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## **Draft Screening Assessment**

### **Certain Organic Flame Retardants Substance Grouping**

**Phosphoric acid, tris(methylphenyl) ester  
(TCP)**

**Chemical Abstracts Service Registry Number  
1330-78-5**

**Health Canada  
Environment and Climate Change Canada**

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**Canada** 

## Synopsis

Pursuant to section 74 of the *Canadian Environmental Protection Act, 1999* (Canada 1999), the Ministers of the Environment and Climate Change and of Health have conducted a screening assessment of phosphoric acid, tris(methylphenyl) ester, commonly known as tricresyl phosphate or TCP (Chemical Abstracts Service Registry Number 1330-78-5). TCP is a substance within the Certain Organic Flame Retardants (OFR) Substance Grouping under Canada's Chemicals Management Plan, which includes organic substances having similar function: application to materials to slow the ignition and spread of fire. This substance was identified as a priority for assessment based on human health concerns (related to potential for exposure), but not for ecological concerns (did not meet criteria for persistence or potential for bioaccumulation, but met criteria with respect to inherent toxicity to non-human organisms).

TCP does not occur naturally in the environment. Results from a 2011 industry survey indicated that TCP was not manufactured in Canada in 2011 but 1 000 to 10 000 kg of neat TCP substance and between 1 000 and 10 000 kg of TCP in mixtures and consumer or commercial products were imported into Canada. In Canada, confirmed uses of TCP include adhesives and sealants, automobile parts, aircraft applications, fire-resistant lubricant and grease additive, and electrical and electronic applications. Internationally, TCP is used as a flame retardant and plasticizer in household applications such as furniture upholstery backcoating, adhesives and sealants, automobile parts, aircraft applications, electronic and electrical applications, various extruded manufactured items such as flexible polyvinyl chloride (PVC), vinyl tarpaulins, as well as extreme pressure additive in lubricants, and as a fire-resistant hydraulic fluid.

Current commercial products marketed as TCP consists primarily of a mixture of *m*-TCP and *p*-TCP isomers, with the *o*-TCP isomer at approximately 0.05%. The three isomers are considered to possess identical physical chemical properties for the purpose of this assessment. They are characterized by low water solubility and octanol-water partition coefficient, and a low vapour pressure and melting point.

Based on limited experimental and modelled data, TCP is not persistent in water, soil, sediment or air. Furthermore, results from empirical and modelled hydrolysis data suggest a fast degradation rate which increases with increasing environmental pH. Based on TCP's low modelled volatility, short half-life in air (18.74 hr) and estimated Characteristic Travel Distance of 363 km, TCP is not expected to reside in air long enough to be atmospherically transported a significant distance from its emission source.

TCP is considered to have low to moderate bioconcentration and bioaccumulation potentials based on empirical fish bioconcentration studies and modelled data. TCP is considered to be rapidly metabolized in fish.

Based on the available empirical ecotoxicity studies and modelled data, TCP is considered to have a moderate to high level of toxicity to aquatic organisms with acute and chronic effects demonstrated from approximately 0.001 to 1 mg/L. There are no sediment, soil or wildlife toxicity data for TCP.

It is expected that TCP may be released to the Canadian environment as a result of industrial processing activities through wastewater. Although TCP can be found in consumer and commercial products, information on release to the environment from this route is limited, and releases are expected to be diffuse and minimal, particularly when considering the low level of use for this substance identified in Canada. Exposure scenarios were developed for industrial releases, where release to water results in minor TCP partitioning to sediment. Although there are no soil toxicity data, exposure to soil-dwelling mammals from the application of biosolids containing TCP was estimated. To address the potential exposures to wildlife predators consuming fish with accumulated TCP, total daily intake modelling was performed for mink and river otter as representative wildlife species. Risk quotient analyses, integrating conservative estimates of exposure with the available toxicity information, were performed and showed a low potential for risk for aquatic organisms, soil-dwelling mammals, and fish-eating mammals.

Considering all available lines of evidence presented in this draft screening assessment, there is a low risk of harm to organisms and the broader integrity of the environment from TCP. It is proposed to conclude that TCP does not meet the criteria under paragraphs 64(a) or (b) of CEPA as it is not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity or that constitute or may constitute a danger to the environment on which life depends.

No classifications of the health effects of TCP by national or international regulatory agencies were identified. Based on available information, TCP is not carcinogenic or genotoxic. Based on animal studies, the critical health effects of exposure to TCP are effects on the adrenal cortex and ovary. The main sources of exposure for the general population in Canada are expected to be from environmental media (air, dust, soil, and water), food, including breast milk, and from the use of consumer products such as furniture (with treated upholstery or foam) and lubricants. Limited international general population biomonitoring data are available.

The margins of exposure between estimates of exposure from environmental media, food and from contact with consumer products, and effect levels are considered to be adequate to address uncertainties in the exposure and health effects databases. Therefore, it is proposed to conclude that TCP does not meet the criteria under paragraph 64(c) of CEPA, as it is not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

## **Overall Proposed Conclusion**

It is proposed to conclude that TCP does not meet any of the criteria set out in section 64 of CEPA.

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## 1. Introduction

Pursuant to sections 68 and 74 of the *Canadian Environmental Protection Act, 1999* (CEPA) (Canada 1999), the Minister of the Environment and Climate Change and the Minister of Health conduct screening assessments of substances to determine whether these substances present or may present a risk to the environment or to human health.

The Substance Groupings Initiative is a key element of the Government of Canada's Chemicals Management Plan. The Certain Organic Flame Retardants Substance Grouping consists of ten substances identified as priorities for action as they met the categorization criteria under section 73 (1) CEPA and/or were considered a priority based on ecological and/or human health concerns (Environment and Climate Change Canada and Health Canada 2007). All of these substances have a similar function: the application to materials to slow the ignition and spread of fire. Also, these substances are potential alternatives for other flame retardants which are presently subject to regulatory controls or phase-out in Canada and/or globally.

This screening assessment focuses on the substance Phosphoric acid, tris(methylphenyl) ester, commonly known as Tricresyl Phosphate or TCP (CAS RN 1330-78-5). This substance was identified in the categorization of the Domestic Substances List (DSL) under subsection 73(1) of CEPA as meeting criteria for greatest potential for exposure of individuals in Canada. While the substance did not meet categorization criteria for persistence or bioaccumulation, it did meet criteria for inherent toxicity to non-human organisms.

Screening assessments focus on information critical to determining whether a substance meets the criteria as set out in section 64 of CEPA. Screening assessments examine scientific information and develop conclusions by incorporating a weight-of-evidence approach and precaution.<sup>1</sup>

This draft screening assessment includes consideration of information on chemical properties, hazards, uses and exposure for TCP. Data relevant to the screening assessment of these substances were identified in original literature, review and

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<sup>1</sup> A determination of whether one or more of the criteria of section 64 are met is based upon an assessment of potential risks to the environment and/or to human health associated with exposures in the general environment. For humans, this includes, but is not limited to, exposures from ambient and indoor air, drinking water, foodstuffs, and the use of consumer products. A conclusion under CEPA is not relevant to, nor does it preclude, an assessment against the hazard criteria specified in the *Hazardous Products Regulations* and the *Controlled Products Regulations*, which are part of the regulatory framework for the Workplace Hazardous Materials Information System for products intended for workplace use. Similarly, a conclusion based on the criteria contained in section 64 of CEPA does not preclude actions being taken under other sections of CEPA or other Acts.

assessment documents, stakeholder research reports and from recent literature searches, up to September 2014 for the ecological and human health sections. However, a cursory search was conducted to include any salient literature up to June 2015. Empirical data from key studies as well as some results from models were used to reach proposed conclusions. When available and relevant, information presented in assessments from other jurisdictions was considered.

The draft screening assessment does not represent an exhaustive or critical review of all available data. Rather, it presents the most critical studies and lines of evidence pertinent to the proposed conclusion.

This draft screening assessment was prepared by staff in the Existing Substances Programs at Health Canada and Environment and Climate Change Canada and incorporates input from other programs within these departments. The ecological and human health portions of this assessment have undergone external written peer review and/or consultation. Comments on the technical portions relevant to the environment were received from Dr. Jon Arnot (Arnot Research and Consulting) and Mr. John A. Biesemeier (Chemtura Corporation). Comments on the technical portions relevant to human health were received from Raymond York, R.G. York & Associates; Donna Vorhees, The Science Collaborative; and Bernard Gadagbui, Toxicology Excellence for Risk Assessment (TERA). While external comments were taken into consideration, the final content and outcome of the screening assessment remain the responsibility of Health Canada and Environment and Climate Change Canada.

The critical information and considerations upon which the draft screening assessment is based are given below.

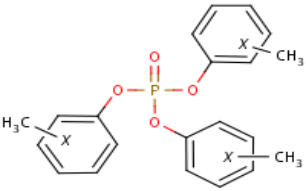
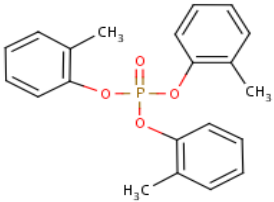
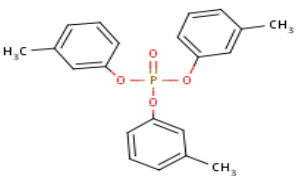


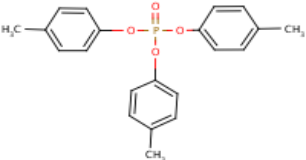
## 2. Substance Identity

This screening assessment focuses on the substance Phosphoric acid, tris(methylphenyl) ester (CAS RN 1330-78-5) within the Certain Organic Flame Retardants Substance Grouping. Phosphoric acid, tris(methylphenyl) ester is also known as Tricresyl Phosphate (TCP). A list of its additional chemical names (i.e. trade names) is available from the National Chemical Inventory (NCI 2013). For the purposes of this assessment, the substance will be referred to as TCP. Substance identity for TCP is shown in Table 2-1 and is described by a structure with undefined methyl group positions.

There are three isomers of TCP based on methyl group positions: tri-ortho-cresyl phosphate, tri-meta-cresyl phosphate, and tri-para-cresyl phosphate. They are referred to as *o*-TCP (CAS RN 78-30-8), *p*-TCP (CAS RN 78-32-0) and *m*-TCP (CAS RN 563-04-2), respectively, for this assessment. Substance identity of TCP and its isomers are presented in Table 2-1. Other names for TCP and its isomers are available in Environment and Climate Change Canada (2015a).

**Table 2-1. Substance identity for TCP**

CAS RN (acronym)	Chemical structure	Molecular mass	Chemical formula
1330-78-5 (TCP)		368.37 g/mol	C <sub>21</sub> H <sub>21</sub> O <sub>4</sub> P
78-30-8 ( <i>o</i> -TCP)		368.37 g/mol	C <sub>21</sub> H <sub>21</sub> O <sub>4</sub> P
563-04-2 ( <i>m</i> -TCP)		368.37 g/mol	C <sub>21</sub> H <sub>21</sub> O <sub>4</sub> P

CAS RN (acronym)	Chemical structure	Molecular mass	Chemical formula
78-32-0 ( <i>p</i> -TCP)		368.37 g/mol	C <sub>21</sub> H <sub>21</sub> O <sub>4</sub> P

Most data, which were reported in studies on TCP, were assessed using commercial products of TCP. Commercial TCP mixtures may contain 65-70% tricresyl phosphate (mixture of *m*-TCP and *p*-TCP isomers and 0.05% *o*-TCP) with 0.5% triphenyl phosphate and less than 0.05% free phenol and cresol (Bayer 2002). TCP is typically produced by the reaction of a synthetic mixture of *m*- and *p*-cresol with phosphorus oxychloride (Ashford 1994; UK EA 2009) to limit the formation of unwanted isomers (e.g., *o*-TCP) and contaminants (Sjögren et al. 2010). Early manufacturing practices in general used petroleum or coal tar derived cresols (naturally derived cresols) (Sjögren et al. 2010). While TCP manufacturing from naturally derived cresols has been reported to exist today (e.g., Great Lakes 2010; Chemnet 2014), manufacturing activities have changed over time, and the amount of *o*-TCP present has been minimized (UK EA 2009; Sjögren et al. 2010). However, it is difficult to obtain data on the amount of *o*-TCP and other orthocresyl isomers in commercially available materials containing TCP marketed worldwide (Sjögren et al. 2010). Conservative estimates of 0.1 to 1% of *o*-TCP have been reported (Sjögren et al. 2010; ACGIH 2012 cited in HSDB 2014); however, it has also been reported that the concentration is usually below 0.1% (Sjögren et al. 2010). Also, “new generation” materials typically claim to have an even lower *o*-TCP content (Sjögren et al. 2010). Based on the collective information, it is reasonable to consider that the TCP mixture contains less than 0.1% *o*-TCP for the purpose of this assessment.

### 3. Physical and Chemical Properties

Environment and Climate Change Canada (2015a) contains experimental and modelled physical and chemical properties for TCP and its isomers that are relevant to their environmental fate. Key physical and chemical property data for TCP and its isomers presented in Table 3-1, which were reported from empirical studies, were critically reviewed for data quality.

Models based on QSARs were used to generate data for some of the physical and chemical properties of TCP. These models are mainly based on fragment addition methods, i.e. they sum the contributions of sub-structural fragments of a molecule to make predictions for a property or endpoint. Most of these models rely on the SMILES notation as indicated in Environment and Climate Change Canada (2015a)

While, the Least Square Adjustment (LSA) method was applied to harmonize physical chemical properties for TCP (Schenker et al. 2005), the original empirical data were used in preference as key physical and chemical properties for this assessment. TCP (the mixture of isomers) is a clear, colourless liquid with a very slight aromatic odour (IPCS 1990). The commercially marketed TCP is a clear colourless to slightly yellow liquid (UK EA 2009, Ashford 1994, Bayer 2002, Wildlife International Ltd. 2002, WHO 1990). TCP has a low melting point of -33 °C, while its three isomers have higher melting points, ranging from 11 to 78°C (UK EA 2009, WHO 1990). The boiling point of TCP is at 476.06°C at standard atmospheric pressure, while its isomers have lower values at various measured pressures. TCP has a density of 1160 kg/m<sup>3</sup> at 20°C that is comparable among its three isomers.

TCP is characterized by low water solubility at room temperature and very low volatility based on its low vapour pressure and low Henry's Law constant. This substance also has a moderate to high octanol/water partition coefficient (see Table 3-1). TCP can easily be hydrolyzed to dicresyl phosphate and cresol in an alkaline medium, but it is stable in neutral and acidic media (IPCS 1990; van der Veen and de Boer 2012; WHO 1990). Cresol was assessed by Environment and Climate Change Canada and was concluded not to meet the criteria under paragraphs 64(a) or (b) of CEPA in July 2014 (Environment and Climate Change Canada 2014). Therefore, cresol is not discussed in this assessment.

**Table 3-1. Key physical and chemical properties of TCP<sup>a</sup>**

Property	Value	Temperature (°C)	Reference
Melting point (°C)	-33	NA	US EPA 2010 (Midwest Research Institute, 1977) UK EA 2009 (WHO 1990)
Boiling point (°C)	476.06 (standard atmospheric pressure at 101 325 Pa)	NA	MPBPVP v.1.43
Density (kg/m <sup>3</sup> )	1160	20	UK EA 2009 (Ashford 1994)
Vapour pressure (Pa)	6.6 x 10 <sup>-5</sup>	25	UK EA 2009 (extrapolated)
Henry's Law	6.75 x 10 <sup>-2</sup>	25	Calculated from

Property	Value	Temperature (°C)	Reference
constant (Pa·m <sup>3</sup> /mol)	(6.843 x 10 <sup>-7</sup> atm.m <sup>3</sup> /mol)		molecular weight, vapour pressure and water solubility listed in this table
Log K <sub>ow</sub> (dimensionless)	5.11	25 (room temperature)	Saeger et al. 1979
Log K <sub>oc</sub> (dimensionless)	3.52	NA	KOCWIN v.2.00
Log K <sub>oa</sub> (dimensionless)	9.59	NA	KOAWIN v.1.10
Log K <sub>aw</sub> (dimensionless)	-4.564	25	Calculated from Henry's Law constant listed in this table
Water solubility (mg/L)	0.36	25 <sup>b</sup>	Saeger et al. 1979
pK <sub>a</sub> (dimensionless)	-	-	-

Abbreviations: WS, water solubility; VP, vapour pressure; log K<sub>ow</sub>, octanol-water partition coefficient; log K<sub>oc</sub>, organic carbon-water partition coefficient; log K<sub>oa</sub>, octanol-air partition coefficient; pK<sub>a</sub>, acid dissociation constant; NA, not applicable; NS, not specified (likely experimental).

<sup>a</sup> Values in parentheses represent the original ones as reported by the authors or as estimated by the models.

## 4. Sources

TCP is a synthetic substance and does not occur naturally. Based on responses to a survey conducted under section 71 of CEPA in 2001, there was no manufacture of this substance in Canada in 2000; however, approximately 1 000 000 to 10 000 000 kg of TCP were imported into Canada during that year (ECCC 2001). Based on the responses to a more recent survey pursuant to Section 71 of CEPA (calendar year 2011), TCP was not manufactured in Canada; however 1 000 to 10 000 kg of TCP were imported into Canada during that year as a neat substance (1 000–10 000 kg), and in consumer or commercial products (100–1 000 kg) (ECCC 2013-2014). While the survey included products, there is the possibility that the import volume of consumer or commercial products is underestimated.

TCP is a high-production volume (HPV) chemical in the U.S., where TCP production is

estimated to range from 1 to 10 million pounds (US EPA 2010). In 1998, 2002 and 2006, 373 to 4082 tonnes (454 to 4500 tonnes) of TCP were produced in the U.S. (van der Veen and de Boer 2012) of which, 0.73 tonnes, 0.54 tonnes, 3.3 tonnes, 4.5 tonnes were produced/used in Norway, Denmark, Finland and Sweden, respectively, in 2008 (van der Veen and de Boer 2012). There are two known European production sites; however information on production volume and market size is confidential (UK EA 2009). In 1990, about 800 to 1 000 tonnes of TCP were produced annually in China (IPCS 1990).

## 5. Uses

According to submissions under section 71 of CEPA, TCP is used in Canada as adhesives and sealants, in automobile parts, aircraft applications, as a fire-resistant lubricant and grease additive, and in electrical and electronic applications (ECCC 2013-2014). In preliminary product testing conducted by Health Canada of children's manufactured items purchased in Canada in 2014, TCP was detected in a foam chair above the limit of detection of quantitation at a concentration reported as  $\geq 0.7\%$ ; however, TCP was not detected in the remaining 23 children's manufactured items (e.g. nursing pillows, toys) (Health Canada 2014a). According to manufacturer literature (ICL 2013c), TCP is marketed for flexible foam used in furniture.

TCP appears on the List of Prohibited and Restricted Cosmetic Ingredients (more commonly referred to as Health Canada's Cosmetic Ingredient Hotlist or simply the Hotlist), an administrative tool that Health Canada uses to communicate to manufacturers and others that certain substances, when present in a cosmetic, may contravene (a) the general prohibition found in section 16 of the *Food and Drugs Act* or (b) a provision of the *Cosmetic Regulations*. The Hotlist prohibits the ingredient TCP (synonym: tritolyl phosphate) (Health Canada 2014b).

TCP is not listed as an approved food additive in the Lists of Permitted Food Additives as regulated under the *Food and Drugs Act* (Health Canada 2013). TCP has not been identified as being used /present in formulations of food packaging materials, but is present in incidental additives used as a lubricant on equipment or machine parts where there is no contact with food (2013 email from Food Directorate, Health Canada, to Risk Management Bureau, Health Canada; unreferenced). TCP is not listed in the Drug Products Database, the Therapeutic Products Directorate's internal Non-Medicinal Ingredient Database, the Natural Health Products Ingredients Database or the Licensed Natural Health Products Database as a medicinal or non-medicinal ingredient present in final pharmaceutical products, natural health products or veterinary drugs in Canada (DPD 2013, NHPID 2013, LNHPD 2013, 2013 email from the Therapeutic Products Directorate, Health Canada, to Risk Management Bureau, Health Canada; unreferenced).

Internationally, TCP applications also include several manufactured items such as furniture and electronics. TCP was reported to be applied as a backcoating to furniture

upholstery in the U.S. in 2000 (US CPSC 1998; Piccirillo 1999; NRC 2000). TCP is used in synthetic leather furniture upholstery based on a report by the European Commission (2011), in PVC seat covers (SinoHarvest 2011). Curtains, wallpaper, flooring and electronics in Japan have been reported to contain TCP (Kajiwara et al. 2011). TCP is used as a flame retardant in polystyrene plastics that are commonly used in computers, cabinets for display units and refrigerators. As well, TCP use as a flame retardant has been identified in printed circuit boards (GFEA 2001). TCP may also be used in various utility articles including footwear, raincoats and handbags (SinoHarvest 2011), in addition to PVC gloves (Siret-Alatrissa et al. 2010) or garments that are made of imitation leather (IPCS 1990; Ash and Ash 2000; Ash and Ash 2003). Several other applications of TCP involve automobile interiors (IPCS 1990; ATSDR 1997). Minor uses have also been reported for glasses frames (Siret-Alatrissa et al. 2010) and a prosthetic leg (Grimalt et al. 2009). TCP is also used in various extruded products such as flexible polyvinyl chloride (PVC) cable insulation and films, hoses, mine conveyor belts, air ducts, as well as polystyrene and vinyl tarpaulins (Weil 2001; Ash and Ash 2003; UK EA 2009; SinoHarvest 2011).

Internationally, TCP is also used as an additive flame retardant and plasticizer in a range of products. TCP finds use in cellulose nitrate, ethylcellulose, lacquers, adhesives, pigment dispersion, photographic film and clarifying agent in casein polymer production (IPCS 1990; Weil 1993, Ashford 1994; UK EA 2009). TCP is also used as an extreme pressure additive in lubricants, as a fire-resistant hydraulic fluid and a petrol/diesel fuel anti-preignition additive (IPCS 1990). Due to its anti-wear, anti-corrosion, anti-foaming, lubricating and flame retardant properties, TCP is used as an additive in engine turbine oils and hydraulic fluids in aircraft hydraulic systems (IPCS 1990; Okazaki et al. 2003).

## **6. Releases to the Environment**

Anthropogenic releases to the environment depend upon various losses occurring during the manufacture, industrial use, consumer or commercial use, service life and disposal of a substance. Releases of TCP to the Canadian environment, due to the substance's use as a flame retardant, are expected to be diffuse, with some point sources (e.g. from processing facilities). Releases from consumer and commercial products may occur in both indoor and outdoor environments.

According to submissions made under section 71 of CEPA, TCP is imported into Canada in neat form, and as consumer and commercial products (ECCC 2013-2014). TCP is used in Canada as a flame retardant within several sectors; TCP use activities in Canada likely to result in point source TCP releases to the environment include blending into products and potentially from container cleaning.

TCP release to the environment is likely to occur during industrial activities. Releases to the environment are expected to occur primarily to the water compartment via wastewater. Release to the soil could also occur through the application of biosolids to

agricultural and pasture lands. TCP is not a reportable substance in the National Pollutant Release Inventory (NPRI 2011; data from 1994–2009).

## **7. Measured Environmental Concentrations**

Internationally, levels of TCP in air and water appear to be low, with somewhat higher levels in sediments and fish (Boethling and Cooper 1985). A detailed listing of the available concentrations of TCP and its isomers in air, water, sediment, soil, biota and other media from the open literature are available in supporting documentation (Environment and Climate Change Canada 2015b). However, data concerning concentrations of TCP and its related isomers in the Canadian environment are limited and available for water and some biota.

### **7.1 Air**

In Canada, no data are available for the concentrations of TCP in air (Environment and Climate Change Canada 2015b).

Air samples collected near the facilities which produced aryl phosphates in Nitro and Gallipolis Ferry in West Virginia, USA were found to contain concentrations of TCP ranging from 0.01 to 2 ng/m<sup>3</sup> (Boethling and Cooper 1985).

