDCCP) were synthesized by Dr. Vladimir Belov (Göttingen, Germany). PBDE calibration standards were purchased from AccuStandard (New Haven, CT), and 2-ethylhexyl-2,3,4,5-tetrabromobenzoate (TBB) and bis(2-ethylhexyl)-2,3,4,5-tetrabromophthalate (TBPH) were purchased from Wellington Laboratories. TCEP and tris(4-butylyphenyl) phosphate (TBPP) were purchased from Sigma-Aldrich (St. Louis, MI), while TDCPP and tris(2-methyl phenyl) phosphate were purchased from ChemService (West Chester, PA). A commercial mixture of V6 was purchased from a flame retardant manufacturer in China (wishes to be anonymous) and purified to greater than 98%. All solvents used throughout this study were HPLC grade.

**Foam Sample Collection.** Polyurethane foam samples were solicited from volunteers during 2010–2011 using e-mail list-serves and requests at lectures and meetings that reached individuals from all over the US. To qualify for this study, the participant had to own a couch that met four criteria: 1.) The couch was purchased new by the owner and never reupholstered (No previously owned or used couches, sofa-beds, futons, or day beds were included in the study); 2.) The owner knew the state and year of purchase of the couch; 3.) The couch was for home use, rather than for an office or public place; and 4.) The couch had a label that stated it contained polyurethane foam or the couch had no labels when purchased. The label could also state that the couch contained polyester fibers or other materials in addition to polyurethane foam.

The foam sample donor was instructed to cut or tear a 1/2 to 1 cubic inch foam sample from the couch, wrap the sample in aluminum foil, and seal it in an inner Ziploc bag which was placed into an outer Ziploc bag. The donor filled out a questionnaire including where and when the couch was purchased, the filling material as specified on the label, and whether a Technical Bulletin 117 (TB117) or other flammability labels were found on the product. A product was considered to have a TB117 label if it contained the text: THIS ARTICLE MEETS THE FLAMMABILITY REQUIREMENTS OF CALIFORNIA BUREAU OF HOME FURNISHINGS TECHNICAL BULLETIN 117 (TB117). The questionnaire was placed in the outer Ziploc bag. The donor and sample information was logged into a database, unique ID numbers were given to each sample, and they were then shipped to Duke University for blind analysis of flame retardants.

**Sample Analysis by Mass Spectrometry.** All foam samples were first screened for flame retardant additives. Briefly, small pieces of foam (approximately 0.05 g) were sonicated with 1 mL of dichloromethane (DCM) in a test tube for 15 min. The DCM extract was syringe-filtered to remove particles and then transferred to an autosampler vial for analysis by GC/MS. All extracts were analyzed in full scan mode (collecting data on all mass spectra generated) using both electron ionization (GC/EI-MS) and electron capture negative chemical ionization (GC/ECNI-MS). Pressurized temperature vaporization injection was employed in the GC. GC/MS method details can be found in ref 24. Peaks observed in the total ion chromatograms were compared to a mass spectral database (NIST, 2005) and to authentic standards when available.
If a potential flame retardant chemical was identified either by comparison to authentic standards or by a match to the NIST MS database (>90% match) during the initial screening, a second analysis of the foam sample, using a separate piece of the foam, was conducted for quantitation. To measure the FRs in foam, a piece of the foam was accurately weighed (approximately 100 mg) and then extracted using Accelerated Solvent Extraction (ASE 300 Dionex Corp., Sunnyvale, CA) with 100% dichloromethane (DCM). Extracts were reduced in volume to approximately 3 mL and transferred to a precleaned 100 mL amber vial. The mass of the extract was recorded, and then a 100 μL aliquot was transferred to a 100 mL volumetric flask and diluted to 100 mL in DCM. One mL of the diluted extract was transferred to an autosampler vial, and the appropriate internal standards were added. A five point calibration curve was established for all analytes with concentrations ranging from 20 ng/mL to 2 μg/mL. PBDEs were quantified by GC/ECNI-MS by monitoring bromide ions (m/z 79 and 81), and TBB and TBPH were monitored by molecular fragments m/z 357/471 and 463/515, respectively. TCEP and TDCPP were quantified by GC/EI-MS by monitoring m/z 249/251 and 381/383, respectively. TBPP was monitored in GC/EI-MS mode by monitoring m/z 479.5 and 480.5, respectively. V6 was detected and quantified using liquid chromatography−mass spectrometry. The HPLC (Agilent 1200; Agilent, Santa Clara, CA) separation was achieved with a Zorbax Eclipse XDB-C18 column (1.8 μm, 4.6 x 50 mm; Agilent). The mobile phase consisted initially of 60% methanol and 40% water at a flow rate of 0.4 mL min⁻¹ that was ramped to 100% methanol from 0 to 6 min and then maintained under isocratic conditions of 100% methanol to 12 min, after which the mobile phase returned to 60% methanol from 12 to 15 min. V6 was detected by multiple reflection monitoring (MRM) using tandem mass spectrometry with positive atmospheric pressure chemical ionization (Agilent 6410B triple quadrupole spectrometer, Santa Clara, CA) by monitoring the transition from m/z 582.7 to 63.0 (quantifier), 582.7 to 360.8 (qualifier), and 582.7 to 234.8 (qualifier). The internal standard used was dTDCPP (108 ng). Fragmentor voltages were set at 160 V, and the collision energy was set at 55 V.

Ten foam extracts were also screened using HPLC-high resolution mass spectrometry (HPLC/HRMS) to provide more detail on potential structures of several unknown chemicals detected during the preliminary GC/MS screening. These analyses were conducted using a LTQ-Orbitrap Velos tandem mass spectrometer (ThermoFisher Scientific, Bremen, Germany) with a Thermo Fisher Scientific Accela series UPLC system. Sample extracts (25 μL) were separated on a Hypersil Gold 100 × 2.1-mm C18 column with 1.9 μm particles (ThermoFisher Scientific) using a flow rate of 0.4 mL/min and a linear gradient from 40 to 99% methanol/water in 15 min, followed by a 4-min hold at 99% methanol before returning to initial conditions for 3 min. Sample extracts were analyzed using positive polarity electrospray ionization (ESI) mode. Prior to analysis, mass calibration was performed daily by direct infusion of a calibration mixture prepared according to the instrument manufacturer’s instructions. Mass spectral acquisition for initial sample screening was programmed into four scan events running concurrently throughout the chromatographic separation. The first scan event was programmed to acquire full-scan (50–2000 m/z), high-resolution (R = 60,000) Orbitrap MS data with external mass calibration (<2 ppm accuracy). The subsequent three scan events were low-resolution data-dependent MS/MS analyses in the LTQ ion trap analyzer, triggered by the three most intense ions selected from the previous high-resolution Orbitrap MS spectrum. After identifying chromatographic features of interest by unsupervised peak picking and molecular formula assignment (ExactFinder 2.0, Thermo Scientific), subsequent targeted multistage HRMS experiments (HRMS² and HRMS³) were performed to acquire high-resolution accurate-mass fragmentation spectra for the structural elucidation of suspected contaminants. Conditions were similar to those reported in our previous paper.²²

As flame retardants are typically added to polyurethane foam at percent levels, we defined samples with detected concentrations (when authentic standards were available) less than 0.2 mg/g as having very small amounts. A majority of the samples contained FRs at levels >1.0 mg/g, while 3 samples contained detectable levels of FRs that ranged from 0.02 to 0.17 mg/g. Therefore, we set our threshold at 0.2 mg/g for “low detection.”

### Table 1. Flame Retardant (FR) Measurements and Descriptive Statistics of Polyurethane Foam Samples (n = 102). (Values in parenthesis represent percentage of the total number of samples for that specific column)

<table>
<thead>
<tr>
<th>flame retardant</th>
<th>number of detects</th>
<th>average FR level (mg/g)</th>
<th>purchased prior to 2005$^b$</th>
<th>purchased 2005 or later$^c$</th>
<th>purchased in California$^a$</th>
<th>purchased outside California$^a$</th>
<th>yes TB 117$^{d}$</th>
<th>no TB 117$^{d}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>PentabDE</td>
<td>17</td>
<td>20.23$^d$</td>
<td>16 (39%)</td>
<td>1 (2%)$^f$</td>
<td>7 (29%)</td>
<td>9 (12%)</td>
<td>8 (24%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>TDCPP</td>
<td>42</td>
<td>44.87</td>
<td>10 (24%)</td>
<td>32 (76%)</td>
<td>10 (42%)</td>
<td>30 (41%)</td>
<td>33 (50%)</td>
<td>9 (26%)</td>
</tr>
<tr>
<td>FM 550</td>
<td>13</td>
<td>19.76</td>
<td>2 (5%)</td>
<td>11 (18%)</td>
<td>3 (13%)</td>
<td>8 (11%)</td>
<td>12 (18%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>V6/TCEP</td>
<td>1</td>
<td>41.77$^c$</td>
<td>0</td>
<td>1 (2%)$^d$</td>
<td>1 (4%)</td>
<td>2 (3%)</td>
<td>0</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>TBPP mix</td>
<td>8</td>
<td>7.90$^c$</td>
<td>0</td>
<td>8 (13%)</td>
<td>1 (4%)</td>
<td>7 (10%)</td>
<td>6 (9%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>MPP mix</td>
<td>2</td>
<td>3.23$^c$</td>
<td>0</td>
<td>2 (3%)</td>
<td>0</td>
<td>2 (3%)</td>
<td>1 (2%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>TDCPP and PentabDE</td>
<td>2</td>
<td>22.64</td>
<td>2 (5%)</td>
<td>0</td>
<td>1 (4%)</td>
<td>1 (1%)</td>
<td>1 (2%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>TDCPP and FM 550</td>
<td>2</td>
<td>19.06</td>
<td>0</td>
<td>2 (3%)</td>
<td>0</td>
<td>2 (3%)</td>
<td>3 (4%)</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>FR &lt; 0.2 mg/g</td>
<td>3$^f$</td>
<td>0.11</td>
<td>1 (2%)</td>
<td>2 (3%)</td>
<td>0</td>
<td>3 (4%)</td>
<td>0</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>none detected</td>
<td>12</td>
<td>-</td>
<td>10 (24%)</td>
<td>2 (3%)</td>
<td>1 (4%)</td>
<td>11 (15%)</td>
<td>1 (2%)</td>
<td>11 (32%)</td>
</tr>
</tbody>
</table>

*Includes measurement of TPP only. $ Two samples contained TDCPP; one sample contained BDE47 and BDE99.

$ Indicates the number of samples collected from couches containing the FR and purchased during this time frame. $ Some participants reported purchasing their couch online or through a catalog, and thus the state of purchase was not included in the sum (n = 5). $ Indicates the number of samples that did or did not contain a TB 117 label on the product (no data available for 2 samples). $ Includes PBDE congeners plus TTP. $ Sample purchased in 2005. $ Measurement is the sum of TPP, TBB, and TBPH. $ Measurement is for V6 + TCEP. $ Measurement is the sum of TPP and tris(4-(tert-butyl)phenyl)phosphate (TBPP). $ Includes measurement of TPP only. $ Two samples contained TDCPP; one sample contained BDE47 and BDE99.
RESULTS AND DISCUSSION

A total of 102 polyurethane foam samples obtained from residential couches were collected for this study. When providing a sample, participants provided information on whether the couch contained a label indicating that it met the requirements of California’s TB 117 flammability standard, the US state where the couch was purchased, and the year of purchase. There were some cases in which the participant indicated that the couch was purchased online, thus information on the state of purchase was not included for 5 samples. Data were missing on TB 117 tags for two samples.

