DEPARTMENT OF ECOLOGY
State of Washington

Children's Safe Products Reporting Rule

Rationale for Reporting List of Chemicals of High Concern to Children 2011–2017

Revised May 2021

Publication 18-04-025

Publication and Contact Information

This document is available on the Department of Ecology's website at:
https://apps.ecology.wa.gov/publications/summarypages/1804025.html

For more information contact:

Hazardous Waste and Toxics Reduction Program
P.O. Box 47600
Olympia, WA 98504-7600
Phone: 360-407-6700

Washington State Department of Ecology: www.ecology.wa.gov

- Headquarters, Olympia: 360-407-6000
- Northwest Regional Office, Shoreline: 206-594-0000
- Southwest Regional Office, Olympia: 360-407-6300
- Central Regional Office, Union Gap: 509-575-2490
- Eastern Regional Office, Spokane: 509-329-3400

ADA Accessibility

The Department of Ecology is committed to providing people with disabilities access to information and services by meeting or exceeding the requirements of the Americans with Disabilities Act (ADA), Section 504 and 508 of the Rehabilitation Act, and Washington State Policy #188.

To request an ADA accommodation, contact Ecology by phone at 360-407-6700 or email at hwtrpubs@ecy.wa.gov. For Washington Relay Service or TTY call 711 or 877-833-6341. Visit Ecology's website[1] for more information.

[1] http://ecology.wa.gov/accessibility

Children's Safe Products Reporting Rule

Rationale for Reporting List of Chemicals of High Concern to Children 2011-2017

Hazardous Waste and Toxics Reduction Program

Washington State Department of Ecology

Olympia, Washington

This page is purposely left blank

Table of Contents

List of Tables

Page

Tables

Introduction

This publication is the product of two previous publications:

- Publication 17-04-021: *Children's Safe Products Reporting Rule: Chemicals of High Concern to Children Proposed for Addition or Delisting during the 2017 Rule Update*.[2]
- Publication 17-04-023: *CSPA Rationale for Reporting List of Chemicals of High Concern to Children 2011*.[3]

We made this publication to make it easier to find the full list of CHCC rationales in one place rather than two.

The CHCC listing process prioritized three toxicity endpoints: carcinogenicity, reproductive/developmental toxicity, and endocrine disruption. Other toxic endpoints (like liver toxicity, neurotoxicity, or aquatic toxicity) were not considered for listing purposes. The process also prioritized potential for exposure as being in children's products or in people.

CHCCs selected for addition or delisting either did or did not meet the listing criteria. CHCC listing criteria are based on authoritative sources that identify chemical toxicity in the Children's Safe Products Act (RCW 70.240.010)[4] and evidence of potential for exposure (RCW 70.240.030(1)).

Authoritative sources used to determine toxicity:

- California's Proposition 65 list for cancer, birth defects, or other reproductive harm (OEHHA).[5]
- National Toxicology Program (NTP) Center for the Evaluation of Risks to Human Reproduction monographs and Report on Carcinogens (NTP 2016).[6]
- The International Agency for Research on Cancer (IARC).[7]

---

[2] https://apps.ecology.wa.gov/publications/SummaryPages/1704021.html
[3] https://apps.ecology.wa.gov/publications/SummaryPages/1704023.html
[4] app.leg.wa.gov/rcw/default.aspx?cite=70.240&full=true
[5] California Office of Environmental Health Hazard Assessment (OEHHA). Website that contains the *Proposition 65 List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity*. http://oehha.ca.gov/proposition-65/proposition-65-list
[6] National Toxicology Program (NTP). 2016. *14th Report on Carcinogens.* U.S. Department of Health and Human Services, Public Health Service. https://ntp.niehs.nih.gov/pubhealth/roc/index-1.html
[7] International Agency for Research on Cancer (IARC). *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*. http://publications.iarc.fr/Book-And-Report-Series/Iarc-Monographs-On-The-Evaluation-Of-Carcinogenic-Risks-To-Humans

- U.S. Consumer Product Safety Commission's Chronic Hazard Advisory Panel Report on Phthalates (CPSC 2014).[8]
- U.S. EPA sources:
    - Alternatives assessments on flame retardants (EPA 2015).[9]
    - Integrated Risk Information System (IRIS).[10]
- European Union sources:
    - Substances restricted or authorized under the EU Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) regulation (ECHA).[11]
    - Candidate list of Substances of Very High Concern (SVHC) under REACH (ECHA).
    - Existing Substances Regulation (ECHA).
    - Priority list of chemicals identified as suspected endocrine disruptors (EC).[12]

Authoritative sources used to determine potential for exposure:

- Scientific studies published in peer-reviewed journals showing presence in children's products, house dust, indoor air, or biomonitoring data.
- Danish Environmental Protection Agency surveys on chemicals in consumer products (DEPA).[13]
- Centers for Disease Control (CDC) National Health and Nutrition Examination Survey (NHANES).[14]

Washington State list of persistent, bioaccumulative, and toxic (PBT) chemicals (Chapter 173-333 WAC).[15]

---

[8] Consumer Product Safety Commission (CPSC). 2014. *Chronic Hazard Advisory Panel Report on Phthalates and Phthalate Alternatives*. https://www.cpsc.gov/s3fs-public/CHAP-REPORT-With-Appendices.pdf

[9] U.S. Environmental Protection Agency (EPA). 2015. *Flame Retardants Used in Flexible Polyurethane Foam: An Alternatives Assessment Update*. EPA 744-R-15-002. https://www.epa.gov/sites/production/files/2015-08/documents/ffr_final.pdf

[10] U.S.EPA, Integrated Risk Information System (IRIS). Website containing IRIS chemical toxicity assessments. https://cfpub.epa.gov/ncea/iris2/atoz.cfm

[11] European Chemicals Agency (ECHA). Registration, Evaluation, Authorisation and Restriction of Chemicals. Online database https://echa.europa.eu/regulations/reach/understanding-reach

[12] European Commission (EC). Endocrine disruptor website. http://ec.europa.eu/environment/chemicals/endocrine/strategy/substances_en.htm

[13] Danish Environmental Protection Agency (DEPA). Website containing DEPA surveys on chemicals in consumer products. https://eng.mst.dk/chemicals/chemicals-in-products/consumers-consumer-products/danish-surveys-on-consumer-products/

[14] Centers for Disease Control (CDC). Website containing the results of the National Health and Nutrition Examination Survey (NHANES). https://www.cdc.gov/nchs/nhanes/about_nhanes.htm

[15] app.leg.wa.gov/wac/default.aspx?cite=173-333&full=true

Chemicals of High Concern to Children (CHCCs)

CAS 50-00-0 Formaldehyde

Summary of Toxicity

Formaldehyde is classified as a carcinogen by a number of authoritative sources [1,2,3,4]. Inhalation of formaldehyde is associated with cancer in the respiratory tract in humans and laboratory animals. Oral exposures in animals are also carcinogenic. Formaldehyde is a skin, eye, and respiratory tract irritant and sensitizer.

Summary of Potential for Exposure

Formaldehyde is used in the production of resins which are commonly used as adhesives and binders in wood products, pulp and paper, and in the production of plastics and coatings. It is also used in the finishing treatment of fabrics used in clothing and other products [5]. Aqueous formaldehyde (formalin) is used as a preservative and antimicrobial agent in some soaps, shampoos, hair preparations, deodorants, lotions, cosmetics, and nail products [6]. Some of these may be marketed to children. Formaldehyde has been detected in a wide range of children's' products including feeding pillows, nursing pillows, glitter glues, infant mittens, infant jackets, disposable diapers, bed linens, children's tents, and glue sticks [7].

List of References

1. WHO International Agency for Research on Cancer (2006) IARC Monograph on the Evaluation of Carcinogenic Risks to Humans, Vol. 88: Formaldehyde, 2-Butoxyethanol and 1-tert-Butoxypropan-2-ol.
2. U.S. EPA Integrated Risk Information System (IRIS) for Formaldehyde (last revised 1991).
3. U.S. DHHS, PHS, National Toxicology Program. Report on Carcinogens, Eleventh Edition. 2005.
4. California Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. Feb 5, 2010.
5. U.S. DHHS, Agency for Toxic Substances & Diseases Registry. Toxicological Profile for Formaldehyde. July 1999.
6. U.S. EPA, Office of Pesticide Programs. Reregistration Eligibility Decision for Formaldehyde and Paraformaldehyde. EPA 739-R-08-004. June 2008
7. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in consumer products.

CAS 62-53-3 Aniline

Summary of Toxicity

Aniline is classified as a carcinogen by a number of authoritative sources [1,2,3]. Tumors of the spleen are observed in test animals. Bladder cancers have been reported in occupationally exposed groups but coexposures with other chemicals limits conclusions. Animal testing also shows that aniline damages red blood cells and causes toxic effects in the blood system (i.e., spleen, bone marrow, kidney, and liver) [2]. Overexposure in humans causes methemoglobinemia and cyanosis [2,4].

Summary of Potential for Exposure

Aniline is used primarily as a chemical intermediate in production of MDA (methylene di-aniline), a starting product for polyurethane plastics. In the rubber industry, aniline is used in the manufacture of antioxidants and rubber accelerators. It is also used in the manufacture of dyes, agricultural chemicals, optical whitening agents, resins, marking inks, perfumes, and certain pharmaceuticals. Aniline has been an ingredient in household products including shoe polish and inks [2,4,5].

Aniline has been detected in a variety of children's products including balloons, marker pens, infant bed linens, and the outer material of an infant jacket [6]. The CDC has not assessed whether aniline is present in peoples' bodies in the U.S. but biomonitoring in the general population of Bavaria showed detectable levels of aniline in urine of 94 percent of participants [7]. Aniline detected may be from degradation of polyurethane plastics.

List of References

1. U.S. EPA Integrated Risk Information System (IRIS) for Aniline (CASRN 62-53-3). Last revised 1994. https://www.epa.gov/aboutepa/about-national-center-environmental-assessment-ncea
2. European Commission Joint Research Centre: Institute for Health and Consumer Protection, ORATS. Summary Risk Assessment Report for Aniline (CAS 62-53-3)
3. California Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. Feb 5, 2010.
4. "Aniline" in REPROTEXT Database Version 5.1 Greenwood Village, CO: Thomson Reuters (Healthcare) Inc. (accessed 2009).
5. Health Canada and Environmental Canada (1994) Priority Substances Assessment Report: Aniline (Catalogue No. En 40-215/35E)
6. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in consumer products.

7. Kütting, B, et al. (2009) Monoarylamines in the general population – A cross-section population-based study including 1004 Bararian subjects. Int J Hyg Environ Health 212: 298-309.

CAS 62-75-9 N-Nitrosodimethylamine (NDMA)

Summary of Toxicity

N-Nitrosodimethylamine is classified as a carcinogen by a number of authoritative sources based on animal evidence of liver, kidney, and lung tumors after oral, inhalation, or injection exposures. Exposure to rodents during pregnancy resulted in tumors in offspring [1,2,3,4].

Summary of Potential for Exposure

Nitrosamines can be formed as process contaminants when carbamate chemicals are used during rubber production [5]. According to the National Toxicology Program, it is also used as a plasticizer for rubber and acrylonitrile polymers and as a solvent in the fiber and plastics industry [2]. NDMA has been detected in children's products including silicone and natural rubber baby bottle nipples and pacifiers [5,6], balloons [7,8,9], and personal care products such as baby shampoo and bath foam [9].

List of References

1. U.S. EPA Integrated Risk Information System (IRIS) for N-Nitrosodimethylamine (last revised 1993).
2. U.S. DHHS, PHS, National Toxicology Program. Report on Carcinogens, Eleventh Edition. 2005.
3. European Commission Joint Research Centre: Institute for Health and Consumer Protection, European chemical Substances Information System
4. California Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. Feb 5, 2010.
5. Dutch Inspectorate for Health Protection and Veterinary Public Health (VWA/KvW). Teats and soothers: migration of N-nitrosaminess and n-nitrosatable substances and MBT. Report No. NDTOY003/01. June 2002.
6. K. Mizuishi, T. Hamano, and S. Ogino (2009) N-nitrosoamine content in rubber nipples and pacifiers, 1988-2007. Tokyo-to Kenko Anzen Kenkyu Senta Kenyu Nenpo 59: 121-125. (abstract in English)
7. Danish Ministry of the Environment. Environmental Protection Agency. Survey of Chemical Substances in Consumer Products, Report No. 89, Analysis of chemical substances in balloons, 2007.
8. Dutch Inspectorate for Health Protection and Veterinary Public Health (VWA/KvW). Migration of N-nitrosaminess and n-nitrosatable substances from latex balloons. Report No. ND04o063/02. January 2005.

9. European Commission, Scientific Committee on Consumer Products. Opinion on the presence and release of nitrosamines and nirtosatable compounds from rubber balloons, December 2007.

CAS 71-43-2 Benzene

Summary of Toxicity

Benzene is considered a known human carcinogen by authoritative sources [1,2,3]. All routes of exposure are considered carcinogenic based on convincing occupational evidence and supporting evidence from animal studies [4]. Benzene is toxic to blood cells. Evidence in animals suggests that exposure to benzene *in utero* can alter fetal maturation of lymphocytes, erythrocytes, and granulocytes and that the damage to the hematopoietic system during development can last into adulthood [5].

Summary of Potential for Exposure

Biomonitoring by the CDC shows that benzene exposure is widespread in the U.S. population [6]. Vehicle exhaust and cigarette smoke are common sources of exposure. Benzene is also used in the manufacture of plastics, synthetic rubber, dyestuffs, resins, raw materials for detergents, and plant protection agents [3]. Testing by the Danish EPA found quantifiable benzene in one out of four balloons tested and in two scented children's toys [7]. Benzene was found infrequently in a large study of common household products in the USA [8].

List of References

1. WHO, International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Supplement No 7: Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs Volumes 1 to 42. 1987
2. Centers U.S. EPA, Integrated Risk Information System (IRIS). Benzene (last revised 2003).
3. European Commission, Joint Research Centre, Institute for Health and Consumer Protection. European Union Risk Assessment Report: Benzene Final Risk Assessment. 2008.
4. U.S. EPA, National Center for Environmental Assessment. Carcinogenic Effects of Benzene: an update. EPA/600/p-97/1001F. April 1998.
5. California EPA, Office of Environmental Health Hazard Assessment (1997) Hazard Identification of the Developmental and Reproductive Toxic Effects of Benzene.
6. Centers for Disease Control and Prevention. Fourth National Report on Human Exposure to Environmental Chemicals, 2009.
7. Danish Ministry of the Environment, Environmental Protection Agency. Survey of Chemical Substances in Consumer Products Reports 89 and, 68.

8. http://www.mst.dk/English/Chemicals/Consumer_Products/Surveys-on-chemicals-in-consumerproducts.htm
9. Sack, TM et al. (1992) A survey of household products for volatile organic compounds. Atmospheric Environment Vol. 26A (6):1063-1070.

CAS 75-01-4 Vinyl chloride

Summary of Toxicity

Vinyl chloride is classified as a human carcinogen by authoritative sources [1,2,3]. Evidence indicates that it causes liver and other cancers in occupationally exposed people and in test animals [1]. Vinyl chloride is considered mutagenic and genotoxic [1]. Young animals are particularly prone to the formation and persistence of vinyl chloride-induced adducts and are more likely than adults to develop tumors [4].

Summary of Potential for Exposure

Vinyl chloride is used primary to make polyvinyl chloride (PVC). Children's products such as bath toys, squeeze toys, and dolls are often made from PVC. PVC can be softened with plasticizers into the plastic commonly known as vinyl. Vinyl is used in numerous children's products including inflatable pools, inflatable play structures, play mats, clothing, mattress covers, and bibs. Chewing or sucking on these products has the potential to release any unpolymerized vinyl chloride from the object [4]. We did not locate product testing data for vinyl chloride monomer from children's products.

List of References

1. WHO, International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume No 97: 1,3-Butadiene, Ethylene Oxide and Vinyl Halides (Vinyl Fluoride, Vinyl Chloride and Vinyl Bromide). 2008.
2. U.S.EPA, Integrated Risk Information System (IRIS). Vinyl Chloride (last revised 2000).
3. U.S. DHHS, PHS, National Toxicology Program. Report on Carcinogens, Eleventh Edition. 2005.
4. US Department of Health and Human Services, Agency for Toxic Substances & Disease Registry. Toxicological Profile for Vinyl Chloride, 2006.

CAS 75-07-0 Acetaldehyde

Summary of Toxicity

Acetaldehyde is classified as a carcinogen by authoritative sources [1,2,3]. Prolonged inhalation exposure causes nasal cancers in test animals. Human evidence from workplace exposures is supportive but not conclusive [2]. Acetaldehyde is a major metabolite of ethanol in mammals and

may be involved in fetal alcohol syndrome. For this reason, Reprotext classifies acetaldehyde as an A- unconfirmed human reproductive hazard [4].

Summary of Potential for Exposure

Acetaldehyde is used primarily as a feedstock in the production of other chemicals. Other uses are or have been in leather tanning, in glues, in the paper industry, in the manufacture of cosmetics and plastics, and as a food flavoring agent [1,4]. Acetaldehyde was detected in 6 out of 6 children's tent samples in testing by the Danish EPA [5]. Acetaldehyde is listed as an ingredient in school glue and other arts and craft glues in the NLM Household Products Database [6].

List of References

1. WHO, International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume No 71: Re-evaluation of Some Organic Chemicals, Hydrazine and Hydrogen Peroxide, Part Two. 1999.
2. U.S. DHHS, PHS, National Toxicology Program. Report on Carcinogens, Eleventh Edition. 2005.
3. U.S. EPA, Integrated Risk Information System (IRIS). Acetaldehyde (last revised 1991).
4. Health Canada, Priority Substances List Assessment Report for Acetaldehyde. 2000.
5. Danish Ministry of the Environment, Environmental Protection Agency. Survey of Chemical Substances in Consumer Products, Report 46, 2004.
6. National Institutes of Health, National Library of Medicine, Household Products Database.

CAS 75-09-2 Methylene chloride (also called dichloromethane)

Summary of Toxicity

Methylene chloride is classified as a carcinogen by authoritative sources [1,2,3]. Inhalation exposures in laboratory animals result in lung and liver cancers and mammary gland tumors [2]. Methylene chloride is metabolized to carbon monoxide in mammals [3]. Because carbon monoxide increases the levels of carboxyhemoglobin in the blood and is a known reproductive hazard, Reprotext classifies methylene chloride as a Class A+ reproductive hazard [4].

Summary of Potential for Exposure

Methylene chloride is used as an industrial solvent in paint removers and degreasers, as a carrier solvent in the textile industry, and as a blowing agent in foam production. It is used in inks and adhesives and in plastics manufacture, as an extraction solvent for spices and hops, and is used to extract caffeine from coffee [1,2,5]. Methylene chloride is also used in spray shoe polish and

water repellent and in wood stains, varnishes and finishes [2]. It was detected in 1 of 14 slimy toys tested by the Danish EPA [7].

List of References

1. WHO, International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume No 71: Re-evaluation of Some Organic Chemicals, Hydrazine and Hydrogen Peroxide, Part One, 1999.
2. U.S. DHHS, PHS, National Toxicology Program. Report on Carcinogens, Eleventh Edition. 2005.
3. U.S.EPA, Integrated Risk Information System (IRIS). Dicloromethane http://www.epa.gov/iris/subst/0070.htm and External Review Draft of the Dichloromethane Assessment, March 2010.
4. "Methylene Chloride" in REPROTEXT Database Version 5.1 Greenwood Village, CO: Thomson Reuters (Healthcare) Inc. (accessed 2009).
5. Health Canada, Priority Substances List Assessment Report: Dichloromethane. 1993.
6. Danish Ministry of the Environment, Environmental Protection Agency. Survey of Chemical Substances in Consumer Products, Report 67, 2005.

CAS 75-15-0 Carbon disulfide

Summary of Toxicity

Carbon disulfide is neurotoxic and is identified as a reproductive and developmental toxicant by authoritative sources [1-5]. Evidence comes from laboratory animal testing as well as supportive data from epidemiological studies of workplace exposures in men and women.

Summary of Potential for Exposure

Carbon disulfide is a thermal decomposition product of zinc dibutyldithiocarbamate, a chemical used in rubber production. Consequently, it may be present in rubber as a degradation product [6]. The most prominent industrial use of carbon disulfide is in the production of viscose rayon fibers. Carbon disulfide is also used in the production of carbon tetrachloride and cellophane, and as a solvent for rubber, sulfur, oils, resins, and waxes [2]. Carbon disulfide was detected at low concentrations in 4 out of 4 balloon samples in consumer product testing by the Danish EPA [7]. It was detected in 1 out of 2 natural rubber pacifiers in testing by the Dutch government [6].

List of References

1. California EPA, Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. February 5, 2010.
2. California EPA, Office of Environmental Human Health Assessment (OEHHA). Chronic Toxicity Summary for Carbon Disulfide (2002).

3. U.S. EPA, Integrated Risk Information System (IRIS). Carbon Disulfide (Oral RfD revised 1990, inhalation RfC last revised 1995).
4. HSDB. Tributyl Phosphate, (CASRN: 126-73-8). 2015 Updated 02/18/2015.
5. Hiroyuki Kojima, S.T., Nele Van den Eede, Adrian Covaci, Effects of primary metabolites of organophosphate flame retardants on transcriptional activity via human nuclear receptors. Toxicology Letters, 2016. 245: p. 31-39.
6. Kojima, H., et al., In vitro endocrine disruption potential of organophosphate flame retardants via human nuclear receptors. Toxicology, 2013. 314(1): p. 76-83.
7. EPA. Chemical Data Access Tool (CDAT) - Chemical Data Reporting (CDR) information on the production and use of chemicals manufactured or imported into the United States. 2012.

CAS 78-93-3 Methyl ethyl ketone (also called MEK or 2-butanone)

Summary of Toxicity

MEK is listed in Reprotext as a class A- for its potential to be a human reproductive hazard [1]. Evidence is principally based on animal evidence of developmental effects at high doses [2-5]. Some of the animal evidence for MEK comes from studies of 2-butanol which is rapidly converted to MEK in mammals. EPA's oral reference dose for MEK is based on developmental effects seen in a reproductive and developmental toxicity study of 2-butanol in rats [6]. Human evidence of reproductive and developmental effects is limited and is not specific to MEK as workers were also exposed to other solvents [1,6].

Summary of Potential for Exposure

MEK is a solvent used in various coatings, adhesives, and inks. It is a solvent for nitrocellulose, lacquers, rubber cement, printing inks, paint removers, vinyl films, resins, rosins, polystyrene, chlorinated rubber, polyurethane, acrylic coatings, and cleaning solutions [7]. MEK was detected in a children's slimy toy and in 3 out of 6 tents in testing by the Danish EPA [8]. MEK is listed as an ingredient in over 30 arts and crafts products [9].

List of References

1. "Methyl Ethyl Ketone" in REPROTEXT Database Version 5.1 Greenwood Village, CO: Thomson Reuters (Healthcare) Inc. (accessed 2009).
2. Schwetz, BA; Leong, BKJ; Gehring, PJ. (1974) Embryo- and fetotoxicity of inhaled carbon tetrachloride, 1,1-dichloroethane and methyl ethyl ketone in rats. Toxicol Appl Pharmacol 28: 452-64.
3. Deacon, MM; Pilny, MD; John, JA; et al. (1981) Embryo- and fetotoxicity of inhaled methyl ethyl ketone in rats. Toxicol Appl Pharmacol 59: 620-2.

4. Schwetz, BA; Mast, TJ; Weigel, RJ; et al. (1991) Developmental toxicity of inhaled methyl ethyl ketone in mice. Fundam Appl Toicol 16: 742-8.
5. Saillenfait AM, Fallissot F, Sabate JP, et al. (2006) Developmental toxicity of combined ethylbenzene and methylethylketone administered by inhalation to rats. Food Chem Toxicol 44(8):1287-1298.
6. U.S. EPA, Toxicological Review of Methyl Ethyl Ketone in support of summary information on the Integrated Risk Information System (IRIS). September 2003.
7. US Department of Health and Human Services, Agency for Toxic Substances & Disease Registry. Toxicological Profile for 2-Butanone, July 1992.
8. Danish Ministry of the Environment, Environmental Protection Agency. Survey of Chemical Substances in Consumer Products, Report 67, 2005 and Report 46, 2004.
9. National Institutes of Health, National Library of Medicine, Household Products Database.

CAS 79-34-5 1,1,2,2-Tetrachloroethane

Summary of Toxicity

1,1,2,2-Tetrachloroethane (1,1,2,2-TCA) is listed as a carcinogen by authoritative sources [1,2]. Evidence is based on liver cancers in male and female mice and inconclusive information in humans [2,3]. 1,1,2,2-TCA is also acutely toxic in people and animals; the primary effects are damage to liver and kidney, the nervous system, and blood system [4].

Summary of Potential for Exposure

1,1,2,2-TCA was historically used as a solvent and extractant. According to multiple sources, it is no longer widely used for this purpose [3,4,5]. In Europe, 1,1,2,2-TCA is only used as a feedstock for the production of other chlorinated hydrocarbons. It may also be an incidental byproduct of other production processes for chlorinated hydrocarbons such as the production of vinyl chloride [4]. Testing of children's products by the Danish EPA detected 1,1,2,2-TCA in 2 out of 2 baby feeding pillow pellets [6]. It was not detected in a large biomonitoring study of the general U.S. population in 2003-2004 [7].

List of References

1. California Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. Feb 5, 2010.
2. U.S. EPA, Integrated Risk Information System (IRIS). 1,1,2,2 tetrachloroethane (last revised 2006).
3. California EPA, Office of Environmental Health Hazard Assessment. Public Health Goals for Chemicals in Drinking Water: 1,1,2,2-Tetrachloroethane. September 2003.

4. UNEP, OECD Screening Information Dataset (SIDS)for High Production Volume Chemicals: Initial Assessment Report for 1,1,2,2-Tetrachloroethane, October 2002.
5. National Institutes of Health, National Library of Medicine Hazardous Substances Data Bank.
6. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Report 90, 2008.
7. Centers for Disease Control and Prevention (CDC), Fourth National Report on Human Exposure to Environmental Chemicals, December 2009.

CAS 79-94-7 Tetrabromobisphenol (TBBPA)

Summary of Toxicity

An oral study in pregnant rats with TBBPA in its formulated product, Saytex 111, reported reduced fetal weight, increased malformations, and fetal death (ICI Americas 1985 study cited in NIEHS [1]). Multiple subsequent studies on the technical compound did not show consistent reproductive or developmental toxicity [2]. Kidney toxicity following oral dosing was reported in newborn rats [3].

TBBPA has been shown to compete with thyroid hormone (T4) in binding to transthyretin serum binding protein *in vitro* [1,2]. It also appears to have potential to act as a thyroid hormone antagonist [4,5]. TBBPA binds to the estrogen receptor but does not appear to be a receptor agonist or to have significant estrogenic potential [2,6]. It is not currently listed as an endocrine disruptor by the European Union.

Summary of Potential for Exposure

This substance is listed as a Persistent, Bioaccumulative and Toxic (PBT) chemical under Washington State's PBT rule (WAC 173-333-320). [7] TBBPA has been detected in breast milk in several small studies of the general population in Europe [2,8].

TBBPA is a high production volume (HPV) chemical that is used as both a reactive and additive flame retardant in plastics, adhesives, paper, and textiles [1,2]. It may constitute up to 22 percent of ABS polymer resins [2]. It is used primarily in electrical and electronic equipment. TBBPA is also used as a plasticizer, a component in adhesives and coatings, and a chemical intermediate for the synthesis of other flame retardants (e.g., TBBPA allyl ether) [2].

List of References

1. National Institute of Environmental Sciences, Research Triangle Park. Tetrabromobisphenol A: Review of Toxicological Literature. June 2002.

2. European Commission, European Chemicals Bureau. European Union Risk Assessment Report for 2,2',6,6'-tetrabromo-4,4'-isopropylidenediphenol (tetrabromobisphenol-A or TBBP-A) Part II – human health. 2006 Final Report.
3. Fukuda, N et al. (2004) Unexpected nephrotoxicity induced by tetrabromobisphenol A in newborn rats. *Toxicol. Lett. 150 (2)*: 145-155.
4. Kitamura, S et al. (2005) Anti-thyroid hormone activity of tetrabromobisphenol A, a flame retardant, and related compounds: Afinity to the mammalian thyroid hormone receptor, and effect on tadpole metamorphosis. *Life Sci. 76(14):*1589-601.
5. Sun, H et al. (2009) Anti-thyroid hormone activity of bisphenol A, tetrabromobisphenol A and tetrachlorobisphenol A in an improved reporter gene assay. *Toxicol. In Vitro* 23(5): 950-4.
6. Dorosh, A et al. (2011) Assessing estrogenic effects of brominated flame retardants hexabromocyclododecane and tetrabromobisphenol A on MCF-7 cells. *Folia. Biol. 57 (1):*35-9.
7. WA Department of Ecology. Summary of Technical Background Information for the Proposed PBT List (Revised Draft) October 2005.
8. Abdallah, MA and S. Harrad (2011) Tetrabromobisphenol-A, hexabromocyclododecane and its degradation products in UK human milk: relationship to external exposure. *Environ. Int. 37(2*): 443-8.

CAS 80-05-7 Bisphenol A (BPA)

Summary of Toxicity

Bisphenol A causes reproductive and developmental toxicity in laboratory animals at high doses [1,2,3]. At low doses that are similar to estimated exposures in people, bisphenol A can affect the developing rodent brain and behavior, prostate and mammary gland development, and cause early onset of puberty in females [1]. There is wide variability in reported results from studies at low doses [1,2,3].

Summary of Potential for Exposure

Bisphenol A is used to manufacture polycarbonate plastics which are used in many children's toys, dishware, and bottles. BPA is also used in epoxy resins used in food can liners and dental sealants [4,5]. Consumer product testing by the Danish EPA found BPA in polycarbonate components of pacifiers, in infant baby bottles, and in plastic spoons [6]. In a large biomonitoring study in the USA, BPA was detected in 92.6 percent of the general population aged 6 years and older. Children had higher levels than adults. This indicates widespread exposure to children and adults [7].

List of References

1. US Department of Health and Human Services, National Toxicology Program, Center for the Evaluation of Risks to Human Reproduction (CERHR) Monograph on the potential human reproductive and developmental effects of Bisphenol A. September 2008.
2. European Commission, Joint Research Centre. European Risk Assessment Report: 4,4'isopropylidenediphenol (bisphenol A) Risk Assessment, February 2010.
3. California EPA, Office of Environmental Health Hazard Assessment (OEHHA). Evidence on the developmental and reproductive toxicity of Bisphenol A. October 2009.
4. Centers for Disease Control and Prevention (CDC), Fourth National Report on Human Exposure to Environmental Chemicals, December 2009.
5. National Institutes of Health, NIEHS Factsheet on BPA.
6. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Report 102, 2009.
7. Calafat AM, Ye X, Wong LY, Reidy JA, Needham LL. Exposure of the U.S. Population to Bisphenol A and 4-tertiary-Octylphenol: 2003–2004. Environ Health Perspect 2008 Jan;116(1):39-44.
8. CAS 80-09-1 Bisphenol S (BPS).