In Japan, three studies conducted from 1974 to 2000 reported TCP concentrations in air. Among them, concentrations of TCP ranging from non-detect to 70.3 ng/m<sup>3</sup> were measured in 3 out of the 19 air samples collected from heavily-industrialized cities in Shikoku, Japan (IPCS 1990). Another two studies, however, reported lower concentrations of TCP ranging from non-detected to 21.4 ng/m<sup>3</sup> (IPCS 1990; Kishi and Sekine 2003; Takimoto et al. 1999). Takimoto et al. (1999) concluded that in the Kurose River Basin area of Japan, the main source of TCP in air, likely sorbed onto particulate matter, were motorcycle and automobile exhausts.

In a more recent study out of Finland, TCP was not found above the detection limit of 0.0007 ng/m<sup>3</sup> (a semi-quantitative value determined against another organophosphate flame retardant) in a sample of air collected in July 2004 from a rural area in Northern Finland—a site selected to verify potential long-range atmospheric transport (Marklund et al. 2005).

### **7.2 Water**

There are limited studies characterizing concentrations of TCP in water (Environment and Climate Change Canada 2015b). In Canada, TCP was not detected in the open waters of the Great Lakes, but the tributaries of Lake Ontario and Lake Erie contained TCP ranging from 11 to 22 ng/L and from 2.5 to 10 ng/L, respectively in 2010 and 2011 (Lee et al. 2011).

In the United States, various studies have sought to determine levels of TCP in surface waters (Boethling and Cooper 1985). However, because many of these studies had high detection limits (e.g.  $\geq 100$  ng/L), only one surface water sample included a detected concentration of 20 ng/L which was reported downstream of a facility that produced aryl phosphates (Boethling and Cooper 1985).

In Europe, concentrations of TCP were reported below detection limit by three independent studies conducted in rivers in Denmark, Rome and Austria (Bacaloni et al. 2007; Martinez-Carballo et al. 2007; UK EA 2009).

In Japan, river and lake waters were tested for TCP in the 1970s and 1990s; however, only a limited number of studies reported measuring TCP concentrations above the detection limit. Concentrations of *o*-TCP, *p*-TCP and *m*-TCP were reported at below 500 ng/L (detection limits ranged from 5 to 2500 ng/L (UK EA 2009; Cho et al. 1994, 1996)). These studies also noted that concentrations of TCP above the detection limit were generally found in highly-polluted areas and were often detected in water samples containing suspended sediments and sediments (UK EA 2009). In China, water samples were collected from 17 sites at Songhua River, and *m*-TCP was detected at concentrations between 5.2 and 45 ng/L (Wang et al. 2011).

### **7.3 Sediment**

No data were found on concentrations of TCP in sediment in Canada. Studies conducted elsewhere before 2005, mainly in the 1980s and 1990s, report detection of TCP in sediments near industrialized areas (Environment and Climate Change Canada 2015b).

In the United States, sediments from freshwater rivers and lakes were monitored for TCP. In the early 1980s, sediment concentrations of TCP in industrialized areas of the Delaware River, Kanawha River, Saginaw River, Baltimore Harbor and Detroit River ranged from non-detect (detection limit: 0.2 mg/kg) to 1.3 mg/kg (Boethling and Cooper 1985). In 1988-1990, sediment concentrations of TCP ranging from 0.05 to 3.40 mg/kg dry weight (dw) (mean level was 1.1 mg/kg dw) were measured in all 10 samples in the Grand Calumet River in Indiana, U.S. (Hoke et al. 1993).

In Europe, TCP in sediments from freshwater sources was measured at concentrations ranging from non-detect to 0.39 mg/kg in Denmark, Norway, Austria and Germany (Ricking et al. 2003; Martinez-Carballo et al. 2007; UK EA 2009; van der Veen and de Boer 2012). Concentrations in marine sediment ranged from non-detect to 0.37 mg/kg in Denmark (UK EA 2009).

Kawagoshi et al. (1999) reported TCP concentrations ranging from non-detect to 2.558 mg/kg over a 7-year period (1991–1997) at a solid waste disposal site in Japan. In 1992, sediment concentrations of TCP isomers ranged from non-detect to 0.08 mg/kg in Kurose River Basin, Japan (Cho et al. 1994). TCP was also measured in a marine



sediment sample at a concentration of 0.004 mg/kg at Tokyo, Japan (Wakabayashi 1980).

## 7.4 Soil

The existing literature contains few references to soil concentrations of TCP (Environment and Climate Change Canada 2015b) and those identified are older (before 1996). No soil concentrations of TCP are available for Canada.

In the United States, concentrations of TCP were detected in soils at US air force bases contaminated with hydraulic fluids, ranging from 0.02 to 130 mg/kg (David and Seiber 1999b). Also, TCP was detected in soils near facilities that produce aryl phosphates in Gallipolis Ferry, West Virginia, with concentrations ranging from 1.0 to 4.0 mg/kg (Boethling and Cooper 1985).

In Japan, concentrations of TCP isomers measured in soils near a highway and in a forest ranged from non-detect to 1.52 mg/kg (Takimoto et al. 1999). Concentrations of m- isomer exceeded concentrations of o- and p-isomers (Takimoto et al. 1999).

## 7.5 Biota

Few studies report concentrations of TCP in biota (Environment and Climate Change Canada 2015b). In Canada, 0.12 ng/g wet weight of TCP has been detected in herring gull egg homogenate taken from the Great Lakes area (Chen et al. 2012). No other TCP concentrations are available for biota in Canada.

In the United States, concentrations of TCP in vegetation near facilities that produce aryl phosphates in Gallipolis Ferry, West Virginia, were between 1 and 20 mg/kg (Boethling and Cooper 1985). TCP was also detected in fish near a triaryl phosphate manufacturing plant in the United States at a concentration of 2–5 µg/kg (Muir 1984). A TCP concentration of 40 µg/kg ww was measured in sturgeon from the Columbia River, USA in an area downstream of several metal processing plants (Lombardo and Egry 1979; cited in UK EA 2009).

In Sweden, TCP has been measured in the muscle of various fish from lakes and coastal areas of Sweden (2003–2007) at concentrations ranging from 1.8 to 110 ng/g lipid (Sundkvist et al. 2010).

TCP at a concentration of 45.4 ng/g lipid was detected in *Epinephelus corallicola* collected from Manila Bay, the Philippines (UK EA 2009; Kim et al. 2011).

## 7.6 Other Media

Few data are available on the concentration of TCP in effluent, sludge or biosolids (Environment and Climate Change Canada 2015b). TCP was measured in wastewater

treatment plant (WWTP) effluent in Canada at a concentration of 1.14 ng/L (Woudneh et al. 2015), and in Austria and Denmark at concentrations ranging from non-detect to 55 ng/L in 2005 (Martinez-Carballo et al. 2007) and non-detect to 530 ng/L (0.53 mg/L; detection limit (DL= 0.02 mg/L), respectively (UK EA 2009). TCP was measured in one wastewater sludge sample and one biosolids at a concentration of 97.6 ng/g and 69.0 ng/L, respectively (Woudneh et al. 2015). TCP was also measured in 3 of the 15 wastewater sludge samples collected in Denmark at a mean concentration of 613 µg/kg dw (UK EA 2009).

In Japan, TCP was measured in effluent from five industrial machinery complexes at concentrations of non-detect to 0.56 µg/L (Cho et al. 1994). It was also measured in effluent from five WWTPs in Kitakyushu City, at concentrations ranging from 0.4 to 0.58 µg/L (DL = 0.06 µg/L) (Ishikawa et al. 1985c, cited in UK EA 2009).

## 8. Environmental Fate and Behaviour

### 8.1 Environmental Distribution

TCP is expected to be released primarily via wastewater from industrial facilities using the substance as an additive flame retardant. TCP is partially removed by adsorption to sludge in wastewater treatment systems, which in turn can be applied to agricultural soils during biosolids amendment. Level III fugacity modelling (Table 8-1) using the updated EQC model (2012), was applied to describe the environmental distribution of TCP following release to air, water and soil.

Results from the HYDROWIN model suggest that the rate of hydrolysis for TCP increases with increasing pH of the water (half-life of 192.6 years at pH 5, 11.58 years at pH 6, 1.17 years at pH 7, 42.87 days at pH 8, 4.287 days at pH 9, and 10.29 hours at pH 10). The half-life for the more environmentally-relevant pH of 8 (pH 8.2 in natural water of Lake Ontario (Howard and Deo 1979)) of 42.87 days (or 1029 hours) was used in this assessment for making predictions about the fate of TCP in water. Half-lives of 1.5 years and 2 years for the acidic environment at less than pH 7 were also considered, however, the results showed similar modelling fate outcome of TCP in water using the half-life of 42.87 days at pH 8.

**Table 8-1. Results of the Level III fugacity modelling for TCP (EQC v1.0 2012)<sup>a</sup>**

TCP released to:	Percentage of TCP partitioning into air	Percentage of TCP partitioning into water	Percentage of TCP partitioning into soil	Percentage of TCP partitioning into sediment
Air (100%)	3.32	4.54	91.6	0.6
Water (100%)	negligible	88.7	0.1	11.1
Soil (100%)	negligible	0.2	99.8	negligible

<sup>a</sup> Physical and chemical properties and environmental half-lives ( $t_{1/2}$ ) of TCP in environmental media are required for

modelling and are listed in Appendix A

When TCP is released to air, about 3% of the substance is expected to reside in air in the gas phase while most is expected to partition to the particulate phase in air, given this substance's moderate  $\log K_{oa}$ . This substance has a very low predicted half-life ( $\leq 1$  day) due to reaction with hydroxyl radicals, and therefore, in the gas phase, TCP is not expected to have long-range transport potential to remote regions in air. The particulate phase is deposited to land and water as wet and dry deposition. For the amount transferred from air to soil, the majority (~92%) will remain in soil while a smaller fraction can be further transported as surface runoff to aqueous systems and when combined with atmospheric inputs, results in approximately 0.6% of the mass fraction in sediment.

Further modelling was conducted to clarify the long-range atmospheric transport potential for TCP. Model estimates of the Characteristic Travel Distance (CTD) of 222 and 363 km in air, respectively, using the Transport and Persistence Level III Model (TaPL3) (TaPL3 2003) and the OECD POPs Screening Model (OECD QSAR Tool 2012; Scheringer et al. 2009) also support that TCP has a low potential for transport in air. In addition, the estimated persistence of TCP in air by TaPL3 and OECD POPs are 38.3 days and 7 days, respectively. Results from AEROWIN suggest that about 47% of TCP released to air will be associated with the particulate phase due to its higher  $\log K_{oa}$  value (9.59) (AEROWIN 2010). While the percentage of the substance adsorbed to aerosols as predicted by the OECD POPs Screening Model is lower (4%); both AEROWIN and the OECD POPs Screening Model indicate that particle-associated long-range transport may be a factor for TCP.

The transfer efficiency (TE) is the percentage of emission flux to air that is deposited to the surface (water and soil) in a remote region ( $TE \% = D/E \times 100$ , where E is the emission flux to air and D is the deposition flux to surface media in a target region). The estimated TE for TCP at 0.0167% is well below the boundary of 2.248% established based on the model's reference substance (PCB 28) meaning that TCP is unlikely to be deposited to Earth's surface in a remote region.

When released to surface water, the vast majority (88.7%) of TCP is expected to stay in water. With a low to moderate water solubility (0.36 mg/L), a small fraction (11.1%) of TCP is expected to adsorb to suspended solids and/or sediments. Volatilization from surface water to air is very low. Thus, loss of TCP from aqueous systems is primarily a result of sediment burial (from the natural process of sedimentation) and from degradation (Environment and Climate Change Canada 2015c and Table 8-2).

When TCP is released to soil as a result of applying biosolids to agricultural lands, it is expected to become adsorbed to soil (~100%) due to its hydrophobic nature. Evaporation from soil into air is not expected due to an extremely low vapour pressure.

## **8.2 Environmental Persistence**

Based on likely TCP releases and partitioning characteristics, environmental persistence is most relevant for the water, sediment and soil compartments where the majority of the substance is expected to be found. Empirical and modelled data were considered in the weight-of-evidence for TCP persistence.

Modelled predictions for TCP in air suggest a half-life < 1 day (gas phase) and or an overall persistence (Pov) of 108 days (OECD POPs model). TCP testing under longer-term, environmentally-relevant conditions to determine the degradation pathways and transformation products is lacking.

Environment and Climate Change Canada (2015c) and Table 8-2 present empirical and modelled degradation data for TCP.

### 8.2.1 Empirical Data for Persistence

TCP can easily be hydrolyzed to dicresyl phosphate and cresol in an alkaline medium, but is stable in neutral and acidic media (IPCS 1990; van der Veen and de Boer 2012; WHO 1990). Cresol was assessed by Environment and Climate Change Canada and was concluded not to meet the criteria under paragraphs 64(a) or (b) of CEPA in July 2014 (Environment and Climate Change Canada 2014). Therefore, cresol is not discussed in this assessment.

Hydrolysis of TCP, *o*-TCP and *p*-TCP at pH 10.3 resulted in half-lives of 70 minutes, 70 minutes and 27 minutes, respectively (David and Seiber 1999a). Hydrolysis of TCP, *o*-TCP and *p*-TCP at pH 10.7 resulted in half-lives of 200 minutes, 280 minutes and 670 minutes, respectively (David and Seiber 1999a). At these basic pHs, TCP is not stable in water. Although this study did not report the experimental temperature, heating the slurries will almost certainly increase hydrolysis (David and Seiber 1999a).

A hydrolysis study conducted using Lake Ontario water found that at 21°C TCP was 100% degraded within 5 to 6 days, and a mixture of *m*- and *p*-TCP degraded rapidly (< 4 days) after a two-day lag period (Howard and Deo 1979). Due to this initial lag phase prior to degradation, microbial degradation instead of hydrolysis was probably the dominant degradation process occurring in these samples (UK EA 2009).

Several studies (Saeger et al. 1979; Ku and Alvarez 1982; Cho et al. 1996; David and Seiber 1999a; NITE 2002) have documented the aerobic biodegradation of TCP using tests of “inherent biodegradability” and the more stringent “ready biodegradability.” Although ready biodegradability was not shown, tests did show that TCP was inherently biodegradable (Saeger et al. 1979; US EPA 2010).

Muir et al. (1985) studied degradation of TCP in water and sediment of an artificial pond system, and in natural sediments. The half-life of *m*-TCP in natural river sediments was 10.1 days at 25°C. Using the Boethling et al. (1995) ratio of biodegradation in water to that in soil and sediment (1:1:4) yields half-lives of 2.5 days for both water and soil.

These data are generally consistent with the half-life reported from other empirical studies, i.e. TCP has a short half-life in water, soil and sediment.

## 8.2.2 Modelling of Persistence

A QSAR-based weight-of-evidence approach (Environment and Climate Change Canada 2007) was also applied using the degradation models shown in Table 8-2. Given the ecological importance of the water, soil and sediment compartments and the fact that TCP is expected to partition mainly to these compartments, it is considered reasonable and relevant to examine biodegradation in water, soil and sediment.

The probability of biodegradation using the TOPKAT model (2004) suggests that TCP is 100% biodegradable within 28 days. Results are within the optimum prediction space (OPS), the structural domain of the model. The CATALOGIC model (2012) predicts that 72% of TCP biodegraded under aerobic conditions within 28 days reporting an ultimate half-life of 15.4 days. Both TOPKAT and CATALOGIC suggest moderate and high rates of mineralization from biodegradation consistent with empirical data. Biodegradation was predicted using BIOWIN 3 and BIOWIN 4 Expert-Survey models. These models also suggest that TCP is not persistent in water although BIOWIN 5 MITI Linear Probability, and BIOWIN 6 MITI Non-Linear Probability suggest otherwise. In addition, results from the HYDROWIN model suggest that the rate of hydrolysis for TCP increases with increasing pH of the water (11.58 years at pH 6, 1.17 years at pH 7, 42.87 days at pH 8 and 10.29 hours at pH 10) (Table 8-2).

In summary, results of empirical and modelled biodegradation data suggest that the half-life in water is likely in the order of several hours to less than 40 days. Applying a half-life extrapolation procedure based on Boethling et al. (1995) using a ratio of 1:1:4 for water:soil:sediment, it is expected that TCP will break down quickly in soil and sediment and not present long-term exposure in these media. Furthermore, results from empirical and modelled hydrolysis data suggest a faster degradation rate at an increasing pH in water, soil and sediment.

**Table 8-2. Summary of modelled data for degradation of TCP**

Medium	Fate process	Model and model basis	Model result and prediction	Extrapolated half-life (days)
Air	Atmospheric oxidation	AOPWIN 2010 <sup>a,b</sup>	$t_{1/2} = 0.78$ days	$\leq 2$
Air	Ozone reaction	AOPWIN 2010 <sup>b</sup>	NA <sup>c</sup>	NA
Water	Hydrolysis	HYDROWIN 2010 <sup>b</sup>	11.58 years (pH 6) 1.17 years (pH 7) 42.87 days (pH 8)	NA
Primary Biodegradation	Biodegradation (aerobic)	BIOWIN 4.10 <sup>b</sup>	Classification value of 3.58	< 182

		Sub-model 4	"biodegrades fast"	
Ultimate Biodegradation	Biodegradation (aerobic)	BIOWIN 4.10 <sup>b</sup> Sub-model 3	Classification value of 2.31 "biodegrades fast"	< 182
Ultimate Biodegradation	Biodegradation (aerobic)	BIOWIN 4.10 <sup>b</sup> Sub-model 5: MITI linear probability	Probability value of -0.0061; "biodegrades very slowly"	> 182
Ultimate Biodegradation	Biodegradation (aerobic)	BIOWIN 4.10 <sup>b</sup> Sub-model 6: MITI non-linear probability	Probability value of 0.0098; "biodegrades very slowly"	> 182
Ultimate Biodegradation	Biodegradation (aerobic)	TOPKAT 2004 (v. 6.1) Probability	1.000 "biodegrades fast"	< 182
Ultimate Biodegradation	Biodegradation (aerobic)	CATALOGIC 2012 % BOD (biological oxygen demand)	% BOD = 72 "biodegrades fast" Primary half-life: 11.613 days Ultimate half-life: 15.434 days	< 182

Abbreviations: NA, not applicable;  $t_{1/2}$ , half-life; %, percent.

<sup>a</sup> Based on a day length of 12 hours, a hydroxyl radical concentration of  $1.5 \times 10^6$  molecules/cm<sup>3</sup> (12-hour annual average), and a system temperature of 25°C.

<sup>b</sup> EPI Suite (2012)

### 8.3 Bioaccumulation

The discussion on the potential for bioaccumulation examines several potential parameters, including properties of the substance (i.e. log  $K_{ow}$ , log  $K_{oa}$ , molecular size and cross-sectional diameters), bioconcentration factor (BCF), biomagnification factor (BMF), trophic magnification factor (TMF) and bioaccumulation factor (BAF). The potential derivation and role of metabolic biotransformation rate constants in determining bioaccumulation potential is also examined.

The empirical log  $K_{ow}$  value of 5.11 for TCP suggests some potential to bioaccumulate or biomagnify in biota. Strong sorption to solids as indicated by a moderate log  $K_{oc}$  suggests a potential for bound residues in the environment reducing the bioavailable fraction of TCP. There is uncertainty with estimates of the partition coefficients, but it is

reasonable to assume that these will be high values, based on the chemical structure of TCP alone.

The bioconcentration of TCP has been examined in a number of studies on fish (Environment and Climate Change Canada 2015c). Low to moderate BCFs were reported in these studies. No empirical studies on BMFs, TMFs, or BAFs are available in the literature at the time of this assessment. Because publicly available TMF models are limited, TMF cannot currently be reliably modelled. Therefore, modelled bioconcentration and bioaccumulation data are considered to provide the best possible weight-of-evidence for the bioaccumulation potential of TCP.

### 8.3.1 Empirically Determined Bioaccumulation

#### 8.3.1.1 Bioconcentration Factor (BCF)

A few studies examining the bioconcentration of TCP on fish were discussed in this section and listed in Table 8-3. A detailed listing of the available bioconcentration of TCP (CAS RN 1330-78-5) on fish from the open literature is available in supporting documentation (Environment and Climate Change Canada 2015c).

In the first, a commercial product containing TCP was tested for uptake into Common Bleak (*Alburnus alburnus*) in natural brackish water (7% salinity) at 10°C for 14 days (Bengtsson et al. 1986). The steady state BCF was 800 L/kg. TCP was rapidly eliminated from the fish, with a depuration half-life of four days or less, and almost complete elimination within 14 days (Bengtsson et al. 1986). In the second study, the bioconcentration of TCP in Fathead Minnows (*Pimephales promelas*) was studied at 25°C over 32 days (Veith et al. 1979). A BCF of 165 L/kg was determined based on total radioactivity.

BCFs also have been measured in Rainbow Trout (*Oncorhynchus mykiss*) and Fathead Minnow (*Pimephales promelas*) for the *p*- and *m*-TCP isomers (Muir et al. 1983) (Environment and Climate Change Canada 2015c). Due to the short test duration (24 hours), steady state was not reached for Rainbow Trout. Estimated BCFs based on total radioactivity varied from 165 to 2768 L/kg according to the method used to calculate or model the value (Environment and Climate Change Canada 2015c). A 4-week BCF study using Bluegill Sunfish (*Lepomis macrochirus*) for *p*-TCP determined a BCF of 1589 L/kg based on total radioactivity (Sitthichaikasem 1978). However, due to the possible uptake of TCP from food as well as water, this value may be more relevant for bioaccumulation (UK EA 2009).

**Table 8-3. Empirical bioaccumulation data for TCP (CAS RN 1330-78-5) and related isomers (CAS RNs 78-30-8, 78-32-0, 563-04-2)**

CAS RN	Test organism	BCF	Kinetic and/or steady-state value (L/kg) <sup>a</sup>	Reference
1330-	Bleak, <i>Alburnus</i>	BCF	800 (14 d, 50 µg/L of	Bengtsson et al.

78-5	<i>alburnus</i>		the triaryl phosphate product)	1986
1330-78-5	Fathead Minnow, <i>Pimephales promelas</i>	BCF	165 (32 d; mean concentration 31.6 µg/L)	Veith et al. 1979
78-32-0	Fathead Minnow, <i>Pimephales promelas</i>	BCF	2199 ± 227 (initial rate method); 928 ± 8 (static test method); 588 ± 129 (BIOFAC model) (24 hr, 5 µg/L nominal)	Muir et al. 1983
78-32-0	Rainbow Trout, <i>Oncorhynchus mykiss</i>	BCF	2768 ± 641 (initial rate method); 1420 ± 42 (static test method); 1466 ± 138 (BIOFAC model); (24 hr, 5 µg/L nominal) *Steady-state concentration was not reached in 24 hours.	Muir et al. 1983
563-04-2	Fathead Minnow, <i>Pimephales promelas</i>	BCF	1653 ± 232 (initial rate method); 596 ± 103 (static test method); 385 ± 92 (BIOFAC model) (24 hr, 5 µg/L nominal)	Muir et al. 1983
563-04-2	Rainbow Trout, <i>Oncorhynchus mykiss</i>	BCF	1162 ± 313 (initial rate method); 784 ± 82; (static test method); 1102 ± 137 (BIOFAC model); (24 hr, 5 µg/L nominal) *Steady-state concentration was not reached in 24 hours.	Muir et al. 1983
78-32-0	Bluegill Sunfish,	BCF	1589 (4 wk, NS)	UK EA 2009



	<i>Lepomis macrochirus</i>			(Sittichaikasem 1978)
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Abbreviations: BAF, bioaccumulation factor; BCF, bioconcentration factor; NA, not applicable; NS, not specified.

<sup>a</sup> Values in parentheses represent the duration and/or test concentrations at which the BAFs or BCFs were derived.

### 8.3.1.2 Biomagnification Factor (BMF) and Trophic Magnification Factor (TMF)

Biomagnification describes the process in which the concentration of a chemical in an organism reaches a level that is higher than that in the organism's diet due to dietary absorption (Gobas and Morrison 2000). A BMF exceeding 1 indicates that biomagnification is potentially occurring. BMF data may be considered indicators of the potential for uptake and accumulation in biota and are considered in the overall weight-of-evidence. The TMF is a measure of the biomagnification potential of a substance within a studied food web under field conditions. It is estimated by correlating the normalized substance concentrations in biota at different trophic levels.

No experimental BMF or TMF studies were identified for TCP.