FR Screening. All foam sample extracts were first screened for potential flame retardant additives in both GC/EI-MS and...
Preliminary screening indicated that 90 of the 102 samples (88%) contained a likely flame retardant chemical, either by comparison to authentic standards or by a significant (>90%) match to the NIST 2005 mass spectral database. The FRs detected and the sample information are presented in Table 1. No significant peaks were observed in the total ion chromatograms (TIC) for 12 of the sample extracts. Inspection of the TICs during the screening step revealed that 80 of the samples contained a flame retardant previously identified in our baby products study. These included FRs such as TDCPP, PBDE congeners commonly found in the PentaBDE commercial mixture, or chemicals found in the commercial mixture known as Firemaster 550 (FM 550). In our baby product study, we found that tris(2-chloroethyl) phosphate (TCEP) was frequently associated with a new flame retardant mixture known as V6. Based on this, the detection of TCEP in one sample suggested the possible presence of V6. Therefore, this sample was further analyzed by LC/MSMS (V6 is not detectable by GC/MS), and the presence of V6 was confirmed during the LC/MSMS analysis by comparison with a purified commercial V6 mixture. The material safety data sheet for Albemarle’s (Baton Rouge, LA) Antiblaze V6 reports the presence of TCEP as a 10% impurity, which is consistent with our findings. To our knowledge, V6 is manufactured both within and outside the USA.

Ten extracts contained significant responses in the TICs for several different types of triaryl phosphate compounds that are believed to be used as flame retardants. Eight of these extracts...
were very similar in response and contained four significant peaks, as seen in Figure 1. The first and last eluting peaks were identified as triphenyl phosphate (TPP) and tris(4-(tert-butyl)phenyl phosphate (TBPP) by comparison to authentic standards. TPP is a common organophosphate flame retardant that is used in a variety of halogenated and nonhalogenated flame retardant mixtures.25 The second and third eluting peaks did not have authentic standards available, and thus Structures 2 and 3 in Figure 1 are hypothesized based on HPLC/HRMS analysis (see the Supporting Information). These four flame retardants together may be a mixture marketed by Supresta (Ardlesey, NY) known as AC073. Information in the EPA’s 2005 report from the Furniture Flame Retardancy Partnership states that AC073 contains TPP (38–48%) and three proprietary ary phosphates in the approximate ratio of 40–46%, 12–18%, and 1–3%, which is very similar to the mass spectral signal responses observed in Figure 1.

The TICs of two foam extracts revealed the presence of TPP and at least 4 additional significant responses for structures containing organophosphate features (see Figure 2). Two of the significant responses were an 87 to 93% match to methylphenyl diphenyl phosphate (Structure 2 in Figure 2), while the other two responses were a 95–96% match to bis(4-methylphenyl) phenyl phosphate (Structure 3 in Figure 2), according to the NIST mass spectral database. The structures of the latter two compounds are hypothesized based on comparison to the NIST database and further analysis by HPLC/HRMS (see the Supporting Information). To the authors’ knowledge, this mixture of flame retardants has not been reported in products or in the environment in the past.

FR Quantification. Following the screening analysis of the foam samples, quantitative measurements were then performed on all samples in which a FR was positively identified. Table 1 provides information on the average FR content measured in the foam samples. The most commonly detected flame retardant was tris(1,3-dichloroisopropyl)phosphate (TDCPP), in 42 of the 102 samples. The average concentration of TDCPP in the foam was 43.53 mg/g and ranged from 1.6 (couch purchased in 1999) to 110.2 (purchased in 2009) mg/g of foam.

PentaBDE was the second most frequently detected FR (n = 17) with an average concentration of 18.34 mg/g of foam and ranging from 6.54 to 43.17 mg/g of foam. All but one of these foam samples containing PentaBDE was purchased prior to 2005, the year of its phase-out in the U.S. The one remaining sample was purchased in 2005. These data suggest that since 2005, PentaBDE is no longer being used in new furniture. However, finding PentaBDE in 17% of the couches studied highlights the fact that, several years after the phase-out, the general population continues to be exposed to PentaBDE-containing products. Furthermore, because there is currently no strategy in place for the identification or safe disposal of FR containing furniture, this chemical will continue to be introduced into the outdoor environment via air, dust, and discarded furniture.

The third most common FR was a mixture of chemicals known to be associated with Chemtura’s FM550 mixture. Thirteen samples contained TPP, a suite of isopropylated triarylphtalates, and two brominated compounds that are associated with FM 550, 2-ethylhexyl-tetrabromobenzoate (TBB), and bis(2-ethylhexyl) tetrabromophthalate (TBPH). No authentic standards were available for the isopropylated triaryl phosphates so they were not measured in this study. The sum concentration of the remaining three compounds in the 13 samples averaged 19.76 mg/g of foam and ranged from 5.18 to 36.85 mg/g of foam. The values are similar to measurements made for these three chemicals in polyurethane foam collected from baby products.22 Since we were unable to measure the isopropylated triarylphtalates present in these samples, the total concentration of FRs actually applied to these samples is higher than reported here.

Quantification of TPP and TBPP was performed in the 10 samples found to contain mixtures of nonhalogenated organophosphate compounds (Figures 1 and 2). The 8 samples that contained both TPP and TBPP (Figure 1, listed as TBPP mix in Table 1) averaged a sum concentration of 7.53 mg/g of foam. It is likely that the two additional isomers (peaks 2 and 3 in Figure 1 for which no authentic standards were available) contribute a larger amount of the total flame retardant mass than TPP and TBPP. Only TPP was measured in the two samples containing a mixture of methylated phenyl phosphate (MPP) isomers (Figure 2, listed as MPP mix in Table 1) and averaged 3.23 mg/g. Again this value underestimates the true FR load in the foam since we could not measure the concentration of the remaining organophosphate FRs.

As mentioned already, one sample contained V6, a chlorinated organophosphate FR that contains two phosphate groups. Similar to what we found in our baby products study, both V6 and TCEP were detected together in one sample, measuring 36.30 and 5.47 mg/g of foam, respectively. Two samples purchased prior to 2005 contained TDCPP and PentaBDE, whereas two samples purchased in 2005 or after contained a mixture of TDCPP and FM 550. In our previous study on flame retardants in baby products, we also found some foam samples treated with more than one commercial mixture.22 Two possible explanations are as follows: (1) Manufacturers may be using a mixture containing multiple flame retardants or (2) Since the large mixing vats are not cleaned between batches of foam, flame retardants from one batch could be transferred into the next batch.

In summary, 85% of the samples contained FRs at greater than 0.2 mg/g, 3% contained small amounts (<0.2 mg/g), while 12% contained no detectable levels.

FR Trends Pre- and Post-2005. Since the phase-out of Penta- and OctaBDE commercial mixtures in the US starting in 2005, there have been no reports documenting the primary flame retardants currently used in residential furniture. In this study, we were able to evaluate trends in flame retardant use in furniture before and after the phase-out. Of the 102 samples analyzed, 41 samples were purchased between 1985 and 2004, 16 (39%) of which were found to contain PentaBDE along with TPP, which we found was associated with PentaBDE use in our previous analysis of baby products.22 The second most common flame retardant detected in samples purchased prior to 2005 was TDCPP, detected in 24% of samples as the sole FR and in 5% of samples in combination with PentaBDE. This observation suggests that TDCPP was being used as a FR at the same time as PentaBDE in residential furniture. This may explain why levels of TDCPP in indoor dust are just as high as PBDE levels.24 Five percent of samples purchased prior to 2005 contained congeners associated with FM 550 (TBB, TBPH, TPP, and isopropylated TPP). These samples were purchased in 2002 and 2003, suggesting that use of FM 550 started at least three years prior to the phase-out of PentaBDE. Of the remaining samples purchased prior to 2005, 24% contained no trace of any flame retardant, and one sample contained very low
levels (<0.2 mg/g) of PentaBDE. This may indicate that prior to 2005, some manufacturers may not have been producing furniture to meet TB 117.

Samples purchased between 2005 and 2010 (n = 61) were found to contain a more varied group of FRs. A large majority of these samples (93%) contained high levels (>0.2 mg/g) of FRs, in contrast to couches purchased prior to 2005. This was a significant increase (p < 0.01) in FR use observed pre- and post-2005 using a Chi-Square test. The two most common FRs detected in the newer furniture were TDCPP and the FM 550 components (or a mixture of the two), in 74% of the samples purchased since 2005. While TDCPP was also detected in samples purchased before 2005, the increased detection of TDCPP in more recent furniture (52% compared to 24%) was statistically significant (p < 0.01). Sixteen percent of foam samples from couches purchased in 2005 or later were found to contain mixtures of nonhalogenated organophosphate based FRs, indicating that the use of nonhalogenated FRs is increasing. Of these samples, 13% contained TPP, TBPP, and several butylphenyl phosphate isomers (Figure 1), while 3% contained TPP and several methyl- or dimethyl-phenyl phosphate isomers (Figure 2). More research is needed to determine if these organophosphate FRs are detected in indoor air and dust.

FRs in Samples Purchased in and outside of California. Participants that donated foam samples from their couches were also asked whether or not their couch was purchased in California. Previous studies showing higher PBDE exposures in California residents23,26 suggest that more furniture may be treated with FRs in California compared to other states in the US. In our study, 24% of the samples were purchased within California, while 72% were purchased in other states (5 individuals reported buying their couches online). All but one of the samples purchased within California was treated with a flame retardant. The one sample from California that did not contain detectable levels of flame retardants was purchased in 1989. Of the 72 samples purchased outside California, 19% did not contain FRs over 0.2 mg/g. Overall, the prevalence of PentaBDE in California couches (29%) was about twice as high as those purchased elsewhere (12%), but the difference was not quite statistically significant (p = 0.054). Analysis of the data pre- and post-2005 suggests that furniture sold in California prior to 2005 was more likely to be treated with FR compared to furniture sold outside California (p = 0.07). FR applications increased overall in furniture post-2005 (p < 0.01), and there was no significant difference in FR use in furniture sold within or outside California after 2005. Thus, the higher prevalence of PentaBDE in California couches appears to be due to the higher prevalence of FR use prior to 2005 when PentaBDE was the dominant FR.

TB117 Labeling and the Use of FRs in Furniture. We also investigated whether the presence of a TB 117 label was associated with the use of FRs in a product. Of the samples analyzed, 64% contained a label indicating they met TB 117, and significant levels of FRs (>0.2 mg/g of foam) were detected in all but one of these samples (98%). Thirty-four % of samples did not have a TB117 label (no data were available for two), and in 40% of the cases, no identifiable FRs were observed, or levels were very low (<0.2 mg/g). Twenty-one samples (60%) that did not contain a TB 117 label did in fact have detectable levels of FRs present in the foam (>0.2 mg/g). These data suggest that the presence of a TB 117 label indicates that a FR is very likely present, but the absence of the label is indeterminate, i.e., use of the label as a screen has good sensitivity but poor specificity.

In summary, our study has provided unique data on the types and amounts of flame retardants used in US residential furniture as well as examining time and geographic trends. We think it is unfortunate that such data are not publicly available to both environmental health scientists and consumers. Information on flame retardant applications in specific consumer products could help elucidate human exposure pathways and provide more insight into sources of flame retardants detected in the environment. One limitation of the current study is that we only examined residential couches. FR use in furniture designed for offices and other public places may differ as they are regulated separately in some locales. While we analyzed a relatively large number of samples (102), our sampling scheme was not random and therefore may not be easily generalizable to the US as a whole. For example, FR prevalence may be different in couches used by people not well represented in our sampling frame.

