

Tab F

CPSC Staff Preliminary Risk Assessment of Flame Retardant (FR) Chemicals in Upholstered Furniture Foam

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Michael A. Babich, Ph.D.; Treye A. Thomas, Ph.D.; and Kristina M. Hatlelid, Ph.D.

Directorate for Health Sciences

U.S. Consumer Product Safety Commission

Bethesda, MD 20814

This report was prepared by the CPSC staff; it has not been reviewed or approved by, and may not necessarily reflect the views of, the Commission.

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Summary

The CPSC staff has developed a draft performance standard to address the hazards associated with fires involving residential upholstered furniture. Manufacturers are likely to treat some products with flame retardant (FR) chemicals if the draft standard is adopted. The CPSC staff previously assessed the potential health risks associated with the use of FR chemicals in upholstered furniture cover fabrics. In this report, the CPSC staff presents a preliminary assessment of the potential health risks associated with the use of selected FR chemicals in upholstered furniture foam. Foam samples treated with three different FR chemicals or mixtures that could be used to meet the draft standard were available to the staff for exposure studies: melamine; tris(1,3-dichloro-2-propyl)phosphate (TDCP) (13674-87-8); and Firemaster® 550 (FM-550). FM-550 is a mixture containing triphenyl phosphate (TPP) (1145-86-6), a proprietary isopropylated triaryl phosphate (ITP), and proprietary brominated aryl esters (BAE's). Samples with the highest available TDCP or FM-550 levels were included in the study. Numerous other FR treatments that could be used in foam have been discussed by the U.S. EPA's Design for the Environment Program.

Melamine does not satisfy the regulatory definition of toxic, even though it has been well studied in chronic bioassays. Thus, melamine-treated foam would not pose an appreciable risk to consumers. Exposure studies with melamine-treated foam were not necessary. TDCP is considered a probable human carcinogen, based on sufficient evidence in animal studies. TDCP also induces non-cancer chronic health effects in animals. Little toxicity data on FM-550 and its components is available. However, the CPSC staff has previously reviewed the toxicity of compounds and mixtures closely related to TPP and ITP.

Mock-ups made with the foam samples were tested by the staff to assess the liquid-mediated migration of FR chemicals. These data were used to estimate dermal and oral exposures. The mock-ups were also subjected to an accelerated wear procedure to measure the release of airborne particles containing FR chemical. Two foam samples containing TDCP and one containing FM-550-treated foam were tested. Exposure to vapor phase chemicals that may be emitted from the foam was assessed using a mathematical model.

The following conclusions are based on limited exposure and/or toxicity data, and should be regarded as preliminary. Estimated exposures to TDCP were near or above the acceptable daily intake (ADI) for non-cancer health effects. The hazard index (HI) values were 0.9 for adults and 1.7 for children. That is, the estimated exposures were just below the ADI in adults and 1.7-fold greater than the ADI in children. The estimated cancer risk for a lifetime of exposure to TDCP-treated upholstered furniture was 140 per million. In children, the estimated cancer risk from exposure during the first two years of life was 7 per million. Thus, based on the available data, TDCP in some upholstered furniture could pose an appreciable health risk to consumers. Tests with additional foam or furniture samples are needed to confirm this preliminary conclusion.

Limited toxicity data were available for TPP and ITP. Thus, the range of ADI values for other aromatic phosphates or blends previously reviewed by the CPSC staff was used as a surrogate. Using these surrogate toxicity data, HI values were estimated to be between 0.003 and 0.3 in adults and between 0.006 and 0.6 in children. Assuming that TPP and ITP are no more toxic than the other aromatic phosphates, they are not expected to pose any appreciable health risk to consumers. The staff will review any additional toxicity data on TPP and ITP that may become available. Additional toxicity data and tests with additional foam or furniture samples are needed to confirm this preliminary conclusion.

Insufficient toxicity data on the BAE's or related compounds were available to assess whether the BAE's in FM-550 could pose any health risks to consumers. However, the estimated exposure to the BAE's was comparatively low. BAE would have to be more toxic than any other additive FR chemical previously reviewed by the CPSC staff to pose an appreciable health risk to consumers. The staff will review any additional toxicity data on BAE's that may become available. Additional toxicity and bioavailability data, as well as tests with additional foam or furniture samples, are needed to assess whether BAE could pose an appreciable health risk to consumers.

List of Abbreviations

ADD	Average daily dose
ADI	Acceptable daily intake
AFSC	American Fire Safety Council
AT	Antimony trioxide
BAE	Brominated aryl ester
BDE	Butanedioic acid, ((dimethoxyphosphinothioyl)thio)-, diethyl ester
CPSC	U.S. Consumer Product Safety Committee
DBDPO	Decabromodiphenyl oxide
DE	Design for the Environment (U.S. EPA)
EPA	Environmental Protection Agency (U.S.)
FHSA	Federal Hazardous Substances Act
FM-550	Firemaster® 550
FR	Flame retardant
FRCA	Fire Retardant Chemicals Association (currently AFSC)
HBCD	Hexabromocyclododecane
HI	Hazard index
IPCS	International Program on Chemical Safety
ITP	Isopropylated triaryl phosphate
LADD	Lifetime average daily dose
LD ₅₀	Median lethal dose
LOAEL	Lowest observed adverse effect level
MM	Molecular mass
MSDS	Material safety data sheet
NOAEL	No observed adverse effect level
NRC	National Research Council
PA	Phosphonic acid, (3-{{hydroxymethyl}amino}-3-oxopropyl)-, dimethyl ester
Penta-BDE	Pentabromodiphenyl ether
PIP	Phenol isopropylated phosphate
PUF	Polyurethane foam
RfD	Reference dose
SD	Sprague-Dawley
SNUR	Significant New Use Rule
TCP	Tricresyl phosphate
TDCP	Tris(1,3-dichloro-2-propyl)phosphate
THPC	Tetrakis(hydroxymethyl)phosphonium chloride
TPP	Triphenyl phosphate
VCCEP	Voluntary Children's Chemical Evaluation Program

I. Introduction

Upholstered furniture fires account for more fire deaths than any other category of products under the jurisdiction of the U.S. Consumer Product Safety Commission (CPSC). From 1999-2002, upholstered furniture fires were associated with an average of 9,000 fires, 520 deaths, 1,040 injuries and \$242 million in property damage annually (Levenson 2005). These fires are most commonly ignited by either smoldering sources, such as cigarettes, or open flame sources, such as cigarette lighters and candles. The U.S. Consumer Product Safety Commission (CPSC) initiated a regulatory proceeding in 1994 to address the hazard of small open flame ignitions of upholstered furniture (CPSC 1994). The CPSC staff has developed a draft performance standard to address the hazards associated with both small open flame and cigarette ignitions. The staff estimates that 4,800 fires, 360 deaths, 740 injuries, and \$133 million in property damage could be prevented if the draft standard is enacted.

While furniture manufacturers would be free to choose the means of complying with the draft standard, it is likely that some products would be treated with flame retardant (FR) chemicals if the draft standard were adopted. In addressing the hazard associated with the flammability of upholstered furniture, the CPSC staff is working to develop a performance standard to reduce furniture fires without creating other hazards to consumers. Thus, the CPSC staff has been assessing the potential for health risks associated with the use of selected FR chemicals in upholstered furniture. The purpose of this report is to assess the potential health risks associated with the use of selected FR chemicals in upholstered furniture foam.

A. Upholstered Furniture Cover Fabrics

The first version of the draft flammability standard developed by the CPSC staff involved exposing the upholstered furniture cover fabric to a gas flame that was roughly equivalent to a cigarette lighter (CPSC 1997). As part of the risk assessment process for FR chemicals, the Commission held a public hearing in May 1998. In its testimony, the Fire Retardant Chemicals Association (FRCA) (currently the American Fire Safety Council, AFSC) reported that in many cases the furniture cover fabric would be treated with FR chemicals if the draft standard were adopted (Parkes 1998). The FRCA also provided a list of 16 chemicals or chemical classes that its members would market for use in upholstered furniture.

The 16 FR chemicals and classes included over 50 individual compounds. The CPSC staff reviewed all the available toxicity data on these chemicals and derived acceptable daily intake (ADI) levels where sufficient data were available (Babich et al. 2004; Babich and Saltzman 1999; Bittner 1999a-d; Bittner 2001; Bittner et al., 2001; Bittner and Ferrante, 1999; Ferrante 1999a-f; Hatlelid 1999a-h). Overall, a considerable number of toxicological studies were available for review. While some FR chemicals have been well studied, only limited data were available for others.

The CPSC staff performed risk assessments for five FR chemicals: antimony trioxide (AT) (CAS no. 1309-64-4); decabromodiphenyl oxide (DBDPO) (1163-19-5); hexabromocyclododecane (HBCD) (3194-55-6); phosphonic acid, (3-[[hydroxymethyl]amino]-3-oxopropyl)-, dimethyl ester (PA) (20120-33-6); and tetrakis (hydroxymethyl) phosphonium chloride (THPC)

(124-64-1) (Babich and Thomas 2001). These FR's were selected for study because they are used to comply with the U.K. upholstered furniture flammability standard (except THPC) and fabric samples were available for testing. The staff concluded that DBDPO, HBCD, and PA would not present a hazard to consumers, and that additional data would be needed to assess AT and THPC.

Prior to the completion of the CPSC staff risk assessment, the National Research Council (NRC) performed a risk assessment of 16 FR chemicals that might be used in upholstered furniture cover fabrics (NRC 2000). The NRC subcommittee, which had minimal exposure data available to them, selected the most toxic chemical to represent each of the same 16 chemicals or classes described by the FRCA. The NRC concluded that eight of these chemicals could be used without presenting a hazard to consumers, including DBDPO, HBCD, PA, and THPC. They recommended that additional exposure or toxicity data were needed for the remaining chemicals, including AT, TDCP, and aromatic phosphates. Following the completion of the NRC report, the CPSC staff found that unidentified compounds were released from THPC-treated fabrics. Thus, the staff concluded that additional information on the identity and toxicity of the THPC by-products was needed.

The CPSC staff is participating in several regulatory and voluntary programs of the U.S. Environmental Protection Agency (EPA) that involve the potential health and environmental effects of FR chemicals. EPA is developing a significant new use rule (SNUR) for FR chemicals that may be used in upholstered furniture. A SNUR requires manufacturers to notify EPA before engaging in activities subject to the SNUR. The SNUR process can be used to obtain additional toxicity or exposure data if needed. The EPA Design for the Environment program is a cooperative effort with industry that is evaluating the potential health risks of FR chemicals that may be used in polyurethane foam (PUF). The EPA Voluntary Children's Chemical Evaluation Program (VCCEP) is investigating children's exposure to penta- and octa-bromodiphenyl ether and DBDPO.

B. Upholstered Furniture Foam

In 2003, the Commission amended the rulemaking activity for upholstered furniture to include smoldering ignition sources, such as cigarettes, and the staff revised the draft performance standard (CPSC 2003). Due to the changes in the draft standard, fewer upholstery cover fabrics are likely to be treated with FR chemicals if the standard is adopted. Rather, in many cases the flexible polyurethane foam (PUF) or other filling materials may require FR treatment to meet the draft standard.

Mixtures containing pentabromodiphenyl ether (penta-BDE) and aromatic phosphate esters were the principal FR chemicals for flexible PUF. However, the sole U.S. manufacturer of penta-BDE voluntarily ceased production in December 2004 due to concerns about environmental persistence and bioaccumulation. A number of alternative treatments are available, including several new proprietary formulations (reviewed in EPA 2005). The CPSC staff has concluded that the FR treatments most likely to be used in upholstered furniture foam include tris(1,3-dichloro-2-propyl) phosphate (TDCP) (13674-87-8), melamine, and a proprietary formulation marketed as Firemaster® 550 (FM-550). FM-550 is a mixture containing triphenyl phosphate

(TPP) (1145-86-6), a proprietary isopropylated triaryl phosphate (ITP), and proprietary brominated aryl esters (BAE's) (EPA 2005). According to its material safety data sheet (MSDS), FM-550 contains 6-24% TPP, 24-51% ITP, and 40-60% BAE's. Several other alternatives are mixtures that include various aromatic phosphates.

Although melamine has been tested in chronic animal studies, it does not satisfy the regulatory definition of "toxic" (Thomas and Brundage 2004). Therefore, it does not pose any appreciable health risks to consumers. Exposure studies are not necessary. Samples of PUF treated with TDCP and FM-550 are available for exposure studies. This report will assess the potential chronic health risks associated with the use of TDCP and FM-550 in upholstered furniture foam.

II. Hazard Identification and Dose Response

A. Tris(1,3-Dichloro-2-Propyl) Phosphate (TDCP)

1. Hazard Identification

The toxicity of tris(1,3-dichloro-2-propyl)phosphate (TDCP) has been reviewed by the CPSC staff (Bittner et al. 2001; Ferrante 1999b) and others (Brandwene 2001; EPA 2005; IPCS 1998; NRC 2000). TDCP is acutely toxic by oral administration, with median lethal dose (LD₅₀) values ranging from 1.85 to 6.8 g/kg (reviewed in Ferrante 1999b). The associated symptoms include ataxia, irritability, hyperactivity, tetanus, and convulsions, suggesting neurological effects. However, the only reported histological lesions were fatty degeneration and necrosis in the kidneys.

TDCP has been studied in a 24-month dietary bioassay in Sprague-Dawley (SD) rats (Biodynamics 1981; Freudenthal and Henrich 2000; Henrich 1998). Animals were exposed to TDCP in feed at doses of 5, 20, or 80 mg/kg-d in groups of 60 per dose and sex. Ten animals from each dose group were sacrificed at 12 months. Non-cancer effects included convoluted tubule hyperplasia at the mid-and high dose in males and the high dose in females; parathyroid hyperplasia in high dose males; and hyperplasia of the spleen in high dose females (reviewed in EPA 2005, NRC 2000). In addition, there were reproductive system lesions in males, including the seminal vesicles (all doses), testes (mid and high doses), and epididymis (high dose). The NRC subcommittee considered the low dose (5 mg/kg-d) as a lowest observed adverse effect level (LOAEL) (NRC 2000). TDCP may be considered probably toxic to humans (see CPSC 1992), based on sufficient evidence of chronic toxicity (reproductive system effects in males) in animals.

Several neoplastic lesions were also reported (Biodynamics 1981; Freudenthal and Henrich 2000; Henrich 1998 and reviewed in EPA 2005; Ferrante 1999b; NRC 2000). The incidence of renal cortical tumors was significantly elevated relative to the controls in mid- and high-dose males and females (Table 1). Benign interstitial cell tumors were also significantly elevated in mid- and high-dose males. Hepatocellular adenomas were significantly elevated at the high dose in both sexes, while hepatocellular carcinomas were non-significantly elevated in high dose males. The combined incidence of hepatocellular adenoma and carcinoma was significantly elevated at the high dose in males and the mid- and high dose in females. Adenomas of the

adrenal cortex were significantly elevated in mid-dose males (not at the high dose) and significantly reduced in mid-dose females.

TDCP is genotoxic in *Salmonella* following metabolic activation (reviewed in EPA 2005; Ferrante 1999b; NRC 2000). Studies in mammalian systems have given mixed results. TDCP exposure induced tumors at multiple doses in the kidneys and liver of both male and female rats. Therefore, TDCP 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 evidence of genotoxicity and structural similarity to another animal carcinogen, tris(1,3-dibromopropyl) phosphate.

2. Dose Response Assessment

The LOAEL for non-cancer effects in the two-year rat study was 5 mg/kg-d (Biodynamics 1981; EPA 2005; NRC 2000). The most sensitive endpoint was the reproductive system in males. An overall uncertainty factor of 1,000 was applied, including 10-fold for animal to human extrapolation, 10-fold for inter-individual variability, and 10-fold because a no-observed-adverse-effect level (NOAEL) was not established. This results in an ADI level of 0.005 mg/kg-d. The NRC subcommittee derived a reference dose (RfD)* of 0.005 mg/kg-d (NRC 2000).

The cancer unit risk (potency) estimate for TDCP is based on the incidence of hepatocellular tumors (carcinoma plus adenoma) and tumors of the renal cortex. Benign tumors of the testes and adrenal cortex were not included (CPSC 1992, p. 46636). Hepatocellular carcinomas and adenomas are combined, because hepatocellular adenomas are known to progress to carcinomas (CPSC 1992, p. 46636). Unit risks for liver and renal tumors were calculated separately and then added, as described in the CPSC chronic hazard guidelines (CPSC 1992, p. 46654). Tumor incidence data for males and females were combined, because their unit risks differed by less than a factor of two when computed separately.

Animal bioassay data were fitted to the multistage model using Global83 (Howe and Crump, 1983; Crump, 1984), as described in the chronic hazard guidelines (CPSC 1992, p. 46654). The unit risk was based on the maximum likelihood estimate of extra risk, that is, the linear term (q_1) in the model. Animal-to-human extrapolation was by the surface area correction, that is, the unit risk is proportional to body weight to the three-quarters power (CPSC 1992, p. 46654; EPA 1992). Mean terminal body weights in untreated controls were 612 g in males and 386 g in females (Freudenthal and Henrich 2000). The average of males and females was 499 g. Thus, humans are estimated to be 3.5-fold more sensitive than the rats. By this methodology, the unit risk for kidney and liver tumors combined is estimated to be $0.031 \text{ (mg/kg-d)}^{-1}$. The NRC subcommittee derived a unit risk of $0.06 \text{ (mg/kg-d)}^{-1}$ (NRC 2000).

* Both the acceptable daily intake (ADI) and reference dose (RfD) are estimates of the amount of a chemical a person can be exposed to on a daily basis over an extended period of time (up to a lifetime) with a negligible risk of suffering deleterious effects.