### 8.3.1.3 Bioaccumulation Factor (BAF)

Bioaccumulation factors are measured under field conditions as the ratio of the whole body burden of chemical taken up from all exposures to that of the ambient water concentrations. Measures of BAF are a preferred metric for assessing the bioaccumulation potential of substances because it incorporates all chemical exposures including the diet, which predominates for substances with  $\log K_{ow} > \sim 4.0$  (Arnot and Gobas 2003a).

One empirical study reported a rough estimation of maximum accumulation factor of 0.08–0.13% w/w, from food in Common Minnows (*Phoxinus phoxinus*) for TCP (Bengtsson et al. 1986; Environment and Climate Change Canada 2015c). No acceptable empirical BAF values were available for TCP at the time of this analysis and therefore metabolic biotransformation corrected kinetic mass-balance modelling was used to fill this data gap.

## 8.3.2 Modelling Bioconcentration and Bioaccumulation

Environment and Climate Change Canada estimated the BCF and BAF of TCP using both structure-based models, QSARS, and a three-trophic-level kinetic mass-balance model (Arnot and Gobas 2003b). All estimates of BCF and BAF, except sub-model 1 of the BCFBAF model in EPIWIN v4.0, were corrected for metabolism because it represents a fundamental elimination pathway for many chemicals like TCP. This correction was performed by deriving metabolic biotransformation rate constants ( $k_M$ ) using available empirical BCF or BMF study information or using a structure-based QSAR method.

The metabolic rate constant is a very sensitive input parameter for bioaccumulation modelling and can be highly variable (Arnot et al. 2008a, Arnot et al. 2008b). An empirical  $k_M$  for TCP (CAS RN 1330-78-5) for a 10 g fish at 15°C of 0.20/ d has been estimated (Arnot et al. 2008a, Arnot et al. 2008b) from a reliable quality BCF study for Common Bleak (*Alburnus alburnus*) (Bengtsson et al. 1986). The metabolic rate constant for TCP was also estimated as 0.015 /d using the  $k_M$  (Q)SAR sub-model in BCFBAF model v3.10 2010 in EPIWIN v4.0 2012 (based on Arnot et al. 2009), and the QSAR  $k_M$  for a 10 g fish at 15°C. The empirical and QSAR estimates are in good agreement with each other and these rates are regarded as relatively “fast” (greater than 0.1) (Arnot and Gobas 2006; Nichols et al. 2009). The  $k_M$  value of 0.15 /d was then normalized to model the BCF and BAF of a middle-trophic-level fish using a three-trophic-level modification of the fish bioaccumulation mass-balance model from Arnot and Gobas (2003a). The results of the BCF and BAF modelling for TCP are 1589 and 2043 L/kg wet weight, respectively.

The BCF<sub>max</sub> model with Mitigating Factors (Dimitrov et al. 2005) was also applied and predicted a corrected BCF of 1251 (log BCF of 3.0974), correcting for the mitigating effects of acids, metabolic biotransformation, phenols, size, and water solubility. It predicts a metabolic biotransformation rate constant of 0.05 /day. However, these results are considered with caution since the substance is considered outside of the model's structural domain.

With an empirical log  $K_{ow}$  of 5.11, the predicted bioavailable fraction of TCP in the water column according to mass-balance fish models (BAF-QSAR v. 1.2) is 97%, which suggests that almost all of the chemical present in typical surface waters is bioavailable for chemical uptake at the gill surface.

In summary, with empirical BCFs ranging from 165 L/kg and 800 L/kg at TCP concentrations of 0.0316 mg/L and 0.050 mg/L (both less than the empirical water solubility value of 0.36 mg/L), respectively, the available empirical fish bioaccumulation studies collectively indicate a low bioconcentration potential. Both modelled BCF (1589 L/kg) and BAF (2043 L/kg) also support that TCP does not have a high bioaccumulation potential.

### 8.3.3 Bioaccumulation in Plants

The uptake of *p*-TCP (CAS RN 78-32-0) from soil into plants was measured only in soybeans (Casterline et al. 1985). Seeds were planted in 2 cm of untreated soil overtop of the TCP-treated soil (10 mg/kg). The fresh weight BAF (plant shoot) was 0.17, where 1.72 µg/g and 10.14 µg/g *p*-TCP concentration were detected in shoot and soil, respectively (about 1:6 in shoot/soil ratio). The outcome of this study is uncertain because it was not a GLP study, it used sterilized soil, and the nominal concentrations were not verified.

## 8.4 Summary of Environmental Fate

TCP is expected to be predominantly released from industrial sources via wastewater. Once released to water, a high proportion (88.7%) of TCP is expected to remain in water. A strong tendency to sorb to the solid phase in various media (including particulate matter suspended in air) means that this chemical will reside in biosolids, soil and suspended air particles and be transferred to soil from dry deposition and application of biosolids to agricultural lands. In summary, high sorption characteristics indicate that TCP will reside in water, biosolids, sediments and soil.

## **9. Potential to Cause Ecological Harm**

### **9.1 Ecological Effects Assessment**

Empirical ecotoxicity data for TCP was considered for assessing the ecological effects of TCP. TCP is expected to be predominantly released from industrial sources via wastewater. Exposure to aquatic organisms may be expected because, once released to water, a high proportion (88.7%) of TCP is expected to remain in water. A strong tendency to sorb to the solid phase in various media (including suspended air particles) indicates that TCP will reside in water, biosolids, sediments and soil. There are a number of available empirical aquatic toxicity data for TCP. Modelled data were used to support the empirical data. There are no available sediment toxicity data for TCP at the time of this assessment and, therefore, the focus of the assessment is for aquatic species. However, available terrestrial toxicity data for TCP is also considered in this assessment which are relevant for exposures to soil-dwelling and piscivorous mammals.

As detailed below, an empirical 35-day chronic study for early life stage of Three-spined Sticklebeak (*Gasterosteus aculeatus*) was selected for the derivation of the predicted no-effect concentration (PNEC) for water. When compared to empirical studies, the results from the QSAR toxicity models are in the same order of magnitude as empirical results. A soil exposure scenario was also developed to reflect potential concentrations of TCP in agricultural soil resulting from the possible application of biosolids originating from a wastewater treatment system receiving effluent from industrial activities. Soil concentrations and potential uptake rates and concentrations in a small mammal (i.e. shrew) were estimated using a fugacity-based model that involves equilibrium partitioning principles to estimate the overall fate of the substance in the soil and exposure to soil biota (BASL4 2011). An empirical study of a two-year oral feed study with male rats was used as critical toxicity value (CTV) for wildlife.

#### **9.1.1 Empirical Studies in Water**

A number of studies are available characterizing the toxicity of TCP to algae. One study on *Scenedesmus pannonicus* determined a chronic 96-hr EC<sub>50</sub> and no observed effect concentration (NOEC) for TCP for growth of 1.5 and 0.32 mg/L, respectively (UK EA 2009). Additional chronic, 72-hr toxicity data for TCP for the green alga *Pseudokirchneriella subcapitata* were available from NITE (2008) and ECHA (c2007-2013). The lowest NOEC for growth rate was 0.088 mg/L. Other NOECs from these

studies for growth rate, biomass and cell number were 4.7, >2.5, and 2.4 mg/L, respectively

Aquatic toxicity data for invertebrates are also available for TCP. A 48-hr unpublished acute study with *Daphnia magna* reported an EC<sub>50</sub> for mortality/immobility of 0.27 mg/L and a NOEC of 0.1 mg/L. Two other 48-hr EC<sub>50</sub>s (Adema et al. 1983; ECHA c2007-2013) were much higher (5.6 mg/L and 146 mg/L).

Two chronic toxicity studies on *Daphnia magna* were identified in the open literature (Adema et al. 1981, 1983). A 21-d EC<sub>50</sub> was reported to be between 0.1 and 0.3 mg/L (Adema et al. 1981) and a 21-d NOEC (mortality, reproduction) was determined to be 0.1 mg/L (Adema et al. 1983).

Van den Dikkenberg et al. reported embryo-larval studies on four fish species: Three-spined Stickleback (*Gasterosteus aculeatus*); Zebrafish (*Brachydanio rerio*); Medaka (*Oryzias latipes*); and Flagfish (*Jordanella floridae*). Among them, the NOEC and EC<sub>50</sub> (early life stage (after 4-week-old fish stage) mortality, sublethal effects excluding growth), and the LC<sub>50</sub>, for Three-spined Stickleback exposed for 35 days were 0.001 mg/L, 0.0013 mg/L and 0.0017 mg/L, respectively (Van den Dikkenberg et al. 1989). The NOECs for growth and sublethal effects on the embryonic stage were lower at 0.00032 mg/L and 0.0032 mg/L, respectively (Van den Dikkenberg et al. 1989).

The NOECs from a six-week embryo-larval study on Zebrafish, Medaka and Flagfish were greater (0.0056 mg/L, 0.01 mg/L and 0.01 mg/L, respectively) than those for Three-spined Stickleback (Adema et al. 1983). The NOEC from a four-week chronic study of guppies was significantly greater at 1 mg/L (Adema et al. 1983).

Results from the ECOSAR model (v.1.00) are available in Environment and Climate Change Canada (2015d). These are generally consistent with the empirical data and support the calculated PNEC used for the risk analysis (see below). Although the log K<sub>ow</sub> of TCP (5.11) is greater than the model's cut-off for acute toxicity estimation (~5), it is close, and thus, the ECOSAR predicted fish 96h-LC<sub>50</sub> and *Daphnia* LC<sub>50</sub> values (0.057 – 0.165 mg/L) are nevertheless considered but not used to estimate a PNEC for the risk analysis. Predictions for chronic toxicity, however, were below the model's cut-off (log K<sub>ow</sub> ~8). These results ranged from 0.005 mg/L to 0.04 mg/L.

The lowest EC<sub>50</sub> obtained from the more reliable studies is a 35-day EC<sub>50</sub> of 0.0013 mg/L for early life stage (after 4-week-old fish stage) mortality and sublethal effects of embryo-larval study with *Gasterosteus aculeatus* (Three-spined Stickleback) (Van den Dikkenberg et al. 1989). This value is selected as the critical toxicity value (CTV) for pelagic organisms. The selection of this CTV is considered reasonable in comparison with modelled results from ECOSAR (0.005 mg/L chronic lethal toxicity; Environment and Climate Change Canada 2015d).

Overall, there is high confidence in the dataset on aquatic toxicity with data on several

endpoints and organisms. To calculate the PNEC, an application factor of 3 is selected to account for differences in species sensitivity. Although there are a lot of data, the chronic toxicity data spans only two taxa: vertebrates and invertebrates. The resulting PNEC is thus 0.00043 mg/L.

### **9.1.2 Empirical Studies in Sediment**

There are no available data characterizing the toxicity of TCP to benthic organisms.

### **9.1.3 Empirical Studies for Soil Organisms and Terrestrial Wildlife**

One study is available using a commercial product (Durad 310M) with TCP present at <5% w/w. This study resulted in an LC<sub>50</sub> (seedling emergence) of >100 mg/kg. This study cannot be interpreted to characterize the toxicity of TCP to plants given the low purity of the test substance.

There are also a few studies characterizing the effects to insects from contact with TCP (WHO 1990). These data, however, are not relevant for the derivation of a PNEC for terrestrial organisms.

A PNEC for small soil-dwelling mammals is derived based on a review of mammalian toxicity. A thorough review of mammalian toxicity is presented in the human health component of this assessment; however, some of the key studies considered for the derivation of the toxicity reference value (TRV, considered equivalent to a PNEC) are summarized below.

Terrestrial toxicity data for TCP and related isomers are compiled and available in Environment and Climate Change Canada (2015d). Several sub-chronic repeated-dose toxicity studies for TCP (mixed isomers) are available. Data from the 13-week oral feed study conducted by NTP (1994) are selectively compiled in Environment and Climate Change Canada (2015d) to allow for comparison of sub-chronic and chronic data. Given the availability of chronic studies, sub-chronic data are not recommended as critical for the screening assessment of TCP.

A single repeated-dose chronic oral study was available. NTP (1994) conducted a 2-year feeding study, investigating repeated-dose toxicity of a commercial mixed-isomer preparation to rats and mice. Survival was the only ecologically-relevant endpoint measured in these studies. The lowest no observed adverse effect levels (NOAEL) for survival in rats and mice were 13 mg/kg/day and 27 mg/kg/day, respectively. These data are not recommended for use as critical endpoints for assessment of risk to wildlife since they represent the highest tested concentrations (i.e. lowest observed adverse effect levels (LOAEL) were not established) and may overestimate potential for effects on survival. In this two-year oral feed study, TCP was fed to male rats (F344/N) with an average body weight of 0.16 kg. NOAEL and LOAEL for all measured endpoints were reported to be at 13 mg/kg/day and 26 mg/kg/day, respectively.

UK EA (2009) reported data from a high-quality mouse reproductive toxicity study by Chapin et al. (1988). The study comprised a 14-day range-finding test, a 98-day continuous breeding phase of the parental generation and a cross-over mating to determine the effects on breeding (UK EA 2009). A LOAEL of 0.05% TCP in the feed (approximately equivalent to 35 mg/kg/day) for reproductive toxicity was established.

The reproductive toxicity endpoint (LOAEL of 0.05% TCP) for mice from NTP (1994) (cited in Chapin et al. 1988) was also recommended by US EPA (2010), although an equivalent dose of 62.5 mg/kg/day was calculated by the agency.

Toxicity tests for TCP have been performed using 95 female rats (F344/N; up to 15 females per group) in a two-year oral feed study (NTP 1994). For this study, dietary levels of 0, 75, 150, and 300 mg/kg TCP were estimated to deliver average daily doses of 0, 4, 7, or 15 mg/kg to females. Over this two-year study, the body weights of female rats started with a mean of 91 g (91, 91, 92, 90 g, respectively, for four different concentrations of TCP in feeds) in the first week of the study, and ended with a mean of 320 g (315, 320, 332, 313 g, respectively, for four different concentrations of TCP in feeds) in the 104<sup>th</sup> week of the study. Endpoints of NOAEL and LOAEL for cytoplasmic vacuolization of the adrenal cortex were reported at 4 mg/kg/day and 7 mg/kg/day, respectively. This study is selected for the derivation of the toxicity reference value (TRV). The CTV of 5.3 mg/kg-bw/day is therefore calculated using a geomean of the NOAEL and the LOAEL values.

The rat toxicity endpoints (NOAEL of 4 mg/kg/day and LOAEL of 7 mg/kg/day) from this study and a body weight of 10 grams, derived from BASL 4, were used as input to estimate TRV of TCP for shrew. An assessment factor of 10 was applied to account for extrapolation from laboratory to field conditions. The resulting TRV of TCP for shrew is 1.259 mg/kg-bw/day (Appendix B).

The same rat toxicity endpoints used to calculate the TRV for shrew were also used to calculate TRVs of TCP for mink and river otter. The body weights of 1.08 kg and 7.98 kg were used to derive their corresponding TRVs. An assessment factor of 10 was applied to account for extrapolation from laboratory to field conditions. The resulting predicted TRVs of TCP for mink and river otter are 0.390 mg/kg-bw/day and 0.237 mg/kg-w/day, respectively (Appendix B).

## **9.2 Ecological Exposure Assessment**

### **9.2.1 Industrial Release**

Limited data concerning concentrations of TCP in water in Canada have been identified. Therefore, environmental concentrations have been estimated from available information, including estimated substance quantities, estimated release rates, and characteristics of the receiving environment. Environmental concentrations have been estimated for industrial release scenarios, as described in the following sections.

### 9.2.1.1 Exposure Scenarios and Predicted Environmental Concentrations

#### Aquatic Exposure

Aquatic exposure to TCP is expected if the substance is released from industrial activities either to a wastewater system or directly to a receiving surface water body. The concentration of the substance in the receiving water near the discharge point of the wastewater system is used as the predicted environmental concentration (PEC) in evaluating the aquatic risk of the substance. It can be calculated using the equation:

$$C_{\text{water-ind}} = \frac{1000 \times Q \times L \times (1 - R)}{N \times F \times D}$$

Where:

$C_{\text{water-ind}}$ : aquatic concentration resulting from industrial releases, mg/L

Q: total substance quantity used annually at an industrial site, kg/yr

L: loss to wastewater, fraction

R: wastewater system removal rate, fraction

N: number of annual release days, d/yr

F: wastewater system effluent flow, m<sup>3</sup>/d

D: receiving water dilution factor, dimensionless

These parameters are described in detail in Environment and Climate Change Canada (2015e).

As TCP is used by industrial facilities and is expected to be released to water, conservative aquatic industrial release scenarios were developed to cover a range of different potential industrial activities in Canada. For TCP, the relevant scenario includes blending of the substance at industrial facilities. The blending scenario estimates releases of TCP which is blended into various applications.

As TCP is imported in bulk in a pure liquid form or part of a liquid mixture which may generate residues in transport containers, container cleaning operations may lead to environmental releases of these substances. Although environmental concentrations of TCP resulting from these releases may be high, these releases would likely be episodic in nature and probably of short duration. Given these considerations and the current data gaps associated with container cleaning operations and practices, a quantitative exposure characterization was not developed for these releases.

Table 9-1 presents the range of inputs used to estimate resulting aquatic concentrations close to the industrial points of discharge. Based on these assumptions, these industrial scenarios yield total PECs of  $7.3 \times 10^{-8}$  to  $2.7 \times 10^{-6}$  mg/L (Table 9-2). These aquatic PEC values represent the *total* TCP concentrations (dissolved and particle associated)

in the receiving water near the point of discharge at each site. It is noted that these calculated PECs are similar to water concentrations of  $2.5 \times 10^{-6}$  to  $2.2 \times 10^{-5}$  mg/L (11–22 ng/L and 2.5–10 ng/L) detected in Lake Ontario, the St. Lawrence River and Lake Erie in Canada in 2010 and 2011 studies.

**Table 9-1. Summary of input values used for scenarios estimating aquatic concentrations resulting from industrial releases of TCP**

Input	Value	Justification and Reference
Yearly quantity used at site (kg/yr)	<10 000	As reported in ECCC (2013-2014)
Loss to wastewater (%)	0.25 to 1.0	Standard assumption based on OECD (2009)
Wastewater system removal efficiency (%)	47 to 90	ASTreat 1.0 model prediction for off-site primary level treatment, secondary level treatment
Number of annual release days (days)	250 to 350	Based on NPRI data, site specific information or professional assumption (NPRI 2011 and Environment and Climate Change Canada internal database)
Wastewater system effluent flow (m <sup>3</sup> /d)	15 000 to 22 400 000	Site-specific data for wastewater treatment system
Dilution factor (–)	10	Site-specific wastewater treatment system flow rate/ receiving environment flow rate. When a dilution factor was greater than 10, a maximum default value of 10 was used.

**Table 9-2. Summary of Predicted Environmental Concentrations (PECs) in water, sediment, and soil, for TCP industrial release scenarios**

Use/Sector	PEC Water (mg/L)	PEC Sediment (4% OC) (mg/kg dw)	PEC Soil (2% OC) (mg/kg dw)
Blending	$7.27 \times 10^{-8}$ to $2.70 \times 10^{-6}$	0.00001 to 0.00036	0.00001 to 0.00030

To estimate the concentration of TCP in the bottom sediment, an equilibrium sediment-water partition approach was used. This approach is based on a partitioning principle described by the European Chemicals Agency (ECHA 2010) and incorporates two additional calculation methods. The first is to estimate the substance's concentration in



the aqueous phase (dissolved) of the overlying water from its total concentration, according to studies by Gobas et al. (2003) and Gobas (2010). The second is to estimate a substance's concentration in bottom sediment from its concentration in the aqueous phase of the overlying water based on an equilibrium partitioning assumption between bottom sediment and overlying water described by the US EPA's National Center for Environmental Assessment (US EPA 2003). At equilibrium, the PEC in bottom sediment can linearly correlate with the concentration in the aqueous phase of the overlying water. Sediment exposure scenarios were developed as an extension of the industrial aquatic release scenarios described above to determine equilibrium sediment PECs, standardized to 4% organic carbon (a typical organic carbon content in bottom sediment for rivers and lakes). The resulting sediment PEC value of TCP ranges from 0.00001 to 0.00036 mg/kg dw.

### **Soil Exposure:**

In the absence of suitable data, a soil exposure scenario was developed to reflect potential agricultural soil concentrations resulting from the possible application of biosolids originating from a wastewater treatment system receiving effluent from the manufacturing plant.

Soil concentrations and exposure to a small mammal (i.e. shrew or vole) were estimated using a fugacity-based model that involves equilibrium partitioning principles to estimate the overall fate of the substance (BASL4 2011). There is only one study available on the concentrations of TCP in biosolids (conducted in Denmark), but no studies conducted in Canada. Miljøstyrelsen 2002a (cited in UK EA 2009) reported a mean concentration of 0.613 mg/kg dw (613 µg/kg dw) detected in wastewater sludge samples collected in Denmark. The maximum biosolids concentration for TCP in Canada based on an estimate from a wastewater treatment plant was 0.44 mg/kg. Given the small difference between these two concentrations and the concentration of 0.44 mg/kg estimated in Canada, the biosolids concentration of 0.44 mg/kg was input to the BASL4 model as the worst case scenario.

The estimated total daily intake (TDI) of TCP to shrew via soil food chain pathway (standardized to 2% OC) at 0.045 mg/kg-bw/day is therefore selected as the TDI value, the estimated mammal uptake exposure rate. This value is considered conservative because the BASL4 model does not consider metabolism in its estimate.

### **Wildlife Exposure:**

A wildlife TDI was derived for Mink (*Mustela vison*) and River Otter (*Lontra canadensis*) consuming fish following the approach of the US EPA (1993). In calculating TDI, the BAF of 2043 (log BAF 3.31) (see Section 9.1.4 Empirical Studies for the Terrestrial Compartment (Wildlife)) was used in conjunction with the maximum water PEC value of 0.0000027 mg/L resulting in estimated TDIs of 0.0010 and 0.0008 mg/kg-bw/day for the Mink and River Otter, respectively.

### **9.2.2 Consumer or Commercial Release**

Although TCP can be found in consumer or commercial products, it is expected that these releases will be minimal. Additive use of TCP in products suggests diffuse emissions may occur from consumer or commercial products, and although there are uncertainties, the rate is also expected to be very low in comparison to industrial point sources during incorporation of the substance into products. Emissions from industrial scenarios presented in this assessment would result in much higher environmental concentrations. Given that products made with TCP will generally not be in contact with water on a regular basis, leaching to water is likely to be minimal.

In the absence of information on the leaching of TCP from products, the UK EA (2009) estimated a potential of release of 0.25% over the lifetime of the TCP product if the product is for indoor use and 7.25% if it is for outside use. The potential release of OFRs from plastics during their service life is estimated at 0.05% to water if the substance is for indoor use or 0.16% over lifetime for outdoor use (OECD 2009). The large majority of products would be enclosed or used indoors; therefore, the release rate of 0.05% is most applicable and may likely be an overestimate since contact with water is not expected.

Therefore, the extreme worst-case scenario for the diffuse release of EBTBP throughout Canada (via WWTP and disperse release directly to the environment), using the indoor release rate of 0.05% over service life information from OECD 2009, was estimated at 10.5 kg. This scenario includes a number of assumptions: the maximum values from each range of import (1 000 kg for consumer or commercial products; 10 000 kg for formulation; and 10 000 kg for neat substances); complete use of TCP in products; low exposure to water over the service lifetime and indoor use. This result suggests that significant release of TCP products is unlikely. The scenario result is considered to be highly uncertain.

Assessments of TCP in household dust and in dust from other microenvironments in Canada and abroad are discussed in the section on Exposure Assessment for Human Health of this assessment (10.1.1 Environmental Media and Food). TCP exposure from consumer products is described in the section on Exposure Assessment for Human Health of this assessment (10.1.2 Consumer Products).

## **9.3 Characterization of Ecological Risk**

The approach taken in this ecological screening assessment was to examine various sources of information and develop conclusions based on a weight-of-evidence approach (Appendix C) and using precaution as required under CEPA. Lines of evidence considered include results from a conservative risk quotient calculation, as well as information on persistence, bioaccumulation, inherent or ecological toxicity, sources and fate of the substance and presence and distribution in the environment.