With the addition of TDCPP to California’s Proposition 65 list in 2011, products containing this chemical are now required to have a label stating “This product contains a chemical known to the state of California to cause cancer”. Our current study suggests that approximately 50% of the residential couches in use by average Americans are treated with TDCPP, indicating that a large percentage of the population may have increased cancer risks due to exposure to TDCPP treated furniture, according to the CPSC model. The addition of TDCPP to Proposition 65 may lead to decreased applications of TDCPP in furniture, but future studies are warranted to evaluate these trends.

Following the PentabDE phase out we also found that a larger variety of FRs are now being used in residential furniture to meet TB 117, increasing the complexity of FR exposures. Given that these alternate FRs are additive, one might suspect that they will also migrate out of furniture over time, leading to exposure concerns in indoor environments, similar to PBDEs and TDCPP. Future studies evaluating human exposure, particularly children’s exposure, to these mixtures of flame retardants in indoor environments are therefore also warranted.

ASSOCIATED CONTENT

Supporting Information

Additional information supportive of our study identified above. Figures S1 through S3 display the mass spectrum of several organophosphate FRs previously unidentified. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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Exhibit 6
Identification of Flame Retardants in Polyurethane Foam Collected from Baby Products

Heather M. Stapleton,*‡ Susan Klosterhaus,† Alex Keller,‡ P. Lee Ferguson,‡ Saskia van Bergen,§ Ellen Cooper,† Thomas F. Webster,‖ and Arlene Blum‡

ABSTRACT: With the phase-out of PentaBDE in 2004, alternative flame retardants are being used in polyurethane foam to meet flammability standards. However, insufficient information is available on the identity of the flame retardants currently in use. Baby products containing polyurethane foam must meet California state furniture flammability standards, which likely affects the use of flame retardants in baby products throughout the U.S. However, it is unclear which products contain flame retardants and at what concentrations. In this study we surveyed baby products containing polyurethane foam to investigate how often flame retardants were used in these products. Information on when the products were purchased and whether they contained a label indicating that the product meets requirements for a California flammability standard were recorded. When possible, we identified the flame retardants being used and their concentrations in the foam. Foam samples collected from 101 commonly used baby products were analyzed. Eighty samples contained an identifiable flame retardant additive, and all but one of these was either chlorinated or brominated. The most common flame retardant detected was tris(1,3-dichloroisopropyl) phosphate (TDCPP; detection frequency 36%), followed by components typically found in the Firemaster550 commercial mixture (detection frequency 17%). Five samples contained PBDE congeners commonly associated with PentaBDE, suggesting products with PentaBDE are still in-use. Two chlorinated organophosphate flame retardants (OPFRs) not previously documented in the environment or in consumer products. Based on exposure estimates conducted by the Consumer Product Safety Commission (CPSC), we predict that infants may receive greater exposure to TDCPP from these products compared to the average child or adult from upholstered furniture, all of which are higher than acceptable daily intake levels of TDCPP set by the CPSC. Future studies are therefore warranted to specifically measure infants exposure to these flame retardants from intimate contact with these products and to determine if there are any associated health concerns.

INTRODUCTION

Prior to 2004, PentaBDE was one of the most common flame retardant mixtures added to polyurethane foam in furniture and other consumer products, particularly in the US. Because of concerns regarding the persistence, bioaccumulation, and potential toxicity of the polybrominated diphenyl ethers (PBDEs) present in this commercial mixture, California passed legislation banning its use in 2003. Eight other states and the European Union (EU) followed with similar bans and the sole U.S. manufacturer, Great Lakes Chemical (now Chemtura), voluntarily phased out production in 2004.1,2 Alternative chemical flame retardants have since been used and identified as PentaBDE replacements in polyurethane foam.3-5 However, basic information on these alternative flame retardants, such as chemical identity, specific product applications, and volumes used, are typically not available.

Supporting Information
significantly restricting human and environmental health evaluations. Many of the chemical ingredients in flame retardant mixtures are proprietary and are not disclosed by the chemical manufacturers, even to manufacturers using these chemicals in their final end products (e.g., furniture).

The flammability standard primarily driving the use of flame retardant chemicals in polyurethane foam in the US is Technical Bulletin 117 (TB117), promulgated by the California Bureau of Electronic and Appliance Repair, Home Furnishings and Thermal Insulation. TB117 requires that polyurethane foam in upholstered furniture sold in the State of California withstand exposure to a small open flame for 12 s. Though the standard does not specifically require the addition of flame retardant chemicals to the foam, polyurethane foam manufacturers typically use chemical additives as an efficient method for meeting the TB117 performance criteria. Throughout the 1980s and 1990s, PentaBDE was used often in the US to comply with TB117. Numerous studies have since documented widespread contamination of the PBDE congeners found in the PentaBDE mixture in both humans and wildlife. PBDEs have also recently been identified in children’s toys. Despite the fact that compliance with TB117 is only required for residential upholstered furniture sold in the State of California, a significant fraction of products sold elsewhere in the US also complies with TB117 and therefore also contains flame retardant additives.

It is less well-known that some baby products are considered juvenile furniture and that the polyurethane foam used in baby products must also comply with TB117. However, the extent of baby product compliance with TB117 and whether or not the types of chemicals added to the polyurethane foam are similar to those in nonjuvenile furniture is unknown. Flame retardant additives can escape from products over time, accumulate in dust, and are a primary route of exposure to humans.

Exposure to children is a particular concern due to their frequent hand to mouth behavior and higher contact with toys. Exposure to chemical additives in baby products is of even greater concern for infants, who are in intimate contact with these products for long periods of time, at very critical stages of their development. Knowledge of the types of chemicals in use and the products they are used in are essential first steps for evaluating the potential for human exposure and subsequent health effects. Structural identities are also needed to track the fate and transport of these chemicals in the environment.

The objective of this study was to survey a large number of baby products that contain polyurethane foam to investigate whether flame retardant chemicals were present and to determine the concentrations in the foam, in order to understand whether they may be a significant source of exposure, particularly to infants. To do this we analyzed foam samples from baby products purchased in the US, primarily targeting the most commonly used products that contain polyurethane foam. A secondary objective was to determine whether portable X-ray fluorescence (XRF) is a useful method for predicting the presence of bromine or chlorinated flame retardant additives in these products. In a previous study, XRF-measured bromine was highly correlated with gas chromatography—mass spectrometry (GC/MS)-measured bromine in a limited number of pieces of furniture foam and plastics from electronics. However, Allen et al. focused on estimating PBDE content, and it is not known whether XRF is a useful indicator of the presence of other brominated and chlorinated flame retardants. Portable XRF has potential for use as a less expensive screening tool for researchers studying potential sources of flame retardant chemicals as well as concerned members of the public interested in avoiding products containing flame retardant chemicals. Data generated from this study will be useful for informing general consumers and scientists about specific flame retardants in use to better understand their fate, exposure, and potential health effects from using these chemicals in consumer products.

### MATERIALS AND METHODS

**Materials.** Internal standards were purchased from Chiron (Trondheim, Norway) and Wellington Laboratories (Guelph, Ontario). PBDE calibration standards were purchased from AccuStandard (New Haven, CT); 2-ethylhexyl-2,3,4,5-tetrabromobenzene (TBB) and bis(2-ethylhexyl)-2,3,4,5-tetrabromophthalate (TBPB) were purchased from Wellington Laboratories. Tris(2-chloroethyl) phosphate (TCEP), tris(1-chloro-2-propyl) phosphate (TCP), and tris(1,3-dichloroisopropyl) phosphate (TDCCP) were purchased from Sigma-Aldrich (St. Louis, MI), Pfaltz & Bauer (Waterbury, CT), and ChemService (West Chester, PA), respectively. All solvents used throughout this study were HPLC grade.

**Sample Collection.** Foam samples were solicited from volunteers via email distributions to colleagues and listserve members primarily in the United States. Requests were made for samples of polyurethane foam from baby products, with specific requests for samples of car seats, strollers, changing table pads, nursing pillows, portable crib mattresses, and infant sleep positioners. Individuals interested in participating in our study were asked to cut out a small piece of the foam (approximately 2 cm × 2 cm), wrap the foam in aluminum foil, and enclose it in a resealable plastic bag. Participants were also asked to complete a brief survey to collect information on the type of product, year of purchase, manufacturer, and whether the product possessed a label indicating that it met the criteria for TB117 or Technical Bulletins 116 (TB 116) or 603 (TB603). These latter two California flammability standards regulate flammability in upholstered furniture and mattresses, respectively. The samples were logged into a database and then split into two pieces, one for chemical analysis by mass spectrometry and one for elemental analysis using a portable XRF analyzer. Each analysis was conducted blind.

**Sample Analysis by Mass Spectrometry.** All foam samples were first screened for flame retardant additives. Briefly, small pieces of foam (approximately 0.05 g) were sonicated with 1 mL of dichloromethane (DCM) in a test tube for 15 min. The DCM extract was syringe-filtered to remove particles and then transferred to an autosampler vial for analysis by GC/MS. All extracts were analyzed in full scan mode using both electron ionization (GC/EI-MS) and electron capture negative chemical ionization (GC/ECNI-MS). Pressurized temperature vaporization injection was employed in the GC. GC/MS method details can be found in ref 3. All significant peaks observed in the total ion chromatograms were compared to a mass spectral database (NIST, 2005) and to authentic standards when available.

If a flame retardant chemical was detected during the initial screening, a second analysis of the foam sample, using a separate piece of the foam, was conducted for quantitation using accelerated solvent extraction. Our methods for extracting and measuring flame retardants in foam are reported in Stapleton et al. A five point calibration curve was established for all analytes with concentrations ranging from 20 ng/mL to 2 μg/mL. PBDEs were quantified by GC/ECNI-MS by monitoring bromide ions.
Table 1. Description of Baby Products Analyzed in This Study and a Summary of the Flame Retardants Detected in These Products at Concentrations >1 mg/g Foam

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<th>U_OPFR</th>
<th>TPP</th>
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<th>Concentration range (mg/g)</th>
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<td>16.6 – 51.54</td>
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The brominated compounds present in FM 550. All samples containing TBB/TBPH also contained TPP. Infers either no detection of chemicals or peaks were unidentifiable. N/M indicates not measured due to absence of calibration standard.
use in this study. Most samples were collected from products currently in use. However, 14 of the products were purchased new in 2010 specifically for this study. Samples were donated from participants residing in 13 US states, although one sample was submitted from Vancouver, Canada. A summary of the number and types of products included in this study is shown in Table 1. Most samples were from car seats (n = 21), changing table pads (n = 16), infant sleep positioners (n = 15), portable crib mattresses (n = 13), and nursing pillows (n = 11). A few additional samples were collected from high chairs, nursery rocking chairs/gliders, baby walkers, baby carriers, and miscellaneous bathroom items.