CAS 80-05-7 Bisphenol S (BPS)

Summary of Toxicity

EPA classified Bisphenol S (BPS) as high hazard for toxicity from repeated exposure based on no-observed-adverse-effect-level (NOAEL) of 10 and 40 mg/kg-day in repeated dose rat studies [1]. A 28-day oral study of BPS in rats showed effects on body weight, increased kidney weight, hyperplasia, necrosis in mucosal epithelium of the cecum, and increased incidence of proteinuria and urobilinogen at 200 mg/kg-day. The NOAEL was 40 mg/kg-day [1].

EPA classified BPS as a moderate hazard for reproductive and developmental toxicity based on prolonged estrus cycle, decreased fertility index, decreased number of live offspring, and liver effects observed at 300 mg/kg-day in a reproductive and developmental toxicity test in orally exposed rats. Although the NOAEL for reproductive effects was 60 mg-kg-day, pathology was noted at this dose in the cecum [1]. A recent 90-day oral study in rats reported atrophy of mammary glands in male rats treated with at 300 mg/kg-day of BPS. This study also observed a dose-dependent increase in focal squamous cell metaplasia of glandular epithelium in the uterus of female rats across all doses (100, 300, and 1000 mg/kg-day) but it was unclear when the increase became statistically significant [2].

BPS has been assessed as part of the NTP's Tox21 High Throughput Screening Program where it was classified as an estrogen agonist with some affinity for the estrogen receptor [3]. *In vitro* assays demonstrate that BPS can bind to estrogen receptors, elicit estrogen-induced gene

transcription, induce cell proliferation in MCF7 cancer cells, and inhibit the androgenic activity of dihydrotestosterone [1]. In a systematic review of BPS, BPA, and BPF endocrine studies, BPS had estrogenic activity in whole organism testing (Zebrafish, Daphnia magna) and in a number of *in vitro* tests. On average, BPS was about 1/3 as potent as BPA in estrogenic activity *in vitro* assays [4].

Summary of Potential for Exposure

BPS exposures can occur through oral, dermal, or inhalation routes. However, primary exposure likely occurs through the oral route. Information on distribution in the body, metabolism, and excretion is mostly lacking [3].

Washington State banned BPA for use in baby bottles, infant sippy cups, and sports water bottles starting in 2010 (Washington State Law; Chapter 70.280 RCW). BPS is used as a replacement for BPA in polymer production and thermal papers. BPS is used in polyethersulfone (PES) plastics used to make baby bottles [3,5,6]. BPS has been detected in personal care products [7], sales receipt paper, and other paper products [8,9]. National U.S. production volume was reported to be 1-10 million pounds in 2012 [10].

BPS was found in 81 percent of the human urine samples analyzed from general populations in the United States and several Asian countries collected in 2010-2011. Urine concentrations in U.S. samples had a median of 0.26 ng/mL and a maximum detection of 21 ng/mL [11]. In another biomonitoring study, archived urine samples from U.S. adults collected from 2000-2014 showed increasing levels of BPS over time 12]. BPS was also measured in the serum and urine of cashiers and a control group of adults in a North Carolina study. Urinary levels of BPS were higher in cashiers following a shift handling receipt paper that contained BPS [9]. BPS was detected in 100 percent of 38 indoor dust samples collected in New York in 2006 and 2010. Median detected concentration was 630 ng/g dust and the maximum was 25,500 ng/g dust [13]. BPS has also been found in a variety of foods collected from retail grocery stores in Albany, NY, in 2008-2010. It was detected in 43 percent of meats and meat products and about 25 percent of seafood, fruit, and vegetable samples [14].

BPS was considered to have moderate persistence and low potential for bioaccumulation by EPA [1].

List of References

1. EPA. Bisphenol A Alternatives in Thermal Paper. Final Report August 2015. Design for the Environment Program. www.epa.gov/sites/production/files/2015-08/documents/bpa_final.pdf.
2. ECHA, *Decision on Substance Evaluation Pursuant to Article 46(1) of Regulation (EC) NO 1907/2006 For 4,4'-sulfonyldiphenol, CAS No 80-09-1 (EC No 201-250-5)*. 2016.

3. National Toxicology Program (NTP) Research Concept: Bisphenol S (Draft). NTP Board of Scientific Counselors Meeting, June 2014. https://ntp.niehs.nih.gov/ntp/about_ntp/bsc/2014/june/bisphenols_concept_508.pdf.
4. Rochester JR and Bolden AL (2015) Bisphenol S and F: Systemic review and comparison of the hormonal activity of bisphenol A substitutes. *Environ. Health Perspect. 123* (7):643-650.
5. Ben-Johnson N and Hugo ER (2016) Bisphenols come in different flavors: is "S" better than "A"? *Endocrinology 157 (4):*1321-11323.
6. Minnesota Pollution Control Agency. BPA and BPS in Thermal Paper: Results of Testing in Minnesota Hospitality Industry. March 2014. www.pca.state.mn.us/sites/default/files/p-p2s10-13.pdf.
7. Liao C, Kannan K. (2014) A survey of alkylphenols, bisphenols, and triclosan in personal care products from China and the United States. *Arch Environ Contam Toxicol* 67(1):50–59.
8. Liao C, Liu F, Kannan K. (2012) Bisphenol S, a new bisphenol analogue, in paper products and currency bills and its association with bisphenol a residues. *Environ Sci Technol. 46(12):*6515-22. doi: 10.1021/es300876n.
9. Thayer KA, Taylor KW et al. (2016) Bisphenol A, Bisphenol S and 4-hydroxyphenyl 4-isoprooxy-phenylsulfone (BPSIP) in urine and blood of cashiers. *Environ. Health Perspect.* 124(4): 437-444.
10. EPA. Chemical Data Access Tool (CDAT) - Chemical Data Reporting (CDR) information on the production and use of chemicals manufactured or imported into the United States. 2012 10/15/2015 10/30/2015]. http://java.epa.gov/oppt_chemical_search/.
11. Liao et al. (2012) Bisphenol S in urine from the United States and Seven Asian Countries: Occurrence and Human Exposures. *Environmental Science and Technology* 46: 6860-6866.
12. Ye, X., et al. (2015) Urinary Concentrations of Bisphenol A and Three Other Bisphenols in Convenience Samples of U.S. Adults during 2000-2014. *Environ Sci Technol* 49(19): p. 11834-9.
13. Liao et al. (2012). Occurrence of Eight Bisphenol Analogues in Indoor Dust from the United States and Several Asian Countries: Implication for Human Exposure. *Environmental Science and Technology 46*:9138-45.
14. Liao C. and Kurunthachalam K. (2013) Concentrations and Profiles of Bisphenol A and Other Bisphenol Analogues in Foodstuffs from the United States and Their Implications for Human Exposure. *J. Agricultural and Food Chemistry 61*, 4655−4662.
15. Ecology, 2011, Children's Safe Products Reporting Rule – Supporting Documents for the 2011 Rulemaking. Rule documents from the 2011 rulemaking were merged into a publication in April of 2017. Publication 17-04-022. https://apps.ecology.wa.gov/publications/SummaryPages/1704022.html

CAS 84-61-7 Dicyclohexyl phthalate (DCHP)

Summary of Toxicity

Dicyclohexyl phthalate (DCHP) is identified as an endocrine disruptor based on the EU Category 1 designation as an endocrine disruptor [1]. The EU developed the priority list in stages (2000, 2002, and 2007), putting chemicals in three categories. The EU **Category 1** endocrine distruptor designation has been used as an authoritative source for CSPA. Category 1 requires evidence of endocrine disrupting activity in at least one species using intact animals. **Category 2,** which requires at least some in vitro evidence, is too preliminary. **Category 3** is no evidence of endocrine disrupting activity or no data available.

The Consumer Product Safety Improvement Act of 2008 (CPSIA) directed the U.S. Consumer Product Safety Commission (CPSC) to convene the CHAP on Phthalates and Phthalate Alternatives "to study the effects of all phthalates and phthalate alternatives as used in children's toys and child care articles." The CHAP assessed the risks of fourteen phthalates and six phthalate alternatives, including three phthalates permanently banned by the CPSIA and three phthalates subject to an interim ban. CHAP is an authoritative source for CSPA [2].

DCHP was included in the CHAP report, which found studies in rodents suggest that exposure to DCHP can induce adverse effects in reproductive organs and suggests that DCHP is a developmental toxicant [2]. The CHAP panel found the toxicological profile of DCHP is very similar to other antiandrogenic phthalates and thus, exposure to DCHP contributes to the cumulative risk from other antiandrogenic phthalates. The CHAP report recommends that DCHP be permanently banned from use in children's toys and child care articles at levels greater than 0.1 percent.

Summary of Potential for Exposure

There is new information on the presence of DCHP in indoor dust (2.9 ug/g, 0.3 ug/g) and air (4-5 ng/m^3, 0.07 ug/m^3) in several studies [3]. DCHP was also found in soap (100 ug/g), modeling clay (4,000 mg/kg), and pajamas (3,400 mg/kg), but they are not noted as being for children [3].

List of References

1. EU-Strategy for Endocrine Disruptors database EDS_2003_DHI2006.mdb. Accessed 10/17/16.
2. Chronic Hazard Advisory Panel on Phthalates and Phthalate Alternatives (CHAP), July, 2014. Report to the U.S. Consumer Product Safety Commission Directorate for Health Services.
3. European Chemicals Agency (ECHA), Sweden and Denmark, 2015. Annex XV Report: Proposal for Identification of a Substance of Very High Concern on the Basis of the Criteria Set Out in REACH Article 57 Substance Name(s): Dicyclohexyl phthalate

(DCHP) EC Number(s): 201-545-9 CAS Number(s): 84-61-7.
http://echa.europa.eu/documents/10162/b2fbb22c-72d7-491d-b417-39105e35b792

CAS 84-66-2 Diethyl phthalate (DEP)

Summary of Toxicity

Diethyl phthalate has been classified as a Category 1 endocrine disruptor by the European Union based on reproductive effects [1]. In a multi-generation mouse study, epididymal sperm concentration in second generation offspring of the group treated with diethyl phthalate was reduced by 30 percent compared to controls [2]. Human studies show an association between increased prenatal urinary concentrations of MEP, the primary urinary metabolite of DEP, and changes in hormone concentrations and anogenital distance in male infants. They also report decreased sperm concentrations and decreased sperm motility associated with higher urinary MEP in adult males [3-7].

Summary of Potential for Exposure

The Danish EPA found diethyl phthalate in plastic components of baby carriers, [8] in activity carpet [9], and in 4 out of 5 PVC soap containers [10]. Monoethyl phthalate, a metabolite indicative of diethyl phthalate exposure, was found in most of the U.S. population sampled in the NHANES survey [11].

List of References

1. European Commission DG Environment (2002). Endocrine disruptors: study on gathering information on 435 substances with insufficient data. Final report B4-3040/2001/325850/MAR/C2.
2. Lamb, J, Reel, J, and Lawton, D. (1997) Diethyl phthalate. *Environ Health Perspect 105* (Suppl 1): 245-6.
3. Swan, S.H. et al. (2005). Decrease in anogenital distance among male infants with prenatal phthalate exposure. *Environ Health Perspect 113*: 1056-1061.
4. Sathyanarayana S. (2008). Phthalates and children's health. Curr Probl Pediatr Adolesc Health Care 38(2):34-49.
5. Main, K.M. et al. (2006) Human breast milk contamination with phthalates and alterations of endogenous reproductive hormones in infants three months of age. *Environ Health Perspect 114*: 270-276.
6. Jonsson, B.A., et al. 2005. Urinary phthalate metabolites and biomarkers of reproductive function in young men. *Epidemiology 16(4)*:487-493.
7. Hauser R, et al (2007) DNA damage in human sperm is related to urinary levels of phthalate monoester and oxidative metabolites. *Hum Reprod 22(3)*:688-95.
8. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Report 90, 2008.

9. Danish Ministry of the Environment, Environmental Protection Agency. Survey of Chemical Substances in Consumer Products, Report 70, 2006.
10. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Report 102, 2009.
11. Silva, MJ, Barr, DB, Reidy, JA, Malek, NA, Hodge, CC, Caudill, SP, Brock, JW, Needham, LL, and Calafat, AM. (2004). Urinary levels of seven phthalate metabolites in the U.S. population from the National Health and Nutrition Examination Survey (NHANES) 1999-2000. Environ Health Perspect 112: 331-8.

CAS 84-69-5 Diisobutyl phthalate (DIBP)

Summary of Toxicity

Diisobutyl phthalate's (DIBP) is identified as a SVHC as toxic for reproduction [1]. Substances that may have serious and often irreversible effects on human health and the environment can be identified as SVHCs under the EU Registration, Evaluation, Authorisation, and Restriction of Chemicals (REACH) law. If a substance is identified as an SVHC, it is added to the Candidate List for eventual inclusion in the Authorisation List.

The Consumer Product Safety Improvement Act of 2008 (CPSIA) directed the U.S. Consumer Product Safety Commission (CPSC) to convene a Chronic Hazard Advisory Panel (CHAP) on Phthalates and Phthalate Alternatives "to study the effects of all phthalates and phthalate alternatives as used in children's toys and child care articles." The CHAP assessed the risks of fourteen phthalates and six phthalate alternatives, including three phthalates permanently banned by the CPSIA and three phthalates subject to an interim ban. CHAP is an authoritative source for CSPA [2].

DIBP was included in the CHAP report [2], which found that animal and human studies suggest that exposure to DIBP can cause reproductive and developmental effects. The CHAP found the toxicological profile of DIBP is very similar to other antiandrogenic phthalates and thus, exposure to DIBP contributes to the cumulative risk from other antiandrogenic phthalates and its use should be permanently banned from use in children's toys and child care articles at levels greater than 0.1 percent.

Summary of Potential for Exposure

DIBP and its metabolites have been detected in people in biomonitoring studies [2]; in blood samples up to 541 ng/g [3], and DIBP metabolites in urine samples from 6 to 9 year old girls up to 363 ug/L [4].

DIBP has been reported in indoor air (0.50 ug/m^3 [5] and max 990 ng/m3 [6]) and dust (max 39.1 ug/g [6] and 3.81 mg/g [7]). DIBP has been reported in children's products [8, 9, 10, 11, 12].

List of References

1. European Chemicals Agency (ECHA) Candidate List of substances of very high concern (SVHC) for Authorisation. http://echa.europa.eu/candidate-list-table.
2. Centers for Disease Control and Prevention (CDC). 2015. Fourth National Report on Human Exposure to Environmental Chemicals: Updated Tables February 2015. Atlanta, GA. www.cdc.gov/exposurereport/.
3. Peters, R. J. B. 2005. Man-Made Chemicals in Maternal and Cord Blood. Netherlands Organisation for Applied Scientific Research. Greenpeace International and WWF-UK. March 2005.
4. Wolff, Mary S. Teitelbaum, Susan L., Windham, Gayle, Pinney, Susan M., Britton, Julie A., Chelimo, Carol, Godbold, James, Biro, Frank, Kushi, Lawrence H., Pfeiffer, chritine M., and Calafat, Antonia M. Pilot Study of Urinary Biomarkers of Phytoestrogens, Phthalates, and Phenols in Girls. Environmental Health Perspectives 115[No. 1], 116-121. 2006.
5. Adibi, J. J., Whyatt, R. M., Willaims, P. L., Calafat, A. M., Camann, D., Herrick, R., Nelson, H., Bhat, H. K., Perera, F. P., Silva, M. J., & Hauser, R. 2008. Characterization of Phthalate Exposure among Pregnant Women Assessed by Repeat Air and Urine Samples. *Environmental Health Perspectives*, 116(4): 467-473.
6. Rudel 2003 Rudel, Ruthann. Camann, David E., Spendler, John D., Korn, Leo R., and Brody, Julia G. Phthalates, Alkylphenols, Pesticides, PBDEs, and Other Endocrine-Disrupting Compounds in Indoor Air and Dust. Environ.Sci.Technol. 37, 4543-4553. 2003.
7. Bornehag 2005 Bornehag, C.-G., Lundgren, B., Weschler, C. J., Sigsgaard, T., Hagerhed-Engman, L., & Sundell, J. 2005. Phthalates in Indoor Dust and Their Association with Building Characteristics. *Environmental Health Perspectives*, 113(10): 1399-1404.
8. DEPA No. 60, Hansen, Ole Chr., Pedersen, Eva, and Danish Technological Institute. Migration and Health assessment of chemical substances in surface treated wooden toys. 2005. Survey of Chemical Substances in Consumer Products.
9. DEPA No. 70, Borling, Pernille, Engelund, Birgit, Sorensen, Hanne, Cohr, Karl-Heinz, and DTC Health and Environment. Survey, migration and health evaluation of chemical substances in toys and childcare products produced from foam plastic, 2006. Survey of Chemical Substances in Consumer Products.
10. DEPA No. 84, Svendsen, Nanna, Bjarnov, Erik, and Poulsen, Pia Brunn. Survey as well as health assessment of chemical substances in school bags, toy bags, pencil cases and erasers, 1-153. 2007. Survey of Chemical Substances in Consumer Products.
11. DEPA No. 90, Tonning, Kathe, Pedersen, Eva, Lomholt, Anette Drojdahl, Malmgren-Hansen, Bjorn, Woin, Per, Moller, Lise, and Bernth, Nils. Survey, emission and health assessment of chemical substances in baby products. 2008. Survey of chemical Substances in Consumer Products.
12. DF. Migration of Bisphenol A and Plasticizers from Plastic Feeding Utensils for Babies. ND05o410, 1-19. 2005b.

CAS 84-74-2 Di-n-butyl phthalate (DBP)

Summary of Toxicity

Dibutyl phthalate has been classified as a developmental and a reproductive toxicant by the National Toxicology Program Center for the Evaluation of Risks to Human Reproduction [1] and by the state of California [2]. The National Toxicology Program concluded that there is clear evidence of developmental and reproductive toxicity [1]. Adverse effects in animals included reduced fetal survival, reduced birth weight, reduced fertility in females, and damage to the developing male reproductive tract [1]. Dibutyl phthalate has been classified as a Category 1 endocrine disruptor by the European [3].

Summary of Potential for Exposure

The Danish EPA found dibutyl phthalate in numerous children's products including clothing (infant), foam toys, a fluorescent light stick, school supplies, and coatings on wood toys [4]. A Dutch study found dibutyl phthalate in a wide range of plastics in children's products [5]. Mono-n-butyl phthalate, a metabolite indicative of dibutyl phthalate exposure, was found in more than 99 percent of the U.S. population sampled in the NHANES survey [6].

List of References

1. U.S. Department of Health and Human Services, National Toxicology Program, Center for the Evaluation of Risks to Human Reproduction (CERHR). NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Di-*n*-Butyl Phthalate (DBP).
2. California EPA, Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. February 5, 2010.
3. European Commission DG Environment (2002). Endocrine disruptors: study on gathering information on 435 substances with insufficient data. Final report B4-3040/2001/325850/MAR/C2.
4. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Reports 40, 60, 70, 84, 102.
5. Dutch Inspectorate for Health Protection and Veterinary Public Health (VWA/KvW). Screening of Plastic Toys for Chemical Composition and Hazards, Report ND05o610/01, July 2005.
6. Hatch, EE, Nelson, JW, Mustafa Qureshi, M, Weinberg, J, Moore, LL, Singer, M, and Webster, TF. (2008). Association of urinary phthalate metabolite concentrations with body mass index and waist circumference: a Cross-sectional study of NHANES data 1999-2002. Environ Health 7: 27-41.

CAS 84-75-3 Di-n-hexyl Phthalate (DnHP)

Summary of Toxicity

Di-n-hexyl phthalate is considered a reproductive toxicant by the state of California and the National Toxicology Program [1,2]. Di-n-hexyl phthalate reduced fertility in both male and female rodents, reduced survival of offspring after birth, and caused severe degenerative changes in the seminiferous epithelium of male rats [1,2]. There is also evidence that exposure *in utero* can damage the male reproductive system, cause fetal growth retardation, malformations, and fetal loss [1,3].

Summary of Potential for Exposure

Di-n-hexyl phthalate is mainly a component of other phthalates. Phthalates are used primarily as plasticizers to add flexibility to plastics. Available information indicates that DnHP is manufactured in relatively small amounts but occurs in industrially important phthalates such as diisohexyl phthalate (up to 25 percent) [1]. Commercial phthalate substances containing DnHP may be added to the polyvinyl chloride (PVC) utilized in the manufacture of notebook covers, toys, and shoes [1,4]. We did not locate biomonitoring data nor could we find testing results that reported its presence in children's products.

List of References

1. U.S. Department of Health and Human Services, National Toxicology Program, Center for the Evaluation of Risks to Human Reproduction (CERHR) Monograph on the potential human reproductive and developmental effects of Di-*n* -Hexyl Phthalate (DnHP), NIH Publication No.03-4489. May 2003.
2. OEHHA, Reproductive and Cancer Hazard Assessment Branch, Proposition 65 Maximum Allowable Dose Level (MADL) for Reproductive Toxicity for Di-*n*-Hexyl Phthalate (DnHP) March 2008.
3. Saillenfait, AM et al. (2009) Differential developmental toxicities of di-n-hexyl phthalate and dicyclohexyl phthalate administered orally to rats. J Applied Toxicology Vol 29 (6): 510-521.
4. Australian Department of Health and Aging, Existing Chemical Hazard Assessment Report for Di-n-hexyl Phthalate, June 2008.

CAS 85-68-7 Butyl benzyl phthalate (BBP)

Summary of Toxicity

Butyl benzyl phthalate has been classified as a developmental and a reproductive toxicant by the National Toxicology Program Center for the Evaluation of Risks to Human Reproduction [1] and by the state of California [2]. The National Toxicology Program concluded that there is clear evidence of developmental toxicity and some evidence of male reproductive toxicity [1]. Effects

in animals included reduced sperm counts, reduced male fertility, prenatal mortality, and skeletal, visceral, and external malformations [1]. Butyl benzyl phthalate has been classified as a Category 1 endocrine disruptor by the European Union [3].

Summary of Potential for Exposure

The Danish EPA found butyl benzyl phthalate in the coating of a wood toy [4]. A Dutch study of plastics in children's products found butyl benzyl phthalate in 2 out of 7 polyurethane plastics [5]. Mono-benzyl phthalate, a metabolite indicative of butyl benzyl phthalate exposure, was found in more than 98 percent of the U.S. population sampled in the NHANES survey [6].

List of References

1. U.S. Department of Health and Human Services, National Toxicology Program, Center for the Evaluation of Risks to Human Reproduction (CERHR). NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Butyl Benzyl Phthalate (BBP). 2003.
2. California EPA, Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. February 5, 2010.
3. European Commission DG Environment (2002). Endocrine disruptors: study on gathering information on 435 substances with insufficient data.
4. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Report 70, 2006.
5. Dutch Inspectorate for Health Protection and Veterinary Public Health (VWA/KvW). Screening of Plastic Toys for Chemical Composition and Hazards, Report ND05o610/01, July 2005.
6. Hatch, EE, Nelson, JW, Mustafa Qureshi, M, Weinberg, J, Moore, LL, Singer, M, and Webster, TF. (2008). Association of urinary phthalate metabolite concentrations with body mass index and waist circumference: a Cross-sectional study of NHANES data 1999-2002. *Environ Health* 7: 27-41.

CAS 86-30-6 N-Nitrosodiphenylamine

Summary of Toxicity

N-nitrosodiphenylamine is considered a carcinogen by two authoritative sources [1,2]. In laboratory animals it causes bladder tumors, and reticulum cell sarcomas. It is structurally similar to other carcinogenic nitrosamines [1,2].

Summary of Potential for Exposure

N-nitrosodiphenylamine has been used as an additive in the manufacturing process for vehicle tires and some other rubber products [3]. Use and production has declined since the 1970s as it

was replaced by other chemicals [3]. The Danish EPA found N-nitrosodiphenylamine in one out of 4 balloons tested [4].

List of References

1. U.S. EPA Integrated Risk Information System (IRIS) for n-nitrosodiphenylamine (last revised 1993).
2. California Office of Environmental Health Assessment. Chemicals Known to the State of California to Cause Cancer or Reproductive Toxicity. September 11, 2009.
3. U.S. Department of Health and Human Services, Agency for Toxic Substances and Disease Registry. Toxicological Profile for N-Nitrosodiphenylamine. April, 1993.
4. Danish Ministry of the Environment, Environmental Protection Agency. 2007. Analysis of chemical substances in balloons. Survey of chemical substances in consumer products, No 89.

CAS 87-68-3 Hexachlorobutadiene (HCDB)

Summary of Toxicity

Hexachlorobutadiene is classified as a possible human carcinogen by the U.S. EPA [1] HCBD is genotoxic in mammalian cell cultures and binds with DNA in rats and mice *in vivo* [2]. Studies in animals show a selective adverse effect of HCBD on the kidney, specifically the proximal tubule [3,4]. HCBD accumulates in brain tissue and is neurotoxic in animal studies [3,4]. HCBD caused reproductive and developmental effects at oral doses that were neurotoxic and damaged the kidney of the mothers [4].

Summary of Potential for Exposure

This substance is listed as a Persistent, Bioaccumulative and Toxic (PBT) chemical under Washington State's PBT rule (WAC 173-333-320) [5]. HCBD is used as an industrial solvent and chemical intermediate in the manufacturer of rubber compounds, chlorofluorocarbons, and lubricants. It is also formed as a byproduct during the manufacture of some chlorinated compounds [2]. It has been widely detected in ambient air, water, foods, and human tissues [6].

List of References

1. U.S. EPA Integrated Risk Information System (IRIS) for Hexachlorobutadiene (CASRN 87-68-3). Last revised 1991.
2. California, EPA, Office of Environmental Health Hazard Assessment, Reproductive and Cancer Hazard Assessment Section. Evidence on the Carcinogenicity of 1,3-Hexachlorobutadiene, December 2000.
3. U.S. DHHS, Agency for Toxic Substances & Disease Registry Toxicological Profile for Hexachlorobutadiene, May 1994.

4. U.S. EPA, Office of Water, Health and Ecological Criteria Division. Health Effects Support Document for Hexachlorbutadiene, February 2003.
5. WA Department of Ecology. Summary of Technical Background Information for the Proposed PBT List (Revised Draft) October 2005.
6. WHO, International Agency for Research on Cancer (IARC), Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 73, Some Chemicals that Cause Tumors of the Kidney or Urinary Bladder in Rodents and Some Other Substances, 1999.

CAS 94-13-3 Propyl paraben

CAS 94-26-8 Butyl paraben

CAS 99-76-3 Methyl paraben

CAS 99-96-7 4-Hydroxybenzoic acid

CAS 120-47-8 Ethyl paraben

Due to similarities in use, exposure, and toxicity; the parabens are grouped in one summary.

Summary

These five chemicals meet the Department of Ecology's criteria for inclusion on the CHCC list. There is widespread exposure to parabens and p-hydroxybenzoic acid (PHBA) in the U.S., and because of evidence of endocrine disruption, it is important to collect more information about the use of these chemicals in children's products. Although there were both positive and negative studies for many potentially harmful effects, the weight of evidence indicates that these chemicals have estrogenic activity, can interfere with normal sperm development, and can alter testosterone levels. Several parties contend that parabens are safe at the levels used in products, but there is some debate about the margin of safety. While toxicity studies have focused on the effects of individual compounds, children's products often contain mixtures of two or more parabens. The parabens and phydroxybenzoic acid are structurally related compounds that often appear to have similar biological activities in experimental studies, and it is therefore important to consider the potential for additive or synergistic effects from exposure to mixtures of these chemicals.

Summary of Toxicity

All five chemicals have been classified as Category 1 endocrine disruptors by the European Union [1].

Estrogenic effects: All the widely used parabens have been shown to possess estrogenic activity to different extents in different assay systems *in vitro* and *in vivo*. Twenty-four out of twenty-five *in vitro* studies of estrogenic effects reported positive findings for parabens [2]. The estrogenic effects of treatment with multiple parabens appear to be additive [3]. The estrogenic activity of parabens is known to increase with increasing chain length and with branching of the alkyl chain. Estrogenic activity of PHBA has been demonstrated in several assays [2].

In uterotrophic assays, all four parabens and PHBA showed estrogenic activity in at least one *in vivo* study, while at least one other study showed negative results for each compound [2]. The lowest NOAELS and LOAELS are shown in the table below [2].

Table 1: Lowest NOAELS and LOAELS

Compound	NOAEL (mg/kg bw)	LOAEL (mg/kg bw)
Methyl paraben	5.5	16.5
Ethyl paraben	6	18
Propyl paraben	6.5	20
Butyl paraben	0.7	7
PHBA	0.5	5

Parabens generally have lower binding affinity to estrogen receptors than some other estrogenic ligands (such as 17*β*-estradiol or DES), and parabens are often termed “weak estrogens”. The estrogenic potentials of parabens have been studied in estrogen receptor (ER) *α* competitive binding assays, as well as studies that examined other aspects of estrogenicity including ligand ability to regulate an estrogenresponsive gene (ERE-CAT) transfected into MCF-7 cells, and ligand ability to regulate estrogendependent proliferation of MCF-7 cells. In the competitive binding assay, all parabens studied were at least 10,000 to 100,000 times less potent than 17*β*-estradiol [4]. In MCF-7 cells with a stably transfected estrogen-regulated ERE-CAT reporter gene, the tested parabens showed effects similar to 17*β*-estradiol, although at 1000–10,000 times greater concentrations. Depending on the endpoint measured and the specific paraben under study, these compounds are from 1000 to 1,000,000 times less potent than 17*β*estradiol [4].

However, with sufficient concentrations, the parabens gave responses in whole cell assays in terms of increased gene expression and cell proliferation in human breast cancer cells of the same magnitude as 17α-estradiol. This shows that parabens are not partial agonists, as might be implied by the term “weak,” but give full agonist responses in whole cells at sufficiently high concentrations. There is some indication that blood levels of parabens and their metabolites are

significantly higher than levels of natural estradiol and therefore, despite their lower binding affinity, could interfere with normal functioning of processes regulated by estrogens [2].

Effects on males: Studies in young male rats have shown adverse effects on sperm production and testosterone levels following oral exposure to parabens with longer side chains, specifically butyl paraben and propyl paraben.

Propyl paraben (8 weeks of dietary exposure) reduced daily sperm production at all doses tested (10 mg/kg, 100 mg/kg, and 1000 mg/kg). Similarly, serum testosterone levels were reduced at all three dose levels, but the effect was statistically significant only at 1000 mg/kg [5].

Butyl paraben reduced daily sperm production (testis sperm counts) as well as epididymal cauda sperm counts in a dose-related manner in all applied doses of approximately 10, 100, and 1000 mg/kg bw/day. Serum testosterone was reduced at 100 and 1000 mg/kg bw/day showing a dose-response relationship.

Relative epididymis weight was reduced at 100 and 1000 mg/kg bw/day with a dose-response relationship [6,7]. These results suggest a LOAEL of 10 mg/kg bw/day and no identifiable NOAEL for propyl paraben and butyl paraben.

Hoberman et al. [8] performed a repeat of the 2001 study by Oishi[6] by exposing young male rats in the diet to 10, 100, and 1000 mg/kg bw/day of butylparaben. This study was performed under Good Laboratory Practices conditions and included a higher number of animals than the Oishi study. The authors reported "no adverse effects" at all dose levels concluding a NOAEL of 1000 mg/kg bw/day. However, serum testosterone was reduced significantly after 3 weeks of dosing at 100 and 1000 mg/kg bw/day.