### 9.3.1 Risk Quotient Analysis

Risk quotient analysis was performed for aquatic, soil and wildlife scenarios (Table 9-3; Appendix B) to determine whether there is potential risk of harm in the vicinity resulting from industrial releases in Canada.

#### Water

The site-specific industrial release scenarios presented above yielded aquatic PEC of  $7.27 \times 10^{-8}$  to  $2.70 \times 10^{-6}$  mg/L. These PEC values represent the level of exposure in the receiving water near the point of the discharge of the wastewater treatment system at each site. A PNEC of 0.00043 mg/L was derived from the 35-day  $EC_{50}$  of 0.0013 mg/L (early life stage mortality) for *Gasterosteus aculeatus* (Three-spined Stickleback) (van den Dikkenberg et al. 1989) (see 9.1.1 Empirical studies in Water under the Ecological Effects Assessment section). The resulting risk quotients (PEC/PNEC) range from 0.0002 to 0.006 (Appendix B). Therefore, harm to pelagic organisms is unlikely at these sites.

#### Soil

BASL4 was employed to estimate exposure (TDI) to shrew via the soil food chain pathway. A value of 0.045 mg/kg-bw/day is selected as the TDI value, the estimated mammalian uptake rate. This is compared with a TRV of 1.259 mg/kg-bw/day (see Section 9.1.3) resulting in a risk quotient of 0.036 TCP, which is not expected to have food chain effects so there is little concern for harm to soil organisms.

#### Wildlife

TDIs for wildlife piscivores were estimated following the approach of US EPA (1993). In calculating TDI, the BAF of 2043 (see Section 8.3.2) was used in conjunction with the maximum water PEC value of 0.0000027 mg/L resulting in estimated TDIs of 0.0010 and 0.0008 mg/kg-bw/day for the Mink and River Otter, respectively. The derived TRVs for Mink and River Otter calculated in Section 9.1.3 are 0.390 and 0.237 mg/kg-bw/day, respectively. The resulting risk quotients (TDI/TRV) are 0.0026 (mink) and 0.0032 (river otter) (Appendix B). Therefore even with conservative assumptions, current use of TCP in Canada is unlikely to exceed minimum effects levels for Mink and River Otter.

**Table 9-3. Risk quotients obtained for different media and exposure scenarios for TCP**

Media	Scenario	PNEC/TRV	PEC/TDI	RQ
Water	Industrial release to water	0.00043 mg/L	$7.27 \times 10^{-8}$ to $2.70 \times 10^{-6}$ mg/L	0.0002 to 0.006
Soil	Biosolids application to soil	1.259 mg/kg-	0.045 mg/kg-bw/day	0.036

Media	Scenario	PNEC/TRV	PEC/TDI	RQ
		bw/day (TRV)	(TDI)	
Wildlife	Piscivore TDI (mink/fish)	0.39 (mink) and 0.237 (otter) mg/kg- bw /day	0.0010 (mink) and 0.0008 (otter) mg/kg- bw /day	0.0026 (mink) 0.0032 (otter)

### 9.3.2 Consideration of Lines of Evidence and Conclusion

The low import volumes of TCP into Canada along with information on its uses indicate low potential for widespread release into the Canadian environment. TCP has been detected at low levels in samples of air, water, sediment, soil and biota found near sources. Therefore, the main concern for TCP is for near-field exposure.

The empirical log  $K_{ow}$  value of 5.11, the fast rate of metabolic biotransformation ( $k_M$ ) and the low to moderate BCF and BAF for TCP suggest a limited potential to bioaccumulate or biomagnify in biota. Weak sorption to solids as indicated by a relatively low log  $K_{oc}$  and the moderate water solubility (0.36 mg/L) suggests a limited potential for bound residues in the environment increasing the bioavailable fraction of TCP in water. TCP is expected to have low potential for persistence in air, water, sediment and soil and is not likely to present long-term exposures in these media (Section 8.2 Environmental Persistence). TCP is not expected to have long-range transport potential in the air and is unlikely to be deposited to the earth's surface in significant quantities in remote regions.

The site-specific industrial scenarios provided a level of exposure in the receiving water near the point of discharge of the wastewater treatment system at each site. The risk quotients showed that harm to pelagic organisms is unlikely at these sites. The importance of releases from products is an area of uncertainty due to the absence of data to inform accurate quantitation of environmental exposure due to the leaching of additive flame retardants from manufactured items; however, it is expected that releases to the environment via this route are minimal and diffuse.

TCP has a predicted short residence time in soil so the chemical is not expected to build up over time. Therefore, at potential current levels of use and based on low persistence and limited bioconcentration and bioaccumulation, TCP is not expected to have food chain effects and is not expected to result in harm to small soil-dwelling mammals. Even with conservative assumptions, current use of TCP in Canada is also unlikely to involve risk of harm to wildlife-consuming fish.

Considering all lines of evidence presented in this screening assessment, TCP does not have the potential to cause ecological harm in Canada.

## **9.4 Uncertainties in Evaluation of Ecological Risk**

The assessment recognizes that there is limited information characterizing potential releases from consumer or commercial products in use and during dismantling or disposal at the end of their service life. No Canadian TCP landfill leachate data have been reported to date, but such data could help interpret end-of-life releases. However, based on available information on low vapour pressure for TCP, releases are considered minimal. Environmental release of the substance from plastic polymers via leaching is considered possible, albeit low. Furthermore, many products identified with TCP will not be in contact with water on a regular basis, e.g. electronics. In this assessment, the low estimated extreme worst-case scenario for TCP release suggests that products of TCP are not likely to be a significant path of release. Based on available information, it is assumed that major TCP pathways of release from products in service are covered under the current industrial release scenarios. Generally, there is moderate confidence in the TCP exposure scenarios.

Finally, this assessment recognizes that there are information gaps on the toxicity of TCP to sediment and soil. However, TCP is not used in high quantities in Canada, and releases are likely low. Moreover, based on the analysis in this assessment, most exposure would be to pelagic organisms and, thus, the risk assessment for water is assumed to be more relevant than potential risks for sediment-dwelling organisms. In addition, TCP is expected to have low potential for persistence in air, water, sediment and soil and is not likely to present long-term exposures to organisms via these media (Section 8.2 Environmental Persistence).

## **10. Potential to Cause Harm to Human Health**

### **10.1 Exposure Assessment**

#### **10.1.1 Environmental Media and Food**

TCP has been monitored in various environmental compartments in Canada and elsewhere (see Section 7). When released to air, TCP is expected to degrade rapidly ( $t_{1/2} \leq 1$  day) or to partition to the particulate phase in air. Due to its low to moderate water solubility, when released to surface water, the majority of TCP is expected to stay in water and a small fraction is expected to adsorb to suspended solids and eventually sink to sediment. Volatilization from surface water to air is very low. When TCP is released to soil as a result of applying biosolids to agricultural lands, the mass fraction is expected to become adsorbed to soil (~100%) due to its hydrophobic nature. TCP is also expected to be stable in soil and resistant to degradation, and thus the loss process in soil will also mainly be driven by soil burial or surface runoff.

Upper-bounding estimates of daily intake of TCP from environmental media for the general population of Canada are presented in Appendix D. For most age groups, the main contribution to the estimated daily intake was from the ingestion of dust, followed by food. Exposure intakes from air and water were very low and considered negligible. The highest estimate of daily intake was derived for breastfed infants (0-6 months), with

an estimated intake of 0.10 ug/kg-bw/d, predominantly from dust and breast milk.

#### 10.1.1.1 Ambient Air

TCP concentrations in ambient air in Canada were not identified (see Section 7.1). TCP was monitored in outdoor air samples collected in the U.S. in the late 1970s at a TCP production site in West Virginia, where concentrations ranged from 0.01 to 2 ng/m<sup>3</sup> (Boethling and Cooper 1985; MRI 1979). In a recent study out of Finland, TCP was not detected (0.0007 ng/m<sup>3</sup>, a semi-quantitative value based on another organophosphate flame retardant) in a sample of air collected in July 2004 from a rural area in Northern Finland (Marklund et al. 2005). TCP was previously monitored in Japanese outdoor air studies, with TCP being detected in a limited number of samples (3 out of 19) collected in 1974 up to 70.3 ng/m<sup>3</sup> from heavily-industrialized cities (IPCS 1990). TCP may be present in industrialized cities due to vehicular exhaust. *o*-TCP and *m*-TCP were found in exhaust gases from motor bikes and cars, where ratios were approximately the same for both isomers in exhaust from motor bikes (0.15-0.30 µg/m<sup>3</sup>) and the proportion (*o*-TCP/*m*-TCP) was the same before and after combustion. The levels were somewhat lower in exhaust from cars (0.14 µg/m<sup>3</sup>) (Takimoto et al. 1999). Two more recent studies, however, reported lower concentrations of TCP, ranging from non-detected to 21.4 ng/m<sup>3</sup> (Takimoto et al. 1999; Kishi and Sekine 2003).

#### 10.1.1.2 Indoor Air

TCP concentrations in indoor air in Canada or the U.S. were not identified. TCP has been monitored in several indoor environments in Europe and China (Appendix E, Table E-1).

In studies in Europe, TCP has not been widely detected in indoor environments. In a recent study on 63 daycare centers in Germany, TCP was not detected in indoor air and dust although LODs were not specified (Fromme et al. 2014). In a study by Tollbäck et al. (2006), air samples were collected in a kindergarten and a lecture room in Sweden. The concentration of TCP detected in the lecture room was 0.4 ng/m<sup>3</sup>, but TCP was not detected in the kindergarten classrooms. Cequier et al. (2014) investigated the occurrence of TCP in Norwegian households (n=48) and classrooms from two primary schools (n=6). TCP was not detected in classrooms and median concentrations of TCP in residential samples were below the mdl (ranging from 18 to 44 pg/m<sup>3</sup> for organophosphate flame retardants), with a maximum of 0.644 ng/m<sup>3</sup>. TCP (reported as tritoly phosphate) was not detected above the detection limit (1 ng/m<sup>3</sup>) in any of the samples collected in Swedish households (n=50) and non-residential environments (e.g. bakery, carpet store, garages) (n=55) (year unspecified) (Staaf and Östman 2005). In a separate study, *o*-TCP was not measured above the limit of quantitation (4.1 ng/m<sup>3</sup>) in any samples (n=12) collected in various non-residential environments (e.g. electronics and furniture stores) in Zurich, Switzerland (Hartmann et al. 2004). However, in this same study, *o*-TCP was detected above the detection limit of 0.41 ng/m<sup>3</sup> in the sample collected from a theatre (2.1 ng/m<sup>3</sup>) (year unspecified) (Hartmann et al. 2004).

A recent study reported particle size-specific concentrations of TCP (reported as TCrP) ranging in total from 0.03 to 0.2 ng/m<sup>3</sup> in Chinese offices equipped with common office furniture and electronic products, away from industrial and high traffic zones (Yang et al. 2014). TCP concentrations peaked in the 0.7 to 1.1-µm particle size fraction, i.e. the ultrafine particle fraction ( $\leq 1$  µm) (Yang et al. 2014).

Time spent in automobiles may also represent potential sources of exposure to TCP. TCP levels in vehicle air have been monitored in a few studies in the international literature. In Germany, a study of the emission of organophosphate esters to automobile interior air determined that TCP was not detected above the detection limit range of 10 to <50 ng/m<sup>3</sup> in eight new vehicles, whether at room temperature or heated at 65°C (Wensing et al. 2005). TCP was not detected in any of the air samples collected from three cars in Zurich, Switzerland, including a new car, a one-year-old car and a nine-year-old car (Hartmann et al. 2004). TCP was not detected in air samples (n=5 for each vehicle) collected in a car (near the driver's breathing zone), two buses and a subway car in Sweden, nor was it detected in any of the samples that were simultaneously collected from outside the vehicles in the parking garages (Staaf and Östman 2005).

Time spent in aircraft may also represent potential sources of exposure to TCP. Several studies have also investigated potential exposure in aircraft cabins due to the use of TCP in engine turbine oils and hydraulic fluids in the hydraulic system of aircrafts. van Netten (2008) reported that TCP was detected in cabin air during flight based on personal air monitoring. Two air samples were taken during two separate flights. The airline, country of departure or arrival, and sampling year were not specified. TCP concentrations adjusted for the sampler's efficiency were found to be 108 ng/m<sup>3</sup> and 36 ng/m<sup>3</sup> for flights A and B, respectively. The authors noted that for flight A, the auxiliary power unit (APU) was used which was later associated with a failing oil seal (van Netten 2008). Another study showed that TCP, which was present in all turbine/engine oils in use in the aircraft included in this study, was determined in four out of 95 samples (4.2%) (Solbu et al. 2011). TCP concentrations in samples ranged from LOQ–0.29 µg/m<sup>3</sup>. TCP was however detected in 39% of the wipe samples (n=56; representing longer-term sampling) and in all HEPA-filters (n=6; spot samples), although for the latter no *o*-TCP was detected. TCP concentrations in cockpit air were below 4 µg/m<sup>3</sup> with two exceptions (22 and 49 µg/m<sup>3</sup>). Ground engine starts at high power gave rise to the highest concentrations. All samples were collected under normal flight conditions. However, the TCP concentration during ground testing in an airplane that had experienced leakage of turbine oil with subsequent contamination of the cabin and cockpit air was an order of magnitude higher as compared to after engine replacement.

Daily intake estimates of exposure to TCP from air (both indoor and outdoor over a 24-hour period) for the general population of Canada were based on a limit of detection of 1 ng/m<sup>3</sup> from the most extensive and recent air study including homes (n=55) in Sweden (Staaf and Östman 2005). While TCP outdoor air studies were identified, these were not considered as robust for characterizing exposure. While TCP has not been monitored in North America, other organophosphate flame retardants have been

measured recently, e.g. in Canada, in concentrations up to 2.2 ng/m<sup>3</sup> (Shoeib et al. 2014) and in American urban and rural cities along the Great Lakes in concentrations up to 0.85 ng/m<sup>3</sup> (Salamova et al. 2013). As such, the selected value of 1 ng/m<sup>3</sup> is considered appropriate for estimating indoor and outdoor air exposures. As for other indoor environments, these air levels are considered to take into account the variability in environmental concentrations associated with different settings (e.g. daycare, office, gym, vehicles, aircraft). Furthermore, these potential sources of exposure are expected to be lower than those conservatively estimated for homes based on lower frequency and duration of exposure and, for vehicles, the absence of detectable levels of TCP in the available studies.

#### **10.1.1.3 Dust**

TCP has been monitored in household dust as well as in dust from other environments in Canada and elsewhere (Appendix E, Table E-2.1 and Table E-2.2).

TCP (reported as TCrP) was included in the Canadian baseline study of organophosphate flame retardants in archived house dust samples (n=818) collected in 2007–2008 from various Canadian cities within the Canadian House Dust Study (CHDS) (CHDS preliminary data; Kubwabo et al., manuscripts in preparation, Environmental Health Science and Research Bureau, Health Canada; unreferenced, dated December 13, 2013). The CHDS dust sampling technique was considered adequate for determining representative organophosphate flame retardant concentrations based on a comparison of dust sampling techniques (Fan et al. 2014). TCP was detected in 99.9% of the baseline study samples, and concentrations ranged from not detected (detection limit = 30 ng/g) to 295 000 ng/g. The median and 95<sup>th</sup> percentile found were 4 860 and 17 700 ng/g, respectively. The maximum concentration of TCP was the highest among all organophosphate flame retardants measured in this study.

A U.S. monitoring study of household dust carried out in California in 2011 and earlier, in 2006, showed relatively lower concentrations (Dodson et al. 2012). TCP median concentrations in samples collected from the living area surfaces of 16 homes in 2011 and 2006 were found to be 680 and 1000 ng/g, respectively, with concentrations ranging from 180 to 10 000 ng/g and 330 to 4 400 ng/g, respectively (Dodson et al. 2012). TCP concentrations reported in house dust studies in Europe and elsewhere were generally lower than those measured in the Canadian baseline study (Kersten and Reich 2003; Brommer et al. 2012; Dirtu et al. 2012; Van den Eede et al. 2011). A recent study in the Netherlands investigated electronic equipment (electronics) as a source of TCP (reported as tris(methylphenyl) phosphate or TMPP) in house dust. TCP levels in house dust on electronics (median of 330 ng/g) were significantly higher than those collected around electronics (110 ng/g) (Brandsma et al. 2014). The findings of higher TCP concentrations in dust on electronics is consistent with the results of Kajiwara et al. (2011) who observed TCP to be a major organophosphate flame retardant detected in electronic equipment (LCD televisions) from the Japanese market in 2008. In New



Zealand, dust was collected from carpets and floors, as well as mattresses in rural and urban locations during 2008 (Ali et al. 2012). In carpet and floor dust, the median concentration (120 ng/g; n=34) was lower than that found in mattress dust (157 ng/g; n=16).

In a recent study in Germany, organophosphate substances were measured in paired indoor air and dust samples from 63 daycare centers (Fromme et al. 2014). TCP was not detected in indoor air and dust from the daycares although LODs were not specified (Fromme et al. 2014). In a separate study, dust samples (n=15) from a variety of retail outlets in Belgium, including an electronics store, a mattress store, pharmacies, a thrift shop and a furniture store, were collected in 2008 and analyzed for multiple flame retardants, including TCP (Van den Eede et al. 2011). TCP concentrations ranged from not detected (LOD =0.04) to 12.5 ng/g with a mean of 1.53 ng/g (Van den Eede et al. 2011)

TCP has been measured in dust from 12 automobile interiors in Germany by Brommer et al. (2012). Samples were collected between December 2010 and January 2011 using the vacuum cleaner typically used by the owner to clean the vehicle. TCP concentrations were much greater than those measured in household dust from the same study as concentrations ranged from not detected (detection limit = 40 ng/ng) to 150 000 ng/g with a mean of 24 000 ng/g (Brommer et al. 2012). Brandsma et al. (2014) recently reported TCP (reported as TMPP) concentrations in cars from the Netherlands. Eight cars were included in the study: two older cars (2003 and 2004) and four others manufactured between 2008 and 2012. Dashboard samples (n=8) and seat samples (n=8) showed TCP median concentrations of 750 ng/g (47 [detection limit] to 9500 ng/g) and 1400 ng/g (250-380 000 ng/g), respectively. The high concentration (particularly the maximum in the seat samples) is consistent with the use of TCP as a plasticizer in automobiles. The TCP levels in car seat dust were also significantly higher than those measured in house dust collected from electronics in the same study (Brandsma et al. 2014).

Daily intake estimates of TCP exposure related to the ingestion of dust for the general population of Canada were based on the 95<sup>th</sup> percentile concentration of 17 700 ng/g from the Canadian House Dust Study (preliminary baseline data from the Canadian House Dust Study (personal communication from Environmental Health Science and Research Bureau, Health Canada, dated December 13, 2013). Evidence based on a limited number of studies in Europe indicate that time spent in a car may represent a source of exposure to TCP in dust; however the exposures derived from the house dust study in Canada were considered appropriately conservative for estimating exposure from dust for the general population in Canada.

#### **10.1.1.4 Soil and Sediment**

No monitoring data on TCP in soil or sediment in Canada were identified (see Sections 7.3 and 7.4). Available soil and sediment data in the U.S. (e.g. Boethling and Cooper

1985; David and Seiber 1999b; Hoke 1993) are older and are not deemed appropriate or relevant for deriving conservative present-day exposure intakes for the general population. A maximum TCP soil PEC of 300 ng/g dw (0.0003 mg/kg dw) was estimated for land application of biosolids on an agricultural field using conservative approaches, as detailed further in the Ecological Exposure Assessment section (see Section 9.2.1.1).

In Europe, TCP in sediments from freshwater sources were measured at concentrations ranging from non-detect to 390 µg/kg in Denmark, Norway, Austria and Germany (Ricking et al. 2003; Martinez-Carballo et al. 2007; UK EA 2009; Van der Veen and de Boer 2012), with the most recent freshwater sediment monitoring (i.e. for 2005) associated with concentrations ranging from 1.5 to 39 ng/g dw (reported as <MQL - 39 ng/g dw) (Martinez-Carballo et al. 2007). Concentrations in marine sediment ranged from non-detect to 370 µg/kg in Denmark (UK EA 2009).

As no appropriate or relevant monitoring studies on TCP in soil were identified, the soil maximum PEC (87.3 ng/g) was selected for deriving intake estimates from the ingestion of soil for the general population in Canada.

#### **10.1.1.5 Drinking Water**

Several studies have monitored TCP in drinking water in Canada (Appendix E, Table E-3). Individual TCP isomers were targeted in the City of Toronto municipal drinking water monitoring program from 2000-2003 and none were found to be present above the detection limit of 60 ng/L (e.g. City of Toronto 2003a, b,c).

TCP has also been monitored in several older studies of drinking water monitoring in Canada, where TCP was not detected in the majority of drinking water samples collected in various municipalities (approximately 35) in Canada during the late 1970s where TCP was detected up to 4.3 ng/L (Lebel et al. 1981; Williams and Lebel 1981). TCP was detected in the drinking water of 5 of 12 Canadian Great Lakes municipalities (Thunder Bay, Owen Sound, Union-Leamington, St Catherines and Toronto) at concentrations of 0.6-1.8 ng/L during a 1980 monitoring study (Williams et al. 1982).

TCP has also been monitored in surface waters (see Section 7.2). In Canada, TCP was not detected in the open waters of the Great Lakes, but was measured in Lake Ontario and Lake Erie tributaries in 2010-11 at concentrations ranging from 2.5 to 22 ng/L (Lee et al. 2011). In recent surface water monitoring in Europe, TCP was not detected in three independent studies conducted in rivers in Denmark, Rome and Austria (Bacaloni et al. 2007; Martinez-Carballo et al. 2007; UK EA 2009).

Upper bounding daily intakes of TCP from drinking water exposure for the general population of Canada were derived using the 60 ng/L detection limit from the City of Toronto drinking water monitoring program for the years spanning from 2000 to 2003 (e.g. City of Toronto 2003a, b,c).

#### **10.1.1.6 Food**

No studies were identified that reported TCP in marketed foods in Canada; however, TCP was previously screened in the U.S. Food and Drug Administration (U.S. FDA) Total Diet Study (Appendix E, Table E-4). The Total Diet Study is an ongoing program conducted by the U.S. FDA to analyze contaminants in 357 different food types (ranging from dairy products to baby food) purchased throughout the U.S. (US FDA 2014). Market basket study results made available on the U.S. FDA website (US FDA 2014) showed that TCP was detected in one out of 44 samples of cracked wheat bread at a concentration of 90 ng/g (0.09 ppm) (resulting in a mean of 2.05 ng/g) in a market basket collected in 2003 (US FDA 2006). However, TCP was not detected in any other foods in all market baskets conducted from 1991 through to 2003, representing approximately 15 000 food items (US FDA 2006). As such, the detection of TCP in a single sample was considered to be an unrepresentative result, and therefore this data point was not included in the exposure assessment.

TCP has also been monitored in biota from the U.S., Europe, and Japan (Appendix E, Table E-5). TCP was monitored in the U.S. in several older studies of fish near industrial facilities (Lombardo and Egry 1979; Muir 1984); however these data are not considered appropriate to characterize present day exposure. TCP was monitored in a wide range of freshwater and marine fish and shellfish collected in 2005 or 2007 across Sweden with a reported range of 1.8 to 110 ng/g lw (or maximum of 1.32 ng/g ww; Sundkvist et al. 2010). The maximum TCP value corresponded to a sample collected in a stream receiving water from an international airport in Marstaän, a suburb of Stockholm, which may explain the higher concentration measured (Sundkvist et al. 2010). This same sample was the only sample observed to have detectable levels of o-TCP of 2.5 ng/g lw. In environmental monitoring by the Ministry of Environment in Japan ([MOE Japan] 2003), TCP was not detected in archived fish collected from various locations in 1975 (n=96) and 1978 (n=93); however, TCP was detected in more recent samples collected in 1993 (n=75), and ranged from 63 to 82 ng/g lw.