The chemical structures for the most commonly detected flame retardants (non-PBDEs) in the baby product foam samples are presented in Figure 1. Table 1 provides an overview of the flame retardants detected in the baby product foam in concentrations greater than 1 mg/g. A threshold value of 1 mg/g was used because while flame retardants are typically added to polyurethane foam at percent levels, some foam samples may contain flame retardant impurities due to changes in flame retardant applications from batch to batch during foam production (personal communication from foam manufacturer who wishes to be anonymous). The most common flame retardant detected was tris(1,3-dichloroisopropyl) phosphate (TDCPP). Chlorinated organophosphate flame retardants (OPFRs) were the dominant class of flame retardants observed and were detected in 60 of the 101 samples analyzed. Firemaster SS0 (FM SS0) was detected in 17 samples, as identified by detection of 2-ethylhexyl-2,3,4,5-tetrabromobenzoate (TBB), bis(2-ethylhexyl)-2,3,4,5-tetrabromophthalate (TBPH), and triphenyl phosphate (TPP) together in the samples.4 FM SS0 also contains several isopropylated triaryl phosphate isomers that are trade secret.14 These isomers were apparent in the GC/MS screening analysis but not quantified due to lack of analytical standards. PBDE congeners commonly associated with the PentabDE mixture were detected in five of the samples examined and were always found in combination with TPP. Despite the fact that Chemtura ceased production of PentabDE in 2004, products containing this flame retardant are obviously still in active use by the general public. Four of the five products found to contain PBDE congeners were purchased prior to 2004, and the fifth sample was purchased in 2007 from a second-hand store, thus making it impossible to determine the original manufacture and purchase date. Lastly, one sample was found to have significant levels of TPP but not TBB or TBPH. HPLC-HRMS analysis of this sample demonstrated the presence of TPP and three polybutylated aryl phosphate compounds, which may be from use of a flame retardant mixture manufactured by Supresta (Ardsley, NY) and sold commercially as AC073. According to information provided in the EPA’s Furniture Flame Retardancy Partnership,15 AC073 consists of TPP (38–48%) and three proprietary aryl phosphate compounds in concentrations ranging from 40 to 46%, 12–18%, and 1–3% for each phosphate compound. These percentages are very similar to the area responses observed for TPP and the butylated aryl phosphates observed in our GC/MS and LC/HRMS analyses.

Identification of New Flame Retardants. In addition to the flame retardants described above, we also detected two OPFRs, which to our knowledge, have not been previously identified in the environmental literature. During our GC/MS analysis of the

Figure 1. Structures of non-PBDE flame retardants detected in polyurethane foam collected from baby products.
foam samples, some samples were found to have either no detectable levels of the targeted flame retardants or to have very low levels of TCEP and TCPP. In addition, GC/MS analysis of some of these samples revealed chromatographically unresolved peaks (i.e., very broad, with significant tailing) eluting after TCEP and TCPP. We considered it very likely that these products had been treated with some kind of flame retardants at a significant (percent-by-mass) level in order to meet flame retardancy standards. During the HPLC/HRMS analysis, several of these samples yielded abundant and chromatographically resolved peaks in both positive-ion electrospray and APCI modes for compounds having mass spectra (e.g., accurate mass and isotope structure) suggestive of a chlorinated organophosphate compound containing two phosphate groups and six chlorine atoms. Furthermore, it appeared that some samples contained a putative chlorinated organodiphosphate with an \([M+H]^+\) ion at 580.91 \(m/z\), while other samples were dominated by a peak giving an \([M+H]^+\) ion at 636.97 \(m/z\). We did not have access to authentic standards for definitive identification of these compounds. However, based on results from both high-resolution electrospray ionization and atmospheric pressure chemical ionization, and from MS/MS and MS\(^3\) analysis, we propose that one compound is 2,2-bis(chloromethyl)propane-1,3-diyl-tetrakis(1-chloropropan-2-yl) bis(phosphate). In this manuscript we will refer to this compound as the “U-OPFR”. As observed in Figure 2, the difference between the predicted (636.9776) and observed (636.9769) \(m/z\) values for monoisotopic \([M+H]^+\) ions for U-OPFR was less than 2 ppm. We can find no reference to the use or manufacture of this compound by any chemical company. However, we did find a patent application submitted by Albermarle in 2008 which describes the potential application and structure of this chemical. Presumably the synthesis of this U-OPFR would be very similar to the synthesis of V6, as these two compounds are structural analogs, suggesting that the U-OPFR would contain TCPP as an impurity, analogous to the presence of TCEP in V6. In fact, in every sample for which we detected this U-OPFR, we also detected TCPP.

It is also of interest to note that many of the products examined contained more than one identifiable flame retardant. For example, in one sample, FM 550 and PentaBDE were detected together in appreciable levels, while in another sample both TDCPP and FM 550 were detected. In addition, every sample containing PentaBDE also contained TPP. It appears likely that TPP was frequently used in combination with PentaBDE, an observation not previously reported to our knowledge. Taken together these
observations indicate that some of these flame retardants are being used in combinations in commercial products or that there is contamination in the foam from one batch to the next.

Of the 101 products examined in this study, 12 samples were observed to have significant peaks present in the extracts, but the identities of the chemicals could not be determined. And nine samples were observed to have no significant peaks in the chromatograms during the screening step. Therefore, 80% of the baby products tested in this study contained a known and identifiable flame retardant, and all but one of these flame retardants were either brominated or chlorinated.

Flame Retardant Associations with Products. In general, the flame retardant chemicals detected were not associated with a particular type of product, manufacturer, or the year of purchase. An exception to this was the detection of V6 in nursing pillows. We analyzed 11 different samples from nursing pillows, all of which were manufactured by one company. Ten of these samples contained V6 and were purchased between 2003 and 2008. The remaining sample was purchased in 2010 and contained primarily TDCPP as well as appreciable levels of TCPP (1.55 mg/g). Five additional nursing pillows from the same company were purchased during the summer of 2010 to determine whether V6 and/or TCEP were present. These samples were screened using GC/MS. The only FR detected was TDCPP, which was found in all five samples. More information on the flame retardants detected in each sample can be found in the Supporting Information.

Flame Retardant Concentrations in Foam. If authentic standards were available, we measured the concentrations of the dominant flame retardants detected in the foam samples (Table 1). TDCPP and PentaBDE were detected in the highest concentrations, with average concentrations of 39.2 and 32.3 mg/g, respectively (approximately 3–4% by weight). These values are similar to previously reported values of flame retardants in furniture by our group but lower than the 32% by weight measurement made by Hale et al. in polyurethane foam. The two brominated compounds in the FM 550 formulation were detected at lower concentrations than TDCPP and PentaBDE, likely because they are parts of a mixture. According to the MSDS for FM 550, TBB and TBPH together comprise approximately 50% of the overall mixture. This likely explains why the sum of TBB and TBPH is approximately 50% of the measured concentrations of TDCPP and PentaBDE in the foam samples.

In general, concentrations of TCEP and TCPP in the samples were much lower than the concentrations of the other three primary flame retardants identified, indicating they may be minor components of flame retardant mixtures, such as V6. In all samples in which TCEP was detected, V6 or TCPP/TDCPP was also detected. In only two samples was TCPP the only identified flame retardant. One sample contained 5.8 mg/g of TCPP, and no other compounds were evident by GC/MS or high resolution MS analysis. However, the second sample, which contained only TCPP (0.8 mg/g), also contained several unidentified chlorinated compounds that appeared to be part of a polymeric series, but no consistent elemental formulas were apparent.

**XRF Analysis.** We investigated whether portable X-ray fluorescence (XRF) could be used as a screening tool for predicting the presence of brominated or chlorinated flame retardant additives in foam from these products. When both XRF and GC/MS analyses detected bromine in the foam samples, a significant correlation (p < 0.001) was observed (Figure 3a). In samples containing FM550, XRF-measured bromine generally overpredicted the GC/MS-measured bromine by about 100%. This overprediction is consistent with that found earlier by Allen et al. and may be due to differences in the sample matrix as the calibration standards used with the XRF device are hard plastics. However, there were seven samples in which XRF analyses detected bromine ranging from 1.4–3.4% by weight, but GC/MS detected only chlorinated OPFRs. This suggests that there are either some instances in which false positives are generated for bromine in polyurethane foam by XRF, possibly due to interferences by other elements, or there are unknown brominated compounds present in some of these foam samples that were not accounted for by GC/MS analysis.

As seen in Figure 3b, there was no significant relationship observed between XRF- and GC/MS-measured chlorine in these samples. The fact that we detected V6, and the U-OPFR, but could not quantify them without an authentic standard, was likely a contributing factor for the poor relationship between the XRF and GC/MS analyses. While removing these compounds from the correlation analysis resulted in a higher correlation coefficient, the slope was still not significant (data not shown). Also, in three samples XRF-measured chlorine ranged from 1.2–3.3% by weight, yet GC/MS determined that only BFRs were present. Chlorinated impurities present in toluene diisocyanate (TDI), a starting material for the synthesis of polyurethane foam, may be responsible for these chlorine signals and would not have been detectable in the GC/MS analysis. These TDI impurities may also have contributed to the much higher concentrations of XRF-measured chlorine observed (2.2–23.7%) compared to the GC/MS results for the OPFRs. Based on these results, we believe that XRF is generally a useful screening tool for identifying the...
presence of BFRs in foam; however, additional work is needed to understand the extent of its use as an effective screening tool for chlorinated flame retardants.

**Infant’s Exposure Potential and Health Concerns.** This study found that more than 80% of the baby products tested contained a halogenated flame retardant additive, many of which were chlorinated OPFRs. This suggests these products could be sources of flame retardant exposures in indoor environments, particularly to infants that come in close contact with these products. In 2006, the Consumer Product Safety Commission (CPSC) released a Risk Assessment of Flame Retardant Chemicals in Upholstered Furniture Foam, which included TDCPP.

This CPSC report states that “...upholstered furniture manufactured with TDCPP treated foam might present a hazard to consumers, based on both cancer and non-cancer end points”. The CPSC estimate of children’s exposure to TDCPP from treated furniture was five times higher than the agency’s acceptable daily intake (i.e., the Hazard Index was 5). Almost 99% of this exposure was from inhalation of TDCPP volatilized from treated furniture (air concentrations were predicted near furniture and in rooms rather than measured, a major source of uncertainty). TDCPP was the most common flame retardant identified in this screening study, with concentrations very similar to those reported in upholstered furniture. For several reasons, infants exposure to TDCPP could be higher than the exposure calculated by the CPSC. Infants have smaller body masses relative to the average child or adult used in their assessment. Infants spend a greater proportion of their time in intimate contact with these materials (e.g., infant sleep positioners, car seats, nursing pillows) over a longer daily time period than the 3 h assumed in the CPSC report. In addition, new studies are suggesting that exposure to semi-volatile organic compounds may be occurring from equilibrium partitioning between the indoor gas phase and skin surfaces/clothing, which can lead to accumulation via skin absorption. TDCPP has been shown to be efficiently absorbed through the skin of rodents, with as much as 85% of the dose absorbed dermally. Therefore, exposure of infants to TDCPP, and likely other flame retardants, may be greater than the Hazard Index of 5 calculated by the CPSC. Further research is warranted to investigate infant exposure to flame retardants in these products, particularly since infants are in a very sensitive development stage and may be more susceptible to adverse effects than an older child or adult.

Previous studies have shown that TDCPP, and its brominated analogue tris (2,3-dibromopropyl) phosphate, were previously used as flame retardants in children’s sleepwear. However, this use was discontinued after studies found that children wearing these clothes absorbed TDBPP. Both TDBPP and TDCPP were observed to be mutagenic in the Ames assay, particularly after metabolism. Rats exposed to TDCPP were found to have increased incidences of tumors, and a recent study also found that TDCPP was as potent a neurotoxicant as chlorpyrifos using an in vitro assay. One study found that TDCPP levels in house dust were significantly correlated with reduced thyroid hormone levels and increased levels of prolactin in men. And one study detected TDCPP and several other OPFRs at concentrations similar to PBDEs in US house dust, suggesting chronic exposure to the population is occurring on a daily basis. In addition, the European Chemical Bureau of the European Union considers TCEP to be a category 3 carcinogen.