In a study of methyl paraben, Hoberman et al. reported statistically significant increases in the number of abnormal sperm in the two highest dose groups (100 mg/kg and 1000 mg/kg), and the testicular spermatid concentration appeared dose-dependently decreased (to 77 percent of control level), although this was not statistically significant [8].

Recent reports have documented that several parabens have the ability to bind to the androgen receptor and anti-androgenic activity was found for all the parabens tested. Additionally, in a recent *in vitro* study, methyl-, propyl- and butyl-4-hydroxybenzoate were shown to be androgen receptor antagonists, and some of the parabens could inhibit testosterone induced transcriptional activity by as much as 40 percent at a concentration of 10μM [9].

Summary of Potential for Exposure

Parabens are the most widely used preservatives in cosmetic products [10]. Various parabens and paraben mixtures are intentionally added to thousands of cosmetic products. Methyl paraben and propyl paraben have been Generally Recognized As Safe (GRAS) by the FDA for direct addition

to foods at levels less than 0.1 percent. Para-hydroxybenzoic (PHBA) acid is a precursor used in the manufacture of parabens and is also a common metabolite in humans following oral or dermal exposure to parabens.

Parabens are used in many children's products.

The Danish EPA identified methyl paraben as a listed ingredient in 95 of 208 children's personal care products, 7 of 28 sunscreens, and 7 of 32 lotions in studies of cosmetics marketed for children [11,12].

Methyl paraben was also found in 2 of 26 marker pen sets [13], 1 of 3 gel pens [13], and several slime toys [14,15]. A Dutch study of plastics in children's products found methyl paraben in 1 out of 18 samples of ethylene vinyl acetate plastic [16].

The Danish EPA identified ethyl paraben as a listed ingredient in 46 of 208 children's personal care products, 2 of 28 sunscreens, and 4 of 32 lotions in studies of cosmetics marketed for children [11,12]. Ethyl paraben was found in 1 of 14 slime toys [14].

The Danish EPA identified propyl paraben as a listed ingredient in 70 of 208 children's personal care products, 5 of 28 sunscreens, and 6 of 32 lotions in studies of cosmetics marketed for children [11,12]. Propyl paraben was found in 3 of 14 slime toys [14].

The Danish EPA identified butyl paraben as a listed ingredient in 48 of 208 children's personal care products, 1 of 28 sunscreens, and 1 of 32 lotions in studies of cosmetics marketed for children [11,12]. Butyl paraben was found in 1 of 14 slime toys [14].

The Danish EPA found para-hydroxybenzoic acid in 1 slime toy [15]. A Dutch study of plastics in children's products found para-hydroxybenzoic acid in 2 out of 18 samples of ethylene vinyl acetate plastic [16].

Analysis for parabens in urine of the general U.S. population was conducted in the NHANES survey during 2005 2006; and two or more were detected in almost all people sampled [17]. Table 4 below shows percent detection for four parabens.

Table 2: Percent detection for four parabens

Compound	Percentage detected
Methyl paraben	99.1 percent
Ethyl paraben	42.4 percent
Propyl paraben	92.7 percent
Butyl paraben	47.0 percent

For some children 6 to 11 years old, urinary excretion exceeded one milligram per day (Table 5) [17].

Table 3: Level of paraben urinary excretion

Compound	Urinary Excretion 50th percentile (µg/L)	Urinary Excretion 95th percentile (µg/L)
Methyl paraben	25	1560
Ethyl paraben	Not detected	9.9
Propyl paraben	2.5	125
Butyl paraben	Not detected	7.5

List of References

1. European Commission DG Environment (2002). Endocrine disruptors: study on gathering information on 435 substances with insufficient data. Final report B4-3040/2001/325850/MAR/C2.
2. Boberg, J., Taxvig, C., Christiansen, S., Hass, U. (2010). Possible endocrine disrupting effects of parabens and their metabolites. *Reproductive Toxicology 30(2):* 301-12.
3. Van Meeuwen, JA, van Son, O, Piersma, AH, de Jong, PC, and van den Berg, M. (2008). Aromatase inhibiting and combined estrogenic effects of parabens and estrogenic effects of other additives in cosmetics. *Toxicol Appl Pharmacol 230(3):* 372-82.
4. Golden, R., Gandy, J., Vollmer, G. (2005). A Review of the Endocrine Activity of Parabens and Implications for Potential Risks to Human Health. *Critical Reviews in Toxicology 35*:435–458.
5. Oishi S. (2002a). Effects of propyl paraben on the male reproductive system. *Food Chem Toxicol 40(12)*:1807–13.
6. Oishi S. (2001). Effects of butylparaben on the male reproductive system in rats. *Toxicol Ind Health 17(1):*31–9.
7. Oishi S. (2002b) Effects of butyl paraben on the male reproductive system in mice. *Arch Toxicol 76 (7):423–9.*
8. Hoberman AM, Schreur DK, Leazer T, Daston GP, Carthew P, Re T, et al. (2008). Lack of effect of butylparaben and methylparaben on the reproductive system in male rats. *Birth Defects Res B: Dev Reprod Toxicol 83(2*):123–33.
9. Chen J, Ahn KC, Gee NA, Gee SJ, Hammock BD, Lasley BL. (2007). Antiandrogenic properties of parabens and other phenolic containing small molecules in personal care products. Toxicol *Appl Pharmacol 221(3)*:278–84.
10. U.S. Food and Drug Administration (accessed March 31, 2011).

11. Danish Ministry of the Environment, Environmental Protection Agency. Survey of Chemical Substances in Consumer Products, Report 88, 2007.
12. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Report 102, 2009.
13. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Report 93, 2008.
14. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Report 67, 2005.
15. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Report 40, 2003.
16. Dutch Inspectorate for Health Protection and Veterinary Public Health (VWA/KvW). Screening of Plastic Toys for Chemical Composition and Hazards, Report ND05o610/01, July 2005.
17. Calafat, A., Ye, X., Wong, L-Y., Bishop, A., Needham, L. (2010). Urinary concentrations of four parabens in the U.S. population: NHANES 2005-2006. *Environ Health Perspect 118(5):* 679-685.
18. CAS 95-53-4 2-Aminotoluene (also called *ortho*-toluidine).

CAS 95-53-4 2-Aminotoluene (also called *ortho*-toluidine)

Summary of Toxicity

2-Aminotoluene is classified as a carcinogen by authoritative sources [1-4]. Animal evidence includes bladder and liver cancers as well as tumors in various tissues. Studies of exposed workers have reported that 2-aminotoluene and 2-aminotoluene hydrochloride exposure are associated with increased bladder cancer in humans. Definitive conclusions are limited by the fact that workers were almost always exposed to multiple chemicals including other possible bladder carcinogens [1,2].

Summary of Potential for Exposure

2-Aminotoluene and its hydrochloride salt are primarily used as chemical intermediates in making over 90 dyes and pigments. They are used in acid-fast dyestuffs, azo pigment dyes, sulfur dyes, indigo compounds, and optical brighteners. 2-Aminotoluene is also used as an intermediate for synthetic rubber and rubber vulcanizing chemicals, pharmaceuticals, and pesticides [1,2,5]. Studies by the Danish EPA detected this compound in 1 out of 4 balloon samples, in infant mittens, and in wool fabric. The source of residues may be synthetic rubber and dyes used in fabrics [6].

List of References

1. International Agency for Research on Cancer (IARC). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 77, Some Industrial Chemicals. Chapter on ortho-Toluidine. 2000.
2. National Toxicology Program, Report on Carcinogens, Eleventh Edition, Substance file for "*o*-Toluidine and *o*-Toluidine Hydrochloride CAS No. 95-53-4 and 636-21-5." Accessed online February 2010.
3. California Office of Environmental Human Hazard Assessment. OEHHA Cancer Potency Values. June 18, 2009. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Report 70, 2006.
4. American Conference of Governmental Industrial Hygienists (ACGIH). *o*-Toluidine in Documentation of the Threshold Limit Values for Chemical Substances and Physical Agents, 2008.
5. National Institutes of Health, National Library of Medicine, Hazardous Substances Data Bank Accessed May 2010.
6. Danish Ministry of the Environment, Environmental Protection Agency. Survey of Chemical Substances in Consumer Products.

CAS 95-80-7 2,4-Diaminotoluene

Summary of Toxicity

2,4-Diaminotoluene is classified as a carcinogen by authoritative sources [1-4]. Evidence is based on liver and mammary gland tumors in rats and mice. The European Union considers it a genotoxic carcinogen [3]. Oral studies in rodents have also shown adverse effects on the male reproductive tissues including testicular atrophy, altered levels of male hormones, and depression in spermatogenesis [3].

Summary of Potential for Exposure

2,4-Diaminotoluene is used in the production of toluene diisocyanate which is used to make polyurethane. It is or has been used in the production of dyes used to color paper, fur, leather, and textile fabrics [2,3]. 2,4-Diaminotoluene was detected in a children's doll fabric in testing of textile toys by the Dutch Government [5].

List of References

1. WHO International Agency for Research on Cancer (IARC) Monographs on the Evaluation of Carcinogenic Risks to Humans, Supplement No 7: Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs Volumes 1 to 42. 1987.
2. U.S. DHHS, PHS, National Toxicology Program. Report on Carcinogens, Eleventh Edition. 2005.

3. European Commission, Joint Research Centre. European Union Risk Assessment Report: 4-METHYL-M-PHENYLENEDIAMINE (TOLUENE-2,4-DIAMINE) RISK ASSESSMENT (CAS-No.: 95-80-7). May 2008.
4. California EPA, Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. February 5, 2010.
5. Dutch Inspectorate for Health Protection and Veterinary Public Health (VWA/KvW). Market Surveillances on Toy Safety: Isophoron and phenol in floatable toys, lead and cadmium in wooden toys, wood preservatives in wooden toys, and Azo dyes in textile toys. Vwa/Kvw Report ND04o063/01. September 2004.

CAS 100-41-4 Ethylbenzene

Summary of Toxicity

Ethylbenzene is classified as a carcinogen by authoritative sources [1,2,3]. Evidence is based on liver and kidney toxicity in rodents, kidney tumors in rats, and lung and liver tumors in mice [4]. Ethylbenzene can produce developmental effects in rabbits, mice, and rats although these effects may be secondary to maternal toxicity [4].

Summary of Potential for Exposure

Ethylbenzene is a high production chemical used primarily in the production of styrene monomer, with smaller amounts used to make several other chemicals [4]. Ethylbenzene is present at up to 25 percent in mixed xylenes which are used as solvents in many products [3]. Ethylbenzene was detected in consumer product testing by the Danish EPA in marker pens, slimy toys, and children's tents [5]. It was also listed on the MSDS of lacquer applied to wooden toys at 1-2.5 percent [5]. Ethylbenzene was detected widely in the blood of the general U.S. population [6].

List of References

1. National Toxicology Program. 1999. NTP technical report on the toxicology and carcinogenesis studies of ethylbenzene in F344/N rats and B6C3F1 mice (inhalation studies). Research Triangle Park, NC: National Toxicology Program, U.S. Department of Health and Human Services. NTP TR 466.
2. California Environmental Protection Agency, Office of Environmental Health Hazard Assessment. Public Health Goal for Ethylbenzene in Drinking Water. December, 1997.
3. WHO, International Agency for Research on Cancer (IARC). Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 77, Some Industrial Chemicals. 2000.
4. U.S. DHHS, Agency for Toxic Substances & Disease Registry. Toxicological Profile for Ethylbenzene. 2010.

5. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Reports 33, 46, 67 and 93 (2003-2008).
6. Centers for Disease Control and Prevention (CDC), Fourth National Report on Human Exposure to Environmental Chemicals, December 2009.

CAS 100-42-5 Styrene

Summary of Toxicity

Styrene is listed as a carcinogen by IARC based on limited evidence of lymphatic and hematopoietic cancer in occupationally exposed people and limited evidence of cancer in animals [1]. Styrene appears to produce developmental effects in laboratory animals but the effects may be secondary to maternal toxicity [2]. Developmental effects reported include reduced growth and survival and alterations in neurochemicals [1,2]. Central and peripheral nervous system effects have also been reported in exposed workers [1].

Summary of Potential for Exposure

Styrene is listed as a carcinogen by IARC based on limited evidence of lymphatic and hematopoietic cancer in occupationally exposed people and limited evidence of cancer in animals [1]. Styrene appears to produce developmental effects in laboratory animals but the effects may be secondary to maternal toxicity [2]. Developmental effects reported include reduced growth and survival and alterations in neurochemicals [1,2]. Central and peripheral nervous system effects have also been reported in exposed workers [1].

List of References

1. WHO, International Agency for Research on Cancer (IARC) Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 82, Some Traditional Herbal Medicines, Some Mycotoxins, Naphthalene and Styrene. February 2002.
2. U.S. DHHS, National Toxicology Program, Center for the Evaluation of Risks to Human Reproduction. Monograph on the Potential Human Reproductive and Developmental Effects of Styrene. NIH Pub. No. 06-4475, February 2006.
3. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Reports 46, 67 and 68.
4. Centers for Disease Control and Prevention. Fourth National Report on Human Exposure to Environmental Chemicals, 2009.

CAS 104-40-5 4-Nonylphenol

Summary of Toxicity

4-nonylphenol has been classified as a Category 1 endocrine disruptor by the European Union [1]. Uterotrophic assays indicate that nonylphenol has estrogenic activity [2-4].

Summary of Potential for Exposure

The Danish EPA found 4-nonylphenol in 1 out of 2 nursing pillows [5]. 4-nonylphenol was found in a variety of plastics in a Dutch survey of plastic children's toys [6]. In a large biomonitoring study of the general U.S. population, 51 percent of people had 4-nonylphenol in their urine [7].

List of References

1. European Commission DG Environment (2002). Endocrine disruptors: study on gathering information on 435 substances with insufficient data. Final report B4-3040/2001/325850/MAR/C2.
2. Odum, J, Pyrah, IT, Foster, JR, Van Miller, JP, Joiner, RL, and Ashby, J. (1999). Comparative activities of p-nonylphenol and diethylstilbestrol in noble rat mammary gland and uterotrophic assays. *Regul Toxicol and Pharmacol 29(2 Pt 1)*: 184-95.
3. Kim, HS, Shin, JH, Moon, HJ, Kang, IH, Kim, TS, Kim, IY, Seok, JH, Pyo, MY, and Han, SY. (2002). Comparative estrogenic effects of p-nonylphenol by 3-day uterotrophic assay and female pubertal onset assay. *Reprod Toxicol 16(3)*: 259-68.
4. Kang, KS, Kim, HS, Ryu, DY, Che, JH, and Lee, YS. (2000). Immature uterotrophic assay is more sensitive than ovariectomized uterotrophic assay for the detection of estrogenicity of p-nonylphenol in Sprague-Dawley rats. *Toxicol Lett 118(1-2)*: 109-15.
5. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Report 90, 2008.
6. Dutch Inspectorate for Health Protection and Veterinary Public Health (VWA/KvW). Screening of Plastic Toys for Chemical Composition and Hazards, Report ND05o610/01, July 2005.
7. Calafat, AM, Kuklenyik, Z, Reidy, JA, Caudill, SP, Ekong, J, and Needham, LL. (2005). Urinary concentrations of bilphenol A and 4-nonylphenol in a human reference population. *Environ Health Perspect 113*: 391-5.

CAS 106-47-8 4-Chloroaniline

Summary of Toxicity

para-Chloroaniline is classified as a carcinogen by authoritative sources [1-3]. Evidence is based primarily on cancers in the spleen and liver of test animals [1]. Both animal and human occupational exposures have resulted in methemoglobinemia, a blood disorder that results in hypoxia. Infants have also suffered from methemoglobinemia when chlorohexidine, which decomposes spontaneously to *para*-chloroaniline, was used in their hospital incubators [1,4].

Summary of Potential for Exposure

para-Chloroaniline has been used in the manufacture of dyes, pigments, and as a chemical intermediate in the production of other chemicals [1,4]. The general public may be exposed to

para-chloroaniline through dyed textiles, printed papers, cosmetics, and pharmaceutical products [4]. Testing on consumer products by the Danish EPA found the chemical in acrylic paints for children and dyed fabric on a stuffed bear [5].

List of References

1. WHO, International Agency for Research on Cancer (IARC) Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume No 57: Occupational Exposures of Hairdressers and Barbers and Personal Use of Hair Colourants; Some Hair Dyes, Cosmetic Colourants, Industrial Dyestuffs and Aromatic Amines. 1993.
2. European Commission, Joint Research Centre ESIS data sheet for 4-chloroaniline (CAS# 106-47-8). Accessed June 2010.
3. California Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. Feb 5, 2010.
4. WHO, International Programme on Chemical Safety (IPCS) Concise International Chemical Assessment Document 48: 4-chloroaniline, 2003.
5. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Report 23and 93 (2003, 2008).

CAS 107-13-1 Acrylonitrile

Summary of Toxicity

Acrylonitrile is classified as a carcinogen by authoritative sources [1-5]. Long term studies in laboratory animals have shown cancers of the digestive tract, mammary gland, and the central nervous system [2,4]. Occupational studies have shown excesses of lung and prostate cancers as well as other sites in humans [2].

Summary of Potential for Exposure

Acrylonitrile is an important industrial chemical intermediate. It is used extensively in the manufacture of synthetic fibers (e.g. acrylic fibers). It is also used in copolymer plastics (e.g., ABS and SAN) for a variety of consumer goods such dinnerware, food containers, toys, luggage, and small appliances [2,4]. It is used in the manufacture of children's products but we were unable to locate any testing data for end use products covered by CSPA.

List of References

1. WHO, International Agency for Research on Cancer. IARC Monograph on the Evaluation of Carcinogenic Risks to Humans, Volume 71, Re-evaluation of Some Organic Chemicals, Hydrazine and Hydrogen Peroxide. 1999.
2. U.S. DHHS, PHS, National Toxicology Program. Report on Carcinogens, Eleventh Edition. 2005.

3. U.S. EPA Integrated Risk Information System (IRIS) for Acrylonitrile (last revised 1993).
4. European Commission, Joint Research Centre. European Risk Assessment Report: Acrylonitrile, 2004.
5. California Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. Feb 5, 2010.

CAS 107-21-1 Ethylene glycol

Summary of Toxicity

Ethlyene glycol causes fetal death and malformations when fed to rodents during pregnancy [1,2]. The National Toxicology Program concluded that "ethylene glycol may adversely affect human development if oral exposures are sufficiently high [1]."

Summary of Potential for Exposure

Ethylene glycol lowers the freezing point of water. It is used in antifreeze, in aircraft deicing fluids, and in condensers and heat exchangers. It is a chemical intermediate in the production of polyester compounds [1,3]. It has also been used as a glycerin substitute in commercial products such as paints, lacquers, detergents, and cosmetic [3].

In two online databases ethylene glycol is listed as an ingredient in a diaper ointment [4] and in body wash/cleansers, acne treatment, athlete's foot treatment, hair color, hair conditioners, and a home hair perm kit [5]. Product testing for the Danish EPA detected ethylene glycol in balloons and tents [6].

List of References

1. U.S. Department of Health and Human Services, National Toxicology Program, Center for the Evaluation of Risks to Human Reproduction (CERHR) Monograph on the potential human reproductive and developmental effects of Ethylene Glycol. January 2004.
2. REPROTEXT Thomson Reuters (Healthcare) Inc. File for Ethylene Glycol. Database Version 5.1 Greenwood Village, CO. (accessed 2009).
3. ACGIH: Documentation of the Threshold Limit Values and Biological Exposure Indices (Supplement), 6th ed, American Conference of Governmental Industrial Hygienists, Inc, Cincinnati, OH, 1996.
4. National Institutes of Health, National Library of Medicine, Household Products Database. Accessed May 2010.
5. Environmental Working Group. Skin Deep Cosmetic Safety Database. Accessed online May 2010.

6. Danish Ministry of the Environment, Environmental Protection Agency. Survey of Chemical Substances in Consumer Products, Report 46 and 89 (2005-2007).

CAS 108-88-3 Toluene

Summary of Toxicity

Toluene is a known neurotoxicant and is listed as a developmental toxicant by the state of California [1]. Studies in laboratory animals indicate that gestational exposure can induce alterations in brain development and result in low birth weight [2]. Studies of human babies born to mothers who abused solvents during pregnancy (e.g., glue sniffers) have reported similar effects: perinatal death, preterm delivery, small brain size at birth, low birth weight, and neurodevelopmental delays [3,4].

Summary of Potential for Exposure

Toluene is a high production chemical that is widely used as a solvent in paints, coatings, adhesives, inks, and cleaning agents [4,5]. It is used in the production of other chemicals such as benzene [3]. Toluene is also used in production of polymers to make nylon, plastic soda bottles, and polyurethanes; and in some pharmaceuticals, and dyes [5]. Toluene is listed as an ingredient in hundreds of paints, sealers, strippers, auto shop and cleaning items [6] but few of these products would be marketed to children. Some hobby glues and liquid nails with toluene might be used by children. Toluene was detected in a wide variety of children's products in consumer product testing by the Danish EPA. It was detected in 1 of 5 infant jackets, 2 of 4 infant mittens, 2 of 3 school erasers, 1 or 4 pencil cases, 6 of 6 tents, 14 of 14 slimy toys, and 2 of 15 wooden toys. It was also reported in hobby adhesives [7].

List of References

1. California Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. Feb 5, 2010.
2. U.S. EPA Integrated Risk Information System (IRIS) Toxicological Review for Toluene 2005.
3. Centers for Disease Control and Prevention (CDC), Fourth National Report on Human Exposure to Environmental Chemicals, December 2009.
4. REPROTEXT Thomson Reuters (Healthcare) Inc., File for Toluene. Database Version 5.1 Greenwood Village, CO. (accessed 2009).
5. U.S. DHHS, Agency for Toxic Substances & Disease Registry. Toxicological Profile for Toluene. September 2000.
6. National Institutes of Health, National Library of Medicine, Household Products Database.
7. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Reports 46, 60, 67, 68, and 84.

CAS 108-95-2 Phenol

Summary of Toxicity

High levels of oral or inhalation exposure during pregnancy resulted in dose-dependent fetotoxicity in animals studies [1,2,3]. The EPA oral reference dose is based on a developmental toxicity study in rats which showed decreased fetal body weight and delayed ossification of bones [4]. Phenolic disinfectants in hospital neonatal units have caused outbreaks of hyberbilirubinemia in infants and some cases of fetal death [5].

Summary of Potential for Exposure

Phenol was found in various children's products in testing by the Danish EPA [6]. It was detected in a nursing pillow, a balloon, glitter glue, an infant jacket, in ABS and PVC plastics, a tent, and a coating on a wooden toy. Phenol is also listed as an ingredient in diaper rash ointment, lip products, and dandruff shampoo in an online database of personal care products [7].

List of References

1. California EPA, Office of Environmental Human Health Assessment (OEHHA) Evidence on the Developmental and Reproductive Toxicity of Phenol, Draft July 2003.
2. U.S. Department of Health and Human Services, Agency for Toxic Substances & Disease Registry. Toxicological Profile for Phenol (ATSDR 2008).
3. REPROTEXT Thomson Reuters (Healthcare) Inc. File for Phenol. Database Version 5.1 Greenwood Village, CO. (Accessed 2010).
4. U.S.EPA, Integrated Risk Information System (IRIS). Phenol (last revised 2002).
5. National Institutes of Health, National Library of Medicine Hazardous Substances Data Bank file for Phenol.
6. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Report 90, 2008.
7. Environmental Working Group. Skin Deep Cosmetic Safety Database. Accessed online May 2010.

CAS 109-86-42 2-Methoxyethanol (also called ethylene glycol monomethyl ether)

Summary of Toxicity

2-Methoxyethanol is listed as a reproductive hazard by the state of California and the European Union [1,2]. It causes reproductive and developmental toxicity in laboratory animals including reduced fertility, effects on sperm and male gonads, fetotoxicity, and low birthweights [3-6]. Cases of occupational exposures associated with testicular effects have been reported [4]. Hematotoxic effects have also been reported [4,5].

Summary of Potential for Exposure

2-Methoxyethanol has been used as a solvent for low viscosity cellulose acetate, varnishes, dyes, and resins. It may also be used in paper board manufacturing.[4] The Danish EPA tested coatings on wooden toys and found it in 1 of the 15 coatings tested.[7]

List of References

1. California Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. Feb 5, 2010.
2. European Commission, Joint Research Centre, Institute for Health and Consumer Protection. European Chemical Substances Information System for 2-methoxyethanol. Accessed online May 2010.
3. European Commission, European Chemcials Bureau. IUCLID dataset for 2-methoxyethanol. 2000.
4. National Institutes of Health, National Library of Medicine Hazardous Substances Data Bank.
5. American Conference of Governmental Industrial Hygienists. Documentation of Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices for 2001. Cincinnati, OH. 2001.
6. U.S. Department of Health and Human Services, National Toxicology Program. Abstracts of NTP Reproductive Studies on Ethylene glycol monomethyl ether.
7. Danish Ministry of the Environment, Environmental Protection Agency. Survey of Chemical Substances in Consumer Products Report 60, 2005.

CAS 110-80-5 Ethylene glycol monoethyl ether (also called 2-ethoxyethanol)

Summary of Toxicity

Ethylene glycol monoethyl ether is listed as a reproductive hazard by the state of California and the European Union [1,2]. Consistent adverse effects on male reproductive organs and sperm have been observed in multiple species. These effects include testicular atrophy, degeneration of testicular tubules, decrease in sperm counts and motility, and an increase in the number of abnormal sperm cells [3]. Ethylene glycol monoethyl ether has been shown to affect fertility in both sexes of rodents and cause developmental effects [3]. Hematotoxic effects, such as hemolytic anemia, have also been reported [3].

Summary of Potential for Exposure

Ethylene glycol monoethyl ether is primarily used as a chemical intermediate in the chemical industry. It is also used as an industrial solvent for nitrocellulose, varnish removers, cleansing solutions, and dye baths. It has been used for the formulation of paints, lacquers, varnishes, and

printing inks [3,4]. It's use as a solvent in cleaning agents and cosmetics may have been phased out in Europe due to concerns about reproductive toxicity [3]. Testing by the Danish EPA found it in marker pen sets, the coatings of wooden toys, and children's tents [5].

List of References

1. California Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. Feb 5, 2010.
2. European Commission, Joint Research Centre, Institute for Health and Consumer Protection. European Chemical Substances Information System for Ethylene glycol monoethyl ether. Accessed online May 2010.
3. European Commission Joint Research Centre: Institute for Health and Consumer Protection, ORATS. European Union Risk Assessment Report for 2-Ethoxyethanol (CAS# 110-80-5) Draft December 2007and Draft Human Health Risk Assessment, October 2008.
4. National Institutes of Health, National Library of Medicine Hazardous Substances Data Bank Accessed May 2010.
5. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Report 93, 60, and 46.

CAS 115-86-6 Triphenyl phosphate (TPP)

Summary of Toxicity

EPA classified Triphenyl phosphate (TPP) as a high hazard for toxicity from repeated exposures [1]. Decreased body weight gain in adult rats was the most sensitive endpoint reported following repeated oral exposure; the lowest-observed-adverse-effect-level (LOAEL) was 161 mg/kg-day. At higher doses, reproductive and fetal effects were observed [1]. TPP appears to be active in endocrine tissues. In a recently published study, mice exposed to 300 mg/kg-day TPP orally for 35 days had decreased testes weight, histopathological damage, decreased testicular testosterone levels, decreased expression of genes related to testosterone synthesis, and signs of oxidative stress in the liver [2]. *In vitro* testing shows that TPP is a moderate androgen-receptor binder and can inhibit receptor function (testosterone-induced androgen-receptor-dependent activity) [1]. TPP and its hydroxylated metabolites acted as estrogen receptor agonists in other *in vitro* studies [3,4]. Only limited human evidence of endocrine disruption is available. A study in Boston, Massachusetts reported that men living in homes with higher TPP in house dust had decreased sperm counts and altered hormone (prolactin) levels [5].

There is also emerging evidence that TPP may cause long-lasting metabolic disruption in rats exposed during fetal and nursing periods [6,7]. Green et al. 2016 showed that developmental exposure to TPP alone caused accelerated onset of type 2 diabetes in a rat diabetes model and increased body fat later in life [7]. The very low dose used in this study (17 µg/rat-day; less than

0.5 mg/kg-day) was not associated with overt toxicity or weight change in treated dams or offspring at birth. It was equivalent to the dose of TPP present in a study by Patisaul et al. 2013, that observed metabolic disruption in offspring following developmental exposure to 1 mg/rat-day of Firemaster® 550 [6]. These study results suggest a high hazard for developmental toxicity.

Investigators at the National Toxicology Program used cell-based *in vitro* assays and assays in rapidly developing whole organisms (in this case, the nematode *C. elegans*) to screen for potential developmental toxicity and neurotoxicity of a number of phosphate flame retardants [8,9]. TPP had a more potent impact on larval development than PBDE[16] flame retardants and was a relatively strong inhibitor of mitochondrial activity in *in vitro* testing [9].

Summary of Potential for Exposure

TPP is a plasticizing flame retardant in polyvinyl chloride (PVC). It is also used as a flame retardant in other polymers, textiles, polyurethane foam, electronic circuit boards, photographic films, and building materials [10,11]. It is a component of Firemaster® 550 used in polyurethane foams and has been detected in baby products [11,12], other children's products, carpet pads, and plastic parts of LCD monitors [13]. TPP is an additive flame retardant and migrates from computer monitors and television sets [11]. TPP is also used as a plasticizer and may be in clothing, textiles, cosmetics, and personal care products [14]. It is listed as an ingredient in nail polish and a recent biomonitoring study showed short-term spikes in exposure following application of nail polish [15]. U.S. national production volume was reported to be 10,796,422 million pounds per year in 2012 [16].

Because of its physical properties, TPP that escapes from consumer products, either by emission or abrasion, is likely to end up in indoor dust. TPP was detected at high levels in indoor dust in studies of homes in North Carolina, Boston, California, and Canada [17-20]. Maximum detected level was 1,800 µg/g dust. It has also been detected in U.S. office and vehicle dust [21]. TPP has also been measured in the indoor air of homes and public buildings in a number of countries. Maximum level reported was 100 ng/m^3 [11].

Diphenyl phosphate (DPHP), a metabolite of TPP, has been found in urine at high frequency (greater than 90 percent) in North American biomonitoring studies including Boston adults [22], New Jersey mothers and toddlers [23], California mothers and their children aged 2-70 months [24], and North Carolina babies [25]. Levels measured in children were higher than their mothers [23,24,26] and were higher in children with more reported hand-to-mouth behaviors [23,24]. Mean and median levels of DPHP in urine reported across these studies have been less than 3.2 ng/mL with a maximum reported level of 140 ng/mL. TPP has been measured up to 140 ng/g lipid in human breast milk in Asian and Swedish studies [27,28]. TPP was detected in 98 percent

[16] Pbde - polybrominated diphenyl ether

of hair samples and 74 percent of finger and toenail samples in a population of young adults in Indiana [29].

TPP appears to be ubiquitous in the environment and has been detected in drinking water, river water, seawater, rainwater, snow, wastewater effluent, ambient air, and indoor air [1,11,18,30-33].