Based on the available information, daily intake estimates of TCP from fish consumption for the general population of Canada were estimated using the maximum concentration (1.32 ng/g ww) of shellfish measured in Europe (Sundkvist et al. 2010). In the absence of recent North American monitoring, this concentration is considered appropriate for deriving chronic upper bound intakes for the general population of Canada. Also, the assumption that TCP is present at this concentration in the entire fish food group (i.e. in fish, shellfish and related food items) consumed by the general population is considered conservative. Although certain northern populations in Canada may, seasonally, consume larger quantities of seafood in their diet, this estimate is considered adequately conservative to account for this variability.

#### **10.1.1.7 Breast Milk**

No studies were identified that reported TCP monitoring in breast milk in Canada;

however, two international studies were identified. Sundkvist et al. (2010) reported TCP breast milk concentrations for samples originating from women in four Swedish towns between 1997 and 2007 (Appendix E, Table E-6). Milk samples were collected from mothers two to three weeks after the delivery of their first baby. Most of the samples per cohort (from a single town for a given year) were pooled, and a single value was reported. TCP concentrations ranged from not detected (detection limit = 0.1 ng/g lipid weight) in 2006 (50 pooled samples) to 3.7 ng/g lipid weight in 1997 (69 pooled samples), both from Uppsala (Sundkvist et al. 2010). The authors noted a similar trend (i.e. higher concentrations in older samples) for another organophosphate flame retardant, and noted the possibility that older samples may have been contaminated, for example, by the sampling equipment such as breast pumps.

TCP (reported as TMPP) was measured in human breast milk collected from Japan (n=20) in 2009–2011, the Philippines (n=41) in 2008, and Vietnam (n=26) in 2008 (Kim et al. 2014). While the overall study detection frequency was 59% (detection limit not specified), TCP was not detected in samples from Japan. The median concentrations in the Philippines (2.3 ng/g lw; range of ND to 11 ng/g lw) were higher than those measured in Vietnam (0.28 ng/g lw, range from ND to 7.9 ng/g lw), which was the same trend observed for total organophosphorus concentrations. The maximum concentrations in Vietnam and the Philippines were associated with samples collected from mothers residing near urban areas and e-waste recycling sites, respectively.

Daily intake estimates for TCP for nursing infants in the general population of Canada were estimated based on the concentration of 3.7 ng/g lipid weight (resulting in a concentration of 0.126 ng/g ww based on the reported lipid content of 3.4%) from the Swedish study (Sundkvist et al. 2010).

### 10.1.2 Consumer Products

TCP is an additive flame retardant with a variety of uses and applications (see Section **Erreur ! Source du renvoi introuvable.**) which may result in general population exposure. Dermal exposure estimates were derived using conservative approaches for scenarios deemed relevant for the general population. TCP is characterized by very low volatility based on its low vapour pressure and low Henry's Law constant (see section 3). As such, releases to air from consumer products are expected to be accounted for through indoor air and dust exposure estimates (see Sections 9.1.1.1 and 9.1.1.3).

#### 10.1.2.1 Manufactured Items

Flame retardants can be found in coatings applied to the inside face of the cover fabric as "backcoating". The use of TCP as backcoating in furniture upholstery has not been reported in Canada, but has been documented in the U.S. Therefore, it is considered reasonable to assume that the general population of Canada can be exposed to TCP in furniture. According to a 2000 report by the U.S. National Research Council (NRC 2000), TCP was applied as a backcoating to furniture upholstery (Piccirillo 1999; NRC

2000). In a U.S. survey conducted by the Fire Retardant Chemicals Association prior to 1998, “aromatic phosphate esters” (such as TCP) were reported to be used in residential furniture based on information from U.S. flame retardant industries with marketing activities with the textiles industry (cited in U.S. CPSC 1998). The Upholstered Furniture Action Council (UFAC), a voluntary coalition of furniture manufacturers, outlined the potential for dermal exposure to backcoating, either via direct contact with the substance from contamination of the outside surface of the fabric (from wet backcoating when textile is rolled up post-production), or from migration and degradation of the backcoating through the textile weave (cited in U.S. CPSC 1998).

Other more recent reports also document furniture-related uses of TCP including its use as a plasticizer in synthetic leather upholstery in Europe (European Commission 2011), and in PVC seat covers (SinoHarvest 2011). Also, according to manufacturer literature, TCP is marketed for flexible foam for furniture (ICL 2013c). In preliminary product testing conducted by Health Canada of children’s manufactured items purchased in retail stores in Ottawa, Ontario, in January and May 2014, TCP was detected in a foam chair above the limit of detection of quantitation at a concentration reported as  $\geq 0.7\%$ ; however, TCP was not detected in the remaining 23 children’s manufactured items (e.g. nursing pillows, toys) (Health Canada 2014a) (Appendix F).

Based on the available information, dermal exposure intakes were estimated for toddlers and adults in direct contact with adult furniture (with treated upholstery backcoating or foam) as a sentinel scenario (Table 10-1). No TCP-specific migration data were identified. As such, a range of migration values for other organophosphate flame retardants were used to account for the migration from both treated upholstery and foam, and the general variability in migration rates. These values were also considered conservative owing to their higher water solubility relative to TCP. Migration rates ranged from  $2.17 \times 10^{-4}$  mg/cm<sup>2</sup>/h for tris(2-chloroethyl) phosphate (TCEP) to  $5.6 \times 10^{-5}$  mg/cm<sup>2</sup>/hr for tris(1,3-dichloroisopropyl)phosphate (TDCPP). The TCEP migration was based on textile backcoating described in the TCEP European Risk Assessment Report (EU RAR 2009), while the rate for TDCPP was based on treated upholstered foam as described by the U.S. Consumer Product Safety Commission (US CPSC 2005). No TCP-specific skin contact factor was identified in the literature; therefore, a skin contact factor of 0.13 based on the average of several substances was applied to account for the dermal adherence of TCP from the surface of the manufactured item (CPSC 2006). Estimates of dermal exposure from contact with adult furniture ranged from  $1.7 \times 10^{-4}$  to  $6.5 \times 10^{-4}$  mg/kg-bw/d for toddlers, and from  $8.6 \times 10^{-4}$  to  $3.3 \times 10^{-3}$  mg/kg-bw/d for adults, where ranges reflect the different migration rates. These estimates were derived using conservative assumptions as described in Appendix F.

Other jurisdictions have conducted furniture-related assessments of TCP (NRC 2000; European Commission 2011); however the approaches used varied substantially, as did intakes and route-specific conclusions due to differences in parameters considered, default values, conservatism, etc. The assessment report on flame retardants in consumer products published by the European Commission included several

recommendations for refining scenarios (European Commission 2011), most of which were considered in this current assessment.

**Table 10-1. Intake estimates from dermal contact with furniture**

Exposure Route	Source	Product	Age Group	Intake
Dermal	Upholstery backcoating or foam	Furniture	Toddler (15.5 kg)	$1.7 \times 10^{-4}$ to $6.5 \times 10^{-4}$ mg/kg-bw/d
Dermal	Upholstery backcoating or foam	Furniture	Adult (70.9 kg)	$8.6 \times 10^{-4}$ to $3.3 \times 10^{-3}$ mg/kg-bw/d

Other uses of TCP in manufactured items in Canada include automobile parts, such as the trunk and headliner (ECCC 2013-2014). TCP has been associated to dust in the interior of vehicles (Brommer et al. 2012; Brandsma et al. 2014; see section 10.1.1.3). As such, it is reasonable to assume that the general population of Canada can be exposed to TCP in the interior of vehicles. TCP uses in other manufactured items found in the international literature include home furnishings, electronics and other utility articles (i.e. footwear, raincoats, imitation leather and handbags) (Kajiwara et al. 2011; SinoHarvest 2011; Siret-Alatrissa et al. 2010; IPCS 1990; Ash and Ash 2003) (Appendix F). While exposure to TCP can occur via these manufactured items, the overall exposure potential (frequency, duration and magnitude) for these scenarios are not expected to result in higher exposures than those quantitatively presented for the furniture scenario.

#### 10.1.2.2 Products

TCP-containing products available to the general population in the area of hydraulic fluids, oils and lubricants may include automatic transmission fluid and automotive and motorcycle engine oils (Chemtura 2007; Takimoto et al. 1999; Solbu et al. 2011; ATSDR 1997; WHO 1990). The concentrations of TCP in various oil-based products is provided in Appendix G. Based on the Canadian industry survey, one consumer product was identified for the general population with plausible direct contact, i.e. power steering fluid (ECCC 2013-2014). The dermal route was considered to be the only route of exposure due to the low vapour pressure of TCP. Using a thin film approach (Westat 1987), the highest short-term dermal exposure (tips of the fingers) to TCP from the use of power steering fluid was estimated to be 2.4 ug/kg-bw (Appendix G).

#### 10.1.3 Biomonitoring

One Canadian study has been identified that reported biomonitoring data for TCP in adipose tissue from 6 municipalities in Ontario. TCP was not detected in any of the 82 samples analyzed with a detection limit of 1 ng/g (LeBel et al. 1989).

In a recent study in Germany, organophosphate substances were measured in paired indoor air and dust samples from 63 daycare centers (Fromme et al. 2014). Moreover, the urine of 312 children between 22 and 80 months old who attend these facilities was analyzed for the presence of eight OP metabolites, including those for TCP isomers. TCP was not detected in indoor air and dust from the daycares, and all three isomeric metabolites of TCP were not found above the LOD (0.1 µg/L) (Fromme et al. 2014).

The aircraft cabin and flight deck ventilation are supplied from partially compressed unfiltered bleed air directly from the engine. Worn or defective engine seals can result in the release of engine oil into the cabin air supply (Liyasova et al. 2011). The highest concentration of *o*-TCP contamination in cockpit air occurs during ground engine starts (Hanhela et al. 2005). This suggests that a person who has taken more flights is more likely to have been exposed to *o*-TCP (Liyasova et al. 2011). Recently, a marker of *o*-TCP exposure (butyrylcholinesterase adduct or phosphorylated butyrylcholinesterase), was found in 6 of 12 blood samples from twelve randomly selected jet airplane passengers. Blood samples were obtained 24 to 48 h after completing a flight. The authors described the levels of exposure as very low, averaging 0.05 to 1% phosphorylated butyrylcholinesterase. Four of the positive subjects were retested 3 to 7 months following their last airplane trip and were found to be negative for phosphorylated butyrylcholinesterase (Liyasova et al. 2011).

## **10.2 Health Effects Assessment**

A summary of the available health effects information for TCP is presented in Appendix H.

No classifications of the health effects of TCP by national or international regulatory agencies were identified. The United States National Toxicology Program (US NTP) has conducted a 2-year oral study in rats and mice, and concluded that there was no evidence of carcinogenic activity of TCP in exposed animals (NTP 1994).

### **10.2.1 Carcinogenicity and Genotoxicity**

The US NTP conducted a 2-year oral study in rats and mice to investigate the carcinogenicity of TCP. Fischer 344/N rats (95 per sex per group) were exposed to TCP in feed at 0, 75, 150 or 300 ppm (approximately 0, 3, 6 or 13 mg/kg-bw/day for males and 0, 4, 7 or 15 mg/kg-bw/day for females) for 2 years. An additional group of rats received 600 ppm TCP in feed for 22 weeks and then received control feed. B6C3F1 mice (95 per sex per dose) were exposed to TCP in feed at 0, 60, 125 or 250 ppm (approximately 0, 7, 13 or 27 mg/kg- bw/day in males and 0, 8, 18 or 37 mg/kg-bw/day in females) for 2 years. Rats and mice were examined at 3, 9 and 15 months and 2 years into the study. There was no evidence of carcinogenic activity of TCP found in the exposed rats and mice. Non-neoplastic effects observed in the 2-year study included cytoplasmic vacuolization of the adrenal cortex in male and female rats, ovarian interstitial cell hyperplasia in female rats, ceroid pigmentation of the adrenal cortex in

male and female mice, as well as increased incidence in clear cell foci, fatty change and ceroid pigmentation of the liver in male mice (NTP 1994). These effects are discussed in more detail in Section 9.2.3.

Studies on genotoxicity of TCP have been conducted *in vitro* and *in vivo*. TCP tested negative in bacteria mutation assays (*Salmonella typhimurium* TA 98, TA100, TA1535, TA1537, TA1538) with or without metabolic activation. It did not induce sister chromatid exchange in Chinese hamster ovary (CHO) cell with or without metabolic activation. In the chromosome aberration assays, TCP tested negative in CHO cells and in mouse lymphoma cell line, but ambiguous in mouse lymphoma L5178Y cells, and positive in BALB/3T3 cell line, with or without metabolic activation. In an *in vivo* assay, TCP did not induce unscheduled DNA synthesis in exposed rats. Therefore, TCP is unlikely to be genotoxic based on the available information.

### 10.2.2 Reproductive and Developmental Effects

The reproductive effects of TCP were examined in mice and rats of both sexes. In a study using continuous breeding protocol, male and female Swiss (CD-1) mice (20 per sex per dose for test group, 40 per sex for control group) were dosed at 0, 0.05, 0.1 or 0.2% of TCP (approximately 0, 63, 124, or 250 mg/kg-bw/day) in feed, for 7 days prior to breeding and 98 days during breeding. A significant ( $p < 0.01$ ) decrease in the number of litters per pair was observed in a dose-dependent manner. The proportion of pups born live and their weight was significantly decreased at 250 mg/kg-bw/day. In the crossover mating phase, impaired fertility was observed in both males and females treated with 250 mg/kg-bw/day, with a greater effect in females. There were dose-related changes in the adrenals for both sexes. Bodyweight was decreased in both males and females at the high dose. A significant ( $p < 0.05$ ) decrease in sperm motility was observed at 63 and 124 mg/kg-bw/day (males in the 250 mg/kg-bw/day dose group were not examined). Atrophy of seminiferous tubules, decreased testis and epididymal weights were observed in F0 males at the high dose, while no histopathological changes were found in the female reproductive tract. A LOAEL was identified at 63 mg/kg-bw/day based on decreased number of litters per pair. No NOAEL was identified (Chapin et al. 1988).

The reproductive effects of TCP were also examined in a one-generation study in Long Evans rats. TCP was administered to male rats (12 per dose) at 0, 100 or 200 mg/kg-bw/day, and to female rats (24 per dose) at 0, 200, or 400 mg/kg-bw/day in corn oil via gavage. Males were dosed for 56 days, and females for 14 days prior to breeding and throughout the 10-day breeding period. The low-dose (100 mg/kg-bw/day) males were mated with the low-dose (200 mg/kg-bw/day) females and the high-dose (200 mg/kgbw/day) males were mated with the high-dose (400 mg/kg-bw/day) females. A dose-dependent abnormal sperm morphology was observed at all doses. Sperm concentration, motility and progressive movement were decreased at 200 mg/kg-bw/day. The number of females delivering live pups was decreased at all doses. Decreased litter size and pup viability were observed at 400 mg/kg-day.



Histopathological changes were observed in the testes and epididymides of male rats, and in the ovaries of female rats. A LOAEL was identified at 100 mg/kg-bw/day, the lowest dose tested, based on fetotoxicity, abnormal sperm morphology, histopathological changes in testis, epididymides and ovaries (Carlton et al. 1987).

In a prenatal developmental toxicity study, pregnant SD rats were administered TCP via gavage at 0, 20, 100, 400 or 750 mg/kg-bw/day during gestation days 0 to 19. Clinical observations included increased salivation at 100 mg/kg-bw/day and higher dose, and alopecia and unkempt appearance at 400 mg/kg-bw/day and higher doses. Fetal body weights were reduced compared to control groups at all dose levels. Incomplete ossification was observed at 750 mg/kg-bw/day. A LOAEL was identified at 20 mg/kg-bw/day, the lowest dose tested, based on reduced fetal body weights while the LOAEL for maternal toxicity was 100 mg/kg-bw/day based on increased salivation. Also, a NOAEL for maternal toxicity was established at 20 mg/kg-bw/day. No NOAEL for developmental toxicity was identified (MPI Research Inc. 2004).

### **10.2.3 Repeated-dose Toxicity**

A number of repeated-dose studies have been identified, which are summarized in Appendix H. Some of these studies are presented below:

One short-term dermal study was identified. Female Sprague-Dawley rats (5 per dose) were exposed to TCP (3% in jet engine oil) via dermal application to the clipped (shaved) skin at 0, 500 or 1000 mg/kg-bw/day, for a total of 20 exposures over four weeks. Serum cholinesterase was significantly ( $p < 0.05$ ) reduced in all exposed rats. Clinical signs of hypersensitivity, such as increased motor activity were observed at 1000 mg/kg-bw/day (Mobil 1990).

The US NTP conducted a 13-week oral study in Fischer 344/N rats and B6C3F1 mice. Animals (10 per sex per dose) were exposed to TCP in corn oil by gavage up to 800 mg/kg-bw/day. No mortalities were observed in either species. Final mean body weights of male rats and mice were significantly lower than controls after exposure to doses of 200 mg/kg-bw/day and higher, whereas in female mice, mean body weights were significantly reduced after receiving doses of 400 mg/kg-bw/day and higher. No significant mean body weight changes were observed in female rats. Cytoplasmic vacuolization of the adrenal cortex was observed in rats and mice of both sexes at all dose groups in a dose-dependent manner. Ovarian interstitial cell hypertrophy was observed in all treated female rats and mice. In addition, atrophy of seminiferous tubules was observed in male rats at doses of 400 mg/kg-bw/day and higher. There were no biologically significant changes in neurobehavioral parameters in exposed rats. However, in mice, multifocal degeneration of the spinal cord was observed at 100 mg/kg-bw/day and higher, in both sexes; and multifocal degeneration of the sciatic nerve was observed at 200 mg/kg-bw/day and higher, in males, and at 100 mg/kg-bw/day and higher, in females. Significantly decreased forelimb grip strength was observed in males treated with doses of 200 and higher and in females treated with

doses of 400 mg/kg-bw/day and higher. Significantly decreased hindlimb grip strength was observed at 200 mg/kg-bw/day and higher in both sexes.. A LOAEL of 50 mg/kg-bw/day, the lowest dose tested, was identified both for rats and mice based on cytoplasmic vacuolization of the adrenal cortex, and ovarian interstitial cell hypertrophy (NTP 1994).

A similar 13-week feeding study was conducted in rats and mice., Fischer 344/N rats (10 per sex per dose) were treated with diets containing 0, 900, 1700, 3300, 6600 or 13,000 ppm TCP (approximately equal to 0, 55, 120, 220, 430 or 750 mg/kg-bw/day for males and 65, 120, 230, 430 or 770 mg/kg-bw/day for females), whereas B6C3F1 mice (10 per sex per dose) were treated with diets containing 0, 250, 500, 1000, 2100 or 4200 ppm TCP (approximately equivalent to 0, 45, 110, 180, 380 or 900 mg/kg-bw/day for males and 0, 65, 130, 230, 530 or 1050 mg/kg-bw/day for females). No mortalities were observed in either rats or mice of either sex. Final mean body weights were significantly decreased in male rats at 430 mg/kg-bw/day and higher, and in female rats at 230 mg/kg-bw/day and higher. In mice, mean body weights were decreased (significance not stated) at 900 mg/kg-bw/day in males, and at 530 mg/kg-bw/day and higher in females. Cytoplasmic vacuolization of the adrenal cortex was observed in all exposed rats and mice except for the male mice treated at 45 mg/kg-bw/day. In addition, ovarian interstitial cell hypertrophy and inflammation of the ovarian interstitium were observed in all female rats. Renal papillary edema and renal papillary necrosis were observed at 750 mg/kg-bw/day in male rats and at 430 mg/kg-bw/day and higher dose in female rats. Basophilic hypertrophy of the pituitary gland pars distalis and atrophy of the seminiferous tubules were observed at 430 mg/kg-bw/day and higher dose in male rats. No biologically significant changes in neurobehavioral parameters were observed in exposed rats.. In mice, papillary hyperplasia of the gallbladder mucosa was observed in males which received doses of 110 mg/kg-bw/day and higher, and in females treated with doses of 230 mg/kg-bw/day and higher. Renal tubule degeneration was observed in all male mice at 900 mg/kg-bw/day. Axonal degeneration was observed in males dosed with 380 mg/kg-bw/day and higher, and in females treated with 230 mg/kg-bw/day and higher. Significant decreases in forelimb grip strength were observed in males and females treated at 380 and 530 mg/kg-bw/day, respectively ( $p \leq 0.05$ ) and in males and females treated at 900 and 1050 mg/kg-bw/day, respectively ( $p \leq 0.01$ ). Significant decreases in hindlimb grip strength were observed in males receiving 900 mg/kg-bw/day and in females receiving 530 mg/kg-bw/day and higher ( $p \leq 0.01$ ).

A LOAEL was identified for male rats at 55 mg/kg-bw/day based on cytoplasmic vacuolization of the adrenal cortex; and for females at 65 mg/kg-bw/day based on hyperplasia of ovarian interstitial cells. No NOAELs were identified in the rats study. In mice, a LOAEL was identified at 110 mg/kg-bw/day for males, and at 65 mg/kg-bw/day, the lowest dose tested, for females based on cytoplasmic vacuolization of the adrenal cortex; a NOAEL was identified at 45 mg/kg-bw/day for the males (NTP 1994).

TCP was further tested in a 2-year feeding study in rats and mice. Fischer 344/N rats

(95 per sex per dose) were fed diets containing 0, 75, 150 or 300 ppm TCP (approximately 0, 3, 6 or 13 mg/kg-bw/day for males and 0, 4, 7 or 15 mg/kg-bw/day for females). An additional group of rats (95 per sex per dose) received diets containing 600 ppm TCP (approximately 26 mg/kg-bw/day for males and 30 mg/kg-bw/day for females) for 22 weeks and then received only control feed. No mortalities occurred. No effect was observed on the final mean body weights. Cytoplasmic vacuolization of the adrenal cortex was observed in males treated at 26 mg/kg-bw/day and in females treated at 7 mg/kg-bw/day and higher at 3 months. At 9 and 15 months, cytoplasmic vacuolization was observed primarily in females treated at 15 mg/kg-bw/day, with the incidence and severity significantly increased at the end of the study. Ovarian interstitial cell hyperplasia was observed in female rats at 15 mg/kg-bw/day and the incidence and severity were increased at the end of the study. A LOAEL was identified at 7 or 26 mg/kg-bw/day for females or males, respectively, based on cytoplasmic vacuolization of the adrenal cortex. A NOAEL was identified at 4 and 13 mg/kg-bw/day for females and males, respectively.

B6C3F1 mice (95 per sex per dose) were treated with diets containing 0, 60, 125 or 250 ppm TCP (approximately 0, 7, 13 or 27 mg/kg-bw/day for males and 0, 8, 18 or 37 mg/kg-bw/day for females). At 3, 9 and 15 months of exposure, up to 15 mice/sex/dose were necropsied and evaluated for histopathological lesions. Body weights, survival and feed consumption of exposed groups were similar to that of controls. Ceroid pigmentation of the adrenal cortex was observed in all exposed groups including controls (with an incidence near or at 100% at 9, 15 and 24 months) throughout most of the 2-year study, except in 8 and 18 mg/kg-bw/day females at the 3-month necropsy. The severity was markedly increased in females at 37 mg/kg-bw/day. Increased incidence in clear cell foci, fatty change and ceroid pigmentation of the liver were observed in males at 13 mg/kg-bw/day and higher doses. A LOAEL was identified at 7 or 37 mg/kg-bw/day for males or females, respectively, based on ceroid pigmentation of the adrenal cortex. A NOAEL was identified at 18 mg/kg-bw/day for the female mice, but no NOAEL was identified for the male mice (NTP 1994).

Since adrenal lesions were observed in all groups of male and female mice including controls, this suggests that in mice, adrenal lesions occur spontaneously and TCP accelerated its onset (ATSDR 2012). Therefore, the NOAEL of 4 mg/kg-bw/day based on cytoplasmic vacuolization of the adrenal cortex observed in female rats is identified as the lowest NOAEL for adrenal lesions.