This study adds to our understanding of flame retardants in consumer products. The comparison of XRF and GC/MS measurements for bromine confirm previous results that this technology is generally useful for screening brominated flame retardants in polyurethane foam. The results for chlorine have not been previously reported and suggest that additional research is needed before XRF can reliably screen for chlorinated flame retardants in polyurethane foam. Levels of up to 12.5% of TDCPP were found in one product, while other products were found to contain up to three different retardants in one product. Lastly, we have identified two flame retardants previously unreported in the environment. Further studies are also warranted to determine whether V6 and the U-OPFR are present in indoor environments and whether human exposure is a concern.

**ASSOCIATED CONTENT**

5 Supporting Information. High resolution tandem mass spectra and proposed fragmentation mechanisms and pathways relevant to the identification of the putative U-OPFR compound described in the manuscript are available in the Supporting Information. We also include a table summarizing the types and relative abundances of flame retardant chemicals analyzed in all samples measured in the present study. This material is available free of charge via the Internet at http://pubs.acs.org.

**AUTHOR INFORMATION**

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**ACKNOWLEDGMENT**

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**REFERENCES**


(17) http://www.epa.gov/iur/.


Exhibit 7
After the PBDE Phase-Out: A Broad Suite of Flame Retardants in Repeat House Dust Samples from California

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Supporting Information

ABSTRACT: Higher house dust levels of PBDE flame retardants (FRs) have been reported in California than other parts of the world, due to the state’s furniture flammability standard. However, changing levels of these and other FRs have not been evaluated following the 2004 U.S. phase-out of PentaBDE and OctaBDE. We analyzed dust collected in 16 California homes in 2006 and again in 2011 for 62 FRs and organohalogens, which represents the broadest investigation of FRs in homes. Fifty-five compounds were detected in at least one sample; 41 in at least 50% of samples. Concentrations of chlorinated OPFRs, including two (TCEP and TDCIPP) listed as carcinogens under California’s Proposition 65, were found up to 0.01% in dust, higher than previously reported in the U.S. In 75% of the homes, we detected TDBPP, or brominated “Tris,” which was banned in children’s sleepwear because of carcinogenicity. To our knowledge, this is the first report on TDBPP in house dust. Concentrations of Firemaster 550 components (EH-TBB, BEH-TEBP, and TPHP) were higher in 2011 than 2006, consistent with its use as a PentaBDE replacement. Results highlight the evolving nature of FR exposures and suggest that manufacturers continue to use hazardous chemicals and replace chemicals of concern with chemicals with uncharacterized toxicity.

INTRODUCTION

California house dust contains some of the highest concentrations of polybrominated diphenyl ether (PBDE) flame retardants (FRs) in the world due to a state-wide furniture flammability standard (Technical Bulletin 117). PBDEs have been associated with thyroid and other endocrine system disruption and adverse neurological development (see Supporting Information (SI)). PBDEs in California homes and residents often exceed risk-based levels for children, raising concerns about exposures to the many other FRs that have not yet been well-characterized. For example, Great Lakes Chemical Corporation, the sole U.S. PBDE manufacturer, introduced Firemaster 550 to replace the PentaBDE commercial mixture in response to prospective bans in Europe and several U.S. states. Little is known about the chemical composition, uses, exposure levels and health effects of this mixture or of other brominated, chlorinated, and organophosphate chemicals used as FRs. Because additive FRs shed from consumer products, they are found in house dust. Measuring dust concentrations over time can identify exposure trends that result from changes in product formulations.

House dust is the primary route of exposure for PBDEs, contributing 82%, on average, of a U.S. adult resident’s exposure. Dust concentrations of PentaBDE were correlated with breast milk levels in 11 women. Although diet may also contribute, dust appears to be particularly important in areas, like California, with high concentrations in dust. Dust is a direct exposure pathway through incidental ingestion, inhalation of resuspended particles, and dermal absorption, and it is a proxy for exposure from product use.

Commercial PentabDE and OctaBDE mixtures were phased-out in 2004 in the U.S.8 DecaBDE is banned in electrical and electronic applications in Europe, and U.S. producers and importers (Chemtura, Albermarle, and ICL Industrial Products) committed to end production, import and sales by the end of 2013. As PBDEs were phased out due to health concerns, other brominated FRs (BFRs) and organophosphate flame retardants (OPFRs) were introduced as replacements. Chemtura, formerly Great Lakes Chemical Corporation, replaced PentaBDE in polyurethane foam with Firemaster 550, a mixture of 2-ethylhexyl-2,3,4,5-tetrabromobenzoate (EH-TBB), bis(2-ethylhexyl)-3,4,5,6-tetramethylphosphonate (BEH-TEBP), triphenyl phosphate (TPHP), and a yet-to-be-fully characterized triaryl phosphate isopropylated mixture. Concerns are emerging about BEH-TEBP’s environmental persistence and toxicity, since BEH-TEBP is the brominated
Table 1. Concentrations (ng/g Dust) of Flame Retardants and Legacy Organohalogens in California House Dust from 16 Homes Sampled in 2006 and 2011

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>Abbreviation</th>
<th>LOQ&lt;sup&gt;a&lt;/sup&gt;</th>
<th>% &gt; LOQ</th>
<th>min.</th>
<th>median</th>
<th>max.</th>
<th>% &gt; LOQ</th>
<th>min.</th>
<th>median</th>
<th>max.</th>
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<td>bis(2-ethylhexyl)-3,4,5,6-tetrabromophthalate</td>
<td>BEH-TBEP (or TBPH)</td>
<td>2 100 36 140 1900 94 &lt;2 260 3800</td>
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<td>TPHP</td>
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<td>Tetramethylbisphenol A</td>
<td>BBPA</td>
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<tr>
<td>Hexabromocyclododecane</td>
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<tr>
<td>α-hexabromocyclododecane</td>
<td>α-HBCYD (or α-HBCD)</td>
<td>5 100 31 62 710 100 17 62 910</td>
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<td>β-hexabromocyclododecane</td>
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<td>γ-hexabromocyclododecane</td>
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<td>5 100 29 94 6700 100 13 73 790</td>
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<td>hexabromocyclododecane</td>
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<td>Other Brominated Flame Retardants (BFRs)</td>
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<td>hexachloroclopetadientyle-dibromocyclooctane</td>
<td>DBHCTCD (or HCDDBC)</td>
<td>5 6 &lt;5 &lt;5 9 25 &lt;5 &lt;5 72</td>
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<td>1,2-bis(2,6,6-trimethylphanenoxo)ethane</td>
<td>BTBPE</td>
<td>2 100 7 30 220 100 3 12 130</td>
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<tr>
<td>decabromodiphenylethane</td>
<td>DBDPE</td>
<td>10 94 &lt;10 51 430 100 18 140 2800</td>
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<td>tetrabromobisphenol A - bis(2,3-dibromopropane)</td>
<td>TBBPA-BDBPE (or TBBPA-dbp)</td>
<td>10 75 &lt;10 22 180 50 &lt;10 7 560</td>
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<tr>
<td>α-1,2-dibromo-4′-(1,2-dibromoethyl)</td>
<td>α-DBE-DBCH (or α-TBCH)</td>
<td>2 6 &lt;2 &lt;2 13 19 &lt;2 &lt;2 25</td>
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<tr>
<td>cyclohexane</td>
<td>β-DBE-DBCH (or β-TBCH)</td>
<td>2 6 &lt;2 &lt;2 11 12 &lt;2 &lt;2 16</td>
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<td>β-1,2-dibromo-4′-(1,2-dibromoethyl)</td>
<td>β-DBE-DBCH (or β-TBCH)</td>
<td>2 6 &lt;2 &lt;2 11 12 &lt;2 &lt;2 16</td>
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<tr>
<td>cyclohexane</td>
<td>γ-DBE-DBCH (or γ-TBCH)</td>
<td>2 6 &lt;2 &lt;2 11 12 &lt;2 &lt;2 16</td>
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<tr>
<td>δ-1,2-dibromo-4′-(1,2-dibromoethyl)</td>
<td>δ-DBE-DBCH (or δ-TBCH)</td>
<td>2 6 &lt;2 &lt;2 11 12 &lt;2 &lt;2 16</td>
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<td>TBP-AE (or ATE)</td>
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<td>2,4,6-tribromophenyl 2,3-dibromopropyl ether</td>
<td>TBP-DPE (or DPE)</td>
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<td>β-TBCO</td>
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<td>octabromo-1,3,3-trimethyl-1-phenylidine</td>
<td>OBTMPI (or OBIND)</td>
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<td>Halogenated Organophosphate Flame Retardants (OPFRs)</td>
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<td>tris(2-chloroethyl) phosphates</td>
<td>TCEP</td>
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<td>tris(1-chloro-2-propyl) phosphates</td>
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<td>TDCIPP (or TDCPP)</td>
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<td>tris(2,3-dibromopropyl) phosphates</td>
<td>TDBPP</td>
<td>20 62 &lt;20 35 8900 38 &lt;20 &lt;20 310</td>
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<tr>
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<td>TEP</td>
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Table 1. continued

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<th>min.</th>
<th>median</th>
<th>max.</th>
<th>% &gt; LOQ</th>
<th>min.</th>
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<td>100</td>
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Dechlorane Plus (DP)

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<td>anti-DP</td>
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<td>Σ DP</td>
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Legacy Compounds

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<th>max.</th>
<th>% &gt; LOQ</th>
<th>min.</th>
<th>median</th>
<th>max.</th>
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<td>100</td>
<td>6</td>
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<td>200</td>
<td>81</td>
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<td>2,2′-4,4′,5,5′-heptachlorobiphenyl</td>
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<td>5</td>
<td>94</td>
<td>&lt;5</td>
<td>16</td>
<td>74</td>
<td>75</td>
<td>&lt;5</td>
<td>8.5</td>
<td>90</td>
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<tr>
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<td>BB 80</td>
<td>3</td>
<td>0</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>6</td>
<td>&lt;3</td>
<td>&lt;3</td>
<td>6</td>
</tr>
<tr>
<td>2,2′,4,5′-pentabromo biphenyl</td>
<td>BB 103</td>
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<td>0</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>6</td>
<td>&lt;3</td>
<td>&lt;3</td>
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</tr>
<tr>
<td>2,2′,4,4′,5,5′-hexabromo biphenyl</td>
<td>BB 153</td>
<td>3</td>
<td>56</td>
<td>&lt;3</td>
<td>4.5</td>
<td>160</td>
<td>44</td>
<td>&lt;3</td>
<td>&lt;3</td>
<td>47</td>
</tr>
<tr>
<td>2,2′,4,4′,5,5′-heptabromo biphenyl</td>
<td>BB 180</td>
<td>5</td>
<td>0</td>
<td>—</td>
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<td>—</td>
<td>0</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>decabromo biphenyl</td>
<td>BB 209</td>
<td>10</td>
<td>0</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>0</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>cis-chlordane</td>
<td>CC</td>
<td>5</td>
<td>94</td>
<td>&lt;5</td>
<td>26</td>
<td>250</td>
<td>94</td>
<td>&lt;5</td>
<td>17</td>
<td>180</td>
</tr>
<tr>
<td>trans-chlordane</td>
<td>TC</td>
<td>5</td>
<td>94</td>
<td>&lt;5</td>
<td>34</td>
<td>280</td>
<td>100</td>
<td>5</td>
<td>22</td>
<td>220</td>
</tr>
<tr>
<td>trans-nonachlor</td>
<td>TN</td>
<td>5</td>
<td>94</td>
<td>&lt;5</td>
<td>19</td>
<td>130</td>
<td>88</td>
<td>&lt;5</td>
<td>11</td>
<td>140</td>
</tr>
<tr>
<td>1,1,1-trichloro-2,2-di(4-chlorophenyl)ethane</td>
<td>pp′-DDT</td>
<td>10</td>
<td>100</td>
<td>44</td>
<td>530</td>
<td>4100</td>
<td>100</td>
<td>50</td>
<td>160</td>
<td>1500</td>
</tr>
<tr>
<td>1,1-bis(4-chlorophenyl)-2,2-dichloroethene</td>
<td>pp′-DDE</td>
<td>10</td>
<td>94</td>
<td>&lt;10</td>
<td>74</td>
<td>430</td>
<td>88</td>
<td>&lt;10</td>
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<td>170</td>
</tr>
<tr>
<td>1,1-dichloro-2-(2-chlorophenyl)-2-(4-phenyl)ethane</td>
<td>pp′-DDD</td>
<td>10</td>
<td>88</td>
<td>&lt;10</td>
<td>36</td>
<td>240</td>
<td>75</td>
<td>&lt;10</td>
<td>14</td>
<td>64</td>
</tr>
</tbody>
</table>