List of References

1. EPA, Flame Retardants Used in Flexible Polyurethane Foam: An Alternatives Assessment Update. 2015, U.S. Environmental Protection Agency.
2. Chen, G., et al., Exposure of male mice to two kinds of organophosphate flame retardants (OPFRs) induced oxidative stress and endocrine disruption. Environ Toxicol Pharmacol, 2015. **40**(1): p. 310-8.
3. Hiroyuki Kojima, S.T., Nele Van den Eede, Adrian Covaci, Effects of primary metabolites of organophosphate flame retardants on transcriptional activity via human nuclear receptors. Toxicology Letters, 2016. **245**: p. 31-39.
4. Boris V. Krivoshiev, F.D., Adrian Covaci, Ronny Blust, Steven J. Husson, Assessing in-vitro estrogenic effects of currently-used flame retardants. Toxicology in Vitro, 2016. **33**: p. 153-162.
5. Meeker, J.D. and H.M. Stapleton, House dust concentrations of organophosphate flame retardants in relation to hormone levels and semen quality parameters. Environ Health Perspect, 2010. **118**(3): p. 318-23.
6. Patisaul, H.B., et al., Accumulation and endocrine disrupting effects of the flame retardant mixture Firemaster(R) 550 in rats: an exploratory assessment. J Biochem Mol Toxicol, 2013. **27**(2): p. 124-36.
7. Green, A.J., et al., Perinatal triphenyl phosphate exposure accelerates type 2 diabetes onset and increases adipose accumulation in UCD-type 2 diabetes mellitus rats. Reprod Toxicol. 2016 Jul 12. doi: 10.1016/j.reprotox.2016.07.009. [Epub ahead of print].
8. Behl, M., et al., Use of alternative assays to identify and prioritize organophosphorus flame retardants for potential developmental and neurotoxicity. Neurotoxicology and Teratology **52** (2015) 181–193.
9. Behl, M., et al., Comparative Toxicity of Organophosphate Flame Retardants and Polybrominated Diphenyl Ethers to Caenorhabditis elegans. Toxicol Sci. 2016 Aug 26. pii: kfw162 [Epub ahead of print].
10. Brooke, D., Crookes, M, Quaterman, P, Burns, J, Environmental Risk Evaluation Report: Triphenyl Phosphate (CAS no. 115-86-6). 2009, Environment Agency, Bristol, UK: United Kingdom. p. 140.
11. Toxicology Excellence for Risk Assessment (TERA), Environmental Concentrations and Consumer Exposure Data for Selected Flame Retardants (TDCPP, TCPP, TEP, TPP). June 1, 2015: Consumer Product Safety Commission contract Number CPSC-D-12-0001.

12. Stapleton, H.M., et al., Identification of flame retardants in polyurethane foam collected from baby products. Environ Sci Technol, 2011. **45**(12): p. 5323-31.
13. Ecology, Flame Retardants in General Consumer and Children's Products. Washington State Department of Ecology, June 2014, Publication No. 14-04-021.
14. ECHA, Brief Profiles: Triphenyl Phosphate [accessed September 2016]. https://echa.europa.eu/information-on-chemicals.
15. Emma Mendelsohn, A.H., Kate Hoffman, Craig M. Butt, Amelia Lorenzo, and T.F.W. Johanna Congleton, Heather M. Stapleton, Nail polish as a source of exposure to triphenyl phosphate. Environment International, 2016. **86**: p. 45-51.
16. EPA. Chemical Data Access Tool (CDAT) - Chemical Data Reporting (CDR) information on the production and use of chemicals manufactured or imported into the United States. 2012 10/15/2015 10/30/2015]. http://java.epa.gov/oppt_chemical_search/.
17. Hoffman, K., et al., Monitoring indoor exposure to organophosphate flame retardants: hand wipes and house dust. Environ Health Perspect, 2015. **123**(2): p. 160-5.
18. Stapleton, H.M., et al., Detection of Organophosphate Flame Retardants in Furniture Foam and U.S. House Dust. Environmental Science & Technology, 2009. **43**(19): p. 7490-7495.
19. Dodson, R.E., et al., After the PBDE phase-out: a broad suite of flame retardants in repeat house dust samples from California. Environ Sci Technol, 2012. **46**(24): p. 13056-66.
20. Fan, X., et al., Simultaneous determination of thirteen organophosphate esters in settled indoor house dust and a comparison between two sampling techniques. Sci Total Environ, 2014. **491-492**: p. 80-6.
21. Springer, C., et al., Rodent thyroid, liver, and fetal testis toxicity of the monoester metabolite of bis-(2-ethylhexyl) tetrabromophthalate (tbph), a novel brominated flame retardant present in indoor dust. Environ Health Perspect, 2012. **120**(12): p. 1711-9.
22. Meeker, J.D., et al., Urinary metabolites of organophosphate flame retardants: temporal variability and correlations with house dust concentrations. Environ Health Perspect, 2013. **121**(5): p. 580-5.
23. Butt, C.M., et al., Metabolites of organophosphate flame retardants and 2-ethylhexyl tetrabromobenzoate in urine from paired mothers and toddlers. Environ Sci Technol, 2014. **48**(17): p. 10432-8.
24. Butt, C.H., K; Chen, A; Lorenzo, A; Congleton, J; Stapleton, HM, Regional comparison of organophosphate flame retardant (PFR) urinary metabolites and tetrabromobenzoic acid (TBBA) in mother-toddler pairs from California and New Jersey. Environment International, 2016. **94**: p. 627-34.
25. Hoffman, K., et al., High Exposure to Organophosphate Flame Retardants in Infants: Associations with Baby Products. Environ Sci Technol, 2015. **49** (24), pp 14554–14559.
26. Cequier, E., et al., Human exposure pathways to organophosphate triesters - a biomonitoring study of mother-child pairs. Environ Int, 2015. **75**: p. 159-65.

27. Kim, J.W., et al., Organophosphorus flame retardants (PFRs) in human breast milk from several Asian countries. Chemosphere, 2014. **116**: p. 91-7.
28. Sundkvist, A.M., U. Olofsson, and P. Haglund, Organophosphorus flame retardants and plasticizers in marine and fresh water biota and in human milk. J Environ Monit, 2010. **12**(4): p. 943-51.
29. Liang-Ying Liu, K.H., Ronald A. Hites, and Amina Salamova, Hair and Nails as Noninvasive Biomarkers of Human Exposure to Brominated and Organophosphate Flame Retardants. Environ. Sci. Technol. 2016, 2016. **50**: p. 3065−3073.
30. van der Veen, I. and J. de Boer, Phosphorus flame retardants: properties, production, environmental occurrence, toxicity and analysis. Chemosphere, 2012. **88**(10): p. 1119-53.
31. Salamova, A., et al., High Levels of Organophosphate Flame Retardants in the Great Lakes Atmosphere. Environmental Science & Technology Letters, 2014. **1**(1): p. 8-14.
32. Cao, S., et al., Levels and distributions of organophosphate flame retardants and plasticizers in sediment from Taihu Lake, China. Environ Toxicol Chem, 2012. **31**(7): p. 1478-84.
33. Stiles, R., et al., Measurement of drinking water contaminants by solid phase microextraction initially quantified in source water samples by the USGS. Environ Sci Technol, 2008. **42**(8): p. 2976-81.

CAS 115-96-8 Tris(2-chloroethyl) phosphate (TCEP)

Summary of Toxicity

Tris(2-chloroethyl) phosphate is classified as a carcinogen by the state of California and a reproductive hazard by the European Union [1,2]. TCEP caused kidney tumors and cancers in rats and mice in studies conducted by the National Toxicology Program [3]. In studies reviewed bythe European Union, TCEP caused significant impairiment of fertility and adverse effects in male reproductive organs and sperm parameters [2].

Summary of Potential for Exposure

TCEP has been used has an additive plasticizer and viscosity regulator with flame-retarding properties for polyesters, polyurethane, polyvinyl chloride, and other polymers [4]. TCEP can be released from items treated with TCEP flame retardant such as foam rubber, carpets, and plastic materials as a result of abrasion [2]. TCEP was detected in the foam and covering fabric of a foam play cube in testing of toys by the Danish EPA [5]. In a study by the Netherland Government, TCEP was detected in ethylene vinyl acetate and polyurethane plastics in toys that are likely to be sucked by children under two years old [6]. TCEP production and use have reportedly declined since other flame retardants were adopted for rigid and flexible polyurethane foams [2].

List of References

1. California Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. Feb 5, 2010. O, International
2. European Commission Joint Research Centre: Institute for Health and Consumer Protection, European Union Risk Assessment Report for TRIS (2-CHLOROETHYL) PHOSPHATE, TCEP. July 2009.
3. NTP (1991). National Toxicology Program: Technical report series No. 391. "Toxicology and carcinogenesis studies of tris(2-chloroethyl)phosphate (CAS No. 115-96-8) in F344/N rats and B6C3F1 mice (gavage studies)", US Department of Health and Human Services.
4. National Institutes of Health, National Library of Medicine Hazardous Substances Data Bank Accessed May 2010.
5. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products Report.
6. Dutch Inspectorate for Health Protection and Veterinary Public Health (VWA/KvW). Screening of Plastic Toys for Chemical Composition and Hazards, Report ND05o610/01, July 2005.

CAS 117-81-7 Di-2-ethylhexyl phthalate (DEHP)

Summary of Toxicity

Di-2-ethylhexyl phthalate (DEHP) has been listed as a carcinogen by authoritative sources [1,2,3]. It has been found to cause hepatocellular carcinomas in laboratory animals [1,2]. DEHP has been classified as a developmental and a reproductive toxicant by National Toxicology Program Center for the Evaluation of Risks to Human Reproduction and the state of California [3,4]. The National Toxicology Program concluded that there is clear evidence it can cause developmental and reproductive toxicity in laboratory animals [4]. Effects included skeletal and cardiovascular malformations, neural tube defects, developmental delays, intrauterine death and adverse effects on the male and female reproductive tract [4]. DEHP has been classified as a Category 1 endocrine disruptor by the European Union [5].

Summary of Potential for Exposure

The Danish EPA found di-2-ethylhexyl phthalate in numerous children's products including clothing (infant), foam toys, pacifiers, school supplies, slimy toys, packaging for cosmetics, a perambulator cover, and the coatings on a wood toy [6]. Dutch studies found it in a wide range of plastics in children's products [7] and in a baby feeding spoon [8]. Several metabolites indicative of di-2-ethylhexyl phthalate exposure were found in the population sampled for the NHANES survey, indicating that greater than 98 percent of the U.S. population is exposed to DEHP [9].

List of References

1. U.S. DHHS, PHS, National Toxicology Program. Report on Carcinogens, Eleventh Edition. 2005.
2. U.S. EPA, Integrated Risk Information System. Di(2-ethylhexyl)phthalate (DEHP) (last revised 1993).
3. California EPA, Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. February 5, 2010.
4. U.S. Department of Health and Human Services, National Toxicology Program, Center for the Evaluation of Risks to Human Reproduction (CERHR). NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Di(2-Ethylhexyl) Phthalate (DEHP). 2006.
5. European Commission DG Environment (2002). Endocrine disruptors: study on gathering information on 435 substances with insufficient data. Final report B4-3040/2001/325850/MAR/C2.
6. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Reports 60, 67, 70, 84,88, 90, 102.
7. Dutch Inspectorate for Health Protection and Veterinary Public Health (VWA/KvW). Screening of Plastic Toys for Chemical Composition and Hazards, Report ND05o610/01, July 2005.
8. Dutch Food and Consumer Product Safety Authority. Migration of Bisphenol A and Plasticizers from Plastic Feeding Utensils for Babies. Report ND05o410, June 2005.
9. Hatch, EE, Nelson, JW, Mustafa Qureshi, M, Weinberg, J, Moore, LL, Singer, M, and Webster, TF. (2008). Association of urinary phthalate metabolite concentrations with body mass index and waist circumference: a Cross-sectional study of NHANES data 1999-2002. *Environ Health* 7: 27-41.

CAS 117-82-8 Di(2-methoxyethyl) phthalate (DMEP)

Summary of Toxicity

In December 2011, the European Union added di(2-methoxyethyl) phthalate (DMEP) to the candidate list of substances of very high concern (SVHC) based on a determination that DMEP is toxic for reproduction [1,2]. This is part of implementing the EU law Registration, Evaluation, Authorisation, and Restriction of Chemicals (REACH). Substances that may have serious and often irreversible effects on human health and the environment can be identified as SVHCs. If a substance is identified as an SVHC, it will be added to the Candidate List for eventual inclusion in the Authorisation List.

Summary of Potential for Exposure

Australian Department of Health reported use of DMEP as a plasticizer in toys, however no product testing results were reported [3,4].

A Canadian screening assessment of DMEP points out many studies where DMEP was tested for but not detected and concludes that "available data do not indicate the existence of consumer products containing DMEP in the Canadian marketplace." For example, DMEP was not detected in a Health Canada survey of phthalates in 70 soft vinyl children's products [5].

In contrast, investigations reported DMEP in vacuum cleaner bag dust and house carpets in Germany in studies conducted between 1998 and 2000 (Kersten 2003 and Pfordt 1999 as cited in BAuA Dossier) [6]. DMEP was detected in 100 percent of the 153 blood samples of Hong Kong residents in 2013 [7]. Phthalate testing of a variety of cosmetic products in Shanghai detected DMEP in one baby care product (shampoo) in 2013 [8].

List of References

1. ECHA Candidate List of substances of very high concern for Authorisation (SVHC). http://echa.europa.eu/candidate-list-table.
2. ECHA Substance Information, Bis(2-methoxyethyl) phthalate CAS # 117-82-8, Summary of Classification and Labelling. https://echa.europa.eu/information-on-chemicals.
3. Australian Government. Department of Health. Australia National Industrial Chemicals Notification and Assessment Scheme (NICNAS). Priority Existing Chemical Assessment Report No. 38. www.nicnas.gov.au/__data/assets/word_doc/0020/34841/PEC38-DMEP.DOCX#cas-A_117-82-8.
4. Australia National Industrial Chemicals Notification and Assessment Scheme (NICNAS), 2016. Di(methoxyethyl) phthalate (DMEP), Existing chemical info sheets. www.nicnas.gov.au/communications/publications/informationsheets/existingchemicalinfosheets/dimethoxyethylphthalatedmp.
5. Environment Canada, Health Canada, 2009. Screening Assessment for the Challenge; 1,2-Benzenedicarboxylic acid, bis(2-methoxyethyl) ester, Chemical Abstracts Service Registry Number 117-82-8. www.ec.gc.ca/ese-ees/F9B6BE6B-C7F5-49DD-8F05-C869D4D05E2D/batch6_117-82-8_en.pdf.
6. BAuA Federal Institute for Occupational Safety and Health, Federal Office for Chemicals, Dortmund, Germany. Annex XV Dossier: Proposal for Identification of a Substance as a CMR (1A or 1BG), PBT, vPvB or a Substance of an Equivalent Level of Concern, Substance Name: Bis(2-methoxyethyl)phthalate, CAS Number 117-82-8. https://echa.europa.eu/documents/10162/38458518-7e1d-49ff-b53d-d07963c1bceb.
7. Wan, H.T., P.Y. Leung , Y.G. Zhao , X. Wei , M.H. Wong , Chris K.C. Wong. 2013. Blood plasma concentrations of endocrine disrupting chemicals in Hong Kong populations. Journal of Hazardous Materials, Volume 261, 15 October 2013. https://doi.org/10.1016/j.jhazmat.2013.01.034.
8. Bao, Jiaqin, Min Wang, Xiaojun Ning, Yaobin Zhou, Yuping He, Jielin Yang, Xi Gao, Shuguang Li, Zhuoping Ding & Bo Chen. 2015. Phthalate Concentrations in Personal Care Products and the Cumulative Exposure to Female Adults and Infants in Shanghai.

Journal of Toxicology and Environmental Health, Part A, Volume 78, 2015, Issue 5. http://dx.doi.org/10.1080/15287394.2014.968696.

CAS 117-84-0 Di-n-octyl phthalate (DnOP)

Summary of Toxicity

The National Toxicology Program found limited evidence that di-n-octly phthalate caused adverse developmental effects in laboratory animals [1]. Multiple animal studies have demonstrated that di-n-octly phthalate can be toxic to the liver, kidney, thyroid, and immune system [2].

Summary of Potential for Exposure

Di-n-octyl phthalate is a common plasticiser in plastic production [2]. The Danish EPA found di-n-octyl phthalate in several children's products including foam toys, PVC soap containers, packaging for cosmetics, and a set of marker pens [3]. A Dutch study found di-n-octyl phthalate in several plastics in children's products [4]. Mono-(3-carboxypropyl) phthalate, a metabolite indicative of di-n-octyl phthalate exposure, was found in greater than 60 percent of the U.S. population sampled in the NHANES survey [5].

List of References

1. U.S. Department of Health and Human Services, National Toxicology Program, Center for the Evaluation of Risks to Human Reproduction (CERHR). NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Di-n-Octyl (DnOP). 2003.
2. U.S. Consumer Products Safety Commission. March 8, 2010. Toxicity Review of Di-n-Octyl Phthalate (DnOP).
3. Danish Ministry of the Environment, Environmental Protection Agency. Survey of Chemical Substances in Consumer Products, Reports 70, 88, 93, and 102.
4. Dutch Inspectorate for Health Protection and Veterinary Public Health (VWA/KvW). Screening of Plastic Toys for Chemical Composition and Hazards, Report ND05o610/01, July 2005.
5. Colacino, JA, Harris, TR, and Schecter, A. (2010). Dietary intake is associated with phthalate body burden in a nationally representative sample. *Environ Health Perspect* 118: 998-1003.

CAS 118-74-1 Hexachlorobenzene (HCB)

Summary of Toxicity

Hexachlorobenzene is classified as a carcinogen by authoritative sources [1-4]. HCB causes liver tumors in laboratory animals. HCB is listed as developmental toxicant by the state of California

primarily based on altered neurobehavioral development in offspring of dosed rodents [5,6]. HCB has been shown to induce structrual and functional changes in primate ovaries [6] and is listed as a Category 1 endocrine disruptor by the European Union [4].

Summary of Potential for Exposure

Hexachlorobenzene is listed as a Persistent, Bioaccumulative and Toxic (PBT) chemical under Washington State's PBT rule (WAC 173-333-320) [7]. No current U.S. commercial uses of hexachlorobenzene were identified but HCB is formed as a by-product or impurity in the manufacture of other chlorinated chemicals [2]. The FDA, Cosmetics Office detected HCB in U.S.-certified color additives. Their analysis suggested that the contamination with HCB may be decreased by avoiding use of starting material (tetrachlorophthalic anhydride) heavily contaminated with HCB [8]. Biomonitoring shows widespread but declining detections in the U.S. general population [9].

List of References

1. WHO, International Agency for Research on Cancer (IARC) Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 79, Some Thyrotropic Agents, 2001.
2. U.S. DHHS, PHS, National Toxicology Program. Report on Carcinogens, Eleventh Edition. 2005.
3. U.S. EPA Integrated Risk Information System (IRIS) for Hexachlorbenzene (last revised 1996).
4. European Commission, Joint Research Centre, Institute for Health and Consumer Protection. European Chemical Substances Information System (ESIS) file for Hexachlorobenzene (CAS# 118-74-1).
5. California EPA, Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. February 5, 2010.
6. California EPA, Office of Environmental Health Hazard Assessment (OEHHA). Public Health Goals for Chemicals in Drinking Water: Hexachlorobenzene, September 2003.
7. WA Department of Ecology. Summary of Technical Background Information for the Proposed PBT List (Revised Draft) October 2005.
8. Andrzejewski, D. and A. Weisz (2000) Rapid quantification of hexachlorobenzene in the color additives D&C Red Nos. 27 and 28 (phloxine B) using solid-phase microextraction and gas chromatography–mass . *Journal of Chromotography A, Vol 863 (1):* 37-46.
9. Centers for Disease Control and Prevention (CDC), Fourth National Report on Human Exposure to Environmental Chemicals, December 2009.

CAS 119-93-7 3,3´-Dimethylbenzidine (also caled *ortho*-Tolidine)

Summary of Toxicity

3,3´-Dimethylbenzidine and dyes metabolized to 3,3´-dimethylbenzidine are listed as carcinogens by authoritative sources [1-4]. Evidence is based on cancer of the skin, liver, oral cavity, intestinal tract, lung, and mammary gland observed in test animals [2,5].

Summary of Potential for Exposure

3,3´-Dimethylbenzidine has been used as a dye or an intermediate for producing a large number of dyestuffs and pigments [2]. These dyes have been used to color leather, textiles, and paper [6]. 3,3´-Dimethylbenzidine is also used in the production of polyurethane-based elastomers, coatings, and rigid plastics [6]. Danish EPA testing of hobby products marketed to children found it in a gel pen [7].

List of References

1. WHO, International Agency for Research on Cancer (IARC), Monographs on the Evaluation of Carcinogenic Risks to Humans, Supplement No 7: Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs Volumes 1 to 42. 1987.
2. U.S. DHHS, PHS, National Toxicology Program. Report on Carcinogens, Eleventh Edition. 2005.
3. California EPA, Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. February 5, 2010.
4. European Commission, Joint Research Centre, Institute for Health and Consumer Protection. European Chemical Substances Information System (ESIS) file for 4,4'-bi-o-toluidine (CAS# 119-93-7).
5. Daniel L. Morgan, June K. Dunnick, Thomas Goehl, Michael R Jokinen, H. B. Matthews, Errol Zeiger and John H. Mennear (1994) Summary of the National Toxicology Program Benzidine Dye Initiative. Environ Health Perspect 102(Suppl 2):63-78.
6. National Institutes of Health, National Library of Medicine Hazardous Substances Data Bank Accessed May 2010.
7. Danish Ministry of the Environment, Environmental Protection Agency. Survey of Chemical Substances in Consumer Products, Report 93, 2008.

CAS 123-91-1 1,4-Dioxane

Summary of Toxicity

1,4-Dioxane is classified as a carcinogen by authoritative sources [1-4]. Evidence is based on liver tumors in multiple animal species as well as tumors at other sites[1-3]. There is some

evidence that 1,4-dioxane acts as a tumor promoter [1-3]. 1,4 dioxane has also caused liver and kidney toxicity in laboratory animals and in people who were occupationally exposed [1].

Summary of Potential for Exposure

1,4-Dioxane is primarily used as a solvent for chemical processing. It is used in the manufacturing of products such as adhesives, cleaning and detergent preparations, cosmetics, deodorant fumigants, emulsions, and polishing compositions. It is unintentionally formed as an impurity during the manufacture of alkyl ether sulfates and other ethoxylated substances which are used in consumer products such as cosmetics, detergents, and shampoos [6]. Testing in the Europe detected 1,4-dioxane in baby lotion, in shampoos and lotions, and in hand dishwashing liquids [5]. The U.S. FDA has detected 1,4-dioxane in ethoxylated raw materials for cosmetics and in finished cosmetic products including baby shampoos and bubble baths [6].

List of References

1. U.S. EPA, Integrated Risk Information System (IRIS). 1,4-Dioxane (last revised 2010)
2. WHO, International Agency for Research on Cancer (IARC) Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume No 71: Re-evaluation of Some Organic Chemicals, Hydrazine and Hydrogen Peroxide (1999).
3. U.S. DHHS, PHS, National Toxicology Program. Report on Carcinogens, Eleventh Edition. 2005.
4. California EPA, Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. February 5, 2010.
5. European Commission, Joint Research Centre, Institute for Health and Consumer Protection. European Union Risk Assessment Report: 1,4-Dioxane Final Risk Assessment. 2002.
6. U.S. DHHS, Agency for Toxic Substances & Disease Registry (ATSDR). Toxicological Profile for 1,4-dioxane. September 2007.

CAS 126-72-7 Tris (2,3-dibromopropyl) phosphate (TDBPP)

Summary of Toxicity

Tris (2,3-dibromopropyl) phosphate (TDBPP) is reasonably anticipated to be a human carcinogen by the National Toxicology Program [1], is listed as carcinogen on California's Proposition 65 List, and is classified as possible 2A carcinogen by the International Agency for Research on Cancer (IARC). According to the European Food Safety Authority (EFSA) (2012), there is convincing evidence that TDBPP is genotoxic and carcinogenic [2].

Summary of Potential for Exposure

TDBPP was used as a flame retardant in children's clothing until banned in 1977 [3]. According to the National Toxicology Program, it has been used as an additive flame retardant in

polyurethane foams, polystyrene foam, acrylic carpets and sheets, water flotation devices, polyvinyl and phenolic resins, paints, lacquers, paper coatings, styrene-butadiene rubber, and latex [1]. These types of materials are used in children's products and the chemical is still available for sale from overseas suppliers. A disclosure requirement could confirm that imported children's products do not contain this flame retardant. No current information on uses or national production volume is available [4].

TDBPP has not been included in many house dust sampling studies. It was identified in one study of house dust in California [5]. No biomonitoring studies were located.

List of References

1. National Toxicology Program. 2016. Report on Carcinogens, Fourteenth Edition; Research Triangle Park, NC: U.S. Department of Health and Human Services, Public Health Service. http://ntp.niehs.nih.gov/go/roc14/.
2. EFSA, *Scientific Opinion on Emerging and Novel Brominated Flame Retardants (BFRs) in Food*. 2012, European Food Safety Authority: Parma, Italy.
3. CPSC. *CPSC Bans TRIS-Treated Children's Garments* 1977 8/12/2015]. www.cpsc.gov/en/Newsroom/News-Releases/1977/CPSC-Bans-TRIS-Treated-Childrens-Garments/.
4. EPA. *Chemical Data Access Tool (CDAT) – Chemical Data Reporting (CDR) information on the production and use of chemicals manufactured or imported into the United States*. 2012 10/15/2015 10/30/2015]; Available from: http://java.epa.gov/oppt_chemical_search/.
5. Dodson, R.E., et al., *After the PBDE phase-out: a broad suite of flame retardants in repeat house dust samples from California.* Environ Sci Technol, 2012. **46**(24): p. 13056-66.

CAS 126-73-8 Tri-n-butyl phosphate (TNBP)

Summary of Toxicity

According to the European Chemicals Agency (ECHA) Tri-n-butyl phosphate (TNBP) is suspected to cause cancer and is a category 2 cancer hazard [1]. TNBP caused dose-related increases in the incidence and severity of urinary bladder tumors in male and female rats with dietary exposure for two years [2]. Male mice with chronic dietary exposure developed liver tumors [3]. The American Conference of Governmental Industrial Hygienists (ACGIH) classified TNBP as a confirmed animal carcinogen with unknown relevance to humans [4].

The U.S. Agency for Toxic Substances and Disease Registry (ATSDR) evaluated available toxicity data for TNBP and developed human health screening values [3]. Acute oral exposure guidelines were based on reduced weight gain in rats dosed during pregnancy. The lowest-observed-adverse-effect-level (LOAEL) for this maternal effect was 125 mg/kg-day [3]. No

observable birth defects in fetuses were observed at gestation day 20 at this dose. Higher oral doses in subacute rat testing caused neurological signs and symptoms, changes in liver and spleen weights, and degenerative changes in the testes (Laham et al. 1983 and Noda et al. 1994 as cited in ATSDR review) [3]. Urinary bladder hyperplasia was the most sensitive effect observed in three oral rat studies of longer duration (Arnold et al. 1997, FMC 1985, Tyl et al. 1997 reviewed in ATSDR) [3]. ATSDR selected the study by Arnold et al. 1997, with a LOAEL of 33 mg/kg/d, to derive human screening levels for both intermediate and chronic duration [3]. ATSDR's human health screening value for TNBP is 0.08 mg/kg-day for intermediate and chronic exposures [3].

In vitro tests show that TNBP, but not its metabolite di-n-butyl phosphate (DNBP), may act as an antagonist for androgen and the glucocorticoid nuclear receptors [4,5]. Neither TNBP nor its metabolite DNBP had an effect on estrogen receptors *in vitro* [5,6].

Summary of Potential for Exposure

TNBP is mainly used as an additive in fire-resistant aircraft hydraulic fluids and as a plasticizer for cellulose esters, lacquers, plastics, and vinyl resins [4]. It may be present in floor finish, floor wax, paints, and glues. It also has a number of industrial applications [3]. U.S. national volume production was reported to be 8,877,744 pounds/year in 2012 [7].

TNBP has been measured in indoor dust and air in U.S. and European studies [8-12]. The maximum level reported was 7,100 ng/g in house dust [10]. Two European studies included air measurements and found TNBP more commonly in indoor air than in dust at homes and daycare centers [8,11]. Recent residential sampling in Norway by Xu et al. reported 98 percent detection in residential indoor air with a median of 14 ng/m^3 and a maximum detection of 119 ng/m^3 [11]. Inhalation exposure was the predominant route of estimated human residential exposure [11].

Biomonitoring studies indicate that TNBP is making its way into people's bodies. Dodson et al. measured metabolites of TNBP in urine from adults in Northern California [13]. Fromme et al. reported slightly higher mean levels of TNBP urinary metabolite in a population of 312 children attending 63 German day care centers [8]. TNBP has been detected in breast milk samples from Sweden and several Asian counties [14,15]. TNBP was recently measured directly in blood of 237 adults in a Chinese study [16]. The median level reported was 37.8 ng/mL, which was much higher than the other organophosphorus flame retardants measured.

There is some evidence of TNBP in the U.S. diet, drinking water, and ambient air. TNBP has been found at low parts per billion levels in cereal products including baby food in the U.S. [3,4,17] Focazio et al. 2008, detected TNBP in a study of 74 public drinking water systems from 25 states and Puerto Rico. TNBP was detected in 8.1 percent of the samples with a maximum of 0.74 µg/L as cited in [3]. TNBP was detected in 100 percent or urban air samples from the Great

Lakes area with an average concentration of 150-250 pg/m^3. Lower air concentrations (average of 34 pg/m^3) were detected at remote locations [4].

List of References

1. ECHA. *Brief Profile: Tributyl phosphate*. August 2016]. https://echa.europa.eu/brief-profile/-/briefprofile/100.004.365.
2. Auletta, C.S., M.L. Weiner, and W.R. Richter, *A dietary toxicity/oncogenicity study of tributyl phosphate in the rat.* Toxicology, 1998. **128**(2): p. 125-34.
3. ATSDR. *Toxicological profile for phosphate ester flame retardants*. 2012 Updated Jan 21, 2015, Available from: www.atsdr.cdc.gov/ToxProfiles/TP.asp?id=1119&tid=239.
4. HSDB. *Tributyl Phosphate, (CASRN: 126-73-8)*. 2015 Updated 02/18/2015; Available from: http://toxnet.nlm.nih.gov/cgi-bin/sis/search2/f?./temp/~qPQDVd:1.
5. Hiroyuki Kojima, S.T., Nele Van den Eede, Adrian Covaci, *Effects of primary metabolites of organophosphate flame retardants on transcriptional activity via human nuclear receptors.* Toxicology Letters, 2016. **245**: p. 31-39.
6. Kojima, H., et al., *In vitro endocrine disruption potential of organophosphate flame retardants via human nuclear receptors.* Toxicology, 2013. **314**(1): p. 76-83.
7. EPA. *Chemical Data Access Tool (CDAT) - Chemical Data Reporting (CDR) information on the production and use of chemicals manufactured or imported into the United States*. 2012; Available from: http://java.epa.gov/oppt_chemical_search/.
8. Fromme, H., et al., *Organophosphate flame retardants and plasticizers in the air and dust in German daycare centers and human biomonitoring in visiting children (LUPE 3).* Environ Int, 2014. **71**: p. 158-63.
9. Dodson, R.E., et al., *After the PBDE phase-out: a broad suite of flame retardants in repeat house dust samples from California.* Environ Sci Technol, 2012. **46**(24): p. 13056-66.
10. Fan, X., et al., *Simultaneous determination of thirteen organophosphate esters in settled indoor house dust and a comparison between two sampling techniques.* Sci Total Environ, 2014. **491-492**: p. 80-6.
11. Xu, F., et al., *Comprehensive Study of Human External Exposure to Organophosphate Flame Retardants via Air, Dust, and Hand Wipes: The Importance of Sampling and Assessment Strategy.* Environ Sci Technol, 2016. **50**(14): p. 7752-60.
12. Zhou, L., et al., *Organophosphate flame retardants (OPFRs) in indoor and outdoor air in the Rhine/Main area, Germany: comparison of concentrations and distribution profiles in different microenvironments.* Environ Sci Pollut Res Int, 2016.
13. Dodson, R.E., et al., *Urinary biomonitoring of phosphate flame retardants: levels in California adults and recommendations for future studies.* Environ Sci Technol, 2014. **48**(23): p. 13625-33.