Information from oral repeated-dose studies indicates that the target organs for TCP are the adrenal gland and ovary in rats. The mechanisms by which these effects occur have not been elucidated, but some studies have provided some insight. Among the possible mechanisms, a potential underlying mechanism of these effects seems to be an alteration in the storage pathway resulting from the inhibition by TCP of neutral cholesteryl ester hydrolase (nCEH), an enzyme that catalyzes the conversion of stored cholesteryl ester to free cholesterol. Such an action would result in accumulation of cholesteryl esters in adrenocortical and ovarian interstitial cells. TCP also inhibited A:

cholesterol acyl transferase (ACAT) in the adrenals. ACAT is involved in the esterification of cholesterol to form cytoplasmic lipid droplets of cholesteryl ester, a mechanism by which the cells store and conserve cholesterol in excess of that required for steroidogenesis. Male B6C3F1 mice showed increased incidences of fatty change, clear foci, and ceroid pigmentation in hepatocytes after exposure to TCP for 2 years, which could indicate a disruption in lipid metabolism. However, since no such effects were reported in females, additional mechanisms are probably involved (ATSDR 2012).

#### **10.2.4 Neurotoxicity**

Exposure to TCP also induced neurotoxicity in mice and rats. In a 16-day gavage study in F344/N rats, a significant reduction of forelimb grip strengths was observed in females at 1450 mg/kg-bw/day and higher doses, and in males at 2900 and 5800 mg/kg-bw/day. A significant reduction in hindlimb grip strengths was observed in males at 2900 and 5800 mg/kg-bw/day, and in females at 5800 mg/kg-bw/day (NTP 1994). In a similar 16-day gavage study in B6C3F1 mice, a significant reduction of forelimb grip strengths was observed at 1450 mg/kg-bw/day in males and at 5800 mg/kg-bw/day in females while a significant reduction of hindlimb grip strengths was observed at 360 mg/kg-bw/day in males, at 730 mg/kg-bw/day in males and females, at 1450 in males and at 5800 mg/kg-bw/day in males and females, on day 14 of the study (NTP 1994).

Neurotoxicological effects of TCP were also observed in mice in the sub-chronic oral studies. In a 13-week gavage study in B6C3F1 mice, multifocal degeneration of the spinal cord was observed at doses of 100 mg/kg-bw/day and higher, both in males and females; multifocal degeneration of the sciatic nerve was observed in males at 200 mg/kg-bw/day and higher, and in females at 100 mg/kg-bw/day and higher. Decreased hindlimb grip strength was observed at doses of 200 mg/kg-bw/day and higher, in both sexes. Decreased forelimb grip strength was observed at 400 mg/kg-bw/day and higher doses in males, and at 200 mg/kg-bw/day and higher doses in females (NTP 1994).

In a similar 13-week feeding study in B6C3F1 mice, axonal degeneration was observed in males at 380 mg/kg-bw/day and higher doses, and in females at 230 mg/kg-bw/day and higher doses. Significant decreases in forelimb grip strength were observed at 380 mg/kg-bw/day and higher dose and at 530 mg/kg-bw/day and higher dose in males and females, respectively. Significant decreases in hindlimb grip strength were observed at 900 and 1050 mg/kg-bw/day in males and females, respectively (NTP 1994).

TCP can also induce neuroeffects via dermal exposure. In the 4-week dermal study in female Sprague-Dawley rats, serum cholinesterase was significantly ( $p < 0.05$ ) reduced at 500 and 1000 mg/kg-bw/day, the only 2 doses tested. Clinical signs of hypersensitivity, such as increased motor activity, were observed at 1000 mg/kg-bw/day (Mobil 1990). This study was conducted in 1990, and the TCP formulation composition used for the study is unknown and may have been different from TCP formulations used commercially today.

### 10.2.5 Sensitization

In a local lymph node assay, twenty female CBA/J Rj mice were allocated to five groups of four animals each. TCP was applied to the surface of ears of mice at concentrations of 100% (undiluted), 50% and 25% (w/v). The negative control group received acetone olive oil (AOO) while the positive control group received 25%  $\alpha$ -Hexylcinnamaldehyde (HCA) in AOO. No mortality, systemic toxicity or local irritation was observed during the study. No treatment-related effects were observed on animal body weights in any treated groups. Stimulation index values of the test item were 3.7, 3.4 and 5.7 at treatment concentrations of 100% (undiluted), 50% and 25% (w/v), respectively. A significant lymphoproliferative response (stimulation index value of 17.2) was noted for the positive control chemical and this result confirmed the validity of the assay. In conclusion, under the conditions of the present assay, Kronitex TCP, tested in a suitable vehicle, was shown to have sensitization potential (sensitizer) in the local lymph node assay (LAB Research Ltd. 2010).

### 10.2.6 Human Studies

There are a number of generally poorly documented case reports of toxic effects caused by accidental ingestion or occupational exposure to TCP with unknown concentration of isomers. An outbreak of acute polyneuropathy in over 20 young females in Sri Lanka during 1977 to 1978 was reported. The cause of the neuropathy was TCP as a contaminant in special cooking oil (gingili oil). Contamination probably occurred during transport of the oil in containers previously used for storing mineral oils (Senanayake and Jeyaratnam 1981). In 1944, three cases of toxic polyneuropathy among workers who had worked for six to eight months in a plant manufacturing TCP in England were reported. Skin penetration and inhalation were deemed to be the main causes of the occupational poisoning (Hunter et al. 1944). A case of severe intoxication in a 4-year-old child following ingestion of a lubricant containing TCP was reported. The clinical findings were vomiting, diarrhea, weakness, drowsiness, delayed cholinergic crisis, and depressed nerve velocity. Full recovery occurred within four weeks (Goldstein et al. 1988). The concentration of the *o*-isomer, which is a potent neurotoxic agent (IPCS 1990), in the TCP mixture manufactured at the time of these human case reports, is believed to have been higher than what is in current TCP formulations.

There was a case report about the allergic contact dermatitis induced by contacting Band-Aid brand adhesive bandages which contains TCP as an ingredient (Norris and Storrs 1990). Also, a maximization test conducted dermally on male human subjects showed that TCP was a moderately strong sensitizer (Dupont 1992).

### 10.2.7 Toxicokinetics

No information on toxicokinetics of the TCP mixture was identified. Kurebayashi et al (1985) conducted a study on the *para*-isomer, *p*-TCP, a component of TCP, in male Wistar rats. Rats were administered a single dose of 7.8 mg/kg  $^{14}\text{C}$ -*p*-TCP in corn oil by

gavage. 41% of the administered dose was excreted in the urine in 7 days, indicating that at least that amount was absorbed.

The distribution of  $^{14}\text{C}$  -*p*-TCP-derived radioactivity was studied in rats for up to 168 hours after administration of a single dose of 89.6 mg/kg  $^{14}\text{C}$ -*p*-TCP by gavage in corn oil. At 24 hours, radioactivity was widely distributed in the tissues. Relatively high concentrations of label were found in adipose tissue, liver and kidneys, in addition to the intestine and stomach, whereas the lungs, testes, spleen, thymus, and blood had intermediate amounts of label and the lowest concentrations of radioactivity were found in the heart, muscle, and brain. At 72 hours, the concentration of radioactivity in tissues had diminished to approximately 25% of that detected at 24 hours. At 168 hours, the radioactivity in tissues had further decreased to approximately 10% of the values reported at 24 hours.

Kurebayashi et al. (1985) also studied the metabolism of *p*-TCP in male Wistar rats. Metabolites were identified in blood, urine, feces and tissues of rats at various times (up to 72 hours) following administration of 7.8 or 89.6 mg/kg  $^{14}\text{C}$ -*p*-TCP by gavage in corn oil. Metabolism involved a series of successive oxidations (in the liver) and hydrolysis (in the intestine) that resulted in *p*-hydroxybenzoic acid, di-*p*-cresyl phosphate, and *p*-cresyl *p*-carboxyphenyl phosphate as the major urinary metabolites. In the bile, the major metabolites were di-*p*-cresyl phosphate, *p*-cresyl *p*-carboxyphenyl phosphate, and the oxidized triesters di-*p*-cresyl *p*-carboxyphenyl phosphate, and *p*-cresyl *p*-carboxyphenyl phosphate. Analysis of the feces revealed metabolites very similar to those monitored in the bile; at the high dose, the main fecal metabolite was the unchanged *p*-TCP, probably due to incomplete absorption. Analysis of expired air showed  $^{14}\text{CO}_2$  that appeared to be formed by decarboxylation of *p*-hydroxybenzoic acid by intestinal microbes.

The excretion of  $^{14}\text{C}$ -labeled *p*-TCP was found in urine and feces from male Wistar rats following the administration of a single dose of 7.8 or 89.6 mg/kg of the compound by gavage in corn oil. With both doses, most of the radioactivity was excreted within 24 hours. At the low dose, 41% of the radioactivity was excreted in the urine and 44% in the feces in 7 days. Expired air accounted for 19% of the administered dose. In rats with cannulated bile ducts, about 28% of the administered radioactivity was excreted into the bile during 24 hours. At the high dose, 12% of the radioactivity was excreted in the urine and 77% in the feces, and 6% in expired air in 7 days. The authors suggested that the enterohepatic circulation and intestinal microflora play an important role in the degradation of *p*-TCP biliary metabolites (Kurebayashi et al. 1985). Elimination via the bile has also been shown after intravenous injection into rabbits (Gross and Grosse 1932), and intraperitoneal injection into rats (Myers et al 1955).

### 10.3 Characterization of Risk to Human Health

No classifications of the health effects of TCP by national or international regulatory agencies were identified. There was no evidence of carcinogenicity of TCP found in a

two-year study in rats and mice exposed to TCP in diets. TCP is unlikely to be genotoxic based on available information.

Based principally on the weight of evidence of available information, the critical effects of exposure to TCP were identified to be cytoplasmic vacuolization of adrenal cortex and interstitial cell hyperplasia in the ovary observed in rats and mice; and the lowest LOAEL was identified at 7 mg/kg-bw/day, based on cytoplasmic vacuolization of adrenal cortex observed in female rats in a two-year feeding study, the corresponding NOAEL was 4 mg/kg-bw/day. Comparison of this NOAEL with the highest estimates of total daily intake via environmental media (0.10 µg/kg-bw/day; breastfed infants of 0-6 months) resulted in a margin of exposure of approximately 39,000. This margin is considered adequate to account for uncertainties in the exposure and effects database. The selection of the lowest NOAEL as the point of departure is also considered protective of developmental and neurotoxicological effects observed in animals at higher dose levels.

With respect to exposure to TCP in certain manufactured items, contact with furniture (with treated upholstery or foam) was identified as a potential source of exposure (Table 10-1). Comparison of the NOAEL of 4 mg/kg-bw/day from the two-year oral study to the highest estimate of daily dermal exposure estimates of chronic dermal exposure ( $3.3 \times 10^{-3}$  mg/kg-bw/day) for adults sitting on furniture resulted in a margin of exposure of 1201. This approach is considered conservative as the estimates of exposure are based on migration rates for organophosphate flame retardants that are more water soluble, i.e. prone to migration, than TCP. Further, these conservative estimates of exposure are compared to a level at which no effect was observed in animals treated for 2 years. Based on this information, the MOE presented is considered adequate to account for uncertainties in the exposure and effects database.

Comparison of the LOAEL of 20 mg/kg-bw/day identified from the developmental study (short-term) to the highest estimate from handling TCP-containing products (power steering fluid) (0.002 mg/kg-bw, per event, infrequent) resulted in a margin of exposure of approximately 10,000. This margin is considered adequate to account for uncertainties in the exposure and effects database.

**Table 10-1. Human health risk characterization for TCP**

<b>Exposure Route and Duration</b>	<b>Source</b>	<b>Age Group (weight)</b>	<b>Intake (mg/kg-bw/day)</b>	<b>Critical effect level (mg/kg-bw/day)</b>	<b>MOE</b>
Oral (primary route)	Environmental media and food	Breastfed infant (7.5 kg)	$1.0 \times 10^{-4}$	4 (NOAEL)	39 000
Dermal (daily)	Furniture	Toddler (15.5 kg)	$1.7 \times 10^{-4}$ to $6.5 \times 10^{-4}$	4 (NOAEL)	6 156 to 23 770

Exposure Route and Duration	Source	Age Group (weight)	Intake (mg/kg-bw/day)	Critical effect level (mg/kg-bw/day)	MOE
Dermal (daily)	Furniture	Adult (70.9 kg)	$8.6 \times 10^{-4}$ to $3.3 \times 10^{-3}$	4 (NOAEL)	1201 to 4 638
Dermal (infrequent; per event)	Power steering fluid	Adult (70.9 kg)	0.002	20 (LOAEL)	10 000

## 10.4 Uncertainties in Evaluation of Risk to Human Health

This draft screening assessment acknowledges uncertainties regarding the exposure database and health effects database.

Intake estimates for drinking water and household dust were based on Canadian empirical data. European data were used to estimate TCP intakes from air as well as fish and breast milk given the absence of Canadian data. No data in the primary literature were available for marketed foods in North America and Europe; however European environmental fish data was available. The assumption that fish is the only source of dietary exposure (with the exception of breast milk for nursing infants) based on levels measured in Europe is an uncertainty. To account for this uncertainty, the dietary assessment for the general population conservatively assumes that all food items in the fish food group (i.e. fish, shellfish and related foods) contain the substances at upper bounding levels. Monitoring selected for several media were not recent, which is an uncertainty in this assessment.

No TCP-specific migration data were identified; however, migration was conservatively estimated based on migration studies of other organophosphate substances expected to result in higher migration. No TCP-specific skin contact factor was identified; therefore, an average of multiple substances was selected and is an uncertainty. While the scenario for the furniture (with treated upholstery and foam) was considered to be an appropriate scenario for assessing upper bounding exposure to consumer products, there is uncertainty regarding the presence of TCP in other manufactured items or products available in the marketplace in Canada.

There is an uncertainty with regard to the concentration of the ortho- isomer of TCP, o-TCP, which can cause organophosphate-induced delayed neuropathy (OPIDN) in humans and experimental animals. However, studies on TCP containing less than 0.1% o-TCP did not show OPIDN in experimental animals. This assessment is based on the assumption that all current commercial products contain less than 0.1% of o-TCP. Although this assumption is deemed to be appropriate based on available information, it cannot be precluded that there might be consumer products containing higher concentrations of o-TCP on the Canadian market.



There is an uncertainty associated with the results of one prenatal developmental toxicity study. in which reduced fetal body weight was observed following in utero exposure at 20 mg/kg- bw/day, the lowest dose tested, a dose lower than the dose at which maternal effects were observed (MPI Research Inc. 2004). However, delayed fetal ossification occurred at a much higher dose than that associated with maternal toxicity. The point of departure (4 mg/kg-bw/day) selected for the characterization of risk to human health is lower than 20 mg/kg-bw/day. Information on effects via dermal route was limited. The margins of exposure derived for dermal exposure scenarios were based on the critical effect level identified from an oral study. With characterization of the risk associated with exposure to TCP from sitting on upholstered furniture, there is uncertainty in the assumption that use of a more realistic migration rate and dermal absorption specific to TCP would result in a higher MOE. However, this assumption is considered reasonable since exposure was estimated based on a) rates of migration from foam or textile for organophosphate flame retardants which are much more soluble in water than TCP, and b) on an equivalent dermal/oral rate that is likely an overestimate given the lower dermal absorption percentage for other organophosphate substances characterized with physical-chemical properties (such as a lower  $K_{ow}$  and/or molecular weight) more amenable to dermal absorption than TCP.

## **10.5 Proposed Conclusion**

On the basis of the adequacy of the margin between the upper-bounding estimates of exposure from environmental media or consumer products and effect levels, it is proposed that TCP does not meet the criteria under paragraph 64(c) of CEPA as it is not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

## **11. Conclusion**

Considering all available lines of evidence presented in this draft screening assessment, there is low risk of harm to organisms and the broader integrity of the environment from TCP. It is proposed to conclude that TCP does not meet the criteria under paragraphs 64(a) or (b) of CEPA as it is not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity or that constitute or may constitute a danger to the environment on which life depends.

On the basis of the adequacy of the margin between the upper-bounding estimates of exposure from environmental media or consumer products and effect levels for chronic or sub-chronic exposure, it is proposed that TCP does not meet the criteria under paragraph 64(c) of CEPA as it is not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.



## References

Abou-Donia MB, Varga PA, Graham DG, Kinnes CG. 1980. Delayed neurotoxicity of a single dermal administration of o-ethyl o-4-nitro-phenyl phenylphosphonothioate and tri-o-cresyl phosphate to cats. *Toxicol Lett.* 1 (Special issue): 141.

Adipose Autopsy Samples from Six Ontario Municipalities. *Bull Environ Contam Toxicol* 43:225–230.

Adema DMM, Canton JH, Slooff W, Hanstveit AO. 1981. Onderzoek naar een geschikte combinatie toetsmethoden ter bepaling van de aquatische toxiciteit van milieugevaarlijke stoffen. Rapport nr RIV 627905001, Rijksinstituut Voor Volksgezondheid en Milieuhygiene, Biltoven, the Netherlands, 112. [cited in UK EA 2009].

Adema DMM, Kuiper J, Hanstveit AO, Canton HH. 1983. Consecutive system of tests for assessment of the effects of chemical agents in the aquatic environment. *Pesticide Chemistry: Human Welfare Environmental Protection. International Congress of Pesticide Chemistry, 5th, Meeting Date 1982, 3, 537-544.* [cited in UK EA 2009].

[AEROWIN] AEROWIN Program for Windows [Estimation Model]. 2010. Version 1.00. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. [cited 2014 January]. Available from: [www.epa.gov/oppt/exposure/pubs/episuite.htm](http://www.epa.gov/oppt/exposure/pubs/episuite.htm)

Ali N, Dirtu AC, Van den Eede N, Goosey E, Harrad S, Neels H, Mannetje A, Coakley J, Douwes J, Covaci A. 2012. Occurrence of alternative flame retardants in indoor dust from New Zealand: Indoor sources and human exposure assessment. *Chemosphere* 88:1276–1282.

[AOPWIN] Atmospheric Oxidation Program for Windows [Estimation Model]. 2010. Version 1.92a. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. [cited 2014 January]. Available from: [www.epa.gov/oppt/exposure/pubs/episuite.htm](http://www.epa.gov/oppt/exposure/pubs/episuite.htm)

Arnot JA, Gobas FAPC. 2003a. A generic QSAR for assessing the bioaccumulation potential of organic chemicals in aquatic food webs. *QSAR Comb Sci* 22(3):337–345.

Arnot JA, Gobas FAPC. 2003b. Categorization of organic substances on the Domestic Substances List for bioaccumulation potential. Report to Environment and Climate Change Canada, Existing Substances Branch. June 2003. Gatineau (QC): Environment and Climate Change Canada.

Arnot JA, Gobas FAPC. 2006. A review of bioconcentration factor (BCF) and bioaccumulation factor (BAF) assessments for organic chemicals in aquatic organisms. *Environ Rev* 14:257–297.

Arnot JA, Mackay D, Bonnell M. 2006. A review of bioconcentration factor (BCF) and bioaccumulation factor (BAF) assessments for organic chemicals in aquatic organisms. *Environ Rev* 14:257-297.

Arnot JA, Mackay D, Parkerton TF, Bonnell M. 2008a. Database of fish biotransformation rate for organic chemicals. *Environ Toxicol Chem* 27(11): 2263–2270.

Arnot JA, Mackay D, Bonnell M. 2008b. Estimating metabolic biotransformation rates in fish from laboratory data. *Environ Toxicol Chem* 27 (2): 341–351.

Arnot JA, Meylan W, Tunkel J, Howard PH, Mackay D, Bonnell M, Boethling RS. 2009. A quantitative structure-activity relationship for predicting metabolic biotransformation rates for organic chemicals in fish. *Environ Toxicol Chem* 28(6): 1168–1177.

Ash M, Ash I. 2000. Handbook of Industrial Chemical Additives. Synapse Information Resources, Inc., Endicott, NY.

Ash M, Ash I. 2003. Handbook of Paint and Raw Coating Materials. Synapse Information Resources, Inc., Endicott, NY.

Ashford RD. 1994. Ashford's Dictionary of Industrial Chemicals. Wavelength Publications Ltd., London, England. p. 908. [cited in US EPA 2010] and [cited in UK EA 2009].

ASTreat [sewage treatment plant removal model]. 2006. Version 1.0. Cincinnati (OH): Procter & Gamble Company. Available from Procter & Gamble Company, Cincinnati, OH, USA.

[ATSDR] Agency for Toxic Substances and Disease Registry. September 2012. Banjeree, BD, Saha, S, Ghosh, KK and Nandy P. 1992. Effect of tricresyl phosphate on humoral and cell-mediated immune responses in albino rats. *Bull Environ Contam Toxicol* 49:312-317.

[ATSDR] Agency for Toxic Substances and Disease Registry. 1997. Toxicological profile for hydraulic fluid. Washington (DC): US Department of Health and Human Services, Public Health Service. [cited June 2013]. Available from: <http://www.atsdr.cdc.gov/toxprofiles/tp99.pdf>

[ATSDR] Agency for Toxic Substances and Disease Registry. 2012. Public Health Statement for Phosphate Ester Flame Retardants. Washington (DC): Division of Toxicology and Human Health Sciences. [cited June 2013]. Available from: <http://www.atsdr.cdc.gov/ToxProfiles/tp202.pdf>

Bacaloni A, Cavaliere C, Foglia P, Nazzari M, Samperi R, Lagana A. 2007. Liquid chromatography/tandem mass spectrometry determination of organophosphorus flame retardants and plasticizers in drinking and surface waters. *Rapid Commun Mass Spectrom* 21:1123–1130.

[BASL4] Biosolids-Amended Soil Level 4 Model. 2011. Version 2.00. Peterborough (ON): Trent University, Canadian Environmental Modelling Centre. [cited 2013 Nov 1] [Available from: <http://www.trentu.ca/academic/aminss/envmodel/models/BASL4110.html>]

Bayer. 2002. Technical information and safety data sheet for Disflamoll TKP. Bayer AG. [cited in UK EA 2009].

[BCFBAF] Bioaccumulation Program for Windows [Estimation Model]. 2010. Version 3.10. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. [cited 2014 January]. Available from: [www.epa.gov/oppt/exposure/pubs/episuite.htm](http://www.epa.gov/oppt/exposure/pubs/episuite.htm)

Bengtsson BE, Tarkpea M, Sletten T, Carlberg GE, Kringstad A, Renberg L. 1986. Bioaccumulation and effects of some technical triaryl phosphate products in fish and *Nitocra spinipes*. *Environ Toxicol Chem* 5:853–861.

Beyer A.; Mackay D, Matthies M, Wania F, Webster E. 2000. Assessing long-range transport potential of persistent organic pollutants. *Environ Sci Technol* 2000, 34, 699–703.

Biomonitoring California. 2014. Biomonitoring California Priority Chemicals May 2013. [Internet]. Available from: [http://biomonitoring.ca.gov/sites/default/files/downloads/PriorityChemicalsList\\_June2014.pdf](http://biomonitoring.ca.gov/sites/default/files/downloads/PriorityChemicalsList_June2014.pdf)

[BIOWIN] Biodegradation Probability Program for Windows [Estimation Model]. 2010. Version 4.10. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. [cited 2014 January]. Available from: [www.epa.gov/oppt/exposure/pubs/episuite.htm](http://www.epa.gov/oppt/exposure/pubs/episuite.htm)

Boethling GRS, Cooper JC. 1985. Environmental fate and effects of triaryl and trialkyl/aryl phosphate esters. *Residue Reviews* 94:49–99.

Boethling RS, Howard PH, Beauman JA, Larosche, ME. 1995. Factors for intermedia extrapolation in biodegradability assessment. *Chemosphere* 30:741–752.

Brommer S, Harrad S, Van Den Eede N, Covaci A. 2012. Concentrations of organophosphate esters and brominated flame retardants in German indoor dust samples. *J Environ Monit* 14(9):2482–2487.

Canada Dept. of the Environment. 2013. Canadian Environmental Protection Act, 1999: Notice with respect to certain organic flame retardant substances. Canada Gazette, Part I, vol. 147, no. 13, p. 613–633. Available from: <http://gazette.gc.ca/rp-pr/p1/2013/2013-03-30/html/notice-avis-eng.html#d119>

Carlton BD, Hasaran AH, Mezza LE, Smith MK. 1987. Examination of the reproductive effects of tricresyl phosphate administered to Long-Evans rats. Toxicology 46: 321-328. [cited in UK EA 2009, IPCS 1990, GLCC 2001].

Casterline JL Jr., Ku Y, Barnett NM. 1985. Uptake of tri-p-cresyl phosphate in soybean plants. Bulletin of Environ Contam Toxicol 35:209-212.