*aCompounds were named following the newly proposed nomenclature presented by Bergman et al,62 with the older name give in parentheses.
*bLOQ limit of quantification; — indicates insufficient number of detects to calculate summary statistics.

version of bis(2-ethylhexyl)phthalate (DEHP) that adversely affects reproductive development.16 The U.S. EPA recently announced plans to conduct risk assessments for BEH-TEBP and EH-TBB.17

Several OPFRs are used as PBDE replacements. In the late 1970s, tris(2,3-dibromopropyl) phosphate (TDBPP or brominated “Tris”) was banned from children’s pajamas because of its mutagenic and carcinogenic properties.18,19 Exposure data are limited, although the toxic breakdown product, 2,3-dibromo-1-propanol, was detected in U.S. homes.20 The chlorinated analog, tris(1,3-dichloro-2-propyl) phosphate (TDCIPP), also a carcinogen,14,21 has been found in U.S. house dust and baby products.22,23 TDCIPP concentrations in U.S. house dust were recently associated with altered thyroid (free T4) and prolactin hormone levels in men.24 Little information exists on exposure.25

Elevated PentaBDE concentrations in California relative to other parts of the U.S. and world have been well established; however, little is known about levels of other FRs. We expect that FRs used in polyurethane foam, including PentaBDE replacements, may be elevated due to the furniture flammability standard. Exposure patterns for FRs in other applications, such as electronics, are not known because of limited data, including for BDE 209.5

To provide data on a wider range of FRs and on changing exposure patterns, this study measured a broad array of FR chemicals in repeat dust samples collected from 16 California homes. Dust collected in California homes in 2006 and in the same homes in 2011 was analyzed for a broad suite of BFRs and OPFRs (n = 49). We also measured 13 “legacy” chemicals: persistent organochlorines (OCs) banned long ago (e.g., DDT). We expected OC concentrations to remain relatively constant or decrease between sampling dates.26 Correlation and cluster analysis of simultaneous FR measurements were used to shed light on mixtures and potential sources. Measurement at two time periods allows for the investigation of changes in residential levels, which likely reflect patterns of use. This work contributes to the ongoing characterization of evolving exposures to FR chemicals in homes.

**MATERIALS AND METHODS**

**Sample Collection.** Dust samples were collected in 16 northern California homes in 2006 and again in the same homes with the same participants in 2011. These homes were a subset of 50 homes in two San Francisco Bay Area communities further described in Brody et al.27 and Rudel et al.28 Samples were collected by trained field staff using a Eureka Mighty-Mite vacuum cleaner fitted with a specially designed PTFE Teflon crevice tool attachment modified to collect dust into a cellulose extraction thimble (19 × 90 mm). Samples were collected by slowly dragging the crevice tool for approximately 30 min over surfaces in the living areas of the home. Samples were sieved to <150 μm prior to long-term storage (−16 °C ± 10 °C) and extraction. Residents were surveyed about the presence of furniture, carpets, and electronics, particularly if any...
Analyte Selection. Analytes were selected based on previous research, current understanding of potential replacements for PBDEs, health concerns, and analytical capability. Based on production volumes, HBCYD and TBBPA are important BFRs. Other potential PBDE-replacements were included. The health effects of chlorinated and brominated OPFRs are of concern and recent work suggests they are found at levels similar to PBDEs. Nonhalogenated FRs are expected to be used in various FR mixtures and may be pervasive given their many other uses in the home. Legacy OCs were included to evaluate concentration consistency over time. The 62 target chemicals are listed in Table 1.

Analytical Methods. Due to the comprehensive list of target analytes and differences in physical-chemical properties, two different sample preparation methods were used in four extracts per sample (two fractions per method) for chemical analysis. One sample preparation method, which was used to measure the bulk of BFRs, OCs, and OPFRs, involved

<table>
<thead>
<tr>
<th>FR class</th>
<th>≥ 1 M lbs produced/yr</th>
<th>EPA action plan</th>
<th>REACH SVHC uses</th>
<th>health concerns</th>
</tr>
</thead>
<tbody>
<tr>
<td>PBDEs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PentaBDE</td>
<td>•</td>
<td></td>
<td>polyurethane foams</td>
<td></td>
</tr>
<tr>
<td>OctaBDE</td>
<td>•</td>
<td></td>
<td>phase-out in U.S. in 2004</td>
<td></td>
</tr>
<tr>
<td>DecaBDE</td>
<td>• • •</td>
<td></td>
<td>electrical equipment, textiles and fabric backings; 80% of total PBDE production</td>
<td></td>
</tr>
<tr>
<td>Firemaster 550</td>
<td>•</td>
<td></td>
<td>replacement for PentaBDE in foams</td>
<td></td>
</tr>
<tr>
<td>HBCYDs</td>
<td>• • •</td>
<td></td>
<td>thermoplastic (moldable) polymers and styrene resins;</td>
<td></td>
</tr>
<tr>
<td>TBBPA</td>
<td>•</td>
<td></td>
<td>reactive in circuit boards; additive in polymers;</td>
<td></td>
</tr>
<tr>
<td>Other BFRs</td>
<td></td>
<td></td>
<td>most widely used flame retardant</td>
<td></td>
</tr>
<tr>
<td>TBBPA: DDBPE</td>
<td>•</td>
<td></td>
<td>plastics, including pipes, water barriers, kitchen hoods and electronics</td>
<td></td>
</tr>
<tr>
<td>HBB</td>
<td>•</td>
<td></td>
<td>paper, wood, textiles, electronics and plastics; not used in Europe</td>
<td></td>
</tr>
<tr>
<td>BTBPE</td>
<td>•</td>
<td></td>
<td>replacement for OctaBDE</td>
<td></td>
</tr>
<tr>
<td>DBDPE</td>
<td>• • •</td>
<td></td>
<td>alternative to DecaBDE</td>
<td></td>
</tr>
<tr>
<td>Halogenated OPFRs</td>
<td>•</td>
<td></td>
<td>polyurethane foams, plastics, polyester resins, and textile</td>
<td></td>
</tr>
<tr>
<td>TCEP</td>
<td>• • •</td>
<td></td>
<td>banned from children’s products in NY in 2011</td>
<td></td>
</tr>
<tr>
<td>TCIPP</td>
<td>• • •</td>
<td>polyurethane foams</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TDCIPP</td>
<td>• • •</td>
<td>polyurethane foams, plastics, and textiles</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TDBPP</td>
<td>• • •</td>
<td>polyurethane foams</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Halogenated OPFRs</td>
<td>•</td>
<td></td>
<td>also used as plasticizer and in antifoam agents and lacquers</td>
<td></td>
</tr>
<tr>
<td>TEP</td>
<td>•</td>
<td></td>
<td>also used as plasticizer and in antifoam agents and lacquers</td>
<td></td>
</tr>
<tr>
<td>TIBP</td>
<td>•</td>
<td></td>
<td>also used as plasticizer and as a lubricant in hydraulic fluids</td>
<td></td>
</tr>
<tr>
<td>TNBP</td>
<td>•</td>
<td></td>
<td>also used in floor wax, lacquers, rubber and plastics</td>
<td></td>
</tr>
<tr>
<td>TBOEP</td>
<td>• • •</td>
<td></td>
<td>clothing, also used as plasticizer and as a solvent</td>
<td></td>
</tr>
<tr>
<td>TEHP</td>
<td>• • •</td>
<td></td>
<td>also used as plasticizer and as lubricants in hydraulic fluids</td>
<td></td>
</tr>
<tr>
<td>TMPP</td>
<td>•</td>
<td></td>
<td>also used as plasticizer and as lubricants in hydraulic fluids</td>
<td></td>
</tr>
<tr>
<td>DP</td>
<td>• • •</td>
<td></td>
<td>electronic</td>
<td></td>
</tr>
</tbody>
</table>

References for health effects can be found in SI Table SI4. Chemicals produced in the U.S. ≥ 1 million pounds per year are typically designated by the EPA as High Production Volume chemicals, a voluntary reporting program (data from 2006). U.S. EPA Action Plans have been developed for 10 chemicals considered high priority for risk management. The European Union’s system of Registration, Evaluation, Authorization, and Restriction of Chemical substances (REACH) identifies Substances of Very High Concern (SVHC), which are public health hazards proposed for regulation under REACH. Congeners BDE 28, BDE 47, BDE 66, BDE 85, BDE 99, BDE 100, BDE 153, and BDE 154. Congeners BDE 183, BDE 196, BDE 197, and BDE 203. Congener BDE 209. Based on structural considerations.
extraction using Hex-Ac (3:1, v:v) and fractionation on Florisil. The obtained fractions F1 and F2 were subjected to analysis by GC-ECNI/MS and GC-EI/MS (see SI Table S1). A second sample preparation method, involving similar extraction and fractionation on silica, was employed to measure HBCYDs, TBBPA, and to confirm PBDEs. The fraction containing PBDEs was subjected to GC-ECNI/MS and the fraction containing HBCYDs and TBBPA was subjected to LC-MS/MS analysis. Additional analytical details are in the SI.

Quality Control. Six procedural blanks were analyzed in the same batches as the samples and concentrations were blank-corrected by subtracting the mean blank values (in pg) from the raw analyte values. Method limits of quantification (LOQ) were calculated as $3 \times$ standard deviation of blank values and divided by the amount of dust used for analysis (typically 50 mg). For compounds not detected in the blanks, the LOQ was calculated based on the signal-to-noise ratio 10/1. Since LOQs are compound-specific variables, they spanned a large range of concentrations. Certified reference material SRM 2585 (Organics in Indoor Dust) was used to test the accuracy. Additional details are in the SI.

Data Analysis. Summary statistics were calculated for all analytes within each sampling round. Nondetectable concentrations were left at zero for summary statistics, which results in lower values than if other replacement methods were used. Concentration ratios (2011/2006 concentrations) were calculated to evaluate changes between the two sampling periods. Nondetectable concentrations were set to the LOQ for concentration ratios. Ratios above 1 indicate higher concentrations in 2011 and ratios below 1 indicate higher 2006 concentrations. Spearman rank correlations were used to evaluate associations between absolute concentration differences between rounds (2011−2006 concentrations) and total number of reported new FR-relevant items (e.g., electronics, carpets) in 2011. Kendall’s tau rank correlation estimates were calculated to investigate relationships between analytes within each sampling round and for each analyte across rounds. These estimates were used in cluster analysis to elucidate common mixtures and potential sources. Additional details are in the SI. Data analysis was performed in R (version 2.15).