Table 1. Tumor Incidence in Sprague-Dawley Rats Exposed to TDCP in Feed^a

Tumor	Sex		<u>Dose (mg/kg-d)</u>			
			0	5	20	80
Renal cortex tumor	M	Incidence	1/60	3/60	9/60	32/59
		P ^b		0.309	8.3x10⁻³	1.1x10⁻¹¹
	F	Incidence	0/60	1/60	8/57	29/60
		P		0.500	2.4x10⁻³	2.0x10⁻¹¹
Testicular interstitial cell adenoma	M	Incidence	7/57	8/60	26/60	39/56
		P		0.540	1.6x10⁻⁴	2.5x10⁻¹⁰
Hepatocellular adenoma	M	Incidence	2/60	7/60	1/60	16/60
		P		0.081	0.878	2.7x10⁻⁴
	F	Incidence	1/60	1/60	4/55	9/60
		P		0.752	0.156	8.3x10⁻³
Hepatocellular carcinoma	M	Incidence	1/60	2/60	3/60	7/60
		P		0.500	0.309	0.031
	F	Incidence	0/60	2/60	2/55	4/60
		P		0.248	0.227	0.059
Hepatocellular adenoma or carcinoma	M	Incidence	3/60	9/60	4/60	23/60
		P		0.220	0.500	5.7x10⁻⁴
	F	Incidence	1/60	3/60	6/55	13/60
		P		0.309	0.044	4.9x10⁻⁴
Adrenal cortex adenoma	M	Incidence	5/59	3/14	5/16	5/57
		P		0.421	0.031	0.607
	F	Incidence	13/59	5/27	2/33	20/59
		P		0.740	0.040	0.109

^a Tumor data are from NRC 2000, Table 16-5.

^b One-tailed Fisher's exact test performed by CPSC staff. Values <0.05 are in bold.

B. Aromatic Phosphates

The toxicity of aromatic phosphates has been reviewed by the CPSC staff (Bittner 2001; Bittner et al. 2001; Ferrante 1999a) and others (EPA 2005; NRC 2001). The toxicity of the aromatic phosphates varies among individual compounds and commercial mixtures. Tricresyl phosphate (TCP) (mixture of isomers) (1330-78-5) and *o*-tricresyl phosphate are among the more toxic members of the class. They are acutely toxic and neurotoxic in animals and humans. For the most part, the other aromatic phosphates are not acutely toxic by the oral or dermal route (Bittner et al. 2001; Ferrante 1999b). In subchronic studies, aromatic phosphates have generally targeted the liver and nervous system. Only 2-ethylhexyl diphenyl phosphate (EHDP) (1241-94-7) has been subjected to a chronic study in animals. Sufficient data from subchronic studies were available to derive ADI values for three of the 10 aromatic phosphates or mixtures that the staff reviewed: Santicizer 148 (roughly 90% isodecyl diphenyl phosphate), 0.01 mg/kg-d; TCP isomers, 0.05 mg/kg-d; and 2-ethylhexyl diphenyl phosphate, 1.0 mg/kg-d (Bittner et al. 2001; Ferrante 1999b). The NRC subcommittee derived an RfD of 0.07 mg/kg-d for TCP isomers. FM-550 contains two aromatic phosphates—triphenyl phosphate (TPP) (1145-86-6) and a proprietary isopropylated triaryl phosphate (EPA 2005).

1. Triphenyl Phosphate (TPP)

The CPSC staff reviewed the toxicity data for TPP (Bittner et al. 2001; Ferrante 1999b). The range of studies on TPP was limited. TPP appears to be less neurotoxic than TCP. The lowest NOAEL reported for TPP was 160 mg/kg-d for effects on body weight gain in male SD rats fed TPP for 90 days in a neurotoxicity screen (Sobotka et al. 1986). The staff concluded that TPP is possibly toxic in humans, based on limited evidence of neurotoxicity and chronic organ toxicity in animals. The staff also concluded that there is insufficient information to derive an ADI value. The conclusion that TPP is possibly toxic in humans is not sufficient to satisfy the regulatory definition of “toxic” (CPSC 1992). However, this conclusion is based on limited data. It does not mean that TPP is not toxic. Rather, it means that additional information is needed to assess its toxicity and derive an ADI. Other aromatic phosphates were toxic to the liver in animals and were neurotoxic in animals and/or humans.

2. Isopropylated Triaryl Phosphate

Limited data are available for the proprietary isopropylated triaryl phosphate (ITP) (reviewed in EPA 2005). ITP is not acutely toxic. Repeat dose studies in animals suggest that ITP may induce systemic effects, reproductive and developmental effects, and neurotoxicity. The CPSC staff concludes that ITP is possibly toxic in humans, based on limited evidence of chronic toxicity in animals. There is insufficient information to derive an ADI level. The conclusion that ITP is possibly toxic in humans is not sufficient to satisfy the regulatory definition of toxic. However, this conclusion is based on limited data. It does not necessarily mean that ITP is not toxic. Rather, it means that additional information is needed to assess its toxicity and derive an ADI level. Other aromatic phosphates were toxic to the liver in animals and were neurotoxic in animals and/or humans.

The staff reviewed the toxicity of phenol isopropylated phosphate (PIP) (68937-41-7) (Ferrante 1999a), which is structurally related to ITP. The staff concluded that PIP is possibly toxic in humans, based on limited evidence of neurotoxicity and chronic organ toxicity in animals. The staff also concluded that there is insufficient information to derive an ADI value.

3. Dose Response Assessment

Insufficient data are available to derive ADI values for either TPP or ITP. For the purpose of the present risk assessment, estimated exposures to these compounds will be compared to the ADI values for other aromatic phosphates, which range from 0.01 to 1.0 mg/kg-d (Bittner 2001; Bittner et al. 2001; Ferrante 1999a).

C. Brominated Aryl Esters

Limited toxicity data for the proprietary brominated aryl esters (BAE's) are available (reviewed in EPA 2005). SD rats were given single oral doses of either BAE compound. There were no deaths, although exposed animals exhibited effects including piloerection and hunched posture. Thus, both compounds have oral LD₅₀ values >2000 mg/kg in rats. No other animal or human toxicity data or empirical physico-chemical properties are available. There is insufficient information to determine whether the BAE's are "toxic" under the Federal Hazardous Substances Act (FHSA) or to derive an ADI level. No toxicity data on structural analogues were identified in National Library of Medicine databases.

III. Exposure and Bioavailability

As in previous risk assessments involving FR chemicals, exposure was estimated by analyzing various exposure scenarios (Babich and Thomas 2001; Thomas and Brundage 2005). This was accomplished through a combination of laboratory studies and mathematical models. Dermal, inhalation, and oral exposure routes were included. Inhalation exposure considered both vapor phase and particles. Separate exposure estimates were made for adults and small children.

A. Laboratory Studies

The CPSC staff conducted laboratory studies to estimate the possible migration of FR chemicals from upholstery foam (Cobb and Bhooshan 2005). Experiments utilized a mock-up consisting of a 9x9x½-inch (23x23x1.25 cm) sheet of plywood supporting a 3-inch thick slab of the FR-treated upholstery foam to be tested (Figure 1). The foam was covered by a standard non-FR fabric (50-50 cotton-polyester blend). No interliner or batting was present in the mock-up, because some upholstered furniture does not have these components. The presence of an interliner or batting might be expected to reduce migration. The mock-up and experimental methods were adapted from the staff exposure and risk assessment for mattresses (Cobb 2005; Thomas and Brundage 2005). Three foam samples that could be used to meet the draft flammability standard were tested. Foam "S" contained 6.6% TDCP, foam "Y" contained 3.5% TDCP and 11% melamine, and foam "Z" contained 6% FM-550 and 2.8% melamine (Cobb and Chen 2005). Foams S and Z contained the highest TDCP and FM-550 concentrations among the available samples.

To study the potential for dermal or oral exposure, the mock-up was wetted with 25 mL of isotonic saline solution (0.9% NaCl). Two 55 mm diameter pieces of #2 filter paper were placed on the wetted portion and covered with weights. The weights were 2-inch diameter (5.1 cm) steel rods weighing 3.14 pounds (1.4 kg), resulting in one pound per square-inch (psi) of pressure (6.9 kPa). After 6 hours, the filter paper was removed and analyzed for FR content. The test was repeated with the same foam sample for up to eight consecutive days. FR chemical in the filter paper is assumed to be available for transfer to the skin or mouthing by children (Thomas and Brundage 2005). FR chemicals on the skin can be absorbed percutaneously or transferred to the mouth by hand-to-mouth activity. Foams S and Y were tested once. Two specimens of foam Z were tested, one for 4 days and the second for 8 days. The average migration from each iteration was used to estimate exposure.

Experiments were also conducted to estimate the release of particles containing FR chemicals into air (Cobb and Bhooshan 2005). Mock-ups were subjected to repetitive impaction with an air-driven piston attached to a 4-inch diameter semi-spherical form. Mock-ups were impacted 100,000 times at a rate of 1 per second and 3 pounds per square inch pressure. Tests were done inside a closed, inflatable glove bag supported by a metal frame, with a volume of 216 L. Recirculated air was continuously sampled at a rate of 2 L per minute to collect inhalable particles. The total amount of particulate phase FR chemical collected was assumed to be released during the lifetime of the furniture. Duplicate samples of foam S and Z were tested. Foam Y was not subjected to this test. Three filter cassettes were used in each test.

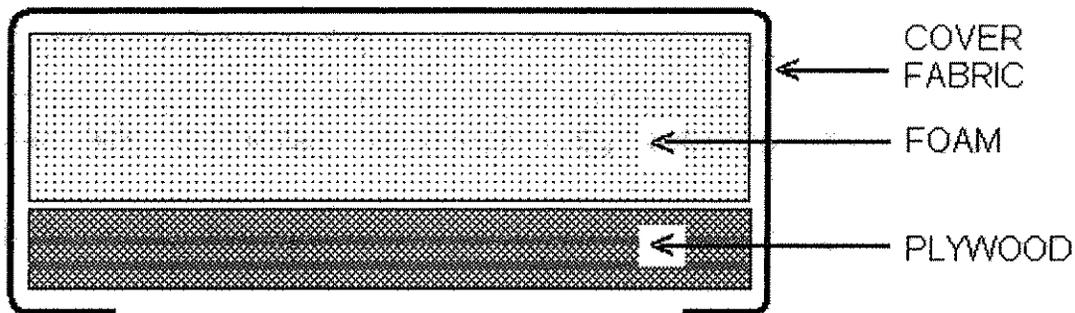


Figure 1. Mock-up for exposure studies

B. Calculations

To estimate dermal exposure, it is assumed that an external liquid phase facilitates the transfer of FR chemical from the foam to the surface of the cover fabric and then to the skin (compare NRC 2000). During normal use, that is, while sitting on furniture, perspiration is assumed to be the liquid phase. The amount of FR chemical migrating to the fabric surface was measured in the laboratory as described above (Cobb and Bhooshan 2005). The average daily dose (ADD) from dermal exposure was calculated by:

$$ADD_D = \frac{M \cdot F \cdot S \cdot K_T \cdot T}{W} \quad (1)$$

where: ADD_D , average daily dose from dermal exposure, mg/kg-d; M , amount of FR chemical that migrates to the fabric surface, mg/cm²; F , fraction of liquid phase transferred to the skin, unitless; S , skin surface area exposed, cm²; K_T , percutaneous absorption rate, h⁻¹; T , exposure duration, h/d; and W , body weight, kg.

Oral exposure occur either by direct mouthing of furniture cover fabric or by hand-to-mouth activity. As with dermal exposure, migration of FR chemical from foam is assumed to be mediated by an external liquid phase, in this case saliva. The amount of FR chemical migrating to the surface of the cover fabric was estimated in laboratory studies as described above (Cobb and Bhooshan 2005). The average daily dose from indirect mouthing, that is, hand-to-mouth act activity was calculated by:

$$ADD_{OH} = \frac{M \cdot F \cdot S_H \cdot F_H}{W} \quad (2)$$

where: ADD_{OH} , average daily dose from hand-to-mouth activity, mg/kg-d; M , amount of FR chemical that migrates to the fabric surface, mg/cm²; F , fraction transferred from the fabric to the hand; S_H , surface area of the hand that is mouthed, cm²; F_H , hand to mouth transfer factor, d⁻¹; and W , body weight, kg.

The average daily dose from direct mouthing activity was calculated by:

$$ADD_{OM} = \frac{M \cdot S_M \cdot F_M}{W} \quad (3)$$

where: ADD_{OM} , average daily dose from direct mouthing activity, mg/kg-d; M , amount of FR chemical that migrates to the fabric surface, mg/cm²; S_M , surface area of fabric that is mouthed, cm²; F_M , fabric to mouth transfer factor, d⁻¹; and W , body weight, kg.

The total oral exposure is given by:

$$ADD_O = \frac{M(F \cdot S_H \cdot F_H + S_M \cdot F_M)}{W} \quad (4)$$

where: ADD_O , average daily dose from oral exposure, mg/kg-d; M , amount of FR chemical that migrates to the fabric surface, mg/cm²; F , fraction transferred from the fabric to the hand; S_H , surface area of the hand that is mouthed, cm²; F_H , hand to mouth transfer factor, d⁻¹; S_M , surface area of fabric that is mouthed, cm²; F_M , fabric to mouth transfer, d⁻¹; and W , body weight, kg.

Inhalation exposure may occur from the release of semi-volatile FR chemicals into the vapor phase or from the release of FR-containing particles during normal wear or aging. The release of FR-containing particles was measured in the laboratory as described above (Cobb and Bhooshan 2005). The total amount of particle-bound FR chemical released during the accelerated wear test was assumed to be released over the lifetime of the furniture (compare Thomas and Brundage 2005).

The average daily dose from inhalation exposure to vapor phase FR chemical was calculated by:

$$ADD_{IV} = \frac{C_v \cdot I \cdot T}{W} \quad (5)$$

where: ADD_{IV} , average daily dose from inhalation exposure of vapor phase chemical, mg/kg-d; C_v , concentration of vapor phase FR chemical in air, mg/m³; I , average inhalation rate, m³/h; T , exposure duration, h/d; and W , body weight, kg.

The concentration of vapor phase chemical was calculated from a one-zone mass-balance model (NRC, 1981):

$$C_v = \frac{E_v}{V \cdot (A + K_v)} \quad (6)$$

where: C_v , concentration of vapor phase FR chemical in air, mg/m³; E_v , source strength for vapor phase chemical, mg/h; V , house volume, m³; A , air infiltration rate, h⁻¹; and K_v , decay rate for vapor phase chemical.

The source strength, E_v , estimated by means of a mathematical model (Babich and Thomas 2001) that is algebraically equivalent to the model described by the NRC subcommittee (NRC 2000):

$$E_{v1} = \frac{C_{Sat} \cdot H}{\frac{1}{A \cdot V} + \frac{1 \times 10^{-4} \cdot S_p \cdot D_{Air}}{H}} \quad \text{for } T_{Max} \geq P \text{ years} \quad (7)$$

$$E_{v2} = \frac{T_{Max} \cdot E_{v1}}{P} \quad \text{for } T_{Max} < P \text{ years}$$

where:

$$T_{Max} = \left[\frac{10,000 \cdot FRL \cdot H}{C_{Sat} \cdot D_{Air} \cdot 8,766} \right] \cdot \left[1 + \frac{1 \times 10^{-4} \cdot S_p \cdot D_{Air}}{A \cdot V \cdot H} \right] \quad (8)$$

and where: T_{max} , maximum time that vapor phase FR can be released at the estimated rate, y; 1×10^{-4} , to convert from cm² to m²; 10,000, to convert from mg/cm² to mg/m²; FRL, FR chemical loading rate, mg/cm²; H , boundary layer height, m; C_{sat} , saturation concentration in air, mg/m³; D_{air} , diffusivity in air, m²/h; 8,766, number of hours per year; S_p , surface area

of foam in a suite of furniture, cm²; A, air infiltration rate, h⁻¹; V, house volume, m³; P, product lifetime, y; and E_v, source strength, mg/h.

C_{Sat} was estimated as previously (Babich and Thomas 2001):

$$C_{Sat} = \frac{MM \cdot VP \cdot 1 \times 10^6}{R \cdot Temp} \quad (9)$$

where: MM, molecular mass, grams/mole; VP, vapor pressure, torr; 1x10⁶, to convert from grams per liter to mg/m³; R, gas constant, 62.4 torr-L/mole-degree Kelvin; T, temperature (298°K).

D_{Air} was estimated as described by Schwoppe et al. (1999):

$$D_{Air} = \frac{3.3}{(2.5 + MM^{1/3})^2} \quad (10)$$

where: MM, molecular mass, grams/mole.

The average daily dose from inhalation of particle-bound FR chemical is given by:

$$ADD_{IP} = \frac{C_p \cdot I \cdot T}{W} \quad (11)$$

where: ADD_{IP}, average daily dose from inhalation exposure of particle-bound chemical, mg/kg-d; C_p, concentration of particle-bound FR chemical in air, mg/m³; I, average inhalation rate, m³/h; T, exposure duration, h/d; and W, body weight, kg.

The concentration in air (C_p) was calculated from the one-zone mass balance model:

$$C_p = \frac{E_p}{V(A + K_D)} \quad (12)$$

where: C_p, concentration of particle-bound FR chemical in indoor air, mg/m³; E_p, source strength for particle-bound FR chemical, mg/h; V, room volume, m³; A, air infiltration rate, h⁻¹; and K_D, particle decay (deposition) rate, h⁻¹.

The source strength (E_p) was estimated by:

$$E_p = \frac{M_p \cdot F_p}{24 \cdot 365 \cdot P} = \frac{M_p \cdot F_p}{8,760 \cdot P} \quad (13)$$

where: E_p, source strength, mg/h; M_p, mass of FR chemical released in the impaction experiment, µg; F_p, scaling factor, unitless; 24, hours per day; 365, days per year; and P,

average product lifetime, years. F_p is the ratio of the total surface area of foam in the product to the area of the mock-up.

The overall ADD value was obtained by summing the ADD values for each route of exposure:

$$ADD = ADD_D + ADD_O + ADD_I \quad (14)$$

The lifetime average daily dose (LADD) was calculated from the ADD as follows:

$$LADD = \frac{ADD \cdot Y}{L} \quad (15)$$

where: LADD, lifetime average daily dose; ADD, average daily dose, mg/kg-d; Y, number of years the consumer is exposed, y; L, average life expectancy, y.