CATALOGIC [Computer Model]. 2012. Version 5.11.13. Bourgas (BG): Bourgas Prof. Assen Zlatarov University, Laboratory of Mathematical Chemistry. Available from: [www.oasis-lmc.org/?section=software&swid=1](http://www.oasis-lmc.org/?section=software&swid=1)

Cequier E, Ionas AC, Covaci A, Marcé RM, Becher G, Thomsen C. 2014. Occurrence of a broad range of legacy and emerging flame retardants in indoor environments in Norway. Environ Sci Technol. 48: 6827-6835.

Chapin RE, George JD, Lamb JC. 1988. Reproductive toxicity of tricresyl phosphate in a continuous breeding protocol in Swiss CD-1 mice. Fund Appl Toxicol 10:344-354. [cited in IPCS 1990, UK EA 2009]

Chemtura Corporation. 2007. Kronitex® TCP Technical Data Sheet. West Lafayette (IN): Chemtura Corporation. Available from: [http://www.chemtura.com/deployedfiles/Business%20Units/Polymer\\_Additives-en-US/BU%20Documents/Technical%20Data%20Sheets/Flame%20Retardants/Phosphorus%20Based%20Flame%20Retardants/Files/Kronitex\\_TCP\\_TDS.pdf](http://www.chemtura.com/deployedfiles/Business%20Units/Polymer_Additives-en-US/BU%20Documents/Technical%20Data%20Sheets/Flame%20Retardants/Phosphorus%20Based%20Flame%20Retardants/Files/Kronitex_TCP_TDS.pdf)

[ChemFate] Interactive ChemFate Database [database on the Internet]. 2012. Syracuse (NY): Syracuse Research Corporation. [cited 2014 June 11] Available from: <http://www.srcinc.com/what-we-do/environmental/scientific-databases.html>  
TCP results from SRC PHysProp Database: available from: <http://esc.syrres.com/fatepointer/webprop.asp?CAS=1330785>

Chen D, Letcher RJ, Chu S. 2012. Determination of non-halogenated, chlorinated and brominated organophosphate flame retardants in herring gull eggs based on liquid chromatography–tandem quadrupole mass spectrometry. J Chromatogr A 1220:169–174.

Cho KJ, Kirakawa T, Mukai T, Takimoto K, Okada M. 1996. Origin and stormwater runoff of TCP (tricresyl phosphate) isomers. Water Research 30(6):1431–1438.

Cho KJ, Takimoto K, Okada M. 1994. Fate of tricresyl phosphate isomers in Kurose

River (Japan). Water Science and Technology 30(10):189-197.

Zarfl C, Scheringer M, Matthies M. 2011. Screening Criteria for Long-Range Transport Potential of Organic Substances in Water. Environ. Sci. Technol. 45, 10075-10081.

City of Toronto. 2003a. Water quality quarterly report (January–March 2003). Works and Emergency Services, Toronto.

City of Toronto. 2003b. Water quality quarterly report (April–June 2003). Works and Emergency Services, Toronto.

City of Toronto. 2003c. Water quality quarterly report (July–September 2003). Works and Emergency Services, Toronto.

Crockett AB. 1978 a. U.S. EPA: Letter to M.P. Halper, U.S. EPA, Oct. 26. [cited in Boethling and Cooper 1985].

Crockett AB. 1978b. U.S. EPA: Letter to P. Hilgard, U.S. EPA. [cited in Boethling and Cooper 1985].

Crockett AB. 1978c. U.S. EPA: Letter to G. B. Wiersma, U.S. EPA, June 2. [cited in Boethling and Cooper 1985].

Crockett A B. 1979. U.S. EPA: Letter to P. Hilgard, U.S. EPA, March 6. [cited in Boethling and Cooper 1985].

Daughtrey, W., Biles, R., Jortner, B, and Ehrich, M. (1996) Subchronic delayed neurotoxicity evaluation of jet engine lubricants containing phosphorus additives. Fundam Appl Toxicol 32:244–249

David MD, Seiber JN. 1999a. Accelerated hydrolysis of industrial organophosphates in water and soil using sodium perborate. Environmental Pollution 105:121-128.

David MD, Seiber JN. 1999b. Analysis of organophosphate hydraulic fluids in U.S. Air force base soils. Arch Environ Contam Toxicol 36:235–241.

De Nola G, Kibby J, Mazurek W. 2008. Determination of *ortho*-cresyl phosphate isomers of tricresyl phosphate used in aircraft turbine engine oils by gas chromatography and mass spectrometry. 2008. J Chromatogr A 1200:211–216.

Dimitrov S, Dimitrova N, Parkerton T, Comber M, Bonnell M, Mekenyan O. 2005. Base-line model for identifying the bioaccumulation potential of chemicals. SAR QSAR Environ Res 16(6):531–554.

Dirtu AC, Ali N, Van den Eede N, Neels H, Covaci A. 2012. Country specific comparison

for profile of chlorinated, brominated and phosphate organic contaminants in indoor dust. Case study for Eastern Romania, 2010. *Environ Int* 49:1–8.

Dodson R, Perovich LJ, Covaci A, Van den Eede N, Ionas AC, Dirtu AC, Brody JG, Rudel RA. 2012. After the PBDE Phase-Out: A Broad Suite of Flame Retardants in Repeat House Dust Samples from California. *Environ Sci Technol* 46:13056–13066.

Dupont Chemical. 1992. Initial submission: study synopsis regarding tricresyl phosphate and 2,3-dibromopropyl phosphate with cover letter dated 101592. NTIS/OTS Fiche # 0571488.

[ECHA] European Chemicals Agency. 2010. Guidance on information requirements and chemical safety assessment. Chapter R.16:Environmental exposure estimation. May 2010. Guidance for the implementation of REACH. Helsinki (FI): European Chemicals Agency.

[ECHA] European Chemicals Agency. c2007-2013. Registered Substances database. Search results for CAS RN 1330-78-5. Helsinki (FI): ECHA. [updated 2013 July 26; cited 2013 July 17]. Available from: [www.echa.europa.eu/information-on-chemicals/registered-substances](http://www.echa.europa.eu/information-on-chemicals/registered-substances)

Environment Agency Japan. 1996. Chemicals in the environment. Report on environmental survey and wildlife monitoring of chemicals in F.Y. 1994. Environmental Health and Safety Division, Environment Agency Japan, May 1996. [Cited in UK EA 2009].

[ECCC] Environment and Climate Change Canada. 2001. Canadian Environmental Protection Act, 1999. Notice with respect to certain substances on the Domestic Substances List (DSL). *Canada Gazette* 135(46):4194–4211. <http://canadagazette.gc.ca/part1/2001/20011117/pdf/g1-13546.pdf>

Environment and Climate Change Canada 2003. Guidance Manual for the Categorization of Organic and Inorganic Substances on Canada's Domestic Substances List. Determining persistence, bioaccumulation potential, and inherent toxicity to non-human organisms. Existing Substances Branch. June 2003.

Environment and Climate Change Canada. 2007. Guidance for Conducting Ecological Assessments under CEPA, Science Resource Technical Series, Technical Guidance Module: QSARs. Reviewed Draft Working Document. Gatineau (QC): Environment and Climate Change Canada, Ecological Assessment Division.

Environment and Climate Change Canada, Health Canada. 2007. Chemical substances: Categorization [Internet]. Ottawa (ON): Government of Canada. [updated 2007 April 20; cited 2014 June 10]. Available from: <http://www.chemicalsubstanceschimiques.gc.ca/approach-approche/categor-eng.php>



[ECCC] Environment and Climate Change Canada. 2013-2014. Data for certain organic flame retardants substance grouping collected under the *Canadian Environmental Protection Act, 1999, section 71: Notice with respect to certain organic flame retardant substances*. Data prepared by: Environment and Climate Change Canada, Health Canada; Existing Substances Program.

Environment and Climate Change Canada. 2014. Ecological screening assessment report on Cresol (phenol, methyl-) Substances, CEPA, July 2014. Environment and Climate Change Canada, Ecological Assessment Division. Available from: <http://ec.gc.ca/es-ees/default.asp?lang=En&n=6ED0027C-1>

Environment and Climate Change Canada. 2015a. Supporting documentation: Summary tables of substance identity and physical chemical property information for Tricresyl phosphate. Gatineau (QC): Environment and Climate Change Canada. Information in support of the Screening Assessment for Phosphoric acid, tris(methylphenyl) ester. Available on request from: [substances@ec.gc.ca](mailto:substances@ec.gc.ca)

Environment and Climate Change Canada. 2015b. Supporting documentation: Summary tables of environmental concentrations information for Tricresyl phosphate. Gatineau (QC): Environment and Climate Change Canada. Information in support of the Screening Assessment for Phosphoric acid, tris(methylphenyl) ester. Available on request from: [substances@ec.gc.ca](mailto:substances@ec.gc.ca)

Environment and Climate Change Canada. 2015c. Supporting documentation: Summary tables of environmental fate and behaviour information for Tricresyl phosphate. Gatineau (QC): Environment and Climate Change Canada. Information in support of the Screening Assessment for Phosphoric acid, tris(methylphenyl) ester. Available on request from: [substances@ec.gc.ca](mailto:substances@ec.gc.ca)

Environment and Climate Change Canada. 2015d. Supporting documentation: Summary tables of ecotoxicity data information for Tricresyl phosphate. Gatineau (QC): Environment and Climate Change Canada. Information in support of the Screening Assessment for Phosphoric acid, tris(methylphenyl) ester. Available on request from: [substances@ec.gc.ca](mailto:substances@ec.gc.ca)

Environment and Climate Change Canada. 2015e. Supporting documentation: Summary tables of ecological exposure information for Tricresyl phosphate. Gatineau (QC): Environment and Climate Change Canada. Information in support of the Screening Assessment for Phosphoric acid, tris(methylphenyl) ester. Available on request from: [substances@ec.gc.ca](mailto:substances@ec.gc.ca)

[EPI Suite] Estimation Programs Interface Suite for Microsoft Windows [Estimation Model]. 2012. Version 4.11. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. Available from: [www.epa.gov/oppt/exposure/pubs/episuitedl.htm](http://www.epa.gov/oppt/exposure/pubs/episuitedl.htm)

[EQC] Equilibrium Criterion Model. 2012. Version 1.00. Peterborough (ON): Trent University, Canadian Environmental Modelling Centre. Available from: <http://www.trentu.ca/academic/aminss/envmodel/models/NewEQCv100.html>

European Commission. 2011. Identification and evaluation of data on flame retardants in consumer products. Final Report. Brussels, Belgium: prepared for the European Commission, Health and Consumers Department, by ARCADIS Belgium, Contract no. 17.020200/09/549040. Available from: [http://ec.europa.eu/consumers/archive/safety/news/flame\\_retardant\\_substances\\_study\\_en.pdf](http://ec.europa.eu/consumers/archive/safety/news/flame_retardant_substances_study_en.pdf)

[EU RAR] European Union. 2008. European Union Risk Assessment Report. Tris(2-chloro-1-methylethyl)phosphate (TCPP). Luxembourg: Office for Official Publications of the European Communities. [Internet]. [cited 2014 Jun 18]. Available from: [http://esis.jrc.ec.europa.eu/doc/risk\\_assessment/REPORT/tcppreport425.pdf](http://esis.jrc.ec.europa.eu/doc/risk_assessment/REPORT/tcppreport425.pdf)

[EU RAR] European Union. 2009. European Union Risk Assessment Report. Tris(2-chloroethyl)phosphate (TCEP). July 2009. Available from: [http://esis.jrc.ec.europa.eu/doc/risk\\_assessment/REPORT/tcepreport068.pdf](http://esis.jrc.ec.europa.eu/doc/risk_assessment/REPORT/tcepreport068.pdf)

Evenset A, Leknes H, Christensen GN, Warner N, Remberger M, Gabrielsen GW. 2009. Screening of New Contaminants in Samples from Norwegian Arctic. NIVA Report 4351-1, SPFO-Report 1049/2009. TA-2510/2009. ISBN:978-82- 449-0065-2. [cited in Van der Veen and de Boer 2012].

Fan, X., Kubwabo, C., Rasmussen, P. E., Wu, F. (2014). Simultaneous determination of thirteen organophosphate esters in settled indoor house dust and a comparison between two sampling techniques. *Sci. Tot. Environ.* 491–492; 80–86.

FMC Corporation. 1995. Tricresyl phosphate/Durad 125L Acute delayed neurotoxicity study in hens (study # I94-1925). NTIS/OTS #0572164.

Food and Drug Research Laboratories, Inc. 1975a. Acute Dermal Toxicity Study in Rabbits. Conducted for FMC Corporation. Cited in IUCLID 2001

Food and Drug Research Laboratories, Inc. 1975b. Eye Irritation Test in Rabbits. Conducted for FMC Corporation. Cited in IUCLID 2001

Foster D. Snell, Inc. 1976. 28-Day Oral Administration in Rats. Conducted for FMC Corporation. Cited in IUCLID 2001

Freeman GB, Irwin R, Trejo R, Hejtmancik M, Ryan M, Peters AC. 1988. Reversibility and tolerance to tricresyl phosphate-induced neurotoxic effects in F344 rats. *Toxicologist*, 8, 76 (cited in IPCS, 1990).

Freudenthal RI, Rausch L, Gerhart JM, Barth ML, Mackerer, CR, Bisinger, EC. 1993. Subchronic neurotoxicity of oil formulations containing either tricresyl phosphate or tri-orthocresyl phosphate. *J Am Coll Toxicol* 12:409–416.

Fromme H, Lahrz T, Kraft M, Fembacher L, Mach C, Dietrich S, Burkardt R, Völkel W, Göen T. 2014. Organophosphate flame retardants and plasticizers in the air and dust in German daycare centers and human biomonitoring in visiting children (LUPE 3). *Environ. Int.* 71: 158-163.

Fukushima M, Kawai S, Yamaguchi Y. 1992. Behavior of organophosphoric acid triesters in Japanese riverine and coastal environment. *Water Science and Technology* 25:271–278. UK EA 2009 (Glob 1998). [cited in UK EA 2009].

[GFEA] German Federal Environmental Agency. 2001. Substituting Environmental Relevant Flame Retardants: Assessment Fundamentals–Results and summary overview. Research report 204 08 542 (old) 297 44 542 (new) UBA-FB 000171/le. By Andre Leisewitz, Hermann Kruse, Engelbert Schramm. Commissioned by the German Federal Environmental Agency (Umweltbundesamt, UBA) June 2001. ISBN 0722-186X. Available from: [www.oekorecherche.de/english/berichte/volltext/FSM-cont.pdf](http://www.oekorecherche.de/english/berichte/volltext/FSM-cont.pdf)

[GLCC] Great Lakes Chemical Corporation. 2001. High Production Volume (HPV) Challenge Program, Test Plan and Robust Summaries for Phosphoric acid tris(methylphenyl)ester (Tricresyl phosphate) CAS No. 1330-78-5. [Internet]. November 28, 2001. West Lafayette, IN. [cited 2013 June 23]. Available from: <http://www.epa.gov/chemrtk/pubs/summaries/tricphos/c13318tc.htm>

Glob E. 1998. Miljøfremmede stoffer i havbunden. Lillebætsamarbejdet. [cited in UK EA 2009].

Gobas FAPC, Kelly BC, Arnot JA. 2003. Quantitative Structure Activity Relationships for Predicting the Bioaccumulation of POPs in Terrestrial Food-Webs. *QSAR Comb. Sci.* 22: 329–336.

Gobas FAPC. 2010. Comments on approach to sediment exposure. Burnaby (BC): Simon Fraser University, School of Resource & Environmental Management, March 25.

Gobas FA, Morrison HA. 2000. Bioconcentration and biomagnification in the aquatic environment. In: Boethling RS, Mackay D, editors. *Handbook of property estimation methods for chemicals, environmental and health sciences*. Boca Raton (FL): CRC. p 189C.

Goldstein DA, McGuigan MA, Ripley BD. 1988. Acutetricresyl phosphate intoxication in childhood. *Hum Toxicol* 7:179–182. Cited in IPCS 1990.

Great Lakes Chemical Company. 2004. Submission of maternal and developmental

fetal body weight effects in the rat via an OECD 421 Guideline Screening Study of tricresyl phosphate; (CAS No.:1330-78-5). Submitted to EPA under Toxic Substance Control Act Section 8(e) (Reference # 8EHQ-0604-15587) and posted on EPA website (accessed Aug 12, 2004):

[http://www.epa.gov/oppt/tsca8e/doc/8esub/8e0614\\_062504.htm](http://www.epa.gov/oppt/tsca8e/doc/8esub/8e0614_062504.htm)

Grimalt R, Romaquera C, Vilaplana J. 2009. Allergic Contact Dermatitis from Tricresyl Phosphate. *Dermatitis* 20(5):297–298

Gross E, Grosse A. 1932. A contribution to the toxicology of ortho-tricresylphosphates. *Naunyn-Schmiedeberg's Archives of Pharmacology*, 168:473–514 (in German). Cited in IPCS 1990.

Haggerty GJ, Hejtmancik M, Deskin R, Ryan MJ, Peters AC, Irwin R. 1986. Effects of subchronic exposure to tricresyl phosphate in F344 rats and B6C3F1 mice: behavioural and morphological correlates. *Toxicologist* 6:218 (cited in IPCS, 1990).

Hanhela PJ, Kibby J, DeNola G, Mazurek W. 2005. Organophosphate and amine contamination of cockpit air in the Hawk, F-111 and Hercules C-130 aircraft. Australian Govt Defence Science and Technology Organisation. DSTO-RR-0303 online, 1–21. [cited in Liyasova et al. 2011]

Hann RW Jr, Jensen PA. 1977. Water quality characteristics of hazardous materials; NTIS-PB-285946. Texas A&M Univ., College Station Environmental Engineering Div. 1751 pp. 1977 [cited in ChemFate 2012]. Available from: [www.pesticideinfo.org/references/25265-71-8hsdb.doc](http://www.pesticideinfo.org/references/25265-71-8hsdb.doc)

Hartmann PC, Burgi D, Giger W. 2004. Organophosphate flame retardants and plasticizers in indoor air. *Chemosphere* 57:781–787.

Haworth, S., Lawlor, T., Mortelmans, K., Speck, N., and Zeiger, E. (1983) Salmonella mutagenicity test results for 250 chemicals. *Environ. Mutagen. Suppl.*, 1, 3-142 (cited in IPCS, 1990).

Health Canada. 1994 *Canadian Environmental Protection Act: Human health risk assessment for priority substances*. Ottawa, Ontario

Health Canada. 2014a. Preliminary Product Testing. Consumer Product Safety Directorate. (unpublished)

Health Canada. 2014b. List of Prohibited and Restricted Cosmetic Ingredients ("Hotlist"). Available from: <http://www.hc-sc.gc.ca/cps-spc/cosmet-person/hot-list-critique/hotlist-liste-eng.php>

Hine C, Rowe VK, White ER, Darmer KI Jr, Youngblood GT. 1981. In: Clayton, G.D. &

Clayton, F.E., ed. Patty's industrial hygiene and toxicology, 3rd revised ed Vol. 2A. New York, Wiley-Interscience. p. 2362–2363. [cited in IPCS 1990].

Hoke RA, Giesy JP, Zabik M, Unger M. 1993. Toxicity of sediments and sediment pore waters from the Grand Calumet River-Indiana Harbor area of concern. *Ecotoxicity and Environmental Safety*. 26(1):86–112. [cited in UK EA 2009].

Hollifield HC. 1979. Rapid nephelometric estimate of water solubility of highly insoluble organic chemicals of environmental interest. *Bulletin of Environmental Contamination and Toxicology* 23:579–586.

Houde M, Berryman D, de Lafontaine Y, Verrault J. 2014. Novel brominated flame retardants and dechloranes in three fish species from the St. Lawrence River, Canada. *Sci Total Environ* 479–480:48–56.

Howard PH, Deo PG. 1979. Degradation of aryl phosphates in aquatic environments. *Bulletin of Environmental Contamination and Toxicology* 22:337–344.

[HSDB] Hazardous Substances Data Bank [database on the Internet]. 2012. Bethesda (MD): National Library of Medicine (US). [revised 2013 Mar 8; cited 2013 June 15]. Available from: <http://toxnet.nlm.nih.gov/cgi-bin/sis/search/f?./temp/~P0GUgw:1>

Hunter, D., Perry, KMA, Evans RB. 1944. Toxic polyneuritis arising during the manufacture of tricresyl phosphate. *Br. J. Ind. Med.* 1:227–231 (cited in IPCS, 1990).

[HYDROWIN] Hydrolysis Rates Program for Microsoft Windows [Estimation Model]. 2010. Version 2.00. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. [cited 2014 January]. Available from: [www.epa.gov/oppt/exposure/pubs/episuite.htm](http://www.epa.gov/oppt/exposure/pubs/episuite.htm)

[ICL] Israel Chemicals Ltd. Industrial Products, 2012. Flame Retardants [Internet]. Beer Sheva, Israel. [cited June 2013]. Available from: <http://icl-ip.com/wp-content/uploads/2012/01/FR-Brochure-2012-web.pdf>

[ICL] Israel Chemicals Ltd. Industrial Products, 2013a. Application–Phenolic Resins [Internet]. Tel Aviv, Israel. [cited June 2013]. Available from: <http://icl-ip.com/?applications=phenolic-resins>.

[ICL] Israel Chemicals Ltd. Industrial Products, 2013b. Application–PVC [Internet]. Tel Aviv, Israel. [cited June 2013]. Available from: <http://icl-ip.com/?applications=pvc-and-fr-plasticizers>

[ICL] Israel Chemicals Ltd. Industrial Products, 2013c. Segment–Bedding and Seating [Internet]. Tel Aviv, Israel. [cited June 2013]. Available from: [http://icl-ip.com/?segment\\_category=bedding-and-seating](http://icl-ip.com/?segment_category=bedding-and-seating).

Imperial Oil. 1991. Male reproductive toxicity assessment following a fourteen-day oral exposure to phosphate esters in F344 rats. Study # 64412. Obtained from ECCC 2001.

[IPCS] International Programme on Chemical Safety. 1990. Tricresyl Phosphate. Geneva (CH): World Health Organization. (Environmental Health Criteria 110). Jointly sponsored by the United Nations Environment Programme, the International Labour Organization, and the World Health Organization.

Irwin R, Freeman GB, Trejo R, Hehtmancik M, Peters A. 1987. Effects of chronic exposure to tricresyl phosphate I F344 rats and B6C3F1 mice: behavioural and biochemical correlates. Soc Neurosci Abstr 13:90 (cited in IPCS 1990).

[IUCLID] 2001. IUCLID Data set for tris(methylphenyl) phosphate. Great Lakes Chemical Corporation. [cited in UK EA 2009].

Ishikawa S et al. 1985a. Suishitsu Odaku Kenkyu 8: 799–807. [cited in HSDB 2012] .

Ishikawa S, Taketomi M, Shinohara R. 1985b. Determination of trialkyl and triaryl phosphates in environmental samples. Water Research 19:119–125. [cited in UK EA 2009].

Ishikawa S, Taketomi M, Shinohara R. 1985c. Determination of organic phosphate esters in factory effluent and domestic effluent. Japanese Journal of Water Pollution Research 8:529–535. [cited in UK EA 2009].

Izmerov NF, Sanotsky IV, Sidorov KK. 1982. Toxicometric parameters of industrial toxic chemicals under single exposure, Moscow, Centre of International Projects, GKNT, p. 14. (Cited in IPCS 1990).

Johanssen FR, Wright PL, Gordon DE, Levinskas GJ, Radue RW, Graham PR 1977. Evaluation of delayed neurotoxicity and dose-response relationships of phosphate esters in the adult hen. Toxicol Appl Pharmacol 41:291–304. (Cited in IPCS 1990).

Kajiwara N, Noma Y, Takigami H. 2011. Brominated and organophosphate flame retardants in selected consumer products on the Japanese market in 2008. J Hazard Mater 192: 1250–1259.

Kawagoshi Y, Fukunaga I, Itoh H. 1999. Distribution of organophosphoric acid triesters between water and sediment at a sea-based solid waste disposal site. J Mater Cycles Waste Manage 1:53–61.