14. Sundkvist, A.M., U. Olofsson, and P. Haglund, *Organophosphorus flame retardants and plasticizers in marine and fresh water biota and in human milk.* J Environ Monit, 2010. **12**(4): p. 943-51.
15. Kim, J.W., et al., *Organophosphorus flame retardants (PFRs) in human breast milk from several Asian countries.* Chemosphere, 2014. **116**: p. 91-7.
16. Zhao, F., et al., *Levels of Blood Organophosphorus Flame Retardants and Association with Changes in Human Sphingolipid Homeostasis.* Environ Sci Technol, 2016. **50**(16): p. 8896-903.
17. FDA, *U.S Food and Drug Administration – Total Diet Study Market Baskets 2004-1 through 2005-4*. 2005, Food Drug Administration, Public Health Service. FDA/Center for Food Safety and Applied Nutrition.

CAS 127-18-4 Perchloroethylene (also called tetrachlorethene or tetrachloroethylene)

Summary of Toxicity

Perchloroethylene is a halogenated hydrocarbon classified as a carcinogen by authoritative sources [1-3]. Evidence from laboratory animals shows it can cause liver cancer and leukemia in rodents [1,2]. Human evidence comes from studies of people occupationally exposed to perchloroethylene either through manufacturing or dry cleaning. The most consistent evidence across these studies suggests there may be an association between increased exposure and increased incidence of esophageal and cervical cancer and non-Hodgkin's lymphoma [2]. Conclusions are limited by co-exposures to petroleum solvents and other dry cleaning agents [2].

Summary of Potential for Exposure

Perchloroethylene is a high production volume chemical used in dry cleaning garments, metal cleaning, and synthesis of other chemicals [4]. It is used in the textile industry for cleaning, processing, and finishing [1]. It has been used in household products like spot removers, lubricants, and water repellents [4]. Consumer product testing by the Danish EPA detected it in children's tents but not in a study of textiles [5]. Biomonitoring of the general U.S. population detected perchloroethylene in about one quarter of the people tested in 2001-02 [4].

List of References

1. WHO, International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume No 6, Dry Cleaning, Some Chlorinated Solvents and Other Industrial Chemicals. 1995.
2. U.S. DHHS, PHS, National Toxicology Program. Report on Carcinogens, Eleventh Edition. 2005.
3. California Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. Feb 5, 2010.

4. Centers for Disease Control and Prevention. Fourth National Report on Human Exposure to Environmental Chemicals, 2009.
5. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in consumer products. Reports 23 and 46 (2003-04).

CAS 131-18-0 Dipentyl phthalate (DPP)

Summary of Toxicity

Dipentyl phthalate (DPP) is designated by the EU as a Category 1 endocrine disruptor [1,2]. The EU developed their priority list of endocrine disruptors in stages (2000, 2002, and 2007), grouping chemicals into three categories. The EU **Category 1** endocrine distruptor designation has been as an authoritative source, because Category 1 requires evidence of endocrine disrupting activity in at least one species using intact animals. **Category 2** requires at least some *in vitro* evidence but is considered insufficient evidence of endocrine activity, while **Category 3** indicates either no evidence of endocrine disrupting activity or no data available.

DPP has been identified as a SVHC based on a toxic for reproduction designation [3,4]. This is part of implementing the EU law Registration, Evaluation, Authorisation, and Restriction of Chemicals (REACH). Substances that may have serious and often irreversible effects on human health and the environment can be identified as SVHCs. If a substance is identified as an SVHC, it will be added to the Candidate List for eventual inclusion in the Authorisation List.

The Consumer Product Safety Improvement Act of 2008 (CPSIA) directed the U.S. Consumer Product Safety Commission (CPSC) to convene a Chronic Hazard Advisory Panel (CHAP) on Phthalates and Phthalate alternatives "to study the effects of all phthalates and phthalate alternatives as used in children's toys and child care articles." The CHAP assessed the risks of 14 phthalates and 6 phthalate alternatives, including three phthalates permanently banned by the CPSIA and three phthalates subject to an interim ban. CHAP is an authoritative source for CSPA [2].

In 2014, DPP was included in the CHAP report, which found "DPENP is clearly among the most potent phthalates regarding developmental effects [5]." The CHAP panel found the toxicological profile of DPP is very similar to other antiandrogenic phthalates and thus, exposure to DPP contributes to the cumulative risk from other antiandrogenic phthalates and its use should be permanently banned from use in children's toys and child care articles at levels greater than 0.1 percent.

Summary of Potential for Exposure

DPP was detected in house dust in northern California [6]. A metabolite of DPP, MnPeP, was detected in children's urine in Austria [7] and Germany [8].

List of References

1. Ecology, 2011, Children's Safe Products Reporting Rule – Supporting Documents for the 2011 Rulemaking. Rule documents from the 2011 rulemaking were merged into a publication in April of 2017. Publication 17-04-022. https://apps.ecology.wa.gov/publications/SummaryPages/1704022.html
2. EU-Strategy for Endocrine Disruptors database EDS_2003_DHI2006.mdb. Accessed 10/17/16. http://ec.europa.eu/environment/chemicals/endocrine/strategy/substances_en.htm.
3. ECHA Candidate List of substances of very high concern for Authorisation (SVHC). http://echa.europa.eu/candidate-list-table.
4. European Chemicals Agency (ECHA), 2015. Annex XV Report: Proposal for identification of a Substance as a CMR 1A or 1B, PBT, vPvB or a Substance of an Equivalent Level of Concern Name(s): Dipentyl phthalate (DPP) EC Number(s): 205-017-9 CAS Number(s): 131-18-4. https://echa.europa.eu/documents/10162/d55c182b-f063-4955-969d-5684584d17b2.
5. Chronic Hazard Advisory Panel on Phthalates and Phthalate Alternatives (CHAP), July, 2014. Report to the U.S. Consumer Product Safety Commission Directorate for Health Services.
6. Dodson, R. E., et al. (2015). "Semivolatile organic compounds in homes: Strategies for efficient and systematic exposure measurement based on empirical and theoretical factors." Environmental Science & Technology **49**: 113-122.
7. Hartmann, C., et al. (2015). "Human biomonitoring of phthalate exposure in Austrian children and adults and cumulative risk assessment." International Journal of Hygiene and Environmental Health **218**: 489-499.
8. Kasper-Sonnenberg, M., et al. (2014). "Phthalate metabolites and bisphenol A in urines from German school-aged children: Results of the Duisberg Birth Cohort and Bochum Cohort studies." International Journal of Hygiene and Environmental Health 217: 830-838.

CAS 131-55-5 Benzophenone-2 (also called 2,2,4,4-tetrahydroxybenzophenone)

Summary of Toxicity

Benzophenone-2 has been classified as a Category 1 endocrine disruptor by the European Union [1]. It has shown estrogenic activity in rat uterotrophic assays [2]. Studies in mice [3] and rats [4] demonstrated dose dependent estrogenic effects.

Summary of Potential for Exposure

The Danish EPA identified benzophenone-2 as a listed ingredient in 2 of 208 children's personal care products in the mapping study of cosmetics marketed to children [5].

List of References

1. European Commission DG Environment (2002). Endocrine disruptors: study on gathering information on 435 substances with insufficient data. Final report B4-3040/2001/325850/MAR/C2.
2. Koda, T, Umezu, T, Kamata, R, Morohoshi, K, Ohta, T, and Morita, M. (2005). Uterotrophic effects of benzophenone derivatives and a p-hydroxybenzoate used in ultraviolet screens. *Environ Res 98(1)*: 40 – 5.
3. Hsieh, MH, Grantham, EC, Liu, B, Macapagal, R, Willingham, E, and Baskin, LS. (2007) In utero exposure to benzophenone-2 causes hypospadias through an estrogen receptor dependent mechanism. *Journal of Urology 178(4 Pt 2)*: 1637-42.
4. Jarry, H, Christoffel, J, Rimoldi, G, Koch, L, and Wuttke, W. (2004). Multi-organic endocrine disrupting activity of the UV screen benzophenone 2 (BP2) in ovariectomized adult rats after 5 days treatment. *Toxicology 205(1-2)*: 87-93.
5. Danish Ministry of the Environment, Environmental Protection Agency. Survey of Chemical Substances in Consumer Products, Report 88, 2007.

CAS 140-66-9 4-tert-Octylphenol (also called 4-(1,1,3,3-tetramethylbutyl)phenol)

Summary of Toxicity

4-tert-octylphenol has been classified as a Category 1 endocrine disruptor by the European Union [1]. Studies in rats have found 4-tert-octylphenol to have uterotrophic effects,[2] to cause early vaginal opening [3], to disrupt the estrous cycle [4], and to cause abnormal sperm development [5].

Summary of Potential for Exposure

A Dutch study of plastics in children's products found 4-tert-octylphenol in 5 out of 48 polyvinyl chloride plastics and 1 poly(isopropyl methacrylate) plastic [6]. In a large biomonitoring study, 4-tert-octylphenol was detected in 57 percent of the general US population [7].

List of References

1. European Commission DG Environment (2002). Endocrine disruptors: study on gathering information on 435 substances with insufficient data. Final report B4-3040/2001/325850/MAR/C2.
2. Laws, SC, Carey, SA, Ferrell, JM, Bodman, GJ, and Cooper, RL. (2000). Estrogenic Activity of Octylphenol, Nonylphenol, Bisphenol A and Methoxychlor in Rats. *Toxicological Sciences 54*: 154-167.
3. Willoughby, KN, Sarkar, AJ, Boyadjieva, NI, and Sarkar, DK. (2005). Neonatally administered tert-octylphenol affects onset of puberty and reproductive development in female rats. *Endocrine 26(2)*: 161-8.

4. Blake, CA and Ashiru, OA. (1997). Disruption of rat estrous cyclicity by the environmental estrogen 4-tert-octylphenol. *Proc Soc Exp Biol Med 216(3)*: 446-51.
5. Blake CA, Boockfor FR, Nair-Menon JU, Millette CF, Raychoudhury SS, and McCoy GL. (2004). Effects of 4-*tert*-octylphenol given in drinking water for 4 months on the male reproductive system of Fischer 344 rats. *Reprod Toxicol 18*: 43–51.
6. Dutch Inspectorate for Health Protection and Veterinary Public Health (VWA/KvW). Screening of Plastic Toys for Chemical Composition and Hazards, Report ND05o610/01, July 2005.
7. Calafat AM, Ye X, Wong LY, Reidy JA, Needham LL. Exposure of the U.S. Population to Bisphenol A and 4-tertiary-Octylphenol: 2003–2004. *Environ Health Perspect 2008 Jan;116(1)*:39-44.

CAS 140-67-0 Estragole

Summary of Toxicity

Estragole is listed as a carcinogen for the state of California [1]. Estagole has been shown to cause liver cancer and organ toxicity in rodents [1,2]. In its determinations, California also considered that estragole was genotoxic in several short-term tests, caused DNA adduct formation *in vivo* and *in vitro*, was structurally similar to recognized carcinogens, and had a well characterized carcinogenic mode of action that is expected to occur in humans [1].

Summary of Potential for Exposure

Estragole occurs naturally in many culinary herbs such as anise and basil. It is used as an additive, fragrance, and flavoring agent in cosmetics, cleaning products, and food [1,2]. In a survey by the Danish EPA, essential oils and fragrances reported estragole on their Material Safety Data Sheets (MSDS) at over 50 percent estragole in basil oil, and at lower amounts in anise seed star oil, and fennel oil [3].

List of References

1. California EPA, Office of Environmental Health Hazard Assessment (OEHHA) Reproductive and Cancer Hazard Assessment Section. Evidence on the Carcinogenicity of Estragole. 1999.
2. Bristol, D (2011). NTP 3-month toxicity studies of estragole administered by gavage to rats and mice. *National Toxicology Program Toxicity Report Series* Jan(82):1-112.
3. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in consumer products. Report 92, 2008.

CAS 149-57-5 2-Ethylhexanoic acid (2-EHA)

Summary of Toxicity

2-Ethylhexanoic acid is listed as a developmental toxicant by the state of California and a reproductive and developmental toxicant by the European Union [1,2]. The National Toxicology Program Center for the Evaluation of Risks to Human Reproduction also reviewed studies of 2-EHA as part of their evaluation of DEHP [3]. It concluded that there was sufficient animal evidence to identify 2-EHA as a developmental toxicant [3,4].

Summary of Potential for Exposure

Metal derivatives of 2-ethylhexanoic acid are widely used as stabilizers for polyvinyl chloride (PVC). Testing by the Danish EPA found 2-EHA in foam washcloths for babies, baby foam mattresses, nursing pillows, marker pen sets, and a coating on a wooden toy [5]. Testing by the Dutch government showed frequent detections of 2-EHA migrating out of PVC plastic [6].

List of References

1. California EPA, Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. February 5, 2010.
2. European Commission, Joint Research Centre, Institute for Health and Consumer Protection. European Chemical Substances Information System (ESIS) file for 2-ethylhexanoic acid.
3. U.S. Department of Health and Human Services, National Toxicology Program, Center for the Evaluation of Risks to Human Reproduction (CERHR). NTP- CERHR Expert Panel Report on Di (2-ethylhexyl) Phthalate. October 2000.
4. U.S. Department of Health and Human Services, National Toxicology Program, Center for the Evaluation of Risks to Human Reproduction (CERHR) Monograph on the potential human reproductive and developmental effects of Di (2-ethylhexyl) Phthalate (DEHP) November 2006.
5. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in consumer products.
6. Dutch Inspectorate for Health Protection and Veterinary Public Health (VWA/KvW). Screening of Plastic Toys for Chemical Composition and Hazards, Report ND05o610/01, July 2005.

CAS 335-67-1 Perfluorooctanoic acid (PFOA)

Summary of Toxicity

In 2013 PFOA was identified by the European Union to be a substance of very high concern (SVHC) as toxic for reproduction [1]. This is part of implementing the EU law Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). Substances that may have

serious and often irreversible effects on human health and the environment can be identified as SVHCs. If a substance is identified as an SVHC, it will be added to the Candidate List for eventual inclusion in the Authorisation List.

In 2016 the International Agency for Research on Cancer (IARC) classified PFOA as possible carcinogenic to humans (category 2B) [2]. IARC is part of the World Health Organization and its mission is to coordinate and conduct research on the causes of human cancer, the mechanisms of carcinogenesis, and to develop scientific strategies for cancer control. IARC publishes monographs which identify carcinogenic chemicals.

Summary of Potential for Exposure

PFOA has been detected in biomonitoring studies [3,4,5,6] and house dust [7,8].

List of References

1. ECHA Candidate List of substances of very high concern for Authorisation (SVHC). http://echa.europa.eu/candidate-list-table.
2. International Agency for Research on Cancer (IARC), 2016. Monograph 110. Carcinogenicity of perfluorooctanoic acid, tetrafluoroethylene, dichloromethane, 1,2-dichloropropane, and 1,3-propane sultone. http://monographs.iarc.fr/ENG/Monographs/vol110/index.php.
3. Centers for Disease Control and Prevention (CDC). 2015. Fourth National Report on Human Exposure to Environmental Chemicals: Updated Tables February 2015. Atlanta, GA. www.cdc.gov/exposurereport/.
4. Apelberg, B., Witter, F. R., Herbstman, J. B., Calafat, A. M., Halden, R. U., Needham, L. L., & Goldman, L. R. 2007. Cord Serum Concentrations of Perfluorooctane Sulfonate (PFOS) and Perfluorooctanoate (PFOA) in Relation to Weight and Size at Birth. Environmental Health Perspectives, 115(11): 1670-1676.
5. Calafat, Antonia M. Wong, Lee-Yang, Kuklenyik, Zsuzsanna, Reidy, John A., and Needham, Larry L. Polyfluoroalkyl chemicals in the U.S. Population: Data from the National Health and Nutrition Examination Survey (NHANES) 2003-2004 and Comparisons with NHANES 1999-2000. Environmental Health Perspectives , 1596-1602. 2007.
6. Peters, R. J. B. Man-Made Chemicals in Maternal and Cord Blood. Netherlands Organisation for Applied Scientific Research. 2005a.
7. D'Hollander, W., L. Roosens, A. Covaci, C. Cornelis, H. Reynders, K. V. Campenhout, P. Voogt and L. Bervoets (2010). "Brominated flame retardants and perfluorinated compounds in indoor dust from homes and offices in Flanders, Belgium." Chemosphere 81(4): 478-487.
8. Fraser, A. J., T. F. Webster, D. J. Watkins, M. J. Strynar, K. Kato, A. M. Calafat, V. M. Vieira and M. D. McClean (2013). "Polyfluorinated compounds in dust from homes,

offices, and vehicles as predictors of concentrations in office workers' serum." Environ Int 60: 128-136.

CAS 608-93-5 Pentachlorobenzene

Summary of Toxicity

Pentachlorobenzene has been classified as a Category 1 endocrine disruptor by the European Union [1]. In rats, levels of thyroid hormones (T3 and T4) in plasma were decreased after intraperitoneal injection or dietary ingestion of pentachlorobenzene [2,3].

Summary of Potential for Exposure

Pentachlorobenzene is on the Washington state list of PBTs as being persistent, bioaccumulative, and toxic (WAC 173-333-310) [4]. Evidence that pentachlorobenzene is found in children's products was not located. Its use as a fungicide and as a flame retardant were cancelled in U.S. by the early 1980s. The fungicide PCNB (of which pentachlorobenzene is an impurity and a metabolite), was cancelled by the U.S. EPA for residential, school, and golf course uses in 2009 [5]. PCNB is still used agriculturally.

List of References

1. European Commission DG Environment (2002). Endocrine disruptors: study on gathering information on 435 substances with insufficient data. Final report B4-3040/2001/325850/MAR/C2.
2. den Besten, C, Vet, JJ, Besselink, HT, Kiel, GS, van Berkel, BJ, Beems, R, and van Bladeren, PJ. (1991). The liver, kidney, and thyroid toxicity of chlorinated benzenes. Toxicol Appl Pharmacol 111(1): 69-81.
3. den Besten, C, Bennik, MH, Bruggeman, I, Schielen, P, Kuper,F, Brouwer,A, Koeman, JH, Vos, JG, and van Bladeren, PJ. (1993). The role of oxidative metabolism in hexacholorobenzene-induced porphyria and thyroid hormone homeostasis: a comparison with pentachlorobenzene in a 13-week feeding study. Toxicol Appl Pharmacol 119: 181-194.
4. WA Department of Ecology. Summary of Technical Background Information for the Proposed PBT List (Revised Draft) October 2005.
5. U.S. EPA Pentachloronitrobenzene (PCNB) Amendments to Terminate Uses. Federal Register: July 15, 2009 (Volume 74, Number 134) Page 34337-34339.

CAS 620-92-8 Bisphenol F (BPF)

Summary of Toxicity

EPA classified bisphenol F (BPF) as high hazard for toxicity from repeated exposures based on reduced body weight and decreased total serum cholesterol, glucose, and albumin at 20 mg/kg-

day in a 28-day oral rat study. BPF was classified by EPA as a moderate hazard for reproductive toxicity and a high developmental hazard based primarily on toxicity of its structural analog BPA [1].

In a systematic review of BPS, BPA, and BPF endocrine studies, BPF had estrogenic and anti-androgenic activity in *in vitro* testing [2]. On average, BPF was as potent as BPA in estrogenic activity assays and about half as potent as BPA in anti-estrogenic activity assays [2].

Summary of Potential for Exposure

In rodents, bisphenol F is readily absorbed following oral exposure, metabolized, and excreted primarily in the urine [1].

Washington State banned BPA for use in baby bottles, infant sippy cups, and sports water bottles starting in 2010 (Chapter 70.280 RCW). BPF is used as a replacement for BPA in epoxy resins used to line food cans and in polymer plastics [3]. BPF has been detected in personal care products such as lotions and cosmetics [4]. National U.S. production volume was reported to be 355,000 pounds in 2012 [5].

BPF was detected in 68 percent of indoor dust samples collected between 2006 and 2010 in New York. Median detected concentration was 49 ng/g dust and the maximum detected was 240 ng/g. Of eight bisphenol analogs measured, it was the third most common bisphenol detected after BPA and BPS [6].

BPF was detected in urine collected between 2000 and 2014 from U.S. adults. Depending on the collection time, BPF was detected in 42-88 percent of samples and the mean detection was 0.15-0.54 ng/mL [7].

BPF was detected more frequently than other BPA analogs in a variety of foods collected from retail grocery stores in Albany, NY, between 2008 and 2012 [3]. The maximum concentration detected (1130 ng BPF/g sample) was in a salad dressing packaged in a plastic container. BPF was most frequently detected in fats and oils, dairy products, fish and seafood, meat products, and vegetables, and was mostly associated with foods packaged in cans. The authors estimated daily dietary exposure to BPF through U.S. food for different age groups and found toddlers had the highest estimated intakes (mean 22.3 ng/kg bw-day, 95th percentile 70.2 ng/kg bw-day) [3].

BPF may be slower to degrade in the environment than BPA [8], but is not expected to have high persistence or high potential for bioaccumulation [1]. BPF has been reported to occur in surface water, sewage, and sediments [9].

List of References

1. EPA. Bisphenol A Alternatives in Thermal Paper. Final Report August 2015. Design for the Environment Program. www.epa.gov/sites/production/files/2015-08/documents/bpa_final.pdf.
2. Rochester JR and Bolden AL (2015) Bisphenol S and F: Systemic review and comparison of the hormonal activity of bisphenol A substitutes. *Environ. Health Perspect. 123 (7):*643-650.
3. Liao C. and Kurunthachalam K. (2013) Concentrations and Profiles of Bisphenol A and Other Bisphenol Analogues in Foodstuffs from the United States and Their Implications for Human Exposure. *J. Agricultural and Food Chemistry 61*, 4655−4662.
4. Liao C, Kannan K. 2014. A survey of alkylphenols, bisphenols, and triclosan in personal care products from China and the United States. *Arch Environ Contam Toxicol* 67(1):50–59.
5. EPA. Chemical Data Access Tool (CDAT) - Chemical Data Reporting (CDR) information on the production and use of chemicals manufactured or imported into the United States. 2012 10/15/2015 10/30/2015]. http://java.epa.gov/oppt_chemical_search/.
6. Liao et al., 2012b. Occurrence of Eight Bisphenol Analogues in Indoor Dust from the United States and Several Asian Countries: Implication for Human Exposure. *Environmental Science and Technology; 46*:9138-45.
7. Ye, X., et al., *Urinary Concentrations of Bisphenol A and Three Other Bisphenols in Convenience Samples of U.S. Adults during 2000-2014.* Environ Sci Technol, 2015. **49**(19): p. 11834-9.
8. Ike M, Chen MY, Danzl E, Sei K, Fujita M. (2006) Biodegradation of a variety of bisphenols under aerobic and anaerobic conditions Water Sci Technol. 2006;53(6):153-9.
9. Fromme, H.; Küchler, T.; Otto, T.; Pilz, K.; Müller, J.; Wenzel, A. (2002) Occurrence of phthalates and bisphenol A and F in the environment. *Water Res. 36 (6),* 1429−1438.
10. Ecology, 2011, Children's Safe Products Reporting Rule – Supporting Documents for the 2011 Rulemaking. Rule documents from the 2011 rulemaking were merged into a publication in April of 2017. Publication 17-04-022. https://apps.ecology.wa.gov/publications/SummaryPages/1704022.html

CAS 842-07-9 C.I. Solvent Yellow 14

Summary of Toxicity

C.I. Solvent Yellow 14 is listed as a carcinogen by the state of California [1]. The listing is based on evidence of dose-related liver cancer in rats but not mice [2]. Other studies indicate that C.I. Solvent Yellow 14 is genotoxic and that human metabolism would likely activate this chemical to form adducts with DNA [3,4].

Summary of Potential for Exposure

C.I. Solvent Yellow 14 is an azo dye and is used to color waxes, oils, solvents, polishes, cellulose ether varnishes, and styrene resins [5,6]. It was used as a food dye, called Sudan 1, and was common in certain curry and chili powders. The use of Sudan I in foods is now banned in many countries due to reports on its possible health risks [6]. The Dutch gevernment detected C.I. Solvent Yellow 14 in two plastic samples from toys likely to be sucked by children under 2 years old [7].

List of References

1. California EPA, Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. February 5, 2010.
2. U.S. DHHS, PHS, National Toxicology Program (1982) Carcinogenesis bioassay of C.I. Solvent Yellow 14 in F344/N rats and B6C3Fi Mice (feed study). *National Toxicol Tech Rep Ser 226*:1-164.
3. Westmoreland, Westmoreland, C. and DG Gatehouse (1991) The differential clastogenicity of solvent yellow 14 and FD&C yellow No 6 in vivo in the rodent micronuceus test. *Carcinogenesis 12(8):* 1403-1407.
4. Stiborova, M. et al. (2002) Sudan I is a potential carcinogen for humans. *Cancer Research 62*: 5678-84.
5. National Institutes of Health, National Library of Medicine Hazardous Substances Data Bank Accessed May 2010.
6. WHO, International Agency for Research on Cancer (IARC) Monographs on the Evaluation of Carcinogenic Risks to Humans, Supplement No 7: Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs Volumes 1 to 42. 1987. Listed as Sudan 1.
7. Dutch Inspectorate for Health Protection and Veterinary Public Health (VWA/KvW). Screening of Plastic Toys for Chemical Composition and Hazards, Report ND05o610/01, July 2005.

CAS 872-50-4 1-Methyl-2-pyrrolidinon (also called N-methylpyrrolidone or NMP)

Summary of Toxicity

N-Methylpyrrolidone is listed by the state of California and the European Union as a developmental toxiciant [1,2]. In animal studies it caused reduced fetal and birth weights, developmental delays, and impairment of cognitive skills in offspring [1,3,4].

Summary of Potential for Exposure

1-Methyl-2-pyrrolidinon is used as an industrial solvent for resins, paint strippers, and plastics in the semiconductor industry. It is also used as a finishing agent in textiles, as a pigment

dispersant, and as a spinning agent for polyvinyl chloride [1,3,5]. It is listed as an ingredient under the synonym (methyl pyrrolidone) in a nail polish remover and five mascaras in an online cosmetic database [6]. The Danish EPA detected 1-methyl-2-pyrrolidinon in the coatings of children's wooden toys [7].

List of References

1. California EPA, Office of Environmental Human Health Assessment (OEHHA). Maximum Allowable Dose Level (MADL) for Reproductive Toxicity for N-methylpyrrolidone for Dermal and Inhalation Exposures, March 2003.
2. European Commission, Joint Research Centre, Institute for Health and Consumer Protection. European Chemical Substances Information System (ESIS) file for 1-methyl-2-pyrrolidone.
3. EPA Action Memorandum: Inert Reassessment: N-methylpyrrolidone (CAS Reg. No. 872-50-4), June 2006.
4. European Commission, European Chemcials Bureau. IUCLID dataset for 1-methyl-2-pyrrolidone, 2000.
5. National Institutes of Health, National Library of Medicine, Household Products Database. Accessed May 2010.
6. Environmental Working Group. Skin Deep Cosmetic Safety Database. Accessed May 2010.
7. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Report 60. CAS 1163-19-5 2,2',3,3',4,4',5,5',6,6'-Decabromodiphenyl ether (also known as BDE-209).

CAS 1163-19-5 2,2',3,3',4,4',5,5',6,6'-Decabromodiphenyl ether (BDE-209)

Summary of Toxicity

BDE-209 is the primary congener found in Deca-BDE. Thyroid and liver appear to be the most sensitive tissues to toxicity of Deca-BDE in animal studies. In 2008, EPA determined that Deca-BDE had "suggestive evidence of carcinogenic potential" in humans [1]. This is based on liver tumors in rats and male mice, and thyroid gland follicular cell hyperplasia and thyroid tumors in male mice in oral studies with Deca-BDE [1,2]. Rats and mice exposed to Deca-BDE in their early postnatal period, were observed to have neurodevelopmental effects as they matured [3,4,5,6]. In the environment, BDE-209 is likely to degrade into less-brominated, more toxic BDEs [7].

Summary of Potential for Exposure

Deca BDE is listed as a Persistent, Bioaccumulative and Toxic (PBT) chemical under Washington State's PBT rule (WAC 173-333-320) [7]. This chemical is widely used as a flame

retardant in high impact poylstyrene and other polymers, in coatings and adhesive systems such as the back coatings for carpets, and in non-clothing textiles [1,7]. It is a high production volume chemical that has not been reported directly in children's products but has been found in indoor air and dust and in biomonitoring studies [1,7,8,9].

List of References

1. U.S. Environmental Protection Agency. Toxicological review of Decabromodiphenyl Ether (BDE-209), June 2008.

2. National Toxicology Program (1986) Toxicology and carcinogenesis studies of decabromodiphenyl oxide (CAS No. 1163-19-5) in F344/N rats and B6C3F1 mice (feed studies). Public Health Service, U.S. DHHS; NTP TR 309.

3. Viberg, H; Fredriksson, A; Eriksson, P. (2007) Changes in spontaneous behavior and altered response to nicotine in the adult rat, after neonatal exposure to the brominated flame retardant, decabrominated diphenyl ether (PBDE 209). Neurotoxicol 28:136–142.

4. Rice, DC; Reeve, EA; Herlihy, A; et al. (2007) Developmental delays and locomotor activity in the C57BL6/J mouse following neonatal exposure to the fully-brominated PBDE, decabromodiphenyl ether. Neurotoxicol Teratol 29:511–520.

5. Viberg, H; Fredriksson, A; Jakobsson, E; et al. (2003) Neurobehavioral derangements in adult mice receiving decabromodiphenyl ether (PBDE 209) during a defined period of neonatal brain development. Toxicol Sci 76:112–120.

6. Darnerud et al. (2001) Polybrominated diphenyl ethers: occurrence, dietary exposure and toxicology. *Environmental Health Perspectives 109(Supplement 1):* 49-68.

7. WA Departments of Ecology and Health. Washington State Polybrominated Diphenyl Ether (PBDE) Chemical Action Plan. January 2006.

8. Schecter et al., 2003. Polybrominated diphenyl ethers (PBDEs) in U.S. mother's milk. *Environmental Health Perspectives 111(14)*: 1723-1729.

9. Butt et al., 2004. Spatial distribution of polybrominated diphenyl ethers in southern Ontario as measured in indoor and outdoor window organic films. *Environmental Science & Technology 38(3):*724-731.