C. Input Parameters

1. All Routes

General parameters for estimating exposure are summarized in Table 2. The average lifetime of a suite of upholstered furniture (P), 15 years, was estimated by industry representatives (Babich and Thomas 2001; NRC 2000). For the purpose of uncertainty analysis, 5 and 25 years were assumed to be reasonable lower and upper bounds, respectively. The average number of years of exposure to upholstered furniture (Y) is not necessarily the same as the average product life. A consumer may be exposed to several different types of furniture, which may be treated with different FR chemicals or none at all. For calculating cancer risk, it was assumed that adults are exposed to the same FR treatments for a lifetime, which is the most conservative approach. This assumption is only relevant to cancer risk. The average furniture lifetime (15 years) may be considered a reasonable lower bound for exposure duration.

For children, an exposure duration (Y) of two years, the first two years of life, was assumed. Children are most likely to place objects in their mouths between 3 months and 12 months of age; mouthing activity declines significantly by 24 months of age (Greene 1998). Mouthing activity is one of the principal quantifiable differences between children and adults that may affect exposure to FR chemicals. The body weight, surface area, and respiration rate are also different in children.

The average life expectancy (L) and average body weight (W) for adults are from the EPA "Exposure Factors Handbook" (EPA 1997). Body weights for males and females 45-54 years old were averaged (EPA 1997 Tables 7-4, 7-5). The 5th, 50th, and 95th percentile values were used as the lower bound, best estimate, and upper bound, respectively. Children's body weights were for one-year olds (EPA 1997, Tables 7-6, 7-7).

Table 2. General Input Parameters

Parameter	Best Estimate	Lower Bound	Upper Bound	Reference
All Routes				
Body weight, W, kg	72	50	101	EPA 1997, Tables 7-4, 7-5
Children	11	9	14	EPA 1997, Tables 7-6, 7-7
Life expectancy, L, y	ND	75	ND	EPA 1997
Years of exposure, Y, y	75	15	75	Assumption; see text
Children	2	2	2	Assumption; see text
Product lifetime, P, y	15	5	25	Estimate; see text
Product (foam) surface area, S _P , cm ²	28,000	17,000	56,000	Estimate; see text
Dermal				
Fabric to skin transfer, F	0.4	0.07	1	Wester et al. 1996; see text
Surface area of exposed skin, S, cm ²	2,500	1,000	9,000	EPA 1997; Smith 2000
Children	750	400	3400	EPA 1997; Smith 2000
Exposure duration, T, h/d	4	0.5	16	EPA 1997; Smith 2000
Children	3	0.5	12	EPA 1997; Smith 2000
Oral				
Mouthed surface area, hand, S _H , cm ²	450	45	900	EPA 1997; see text
Children	200	20	400	EPA 1997; see text
Hand to mouth transfer, F _H , d ⁻¹	0.4	0.03	7	Hatlelid 2003
Mouthed surface area, fabric, S _M , cm ²	0	0	50	Assumption; see text
Children	10	0	50	CPSC 1983; NRC 2000
Fabric to mouth transfer, F _M , d ⁻¹	0.4	0.03	7	Hatlelid 2003
Inhalation				
Average inhalation rate, I, m ³ /h	0.55	0.4	1.0	EPA 1997; Table 5-23
Children	0.24	0.17	0.4	EPA 1997; Table 5-23
Exposure duration, T, h/d	16	8	24	EPA 1997, p. 15-7
Scaling factor, F _P	60	30	120	Calculated from S _P
House volume, V, m ³	320	170	580	EPA 1997, Table 17-1
Air infiltration rate, A, h ⁻¹	0.4	0.15	1.7	Koontz & Rector 1993
Particle decay rate, K _D , h ⁻¹	2.0	0.5	4.0	EPA 1997; Table 17-13
Vapor phase decay rate, K _V , h ⁻¹	0	0	1	Assumption; NRC 2000
Boundary layer height, H, m	0.01	0.001	0.1	NRC 2000; see text

ND, not determined.

2. Dermal Exposure

For estimating dermal exposure, it was assumed that the consumer is lying on a sofa and wearing a short-sleeved shirt and short pants (Babich and Thomas 2001; Smith 2000). Thus, the surface areas for the lower leg and arms were combined, then divided by two. For adults, median values for males and females were averaged (EPA 1997, Table 6-2, 6-3). The lower bound for adults was assumed to be one-half the combined surface areas for the hands and feet. The upper bound was assumed to be one-half the total surface area.

For children, surface areas were available as the percentage of the total surface area. Mean values for the age groups <1 year and 1 to <2 years old were averaged (EPA 1997, Table 6-8). Data for the lower leg were not provided; thus, the lower leg was assumed to be 40% of the area of the entire leg, which is the case for adults. For children <2 years old, the median surface area-to-body weight ratio is 0.062 (EPA 1997, Table 6-9). Multiplying the average body weight (11 kg) by 0.062 gives a total surface area of 0.68 m². Absolute surface areas were computed from percent areas and the total surface area. Upper and lower bounds were analogous to the adult values.

An average exposure of 4 hours per day (T) for adults was estimated (Babich and Thomas 2001; Smith, 2000) from compiled activity data. This is the amount of time that adults and older children spend in “indoor/leisure” activities (EPA 1997, Table 15-8 to 15-10). Exposure durations of 0.5 hours and 16 hours were assumed as reasonable lower and upper bounds. Children up to 2 years old spend approximately 3 hours per day in “passive leisure” activities (EPA 1997 Table 15-12). An average exposure duration of 3 hours per day, with lower and upper bounds of 0.5 and 12 hours per day, was assumed. The total daily exposure duration may, in fact, be divided among several events. However, dividing the total exposure among several events does not affect the exposure calculation.

Chemical-specific input parameters are summarized in Table 3. Liquid-mediated migration to the fabric surface (M) was measured as described above. FR chemical migrating to the filter paper was assumed to be deposited on the surface of the cover fabric and, therefore, available for transfer to the skin. The components of FM-550 could not be quantified individually (Cobb and Bhooshan 2005). Therefore, the total migration of FM-550 was used to calculate exposure to both the aromatic phosphate (TPP/ITP) and BAE components. The average migration from each iteration (that is, from each daily measurement) was used to estimate exposure. Results from the two TDCP-containing samples (n=16) were averaged. Results from two FM-550-treated specimens were also averaged (n=12).

FR chemical migration from the foam to the filter paper depends, in part, on the volume of liquid phase (25 mL) and the pressure (1 psi) applied to the filter paper. The 1 psi was based on the average peak pressure of an adult lying on a mattress (reviewed in Midgett 2005). Firm mattresses produce higher pressures (Midgett 2005). Upholstered furniture, which is generally less firm than mattresses, might be expected to result in lower pressures. Thus, an average pressure of 1 psi may tend to overestimate exposure.*

* Personal communication from Jonathan Midgett, Division of Human Factors.

The amount of liquid phase was based on the amount of perspiration excreted from the body during an 8-hour period, about 0.05 mL per square centimeter of skin area (reviewed in Thomas and Brundage 2005). Multiplying 0.05 mL/cm² by the surface area of the mock-up (520 cm²) gives approximately 25 mL. However, the average exposure duration of adults to upholstered furniture is estimated as 4 hours. Therefore, the use of 25 mL of saline solution may tend to overestimate exposure. Furthermore, the saline solution is assumed to be distributed evenly across the surface of the mock-up. If the amount of saline solution were greater in the area below the filter paper, then this would also tend to overestimate exposure.

No data were available to estimate the fraction of FR chemical transferred from the fabric surface (represented by the filter paper) to the skin, that is, the fabric-to-skin transfer efficiency. Maibach et al. (1996) compared the *in vitro* percutaneous absorption rates of butanedioic acid, ((dimethoxyphosphinothioyl)thio)-, diethyl ester (BDE) applied to skin either directly or as BDE-impregnated fabric. BDE is relatively hydrophobic, as are the FR chemicals of interest. When applied directly to the skin in an aqueous ethanol vehicle, 8.8% of the applied dose was absorbed. When fabric was treated with the BDE solution and immediately applied to the skin, 3.9% was absorbed. This declined to 0.6% when the fabric was dried prior to application. The ratios between the treated fabric and directly applied chemical were, thus, 0.4 for moistened fabric and 0.07 for dry fabric. For the present risk assessment, 0.4 was assumed to be the best estimate for the transfer efficiency, with 0.07 as the lower bound and one (theoretical maximum) as the upper bound. The percutaneous absorption rate (K_T) is described below (Bioavailability).

3. Oral Exposure

Oral exposure to FR chemical may occur either indirectly by transfer of FR chemical from the fabric surface to the hand or directly by mouthing of upholstered furniture. FR chemical on the hand may be ingested by hand-to-mouth contact or by transfer of FR chemical from the hands to food. Indirect transfer is assumed to occur in both children and adults, while direct mouthing is assumed to occur primarily in children. The relevant surface area for hand-to-mouth activity (S_H) was assumed to be the ventral surface (palm) of the hands or approximately one-half the surface area of the hand. Parameters are summarized in Table 2. One-tenth of the best estimate, roughly equivalent to the fingertips, was assumed as a reasonable lower bound. The entire surface area of both hands, the theoretical maximum, was used as an upper bound.

For adults, the median surface area of the hands is 0.099 m² in men and 0.0817 m² in women (EPA 1997, Tables 6-2 and 6-3). Averaging the two values and dividing by two gives 0.045 m² or 450 cm². For children aged <1 and 1 to <2 years old, the hands represent 5.3 and 5.7 % of the total body surface area, respectively (EPA 2002, Table 8-3). The total surface area was calculated as 0.68 m² (see above). Multiplying the total surface area by 5.5 % (the average of 5.3 and 5.7) and dividing by two gives roughly 0.02 m² or 200 cm².

Table 3. Chemical-Specific Input Parameters

Parameter	Symbol	Units	TDCP	TPP/ITP	BAE
FR weight (mass) percent in foam	FRW	Mass percent	5.1 ^{a,b}	6.8 ^{a,c}	6.8 ^{a,d}
FR loading rate ^d	FRL	mg/cm ²	49	36 ^c	36 ^d
Total FR in product ^d	FRT	mg	1.3x10 ⁶	1x10 ^{6c}	1x10 ^{6d}
Migration to liquid phase	M	mg/cm ²	0.0036 ^{a,b,f}	0.0011 ^{a,c,f}	0.0011 ^{a,d,f}
Mass released from impaction ^{a,g}	M _p	mg	0.0015	<0.0004	<0.0004
Molecular mass	MM	g/mol	430.9	326.29 ⁱ	548.0 ^a
Vapor pressure	VP	torr	<1x10 ^{-6h}	6.3x10 ⁻⁶ⁱ	<1x10 ^{-6h}
Saturation concentration in air ^j	C _{sat}	mg/m ³	0.012	0.11	0.015
Diffusivity in air ^k	D _{air}	m ² /h	0.012	0.013	0.010
Dermal absorption rate	K _T	h ⁻¹	0.08 ^l	0.1 ^m	0.01 ⁿ
Acceptable daily intake	ADI	mg/kg-d	0.005 ^o	0.01—1.0 ^p	ND ^q
Cancer unit risk	Q	(mg/kg-d) ⁻¹	0.031 ^o	NA ^q	NA

^a Measured by CPSC staff (Cobb and Bhooshan 2005; Cobb and Chen 2005).

^b Average from two samples, foam S and foam Y.

^c Total FM-550. Individual components were not identified. Assumes that 100% of FR chemical present in or migrating from FM-500-treated foam is TPP/ITP.

^d Assumes that 100% of FR chemical present in or migrating from FM-500-treated foam is BAE.

^e Estimated from the mass percent (see text).

^f Average migration from up to 8 repeated tests on consecutive days with the same sample (Cobb and Bhooshan 2005). In calculating the average, non-detects were regarded as one-half the detection limit.

^g Five of 6 TDCP replicates (foam S) and 5 of 5 FM-550 replicates (foam Z) were below the method detection limit. Non-detects were regarded as one-half the detection limit.

^h Estimated upper bound (EPA 2005). One-half this value (5×10^{-7}) was used to estimate C_{sat}.

ⁱ Values for TPP (reviewed in Ferrante 1999a).

^j Calculated from the vapor pressure and molecular mass (see text).

^k Estimated as described in Schwope et al. 1989.

^l Estimated from *in vitro* data in (Hughes 2000; Hughes et al. 2001).

^m Estimated from *in vivo* data for *o*-tricresyl phosphate.

ⁿ Assumed (see text).

^o Estimated from two-year study in rats (Biodynamics 1981; Brandwene 2001; Freudenthal and Heinrich 2000).

^p Range of values for aromatic phosphates (Bittner et al. 2001; Ferrante 1999a).

^q NA, not applicable; ND, not determined.

For direct mouthing, a surface area (S_M) of 10 cm^2 was assumed for children. The CPSC staff has previously used values of 10 or 11 cm^2 for direct mouthing (Babich et al. 2004; Babich and Thomas 2001; CPSC 1983). Upper and lower bounds of 0 and 50 cm^2 were assumed. The upper bound is the value used by the NRC subcommittee (NRC 2000). For adults, zero cm^2 was assumed as both the best estimate and lower bound, while 50 cm^2 was assumed for the upper bound.

Few data on the transfer of chemicals from the hand to the mouth (F_H) or fabric to the mouth (F_M) are available. For playground equipment made from pressure-treated lumber, the CPSC staff used an average value of 0.43 for hand-to-mouth transfer, with a range of 0.03 to 7 (Hatlelid 2003). This was derived from the ratio of soil loading on the hands and soil ingestion (Hatlelid 2003; Lee 1990a,b). This value was for a 24-hour period, independent of the number of individual mouthing events. The upper bound is greater than one, because the hand can be “re-loaded” during the course of a day. For the present risk assessment, an average value of 0.4, with lower and upper bounds of 0.03 and 7, was assumed for both hand-to-mouth and fabric-to-mouth transfer.

4. Inhalation Exposure

A daily exposure duration of 16 hours per day (T) was assumed (EPA 1997, p.15-17). This is the time that consumers spend in their residence each day. Long term average inhalation rates (I)— $0.55 \text{ m}^3/\text{h}$ for adults and $0.24 \text{ m}^3/\text{h}$ for children (EPA 1997, Table 5-23)—were used, as the exposure duration includes sleep and other indoor activities. The adult value is the average for men and women. The lower and upper bounds for adults are for rest and light activities, respectively. For children, the upper and lower bounds were assumed to be proportional to the adult values.

The average air infiltration rate (A) is the median value for all seasons and all regions of the U.S. (Koontz and Rector 1993, Table 2). The 5th and 95th percentiles were used as lower and upper bounds. The whole house volume is the median value for U.S. residences (EPA 1997, Table 17-1). The lower and upper bounds were the 10th and 90th percentiles.

Exposure to particles deposited in the nasopharyngeal ($\sim 5\text{-}30 \mu\text{m}$), tracheobronchial ($\sim 1\text{-}5 \mu\text{m}$), and alveolar ($\sim 1 \mu\text{m}$) regions of the respiratory tract are all relevant, because the chemicals of interest are systemic toxicants. Deposition rates for particles roughly corresponding to these size ranges include: 0.5 h^{-1} ($1\text{-}5 \mu\text{m}$), 1.4 h^{-1} ($5\text{-}10 \mu\text{m}$), and 2.4 h^{-1} ($10\text{-}25 \mu\text{m}$) (EPA 1997, Table 17-13). Particles released from the wear and aging of upholstered furniture components are likely to include a broad range of particle sizes (Stevens et al. 2003). A decay rate of 2 h^{-1} , representing particles from 1 to $25 \mu\text{m}$ in diameter, was considered as the best estimate. The lower and upper bound values were for particles in the size ranges $1\text{-to-}5 \mu\text{m}$ and $>25 \mu\text{m}$, respectively.

The mass of FR chemical released from impaction (M_p) was measured as described above. Non-detects were assumed to equal one-half the detection limit. All of the FM-550 samples and most of the TDCP samples were non-detects. The components of FM-550 could not be quantified individually (Cobb and Bhooshan 2005). Therefore, the total migration of FM-550 was used to calculate exposure to both the aromatic phosphate (TPP/ITP) and BAE components. The total

amount of FR chemical retained by the filters was assumed to be released over the lifetime of the product. The seating area and seat back are assumed to be constructed with polyurethane foam. This area was estimated as 2.8 m² (28,000 cm²) for a suite of furniture including a sofa, love seat, and chair (Babich and Thomas 2001). The mock-up has a surface area of 530 cm² or 0.053 m² (9x9 inch). Thus, the scaling factor was calculated by dividing 2.8 m² by 0.053 m², which is approximately 60-fold. The lower bound assumed a suite of furniture in which only the horizontal seating area included foam. The upper bound assumed two suites of furniture in the home, such as in a living room and family room. The source strength (E_p) was calculated using equation (13).

For vapor phase FR chemical, the saturation concentration (C_{sat}) was calculated from the vapor pressure using equation (9). The diffusivity was estimated with equation (10).

The molecular mass and empirical vapor pressure of TPP were used for TPP/ITP (reviewed in Ferrante 1999a). The vapor pressures for TDCP and BAE were model estimates (EPA 2005). Because these were reported as upper bounds, one-half the upper bound was used to estimate exposure. The molecular mass of BAE was estimated by the CPSC staff (Cobb and Bhooshan 2005). The boundary layer height was the value used by the NRC subcommittee (NRC 2000). Values of 0.1-fold and 10-fold were assumed as lower and upper bounds. The decay rate for vapor phase FR was assumed to equal zero (Babich and Thomas 2001; NRC 2000). A value of one was assumed as an upper bound.

5. Bioavailability

In general, little information on the bioavailability of the chemicals of interest was available. The ADI values are based on oral studies. No quantitative data on oral bioavailability was available. Therefore, the default value of one (1) for relative oral bioavailability was assumed. This means that the oral bioavailability in humans was assumed to be equal to that in the test animals (CPSC 1992).

Inhalation exposure may contribute to the overall dose of FR chemical. In the absence of appropriate data, 100% of inhaled FR chemical, whether in the vapor phase or bound to particles, is assumed to be absorbed.

Dermal exposure is likely to be the primary exposure route for FR chemicals in upholstered furniture. Data on percutaneous absorption was available for some chemicals. The percutaneous absorption rate (K_T) for TDCP was derived from *in vitro* studies using mouse skin (Hughes 2000; Hughes et al. 2001). It is the same value used previously by the CPSC staff (Babich and Thomas 2001). The percutaneous absorption rate for *o*-tricresyl phosphate estimated from animal studies was used for the aromatic phosphates TPP and ITP (Babich and Thomas 2001; reviewed in Ferrante 1999a).