RESULTS AND DISCUSSION
Overall, 55 compounds were detected and 41 were found in at least 50% of the 32 samples (Table 1). Detected chemicals were 13 PBDE congeners, 3 components of Firemaster 550, 15 other BFRs, 4 halogenated OPFRs, 7 nonhalogenated OPFRs, and 2 Dechlorane-Plus isomers. Table 2 summarizes information on usage and health concerns of these FRs grouped by common formulations (related to exposure patterns) and chemical
structure (often related to use and toxicity). These FR group names are used throughout the paper.

The highest concentrations, greater than 0.1 mg/g or 0.01%, were for two chlorinated OPFRs, including TCEP, which is listed as a carcinogen under California’s Proposition 65, and TCIIP, and one nonhalogenated OPFR (TBOEP). Over the five years between the sample collection periods, Firemaster 550 components increased, while PentaBDE levels decreased. Legacy pollutants like DDT also decreased, suggesting that the PBDE reduction may be due to decreased loading and/or possibly to differences in sample collection between 2006 and 2011. Figure 1 shows ratios of 2011/2006 concentrations; ratios >1 suggest increasing concentrations with time. Detailed findings are presented below by chemical group.

**Concentrations in House Dust. PBDEs.** We found all targeted PBDE congeners in at least 50% of samples, with the components of PentaBDE (BDE 47 and BDE 99) and DecaBDE (BDE 209) mixtures in 100% of samples. Median concentrations for all PBDE congeners decreased from 2006 to 2011 (Table 1); however, not all of the means decreased (data not shown), with exceptions likely driven by two homes with substantial increases in the congeners of PentaBDE mixture (SI Figure S13). Exposed furniture foam was noted in one of these homes. Ratios of 2011/2006 concentrations are used to evaluate relative concentrations from the two sampling periods. Median concentration ratios were less than 1 for all congeners (Figure 1), suggesting a decrease in concentrations between 2006 and 2011, which could reflect decreased use. However, since we saw decreases for legacy OCs, which should generally have minimal changes between 2006 and 2011, the PBDE reduction may reflect some unidentified but systematic difference in sample collection (see Legacy Chemicals below).

Substantial decreases (up to 20-fold) in concentrations of PentaBDE were observed in three homes where participants reported remodeling or acquiring new furniture and/or rugs/carpets between 2006 and 2011. In fact, there was a significant statistical association between concentration reductions and participant-reported new furniture, electronics, and flooring ($p < 0.05$), suggesting that PentaBDE is no longer present in new household items. Reductions are likely the result of phase-outs (2004) and bans (2006 in CA) of PentaBDE and OctaBDE. Substantial decrease (14-fold) in BDE 209 was observed in a home where the participant did not report changes in electronics and furnishings; possibly some relevant changes were not reported.

We detected BDE 47 and BDE 99 at median concentrations >1000 ng/g in both sampling rounds, which is consistent with previous research showing higher PentaBDE concentrations in California than elsewhere due to the unique furniture flammability standard. In comparison to other studies within California, the median concentration of BDE 47 in 2006 is similar (within 30%); whereas median concentrations of BDE 99 and 100 in 2006 (2,200 ng/g and 520 ng/g, respectively) were lower (up to 2x) than other California studies, which used slightly different vacuum sampling techniques.

Correlation and cluster analysis were used to evaluate mixtures and common sources. SI Figures S14 and S15 show that PBDE congeners measured in each sampling round correlate/cluster together in the three commercial formulations (PentaBDE, OctaBDE, and DecaBDE). OctaBDE levels correlate between sampling rounds (along diagonal in SI Figure S4), suggesting relatively stable concentrations in the homes over time; however, PentaBDE and DecaBDE levels were not significantly correlated over time, likely due to a few homes with substantial changes.

**Firemaster 550.** Chemtura introduced Firemaster 550 in 2004 as a replacement for PentaBDE in polyurethane foam. Besides TPHP, the other constituents of Firemaster 550 were only recently identified as two brominated compounds: EH-TBB and BEH-TEBP. Subsequently, Chemtura developed additional products, with undisclosed composition, including Firemaster 600, Firemaster 800, and Emerald Innovation, with claims of increased efficiency. Firemaster 550 is genotoxic and TPHP was associated with altered prolactin levels and decreased sperm concentration in men. To our knowledge, carcinogenicity, reproductive and development studies have not been conducted on the brominated components of Firemaster 550.

We detected EH-TBB, BEH-TEBP, and TPHP in all but one sample. Concentrations of EH-TBB and BEH-TEBP increased across rounds (median ratio >1; Figure 1), except in one home where BEH-TEBP was found at 1,935 ng/g in the 2006 sample and not detected (<2 ng/g) in 2011 (SI Figure S13). This home also had lower 2011 EH-TBB and TPHP concentrations. The generally increasing trend for EH-TBB and BEH-TEBP suggests that Firemaster 550 is being used as a PentaBDE replacement.

We compared our 2006 results to two sets of dust samples collected in the Boston area (50 vacuum bag samples collected between 2002 and 2007 and 20 field technician collected dust samples collected in 2006) and vacuum bag dust collected in Vancouver, Canada in 2007–2008. The 2006 EH-TBB and BEH-TEBP levels in our study were similar to, if not slightly lower than, levels in Boston. Our 2006 EH-TBB levels were lower than levels in Vancouver whereas the 2011 levels are comparable. In contrast, the levels of BEH-TEBP at both time periods in our study were higher than those in Vancouver. The concentrations in our 2006 samples of TPHP were lower than in Boston.

EH-TBB and BEH-TEBP were significantly positively correlated within each sampling round (SI Figure S14; $\tau = 0.4–0.5; \ p < 0.05$), which is expected since they are both in Firemaster 550. We compared the observed ratio of EH-TBB/BEH-TEBP in our samples with the ratio of the commercial mixture and Boston-area samples to evaluate if Firemaster 550 is the sole source and if EH-TBB and BEH-TEBP have different fates once applied to a product. We observed a mean EH-TBB/BEH-TEBP ratio of 0.6 (0.04–3.1) in the 2006 samples and 1.5 (0.8–11) in the 2011 samples. These ratios are lower than the reported ratio in Firemaster 550 (4) and in Boston dust (mean 4.4; range 0.5–50). This suggests other sources of BEH-TEBP in California or a different fate of the chemicals. TPHP, also present in Firemaster 550, was not significantly correlated with either EH-TBB or BEH-TEBP in either sampling round, although TPHP concentrations increased in homes with substantial increases in EH-TBB and BEH-TEBP. This suggests that, in addition to Firemaster 550, there are other sources of TPHP, for example, as a FR in other formulations or applications or as a plasticizer.

**HBCYD.** HBCYD, the third most used BFR, is used mostly in polystyrene foams in building materials and consumer products. It is being considered for addition to the list of Persistent Organic Pollutants (POPs) under the Stockholm Convention, which would substantially limit its production and use. In 2010, the U.S. EPA released an Action Plan for HBCYD citing its wide use, presence in humans, bioaccum-
lation potential, persistence, toxicity to aquatic organisms and concerns about reproductive, neurological and developmental effects in humans. The Action Plan was followed by a proposed Significant New Use Rule (SNUR) for HBCYD in textiles, where it is often used to meet furniture flammability standards. The SNUR would limit HBCYD in U.S. furnishings.

We detected all HBCYD isomers (α-, β-, and γ-HBCYD) in all samples, and they were significantly correlated (tau = 0.4–0.8; p < 0.05) within each sampling round. Total HBCYD (sum of three isomers) concentrations were similar across time periods, ranging from 82 to 6800 ng/g (median 190 ng/g) in the 2006 samples and 39 to 1800 ng/g (median 160 ng/g) in 2011. It is unclear whether the phase-out of PentaBDE and OctaBDE mixtures influenced the pattern of HBCYD use. Median concentrations were similar to those reported for U.S. and Canadian samples, but less than for UK samples. However, our maxima (2006: 6800 ng/g; 2011: 1800 ng/g) were substantially lower than those reported in Boston living room dust (130 200 ng/g) and UK samples (110 000 ng/g). Commercial mixtures of HBCYD mainly consist of γ-HBCYD (75–89%), while α- and β-HBCYD are found at lower amounts. However, we observed relative abundances of 45–50%, 40–45%, and approximately 10% for γ, α-, and β-HBCYD, respectively. This is likely the result of thermal rearrangement at high temperatures in production and processing of HBCYD-added materials or photolysis. This raises cautions about using only source composition information and not evaluating fate and transport of chemicals.

Other Brominated Flame Retardants. Dust samples were analyzed for 15 other BFRs. BTBPE, in production since the 1970s and now used to replace OctaBDE, and DBDPE, introduced in mid-1980s and available as a replacement for DecaBDE, were detected in nearly 100% of samples. The concentrations of BTBPE, which has limited toxicity data (see SI Table S4 for details and references), were detected in nearly all homes in both rounds with concentrations ranging from <10 to 3400 ng/g in 2006 and from 22 to 2000 ng/g in 2011 (Table 1). We found a significant association between concentration reductions and new electronics suggesting that new electronics contain less BTBPE (rho = −0.69; p = 0.003). Concentrations are higher (17–22× at median) than reported in European homes and similar to Michigan offices.

Another commonly detected FR was the TBBPA derivative tetrabromobisphenol A-bis(2,3-dibromopropylether) (TBBPA-BDBPE), which is being studied by the National Toxicology Program (NTP) because of the structural similarity with the carcinogenic TDBPP (brominated “Tris”). Levels of TBBPA-BDBPE appear fairly stable over time (Table 1 and Figure 1) and lower than levels reported in Belgium.

Hexabromobenzene (HBB), an additive FR used in paper, wood, textiles, plastics and electronics, and not used in Europe, was detected in 50% of 2006 samples and 31% of 2011 samples. Octabromo-1,3,3-trimethyl-1-phenylindane was infrequently detected and one home had substantial (10-fold) reductions over the 5 years. Studies on exposures and health effects of these BFRs are limited.

Halogenated Organophosphate Flame Retardants. Chlorinated and brominated OPFRs have a long history of use in polyurethane foam and textiles and an equally long history of concerns about health effects, particularly cancer. TDBPP or brominated “Tris” was banned from children’s sleepwear in the U.S. in 1977 due to carcinogenicity concerns and detection of its mutagenic metabolite in children. It is listed as a carcinogen in California’s Proposition 65. It is reported to be used as a FR in polyurethane and polystyrene foams, acrylic furnishings, polyvinyl and phenolic resins, paints and lacquers, styrene-butyadiene rubber, and latexes. We detected TDBPP in 62% of 2006 samples and 38% of 2011 samples. As far as we know, this is the first report of TDBPP in house dust, although we previously detected its mutagenic metabolite, 2,3-dibromo-1-propanol, in about 10% of indoor air samples from Cape Cod, MA. Dust concentrations were much lower in 2011 (mean 40 ng/g; maximum 310 ng/g) compared with 2006 (mean 1000 ng/g; maximum 8900 ng/g), though this may be due to whatever factor led to lower concentrations of legacy pollutants (see below).