CAS 1241-94-7 Ethylhexyl diphenyl phosphate (EHDPP)

Summary of Toxicity

Toxicity data for Ethylhexyl diphenyl phosphate (EHDPP) was reviewed by the United Kingdom Environmental Agency in 2009 [1]. Dose-related changes to the blood, liver, kidney, adrenal glands, testes, and ovaries were observed in laboratory rats exposed to 375-425 mg/kg-day of commercial EHDPP in their food over 90 days [1,2]. The lowest-observed-adverse-effect-level (LOAEL)[17] from three 90-day feeding experiments was 15 mg/kg/day for increase in liver enzymes in male rats (NOAEL1 was 6 mg/kg-day). A fertility and reproductive toxicity study in rats reported that mating and reproductive performance were unaffected by treatment (up to 0.8 percent EHDPP in food). Reduced pup weight and survival were noted at mid- and high-doses, respectively. Relative and absolute liver and adrenal weight increased in a dose-dependent manner in both sexes and both generations. Liver and adrenal pathology was also reported. The reproductive NOAEL for both parental and pup generations was 0.2 percent EHDPP in the diet, equivalent to 144 mg/kg/day [1].

U.K. assessors judged EHDPP to have a low potential to cause cancer in humans based on negative results in in vitro and in vivo mutagenicity and genotoxicity assays and an absence of proliferative lesions in repeat-dose studies [1].

Investigators at the National Toxicology Program have used high-throughput assays and rapidly developing whole organisms, such as zebrafish and the nematode C. elegans, to screen for potential developmental toxicity and neurotoxicity of a number of organophosphorus flame retardants [3,4]. Based on results, EHDPP was prioritized for additional neurodevelopmental testing. Briefly, EHDPP reduced firing rate in a neural network assay and inhibited larval development in the nematode C. elegans [3,4]. EHDPP caused significant inhibition of mitochondrial activity which may partly explain the observed developmental arrest in C. elegans [4]. In two developmental rat studies, no clear treatment-related developmental effects were seen at oral doses of up to 3,000 mg/kg- day [1].

Summary of Potential for Exposure

EHDPP is primarily used as a flame retardant and plasticizer in flexible PVC. It is used in food-wrapping films such as those used to wrap meats and skinless sausages [1,2]. According to a 2009 assessment by the U.K., other current uses are in PVC plastics, rubber, polyurethanes, photofilms, paints, pigment dispersions, adhesives, and PVC coatings on textiles and fabrics [1]. These are materials that could be in children's products. It is also used in inflammable hydraulic fluids like those used in large aircraft [2]. U.S. national volume production was reported to be one million to ten million pounds/year in 2012 [5].

[17] LOAEL Low Observed Adverse Effect Level and NOAEL No Observed Adverse Effect Level

EHDPP has been detected in U.S. house dust with levels ranging from 140 to 3,000 ng/g [6]. EHDPP has been detected in U.S. diet studies, primarily in fats and oily foods [1,2]. A sample of margarine for example had 20 ppm. Estimates of mean daily dietary intake in the U.S. by Gunderson et al. 1995, were 339 ng/kg bodyweight for infants and 1236 ng/kg body weight for toddlers based on data from 1986-1991 surveys [2].

Biomonitoring studies have measured EHDPP or metabolites in breast milk, urine, and blood. EHDPP was detected in breast milk of Swedish women and women from three Asian countries [7,8]. It was recently detected in the blood of Chinese adults at a median level three times higher than TPHP [9]. A urinary metabolite of EHDPP called DPHP has also been measured in human urine. It is not specific to EHDPP as it can be generated from at least two other flame retardants, TPHP and RDP [10].[18] The DPHP metabolite has been detected in urine of California adults: 91 percent of children in a German day care study and 93 percent of the infants in a North Carolina study [11-13]. Urinary levels of DPHP in children were higher than their mothers in two studies [14,15].

Two studies looked for evidence that household sources of TPHP flame retardant contributed to children's exposure. No correlations with indoor dust or air concentrations of TPHP were detected in the German study [12]. No correlations between DPHP in infant urine and the number of infant products in the home were detected in the North Carolina study [11]. Either another flame retardant is contributing to this metabolite (for example EHDPP) or there are more important sources of exposure.

If EHDPP is released into the environment, biodegradation is expected to occur with conservative estimated half-lives of 50 days in surface water and 300 days in soil and sediment [1]. It has potential to build up in aquatic organisms [2]. A 2009 review for measurements in environmental media located some soil, water, and air studies conducted in the 1980s; but no positive detections, including in samples collected near industrial production sites [1].

List of References

1. United Kingdom (UK)., Environmental risk evaluation report: 2-Ethylhexyl diphenyl phosphate (CAS no. 1241-94-7). R.H. Environment Agency, Waterside Drive, Aztec West, Almondsbury, Bristol, Editor. 2009.
2. National Laboratory of Medicine. HSDB. Diphenyl-2-ethylhexyl phosphate, (CASRN: 1241-94-7). 2015 Updated 02/18/2015. http://toxnet.nlm.nih.gov/cgi-bin/sis/search2/f?./temp/~efycoF:1.

[18] A variety of hydrolysis products of resorcinol bis(diphenylphosphate) (RDP) and its oligomers were identified by Ballesteros-Gomez, et al. 2015. These metabolites include DPHP. (See ref #10 Ballesteros-Gomez et al.)

3. Behl, M., et al., Use of alternative assays to identify and prioritize organophosphorus flame retardants for potential developmental and neurotoxicity. Neurotoxicol Teratol, 2015.
4. Behl, M., et al., Comparative Toxicity of Organophosphate Flame Retardants and Polybrominated Diphenyl Ethers to Caenorhabditis elegans. Toxicol Sci, 2016.
5. EPA. Chemical Data Access Tool (CDAT) - Chemical Data Reporting (CDR) information on the production and use of chemicals manufactured or imported into the United States. 2012 10/15/2015 10/30/2015]. http://java.epa.gov/oppt_chemical_search/.
6. Dodson, R.E., et al., After the PBDE phase-out: a broad suite of flame retardants in repeat house dust samples from California. Environ Sci Technol, 2012. 46(24): p. 13056-66.
7. Sundkvist, A.M., U. Olofsson, and P. Haglund, Organophosphorus flame retardants and plasticizers in marine and fresh water biota and in human milk. J Environ Monit, 2010. 12(4): p. 943-51.
8. Kim, J.W., et al., Organophosphorus flame retardants (PFRs) in human breast milk from several Asian countries. Chemosphere, 2014. 116: p. 91-7.
9. Zhao, F., et al., Levels of Blood Organophosphorus Flame Retardants and Association with Changes in Human Sphingolipid Homeostasis. Environ Sci Technol, 2016. 50(16): p. 8896-903.
10. Ballesteros-Gomez, A., N. Van den Eede, and A. Covaci, In vitro human metabolism of the flame retardant resorcinol bis(diphenylphosphate) (RDP). Environ Sci Technol, 2015. 49(6): p. 3897-904.
11. Hoffman, K., et al., High Exposure to Organophosphate Flame Retardants in Infants: Associations with Baby Products. Environ Sci Technol, 2015.
12. Fromme, H., et al., Organophosphate flame retardants and plasticizers in the air and dust in German daycare centers and human biomonitoring in visiting children (LUPE 3). Environ Int, 2014. 71: p. 158-63.
13. Dodson, R.E., et al., Urinary biomonitoring of phosphate flame retardants: levels in California adults and recommendations for future studies. Environ Sci Technol, 2014. 48(23): p. 13625-33.
14. Butt, C.M., et al., Metabolites of organophosphate flame retardants and 2-ethylhexyl tetrabromobenzoate in urine from paired mothers and toddlers. Environ Sci Technol, 2014. 48(17): p. 10432-8.
15. Cequier, E., et al., Human exposure pathways to organophosphate triesters - a biomonitoring study of mother-child pairs. Environ Int, 2015. 75: p. 159-65.

CAS 1330-78-5 Tricresyl phosphate (TCP)

Summary of Toxicity

Tricresyl phosphate (TCP) is classified by EPA as a high hazard for reproductive and repeated dose toxicity, and a moderate hazard for developmental and neurological toxicity [1].

Endocrine organs appear to be sensitive to TCP toxicity. Studies carried out by the National Toxicology Program (NTP) in 1994 showed that long-term oral exposure (13 weeks and 104 weeks) to TCP induced adrenal gland and ovarian lesions in rats and adrenal and liver lesions in mice. The lowest-observed-adverse-effect-level (LOAEL) was 7 mg/kg-day for ovarian lesions in female rats in a 2-year bioassay [2,3]. TCP was not carcinogenic in NTP oral bioassays in rats and mice [2]. The TCP used in the NTP studies was a mixed isomer preparation of 79 percent tricresyl phosphate esters consisting of 21 percent tri-m-cresyl phosphate, 4 percent tri-p-cresyl phosphate, less than 1 percent tri-o-cresyl phosphate, and other unidentified tricresyl phosphate esters [2].

At higher doses, TCP reduced fertility and survival of offspring in rodents [2]. Aside from impacts on female ovaries mentioned above, TCP caused a dose-dependent increase in abnormal sperm morphology, reduced sperm concentration, and caused atrophy of seminiferous tubules in male rodents. TCP reduced the number of litters produced and pups per litter especially when males were treated. It also increased pup mortality postnatally [2,4,5]. LOAELs ranged from 63-400 mg/kg-day for these reproductive and developmental effects [1].

NTP studies demonstrated that TCP is neurotoxic to rodents exposed by gavage for 13 weeks to commercial TCP mixtures (with less than 0.1 percent *ortho* TCP isomer). Briefly, TCP caused neuropathy (axonal degeneration in the spinal cord and sciatic nerve) in rats and mice. The LOAEL was 100 mg/kg-d for neurological lesions in male mice [1,3]. The *ortho* isomer is reportedly kept to less than 1 percent of commercial TCP mixtures [1] because it is a known neurotoxic agent in people. In the early 1930s, an outbreak of delayed neuropathy and paralysis in the United States was traced to tri-o-cresyl phosphate that had been added to Jamaican ginger extract and ingested as an alternative alcoholic drink during the Prohibition era [6].

Summary of Potential for Exposure

Commercial TCP is composed of a mixture of methylated triphenyl phosphate isomers with an unspecified amount of methyl substitution[19] including tri-*meta*-cresylphosphate (CAS 563-04-2), tri-*para*-cresylphosphate (CAS 78–32-0), and tri-*ortho*-cresylphosphate (CAS 78-30-8). TCP is often used as a flame retardant and plasticizer in PVC, cellulosic polymers, thermoplastics, and synthetic rubber. It may be added to polyurethane foam as a flame retardant. It also is a flame

[19] Other isomers that might also be present in the TCP mixture include the ortho-ortho-meta (oom), ortho-ortho-para (oop), omm, omp, opp, mmp, and mpp isomers (Van der Veen et al. 2012; reference 14)

retardant additive for industrial lubricants such as hydraulic and brake fluids, and in photographic film [1,2,7]. The NTP report indicated it was used in back-coatings for upholstery fabric [3]. U.S. national volume production was reported to be one million to ten million pounds/year in 2012 [8].

TCP has been measured in 100 percent of dust samples in two North American studies of house dust [9,10]. The largest study sampled 134 urban Canadian homes and reported mean dust concentrations of 990-2600 ng/g depending on the method. Maximum reported dust concentration was 75,000 ng/g dust [10].

TCP has not been widely measured in biomonitoring studies of the general population or children. All three known isomers of TCP were measured but not detected in urine of German children or indoor dust in multiple German day care centers [11]. TCP was detected at low levels in breast milk from Swedish women (median was 0.28 ng/g lipid; maximum was 3.7 ng/g lipid) [12]. Median levels in Asian women were similar, but the maximum detected level in breast milk (85 ng/g lipid) was much higher in this population [13].

TCP has a high bioconcentration factor (BCF) of 8.56 x 10^3 meaning that it is likely to partition to fish and sediments if released into waterways. Potential for TCP bioaccumulation may be low, however. Three fish species cleared this compound after exposure ceased. TCP degraded within five days in river water, and within 7.5 hours in sewage sludge in other studies [5,14]. Rats also are able to excrete TCP in urine, feces, and expired air.

List of References

1. EPA, Flame Retardants Used in Flexible Polyurethane Foam: An Alternatives Assessment Update. 2015, U.S. Environmental Protection Agency.
2. ATSDR. Toxicological profile for phosphate ester flame retardants. 2012 Updated Jan 21, 2015. www.atsdr.cdc.gov/ToxProfiles/TP.asp?id=1119&tid=239.
3. National Toxicology Program (NTP), NTP technical report on the toxicology and carcinogenesis studies of tricresyl phosphate (CAS No. 1330-78-5) in F344/N rats and B6C3F1 mice (gavage and feed studies). TR-433. 1994, National Toxicology Program.
4. Carlton, B.D., et al., Examination of the reproductive effects of tricresyl phosphate administered to Long-Evans rats. Toxicology, 1987. **46**(3): p. 321-8.
5. World Health Organization (WHO). Tricresyl Phosphate - Environmental Health Criteria 110. Environmental Health Criteria 1990. http://apps.who.int/bookorders/anglais/detart1.jsp?codlan=1&codcol=16&codcch=110.
6. National Library of Medicine. HSDB. Tricresyl Phosphate (CAS No. 1330-78-5). Hazardous Substances Data Bank, (accessed September 2016). http://toxnet.nlm.nih.gov/cgi-bin/sis/search2/f?./temp/~Noc1PH:3.

7. Van den Eede, N., et al., Analytical developments and preliminary assessment of human exposure to organophosphate flame retardants from indoor dust. Environ Int, 2011. **37**(2): p. 454-61.
8. EPA. Chemical Data Access Tool (CDAT) - Chemical Data Reporting (CDR) information on the production and use of chemicals manufactured or imported into the United States. 2012 10/15/2015 10/30/2015]. http://java.epa.gov/oppt_chemical_search/.
9. Dodson, R.E., et al., After the PBDE phase-out: a broad suite of flame retardants in repeat house dust samples from California. Environ Sci Technol, 2012. **46**(24): p. 13056-66.
10. Fan, X., et al., Simultaneous determination of thirteen organophosphate esters in settled indoor house dust and a comparison between two sampling techniques. Sci Total Environ, 2014. **491-492**: p. 80-6.
11. Fromme, H., et al., Organophosphate flame retardants and plasticizers in the air and dust in German daycare centers and human biomonitoring in visiting children (LUPE 3). Environ Int, 2014. **71**: p. 158-63.
12. Sundkvist, A.M., U. Olofsson, and P. Haglund, Organophosphorus flame retardants and plasticizers in marine and fresh water biota and in human milk. J Environ Monit, 2010. **12**(4): p. 943-51.
13. Kim, J.W., et al., Organophosphorus flame retardants (PFRs) in human breast milk from several Asian countries. Chemosphere, 2014. **116**: p. 91-7.
14. van der Veen, I. and J. de Boer, Phosphorus flame retardants: properties, production, environmental occurrence, toxicity and analysis. Chemosphere, 2012. **88**(10): p. 1119-53.

CAS 1763-23-1 Perfluorooctane sulphonic acid (PFOS) and its salts

Summary of Toxicity

PFOS is considered a developmental toxicant by the European Union [1]. In rodent studies, it caused high mortality of offspring, reduced weight gain in surviving pups, and developmental delays [2,3]. Recent epidemiological investigations into developmental effects associated with background levels of PFOS in pregnant women provide limited support. Apelberg et al .(2007) reported that PFOS in cord blood had a negative association with birth weight and head circumference in babies [4]. Fei et al. (2007) conducted a similar study but did not observe any association between fetal growth indicators and maternal PFOS levels during pregnancy [5]. The latter study followed children into early childhood and reported , however, that children whose mothers had the highest PFOS during pregnancy had slight delays in meeting two benchmarks: age at sitting without support and age for certain vocal benchmarks [6].

In short and long-term tests in adult rats and primates, PFOS results in liver toxicity and mortality [2,3].

Summary of Potential for Exposure

PFOS is listed as a Persistent, Bioaccumulative, and Toxic (PBT) chemical under Washington State's PBT rule (WAC 173-333-320) [3]. It was historically used in Scotchgard and other waterproofing materials in children's apparel and furniture [3]. According to a 2009 survey, it currently has limited uses in photolithography and as a chemical intermediate in industrial applications. The potassium and ammonium salts of PFOS are used in metal plating and in the manufacture of semiconductors [4]. PFOS is also a degredation product of many other perfluroinated compounds [4]. Biomonitoring is still finding widespread detections of PFOS in the serum of the U.S. general population [5].

List of References

1. European Commission, Joint Research Centre, Institute for Health and Consumer Protection. European Chemical Substances Information System (ESIS) file for heptadecafluorooctane-1-sulphonic acid (CAS# 1763-23-1).
2. Organization for Economic Co-operation and Development (OECD). Co-operation on Existing Chemicals - Hazard Assessment of Perfluorooctane Sulfonate and its Salts, Environment Directorate Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology, Paris, 21 November 2002.
3. U.S. Department of Health and Human Services, Agency for Toxic Substances & Disease Registry. Draft Toxicological Profile for Perfluoroalkyls, May 2009.
4. Apelberg, FJ, Witter FR, Herbstman JB, et al. (2007) Cord serum concentrations of perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) in relation to weight and size at birth. *Environ Health Perspect 115*:1670-1676.
5. Fei C, McLaughlin JK, Tarone RE, et al. (2007) Perfluorinated chemicals and fetal growth: A study within the Danish National Birth Cohort. *Environ Health Perspect 115*:1677-1682.
6. Fei C, McLaughlin JK, Lipworth L, et al. (2008) Prenatal exposure to perfluorooctanoate (PFOA) and perfluorooctanesulfonate (PFOS) and maternally reported developmental milestones in infancy. *Environ Health Perspect 116(10)*:1391-1395.
7. WA Department of Ecology. Summary of Technical Background Information for the Proposed PBT List (Revised Draft) October 2005.
8. Organization for Economic Co-operation and Development (OECD). PFCS: OUTCOME OF THE 2009 SURVEY ON THE PRODUCTION, USE AND RELEASE OF PFOS, PFAS, PFOA PFCA, THEIR RELATED SUBSTANCES AND PRODUCTS/MIXTURES CONTAINING THESE SUBSTANCES. OECD Environment, Health and Safety Publications, Series on Risk Management. No. 24, January 2011.
9. Centers for Disease Control and Prevention (CDC), Fourth National Report on Human Exposure to Environmental Chemicals, December 2009.

CAS 1806-26-4 4-octylphenol

Summary of Toxicity

4-octylphenol has been classified as a Category 1 endocrine disruptor by the European Union [1]. Rats exposed to 4-octylphenol during gestation and for three weeks after birth had decreased testicular size and decreased sperm production as adults when compared to unexposed control animals [2]. Several *in vitro* assays indicate that 4-octylphenol has estrogenic activity [3,4].

Summary of Potential for Exposure

A Dutch study of plastics in children's products found 4-octylphenol in 2 out of 48 polyvinyl chloride plastics [5].

List of References

1. European Commission DG Environment (2002). Endocrine disruptors: study on gathering information on 435 substances with insufficient data. Final report B4-3040/2001/325850/MAR/C2.
2. Sharpe, RM, Fisher, JS, Millar, MM, Jobling, S, and Sumpter, JP. (1995). Gestational and lactational exposure of rats to xenoestrogens results in reduced testicular size and sperm production. Environ Health Perspect 103: 1136-43.
3. Andersen, HR et al. (1999). Comparison of short-term estrogenicity tests for identification of hormone-disrupting chemicals. *Environ Health Perspect 107*(Suppl 1): 89-108.
4. Bonefeld- Jorgensen, EC et al (2007) Endocrine disrupting potential of bisphenol A, bisphenol A dimethacrylate, 4-n-nonylphenol, 4 -n-octylphenol in vitro: new data and a brief review. *Environ Health Perspect 115*(suppl 1): 69-76.
5. Dutch Inspectorate for Health Protection and Veterinary Public Health (VWA/KvW). Screening of Plastic Toys for Chemical Composition and Hazards, Report ND05o610/01, July 2005.

CAS 5466-77-3 2-ethyl-hexyl-4-methoxycinnamate (also called octinoxate)

Summary of Toxicity

2-ethyl-hexyl-4-methoxycinnamate has been classified as a Category 1 endocrine disruptor by the European Union [1]. The compound was found to interfere with the hypothalamic-pituitary-thyroid axis in rats, causing a dose-dependent reduction in thyroid hormones (T3, T4), and thyrotropin (TSH) levels [2]. 2-ethyl-hexyl-4-methoxycinnamate has demonstrated estrogenic properties in the uterotrophic assay and the MCF-7 breast cancer cell line [3].

Summary of Potential for Exposure

The Danish EPA found 2-ethyl-hexyl-4-methoxycinnamate in 2 out of 5 bed linens [4] and 2 out of 28 sunscreens marketed for babies [4]. It is a UV-B filter and is used in many sunscreens, including those marketed for children. It is listed as an ingredient in more than 1700 products including sunscreen, foundation and other facial make-up, lip gloss, and hair products [5].

List of References

1. European Commission DG Environment (2002). Endocrine disruptors: study on gathering information on 435 substances with insufficient data. Final report B4-3040/2001/325850/MAR/C2.
2. Klammer H, Schlecht C, Wuttke W, Schmutzler C, Gotthardt I, Köhrle J, Jarry H. (2007) Effects of a 5-day treatment with the UV-filter octyl-methoxycinnamate (OMC) on the function of the hypothalamo-pituitary-thyroid function in rats. *Toxicology 238(2-3)*: 192-9.
3. Schlumpf M, Cotton B, Conscience M, Haller V, Steinmann B, Lichtensteiger W. (2001) In vitro and in vivo estrogenicity of UV screens. *Environ Health Perspect 109(3)*: 239-44.
4. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Report 102, 2009.
5. Environmental Working Group Skin Deep Database (accessed March 31, 2011).

CAS 7439-97-6 Mercury & mercury compounds

Summary of Toxicity

Mercury exists in three forms that have different properties, usage, and toxicity. The three forms are called elemental (or metallic) mercury, inorganic mercury compounds, and organic mercury compounds. Methylmercury and metallic mercury vapor are well known neurotoxicants. Mercury and mercury compounds are listed as developmental hazards by the European Union and the state of California [1,2]. Animal and human evidence is especially strong for developmental effects of methylmercury and the developing child is considered the most sensitive life stage for exposure [3]. Mercury compounds are listed as possible carcinogens by authoritative sources [2,4,5].

Summary of Potential for Exposure

Metallic mercury is used in some thermometers, dental amalgams, fluorescent light bulbs, some electrical switches, mining, and some industrial processes. Inorganic mercury compounds are used in some industrial processes, in the production of other chemicals and in cosmetics in some countries for skin-lightening soap and creams [3]. Organic mercury compounds, such as Thimerosal and phenylmercuric acetate, are used as preservatives in pharmecueticals [3]. Metallic mercury has been found in imported jewelry marketed to children in WA State. It is also

in button-type batteries used in many children's toys [6]. The Center for Disease Control and Prevention found widespread detections of both organic and inorganic mercury in biomonitoring the general U.S. population [7].

List of References

1. European Commission, Joint Research Centre, Institute for Health and Consumer Protection. European Chemical Substances Information System (ESIS) file for Mecury.
2. California Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. Feb 5, 2010. Listed as mercury and mercury compounds.
3. Centers for Disease Control and Prevention (CDC), Fourth National Report on Human Exposure to Environmental Chemicals, December 2009.
4. WHO, International Agency for Research on Cancer (IARC) Agents Classified by the *IARC Monographs*, Volumes 1–100 (listed as Methylmercury compounds).
5. U.S. EPA, Integrated Risk Information System (IRIS). File for Methylmercury (Last revised 1995).
6. Interstate Mercury Education & Reduction Clearing house (IMERC) database of mercury in consumer products. Accessed July 2011.
7. Caldwell KL, Mortensen ME, Jones RL, Caudill SP, Osterloh JD. Total blood mercury concentrations in the U.S. population: 1999–2006. *Int J Hyg Environ Health 2009; 212*:588-598.

CAS 7440-36-0 Antimony & Antimony compounds

Summary of Toxicity

Antimony trioxide is classified as a carcinogen by authorative sources [1-4]. The listings are based on experimental evidence that demonstrates induction of lung tumors in rats following inhalation of antimony trioxide. There are supportive human data which show an excess of mortality from lung cancer among antimony workers, but these data are not considered conclusive [2,3,5].

Summary of Potential for Exposure

Antimony trioxide (ATO) is used as catalyst in the manufacture of polyester fabrics and polyethylene terephthalate **(**PET) plastics and is used as a synergist to flame retardants in textiles, plastics, paints, adhesives, and sealants. Antimony compounds are also used in the manufacture of pigments, paints, glass, pottery, and enamels. Antimony is common at low percentages in metal alloys [6].

The Danish Environmental Protection Agency (DEPA) detected antimony in their tests of many children's products including perambulator covers, pencil cases, school bags, glitter glue, natural

toys, mattress pads, and fabric samples such as polyester clothing [7]. Antimony was found in a DEPA survey of jewelry that included children's jewelry [7]. Biomonitoring in general U.S. population reported widespread detections in people. Children appear to have higher body burdens than adults [8].

List of References

1. California Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. Feb 5, 2010.
2. WHO, International Agency for Research on Cancer (IARC) Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume No 47, Research on Cancer Some Organic Solvents, Resin Monomers and Related Compounds, Pigments and Occupational Exposures in Paint Manufacture and Painting (1989).
3. American Conference of Governmental Industrial Hygienists TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents and Biological Exposure Indices. Cincinnati, OH, 2008, p. 12.
4. European Commission Regulation on Classification, Labeling and Packaging. 2009. CLP-Regulation (EC) No 1272/2008: Annex VI, Table 3.1.
5. European Union Risk Assessment, Rapporteur Sweden. Diantimony Trioxide Draft Risk Assessment, November 2008.
6. National Institutes of Health, National Library of Medicine Hazardous Substances Data Bank Accessed May 2010.
7. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in consumer products. Reports 23, 58, 67, 84, 90, 93 and 94.
8. Centers for Disease Control and Prevention (CDC), Fourth National Report on Human Exposure to Environmental Chemicals, December 2009.

CAS 7440-38-2 Arsenic & Arsenic compounds

Summary of Toxicity

Arsenic is classified as a carcinogen by a number of authoritative sources [1-4]. In humans, arsenic exposure has been linked to lung cancer, bladder cancer, skin cancer, and cancers at several other sites in the body. The state of California has identified it as a reproductive toxicant [4].

Summary of Potential for Exposure

Historically inorganic arsenic compounds were used in wood preservatives, other pesticides, medicines, metal alloys, and paint pigments [5,6]. The Danish EPA found arsenic in children's products including 3 of 4 pencil cases and 5 of 7 school bags [7].

List of References

1. WHO, International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Supplement No 7: Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs Volumes 1 to 42. 1987.
2. U.S. EPA Integrated Risk Information System (IRIS) for Inorganic Arsenic (last revised 1998).
3. U.S. DHHS, PHS, National Toxicology Program. Report on Carcinogens, Eleventh Edition. 2005.
4. California EPA, Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. February 5, 2010.
5. Centers for Disease Control and Prevention (CDC), Fourth National Report on Human Exposure to Environmental Chemicals, December 2009.
6. U.S. EPA, Office of Pesticide Programs, Pesticide registration, Organic Arsenicals, October 2009.
7. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in consumer products. Report 84, 2007.

CAS 7440-43-9 Cadmium & Cadmium compounds

Summary of Toxicity

Cadmimum and cadmium compounds are classified as carcinogens by authoriative sources [1-4]. Cadmium produces lung and other cancers in laboratory animals by multiple routes of exposures [1]. Studies of people exposed to cadmium have reported excess lung and prostate cancers although co-exposures to other carcinogens often limit the human evidence [1]. It appears that ionic cadmium is genotoxic [1]. Cadmium accumulates in liver and kidney and can cause kidney damage if the levels in the kidney are high enough [3,5]. Cadmium damages male and female reproductive organs and tissues in rats and mice and is classified as a reproductive hazard by the European Union and the state of California [4,7]. Young animals exposed to cadmium before birth have shown impaired growth and neurobehavioral effects [4,5,7].

Summary of Potential for Exposure

Cadmium is used primarily in the manufacture of nickel-cadmium batteries. It is also used as pigments for plastics, ceramic, and glass, as a stabilizer for polyvinyl chloride (PVC); and in alloys and coatings on steel, and other non-ferrous metals [4,5]. The Danish EPA detected cadmium in children's school supplies, such as pencil cases and school bags [6]. A Danish investigation of jewelry from south Asia detected significant amount of cadmium in some "silver" items and demonstated that cadmium could migrate out of these items in artifical sweat [4].

List of References

1. U.S. DHHS, PHS, National Toxicology Program. Report on Carcinogens, Eleventh Edition. 2005.
2. WHO, International Agency for Research on Cancer (IARC) Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume No 58, Beryllium, Cadmium, Mercury, and Exposures in the Glass Manufacturing Industry, 1993.
3. U.S.EPA, Integrated Risk Information System (IRIS). Cadmium (last revised 1994).
4. European Commission, Joint Research Centre. European Union, Risk Assessment Report for Cadmium Metal, Part II Human Health. 2007.
5. ATSDR 2008 Toxicological Profile for Cadmium, Draft for Public Comment, September 2008.
6. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Report 84, Survey as well as health assessment of chemical substances in school bags, toy bags, pencil cases and erasers, 2007.
7. California EPA, Office of Environmental Health Hazard Assessment (OEHHA), Reproductive and Cancer Hazard Assessment Section. Proposition 65 Maximum Allowable Daily Level (MADL) for Reproductive Toxicity for Cadmium (Oral Route), May 2001.

CAS 7440-48-4 Cobalt & Cobalt compounds

Summary of Toxicity

Some cobalt compounds are classified as carcinogens by authoritative sources [1-3]. Inhalation of cobalt compounds can induce lung and other cancers in rats and mice [1,2]. Occupational studies are not conclusive but do indicate that cobalt may be an agent of lung cancer in humans [1,2,5]. Oral exposures to soluble cobalt compounds are associated with testicular atrophy and reduced fertility in male rodents [4]. There is also a limited literature indicating that cobalt had developmental toxicity in rodents [4].

Summary of Potential for Exposure

Cobalt is used in alloys, pigments, and fertilizers, as a drying agent in paints, varnishes and inks, a component in porcelain enamel, and as a catayst in synthesizing polyester and other materials [5]. In testing by the Danish EPA, cobalt was found in samples of fabric, in glass and porcelain colors, and at trace levels in school supplies [6].

List of References

1. WHO, International Agency for Research on Cancer (IARC) Monograph on the Evaluation of Carcinogenic Risks to Humans, Vol. 86: Cobalt in Hard Metals and Cobalt Sulfate, Gallium Arsenide, Indium Phosphide and Vanadium Pentoxide (2006).

2. U.S. DHHS, PHS, National Toxicology Program. Report on Carcinogens, Eleventh Edition. 2005.
3. California Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. Feb 5, 2010.
4. REPROTEXT Thomson Reuters (Healthcare) Inc. File for Cobalt. Database Version 5.1 Greenwood Village, CO. (accessed 2009).
5. Centers for Disease Control and Prevention (CDC), Fourth National Report on Human Exposure to Environmental Chemicals, December 2009.
6. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in consumer products. Reports 23, 59, and 84.