No data relating to percutaneous absorption of BAE were available. The BAE's are expected to be extremely hydrophobic, with predicted log K_{ow} values of 8.75 and 12 (EPA 2004, Volume 1). The molecular mass (MM) is not reported, but was estimated to be 548 (Cobb and Bhooshan 2005). Percutaneous absorption generally increases with increasing K_{ow} and decreases with

increasing MM (Potts and Guy 1992). Other brominated FR chemicals reviewed by the CPSC staff include DBDPO and HBCD. HBCD was absorbed at a rate of approximately 0.003 h^{-1} (Babich and Thomas 2001), based on *in vitro* studies (Hughes 2000). In the same study, DBDPO was absorbed at a rate of 0.001 h^{-1} to 0.01 h^{-1} (Babich and Thomas 2001), depending on the applied dose (Hughes 2000; Hughes et al. 2001). In the absence of appropriate data, a value of 0.01 h^{-1} was assumed for BAE.

Because the ADI values and cancer unit risk are based on oral studies, it would be appropriate to adjust for differences in bioavailability between the different routes (e.g., Babich and Thomas 2001). However, in the absence of data on oral and inhalation bioavailability, no adjustments can be made.

IV. Risk

The potential risk from non-cancer endpoints is evaluated by calculating the hazard index (HI), which is the ratio of the ADD to the acceptable daily intake (ADI), that is:

$$HI = \frac{ADD}{ADI} \quad (16)$$

where: HI, hazard index, unitless; ADD, overall average daily dose, mg/kg-d; and ADI, acceptable daily intake, mg/kg-d.

When the HI is greater than one, the product or exposure scenario under consideration is considered to present a hazard to consumers.

The lifetime individual excess cancer risk was calculated by:

$$R = Q \cdot LADD \quad (17)$$

where: R, lifetime individual excess cancer risk; Q, unit cancer risk or cancer potency, $(\text{mg/kg-d})^{-1}$; and LADD, lifetime average daily dose, mg/kg-d.

The results of the exposure and risk assessment are summarized in Table 4. With TDCP, the estimated HI for non-cancer effects was 0.9 in adults and 1.7 in children. Thus, the estimated exposures are close to the ADI. The estimated lifetime individual cancer risk in adults is 140 per million, based on a lifetime of exposure to furniture with similar levels of TDCP. The estimated risk in children from two-years of exposure is 7 per million. In both adults and children, dermal exposure contributed the largest fraction of total exposure. This was due to the comparatively high liquid-mediated migration of TDCP in laboratory tests with the mock-up. Indirect oral exposure (hand-to-mouth) also contributed significantly in both adults and children. In children, direct mouthing accounted for only 4% of the estimated total exposure.

Thus, with TDCP, the HI for non-cancer effects is greater than one in children, and the estimated cancer risks exceed one-in-a-million. Cancer risks greater than one-in-a-million are considered relevant for regulatory consideration under the CPSC chronic hazard guidelines (CPSC 1992). Based on the available data, TDCP in some upholstered furniture could present an appreciable health risk to consumers. Tests with additional foam or furniture samples are needed to confirm this preliminary conclusion.

Table 4. Exposure and Risk

Parameter	TDCP ^a		TPP/ITP ^b		BAE ^c	
	Adults	Children	Adults	Children	Adults	Children
ADD (mg/kg-d)	4.6x10 ⁻³	8.5x10 ⁻³	2.7x10 ⁻³	5.8x10 ⁻³	1.8x10 ⁻³	3.2x10 ⁻³
<u>Percent of total:</u>						
Dermal	80	65	53	36	80	65
Oral, indirect	18	29	9	13	14	23
Oral, direct	0	4	0	2	0	3
Inhalation, vapor	2	3	38	50	6	9
Inhalation, particles	0	0	0	0	0	0
HI	0.9	1.7	0.003—0.3 ^d	0.006—0.6 ^d	ND	ND
LADD (mg/kg-d)	4.6x10 ⁻³	2.3x10 ⁻⁴	2.7x10 ⁻³	1.6x10 ⁻⁴	1.8x10 ⁻³	8.6x10 ⁻⁵
Cancer risk per million	140	7.0	ND	ND	ND	ND

ADD, average daily dose; HI, hazard index; LADD, lifetime average daily dose; ND, not determined.

^a Migration data from two foam samples were averaged to estimate dermal and oral exposure.

^b Assumes FM-550 is 100% TPP/ITP.

^c Assumes FM-550 is 100% BAE.

^d Insufficient data were available to derive an ADI value for TPP/ITP. The ADI values are based on the range of ADI values for other aromatic phosphates (Ferrante 1999a).

Inhalation of vapor phase TPP/ITP (present in FM-550) contributed 38% of the estimated total TPP/ITP exposure in adults and 50% in children. This is due, in part, to the comparatively low liquid-mediated migration of FM-550. For TPP/ITP, the estimated ADD was 0.0027 mg/kg-d in adults and 0.0058 in children. ADI's for TPP and ITP were not available. ADI's for other aromatic phosphates and commercial mixtures range from 0.01 to 1.0 mg/kg-d. Assuming that the ADI's for TPP and ITP are in this range, the HI's would be between 0.003 and 0.3 in adults and between 0.006 and 0.6 in children. Thus, the estimated exposures are below the range of ADI values. Assuming that TPP and ITP are no more toxic than other aromatic phosphates, they are not expected to present an appreciable health risk to consumers. Additional toxicity data and tests with additional foam or furniture samples are needed to confirm this preliminary conclusion. It should be noted that the model used to estimate inhalation exposure includes a

number of conservative assumptions. That is, the model is likely to overestimate inhalation exposure, which is a significant route of exposure for TPP/ITP. It was also assumed that the total exposure is due entirely to TPP/ITP.

For BAE's (components of FM-550), the ADD was estimated to be 1.8×10^{-3} mg/kg-d in adults and 3.2×10^{-3} mg/kg-d in children. In comparison to TPP/ITP, a greater proportion of exposure was from the dermal route, because a higher percutaneous absorption rate that was assumed for BAE (see above). An ADI value for BAE or closely related compounds was not available. Additional toxicity and bioavailability data, as well as tests with additional foam or furniture samples, are needed to assess whether the BAE's could pose an appreciable health risk to consumers.

Inhalation of particle-bound FR chemicals did not contribute significantly to exposure for any of the FR chemicals under consideration. This was due to the mostly non-detectable levels of FR chemical in the laboratory experiments involving the release of FR chemical-containing particles.

A sensitivity analysis of the exposure model was conducted to assess variability and uncertainty. This was done by individually adjusting input parameters to the lower or upper bound. TDCP exposure to adults, using data from foam S, was the basis for the sensitivity analysis. In most cases, changing individual parameters to the lower or upper bound resulted in small changes in the estimated exposure (Table 5). Only one parameter resulted in greater than a 4-fold increase in exposure when changed to the upper bound.

Varying parameters that apply to all routes, such as body weight and years of exposure, had little effect on the total ADD. Dermal exposure parameters contributed about equally to the overall uncertainty. Increasing the exposure duration to 16 hours per day led to a 4-fold increase in the estimated dermal exposure. For oral exposure, the hand-to-mouth transfer factor was critical. Increasing this to the upper bound resulted in a 17.5-fold increase in oral exposure, while the lower bound led to a 12-fold decrease. However, because oral exposure was not the primary source of exposure, this would lead to only a 4-fold increase in total exposure (not shown). Varying the parameters for inhalation exposure resulted in modest changes in the estimated exposure. Increasing the inhalation rate to the upper bound resulted in a 1.8-fold increase in inhalation exposure. Applying a non-zero decay rate reduced the exposure to vapor phase chemical by 3-fold. Either increasing or decreasing the height of the boundary layer by 10-fold resulted in a decrease in the estimated exposure. Thus, the value assumed by the NRC subcommittee apparently is the optimal value.

Table 5. Sensitivity Analysis

Parameter	Best Estimate	Lower Bound		Upper Bound	
		Value	Ratio	Value	Ratio
All Routes					
Body weight, W, kg	72	50	1.4	101	0.7
Years of exposure, Y, y	75	15	1.0	75	1.0
Product lifetime, P, y	15	5	1.0	25	1.0
Product surface area, S _p , cm ²	28,000	17,000	1.0	56,000	1.0
Dermal					
Fabric to skin transfer, F	0.4	0.07	0.18	1	2.5
Surface area of exposed skin, S, cm ²	2,500	1,000	0.4	9,000	3.6
Exposure duration, T, h/d	4	0.5	0.13	16	4.0
Oral					
Mouthed surface area, hand, S _H , cm ²	450	45	0.1	900	2.0
Hand to mouth transfer, F _H , d ⁻¹	0.4	0.03	0.08	7	17.5
Mouthed surface area, fabric, S _M , cm ²	0	0	--	50	1.3
Fabric to mouth transfer, F _M , d ⁻¹	0.4	0.03	1.0	7	1.0
Inhalation					
Average inhalation rate, I, m ³ /h	0.55	0.4	0.7	1.0	1.8
Exposure duration, T, h/d	16	8	0.5	24	1.5
Scaling factor, F _p	60	30	1.0	120	1.0
House volume, V, m ³	320	170	1.8	580	0.6
Air infiltration rate, A, h ⁻¹	0.4	0.15	2.4	1.7	0.2
Particle decay rate, K _D , h ⁻¹	2.0	0.5	1.0	4.0	1.0
Vapor phase decay rate, K _V , h ⁻¹	0	0	--	0	0.3
Boundary layer height, H, m	0.01	0.001	0.09	0.1	0.1

The sensitivity analysis is based on the estimated TDCP exposure to adults, using data from foam S. The ratio is the relative effect on the ADD when parameters are varied individually from the best estimate to the lower or upper bound. Ratios for parameters affecting all routes are based on the total ADD. Ratios for the dermal, oral, and inhalation parameters are based on ADD(D), ADD(O), and ADD(I), respectively.

V. Discussion

A. Toxicity

Only limited toxicological and bioavailability data are available for the components of FM-550. No toxicological data on the mixture is available. There was insufficient information to derive ADI values for TPP, ITP, or BAE's. TPP and ITP are members of a broader class of compounds that has been reviewed by the CPSC staff. ADI values for other aromatic phosphates, including mixtures, were used as surrogates for TPP and ITP. These ADI values ranged from 0.01 to 1.0 mg/kg-d (Ferrante 1999a; Bittner et al. 2001). Comparing these values to the estimated exposure results in a range of possible HI's that are all less than 1.0. Provided that TPP and ITP are no more toxic than the other aromatic phosphates, they would not pose an appreciable health risk to consumers. Staff will consider any additional toxicity data that may become available. Although several aromatic phosphates have been studied in subchronic studies, only one has been tested in a chronic study. Therefore, there is little information regarding their potential carcinogenicity.

Insufficient toxicity data are available for the BAE's to derive an ADI level. In addition, no data are available on closely related compounds. Therefore, it was not possible to assess whether the BAE's in FM-550 could pose an appreciable health risk to consumers. The CPSC staff will consider any new data that may become available. If, in the future, the ADI level were determined to be greater than the estimated average daily exposures— 1.8×10^{-3} in adults and 3.2×10^{-3} in children—then the BAE's would not pose an appreciable health risk to consumers. The BAE's would have to be more toxic than any of the additive* FR chemicals previously reviewed by the CPSC staff to pose an appreciable health risk to consumers (Bittner et al. 2001).

TDCP has been well studied in comparison to many other FR chemicals, including a two-year study in rats. This study was sufficient to derive a chronic ADI level and cancer potency estimate.

There are no data to evaluate the relative sensitivity of children or juvenile animals or to any of the FR chemicals under consideration. Exposure to carcinogens early in life may lead to an increased cancer risk (reviewed in EPA 2003). No adjustments were applied to account for the possible increased sensitivity of children (CSPC 1992). There are no data relating to possible interactions among aromatic phosphates and the BAE's.

B. Exposure

Generally, the CPSC staff prefers to derive realistic estimates of exposure, rather than an upper bound or worst case estimates. However, in cases where data are lacking, default or conservative assumptions—that is, assumptions that tend to overestimate exposure—are applied (CPSC 1992). Many of the input parameters in the present risk assessment, such as exposure duration and skin surface areas, are the same values used in the previous upholstered furniture risk assessment (Babich and Thomas 2001). Average values (best estimates) of these parameters

* Only THPC would present a hazard at the estimated BAE exposures. THPC is a reactive FR that is not present in the finished product.

were applied whenever sufficient information was available. There are a number of instances, though, where conservative assumptions were applied. This is particularly true for inhalation exposure to vapor phase FR chemicals. Details are discussed below. Although the exposure assessment necessarily includes several conservative assumptions, it should not be regarded as representing a “worst case,” “theoretical worst case,” or “maximum exposed individual.” “Reasonable upper bound” estimates of exposure are discussed below.

The exposure assessment is limited in that only a small number of foam samples were tested. Therefore, it is uncertain whether these results may be applicable to other foam samples treated with the same chemicals. However, with the two TDCP samples, migration was roughly proportional to the TDCP content. Foam S (TDCP) and Foam Z (FM-550) were selected because they contained the highest FR concentrations available. The exposure assessment is also limited in that furniture treated with the FR chemicals was not available for testing.

The individual components of FM-550 were not quantified in the exposure studies; only total FM-550 release was measured. The migration of the different compounds to the fabric surface, or release into airborne particles, may not be the same. Therefore, in estimating exposure to the aromatic phosphate components of FM-550, it was assumed that FM-550 was 100% TPP/ITP. Conversely, it was assumed that FM-550 was 100% BAE in estimating BAE exposure. These assumptions are likely to overestimate exposure. In principle, the true exposure for each component is between zero and the estimated ADD. The alternative approach would be to assume that the components of FM-550 migrating into the liquid phase are in the same proportions as in the foam itself. However, this alternative assumption could underestimate exposure for some components if they migrate at different rates.

The method for estimating the potential for dermal exposure was adapted from exposure studies for mattress filling materials (Thomas and Brundage 2006). The method was intended to provide a realistic exposure estimate. However, some assumptions, such as the amount of liquid phase and the pressure applied, may tend to overestimate exposure from upholstered furniture, in comparison to mattresses. No interliner or batting was present in the mock-up, because some upholstered furniture does not have these components. The presence of an interliner or batting might be expected to reduce migration. As with mattresses, these migration data were also used to estimate oral exposure.

The potential for release of particles containing FR chemicals was also assessed using a method developed for mattresses. For the most part, FR chemicals were not detectable in airborne particles released when the mock-up was subjected to impaction. Therefore, it does not appear that inhalation of particles would contribute significantly to consumer exposure. This is not unexpected, since the foam is resilient and is an internal component.

Inhalation exposure to vapor phase FR chemical was estimated from a mathematical model described by the NRC subcommittee (NRC 2000; see also Babich and Thomas 2001). The model contains several conservative assumptions, including the lack of affinity of the FR for the foam, barriers to vaporization of FR chemical, and sinks or decay processes. In practice, the FR chemicals may have an affinity for the foam matrix due to covalent or non-covalent binding. The foam, interliner, and cover fabric may all impede the release of FR chemical into air. Vapor

phase FR chemical would most likely be absorbed by other household furnishings or materials, including carpets, draperies, and wallboard. Vapor phase FR chemical may also be adsorbed to airborne particles or break down to other substances. Therefore, the model is expected to overestimate exposure to vapor phase FR chemical. Furthermore, in the absence of bioavailability data, 100% absorption and retention of vapor phase chemicals was assumed. These conservative assumptions are especially relevant to the aromatic phosphates TPP and ITP, for which inhalation of vapor phase chemical was estimated to be a significant exposure route (Table 4).

The vapor pressures of TDCP and BAE are upper bound model estimates (EPA 2005). Because they are upper bound estimates, the true vapor pressures and inhalation exposures may be lower. That they are only model estimates implies that they are uncertain. However, it is clear that both TDCP and BAE have low volatility.

Previously, the CPSC staff used a higher vapor pressure for TDCP, which led to higher inhalation exposures (Babich and Thomas 2001). The estimated value used here (EPA 2005) is assumed to be the most reliable value. Using the previous vapor pressure (0.01 torr) for TDCP would lead to greater inhalation exposure and 3-to-4 fold greater HI's and cancer risk estimates.

The CPSC staff was unable to detect vapor phase TDCP or FM-550 at temperatures below 65°C (Cobb and Bhooshan 2005). However, the detection limits were greater than the concentrations predicted by the model. For example, the detection limit for TDCP was 20 mg/m³, while the predicted concentration in air was less than 1 µg/m³ (not shown). The detection limit for FM-550 was 50 mg/m³, while the model-estimated concentrations of TPP and BAE in air were less than 10 µg/m³. Therefore, the mathematical model was used to estimate indoor concentrations, rather than using the detection limits as upper bound estimates of exposure. The low vapor pressures of the FR chemicals under consideration make it difficult to evaluate the potential for exposure to the vapor phase. However, their low volatility is evidence that inhalation is not likely to be a significant exposure route.

In estimating inhalation exposures, the indoor environment was modeled as a single zone the size of a home. Thus, any emissions of vapor or particles are assumed to be evenly distributed throughout the home. In reality, the concentrations of airborne pollutants are greater in the room where the source is located. However, when interior doors are open or when forced air heating and air conditioning are operating, the differences in concentration are relatively small. One alternative would be to model the living room (or living room, dining room, and kitchen) as a single zone, ignoring the other rooms in the home. A second alternative would be to use a multiple zone model. With either alternative, one would need to account for the time spent and activity level in each room. This would add considerable complexity to the model. Treating the entire home as a single zone simply averages the various microenvironments (rooms and activities). The differences in exposure estimates among the alternatives would probably not be sufficient to change the conclusions.

Other than the impaction experiments, the potential effects of accelerated aging or wear on dermal or oral exposure were not evaluated. Small-scale mock-ups were used in lieu of furniture samples, which were not available. The laboratory or mathematical models used to estimate exposure have not been validated by comparison with reliable exposure data, such as from field studies. Appropriate data do not exist.