We also detected three chlorinated OPFRs: TCEP, TCIPP, and TDCIPP (chlorinated “Tris”), which are used in polyurethane foams as replacements for PentaBDE. TDCIPP was voluntarily withdrawn from children’s pajamas after metabolites 1,3-dichloro-2-propanone and 1,3-dichloro-2-propanol were found to be mutagenic. The Consumer Product Safety Commission (CPSC) said TDCIPP was a potential hazard to consumers, based on cancer and noncancer end points. The CPSC estimate of children’s exposure from treated furniture was 5× higher than the agency’s acceptable daily intake, with most of the exposure from inhalation of the chemicals volatilized from treated furniture. TDCIPP was the most commonly detected FR (36%) in a U.S. sample of child care products. Our reported concentrations of TDCIPP comprise tris(1,3-dichloro-2-propyl) phosphate, which makes up approximately 90–95% of TCIPP, and tris(2,3-dibromopropyl) phosphate. Both TCEP and TDCIPP are listed as carcinogens under California’s Proposition 65. TCEP is slated to be banned from children’s products in New York by 2014, and a bill is currently being considered that would expand the ban to TDCIPP. TCIPP is structurally similar to TCEP.

Median concentrations of all chlorinated OPFRs were above 1,000 ng/g, or 1 μg/g, in both sampling rounds, and maxima were >100 000 ng/g or 0.01%, making these the most abundant FRs in this study (Table 1). Levels in some homes changed dramatically. For example, between 2006 and 2011, one home with a new roof installed between sampling rounds had 20-fold increase in TCEP concentration and another home with substantial remodeling had a 14-fold increase in TDCIPP. TCIIP means (2006 mean 1200 ng/g; 2011 mean 1700 ng/g) and medians increased (Table 1), suggesting an increase in use between 2006 and 2011. People who reported new furniture between sampling rounds showed increases in TCIPP concentrations (rho = 0.6; p = 0.02), suggesting that TCIPP is a PentaBDE replacement.
As far as we know, this is the first study to analyze for such a broad range of FRs in house dust and to analyze samples collected in the same home at two different time periods. This design allowed us to evaluate time trends in concentrations; however, rigorous longitudinal analysis was not possible due to the small sample size \((n = 16\) pairs). The sample size also limits assessment of generalizability of our findings. Since our study began in 2006, we did not fully capture the effects of the 2004 PBDE phase-out, and although many participants reported some changes in their homes over the 5 year period, larger differences in FR concentration might be seen in a longer study. We observed differences in concentrations in many homes that reported acquiring furniture, carpets, and electronics; however, our ability to link chemical concentrations with characteristics of products and residences was limited, because our questionnaire relied on residents’ recollections. Residents may have introduced additional chemical sources that were not identified by our questionnaire, removed major sources without replacing them with new items, or failed to report on changes that we did ask about. These limitations raise cautions about relying on questionnaires to classify FR exposures. Finally, while our analyte list is extensive, it is not exhaustive. There are probably additional FRs used in consumer products that are not included because they have not been disclosed by manufacturers.

**FR Burden in California Homes.** We found that PBDEs; components of Firemaster 550; other BFRs, such as HBCYD, TBBPA, BTBPE, DBDPE; and OPFRs, including the carcinogenic TCEP and TDCIPP, were abundant and significantly correlated across sampling rounds, indicating that the rank order was consistent over 5 years. However, the average concentration ratio \((2011/2006)\) was 0.8, which means that 2006 concentrations were generally higher than 2011 concentrations. This may be due to degradation or depletion. However, it may also be due to some unidentified but systematic difference in sample collection between the two sampling rounds, which could also influence results for other chemicals. For example, PentaBDE levels went down between 2006 and 2011, which may reflect decreasing use or may simply be due to the same factor causing decrease in legacy pollutant concentrations. In light of this, the Firemaster 550 increase may be underestimated. Two homes had substantial \((10–30\times)\) decreases in DDT and DDD; one of these homes had significant reductions between rounds, while no explanation was identified for the other home.

We were interested in learning which FRs co-occurred, suggesting common sources, so we conducted correlation analysis for analytes within each sampling round \((SI\ Figure\ SI4)\), and also used these correlation estimates in cluster analysis to visualize relationships \((SI\ Figure\ SI5)\). As expected, many compounds known to co-occur in commercial formulations were correlated in both rounds. We saw strong correlations for: PBDE congeners comprising the PentaBDE and OctaBDE mixtures, DDT and its breakdown products, the legacy pesticides cis- and trans-chlordane and trans-nonachlor, PCB 153 and PCB 180, and the DP isomers. Interestingly, the brominated Firemaster 550 chemicals, EH-TBB and BEH-TEBP, were also clustered consistently, but the third Firemaster 550 constituent, TPHP, did not cluster with them, suggesting other sources. TPHP was correlated with TDCIPP and PentaBDE congeners in 2006 samples. TPHP has reportedly been used in the PentaBDE commercial mixture.\(^{52}\)

**Limitations.** As far as we know, this is the first study to evaluate the effects of the 2004 PBDE phase-out, and although many participants reported some changes in their homes over the 5 year period, larger differences in FR concentration might be seen in a longer study. We observed differences in concentrations in many homes that reported acquiring furniture, carpets, and electronics; however, our ability to link chemical concentrations with characteristics of products and residences was limited, because our questionnaire relied on residents’ recollections. Residents may have introduced additional chemical sources that were not identified by our questionnaire, removed major sources without replacing them with new items, or failed to report on changes that we did ask about. These limitations raise cautions about relying on questionnaires to classify FR exposures. Finally, while our analyte list is extensive, it is not exhaustive. There are probably additional FRs used in consumer products that are not included because they have not been disclosed by manufacturers.
commonly detected, and we hypothesize that they are likely to be found in nearly all California homes. In our study, the levels of individual FRs in dust exceeded 0.01%, with a cumulative level of all FRs almost 0.03% in one home. Such concentration of FRs in dust is expected to lead to 30 μg/day FR ingestion in a typical child. The average total load of FRs in house dust was approximately 80–90 μg/g.

For six chemicals, dust concentrations exceeded risk-based screening levels for residential soil in at least one of the homes, indicating exposure is potentially of health concern. Specifically, concentrations of BDE 47, BDE 99, TCEP, TDCIPP, BB 153, and DDT exceed screening levels, with 13 of 16 homes exceeding at least one chemical screening level in either sampling round. Exposure pathways for residential soil are similar to house dust. Screening levels provided in the SI.

Our previous work showed that elevated PentaBDE levels in California house dust and serum are likely the result of the state’s unique furniture flammability standard. The present study shows California homes still have higher levels of PentaBDEs than the rest of the world and that California also has some of the highest concentrations of halogenated OPFRs, which are also used in furniture foam. The only location with consistently higher OPFR concentrations is Japan, where the elevated OPFRs levels are likely due to the early phase-out of PentaBDE almost 20 years ago. OPFR levels in Japan may foreshadow levels in California.

We also observed that Firemaster S50 concentrations are increasing in California homes, suggesting that Firemaster S50 is being used as a replacement for PentaBDE, which was phased-out in 2004, shortly before our first sample collection. Continued monitoring in California and other locations is warranted because we anticipate levels will continue to increase unless manufacturing practices change.

**Policy Implications.** Following the phase-out of PBDEs due to health concerns, other FRs with considerable evidence of toxicity appear to remain at high or increasing levels of use. Some FRs appear to be replaced by less-studied chemicals whose health implications are unknown. Chlorinated OPFRs, some of the most abundant FRs in our study, continue to be used despite evidence of carcinogenicity, listing as carcinogens under California’s Proposition 65 and IARC, and structural similarity to brominated “Tris” (TDBPP), which was banned in children’s sleepwear in 1977. Despite this ban, we detected TDBPP in approximately half of the homes. We detected HBCYD in all homes, even though it has been identified under Europe’s REACH program as a Substance of Very High Concern and the U.S. EPA initiated a SNUR to limit its use citing its bioaccumulation potential, persistence, toxicity to aquatic organisms and concerns about human reproductive, neurological, and developmental effects. Publicly available health and toxicity information for the PBDE replacements, such as Firemaster S50 and BTBPE, is very limited. The continued use of FRs with established health concerns and introduction of replacement FRs with limited data highlights the need to modernize U.S. chemical policies to require more complete disclosure and safety testing of consumer product chemicals prior to sale.

**ASSOCIATED CONTENT**

2 Supporting Information
Specific details for analytical protocols, quality control (including results from interlaboratory tests), correlation/cluster analysis, and screening levels are in Supporting Information. Detailed use and health information for FRs, including references, is presented in Table S14. Home-specific concentrations (Figure S13), Kendall’s tau correlation estimates (Figure S14) and cluster analysis dendrograms (Figure S15) are also available. This material is available free of charge via the Internet at http://pubs.acs.org.

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**Notes** The authors declare no competing financial interest.

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Exhibit 8
**ABSTRACT**

Organohalogen flame retardants are extensively used in both industrial and consumer products. However, relatively little is known about potential human health effects of these compounds. To address this gap, we conducted a health and environmental hazard screening of almost 100 commercially identified molecules based on the Organization for Economic Cooperation and Development (OECD) guidelines and the Screening Information Guidelines for Organohalogen Compounds (SIG-99) methodology. The principal goals of this work were to: 1) identify any known or potential human health effects of organohalogen flame retardants; and 2) identify any available ecotoxicological data. Key findings are as follows: 1) No human health effects were identified for any organohalogen flame retardant evaluated. 2) Almost 15% of chemicals had a chronic study. 3) Eight chemicals were classified as carcinogens by IARC, NTP or/and California Proposition 65. 4) Some were multi-species tumorigenic, and 5) A major concern included the liver and organs.

**CARCINOGENICITY**

- Less than 1% of chemicals had a chronic study.
- Eight chemicals are classified as carcinogens by IARC, NTP or/and California Proposition 65.
- Some were multi-species tumorigenic, and target sites commonly included the liver and reproductive organs.
- 70% had a structural alert(s) for cancer.
- Halogenated aromatic, aliphatic halogen, epoxides, and aziridines, alkyl (0-9) or benzyl ethers of sulfonic or phosphonic acid.
- No structural alerts (15%) or not in applicability domain (10%).

**REPRODUCTIVE OR DEVELOPMENTAL TOXICITY**

- 25% of chemicals had empirical data generally resulting in High or Moderate concern.
- 50% of chemicals with or without data were predicted developmental toxicants based on training sets with chemicals with empirical data.
- There are currently no widely-used or accepted SAR models for reproductive toxicity.

**PERSISTENCE/ BIOACCUMULATION**

- Half-life predictions in air, soil or water resulted in High or Very High concern for most chemicals.
- Mixed results were obtained for bioaccumulation potential based on Kow (oil/water partition coefficients) and/or bioaccumulation/bioconcentration factors.

**MODIFIED QCAT SCREEN AND GRADING SCHEME**

Assigning the Initial and Revised Grades
- The initial grade does not consider data gaps (dg).
- The initial grade can be based on a High or Very High Hazard for an individual category (Automatic F).
- Grades can be based on a combination of scores for similar categories, such as a chemical with high acute mammalian toxicity and high persistence earns an F.
- For the revised (final) grade, we modified the QCAT screen to include data gaps which can earn additional concern.

**CHALLENGES AND OPPORTUNITIES**

- Lack of availability data was the biggest challenge.
- Inadequate data or SAR models to assess potential for endocrine disruption.
- Chemical manufacturers may have unpublished proprietary data.
- Some model predictions did not agree with actual data.
- There are opportunities to seek safer alternatives.
- This screening approach can be used to identify data gaps and lead to the use of safer organohalogen flame retardants.

**SELECTED REFERENCES**


**RELEVANT TOXICOLOGICAL TOOLS**

- OECD Test No. 405, Toxicity Estimation Software Tools (TEST) for acute mammalian toxicity and ECOLOGIC/EPI SUITE for ecological toxicity