CAS 13674-84-5 Tris (1-chloro-2-propyl) phosphate (TCPP)

Summary of Toxicity

EPA classified Tris (1-chloro-2-propyl) phosphate (TCPP) as a high hazard for reproductive and developmental effects based on increased estrus cycle length, decreased uterine weights, and increased number of runts at the 99 mg/kg dose in a 2-generation oral rat study [1,2]. TCPP has not been tested for cancer, but it is structurally similar to TDCPP and TCEP[20] which are both demonstrated animal carcinogens [2]. The National Toxicology Program has a cancer assay underway to fill this important data gap [3].

Only limited toxicity testing results for TCPP were identified in a review by ATSDR in 2012 [4]. A 1982 study by Kawasaki H. et al. reported that oral dosing in pregnant rats up to 893 mg/kg-day on gestation days 0-20 had no significant effects on the number of implantations or resorptions, fetal weight, external malformations, or pup survival and growth in the first four postnatal weeks [4].

Summary of Potential for Exposure

TCPP is an additive flame retardant used in polyurethane furniture foam, textiles, apparel, leather, electronics, and rigid polyurethane foam insulation and roofing laminates used in building construction [3]. Commercial TCPP is a mixture of isomers: primarily CAS 13674-84-5, with lesser amounts of CAS 76025-08-6, and 76649-15-5 [3]. The U.S. national production volume of TCPP was reported to be 54,673,933 pounds in 2012 [3,5].

TCPP has been detected in U.S. household furniture and in baby products including: polyurethane foam in car seats, changing table pads, sleep positioners, portable mattresses,

[3] TDCPP – Tris(1,3-dichloro-2-propyl)phosphate; TCEP – Tris(2-chloroethyl) phosphate

nursing pillows, and children's furniture [6-8]. Detection rates in foam are reported to be 0.5-2.2 percent by weight in furniture foam; 1-14 percent in baby product foam [3,8].

TCPP has been detected, often with high frequency, in indoor house dust and air by multiple studies in North America [8-12]. Median and mean levels in dust are frequently in the low parts per million (µg/g) with detections up to 140 µg/g dust. Reported air concentration of inhalable TCPP particulate (defined as greater than 4µm) ranged up to 1.36 $\mu g/m^3$ in home indoor air [9]. TCPP has been detected in a variety of foods in the FDA total diet study at low levels (less than 7 ppb).

In biomonitoring studies, two metabolites of TCPP have been measured and detected in human urine: bis (1-chloro-2-propyl) phosphate (BCIPP) and 1-hydroxy-2-propyl bis(1-chloro-2-propyl) phosphate (BCIPHIPP). One or both were detected in toddlers and their mothers in New Jersey,[13] infants in North Carolina [14], mothers and their children in California [15], and in adults in Northern California [16]. While the frequency of detection and levels detected are generally low for the BCIPP metabolite, a recent study measured the BCIPHIPP metabolite in 100 percent of mothers and their children. Maximum concentrations in urine for mothers and children were 104 ng/mL and 23.2 ng/mL, respectively [15]. TCPP has also been detected in breast milk in Sweden at concentrations up to 82 ng/g lipid [17].

EPA considers TCPP to have high hazard for persistence and low hazard for bioaccumulation [1]. In rats, TCPP is readily absorbed, is widely distributed to tissues, especially the liver and kidney, and is excreted primarily in urine but also bile and feces. Tissue elimination time was slowest from adipose tissue (adipose $T_{1/2}$ = 103 hours) [4].

List of References

1. EPA, Flame Retardants Used in Flexible Polyurethane Foam: An Alternatives Assessment Update. 2015, Environmental Protection Agency.
2. EU, Tris(2-chloro-1-methylethyl) phosphate (TCPP) Risk Assessment. 2008, European Union: Dublin, Ireland.
3. EPA, TSCA Work Plan Chemical Problem Formulation and Initial Assessment - Chlorinated Phosphate Ester Cluster Flame Retardants. 2015, Environmental Protection Agency.
4. ATSDR. Toxicological profile for phosphate ester flame retardants. 2012 Updated Jan 21, 2015. Available from: http://www.atsdr.cdc.gov/ToxProfiles/TP.asp?id=1119&tid=239.
5. EPA. Chemical Data Access Tool (CDAT) - Chemical Data Reporting (CDR) information on the production and use of chemicals manufactured or imported into the United States. 2012 10/15/2015 10/30/2015]; Available from: http://java.epa.gov/oppt_chemical_search/.

6. Stapleton, H.M., et al., Identification of flame retardants in polyurethane foam collected from baby products. Environ Sci Technol, 2011. **45**(12): p. 5323-31.
7. Ecology, Flame Retardants in General Consumer and Children's Products. 2014. Washington State Department of Ecology, June 2014, Publication No. 14-04-021.
8. Stapleton, H.M., et al., Detection of Organophosphate Flame Retardants in Furniture Foam and U.S. House Dust. Environmental Science & Technology, 2009. **43**(19): p. 7490-7495.
9. La Guardia, M.J. and R.C. Hale, Halogenated flame-retardant concentrations in settled dust, respirable and inhalable particulates and polyurethane foam at gymnastic training facilities and residences. Environ Int, 2015. **79**: p. 106-14.
10. Dodson, R.E., et al., After the PBDE phase-out: a broad suite of flame retardants in repeat house dust samples from California. Environ Sci Technol, 2012. **46**(24): p. 13056-66.
11. Stapleton, H.M., et al., Flame retardant associations between children's handwipes and house dust. Chemosphere, 2014. **116**: p. 54-60.
12. Fan, X., et al., Simultaneous determination of thirteen organophosphate esters in settled indoor house dust and a comparison between two sampling techniques. Sci Total Environ, 2014. **491-492**: p. 80-6.
13. Butt, C.M., et al., Metabolites of organophosphate flame retardants and 2-ethylhexyl tetrabromobenzoate in urine from paired mothers and toddlers. Environ Sci Technol, 2014. **48**(17): p. 10432-8.
14. Hoffman, K., et al., High Exposure to Organophosphate Flame Retardants in Infants: Associations with Baby Products. Environ Sci Technol, 2015.
15. Butt, C.H., K; Chen, A; Lorenzo, A; Congleton, J; Stapleton, HM, Regional comparison of organophosphate flame retardant (PFR) urinary metabolites and tetrabromobenzoic acid (TBBA) in mother-toddler pairs from California and New Jersey. Environment International, 2016. **94**: p. 627-34.
16. Dodson, R.E., et al., Urinary biomonitoring of phosphate flame retardants: levels in California adults and recommendations for future studies. Environ Sci Technol, 2014. **48**(23): p. 13625-33.
17. Sundkvist, A.M., U. Olofsson, and P. Haglund, Organophosphorus flame retardants and plasticizers in marine and fresh water biota and in human milk. J Environ Monit, 2010. **12**(4): p. 943-51.

CAS 13674-87-8 Tris (1, 3-dichloro-2-propyl) phosphate (TDCPP)

Summary of Toxicity

Tris (1,3-dichloro-2-propyp) phosphate (TDCPP) is considered a carcinogen by California Environmental Protection Agency (EPA), Office of Environmental Health Hazard Assessment

[1]. Evidence of carcinogenicity includes increased incidence of liver and kidney tumors in male and female rats, and testicular tumors in male rats [2]. TDCPP is metabolized in the body to several compounds that are also considered carcinogenic [2]. TDCPP is associated with other health effects including: kidney and testicular abnormalities, changes in blood parameters, and an increase in thyroid, kidney, and liver weights in rodents [3].

Summary of Potential for Exposure

TDCPP is a widely used chemical and is added to polyurethane foams as a flame retardant [3]. Frequent detection of TDCPP was reported in a study of children's products, including car seats, changing table pads, portable mattresses, nursing pillows, and high chairs [4]. Testing by the Dutch government detected TDCPP in one out of seven samples of polyurethane in children's toys [5]. TDCPP is not chemically bound to polyurethane foam and over time it can escape and contaminate indoor air and house dust. TDCPP was detected in 96 percent of house dust samples in a study of 50 homes in Boston [6] and detected in 100 percent of 16 homes tested in San Francisco in 2006 and again in 2011 [7]. Children may be exposed to TDCPP directly by touching or sucking treated products or indirectly by inhaling or ingesting house dust.

List of References

1. California EPA, Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. March 16, 2012.
2. California EPA, Office of Environmental Health Hazard Assessment. Evidence on the Carcinogenicity of Tris (1,3-dichloro-2-propyl) phosphate. July 2011.
3. U.S. DHHS, Agency for Toxic Substances & Disease Registry, Toxicological Profile for Phosphate Ester Flame Retardants. September 2012. *http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=1119&tid=239*
4. Stapleton, H. et al. (2011) Identification of flame retardants in polyurethane foam collected from baby products. *J Environ Sci Technol 45:* 5323 – 5331.
5. Dutch inspectorate for Health Protection and Veterinary Public Health (VWA/KvW). Screening of Plastic Toys for Chemical Composition and Hazards, Report ND05o610/01, July 2005.
6. Stapleton, H. et al. (2009) Detection of organophosphate flame retardants in furniture foam and U.S. house dust. *J Environ Sci & Technol 43(19): 7490-7495.*
7. Dodson, R. et al. (2012) After the PBDE phase-out: a broad suite of flame retardants in repeat house dust samples from California. *J Environ Sci & Technol 46:* 13056-13066.

CAS 25013-16-5 Butylated hydroxyanisole (BHA)

Summary of Toxicity

Butylated hydroxyanisole (BHA) is classified as a carcinogen by authoriative sources [1,2,3]. Oral exposures induced cancers of the forestomach in rats and mice [1,2]. BHA is also listed as a Class 1 endocrine disruptor by the European Union [4]. Their classification is based on evidence of disruption of androgen and thyroid hormonal systems in a number of *in vitro* and *in vivo* tests.

In a rat reproduction study, BHA increased relative organ weights of liver, kidney, adrenal gland, and thyroid gland, decreased the mating rate, resulted in less males being born, shortened anogenital distances in male offspring, lengthened the time to vaginal patency and preputial separation in female offspring, and had measurable effects on sperm [5].

Summary of Potential for Exposure

BHA is used primarily as an antioxidant and preservative in food, food packaging, cosmetics, pharmceuticals, and in rubber and petroleum products [1,2]. BHA was reported in many cosmetics in a large survey of use in consumer products [2]. The highest concentrations were in lipsticks and eye shadows. BHA is listed as an ingredient in baby scalp spray-on sunscreen, diaper rash ointments, and baby oil in an online cosmetics database [6]. It has also been reported in chewing gum samples [2].

List of References

1. U.S. DHHS, PHS, National Toxicology Program. Report on Carcinogens, Eleventh Edition. 2005.
2. WHO, International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Supplement No 7: Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs Volumes 1 to 42. 1987.
3. California Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. Feb 5, 2010.
4. European Commission DG Environment (2002). Endocrine disruptors: study on gathering information on 435 substances with insufficient data. Final report B4-3040/2001/325850/MAR/C2.
5. Jeong S; Kim B; Kim S; Cho J; Kim O (2003). Steroid and thyroid hormonal receptor gene transcription assay and one-generation reproduction study of butylated hydroxyanisole. Toxicologist 2003 Mar; 72(S-1):284.
6. Environmental Working Group. Skin Deep Cosmetic Safety Database. Accessed May 2010.

CAS 25154-52-3 Nonylphenol

Related substance: CAS 84852-15-3 4-Nonylphenol (branched)

Summary of Toxicity

Nonylphenol has been classified as a Category 1 endocrine disruptor by the European Union [1]. Uterotrophic assays indicate that nonylphenol has estrogenic activity, and several other lines of evidence suggest that nonylphenol can adversely affect mammalian reproduction [2].

Summary of Potential for Exposure

The Danish EPA found nonylphenol in 1 of 3 pencil erasers [3] and 1 of 28 infant sunscreens [4]. A Dutch study of plastics in children's products found nonylphenol in many samples (mostly polyvinyl chloride) [5].

List of References

1. European Commission DG Environment (2002). Endocrine disruptors: study on gathering information on 435 substances with insufficient data. Final report B4-3040/2001/325850/MAR/C2.
2. 4-Nonylphenol (Branched) And Nonylphenol, CAS Nos: 84852-15-3 and 25154-52-3, Einecs Nos: 284-325-5 and 246-672-0, Risk Assessment, Final Report, 2002, 2nd Priority List, Volume 10, European Union Risk Assessment Report , European Chemicals Bureau, European Commission Joint Research Centre, 2002.
3. Danish Ministry of the Environment, Environmental Protection Agency. Survey of Chemical Substances in Consumer Products, Report 84, 2007.
4. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Report 102, 2009.
5. Dutch Inspectorate for Health Protection and Veterinary Public Health (VWA/KvW). Screening of Plastic Toys for Chemical Composition and Hazards, Report ND05o610/01, July 2005.
6. Danish Ministry of the Environment, Environmental Protection Agency. Survey of Chemical Substances in Consumer Products, Report 84, 2007. www.mst.dk/English/Chemicals/Consumer_Products/Surveys-on-chemicals-in-consumer-products.htm.
7. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Report 102, 2009.
8. Dutch Inspectorate for Health Protection and Veterinary Public Health (VWA/KvW). Screening of Plastic Toys for Chemical Composition and Hazards, Report ND05o610/01, July.
9. Dutch Inspectorate for Health Protection and Veterinary Public Health (VWA/KvW). Screening of Plastic Toys for Chemical Composition and Hazards, Report ND05o610/01, July 2005.
10. Calafat, AM, Kuklenyik, Z, Reidy, JA, Caudill, SP, Ekong, J, and Needham, LL. (2005). Urinary concentrations of bilphenol A and 4-nonylphenol in a human reference population. *Environ Health Perspect 113*: 391-5.

CAS 25637-99-4 Hexabromocyclododecane (HBCD)

Summary of Toxicity

Hexabromocyclododecane (HBCD) has been associated with reproductive and developmental effects in laboratory animals. Fertility index was reduced, newborn animal mortality was increased, and the number of primordial follicles in rat ovaries was reduced by exposure to HBCD that was ingested [1]. Oral dosing of rats resulted in changes in thyroid weight, levels of thyroid hormones, and levels of thyroid stimulating hormone [1]. The liver is also a target for HBCD toxicity [1].

Summary of Potential for Exposure

This substance is listed as a Persistent, Bioaccumulative, and Toxic (PBT) chemical under Washington State's PBT rule (WAC 173-333-320) [2]. HBCD is a brominated flame retardant that is used for polystyrene and for some fabrics [1]. Its use in child car seats has been reported [1]. HBCD has been found in human breast milk and blood in biomonitoring studies [1].

List of References

1. European Commission, European Chemicals Bureau. Risk Assessment Hexabromocyclododecane. 2008. Final Report.
2. WA Department of Ecology. Summary of Technical Background Information for the Proposed PBT List (Revised Draft) October 2005.

CAS 26040-51-7 Bis (2-ethylhexyl) tetrabromophthalate (TBPH)

Summary of Toxicity

EPA classified bis (2-ethylhexyl) tetrabromophthalate (TBPH) as a moderate hazard for reproductive, developmental, neurological, and repeated dose toxicities based on rodent toxicity of commercial mixtures, structurally similar chemicals, and professional judgement [1]. Significant data gaps were noted. Lowest-observed-adverse-effect-levels (LOAELs) for developmental effects in rats were 100 mg/kg-day in an oral prenatal study of a commercial mixture of TBB and TBPH. A LOAEL of 1 mg/kg-day was reported in a second perinatal oral study with another commercial mixture, Firemaster® 550, which contains TBB and TBPH plus two non-brominated phosphate flame retardants [1]. The latter study, published by Patisaul et al. 2013, found that pregnant rats exposed to the Firemaster® 550 mixture during gestation and lactation had altered thyroid function and produced offspring that were 30–60 percent heavier by weaning, an effect that persisted into adulthood. Female offspring of treated rats entered puberty sooner and had glucose intolerance and elevated anxiety behaviors in maze testing [2].

TBPH is a brominated analog of phthalate DEHP [12] and may be an endocrine disrupter [3]. A metabolite of TBPH induced proliferative damage in rodent liver and altered serum thyroid hormone (T3) in rats after 2 days exposure to 200 mg/kg per day [3]. A study in Boston, MA, reported house dust concentrations of TBPH were positively associated with higher level of thyroid hormone (T3) in men [4].

Summary of Potential for Exposure

TBPH has been detected in foam baby products [5] and U.S. residential furniture [6]. TBPH is an ingredient in additive flame retardant mixtures used in flexible polyurethane foam. TBPH is also used in construction materials and as a non-flammable plasticizer in PVC electrical equipment, electronics, and appliances. In addition, TBPH is a flame retardant in neoprene and certain rubbers [7].

TBPH has been measured with high frequency in residential indoor dust in the United States [3,4,8-10] and Canada [11,12]. It was found in 100 percent of indoor dust samples from childcare centers studied in 2010-2011 in Northern California [13]. Across all these studies, mean levels in indoor dust ranged from 144-734 ng/g dust and the maximum level reported was 47,110 ng/g. In a study of pregnant women in North Carolina, levels of TBPH in dust were correlated positively with levels in hand wipes [14]. TBPH was also detected in 100 percent of office dust and 90 percent of car dust in Boston study [3].

TBPH was detected in human serum in a 2014 Indiana study of adults aged 19-38 [15] and in maternal serum and breast milk collected in a 2008-2009 study of women living in Québec, Canada [16].

TBPH is classified by EPA as a high hazard for persistence and bioaccumulation [1].

List of References

1. EPA, Flame Retardants Used in Flexible Polyurethane Foam: An Alternatives Assessment Update. 2015, Environmental Protection Agency.
2. Patisaul, H.B., et al., Accumulation and endocrine disrupting effects of the flame retardant mixture Firemaster(R) 550 in rats: an exploratory assessment. J Biochem Mol Toxicol, 2013. **27**(2): p. 124-36.
3. Springer, C., et al., Rodent thyroid, liver, and fetal testis toxicity of the monoester metabolite of bis-(2-ethylhexyl) tetrabromophthalate (tbph), a novel brominated flame retardant present in indoor dust. Environ Health Perspect, 2012. **120**(12): p. 1711-9.
4. Johnson, P.I., et al., Associations between brominated flame retardants in house dust and hormone levels in men. Sci Total Environ, 2013. **445-446**: p. 177-84.
5. Stapleton, H.M., et al., Identification of flame retardants in polyurethane foam collected from baby products. Environ Sci Technol, 2011. **45**(12): p. 5323-31.

6. Stapleton, H.M., et al., Novel and high volume use flame retardants in US couches reflective of the 2005 PentaBDE phase out. Environ Sci Technol, 2012. **46**(24): p. 13432-9.
7. EPA, TSCA Work Plan Chemical Technical Supplement - Use and Exposure of the Brominated Phthalates Cluster (BPC) Chemicals - Brominated Phthalates Cluster Flame Retardants. 2015, Environmental Protection Agency, Office of Chemical Safety and Pollution Prevention. p. 54.
8. Dodson, R.E., et al., After the PBDE phase-out: a broad suite of flame retardants in repeat house dust samples from California. Environ Sci Technol, 2012. **46**(24): p. 13056-66.
9. Stapleton, H.M., et al., *Alternate and new brominated flame retardants detected in U.S. house dust.* Environ Sci Technol, 2008. **42**(18): p. 6910-6.
10. Brown, F.R., et al., Levels of non-polybrominated diphenyl ether brominated flame retardants in residential house dust samples and fire station dust samples in California. Environ Res, 2014. **135**: p. 9-14.
11. Shoeib, M., et al., Legacy and current-use flame retardants in house dust from Vancouver, Canada. Environmental Pollution, 2012. **169**(0): p. 175-182.
12. Peng, H.e.a., Detection, identification, and quantification of hydroxylated bis(2-ethylhexyl)-tetrabromophthalate isomers in house dust. Environ Sci & Technol, 2015. **49**(5): p. 2999-2006.
13. Bradman, A., et al., Flame retardant exposures in California early childhood education environments. Chemosphere, 2014. **116**: p. 61-6.
14. Hoffman, K., J.L. Daniels, and H.M. Stapleton, Urinary metabolites of organophosphate flame retardants and their variability in pregnant women. Environ Int, 2014. **63**: p. 169-72.
15. Liang-Ying Liu, K.H., Ronald A. Hites, and Amina Salamova, *Hair and Nails as Noninvasive Biomarkers of Human Exposure to Brominated and Organophosphate Flame Retardants.* Environ. Sci. Technol. 2016, 2016. **50**: p. 3065−3073.
16. Zhou, S.N., et al., Measurements of selected brominated flame retardants in nursing women: implications for human exposure. Environ Sci Technol, 2014. **48**(15): p. 8873-80.

CAS 26761-40-0 (also 68515-49-1) Diisodecyl phthalate (DIDP)

Summary of Toxicity

Diisodecyl phthalate has been classified as a developmental toxicant by the National Toxicology Program Center for the Evaluation of Risks to Human Reproduction and by the state of California [1,2]. The National Toxicology Program concluded that there is clear evidence of developmental toxicity [1]. Effects in animals included abnormal development of the fetal skeleton as well as reduced weight gain and survival of the pups [1].

Summary of Potential for Exposure

The Danish EPA found diisodecyl phthalate in a foam toy [3]. Diisodecyl phthalate has also been found in teething rings and other toys [4,5].

Monocarboxyisononyl phthalate, a metabolite indicative of diisodecyl phthalate exposure, was found in 89.9 percent of the U.S. population sampled in the NHANES survey [6].

List of References

1. U.S. Department of Health and Human Services, National Toxicology Program, Center for the Evaluation of Risks to Human Reproduction (CERHR). NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Di-isodecyl Phthalate (DIDP). 2003.
2. California EPA, Office of Environmental Health Hazard Assessment. List of Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. February 5, 2010.
3. Danish Ministry of the Environment, Environmental Protection Agency. Survey of Chemical Substances in Consumer Products, Report 70.
4. Janssen P, van Veen M, van Apeldoorn M, Speijers G. Phthalates in teething rings/animal figures for infants. Advisory report 5293. Brussels: EU Committee Scientific on Toxicity Ecotoxicity and the Environment, CSTEE, 1997.
5. Rastogi SC. (1998). Gas chromatographic analysis of phthalate esters in plastic toys. *Chromatographia* 47: 724-726.
6. Calafat, AM, Wong, L-Y, Silva, MJ, Samandar, E, Preau, JL, Jia, LT, and Needham, LL. (2011). Selecting adequate exposure biomarkers of diisononyl and diisodecyl phalates: data from the 2005-2006 National Health and Nutrition Examination Survey. *Environ Health Perspect* 119: 50-55.

CAS 28553-12-0 (also 68515-48-0) Diisononyl phthalate (DINP)

Summary of Toxicity

Diisononyl phthalate has been classified as a developmental toxicant by the National Toxicology Program Center for the Evaluation of Risks to Human Reproduction [1]. The National Toxicology Program concluded that there is some evidence of developmental toxicity in animals including reduced birth weight and abnormal development of the fetal skeleton and kidneys [1].

Summary of Potential for Exposure

The Danish EPA found diisononyl phthalate in numerous children's products including pacifiers, mittens, soap containers, school supplies, a slimy toy, packaging for cosmetics, 1 of 2 bath toys, and 1 of 2 nursing pillows [2]. A Dutch study found diisononyl phthalate in polyvinyl chloride in some children's products [3]. Monocarboxyisooctyl phthalate, a metabolite indicative of

diisononyl phthalate exposure, was found in 95.2 percent of the U.S. population sampled in the NHANES survey [4].

List of References

1. European Commission DG Environment (2002). Endocrine disruptors: study on gathering information on 435 substances with insufficient data. Final report B4-3040/2001/325850/MAR/C2.
2. 4-Nonylphenol (Branched) And Nonylphenol, CAS Nos: 84852-15-3 and 25154-52-3, Einecs Nos: 284-325-5 and 246-672-0, Risk Assessment, Final Report, 2002, 2nd Priority List, Volume 10, European Union Risk Assessment Report , European Chemicals Bureau, European Commission Joint Research Centre, 2002.

CAS 38051-10-4 Bis(chloromethyl)propane-1,3-diyl tetrakis-(2-chloroethyl) bis(phosphate) (V6)

Summary of Toxicity

EPA classified V6 a moderate hazard for carcinogenicity based on the toxicity of chemicals with very similar structures [1]. Commercial V6 also contains 4.5-13.5 percent Tris (2-chloroethyl) phosphate (TCEP) as an impurity [1,2]. TCEP is classified as a carcinogen by the State of California [3] and a 1b reproductive hazard by the European Union [4].

EPA considered V6 to have high hazard for developmental toxicity and moderate hazard for reproductive toxicity [1]. In a two-generation oral rat study, doses of 86 mg/kg-day caused thyroid effects (follicular hypertrophy and increased organ weight) in the parental generation and caused retarded fetal and pup growth in offspring [5]. The no-observed-adverse-effect-level (NOAEL) was 29 mg/kg-day.

Summary of Potential for Exposure

V6 has been used as an additive flame retardant in polyurethane foam and has been identified in a number of consumer products including foam carpet pads, tent fabric, and baby products [2,6,7]. Average concentration in the products that tested positive was 4.6 percent by weight of the foam [6]. It is reportedly used in interior foam for automotive and furniture foam at typical loadings of ~6 percent w/w [5]. U.S. national production volume of V6 was between 500,000 and 1 million pounds in 2002, but more current information is withheld as confidential business information [8].

V6 has not been widely studied in house dust or the environment. It was detected in 95 percent of car dust samples and 75 percent of house dust samples in a single Boston area study [2]. Concentrations in car dust were significantly higher than the house dust, which is consistent with its reported higher use in automobile foam. Median levels in car dust were 103 ng/g.

We did not identify any biomonitoring studies for V6. The compound is readily absorbed across the gut and less readily across skin. Half-life for elimination from the body was 99-113 hours in orally exposed rats [1].

List of References

1. EPA, Flame Retardants Used in Flexible Polyurethane Foam: An Alternatives Assessment Update. 2015, U.S. Environmental Protection Agency.
2. Fang, M., et al., Investigating a novel flame retardant known as V6: measurements in baby products, house dust, and car dust. Environ Sci Technol, 2013. **47**(9): p. 4449-54.
3. State of California OEHHA. Chemicals Known to the State to Cause Cancer or Reproductive Toxicity. 2016 August; Available from: http://oehha.ca.gov/proposition-65/proposition-65-list.
4. ECHA, Brief Profiles: Tris(2-chloroethyl) phosphate. [accessed September 2016]. Available at https://echa.europa.eu/information-on-chemicals.
5. ECHA, 2,2-bis(chloromethyl) trimethylene bis[bis(2-chloroethyl) phosphate] (V6) - Summary Risk Assessment Report. 2008, European Union: Ireland and United Kingdom.
6. Stapleton, H.M., et al., Identification of flame retardants in polyurethane foam collected from baby products. Environ Sci Technol, 2011. **45**(12): p. 5323-31.
7. Ecology, Flame Retardants in General Consumer and Children's Products. Washington State Department of Ecology, June 2014, Publication No. 14-04-021.
8. EPA. Chemical Data Access Tool (CDAT) - Chemical Data Reporting (CDR) information on the production and use of chemicals manufactured or imported into the United States. 2012. http://java.epa.gov/oppt_chemical_search/.

CAS 68937-41-7 Isopropylated triphenyl phosphate (IPTPP)

Summary of Toxicity

Isopropylated triphenyl phosphate (IPTPP) is an isomeric mixture of phosphate esters derived from isopropyl phenols. Commercial mixtures may vary in the number of isopropyl substitutions and may contain some triphenyl phosphate and isopropylated diphenyl phosphates, as well. EPA classified IPTPP a high hazard for reproductive, developmental, and neurological toxicities [1]. Changes in organ weights, reduced fertility, and pup survival were observed in an oral rat study of reproduction and development. The lowest-observed-adverse-effect-level (LOAEL) was 25 mg/kg-d for increased female adrenal weights and relative ovary weights. Relative weights of liver, epididymis, and adrenal glands were also observed in male rats at higher doses. IPTPP caused neurotoxicity (ataxia and degeneration of the spinal cord and peripheral nerves) in hens at and above dose of 90 mg/kg-day in a 91-day test submitted by the industry [3]. Brain cholinesterase inhibition was observed in rodent testing of a commercial mixture which contained 80 percent IPTPP and 20 percent TPP [1].

Summary of Potential for Exposure

IPTPP is very likely to be found in children's products. In a European assessment, IPTPP was identified as a flame retardant plasticizer used in a range of PVC products, polyurethanes, textile coatings, adhesives, paints, and pigment dispersions [2]. Uses in the U.S. are largely withheld as confidential business information [4]. However, IPTPP isomers are a listed ingredient of Firemaster®550 which is used as an additive flame retardant in flexible polyurethane foam [5]. U.S. consumer product testing has identified the profile of flame retardants contained in Firemaster®550 in foam baby products and U.S. upholstered furniture [6,7]. The reported U.S. national production volume of IPTPP was 14,904,236 pounds/year in 2012 [3].

U.S. biomonitoring studies indicate that exposure to adults and children is occurring [8-10]. A urinary metabolite of IPTPP was measured in 100 percent of 22 mothers and 92 percent of 26 children in a 2013-14 study of families in Princeton, NJ. Mean and maximum level in the children's urine were 1 ng/mL and 10.1 ng/mL, respectively [9]. This same metabolite was detected at slightly higher mean levels in 100 percent of mothers and babies in a 2015 California study population [10].

EPA considered IPTPP to have very high aquatic toxicity, moderate persistence in the environment, and high potential for bioaccumulation [1].

List of References

1. EPA, Flame Retardants Used in Flexible Polyurethane Foam: An Alternatives Assessment Update. 2015, U.S. Environmental Protection Agency.
2. UK, Environment Agency, Environmental risk evaluation report: Isopropylated triphenyl phosphate (CAS nos. 28108-99-8, 26967-76-0 & 68937-41-7). 2009, Bristol, United Kingdom.
3. EPA, ChemView file for CAS No. 68937-41-7. 2016. https://java.epa.gov/chemview.
4. EPA, Screening-Level Hazard Characterization: Sponsored chemical Isopropylated Triphenyl Phosphate. 2010. U.S. Environmental Protection Agency.
5. Chemtura, Safety Data Sheet Firemaster 550. Revision date 3/31/2015. www.chempoint.com/products/download?grade=3990&type=msds.
6. Stapleton, H.M., et al., Identification of flame retardants in polyurethane foam collected from baby products. Environ Sci Technol, 2011. **45**(12): p. 5323-31.
7. Stapleton, H.M., et al., Novel and high volume use flame retardants in US couches reflective of the 2005 PentaBDE phase out. Environ Sci Technol, 2012. **46**(24): p. 13432-9.
8. Hoffman, K., et al., High Exposure to Organophosphate Flame Retardants in Infants: Associations with Baby Products. Environ Sci Technol, 2015. Dec 15;49 (24):14554-9.

9. Butt, C.M., et al., Metabolites of organophosphate flame retardants and 2-ethylhexyl tetrabromobenzoate in urine from paired mothers and toddlers. Environ Sci Technol, 2014. **48**(17): p. 10432-8.
10. Butt, C.H., K; Chen, A; Lorenzo, A; Congleton, J; Stapleton, HM, Regional comparison of organophosphate flame retardant (PFR) urinary metabolites and tetrabromobenzoic acid (TBBA) in mother-toddler pairs from California and New Jersey. Environment International, 2016. **94**: p. 627-34.