C. Variability and Uncertainty

This risk assessment is constrained by the lack of information in a number of areas, including: (a) the lack of toxicity data for FM-550 or its components; (b) the small number of foam samples tested; and (c) the inability to distinguish the components of FM-550 in migration studies. The potential effects of (a) and (b) on exposure and risk cannot be quantified.

Some sources of variability and uncertainty can be assessed quantitatively. The uncertainty analysis suggests that variability deriving from the model input parameters is modest. The variability of chemical-specific input parameters, such as migration, were not considered due to the limited number of samples tested.

A “reasonable upper bound” estimate of exposure may be derived by setting key parameters for each exposure route to their upper bound, such as the surface area of exposed skin (dermal), mouthed surface area of the hand (oral), and average inhalation rate (inhalation). For TPP/ITP, this would roughly double the range of HI’s to 0.007—0.7 in adults and 0.02—2 in children. Alternatively, setting the surface area of exposed skin (dermal), hand-to-mouth transfer factor (oral), and average inhalation rate (inhalation) to their upper bounds would increase the HI in children to 0.03—3. This increase in the HI is mainly due to the uncertainty in the estimated hand-to-mouth transfer factor, which is estimated as 0.4, with lower and upper bounds of 0.03 and 7 (Table 2). Thus, the estimated upper bound TPP/ITP exposures would exceed the ADI value for the most toxic aromatic phosphate (ADI = 0.01 mg/kg-d). However, this analysis assumes that all of the FM-550 migrating from foam is TPP/ITP. Furthermore, the model for inhalation exposure includes several assumptions that tend to overestimate exposure.

D. Conclusions

The following conclusions are based on limited exposure and/or toxicity data, and should be regarded as preliminary. Conservative assumptions were applied in areas where data were limited. Tests with additional foam samples, tests with furniture samples, and additional toxicity data on TPP, ITP, and BAE’s would significantly reduce the level of uncertainty in this preliminary risk assessment.

Based on tests with two foam samples, upholstered furniture manufactured with TDCP-treated foam in some upholstered furniture could present an appreciable health risk to consumers. The estimated exposures were near or above the ADI for non-cancer effects, and estimated cancer risks exceeded one per million. Tests with additional foam or furniture samples are needed to confirm this preliminary conclusion.

Based on limited data, there is no evidence that upholstered furniture containing foam treated with FM-550 would pose an appreciable health risk to consumers. Based on a single foam sample and toxicity data for structurally related compounds, the TPP and ITP present in FM-550 do not appear to pose any appreciable risk to consumers. Additional toxicity data and tests with additional foam or furniture samples are needed to confirm this preliminary conclusion. The National Toxicology Program (NTP) is considering a request from the CPSC staff to perform additional toxicity studies on aromatic phosphates. The staff will review any additional toxicity data that become available.

Insufficient toxicity data on the BAE's present in FM-550, or structurally related compounds, are available to assess whether the BAE's could pose any health risks to consumers. However, the estimated exposure to BAE's is relatively low. The BAE's would have to be more toxic than any of the additive FR chemicals previously reviewed by the CPSC staff (Bittner et al. 2001) to pose an appreciable health risk to consumers. Additional toxicity and bioavailability data, as well as tests with additional foam or furniture samples, are needed to assess whether the BAE's could pose an appreciable health risk to consumers.

Melamine-treated foam was also available for exposure studies. However, melamine does not satisfy the regulatory definition of toxic, even though it has been well studied in chronic bioassays (Thomas and Brundage 2004). Thus, exposure studies with melamine-treated foam were not necessary. Melamine-treated foam would not pose an appreciable risk to consumers.

A number of other alternative FR treatments that could be used in foam have been discussed by the U.S. EPA's Design for the Environment Program (EPA 2005).

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UNITED STATES
CONSUMER PRODUCT SAFETY COMMISSION
WASHINGTON, DC 20207

Memorandum

Date: July 20, 2004

TO : Dale Ray, Project Manager for Upholstered Furniture
Directorate for Economic Analysis

THROUGH: Mary Ann Danello, Ph.D., Associate Executive Director for Health Sciences *mad*
Lori E. Saltzman, M.S., Director, Division of Health Sciences ✓

FROM : Michael A. Babich, Ph.D., Chemist, Division of Health Sciences *MAB*
Kristina Hatlelid, Ph.D., Toxicologist, Division of Health Sciences *KH*
Cheryl Osterhout, Ph.D., Pharmacologist, Division of Health Sciences *CO*

SUBJECT : Update on the Toxicity of Selected Flame Retardant Chemicals

SUMMARY

Furniture manufacturers would be free to choose the means of complying with the CPSC staff's revised draft flammability standard. However, some upholstered furniture cover fabrics and filling materials would probably require treatment with flame retardant (FR) chemicals to pass the draft standard. In addressing the hazards associated with upholstered furniture fires, the CPSC staff is working to develop a performance standard without creating additional health hazards to consumers, workers, or the environment. Thus, the CPSC staff reviewed all of the available toxicity data on 16 chemicals or chemical classes (over 50 individual chemicals) that could be used to treat upholstery fabric. In 2001, the staff completed a risk assessment of five FR chemicals: antimony trioxide (AT); decabromodiphenyl oxide (DBDPO); hexabromocyclododecane (HBCD); phosphonic acid, (3-[[hydroxymethyl]amino]-3-oxopropyl)-, dimethyl ester (PA); and tetrakis (hydroxymethyl) phosphonium chloride (THPC) polymer (Babich and Thomas 2001). In the view of the staff, these FR chemicals are the most likely to be used to treat upholstery fabrics. The staff concluded that DBDPO, HBCD, and PA (based on limited data) are not likely to present a hazard to consumers. The staff also concluded that additional data are needed on inhalation exposure to AT particles that may be released from the fabric during use. AT is a "synergist" that is generally used in combination with DBDPO and HBCD. The staff further concluded that additional information on the toxicity of unidentified by-products released from THPC-treated fabrics was also needed.

This memorandum reviews new information on these five compounds that has become available since 2001. Studies on inhalation exposure to AT particles are underway in the U.K., although results are not available at this time. New toxicity studies on AT and HBCD provide additional support for, but do not change, the staff's previous conclusions for these compounds. No new significant information is available on PA and THPC. New studies suggest that DBDPO may affect brain development in newborn animals, although the relevance of this to humans is

uncertain. However, even if the staff calculated a new acceptable daily intake level based on this new information, the estimated DBDPO exposure from treated upholstery fabrics would still be below that level. DBDPO has been detected at relatively low levels in the environment, in animals, and in human tissue. It has been suggested that DBDPO in the environment may break down to more toxic compounds, polybrominated diphenyl ethers (PBDE's), although the evidence for this is inconclusive. At this time, the CPSC staff still concludes that DBDPO in upholstered furniture fabrics is not likely to present a hazard to consumers. However, the staff will continue to monitor new data as it becomes available. The staff continues to work with the Environmental Protection Agency (EPA) to ensure that the use of FR chemicals in upholstered furniture does not present a hazard to consumers, workers, or the environment.

INTRODUCTION

Upholstered furniture fires are a leading cause of residential fire deaths involving consumer products. The U.S. Consumer Product Safety Commission (CPSC) is considering the hazards associated with the ignition of upholstered furniture fires by cigarettes and small open flames, such as matches, cigarette lighters, and candles. To reduce these hazards, the CPSC staff is developing a draft performance standard for upholstered furniture. Based on 1995-1999 data, the CPSC staff estimates that annually 460 deaths, 1110 injuries, and \$130 million in property damage could be addressed by the draft standard (Levenson 2004). While furniture manufacturers would be free to choose the means of complying with the draft standard, manufacturers have informed us that they are likely to treat some upholstery cover fabrics with flame retardant (FR) chemicals.

In addressing the hazards associated with upholstered furniture fires, the CPSC staff is working to develop a performance standard without creating additional health hazards to consumers, workers, or the environment. The Fire Retardant Chemicals Association (FRCA) identified 16 FR chemicals or chemical classes that its members would market for use in upholstered furniture if a standard is promulgated (FRCA 1998). The CPSC staff reviewed all of the available toxicity data on the 16 chemicals/chemical classes, comprising over 50 individual compounds (Bittner 1999a-d; Ferrante 1999a-f; Hatlelid 1999a-h; Bittner 2001; Bittner et al. 2001; see also Babich and Saltzman 1999). The toxicity reviews were later updated to include new information (Bittner 2001). The CPSC staff reviews contributed to a National Research Council (NRC) report on 16 FR chemicals, representing each of the 16 classes (NRC 2000).

The CPSC staff evaluated the toxicity data using the criteria in the Federal Hazardous Substances Act (FHSA) regulations and the CPSC chronic hazard guidelines (CPSC 1992; summarized at 16 CFR §1500.135). According to the FHSA supplemental definition of "toxic," a substance is considered "toxic" due to chronic toxicity if it is either known to be, or probably, toxic in humans. 16 CFR §1500.3 (c)(2)(ii). Further, a substance or mixture is classified as "known to be toxic" in humans only if there is sufficient evidence in humans. It is considered "probably toxic" if there is either limited evidence in humans or sufficient evidence in animals (Table 1). If a substance is considered "toxic" due to chronic toxicity, then a quantitative assessment of exposure and risk is performed to evaluate whether the chemical may be considered a "hazardous

substance” under the FHSA. The quantitative risk assessment includes a consideration of dose response, bioavailability, and exposure.

Table 1. Classification of Chronic Hazards under the FHSA.

Evidence	Human studies	Animal studies
Sufficient evidence	Known ^a	Probable ^a
Limited evidence	Probable ^a	Possible
Inadequate evidence	Possible	---

^a Considered “toxic” under the FHSA.

In 2001, the CPSC staff completed risk assessments on selected FR chemicals, including: antimony trioxide (Sb₂O₃) (AT); decabromodiphenyl oxide (DBDPO); hexabromocyclododecane (HBCD); phosphonic acid, (3- {[hydroxymethyl]amino}-3-oxopropyl)-, dimethyl ester (PA) (sold under the trade name Pyrovatex[®]); and tetrakis (hydroxymethyl) phosphonium chloride (THPC) (Proban CC[®]) polymer (Babich and Thomas 2001) (Figure 1). Four of these chemicals—AT, DBDPO, HBCD, and PA—are currently used in the United Kingdom (UK), where a flammability standard for upholstered furniture is in effect. Therefore, they are very likely to be used in the U.S. if a flammability standard is adopted. THPC also was included in the staff risk assessment, because it is currently used in apparel and pre-production upholstery fabric samples were available for testing.

The CPSC staff is cooperating with the U.S. Environmental Protection Agency (EPA) to develop a possible significant new use rule (SNUR) on the use of FR chemicals in upholstered furniture. If adopted, the SNUR could be used to obtain additional toxicity or exposure data where needed.

The purpose of this report is to review new information relating to the toxicity and potential risks associated with five FR chemicals—AT, DBDPO, HBCD, PA, and THPC—and to determine whether the new data would change any of the conclusions in the 2001 staff risk assessment (Babich and Thomas 2001). Recently, the American Furniture Manufacturers Association (AFMA) (Counts 2004) proposed changes to the CPSC draft standard that could affect the use of FR chemicals in upholstered furniture. If the changes proposed by AFMA were adopted, this could result in the use of FR chemicals in upholstery foam in addition to the fabric. Different types of FR chemicals are used in foam and the potential for exposure may differ. This report applies only to the use of FR chemicals in upholstery cover fabrics.

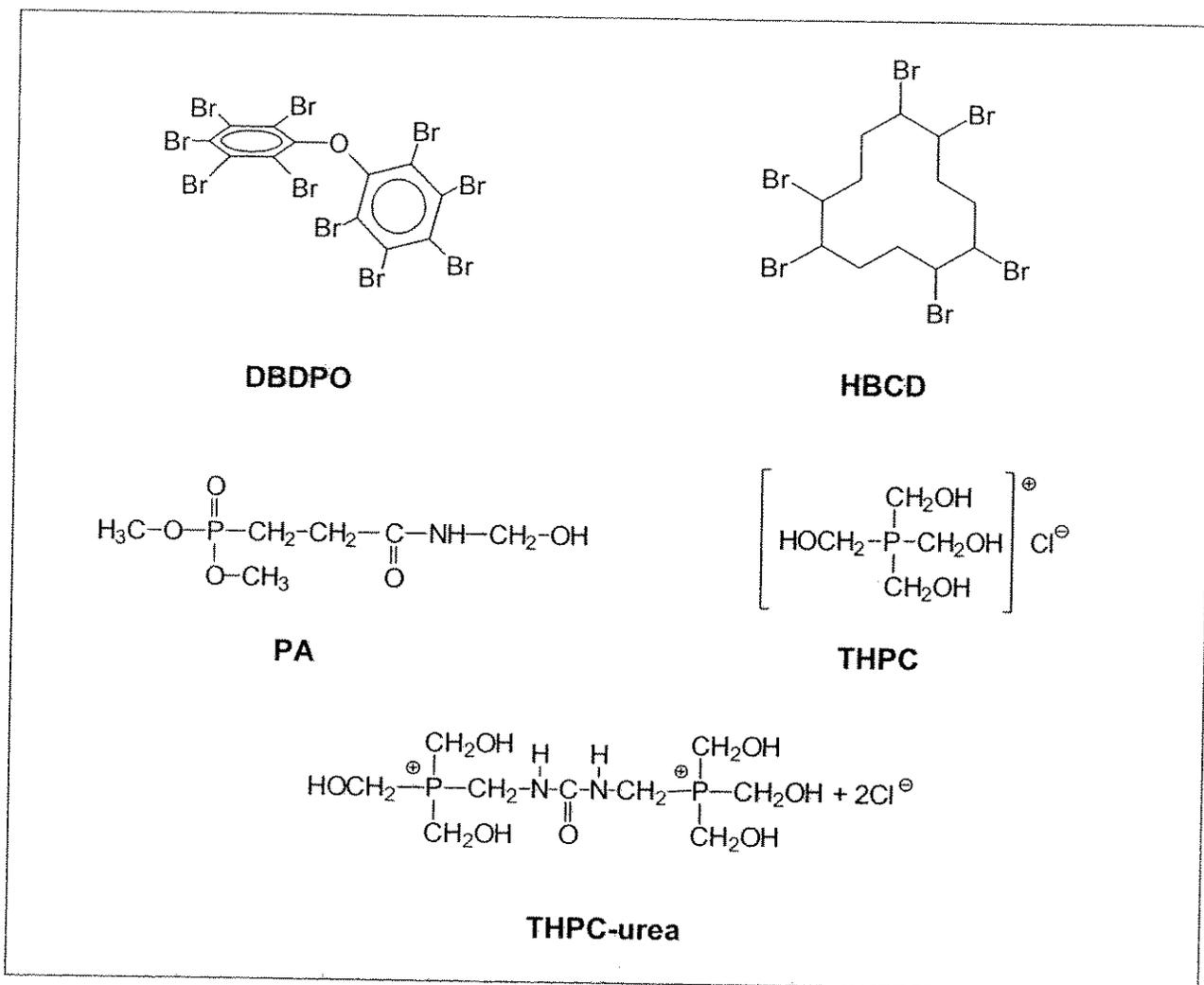


Figure 1. Chemical structures of organic flame retardant chemicals

ANTIMONY TRIOXIDE

AT (1309-64-4) is a synergist that is used in combination with halogenated FR chemicals, including DBDPO and HBCD. The FR chemical mixture is generally applied to upholstery fabrics as a back-coating. Such mixtures are the most common FR's used to treat upholstery fabric for use in the U.K. Previously, the CPSC staff (Hatlelid 1999a) concluded that AT is not acutely toxic by the oral or dermal routes, as defined by FHSA regulations. However, the staff concluded that AT does meet the FHSA definition of "toxic," based on chronic toxicity. AT caused systemic toxicity following oral exposure in experimental animals and non-cancer effects in the lung were observed in animals and humans following inhalation of the dust. The staff further concluded that AT is a probable human carcinogen, based on sufficient evidence of carcinogenicity in animals exposed by inhalation. The staff also considers AT to be a probable skin and eye irritant. The staff calculated an acceptable exposure level for airborne AT particles of 9 ng/m^3 (as antimony) (Hatlelid 1999a; Bittner 2001) and an oral acceptable daily intake

(ADI) of 2.3 mg/kg-d (as antimony), based on systemic toxicity (including liver, gastrointestinal, and hematological effects) in a subchronic study (Hattelid 1999a).*

Systemic Toxicity

Since the 1999 toxicity review and 2001 update, the staff identified additional information. Omura et al. (2002) evaluated testicular toxicity in Wistar rats and CD-1 mice. The animals were dosed with AT equivalent to 1,000 mg/kg antimony suspended in water; the doses were administered for 5 days per week for 4 weeks in mice, and for 3 days per week for 4 weeks in the rats. The evaluation included weights of testis, epididymis, ventral prostate, and seminal vesicles; sperm count, motility, and morphology; and histopathology of the testis. No significant treatment-related effects were reported in either species.

A 90-day feeding study in male and female Wistar rats (Hext et al. 1999) showed that doses up to 1,686 mg/kg-d (as AT) in males or 1,879 mg/kg-d in females resulted in minor hematological (increased erythrocyte count; decreased mean cell volume) and hepatic changes (increased liver weight; lipid perturbations; decreased plasma alkaline phosphatase activity, and increased aspartate aminotransferase activity) in the absence of histopathological changes. A small, but statistically significant decrease in alkaline phosphatase activity was also noted in the mid-dose females (494 mg/kg-d). The authors attributed the decreased alkaline phosphatase activity to effects on nutritional status.

The new 90-day study (Hext et al. 1999) is consistent with other subchronic studies previously reviewed by the staff (Hattelid 1999a). However, some of the previous studies were quite old and all of the studies had limitations such as small number of animals, incomplete histopathology, or durations less than 90 days. If the Hext et al. study were available at the time of the previous staff review, it would have been preferred for setting an ADI. The middle dose (421 mg/kg-d AT or 354 mg/kg-d antimony in males) may be considered to be the no observed adverse effect level (NOAEL). This would result in an ADI of 3.5 mg/kg-d (as antimony), or slightly greater than the current ADI of 2.3 mg/kg-d.

Carcinogenicity, Mutagenicity

The staff previously reviewed data which indicated that AT is not mutagenic in *Salmonella* or *E. coli* strains, but demonstrated evidence of DNA-damaging ability in *B. subtilis*. While AT did not induce chromosomal aberrations in the bone marrow cells of male and female mice after a single oral administration of 330-840 mg/kg-d, repeat dosing for 21 days did (Gurnani et al. 1992).

A more recent study (Elliott et al. 1998) confirmed that AT is not mutagenic in *Salmonella* or mouse lymphoma cells, although a positive response was observed *in vitro* with isolated human peripheral lymphocytes. This study failed to confirm the previously observed clastogenicity in a repeat dose study in mice (Gurnani et al. 1992). In fact, the authors noted that no toxicity was observed in this or other studies at the dose levels reported to be fatal by Gurnani et al. The

* 1.0 mg AT is equivalent to 0.84 mg antimony.

reasons for the different results in these two studies are not known, but Elliott et al. (1998) concluded that AT is not genotoxic *in vivo*.

A study in workers involved in AT fabric treatment (Cavallo et al. 2002) compared AT-exposed workers with unexposed workers as controls. There were no differences in sister chromatid exchanges or micronuclei between the two groups. However, the authors did report an increase in DNA damage in exposed workers using an enzyme (formamidopyrimidine-DNA glycosylase)-modified comet assay that detects 8-OH-dexoyguanosine. The authors stated that the two worker groups in the study had similar chemical exposures and working conditions, except that one group had higher AT exposures. Thus, the authors concluded that AT exposure led to oxidative DNA damage in workers. Oxidative DNA damage may be, for example, an indirect result of chronic inflammation or any other process that releases reactive oxygen species. No data on worker exposures were provided to support this claim. Because the two worker groups were defined based on job description, confounding or effect modification due to other chemical exposures remains a possibility.

The staff concludes that data on the genotoxicity of AT are inconclusive. If AT were found to be genotoxic, this could provide further support for the conclusion that AT is a probable human carcinogen by inhalation. However, inconclusive (as observed) or negative data for the genotoxicity of AT would not be sufficient to alter the staff's original conclusion.

Developmental Toxicity

Schroeder et al. (2004) recently studied the effects of AT on development in rats. Dams were exposed by inhalation on gestation days 0-19. Exposure was by nose only inhalation for 6 hours per day at levels up to 6.3 mg/m³ (as AT). Average particle sizes (mass median aerodynamic diameters) were within the respirable range. Macrophages were found in the lungs of exposed dams and antimony levels were elevated in their erythrocytes at all dose levels, as compared to the controls. The authors reported that there were no statistically significant effects on implantation, resorption, fetal body weight, sex ratios, or crown to rump distances. There was a small, non-significant increase in resorptions per implant at the high dose. The authors also reported no significant increases in external, visceral, or skeletal variations or malformations. The percentage of fetuses with unossified metacarpals was significantly decreased at the mid dose. A single occurrence of anophthalmia (congenital absence of one or both eyes) was reported in 25 litters and 173 fetuses at the high dose, as compared to zero in the controls and other dose groups.

In a previous study in rats, the authors reported increases in pre-implantation loss and fetal growth retardation at doses of 0.068 to 0.23 mg/m³ (Grin et al. 1987). However, another study (Belyaeva 1967) and the study discussed above (Schroeder et al. 2004) did not find statistically significant changes in either of these endpoints at higher doses. The observation of a single occurrence of anophthalmia (Schroeder et al. 2004) was not statistically significant and this rare lesion was not reported in other studies. Therefore, the staff concludes that AT is a possible reproductive/developmental toxicant in humans, based on limited evidence in animals. The original staff conclusion (Hatlelid 1999a) remains unchanged. Nonetheless, any observation of a

rare lesion is a potential concern. The staff will closely monitor any new developments in this area of research.

Exposure and Risk

The Danish Environmental Protection Agency (2003) performed a risk assessment for antimony exposure from polyester apparel. AT and antimony triacetate are used as catalysts in the production of polyester fibers, which leads to residual levels up to 100 mg/kg (parts-per-million) in the finished product. This risk assessment is not directly relevant to the use of AT as an FR chemical, because AT is applied in a different manner and is present at higher levels in FR-treated fabric (~2% by weight) than non-FR treated polyester fabric (≤ 100 mg/kg or 0.01%). The Danish risk assessment is discussed here for the sake of completeness.

The Danish EPA considered exposures from the dermal and oral routes, including mouthing by children. Fabric samples (5x5 mm) were extracted with 100 mL artificial saliva or artificial perspiration for 1 hour at 40°C. No antimony was detected in artificial saliva extracts of four fabrics tested, where the detection limit was 0.5 mg/kg (0.5% to 7% of total antimony). Approximately 8% of total antimony was detected in artificial perspiration extracts from only one of five fabrics tested, at a detection limit of 1 mg/kg (1% to 14%). Estimated exposures ranged from 2.5×10^{-5} mg/kg-d for adults to 8.6×10^{-5} mg/kg-d for children. The estimated exposures are well below both the World Health Organization's ADI of 8.6×10^{-4} mg/kg-d for total antimony and the CPSC ADI of 2.3 mg/kg-d for AT.[†]

The Danish EPA also estimated a maximum theoretical airborne concentration of $10 \mu\text{g}/\text{m}^3$, using a theoretical approach similar to that used by the NRC subcommittee and CPSC staff (NRC 2000; Babich and Thomas 2001). While this level exceeded the Danish ($5 \mu\text{g}/\text{m}^3$) and CPSC staff ($0.009 \mu\text{g}/\text{m}^3$) levels of concern, the authors noted that their exposure estimate was a worst-case value based on a theoretical model (Danish EPA 2003).

The CPSC staff previously concluded that AT probably would not present a hazard to consumers by oral or dermal exposure (Babich and Thomas 2001). A new ADI of 3.5 mg/kg-d could be derived from the new 90-day study (Hext et al. 1999). This is slightly greater than the previous ADI of 2.3 mg/kg-d (Hattelid 1999a). The higher ADI means that consumers could be exposed to slightly more AT and still have a negligible risk. Therefore, staff's previous conclusion is unchanged.

However, the staff also concluded that data on exposure to airborne particles containing AT were needed to evaluate whether AT could present a hazard to consumers (Babich and Thomas 2001). Scientists in the U.K. are in the process of studying the release of AT particles from upholstery fabric into air during simulated wear, using a Martindale fabric wear test for up to 30,000 cycles (Stevens and Horrocks 2002). This test is commonly used in the textile industry to assess the durability of fabrics. The test fabric is placed on an oscillating or rotating head that contacts a stationary surface with a specified force. For a typical fabric, the fibers begin to break down at

[†] The toxicity of antimony depends on the chemical form. The CPSC staff ADI is specific for antimony trioxide, which is poorly absorbed. Organic forms of antimony are absorbed better and are more toxic.

about 30,000 cycles (Stevens and Horrocks 2002). No results are available at this time. Therefore, the staff's previous conclusion that additional data are needed on inhalation exposure to AT dusts remains unchanged. This will be reevaluated when additional data become available.

DECABROMODIPHENYL OXIDE

DBDPO (1163-19-5) is generally applied to upholstery fabrics as part of a back-coating that also contains AT. The staff reported previously that DBDPO caused liver and thyroid effects in subchronic and lifetime feeding studies in rodents (Bittner 1999a). Accordingly, the staff concluded that DBDPO is probably toxic in humans, based on sufficient evidence in animals. The staff derived an oral ADI of 3.2 mg/kg-d (Bittner, 2001).

Pharmacokinetics

Since the previous review and update, the staff has identified additional information. A recent paper on the metabolism and disposition of DBDPO (Mörck et al. 2003) reported that absorption of ¹⁴C-labeled compound from the oral route of administration is at least 10% and that 65% of the radioactivity excreted in the feces was metabolites. Since the compound is minimally soluble in standard solvents, it was prepared for this study in a soya phospholipone/lutrol/water medium to improve absorption of the compound compared with previous studies. The relevance of this to human exposure is not known, but overall, the results of this study do not alter the previous staff discussions concerning the limited bioavailability of this compound.

In the staff risk assessment, it was assumed that the oral bioavailability of DBDPO was similar in animals and humans. Therefore, the absolute value, whether 1% or 10%, would not affect the estimated oral exposure.

The staff applied a route-to-route adjustment when calculating the contribution of dermal exposure to the overall hazard index (ratio of the estimated exposure to the ADI) (Babich and Thomas 2001, p. 26). This adjustment was made, because the ADI was based on oral studies. The adjustment involved dividing the average daily dose by the oral bioavailability. A higher oral bioavailability would result in a lower hazard index for dermal exposure, which was estimated to be the primary route of exposure. Therefore, if the oral bioavailability of DBDPO is greater than assumed in the risk assessment, then the staff overestimated the contribution of dermal exposure to the overall hazard. In other words, the overall risk from DBDPO may be lower than previously estimated.

Developmental Toxicity

A recent study investigated the developmental toxicity of DBDPO in Sprague Dawley rats (Hardy et al. 2002). DBDPO doses of 0, 100, 300, or 1,000 mg/kg were administered daily by gavage in corn oil to dams on gestation days 0 through 19. No adverse clinical signs were observed and no effects were seen in maternal body weight or body weight gain. Food consumption was increased modestly, but significantly in the high dose group from gestation days 0-12. No changes were observed in uterine implantation data, except for a statistically

significant increase in early resorptions per dam at the highest dose, although the authors report that the value was within the range of recent historical data for the laboratory. No effects were observed on liver weight. No statistically significant effects were observed on fetal body weights or sex distribution, or in the external, visceral, or skeletal examinations. However, there was a single pup with enlarged ventricles at 100 mg/kg and another pup with extensive cardiac malformations at 1,000 mg/kg. Previous studies reported a fetal NOAEL of 100 mg/kg-d with a DBDPO product that contained 22% nonabromodiphenyl oxide (reviewed in Bittner 2001).

The observation of two pups with cardiac malformations (Hardy et al. 2002) was not statistically significant and this lesion was not reported in previous studies. Therefore, this would not change the previous staff conclusion that DBDPO is a possible reproductive/developmental toxicant in humans, based on limited evidence in animals (Bittner 1999a, 2001). However, even a low incidence of a rare lesion is a potential concern. The staff will closely monitor any new developments in this area of research.

Another study on developmental toxicity measured neurotoxic effects in adult mice following neonatal dosing with DBDPO on postnatal days (PND) 3, 10, or 19 (Viberg et al. 2003a). The compound was administered by gavage in a 20% fat emulsion prepared with egg lecithin, peanut oil, and water to male NMRI mice. Changes in spontaneous behavior tests (locomotion, rearing, and total activity) were observed in 2-, 4-, and 6-month-old mice that had been dosed with 2.22 or 20.1 mg/kg body weight on PND 3, in contrast to mice exposed on PND 10 or 19. Twenty-four hours after dosing with ¹⁴C-labeled compound, most of the radioactivity was detected in the livers of animals exposed on PND 3 or 10, but about 5% of the radioactivity was found in the brain. After seven days, brain radioactivity increased, while liver levels decreased. The animals exposed on PND 19 showed much less radioactivity retained in body tissues at 24 hours and seven days, respectively. The lowest observed adverse effect level (LOAEL) for neurotoxic effects in adult male mice dosed on PND 3 was 2.22 mg/kg.

Similar results were reported with other polybrominated diphenyl oxides (Eriksson et al. 2002; Viberg et al. 2002; Branchi et al. 2002, 2003; Viberg et al. 2003b). Nonetheless, there are a number of limitations of the study with DBDPO (Viberg et al. 2003a) including: relatively small number of animals per treatment group; dosing was done with a fat emulsion; behavioral tests were conducted only once; only one neurobehavioral endpoint was evaluated; and only one species has been studied (reviewed in BFRIP 2003; Birnbaum and Staskal 2004; Eriksson and Viberg 2004; Vijverberg and van den Berg 2004). The significance of these results and their relevance to human health is not clear. Therefore, the staff concludes that DBDPO is a possible developmental neurotoxicant in humans, based on limited evidence in animal studies. However, due to the potential implications of the adverse effects suggested by this study, the staff will closely follow future developments relating to the neurobehavioral effects of the polybrominated diphenyl oxides.

Exposure and Risk

If one were to consider the dose of 2.2 mg/kg in the neurobehavioral study (Viberg et al. 2003a) as a LOAEL, one could calculate a developmental ADI of 2 µg/kg. In the staff risk assessment,

DBDPO exposures were estimated to range from 0.26 to 2.2 $\mu\text{g}/\text{kg}\cdot\text{d}$ (Babich and Thomas 2001, p. 56). Thus, estimated exposures would be at or below the ADI.

No new data are available on the exposure of consumers to DBDPO from upholstered furniture. Scientists in the U.K. are conducting additional work on DBDPO exposure, but no results are available at this time (Stevens and Horrocks 2002). A new risk assessment was conducted for the Brominated Flame Retardant Industry Panel (BFRIP) as part of the EPA's Voluntary Children's Chemical Evaluation Program (VCCEP) (BFRIP 2003). The study concluded that children's exposure to DBDPO from all sources, including upholstered furniture, was at least five-fold less than the reference dose (RfD)[‡] of 4.0 $\text{mg}/\text{kg}\cdot\text{d}$ derived by the NRC (2000).

Since the previous staff review and update, there have been a number of reports on the occurrence of DBDPO and other polybrominated diphenyl oxides in the environment and in animal and human tissues (reviewed in Birnbaum and Staskal 2004). The significance of these findings will be discussed in a separate report (Babich 2004).

There are no new data to change the staff's previous conclusion that the use of DBDPO in upholstered would not present a hazard to consumers. However, the staff will continue to monitor new data that become available, including any new data on exposure, reproductive/developmental toxicity, and developmental neurotoxicity.

HEXABROMOCYCLODODECANE

Hexabromocyclododecane (HBCD) (25637-99-4) is a cyclic aliphatic flame retardant used primarily in thermal insulating polystyrene foam. It is also used in upholstery textiles and, to a minor extent, in audio and video equipment housings. HBCD is generally applied to upholstery fabrics as part of a back-coating that also contains AT.

Previously, the staff concluded that HBCD is not acutely toxic by the dermal, oral or inhalation routes of exposure, as defined in FHSA regulations (Hatlid 1999b; Bittner 2001). There was limited evidence of liver toxicity, reproductive and developmental effects, and neurotoxicity in animals fed HBCD (reviewed in Hatlid, 1999b). HBCD is considered possibly toxic in humans, based on limited evidence in animals. Therefore, the staff concluded that HBCD does not satisfy the supplemental definition of "toxic." This does not necessarily mean that HBCD is safe, only that there was insufficient data to support a finding of toxicity as defined under the FHSA. This conclusion could be changed if additional toxicity data became available. An ADI was not calculated, because HBCD does not satisfy the FHSA definition of toxic. However, the NRC Subcommittee derived a RfD of 0.2 $\text{mg}/\text{kg}\cdot\text{d}$ (NRC 2000, p. 64). The toxicity of HBCD has also been reviewed by BFRIP (2001).

Additional data are reviewed below. New studies include an *in vitro* mutagenicity study, a contact sensitivity study, and a subchronic 90 day oral study. After careful review of these additional materials, the staff's conclusions regarding the overall toxicity of HBCD remains unchanged.

[‡] The RfD is roughly equivalent to an ADI. Both are estimates of the amount of a chemical a person can be exposed to on a daily basis over an extended period of time (up to a lifetime) with a negligible risk of adverse health effects.

Dermal Effects

Previously, the staff concluded that HBCD exposure resulted in either negative or mild irritation in several studies (Hattelid 1999b). In a recent study sponsored by the American Chemistry Council (ACC), CBA/J mice were subjected to a local lymph node assay to determine the potential for contact sensitization of HBCD (Woolhiser and Anderson 2003). Solutions of 2%, 20%, or 50% HBCD were applied to the dorsal surface of the ear for 3 days. Uptake of ³H-thymidine into the auricular lymph nodes was measured, and sensitivity index was determined. There was a slight irritation and minor increase in ear thickness after 20% and 50% HBCD. However, there were no changes in the sensitivity index, supporting the conclusion that HBCD does not possess the potential for dermal sensitization.

Systemic Toxicity

The ACC sponsored a 90-day oral gavage toxicity study of HBCD in CrI:CD(SD) IGS BR rats (Chengelis 2002). HBCD in corn oil was administered to rats at 0, 100, 300, and 1000 mg/kg-d for 90 days. There were a total of 15 rats/sex/dose group. Ten rats from each sex/dose group were sacrificed following the 90-day exposure period, while 5 rats from each group were allowed to recover for 28 days following exposure to HBCD, and then sacrificed.

During the course of the study there were no mortalities and clinical signs were within normal range or were judged not related to the test article. There were no dose-related changes in body weight, food consumption, functional observational battery, locomotor activity, estrus cycle, sperm, or in the ophthalmic exam. HBCD reached steady state levels after 27 days in adipose tissue in the high dose group. The levels declined during the recovery period. HBCD consists of three stereoisomers (α, β, γ) with relative abundance $\gamma \gg \alpha > \beta$. Interestingly, the relative abundance in adipose tissue was $\alpha \gg \gamma > \beta$. It is unknown whether this is due to preferential absorption, metabolism, or a chemical process.

The authors reported minimal hepatocellular vacuolation in roughly 50% of male and female rats at 100, 300, and 1000 mg/kg-d, and mild to moderate vacuolation in females only at 300 and 1000 mg/kg-d (Table 2). There was also a statistically significant increase in liver weight in male and females at all dose levels. The authors suggested that induction of microsomal enzymes was responsible for this increase in liver weight, as histological changes and clinical chemistry did not support liver damage (discussed below). Following the 28-day recovery period, the increased liver weight was largely reversed in the low and mid dose groups and in the high dose males, but were only partially reversed in the high dose females. The incidence and severity of liver vacuolation declined in the recovery group, accompanied by increased incidence in the controls (Table 2).

At 90 days there were statistically significant changes in serum chemistry including an increase in total protein, albumin, globulin, chloride, and gamma glutamyltransferase. These changes may be indicative of effects in the liver (total protein, albumin, globulin, gamma glutamyltransferase) or kidney (chloride). These changes were not great enough to be considered adverse; these parameters returned to normal levels by the end of the recovery period.