CAS 84852-53-9 Decabromodiphenyl ethane (DBDPE)

Summary of Toxicity

EPA classified decabromodiphenyl ethane (DBDPE) as a high hazard for developmental toxicity based on its structural similarity to decabromodiphenyl ether (decaBDE) [1]. Available toxicity data has been reviewed by the United Kingdom Environment Agency in 2007, by EPA in 2014, and by Health Canada and Environment Canada in 2016 [1-3]**.** Briefly, DBDPE had low acute toxicity in animals, both orally and dermally, and is predicted to have low acute inhalation toxicity. In a 90-day study in rats, minimal systemic effects were reported at the highest dose tested including increased liver size and hepatic cell hypertrophy at 1,000 mg/kg-day (LOAEL). No effects were reported at 320 mg/kg-day (NOAEL).

These liver changes were reversible after 14 days post-exposure, and the effects were interpreted as an adaptive response to increased demand on the liver to metabolize and excrete DBDPE [1]. In another 90-day oral assay in rats, Wang et al. dosed male rats for 90 days with 100 mg/kg-day DBDPE [4]. No alteration in liver, kidney, or body weights was observed, indicating no overt toxicity. Authors reported indications of organ impairment in DBDPE-treated rats (decreased serum creatinine, decreased serum liver enzymes alanine transferase and alkaline phosphatase, and increased total bile acids). Liver tissue was not examined for signs of pathology in this study to investigate this observation. DBDPE-treated rats also showed increased serum thyroid hormones T3 and T4 although the difference was not statistically significant for T4 [4]. Thyroid hormones are central to proper mammalian development, including the brain and reproductive organs, so this observation should be further investigated in assays involving prenatal exposure.

Reproductive toxicity testing has not been conducted. In two developmental toxicity tests in rats and rabbits, neither reported treatment-related malformations at birth or altered pup weight or decrease in survivability. The NOAEL was 1,250 mg/kg-day [1,2]. The developmental tests did not include observations for neurobehavioral effects as the pups matured. DBDPE is structurally similar to decabromodiphenyl ether (decaBDE) and has a similar toxicity profile in acute and short-term toxicity testing [4]. In further investigations of developmental exposures, however, decaBDE has been shown to produce neurodevelopmental toxicity and endocrine disruption in rodents in much lower doses [5-12]. In fact, EPA used a NOAEL of 2.2 mg/kg-day to establish a reference dose for decaBDE based on neurobehavioral effects of prenatal exposure. Lack of

testing for both neurodevelopmental outcomes and endocrine disruption are important data gaps for DBDPE given its very close structural similarity to decaBDE. EPA use of toxicity data from decaBDE to score DBDPE's potential for development toxicity is a reasonable approach to address this important gap in toxicity testing.

No cancer testing was identified. DBDPE was negative in two genotoxicity tests [1].

Summary of Potential for Exposure

DBDPE is a general purpose additive flame retardant for a variety of polymer applications and for textiles. It is a commercially important alternative to decaBDE. It typically comprises 10-15 percent of the weight of treated plastics (e.g., ABS, HIPS, PVC, polypropylene and polyethylene, etc.). It is used in wire and cable coatings for telecommunications, electrical, and automotive industries. To a lesser extent, it can be used in the latex-based back coating for drapery and upholstery fabrics [2]. DBDPE has been manufactured for more than 20 years and is a High Production Volume (HPV) chemical in the United States today. As of 2012, the National Production volume was 50-100 million pounds per year [13].

DBDPE was detected in one third of baby formula and about one quarter of baby cereals collected from the U.S. in 2013 [14]. Median levels of DBDPE detected were 22 and 11 pg/g fresh weight, respectively. The daily median intake for U.S. infants consuming formula and cereal was estimated by authors to be 2.2-3.44 ng DBDPE per day.

DBDPE was detected in a child's tablet and plastics of other consumer products by the Washington Department of Ecology at levels of 1000 ppm or lower [15]. It was also detected at lower levels (less than 100 ppm) in foam, stuffing, and padding of children's products collected by the Washington Department of Ecology [16]. A study that tested a variety of children's toys for sale in China found DBDPE in 80 percent of hard plastic toys, 89 percent of foam toys, 50 percent of the stuffed toys, and 40 percent of rubber or soft plastic toys including baby pacifiers. Maximum levels detected was 237 ppm [17]. Potential migration into saliva was tested by volunteers in this study. One out of 5 volunteers had measurable DBDPE in saliva after lightly chewing a segment of a hard plastic toy in the mouth for 15 min [17].

Because DBDPE is not chemically bound to the treated materials, it can escape into the environment. DBDPE has been widely detected in studies of U.S. house dust [18-21]. The dust levels of DPDPE reported ranged less than 2.6 -11,070 ng/g dust. DBDPE has also been detected in residential indoor air (mean 5 ng/m^3) and at higher levels in a gymnastics facility in Seattle (50 ng/m^3) [22]. In addition to U.S. studies, Harrad et al. 2008, studied DPDPE in dust samples from U.K. homes, offices, and cars. Average (and maximum) concentrations of DPDPE were found to be 270 (3,400), 170 (860) and 900 (2,900) ng/g dust respectively [23].

Only very limited human biomonitoring data are available in the literature for DBDPE. It was measured but not detected in maternal serum in Norway in 2012 [24]. It was detected at low

frequency in maternal serum and breast milk collected between 2008 and 2009 in the Sherbrooke region of Canada [25]. Low dermal and oral absorption may explain the low detections in people [1]. DBDPE is listed as a priority for biomonitoring by the California Biomonitoring Program [26].

Two recent government assessments predict that DBDPE has high environmental persistence but came to different conclusions regarding potential for bioaccumulation [2,3]. In a 90-day oral rat study, DBDPE and its metabolic products accumulated in adipose, liver, and kidney tissue [3]. DBDPE has been detected in environmental media from various parts of the world and in wildlife including birds, dolphins, and pandas. There is limited but positive evidence that DPDPE biomagnifies in aquatic food chains [2,27-28]. More testing is needed to characterize environmental fate, bioavailability, and metabolism of DBDPE in different species. If debromination to nona-, octa-, and hepta-bromodiphenyl ethane occurs following the pathway of debromination established for decaBDE, then degradation products are likely to have high potential for bioaccumulation [3].

List of References

1. EPA. *An Alternatives Assessment for the Flame Retardant Decabromodiphenyl Ether (DecBDE)*. U.S. Environmental Protection Agency 2014. www.epa.gov/saferchoice/partnership-evaluate-flame-retardant-alternatives-decabde.
2. UK Environment Agency, Environmental risk evaluation report: 1,1'-(Ethane-1,2-diyl)bis[penta-bromobenzene] (CAS: 84852-53-9). May 2007, United Kingdom, Environment Agency. ISBN: 978-1-84432-750-8.
3. Health Canada and Environment Canada. Draft Screening Assessment: Decabromodiphenyl ethane (DBDPE), CASRN 84852-53-9. October 2016.
4. Wang, F., et al., Comparative tissue distribution, biotransformation and associated biological effects by decabromodiphenyl ethane and decabrominated diphenyl ether in male rats after a 90-day oral exposure study. Environ Sci Technol, 2010. **44**(14): p. 5655-60.
5. EPA Integrated Risk Information System (IRIS). Chemical Assessment Summary: 2,2',3,3',4,4',5,5',6,6'-Decabromodiphenyl ether (BDE-209) CASRN 1163-19-5. June 30, 2008. https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=35.
6. Rice, D.C., et al., Developmental delays and locomotor activity in the C57BL6/J mouse following neonatal exposure to the fully-brominated PBDE, decabromodiphenyl ether. Neurotoxicol Teratol, 2007. **29**(4): p. 511-20.
7. Tseng, L.H., et al., Developmental exposure to decabromodiphenyl ether (PBDE 209): effects on thyroid hormone and hepatic enzyme activity in male mouse offspring. Chemosphere, 2008. **70**(4): p. 640-7.
8. Viberg, H., A. Fredriksson, and P. Eriksson, Changes in spontaneous behaviour and altered response to nicotine in the adult rat, after neonatal exposure to the brominated

flame retardant, decabrominated diphenyl ether (PBDE 209). Neurotoxicology, 2007. **28**(1): p. 136-42.

9. Tseng, L.H., et al., Postnatal exposure of the male mouse to 2,2',3,3',4,4',5,5',6,6'-decabrominated diphenyl ether: decreased epididymal sperm functions without alterations in DNA content and histology in testis. Toxicology, 2006. **224**(1-2): p. 33-43.
10. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Polybrominated Diphenyl Ethers (PBDEs).* Draft September 2015. www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=183.
11. Costa, L.G. and G. Giordano, *Is decabromodiphenyl ether (BDE-209) a developmental neurotoxicant?* Neurotoxicology, 2011. **32**(1): p. 9-24.
12. Viberg, H., et al., Neurobehavioral derangements in adult mice receiving decabrominated diphenyl ether (PBDE 209) during a defined period of neonatal brain development. Toxicol Sci, 2003. **76**(1): p. 112-20.
13. EPA. Chemical Data Access Tool (CDAT) - Chemical Data Reporting (CDR) information on the production and use of chemicals manufactured or imported into the United States. 2012. http://java.epa.gov/oppt_chemical_search/.
14. Liu, L.Y., A. Salamova, and R.A. Hites, Halogenated flame retardants in baby food from the United States and from China and the estimated dietary intakes by infants. Environ Sci Technol, 2014. **48** (16): p. 9812-8.
15. Ecology, Flame Retardants in General Consumer and Children's Products. Washington State Department of Ecology, June 2014, Publication No. 14-04-021.
16. Ecology, *Consumer Product Testing Database* Washington State Department of Ecology. https://apps.ecology.wa.gov/ptdbreporting.
17. Chen, S.J., et al., Brominated flame retardants in children's toys: concentration, composition, and children's exposure and risk assessment. Environ Sci Technol, 2009. **43**(11): p. 4200-6.
18. Stapleton, H.M., et al., *Alternate and New Brominated Flame Retardants Detected in U.S. House Dust* Environmental Science & Technology, 2008. **42**(18): p. 6910-6916.
19. Brown, F.R., et al., Levels of non-polybrominated diphenyl ether brominated flame retardants in residential house dust samples and fire station dust samples in California. Environ Res, 2014. **135**: p. 9-14.
20. Dodson, R.E., et al., After the PBDE phase-out: a broad suite of flame retardants in repeat house dust samples from California. Environ Sci Technol, 2012. **46**(24): p. 13056-66.
21. Johnson, P.I., et al., Associations between brominated flame retardants in house dust and hormone levels in men. Sci Total Environ, 2013. **445-446**: p. 177-84.
22. Schreder, E., La Guardia, M, Uding, N, Inhalation Exposure to Chlorinated Organophosphate Flame Retardants: Respirable vs. Inhalable intake. 2014, Washington Toxics Coalition: Seattle, Washington.

23. Stuart, H., et al., Concentrations of brominated flame retardants in dust from United Kingdom cars, homes, and offices: causes of variability and implications for human exposure. Environ Int, 2008. **34**(8): p. 1170-5.
24. Cequier, E., et al., Comparing human exposure to emerging and legacy flame retardants from the indoor environment and diet with concentrations measured in serum. Environ Int, 2015. **74**: p. 54-9.
25. Zhou, S.N., et al., Measurements of selected brominated flame retardants in nursing women: implications for human exposure. Environ Sci Technol, 2014. **48**(15): p. 8873-80.
26. California Environmental Contaminant Biomonitoring Program. *List of Priority Chemicals, December 2015.* http://biomonitoring.ca.gov/sites/default/files/downloads/PriorityChemicalsList_December2015.pdf.
27. Law, K., et al., Bioaccumulation and trophic transfer of some brominated flame retardants in a Lake Winnipeg (Canada) food web. Environ Toxicol Chem, 2006. **25**(8): p. 2177-86.
28. Mo, L., et al., Bioaccumulation of polybrominated diphenyl ethers, decabromodiphenyl ethane, and 1,2-bis(2,4,6-tribromophenoxy) ethane flame retardants in kingfishers (Alcedo atthis) from an electronic waste-recycling site in South China. Environ Toxicol Chem, 2012. **31**(9): p. 2153-8.

CAS 85535-84-8 Short-Chain chlorinated paraffins (SCCP)

CAS 108171-26-2 Chlorinated paraffins

Summary of Toxicity

Short-Chain Chlorinated Paraffins (SCCPs) are classified as carcinogens by authoritative sources [1,2]. The National Toxicology Program classifies chlorinated paraffins (C12, 60 percent chlorine) as reasonably anticipated to be human carcinogens based on liver, kidney, and thyroid tumors in rodent testing. California Proposition 65 also lists Chlorinated paraffins (CAS No. 108171-26-2) (average chain length, C_{12}; approximately 60 percent chlorine by weight) as carcinogens.

The European Union lists SCCPs as a substance of very high concern (SVHC), as it meets the criteria for both a persistent bioaccumulative and toxic (PBT) substance and a very persistent, very bioaccumulative substance (vPvB) [3]. This is part of implementing the EU law Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). Substances that may have serious and often irreversible effects on human health and the environment can be identified as SVHCs. If a substance is identified as an SVHC, it will be added to the Candidate List for eventual inclusion in the Authorisation List.

Summary of Potential for Exposure

SCCPs could be present in children's products as they have been used as plasticizers and a flame retardant in plastics, especially PVC. Other minor domestic SCCP uses are as a plasticizer and a flame-retardant additive to a variety of products including: rubber formulations, paints and other coatings, and adhesives, and sealants [8].

SCCPs (CAS No 85535-84-8) are included on Washington State's PBT list (WAC 173-333-320) [4]. SCCPs have been detected in breast milk as well as other human tissues [5,6]. SCCPs are found world-wide in the environment, wildlife, and humans. SCCPs bioaccumulate in wildlife and humans, and are persistent and transported globally in the environment [7].

List of References

1. NTP, *Report on Carcinogens, Thirteenth Edition: Chlorinated Paraffins (C12, 60 percent Chlorine)*. October 2014. National Toxicology Program. https://ntp.niehs.nih.gov/go/roc13.
2. State of California OEHHA. *Proposition 65 list - Office of Environmental Health Hazard Assessment Safe Drinking Water and Toxic Enforcement Act of 1986*. 2016. Available from: http://oehha.ca.gov/media/downloads/crnr/p65single09302016.pdf.
3. ECHA, Substance name: Alkanes, C10-13, chloro: EC number: 287-476-5; CAS number: 85535-84-8. Support Document for Identification of Alkanes, C10-13, Chloro as a Substance of Very High Concern. 2008, European Chemicals Agency. p. 36.
4. Ecology, Concise Explanatory Statement and Responsiveness Summary for the Adoption of Chapter 173-333 WAC, Persistent, Bioaccumulative, Toxins. 2006, Washington State Department of Ecology: Olympia.
5. Thomas, G.O., et al., Short and medium chain length chlorinated paraffins in UK human milk fat. Environ Int, 2006. **32**(1): p. 34-40.
6. Darnerud, O.A., M.; Glynn, A.; Borgen, A., *Chlorinated Paraffins in Swedish breast milk*. 2012, National Food Agency and Norwegian Institute for Air Research.
7. EPA, Short-Chained Chlorinated Paraffins (SCCPs) and Other Chlorinated Paraffins Action Plan. December 30, 2009, U.S. Environmental Protection Agency.

CAS 183658-27-7 2-ethylhexyl-2,3,4,5-tetrabromobenzoate (TBB)

Summary of Toxicity

EPA classified 2-ethylhexyl-2,3,4,5-tetrabromobenzoate (TBB) as a moderate hazard for reproductive, developmental, neurological, and repeated dose toxicities [1]. This was based on the observed toxicity of a closely related confidential analog, and studies of commercial mixtures which contain TBB as a major component. EPA did not release the name or chemical structure of the confidential analog, but reported that the lowest-observed-adverse-effect-level (LOAEL)

for a rodent study of this compound was 25 mg/kg-d for reproductive toxicity. LOAELs for developmental effects of two commercial mixtures were reported at 100 mg/kg-d for Firemaster® BZ-54 and 1 mg/kg-d for Firemaster® 550 [1].

The latter study involved prenatal exposure in rats and was published by Patisaul et al. 2013 [2]. Pregnant rats exposed to the Firemaster® 550 mixture during gestation and lactation had altered thyroid function and produced offspring were 30-60 percent heavier by weaning, an effect that persisted into adulthood. Female offspring of treated rats entered puberty sooner and had glucose intolerance and elevated anxiety behaviors in maze testing [2].

Summary of Potential for Exposure

TBB is an ingredient in common market replacements for PBDEs (polybrominated diphenyl ethers; TBPH – bis (2-ethylhexyl) 2,3,4,5-tetra bromophthalate) in flexible polyurethane foam [3]. Approximately 50 percent of the Firemaster® 550 mixture is TBB and TBPH [1] at a ratio of 4:1 by mass [1,4]. Past and current national production volume of TBB is withheld as confidential business information [4,5]. TBB treated foams may be used in many everyday products such as couches, chairs, upholstered furniture, children's furniture, baby products, office furniture, foam in gymnastic facilities, and auto cushions. TBB may also be present in products made from recycled foam such as carpet backings and pads [4,6,7].

TBB has been measured with high frequency in residential indoor dust in studies in the U.S. [8-11] and Canada [12]. It was found in 100 percent of indoor dust samples from 39 childcare centers in Northern California [13]. Mean levels from these studies ranged from 310-1,062 ng/g in indoor dust. Maximum level reported was 75,000 ng/g dust. In a study of North Carolina adults, levels of TBB in hand wipes correlated positively with a metabolite of TBB in urine suggesting that dermal contact with dust or treated surfaces contributed to overall exposure [14]. In another investigation, median concentrations of TBB and TBPH in paired hand wipe samples were 2-3 times higher after gymnastics practice compared to before indicating skin exposure was occurring during collegiate gymnast practice [15].

Metabolites of TBB were detected in urine of toddlers and their mothers in New Jersey and California studies [16,17]. Levels measured in children tended to be higher than their mothers in both studies. The maximum concentration reported in children's urine reported across both studies was 225 ng/mL. TBB metabolites were also commonly detected in maternal serum (n=102) and breast milk (n=105) collected in a 2008-2009 study in women living in Québec, Canada [18].

TBB is classified by EPA as high hazard for persistence and bioaccumulation [1].

List of References

1. EPA, Flame Retardants Used in Flexible Polyurethane Foam: An Alternatives Assessment Update. 2015, Environmental Protection Agency.
2. Patisaul, H.B., et al., Accumulation and endocrine disrupting effects of the flame retardant mixture Firemaster(R) 550 in rats: an exploratory assessment. J Biochem Mol Toxicol, 2013. **27**(2): p. 124-36.
3. EPA, Furniture Flame Retardancy Partnership: Profiles of Chemical Flame-Retardant Alternatives for Low-Density Polyurethane Foam. 2005, EPA: Washington, D.C. p. 153.
4. EPA, TSCA Work Plan Chemical Technical Supplement - Use and Exposure of the Brominated Phthalates Cluster (BPC) Chemicals - Brominated Phthalates Cluster Flame Retardants. 2015, Environmental Protection Agency, Office of Chemical Safety and Pollution Prevention. p. 54.
5. EPA. Chemical Data Access Tool (CDAT) - Chemical Data Reporting (CDR) information on the production and use of chemicals manufactured or imported into the United States. http://java.epa.gov/oppt_chemical_search/.
6. Stapleton, H.M., et al., Identification of flame retardants in polyurethane foam collected from baby products. Environ Sci Technol, 2011. **45**(12): p. 5323-31.
7. La Guardia, M.J. and R.C. Hale, Halogenated flame-retardant concentrations in settled dust, respirable and inhalable particulates and polyurethane foam at gymnastic training facilities and residences. Environ Int, 2015. **79**: p. 106-14.
8. Dodson, R.E., et al., After the PBDE phase-out: a broad suite of flame retardants in repeat house dust samples from California. Environ Sci Technol, 2012. **46**(24): p. 13056-66.
9. Johnson, P.I., et al., Associations between brominated flame retardants in house dust and hormone levels in men. Sci Total Environ, 2013. **445-446**: p. 177-84.
10. Stapleton, H.M., et al., Alternate and new brominated flame retardants detected in U.S. house dust. Environ Sci Technol, 2008. **42**(18): p. 6910-6.
11. Brown, F.R., et al., Levels of non-polybrominated diphenyl ether brominated flame retardants in residential house dust samples and fire station dust samples in California. Environ Res, 2014. **135**: p. 9-14.
12. Shoeib, M., et al., Legacy and current-use flame retardants in house dust from Vancouver, Canada. Environmental Pollution, 2012. **169**(0): p. 175-182.
13. Bradman, A., et al., Flame retardant exposures in California early childhood education environments. Chemosphere, 2014. **116**: p. 61-6.
14. Hoffman, K., et al., Urinary tetrabromobenzoic acid (TBBA) as a biomarker of exposure to the flame retardant mixture Firemaster(R) 550. Environ Health Perspect, 2014. **122**(9): p. 963-9.
15. Carignan, C.C., et al., Flame Retardant Exposure among Collegiate United States Gymnasts. Environmental Science & Technology, 2013. **47**(23): p. 13848-13856.

16. Butt, C.M., et al., Metabolites of organophosphate flame retardants and 2-ethylhexyl tetrabromobenzoate in urine from paired mothers and toddlers. Environ Sci Technol, 2014. **48**(17): p. 10432-8.
17. Butt, C.H., K; Chen, A; Lorenzo, A; Congleton, J; Stapleton, HM, Regional comparison of organophosphate flame retardant (PFR) urinary metabolites and tetrabromobenzoic acid (TBBA) in mother-toddler pairs from California and New Jersey. Environment International, 2016. **94**: p. 627-34.
18. Zhou, S.N., et al., Measurements of selected brominated flame retardants in nursing women: implications for human exposure. Environ Sci Technol, 2014. **48**(15): p. 8873-80.

CHCC Delistings

These chemicals have been delisted from the CHCC list. An evaluation of each chemical is provided in this document summarizing the reason for the delisting. The evaluations identify the CAS number and chemical name, and summarizes current information about toxicity, potential for exposure, reason for delisting, and provides a list of references.

CAS 71-36-3 n-Butanol

Summary of Toxicity

Workplace exposures to n-butanol have been associated with eye, nose, and throat irritation, and neurological effects such as dizziness, vertigo, and hearing impairment [1,2]. It is classified by Reprotext as a "A-" reproductive hazard [3]. In animals, fetotoxicity and teratogenicity was observed at high doses by both the inhalation and oral routes of exposure [4,5,6,7].

Summary of Potential for Exposure

N-butanol is a widely used industrial solvent used for paints, lacquers, varnishes, resins, and dyes [2]. Product testing by the Danish government detected n-butanol in several categories of children's products including slimy toys, children's tents, coatings on wooden toys, and a scented rubber toy [8]. N-butanol is listed as an ingredient in paints, sharpie markers, dry erase markers, and nail products in the National Library of Medicine Household Products Database [9]. N-butanol occurs naturally as a product of carbohydrate fermentation and is present in food [10].

List of References

1. American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values and Biological Exposure Indices. 6th ed. Volumes I, II, III. Cincinnati, OH: ACGIH, 1991., p. 170.
2. U.S. EPA, Office of Prevention, Pesticides, and Toxic Substances. Inert reassessment for n-butanol and isobutyl alcohol. 2005.
3. "n-butanol" in REPROTEXT Database Version 5.1 Greenwood Village, CO: Thomson Reuters (Healthcare) Inc. (accessed 2009).
4. Nelson et al. (1989) Lack of selective developmental toxicity of three butanol isomers administered by inghalation to rats. *Fundam. Appl Toxicol* 12(3):469-79.
5. Nelson et al. (1990) Developmental toxicology of industrial alcohols: a summary of 13 alcohols administered by inhalation. *Toxicol Ind Health* 6 (3-4): 373-87.
6. Sitarek K, Berlińska B, Barański B. (1994) Assessment of the effect of n-butanol given to female rats in drinking water on fertility and prenatal development of their offspring. *Int J Occup Med Environ Health*. 7(4):365-70.

7. Ema, M et al. (2005) Evaluation of developmental toxicity of 1-butanol given to rats in drinking wtaer throughout pregnancy. *Food Chem Toxicol* 43:325-31.
8. Danish Ministry of the Environment, Environmental Protection Agency. Survey of Chemical Substances in Consumer Products Reports 46, 60, 67, 68. 2004-2006.
9. National Institutes of Health, National Library of Medicine, Household Products Database. Accessed May 2010.
10. National Institutes of Health, National Library of Medicine Hazardous Substances Data Bank. Accessed May 2010.

CAS 85-44-9 Phthalic Anhydride

Summary of Toxicity

In 2011 Ecology based the listing of phthalic anhydride on the Globally Harmonized System (GHS) of Classification and Labelling of Chemicals Cat 2 for reproductive toxicity or germ cell mutagenicity [1]. GHS is a worldwide initiative to promote standard criteria for classifying chemicals according to their health, physical, and environmental hazards.

Since 2011 the European Chemicals Agency (ECHA) reviewed phthalic anhydride and did not classify it for either reproductive toxicity or germ cell mutagenicity under the GHS criteria [2].

Summary of Potential for Exposure

Phthalic anhydride is primarily used in the manufacture of phthalate plasticizers and polyester resins. It is also used in small volume in the production of alkyl resins used in dyes, paints, and lacquers [3,4]. It was detected by the Danish EPA in coatings on 4 out of 15 wooden toys tested [5].

Reason for Delisting

The authoritative source used in 2011 to identify phthalic anhydride as toxic was updated. The updated evaluation no longer classifies phthalic anhydride as reproductively toxic. Phthalic anhydride is delisted from the CHCC list.

List of References

1. Ecology, 2011, Children's Safe Products Reporting Rule – Supporting Documents for the 2011 Rulemaking. Rule documents from the 2011 rulemaking were merged into a publication in April of 2017. Publication 17-04-022. https://apps.ecology.wa.gov/publications/SummaryPages/1704022.html
2. ECHA. REACH Registration Dossier – Phthalic Anhydride. Classification & Labelling & PBT Assessment. https://echa.europa.eu/registration-dossier/-/registered-dossier/15845/1.

3. California EPA, Office of Environmental Health Hazard Assessment (OEHHA). Determination of non-cancer REL for Phthalic anhydride, December 2000. www.oehha.ca.gov/air/chronic_rels/pdf/85449.pdf.
4. ICIS, Chemical Intelligence, Phthalic Anhydride Uses and Market Data, Updated February 2010. www.icis.com/v2/chemicals/9076142/phthalic-anhydride/uses.html.
5. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in Consumer Products. Report 60, 2005 www.mst.dk/English/Chemicals/Consumer_Products/Surveys-on-chemicals-in-consumer-products.htm.

CAS 556-67-2 Octamethylcyclotetrasiloxane (D4)

Summary of Toxicity

Octamethylcyclotetrasiloxane (D4) is included in a European Commission priority list of chemicals identified for further in depth evaluation of their role in endocrine disruption [1,2]. Although this 2007 publication focused on low production volume chemicals, D4 was one of the high production volume chemicals included. This European Commission listing was based on effects in a uterotrophic assay [3]. There is more recent evidence for the lack of effect from D4 in a uterotrophic assay [4].

Summary of Potential for Exposure

In 2003 the Danish EPA identified D4 as a listed ingredient in 1 out of 28 sunscreens, 1 of 32 lotions, and 1 out of 208 cosmetics marketed to children [5]. Recently, Ecology has found children's cosmetics that include D4 on the ingredient list [6].

Reason for Delisting

Under our current process for designating chemicals to be reported under CSPA, determination of toxicity is based on listings by selected authoritative sources that provide a robust evaluation of available data in a public process. In 2011, D4 was identified as toxic (for the purposes of CSPA reporting) based only on the European Commission list of potential endocrine disruptors. The EU does not intend to update this list and a 2015 study found no effect in a similar assay. No other CSPA authoritative source classifies D4 as toxic. D4 is delisted from the CHCC list.

List of References

1. DHI Water and Environment for DG Environment (2007). Study on enhancing the Endocrine Disruptor priority list with a focus on low production volume chemicals. http://ec.europa.eu/environment/chemicals/endocrine/pdf/final_report_2007.pdf.
2. European Commission. 2007. Priority List of suspected endocrine disruptors. Available at http://ec.europa.eu/environment/chemicals/endocrine/strategy/substances_en.htm#priority_list.

3. McKim, JM, Wilga, PC, Breslin, WJ, Plotzke, KP, Gallavan, RH, and Meeks, RG. (2001) Potential estrogenic and androgenic activity of the cyclic siloxane octamethylcyclotetrasiloxane (D4) and the linear siloxane hexamethyldisiloxane (HDMS) in immature rats using the uterotrophic assay. *Toxicological Sciences 63*: 37-46.
4. Lee D, Ahn C, An BS, Jeung EB. (2015) Induction of the estrogenic marker calbindn-d_9k by octamethylcyclotetrasiloxane. *Int J Environ Res Public Health* 12:14610-25.
5. Danish Ministry of the Environment, Environmental Protection Agency. Survey of Chemical Substances in Consumer Products, Report 88, 2007. www.mst.dk/English/Chemicals/Consumer_Products/Surveys-on-chemicals-in-consumer-products.htm.
6. Ecology, October 2016. An Assessment of Children's Safe Product Act Data. Addendum to Quality Assurance Project Plan: Product Testing Program Version 1. Publication 16-03-021.

CAS 7439-98-7 Molybdenum and molybdenum compounds (Mo)

Summary of Toxicity

In 2011 Ecology identified toxicity for Molybdenum (Mo) from a REPROTEXT grade of B for reproductive toxicity [1,2]. Since 2011 we have reconsidered REPROTEXT and determined it is no longer identified as an authoritative source for CSPA. During this review, we also found the REPROTEXT database and scores have not been updated. The information in REPROTEXT is informative, but not sufficient by itself for the purposes of CSPA CHCC listing. We were not able to identify Mo toxicity from another authoritative source.

REPROTEXT a subscription-based database and the University of Washington no longer subscribes to it, which further limits access for residents of Washington.

Summary of Potential for Exposure

Mo is an essential trace nutrient in humans. Biomonitoring in the general U.S. population by the Centers for Disease Control and Prevention (CDC) show that levels in the general population dropped slightly from 1999 to 2004 [3]. Molybdenum was found in testing of children's school supplies by the Danish EPA [4].

Reason for Delisting

The authoritative source used in 2011 to identify Mo as toxic has been determined to be insufficient for CHCC listing. No other authoritative source classifies Mo as toxic. Mo is delisted from the CHCC list.

List of References

1. Ecology, 2011, Children's Safe Products Reporting Rule – Supporting Documents for the 2011 Rulemaking. Rule documents from the 2011 rulemaking were merged into a publication in April of 2017. Publication 17-04-022. https://apps.ecology.wa.gov/publications/SummaryPages/1704022.html
2. REPROTEXT, "Molybdenum" in REPROTEXT Database Version 5.1 Greenwood Village, CO: Thomson Reuters (Healthcare) Inc. (accessed 2009).
3. Centers for Disease Control and Prevention (CDC), Fourth National Report on Human Exposure to Environmental Chemicals, December 2009. www.cdc.gov/exposurereport/data_tables/.
4. Danish Ministry of the Environment, Environmental Protection Agency. Surveys on Chemicals in consumer products. Report 84. www.mst.dk/English/Chemicals/Consumer_Products/Surveys-on-chemicals-in-consumer-products.htm.