Thyroxine (T₄) levels were decreased in a dose-dependent manner. The maximum effect was a 20% decrease at the high dose. However, this effect was largely reversible, as the thyroxine levels were not significantly different from the control levels following the recovery period. There were no changes in thyroid stimulating hormone (TSH) or 3,5,3'-triiodothyronine (T₃).

Table 2. Incidence of selected lesions in rats exposed to HBCD for 90 days (Chengelis 2002)

Dose, mg/kg-d	0		100		300		1,000	
Sex	M	F	M	F	M	F	M	F
13 WEEKS								
Number examined	10	10	10	10	10	10	9	10
LIVER								
Hepatocellular vacuolation	2	3	6	6	5	5	6	9
Minimal	1	3	5	6	4	3	5	5
Mild	1	0	1	0	1	1	1	2
Moderate	0	0	0	0	0	1	0	2
Hepatocellular hypertrophy	0	0	0	0	0	0	0	5
Minimal	0	0	0	0	0	0	0	2
Mild	0	0	0	0	0	0	0	3
THYROID								
Follicular cell hypertrophy	1	0	1	0	5	4	8	7
Minimal	1	0	1	0	5	4	7	3
Mild	0	0	0	0	0	0	1	4
17 WEEKS --Recovery group								
Number examined	5	5	5	5	5	5	5	5
LIVER								
Hepatocellular vacuolation	3	0	0	0	2	1	1	2
Minimal	3	0	0	0	2	1	1	1
Mild	0	0	0	0	0	0	0	1
THYROID								
Follicular cell hypertrophy	2	0	0	0	3	0	3	3
Minimal	2	0	0	0	3	0	3	3

There was minimal thyroid follicular cell hypertrophy in all male dose groups and only the 300 and 1000 mg/kg/day female dose groups. Mild thyroid follicular cell hypertrophy was noted in the high dose female group. There was not a significant increase in thyroid weight. The incidence and severity of follicular cell hypertrophy declined in the recovery group, accompanied by increased incidence in the controls (Table 2). There was an increase in prostate weight in the high dose male group, which was reversible. However, there were no changes in prostate histology or sperm production.

In an amendment to this study, additional gross pathology performed on the kidneys showed irregularities, specifically depressions in the renal cortex, after 90 days of treatment with HBCD. These occurred in one control female and two high dose females and were described as "pinpoint depressions in the renal cortex." Histopathology showed normal tissue in the depressions, with

the following general observations not related to the depressed areas. In the control group, basophilic tubules, papillary tubule mineralization, and subacute inflammation were noted at grade 1.[§] In the high dose animals, focal and diffuse subacute inflammation, and pelvic mineralization were noted at grade 1. The renal cortex depressions do not seem to follow a dose response, nor are there supportive histopathological findings. After the recovery period, depressed areas in the renal cortex were observed in one control male and one high dose male, however, histopathology was not performed in this case.

Gross lesions were noted in the lung and described as “dark red areas.” These occurred in one control male and one high dose male at 90 days. Also, after the recovery period, the gross lung lesions were noted in two control males, one mid dose male, and one high dose male. The authors reported that the dark red areas appeared normal on histopathological examination. Other observations included vascular mineralization and alveolar histiocytosis, both at grade 1.

Genotoxicity

Previously reported *in vitro* mutagenic studies and an 18-month oral carcinogenicity study in mice have produced negative results in response to HBCD (reviewed in Hatlelid 1999, Bittner 2001). A recent study tested the ability of HBCD to induce intragenic recombination in Sp5 and SPD8 hamster cell lines that carry two incomplete hypoxanthine guanine phosphoribosyl-transferase (HPRT) genes (Helleday et al. 1999). Treatment of Sp5 cells with HBCD at concentrations of 0, 2, 5, 10, 15, or 20 µg/mL resulted in 1.0-, 1.0-, 0.8-, 1.1-, 1.4-, and 2.2-fold increases in reversion frequency, respectively. Treatment of SPD8 cells with concentrations of 0, 3, 6, 10, 15 and 20 µg/mL HBCD resulted in reversion frequencies of 1.0-, 0.7-, 0.8-, 0.9-, 1.4-, and 1.9-fold over background. Statistically significant differences in reversion from control levels occurred at 20 µg/mL in both hamster lines.

The report that HBCD induced reversions in mammalian cells suggests that HBCD may be capable of inducing point mutations. However, the effect was relatively small, roughly 2-fold at the highest dose tested. Because this assay is not part of any standard battery of genotoxicity tests, it is difficult to know the reliability of the assay in determining the genotoxic potential of a chemical. The staff concludes that data on the genotoxicity of HBCD are inconclusive. The results do not change the staff's previous conclusion that there are inadequate data for the carcinogenicity of HBCD.

Exposure and Risk

The findings from the subchronic study (Chengelis 2002) include relatively minor effects in the liver (minimal to mild vacuolation and increased liver weight) and thyroid (minimal to mild follicular cell hypertrophy, decrease in serum thyroxine). While some effects were noted at the mid- and low doses, effects were most pronounced at the high dose. In recovery group animals, these effects generally were not significantly different from the controls; however, the incidences and/or severities of these effects did not always return to control levels at the high dose. It is debatable whether the effects at the high dose are truly adverse. The authors suggested that the high dose (1,000 mg/kg-d) should be considered a NOAEL. The staff concludes that these data

[§] Grade 1 generally means low severity, on a scale of 1 to 5.

support, but do not change, their previous conclusion that HBCD is a “possible systemic toxicant”. If the middle dose (300 mg/kg-d) were considered the NOAEL, one could derive an ADI of 3 mg/kg-d, which is greater than the RfD of 0.2 mg/kg-d derived by the NRC (2001). Therefore, this study does not change the overall conclusions in the staff risk assessment (Babich and Thomas 2001). No new data on HBCD exposure from upholstered furniture are available at this time.

PYROVATEX®

PA (20120-33-6) is a reactive flame retardant that is covalently bound to cotton fibers and/or durable press resins. Previously, the staff concluded that there was inadequate evidence of toxicity in animals fed PA for up to 21 days (Bittner 1999b). Thus, PA does not satisfy the FHSA definition of toxic. However, the database on PA is very limited. There was insufficient information to derive an ADI or RfD. No new data relating to toxicity or exposure were identified for PA. Therefore, the previous conclusion remains unchanged. This conclusion could change if additional toxicity data becomes available.

THPC

In the previous review, the staff concluded that there was sufficient evidence of liver toxicity and neurotoxicity in animals exposed to THPC (124-64-1) (reviewed in Bittner 1999c). Thus, the staff considers that THPC may be regarded as probably toxic in humans based on sufficient evidence in animals, as defined in the supplemental definition of “toxic.” In addition, the staff concluded that THPC is a possible developmental toxicant in humans, based on limited evidence in animal studies. THPC is also acutely toxic. The CPSC staff derived an oral ADI of 0.0027 mg/kg-d (Bittner 2001).

THPC is generally applied as a mixture of THPC and THPC-urea (Figure 1), which react to form a polymer (THPC-NH₃) (27104-30-9) within cotton fibers (discussed in Babich and Thomas 2001). Thus, THPC was not detected in extracts of THPC-treated fabrics (Cobb 2000). However, unidentified organic phosphorus compounds were present in aqueous extracts of THPC-treated fabrics. Therefore, the staff concluded that additional information on the identity and toxicity of the compounds migrating from THPC-treated fabric would be needed to determine whether these fabrics could present a hazard to consumers (Babich and Thomas 2001). No new toxicity or exposure data were identified since the previous staff review. Therefore, the staff’s conclusion remains unchanged.

CONCLUSIONS

In 2001, the CPSC staff completed a risk assessment on the use of AT, DBDPO, HBCD, PA, and THPC polymer in upholstery fabric (Babich and Thomas 2001). The staff concluded that DBDPO, HBCD, and PA were not likely to present a hazard to consumers, based on the FHSA supplemental definition of toxic and the CPSC chronic hazard guidelines. The conclusion for PA is based on limited data. The staff also concluded that additional information on AT and THPC polymer was needed. For AT, data on the release of airborne AT particles are needed. For THPC, information on the identity and toxicity of organophosphorus compounds released

from treated fabrics is needed. This report reviewed additional information that became available since 2001. The new information, discussed above, does not change any of the overall conclusions of the previous staff risk assessment (Table 3). However, the staff recommends that scientific developments in the following areas be monitored closely:

1. Studies on the release of airborne AT particles from treated fabric (Stevens and Horrocks 2002). These studies may provide sufficient information to determine whether AT is likely to be hazardous to consumers.
2. Studies on the possible developmental neurotoxicity of DBDPO and related compounds, and its relevance to humans (Viberg et al. 2003a,b).
3. Studies on the possible reproductive/developmental toxicity of DBDPO (Hardy et al. 2002).
4. Studies on the possible subchronic or chronic toxicity study of HBCD, including effects on the liver and thyroid (Chengelis 2002).
5. Occurrence of DBDPO and HBCD in the environment and in human tissue (Birnbaum and Staskal 2004).

Table 3. Potential Chronic Hazards Associated with Flame Retardant Chemicals in Upholstery Fabric^a

FR Chemical	"Toxic" ^b	"Hazardous" ^b
Antimony trioxide (AT)	Yes	Insufficient data
Decabromodiphenyl oxide (DBDPO)	Yes	No
Hexabromocyclododecane (HBCD)	Possibly	No
Phosphonic acid, (3-[[hydroxymethyl]amino]-3-oxopropyl)-, dimethyl ester (PA)	No (based on limited data)	No
Tetrakis (hydroxymethyl) phosphonium chloride (THPC) polymer	Yes	Insufficient data

^a Babich and Thomas 2001.

^b As defined by the FHSA and CPSC chronic hazard guidelines (CPSC 1992).

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UNITED STATES
CONSUMER PRODUCT SAFETY COMMISSION
WASHINGTON, DC 20207

Memorandum

Date: September 1, 2004

TO : Dale Ray, Project Manager for Upholstered Furniture
Directorate for Economic Analysis

THROUGH: Mary Ann Danello, Ph.D., Associate Executive Director for Health Sciences *maD*
Lori E. Saltzman, M.S., Director, Division of Health Sciences *W*

FROM : Michael A. Babich, Ph.D., Chemist, Division of Health Sciences *MAB*

SUBJECT : Brominated Flame Retardant Chemicals

INTRODUCTION

Brominated flame retardant chemicals (BFR's) are a structurally diverse group of chemicals added to plastics, textiles, and other materials to decrease their propensity for ignition and combustion (reviewed in Birnbaum and Staskal 2004). The only feature common to all BFR's is the presence of bromine in the molecular formula. BFR's comprise roughly 25% of the world consumption of flame retardant (FR) chemicals (Hardy 2002). They are used in large quantities because they are efficacious and relatively inexpensive (WHO 1997). The use of BFR's in televisions and other appliances is reported to prevent thousands of fires and save over one-hundred lives each year in the U.S. and Europe (Clarke 1997; Stevens 1998; Simonson et al. 2002; Smith and Mah 2002). However, the detection of certain BFR's in the environment, as well as in human and animal tissues, has led to concerns about the potential environmental and human health effects of all BFR's (reviewed in Alaei and Wenning 2002; McDonald 2002; Birnbaum and Staskal 2004; Gill et al. 2004).

While there are many BFR's, the most significant ones are tetrabromobisphenol A (TBBPA), hexabromocyclododecane (HBCD), and the polybrominated diphenyl oxides (PBDPO's) (WHO 1997). The most widely used BFR worldwide is TBBPA, which is primarily used as a reactive flame retardant (FR) in printed circuit boards and, to a lesser extent, as an additive FR in acrylonitrile-butadiene-styrene (ABS) resin for use in electronic equipment (WHO 1997; Birnbaum 2004). A reactive FR can be incorporated into the chemical structure of a polymer, whereas an additive FR is only mixed with the molten polymer or applied to the surface of a textile. TBBPA is not a candidate for use in upholstery fabric or foam. HBCD is an additive FR used primarily in polystyrene foam and is also used to back-coat textiles (WHO 1997). The PBDPO's* are a family of BFR's that includes decabromodiphenyl oxide (DBDPO or deca-BDPO), octabromodiphenyl oxide (octa-BDPO), and pentabromodiphenyl oxide (penta-BDPO) (WHO 1997). DBDPO, the most important PBDPO and most common BFR in the U.S., is primarily used in high-impact polystyrene (HIPS) used in housings for televisions and other

* Also known as polybrominated diphenyl ethers (PBDE's).

electronic equipment. The use of DBDPO to back-coat textiles is a relatively minor, but important application (Hardy 2002). Approximately 80% of worldwide DBDPO production goes into plastics, with the remainder used in textiles (BFRIP 2001). Octa-BDPO is a mixture that includes hexa- through nona- congeners* and is a relatively minor product used in electronics equipment made from ABS plastic (Table 1). Penta-BDPO is a viscous liquid composed of tetra- through hexa- congeners that has been used in polyurethane foam, but is being replaced by other FR's. Ninety-five percent of total penta-BDPO production has been used in North America.

POLYBROMINATED DIPHENYL OXIDES (PBDPO's)

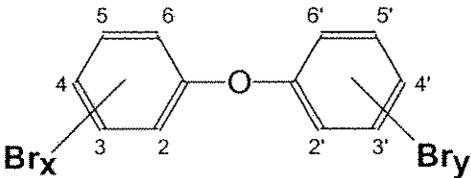
The toxicology of the PBDPO's has been reviewed by several authors (NRC 2000; ECB 2000, 2002, 2003; Hardy 2002; McDonald 2002; BFRIP 2003; Great Lakes 2003a,b; Birnbaum and Staskal 2004; Gill et al. 2004). The CPSC staff has only reviewed the toxicology of DBDPO. Generally the toxicity of the PBDPO's declines as the level of bromination increases (Hardy 2002). DBDPO is the most studied of the three commercial products. For example, DBDPO has been studied in 2-year bioassays in mice and rats, whereas penta- and octa-BDPO have only been studied for 90 days in rats. Common target organs in chronic and subchronic studies include the liver and thyroid. In addition, the PBDPO's are reported to be active in developmental neurotoxicity (Branchi et al. 2002, 2003; Eriksson et al. 2002; Viberg et al. 2002, 2003a,b; Gilbert et al. 2004) and endocrine disruption (antiandrogenic) (Stoker et al. 2004a,b) assays.

Concern regarding the PBDPO's stems primarily from the observation that the lower brominated congeners, especially penta-BDPO, tend to persist in the environment and to bioaccumulate (Alaee and Wenning 2002; McDonald 2002; Birnbaum and Staskal 2004). PBDPO congeners are ubiquitous environmental contaminants (Hale et al. 2003). They have been detected in biota (fish, aquatic mammals, and birds); the environment (lake and river sediments, food, and indoor dust samples); waste streams (sewage sludge); and human tissue (blood and breast milk) (Sjödin et al. 1999, 2001a, 2001b, 2003, 2004; Hale et al. 2001, 2003; Guvenius et al. 2003; Mazdai et al. 2003; Schecter et al. 2003). Furthermore, total PBDPO in human serum is increasing in Americans, while decreasing in Europeans (Sjödin et al. 2004). Some studies have reported higher PBDPO levels in certain occupations, including computer recycling and computer technicians (Sjödin et al. 1999, 2001b). Most human exposure is believed to be from food, especially fish (Sjödin et al. 2004). The most common congeners in environmental samples are BDPO-47 and BDPO-99. DBDPO (BDPO-209), which is less bioaccumulative, is generally detected less frequently and at lower levels than the more common congeners.

Recently, PBDPO's were reported in farmed salmon obtained in Europe and the Americas, and wild Pacific salmon (Hites et al. 2004). Total PBDPO's were greater in farmed salmon, which the authors attributed to the feed, which had PBDPO levels equal to or greater than the levels in salmon. DBDPO was not detected in salmon, but was found in feed at relatively high levels. As with most environmental samples, BDPO-47 was the most common congener found. Congener profiles were similar, regardless of the source. This report is of concern, because most salmon consumed in the U.S. is farmed and consumption of salmon has increased significantly due to reported health benefits related to the presence of omega-3 fatty acids.

* A congener is a geometric isomer with a specific bromine substitution pattern.

Table 1. Principal PBDPO Congeners in Commercial Flame Retardants

Commercial Mixture	Number of Bromines	Chemical Name	Congener Number ^a	Weight percent
Penta-BDPO ^b	4	2,2',4,4'-tetra-BDPO	47	28%
	5	2,2',4,4',5-penta-BDPO	99	43%
	5	2,2',4,4',6-penta-BDPO	100	8%
	6	2,2',4,4',5,5'-hexa-BDPO	153	6%
	6	2,2',4,4',5,6'-hexa-BDPO	154	4%
Octa-BDPO ^c	7	2,2',3,4,4',5',6-hepta-BDPO	183	NR
	8	2,2',3,4,4',5,5',6-octa-BDPO	203	NR
Deca-BDPO ^d	10	2,2',3,3',4,4',5,5',6,6'-deca-BDPO	209	~97%
PBDPO basic structure: 				

^a PBDPO congeners are identified by the International Union of Pure and Applied Chemistry (IUPAC) system developed for polychlorinated biphenyls (PCB's).

^b Commercial penta-BDPO is composed of 24-to-38% tetra-BDPO congeners, 50-to-60% penta-BDPO, and 4-to-8% hexa-BDPO. The primary congeners are 99 and 47 (Great Lakes 2003b).

^c Commercial octa-BDPO is composed of roughly 45% hepta-BDPO congeners, 30% octa-BDPO, 10% hexa-BDPO, 10% nona-BDPO, <2% DBDPO, and <2% penta-BDPO (Great Lakes 2003a). NR, not reported.

^d Commercial DBDPO is comprised of ~97% decabromodiphenyl oxide (209), with the remainder being nona- and octa-BDPO's (BFRIP 2003).

There are many questions regarding the occurrence of PBDPO's in environmental and biological samples. For example, the congener profiles from various sources—sediment, animals, and sludge—differ from each other as well as from the commercial products (Birnbaum and Staskal 2004). This may reflect differences in transport and bioaccumulation. However, it may also be due to conversion of higher congeners to lower ones by chemical or biological processes (Gill et al. 2004). The pathways by which PBDPO's enter the environment, are transported, and lead to human exposure are uncertain. For example, the relative importance of manufacturing processes and disposal of finished products is unknown (Alaee and Wenning 2002; McDonald 2002; Birnbaum and Staskal 2004; Gill et al. 2004).

Laboratory studies have shown that PBDPO's may volatilize from FR-treated polyurethane foam (FR-PUF), which may be a significant source of indoor PBDPO's (Wilford et al. 2003). Recently, investigators reported a study of residential air and dust samples in Massachusetts (Rudel et al. 2003). Penta-BDPO congeners were detected in the dust samples in 20% to 53% of

the homes sampled, but not in air, at levels on the order of part-per-million. However, most residential furniture in the U.S. does not require FR treatment, and much of the total PBDPO production is used in hard plastics (see above). Thus, the sources of penta-BDPO congeners in residential air and dust samples are unknown.

Disposal of FR-PUF in landfills may also be a significant source of environmental contamination. PBDPO's may volatilize or leach from FR-PUF (Wilford et al. 2003). FR-PUF exposed to outdoor conditions may disintegrate and release PBDPO's (Hale et al. 2002). In addition, particles of foam may be consumed by insects that are subsequently consumed by other fauna (Hale et al. 2002). Land application of sewage sludge may also be a significant source of environmental contamination by PBDPO's (Hale et al. 2001).

The European Union (EU) concluded that the risk to consumers from direct exposure to penta-BDPO in upholstery foam is negligible (ECB 2000). Nonetheless, the use of the penta- and octa-BDPO's is being discontinued, due to concerns about their presence in the environment and biota. The EU has banned the use of penta- and octa-BDPO by August 2004 (EU 2003). However, penta-BDPO is not produced in Europe and very little is used there. Octa-BDPO is a relatively minor product. The sole U.S. manufacturer of penta-BDDPO announced that it is discontinuing production of penta-BDPO and octa-BDPO in 2004 (EPA 2003). The California legislature has banned penta-BDPO and octa-BDPO effective in January 2008 (State of California 2003).

DECABROMODIPHENYL OXIDE (DBDPO)

The toxicology of DBDPO has been reviewed elsewhere (Bittner 1999, 2001; NRC 2000; Bittner et al. 2001; Hardy 2002; BFRIP 2003; Babich et al. 2004). DBDPO was found to cause liver and thyroid effects in subchronic and lifetime feeding studies in rodents (NTP 1986). Thus, the CPSC staff concluded that DBDPO is probably toxic in humans based on sufficient evidence in animals, as defined in the CPSC chronic hazard guidelines (CPSC 1992) and supplemental definition of "toxic." 16 CFR §1500.3 (c)(2)(ii). The CPSC staff derived an oral acceptable daily intake (ADI) of 3.2 mg/kg-d (Bittner, 2001). Based on the available information, both the CPSC staff (Babich and Thomas 2001; Babich et al. 2004) and the National Research Council (NRC 2000) concluded that the use of DBDPO in upholstered furniture cover fabrics is not likely to present a hazard to consumers. The EU concluded that consumer exposure to DBDPO is likely to be negligible (ECB 2002). The EU is continuing to assess the potential environmental effects of DBDPO (EBFRIP 2004a).

In comparison to the other PBDPO's, DBDPO is poorly absorbed and less toxic (Hardy 2002). It is not considered to be bioaccumulative, although it is persistent (ECB 2002; Birnbaum 2003; Birnbaum and Staskal 2004; Gill et al. 2004). Due to its low solubility and volatility, DBDPO in the environment is likely to be bound to soil, sediment, or sludge (Hardy 2002; Hale et al. 2003). While DBDPO has been reported in the environment and human tissue, it is generally found less frequently and at lower levels than other PBDPO's (Hale et al. 2003; Sjödin et al. 2003). DBDPO is rarely detected in outdoor air and in wildlife. It was found at 19 to 36 µg/kg (parts-per-billion, ppb) in lake sediment near a PBDE research facility and at levels ranging from 85 to 4890 µg/kg in sewage sludge (Hale et al. 2003).

DBDPO was present in blood serum from U.S. donors at levels ranging from non-detectable (<1) to 35 picomoles per gram of lipid (or 34 nanograms per gram of lipid, ng/g) (Sjödin et al. 2001b). In Sweden, workers who dismantled old electronics equipment for recycling had higher levels (median = 4.8 ng/g) in their blood than other workers (median <0.7 ng/g) (Sjödin et al. 1999). In both studies, levels of BDPO-47 were slightly greater than those of DBDPO (BDPO-209). Particle-bound and semi-volatile (particulate plus vapor phase) DBDPO was detected in the indoor air of an electronics recycling plant, near a dismantling ball (12 to 70 mg/m³) and shredder (150 to 200 ng/m³) (Sjödin et al. 2001a). Levels were lower in other work environments, including electronics assembly and repair facilities and an office with computers (≤ 0.1 ng/m³).

New data published following the CPSC staff and NRC reports have raised two issues regarding DBDPO toxicity and environmental effects (ECB 2002; Birnbaum 2003; Birnbaum and Staskal 2004; Gill et al. 2004):

1. Can DBDPO in the environment break down or be metabolized to other, more toxic congeners?
2. Is DBDPO a developmental neurotoxicant?

Debromination of DBDPO

DBDPO is comparatively less toxic and bioaccumulative than other PBDPO's. However, if DBDPO could be converted to lower brominated congeners (e.g., tetra- and penta-BDPO's) in the environment by chemical or biological processes, then DBDPO could contribute to the overall burden of PBDPO's in the environment (Birnbaum 2003; Birnbaum and Staskal 2004). DBDPO is known to degrade when dissolved in an organic solvent and exposed to UV light. However, this does not represent typical environmental conditions.

Soderstrom et al. (2004) studied the photolytic decomposition of DBDPO under a variety of conditions—either dissolved in toluene or adsorbed to a solid matrix, including silica gel, sand, sediment, and soil. Water was added to the sediment; other solid matrices were dry. DBDPO degraded rapidly in toluene or on silica gel, with half-lives less than 15 minutes. The degradation rate decreased in the order sand > sediment > soil. The half-lives for sand, sediment, and soil were 12, 40-60, and 150-200 hours, respectively. These results were obtained in laboratory studies. Outdoor studies conducted by the authors suggest that environmental decomposition rates are lower and vary greatly, depending on the intensity of natural sunlight for a given location and season.

There were many degradation products, including nona- and octa-BDPO's, a number of lower brominated congeners, and numerous unidentified products. The most common congeners found in environmental samples—congeners 47 and 99—were found only in toluene or on silica gel and then only in small amounts. Because photodegradation of DBDPO does not produce the most common congeners, the CPSC staff concludes that it is uncertain whether this process could contribute significantly to the presence of tetra- and penta-BDPO's in the environment.

Stapleton et al. (2004) exposed juvenile carp to radiolabeled DBDPO in food pellets for 60 days. Although DBDPO was not detected in fish tissues, several penta- through octa-BPDO's were identified. It was not clear whether the transformation of DBDPO occurred by chemical or enzymatic processes. However, the most common congeners found in environmental samples—BDPO 47 and BDPO 99—were not identified. Therefore, the CPSC staff concludes that it is uncertain whether metabolism of DBDPO by fish may contribute to the presence of lower brominated BDPO's in the environment.

In early studies in rats, less than 1% of radiolabeled DBDPO was absorbed when administered in feed or by gavage (reviewed in Bittner 1999a). Most of the absorbed material was concentrated in the liver. Although little DBDPO was absorbed, it appeared that most of the absorbed dose was metabolized and excreted in the bile (NTP 1986). In a more recent study, investigators used a soya phospholipone/lutrol/water medium to improve the absorption of DBDPO (Mörck et al. 2003). When this mixture was administered to rats by gavage, at least 10% of ¹⁴C-labeled DBDPO was absorbed and 65% of the radioactivity excreted in the feces was in the form of metabolites. Metabolites are believed to include methoxy-hydroxylated diphenyl oxides, possibly guaiacols, containing 5 to 8 bromines. Some of the radioactivity found in the tissues was not extractable and, therefore, was probably bound to macromolecules. This suggests the presence of chemically reactive intermediates.

The rat study by Mörck et al. (2003) provides additional evidence that DBDPO can be absorbed and metabolized in animals. Thus, DBDPO may not be as biologically “inert” as previously believed (Hardy 2002). This also tends to support the possibility that other animal species in the environment could contribute to the transformation of DBDPO to less-brominated, more-toxic compounds.

Developmental Neurotoxicity

DBDPO has been reported to induce neurobehavioral effects in adult mice that were exposed on postnatal days (PND) 3, 10, or 19 (Viberg et al. 2003a). The compound was administered by gavage in a 20% fat emulsion prepared with egg lecithin, peanut oil, and water to male NMRI mice. Changes in spontaneous behavior tests (locomotion, rearing, and total activity) were observed in 2-, 4-, and 6-month-old mice that had been dosed with 2.22 or 20.1 mg/kg body weight on PND 3, in contrast to mice exposed on PND 10 or 19. Twenty-four hours after dosing with ¹⁴C-labeled compound, most of the radioactivity was detected in the livers of animals exposed on PND 3 or 10, but about 5% of the radioactivity was found in the brain. After seven days, brain radioactivity increased, while liver levels decreased. The animals exposed on PND 19 showed much less radioactivity retained in body tissues at 24 hours and seven days, respectively. The lowest observed adverse effect level (LOAEL) for neurotoxic effects in adult male mice dosed on PND 3 was 2.22 mg/kg.

Similar results have been reported with other polybrominated diphenyl oxides (Eriksson et al. 2002; Viberg et al. 2002a; Branchi et al. 2002, 2003; Viberg et al. 2003b). Nonetheless, there are a number of limitations of the study with DBDPO (Viberg et al. 2003a) including: relatively small number of animals per treatment group; dosing was done with a fat emulsion; behavioral tests were conducted only once; only one neurobehavioral endpoint was evaluated; and only one

species has been studied (reviewed in BFRIP 2003; Birnbaum and Staskal 2004; Eriksson and Viberg 2004; Vijverberg and van den Berg 2004). The significance of these results and their relevance to human health is not clear. Therefore, the CPSC staff concluded that DBDPO is a possible developmental neurotoxicant in humans, based on limited evidence in animal studies (Babich et al. 2004).

HEXABROMOCYCLODODECANE (HBCD)

The health effects of HBCD have been reviewed by the CPSC staff (Hattelid 1999; Bittner 2001; Bittner et al. 2001; Babich et al. 2004) and others (NRC 2000; BFRIP 2001; Birnbaum and Staskal 2004). The CPSC staff has concluded that there is limited evidence of liver toxicity, reproductive and developmental effects, and neurotoxicity in animals fed HBCD, as described in the CPSC chronic hazard guidelines (Hattelid 1999; Bittner 2001; Bittner et al. 2001; Babich et al. 2004). HBCD may be considered possibly toxic in humans, based on limited evidence in animals. Therefore, the staff concludes that HBCD does not satisfy the supplemental definition of "toxic." This does not necessarily mean that HBCD is safe, only that there was insufficient data to support a finding of toxicity as defined under the FHSA. This conclusion could be changed if additional toxicity data became available. An ADI was not calculated, because HBCD does not satisfy the FHSA definition of toxic.

HBCD is a relatively minor BFR, although it is used more in Europe than in North America (Birnbaum and Staskal 2004). The presence of HBCD in the environment is of concern principally because it is relatively persistent and has a strong tendency to bioaccumulate (reviewed in BFRIP 2001; Birnbaum and Staskal 2004). HBCD has been reported to be present in human milk at a median level of 1.3 µg/kg lipid (parts-per-billion) and ranging from non-detectable to 126 µg/kg (Ryan and Patry 2002).

Commercial HBCD is comprised of three stereoisomers— α -, β -, and γ -HBCD (BFRIP 2001). γ -HBCD is the primary component in the commercial product and in sediment, typically accounting for 80% or more of the mixture. However, α -HBCD is generally the predominant isomer present in animal tissues, and the three isomers are present in roughly equal levels in sewage sludge (Birnbaum and Staskal 2004). These differences in stereoisomer ratios may reflect selective uptake and/or bioconcentration of α -HBCD. They may also be due to chemical transformation in the environment or metabolism by the exposed animals. Differences in the effects of the three stereoisomers on human or ecological toxicity, if any, are unknown.

A recent report suggests that neonatal exposure of mice to HBCD may induce changes in spontaneous behavior in mature animals, similar to the effects reported for PBDPO's (Ericksson et al. 2002). HBCD is also reported to have neurotoxic effects *in vitro* (Mariussen and Fonnum 2002; Reistad et al. 2002). The EU is currently in the process of performing a risk assessment for HBCD (EBFRIP 2004b).

DISCUSSION

Concerns have been raised regarding certain BFR's, because they persist in the environment and accumulate in animal and human tissues. The potential environmental and human health effects of BFR's have been under study in Europe and the U.S. The European Union has, or is in the process of, performing comprehensive risk assessments for several BFR's, including penta-BDPO, octa-BDPO, DBDPO, and HBCD. The comprehensive risk assessments include consumer, occupational, and environmental exposures. The U.S. EPA is also reviewing the same BFR's through its High Production Volume (HPV) Challenge and Voluntary Children's Chemical Evaluation Program (VCCEP). The HPV Challenge includes consumer, occupational, and environmental exposures, whereas the VCCEP focuses on risks to children. In addition, the EPA's Office of Research and Development (ORD) is conducting or sponsoring research on the environmental and human health effects of BFR's. The EPA staff has formed an interagency working group on BFR's, in which the CPSC staff participates, to identify and prioritize research needs and share information and resources. The EPA staff is also working with CPSC staff to develop a possible Significant New Use Rule (SNUR) for FR chemicals used in upholstered furniture. The SNUR process addresses consumer, occupational, and environmental risks. The SNUR could be used to obtain additional toxicity or exposure data where needed. All of these activities will help to ensure that the FR chemicals used in upholstered furniture are not harmful to consumers, workers, or the environment. The status of selected BFR's is summarized below.

Penta-BDPO

Penta-BDPO has been used in upholstery foam, primarily to comply with flammability requirements in the State of California. Most upholstered furniture sold in the U.S. is not FR-treated. Penta-BDPO has never been a candidate for treating upholstery cover fabrics to comply with the CPSC staff draft standard. The CPSC staff has not reviewed the potential risks to consumers from exposure to penta-BDPO in upholstered furniture fabric or foam. However, the EU concluded that penta-BDPO in upholstery foam does not present a hazard to consumers (ECB 2000). The EU and the State of California banned the use of penta-BDPO, because it persists in the environment and accumulates in animal and ultimately in human tissue. The only U.S. producer announced that it will cease production of penta-BDPO in 2004.

Octa-BDPO

Octa-BDPO is a relatively minor BFR that is used in electronics equipment. It is not used in upholstery foam and is not a candidate for use in upholstery cover fabrics. The only remaining U.S. producer has voluntarily ceased production of octa-BDPO. The use of octa-BDPO has been banned by the EU and the State of California for the same reasons that they banned penta-BDPO.

DBDPO

DBDPO is an important FR that is used in primarily electronics equipment, such as televisions and computers. The use of DBDPO in televisions and other appliances is reported to save many lives in North America and Europe each year. DBDPO is also the primary FR used to treat upholstery fabric in the U.K. If the CPSC staff draft standard is enacted, DBDPO would

probably be the FR chemical of choice for upholstered furniture fabrics in the U.S. as well. In comparison to the other PBDPO's, DBDPO is less toxic, poorly absorbed, and does not bioaccumulate. The CPSC staff (Babich and Thomas 2001), the NRC (2000), and EU (ECB 2002) have concluded that direct exposure to DBDPO in upholstery fabrics is not likely to present a hazard to consumers.

Two questions regarding DBDPO remain (Birnbaum 2003). The first is whether DBDPO in the environment can be broken down to lower, more toxic congeners (e.g., penta- or octa-BDPO) by chemical or metabolic processes. Laboratory studies suggest that this may occur to some degree, but there is no evidence that this occurs to a significant degree in nature (Birnbaum and Staskal 2004). New data also suggest that the metabolism of DBDPO may be more extensive than previously believed (Mörck et al. 2003), raising the possibility that animal species could metabolize environmental DBDPO to lower, more toxic congeners. The second question is whether DBDPO is a developmental neurotoxicant. Three-day-old mice exposed to DBDPO exhibited changes in spontaneous behavior as they matured (Viberg et al. 2003a). The relevance of this type of study to humans is unknown. In addition, there are a number of limitations of the study with DBDPO (Viberg et al. 2003a) including: relatively small number of animals per treatment group; dosing was done with a fat emulsion; behavioral tests were conducted only once; only one neurobehavioral endpoint was evaluated; and only one species has been studied (reviewed in BFRIP 2003; Birnbaum and Staskal 2004; Eriksson and Viberg 2004; Vijverberg and van den Berg 2004). Therefore, the staff concludes that additional data are needed to address both questions. The U.S. EPA (BFRIP 2003) and EU (EBFRIP 2004a) continue to study this chemical. While there are questions regarding the potential human health and environmental effects of DBDPO, there does not appear to be strong evidence at this time to support a ban of DBDPO (EBFRIP 2004a).

HBCD

The primary application of HBCD is in polystyrene foam used for building insulation. HBCD is also used to treat upholstery fabric in the U.K., but not to as great an extent as DBDPO. Although toxicity data on HBCD are somewhat limited, both the CPSC staff (Babich and Thomas 2001) and the NRC (2000) concluded that direct exposure to HBCD in upholstery fabric is not likely to present a hazard to consumers. HBCD has been reported in human and environmental samples, but less frequently and at lower levels than the PBDPO's. The primary concern regarding HBCD is that it is bioaccumulative. Thus, environmental levels might be expected to increase over time. In addition, HBCD may be toxic at sufficiently high doses. The EU is in the process of conducting a comprehensive risk assessment for HBCD (EBFRIP 2004b) and it is under review by EPA as part of the HPV Challenge program (BFRIP 2001).

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