Kenmotsu K, Matsunaga K, Ishida T. 1980 [Studies on the mechanisms of biological activities of various environmental pollutants. V. Environmental fate of organic phosphoric acid triesters.] Okayama-ken Kankyo Hoken Senta Nempo, 4:103–110 (in Japanese). [cited in IPCS 1990].

Kim JW, Ramaswamy BR, Chang KH, Isobe T, Tanabe S. 2011. Multiresidue analytical method for the determination of antimicrobials, preservatives, benzotriazole UV stabilizers, flame retardants and plasticizers in fish using ultra high performance liquid chromatography coupled with tandem mass spectrometry. *J Chromatogr A*. 1218:3511-3520.

Kim JW, Isobe T, Sudaryanto A, Malarvannan G, Chang KW, Muto M, Prudent M, Tanabe S. 2013. Organophosphorus flame retardants in house dust from the Philippines: occurrence and assessment of human exposure. *Environ Sci Pollut Res* 20:812–822.

Kim JW, Isobe T, Sudaryanto A, Malarvannan G, Chang KH, Muto M, Tanabe S. 2013. Organophosphorus flame retardants in house dust from the Philippines: occurrence and assessment of human exposure. *Environ Sci Pollut Res* 20(2): 812–822.

Kinkead ER, Bunker SR, Wolfe RE, Wall HG. 1990. The acute delayed neurotoxicity evaluation of two jet engine oil formulations. NTIS/OTS Fiche # 0516607-3.

Kinkead ER, Wolfe RE, Salins SA, Godin CS, Flemming CD. 1992. Acute delayed neurotoxicity evaluation of two jet engine oils using a modified navy and EPA protocol. *Govt Reports Announcements & Index*, Issue 14, 1993; NTIS/AD-A262 580/4.

Kishi H, Sekine Y. 2003. Simple prediction of atmospheric concentration of hydrophilic compounds based on the classification of industrial uses. *QSAR & Combinatorial Science* 22:396–398.

Klimisch HJ, Andreae E, and Tillmann U. 1997. A systematic approach for evaluating the quality of experimental and ecotoxicological data. *Regulatory Toxicology and Pharmacology* 25:1-5.

[KOAWIN] Octanol Air Partition Coefficient Program for Microsoft Windows [Estimation Model]. 2010. Version 1.10. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. [cited 2014 January]. Available from: [www.epa.gov/oppt/exposure/pubs/episuite.htm](http://www.epa.gov/oppt/exposure/pubs/episuite.htm)

[KOCWIN] Organic Carbon Partition Coefficient Program for Windows [Estimation Model]. 2010. Version 2.00. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. [cited 2014 January]. Available from: [www.epa.gov/oppt/exposure/pubs/episuite.htm](http://www.epa.gov/oppt/exposure/pubs/episuite.htm)

Ku Y, Alvarez GH. 1982. Biodegradation of 14C-tri-p-cresyl phosphate in a laboratory activated sludge system. *Appl Environ Microbiol* 43:619–622.

Kurebayashi H, Tanaka A, Yamaha T. 1985. Metabolism and disposition of the flame retardant plasticizer, tri-p-cresyl phosphate, in the rat. *Toxicol Appl. Pharmacol* 77: 395–404.

LAB Research Ltd. Final report: Skin sensitization: Local Lymph Node Assay with Kronitex TCP. Study code :10/160-037E. Date of Final Report: 01 October 2010. (section 71 submission 2014)

Latendresse J, Brooks C, Capen C. 1994a. Pathologic effects of butylated triphenyl phosphate-based hydraulic fluid and tricresyl phosphate on the adrenal gland, ovary, and testes in the Fischer 344 rat. *Toxicol Pathol* 22:341–352. [cited in UK EA 2009, IUCLID 2001].

Latendresse JR, Brooks CL, Capen CC. 1994a. Pathologic effects of butylated triphenyl phosphate-based hydraulic fluid and tricresyl phosphate on the adrenal gland, ovary, and testis in the Fischer-344 rat. *Toxicol Pathol* 22: 341–352.

Latendresse JR, Brooks CL, Flemming CD, Capen CC. 1994b. Reproductive Toxicity of Butylated Triphenyl Phosphate and Tricresyl Phosphate Fluids in F344 Rats. *Fundam Appl Toxicol* 22:392–399.

Latendresse JR, Brooks CL, Capen CC. 1995. Toxic effects of butylated triphenyl phosphate-based hydraulic fluid and tricresyl phosphate in female F344 rats. *Vet Pathol*. 32(4):394–402.

Latourette HK. 1978. FMC Corp.: Letter to U.S. Environmental Protection Agency, attn. 1. Urquhart. [cited in Boethling and Cooper 1985].

Latourette H.K.1980. FMC Corp.: Letter to D. W. Smith, U.S. EPA, July II. [cited in Boethling and Cooper 1985].

LeBel GL, Williams DT, Benoit FM. 1981. Gas Chromatographic Determination of Trialkyl/Aryl Phosphates in Drinking Water, Following Isolation Using Macroreticular Resin. *J Assoc Off Anal Chem* 64(4):991–998.

LeBel GL, Williams DT, Berard D. 1989. Triaryl/Alkyl Phosphate Residues in Human

Lee HB, Peart T, Muir D, Teixeira C, Sett A, Struger J, Backus S. 2011. Organophosphorus flame retardants and benzotriazoles in open waters and tributaries of the Great Lakes. Prepared by Environment and Climate Change Canada (poster).

Lefaux R. 1972. Industrial toxicology. Phosphoric esters. In: *Practical toxicology of plastics*, London, Iliffe Books Ltd, pp 121–127. [cited in IPCS 1990].

Leonards P, Steindal EH, van der Veen I, Berg V, Bustnes JO, van Leeuwen S. 2011.



Screening of Organophosphorus Flame Retardants 2010. SPFO-Report 1091/ 2011. TA-2786/2011. [cited in Van der Veen and de Boer 2012].

Litton Bionetics Inc. 1979a. Evaluation of Phosflex 31 P in the in vitro transformation of BALB3T3 cells. Conducted for Stauffer Chemical Company. Cited in IUCLID 2001

Litton Bionetics Inc. 1979b. Mutagenicity evaluation of Phosflex 31 P in an in vitro cytogenetic assay measuring sister chromatid exchange and chromosomal aberrations. Conducted for Stauffer Chemical Company. Cited in IUCLID 2001

Litton Bionetics Inc. 1979c. Mutagenicity evaluation of phosflex 31 P in the Ames Salmonella microsome plate test. Conducted for Stauffer Chemical Company. Cited in IUCLID 2001

Litton Bionetics Inc. 1979d. Mutagenicity evaluation of Phosflex 31 P in the mouse lymphoma forward mutation assay. Conducted for Stauffer Chemical Company. Cited in IUCLID 2001

Liu X, Ji K, Choi K. 2012. Endocrine disruption potentials of organophosphate flame retardants and related mechanisms in H295R and MVLN cell lines and in zebrafish. *Aquat Toxicol* 114–115:173–181.

Liyasova M, Li B, Schopfer LM et al. 2011. Exposure to tri-o-cresyl phosphate detected in jet airplane passengers. *Toxicol Appl Pharmacol* 256:337–347.

Lombardo P, Egry IJ. 1979. Identification and gas-liquid chromatographic determination of aryl phosphate residues in environmental samples. *J AOAC Int* 62:47–51. [cited in WHO 1990, UK EA 2009].

Mackereer CR, Barth ML, Kreuger AJ, Chawla B, Roy T.A. 1999. Comparison of neurotoxic effects and potential risks from oral administration of ingestion of jet engine lubricants. *J Toxicol Environ Health* 57:293–328.

Marhold, JV. 1972. Collection of results of toxicological assessments of compounds and formulations tested at the Department of Toxicology, Research Institute for Organic Synthesis, Prague, Institute for Management Training in the Chemical industry. (cited in IPCS 1990).

Marklund A, Andersson B, Haglund P. 2005. Traffic as a Source of Organophosphorus Flame Retardants in Snow. *Environ Sci Technol* 39:3555–3562.

Martínez-Carballo E, González-Barreiro C, Sitka A, Scharf S, Gans O. 2007. Determination of selected organophosphate esters in the aquatic environment of Austria. *Sci Total Environ* 388:290–299.

Marzulli FN, Callahan JF, Brown DW. 1965. Chemical structure and skin penetrating capacity of a short series of organic phosphates and phosphoric acid. *J Invest Dermatol* 44:339–344. (cited in Sjögren et al. 2010)

Mayer FL Jr., Ellersieck MR. 1986. *Manual of Acute Toxicity: Interpretation and Data Base for 410 Chemicals and 66 Species of Freshwater Animals*. Resource Publication No. 160, U.S. Department of Interior, Fish and Wildlife Service, Washington, DC. 505 p.

Mele JM, Jensh RP. 1977. Teratogenic effects of orally administered tri-ocresyl phosphate on Wistar albino rats. *Teratology* 15:32A. [cited in IPCS 1990, UK EA 2009]

Michaelis S. 2002. Aircraft cabin fumes: an aviation safety issue. *J Occup Health Safety* – Aust NZ 18(4):291–294.

Midwest Research Institute. 1977. *Assessment of the Need for the Character of and the Impact Resulting from Limitations on Aryl Phosphates*, MRI 4309-L. Midwest Research Institute, Kansas City, Mo., 279 p. [cited in ChemFate 2012, US EPA 2010].

Mirsalis, J. et al. 1985. *Environmental Mutagenesis*, 5:482. Cited in EA 2009

Mobil Oil Corporation. 1987. Determination of the effects of tritolyl phosphate (tricresyl phosphate, Stock 955) on rat serum, erythrocyte and brain cholinesterase activities. Study # 61739. Obtained from ECCC 2001

Mobil Oil Corporation (1990). *Final Report: The Effect of a Generic Jet Engine Oil Formulation on Serum Cholinesterase (ChE) Activity in Female Sprague Dawley Rats Following Two Weeks of Dermal Administration: Range-Finding Study* prepared by Mobil Environmental and Health Science Laboratory. Study # 63114. Obtained from ECCC 2001.

Mobil Oil Corporation (1991e). *Male reproductive toxicity assessment following a fourteen-day oral exposure to Stock 955 in F344 and Long Evans Rats–Range Finding Study*. Study # 64240. Obtained from ECCC 2001.

Mobil Oil Corporation (1992b). *Reproductive toxicity assessment in male F344 rats following a 10-week oral exposure to generic jet engine oil formulations*. Study # 64972. Obtained from ECCC 2001.

[MOE Japan] Japan Ministry of Environment. 2003. *Surveyed Chemical Substances and their Detected Levels in the Environment (A Cumulative List for Fiscal Year 1974 – 1998)*. [cited 2013 June 14]. Available: <http://www.env.go.jp/chemi/kurohon/en/http1998e/cie1998.pdf>

Morrissey RE, Schwetz BA, Lamb JC IV, Ross MD, Teague JL, Morris RW. 1988a. Evaluation of rodent sperm, vaginal cytology, and reproductive organ weight data from

National Toxicology Program 13-week study. *Fundam Appl Toxicol* 11:343—358 (cited in IPCS 1990).

Modern Plastics Encyclopedia. 1975. *International Advertising Supplement* 52(10A), New York, McGraw-Hill Inc. p 697. [cited in IPCS 1990].

[MPBPVP] Melting Point Boiling Point Program for Microsoft Windows [Estimation Model]. 2010. Version 1.43. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. [cited 2014 January]. Available from: [www.epa.gov/oppt/exposure/pubs/episuite.htm](http://www.epa.gov/oppt/exposure/pubs/episuite.htm)

MPI Research Inc. 2004. An oral prenatal developmental toxicity study of tricresyl phosphate in rats. Study# 1038-003. Obtained from ECCC 2013-2014 Muir DCG, Yarechewski AL, Grift NP. 1983. Environmental dynamics of phosphate esters. III. Comparison of the bioconcentration of four triaryl phosphates by fish. *Chemosphere* 12:155–166.

Muir, DCG. 1984. Phosphate esters. In: Hutzinger, O., ed. *The handbook of environmental chemistry*, Berlin, Heidelberg, New York, Tokyo, Springer-Verlag, Vol. 3, Part C, pp. 41–66. [cited in UK EA 2009, WHO 1990]

Muir DCG, Lint D, Grift, NP. 1985. Fate of three phosphate ester flame retardants in small ponds. *Environ Toxicol Chem* 4:663–675.

Myers DK, Rebel JBJ, Veeger D, Kemp A, Simons EGL. 1955. Metabolism of triaryl phosphates in rodents. *Nature (London)*, 176, 259–260. [cited in IPCS 1990]

[NCI] National Chemical Inventories [database on CD-ROM]. 2013. Issue 1. Columbus (OH): American Chemical Society. [cited yr mon date]. Available from: <http://www.cas.org/products/cd/nci/index.html>

New York University 1951. Bellevue Medical Centre April 10, 1951. Data from Exxon Research and Engineering Company, NTIS OTS 206104. [cited in EA 2009]

[NICNAS] National Industrial Chemicals Notification and Assessment Scheme, 2008. Priority Existing Chemicals Program Candidate List of Chemicals (as of Jan 2008) [Internet]. Commonwealth of Australia. [cited June 2013]. Available from: [http://www.nicnas.gov.au/industry/Existing\\_Chemicals/Candidate\\_List/Candidate\\_List\\_Jan2008\\_PDF.pdf](http://www.nicnas.gov.au/industry/Existing_Chemicals/Candidate_List/Candidate_List_Jan2008_PDF.pdf)

[NITE] National Institute of Technology and Evaluation database [database on the Internet]. 2002. Biodegradation and Bioaccumulation of the Existing Chemical Substances under the Chemical Substances Control Law. Available online from: [http://www.safe.nite.go.jp/english/kizon/KIZON\\_start\\_hazkizon.html](http://www.safe.nite.go.jp/english/kizon/KIZON_start_hazkizon.html) as of May 05, 2010.

[cited in US EPA 2010].

[NITE] National Institute of Technology and Evaluation database [database on the Internet]. 2008. [cited 2013 July 29] Available from: [www.safe.nite.go.jp](http://www.safe.nite.go.jp)

NOMO5. 1987. Programs to Enhance PC-Gems Estimates of Physical Properties for Organic Compounds. The Mitre Corp. [cited in US EPA 2010].

Norris P, Storrs F J. 1990. Allergic contact dermatitis to adhesive bandages. *Dermatologic Clinics* 8:147–152. [cited in IUCLID 2001]

[NPRI]. National Pollutant Release Inventory. 2011. Available from: <http://www.ec.gc.ca/inrp-npri/default.asp?lang=en&n=0EC58C98->

NTP (National Toxicology Program). 1994. Toxicology and carcinogenesis studies of tricresyl phosphate (CAS No. 1330-78-5) in F344/N rats and B6C3F<sub>1</sub> mice (gavage and feed studies). Research Triangle Park, North Carolina, National Toxicology Program (Technical Report Series No. 433, PB 95-227377).

[OECD] Organisation for Economic Co-operation and Development. 2005. Manual for Investigation of HPV Chemicals. Annex 1: Guidance for Completing a SIDS Dossier. [Internet]. Paris (FR): OECD, Environment Directorate.

[OECD] Organisation for Economic Co-operation and Development. 2009. Emission scenario document on plastics additives [Internet]. Paris (FR): OECD, Environment Directorate. (Series on Emission Scenario Documents No. 3). Report No.: ENV/JM/MONO(2004)8/REV1. JT03267870. [cited 2014 October]. Available from: [www.oecd.org/chemicalsafety/assessmentofchemicals/publicationsonchemicalsexposureassessment.htm](http://www.oecd.org/chemicalsafety/assessmentofchemicals/publicationsonchemicalsexposureassessment.htm)

OECD QSAR Toolbox. [Read-across tool]. 2012. Version 3.0. Paris (FR): Organisation for Economic Co-operation and Development, Environment Directorate. Available from : [www.oecd.org/document/23/0,3343,en\\_2649\\_34379\\_33957015\\_1\\_1\\_1\\_1,00.html](http://www.oecd.org/document/23/0,3343,en_2649_34379_33957015_1_1_1_1,00.html)

Okazaki ME, D'Souza A, Antika S. 2003. United States Patent No. 6,649,080 B2 Phosphate ester base stocks and aircraft hydraulic fluids comprising the same. <http://ip.com/patent/US6649080> [cited in Schindler et al. 2014]

Oishi H, Oishi S, Hiraga K. 1982. Toxicity of several phosphoric acid esters in rats. *Toxicol Lett* 13:29–34 (cited in IPCS 1990).

[PhysProp] Interactive PhysProp Database [database on the Internet]. 2012. Syracuse (NY): Syracuse Research Corporation. [cited 2013 June 6] Available from: <http://www.syrres.com/esc/physdemo.htm>

Piccirillo , VJ. 1999. Flame-retardant product chemistries, toxicology and hazard evaluations. NPC Inc., Sterling, VA. [cited in NRC 2000]

Quintana JB, Rodil S, Lopez-Mahia P, Muniategui-Lorenzo S, Prada-Rodriguez D. 2007. Optimisation of a selective method for the determination of organophosphorus triesters in outdoor particulate samples by pressurised liquid extraction and large-volume injection gas chromatography–positive chemical ionisation–tandem mass spectrometry. *Anal Bioanal Chem* 388:1283–1293.

Repke VL, Shepherd RC. 1980. United States Patent 4193404. Stretchable and Comfortable pad. Johnson & Johnson (New Brunswick, NJ), Appl. No, 05/896,841. Filed April 17, 1978. Available from: <http://patents.com/us-4193404.html>

Ricking M, Schwarzbauer J, Franke S. 2003. Molecular markers of anthropogenic activity in sediments of the Havel and Spree Rivers (Germany). *Water Research* 37:2607–2617.

Saeger VW, Hicks O, Kaley RG, Michael PR, Mieure JP, Tucker ES. 1979. Environmental fate of selected phosphate esters. *Environ Sci Technol* 13(7):840-844.

Saito C, Kato T, Taniguchi H, Fujita T, Wada H, Mori Y. 1974. Subacute toxicity of tricresylphosphate (TCP) in rats. *Pharmacometrics*, 8:107–118 (cited in IPCS 1990).

Sample BE, Opresko DM, Suter II GW. 1996. Toxicological Benchmarks for Wildlife: 1996 Revision. Health Sciences Research Division, Oak Ridge Tennessee. Submitted to United States Department of Energy. Contract No. DE-AC05-84OR21400.

Sax NI, Lewis RJ Sr. (eds.). 1987. *Hawley's Condensed Chemical Dictionary*. 11th ed. New York: Van Nostrand Reinhold Co. p. 1178. [cited in HSDB 2012]

Schenker U, MacLeod M, Scheringer M, Hungerbuhler K. 2005. Improving data quality for environmental fate models: A least-squares adjustment procedure for harmonizing physicochemical properties of organic compounds. *Environ Sci Technol* 39: 8434-8441.

Scheringer M, MacLeod M, Wegmann F. 2009. The OECD Pov and LRTP Screening Tool, Version 2.2, A manual for the OECD Pov and LRTP Screening Tool 2.2 that is a follow-up version of the software POPorNot 1.0 distributed at the OECD/UNEP Workshop on Application of Multimedia Models for Identification of Persistent Organic Pollutants. ETH Zurich, April 2009. Version 2.2 fixed a bug introduced by changes in Excel 2007. (reference provided by Marie-Claud Sauve)

Schindler BK, Weiss T, Schütze A, Koslitz S, Broding HC, Bünger J, Brüning T. 2013. Occupational exposure of air crews to tricresyl phosphate isomers and organophosphate flame retardants after fume events. *Arch Toxicol* 87(4):645–648.

Schindler BK, Koslitz S, Weiss T, Broding HC, Brüning T, Bünger J. 2014. Exposure of aircraft maintenance technicians to organophosphates from hydraulic fluids and turbine oils: a pilot study. *Int J Hyg Environ Health* 217(1):34–37.

Senanayake N, Jeyaratnam J. 1981. Toxic polyneuropathy due to gingili oil contaminated with tri-cresyl phosphate affecting adolescent girls in Sri Lanka. *Lancet* 10: 88–89 (cited in IPCS 1990).

SinoHarvest, 2011. Tricresyl phosphate (TCP) [Internet]. Shanghai, China. [cited June 2013]. Available from: <http://www.sinoharvest.com/products/Tricresyl-phosphate.shtml>  
<http://www.sinoharvest.com/products/Tricresyl-phosphate.shtml>

Sitthichaikasem S. 1978. Some toxicological effects of phosphate esters on rainbow trout and bluegill. Dissertation, Iowa State University, University Microfilms 7813246 (cited in Zitko 1980). [cited in UK EA 2009]

Sjögren B, Iregren A, Järnberg J. 2010. The Nordic Expert Group for Criteria Documentation of Health Risks from Chemicals. 143. Phosphate triesters with flame retardant properties. *Arbete och Hälsa* 2010; 44(6):1–220.

Solbu K, Daae HL, Thorud S, Ellingsen DG, Lundanes E, Molander P. 2010. Exposure to airborne organophosphates originating from hydraulic and turbine oils among aviation technicians and loaders. *J Environ Monit* 12:2259–2268.

Somkuti SC, Lapadula DM, Chapin RE, Lamb JC IV, Aboudonia MB. 1987a. Reproductive tract lesions resulting from subchronic administration (63 days) of tri-o-cresyl phosphate in male rats. *Toxicol Appl Pharmacol* 89:49–63. [cited in UK EA 2009, IPCS 1990].

Somkuti SC, Lapadula DM, Chapin RE, Lamb JC IV, Aboudonia MB. 1987b. Time course of the tri-o-cresyl phosphate-induced testicular lesion in F-344 rats: enzymatic, hormonal, and sperm parameter studies. *Toxicol Appl Pharmacol* 89:64–72. [cited in UK EA 2009, IPCS 1990].

Stauffer Chemical Company. (1979). Acute inhalation toxicity of Phosflex 31 P in albino rats. study No. T-6682. Cited in IUCLID 2001.

Stauffer Chemical Company. (1988) Test procedures and data summaries for t-butyl phenyl phosphate, tricresyl phosphate, trixylenyl phosphate, mixed triaryl phosphate and isopropyl phenyl diphenyl. (Personal communication as cited in IPCS 1990).

Stumpf AM, Tanaka D, Jr., Aulerich RJ, Bursian SJ. 1989. Delayed neurotoxic effects of tri-o-tolyl phosphate in the European ferret. *J Toxicol Environ Health* 26:61–73.

Sumitomo Chemical Company. 1974. Pharmaceuticals Division Report, Tests of the

subacute toxicity of tricresylphosphate in rats. [cited in IUCLID 2001]

Sundkvist AM, Olofsson U, Haglund P. 2010. Organophosphorus flame retardants and plasticizers in marine and fresh water biota and in human milk. *J Environ Monitor* 12: 943–951.

Takimoto K, Hirakawa T, Ito K, Mukai T, Okada M. 1999. Source and transport of tricresyl phosphate (TCP) isomers in Kurose river basin. *Atmos Environ* 33:3191–3200.

[TaPL3] Long Range Transport and Persistence Level III model [Internet]. 2003. Version 3.00. Peterborough (ON): Trent University, Canadian Environmental Modelling Centre. Available from: <http://www.trentu.ca/academic/aminss/envmodel/models/TaPL3.html>

Tocco DR, Randall JL, York, RG, Smith MK. 1987. Evaluation of the teratogenic effects of tri-ortho-cresyl phosphate in the Long-Evans hooded rat. *Fund Appl Toxicol* 8(3):291-297. [cited in UK EA 2009, IPCS 1990].

Tollbäck J, Tamburro D, Crescenzi C, Carlsson H. 2006. Air sampling with Empore solid phase extraction membranes and online single-channel desorption/liquid chromatography/mass spectrometry analysis: determination of volatile and semi-volatile organophosphate esters. *J Chromatogr A* 1129:1– 8. [cited in van der Veen and de Boer 2012].

[TOPKAT] Toxicity Prediction by Komputer Assisted Technology [Internet]. 2004. Version 6.2. San Diego (CA): Accelrys Software Inc. Available from: <http://www.accelrys.com/products/topkat/index.html>

[UK EA] United Kingdom Environmental Agency. 2009. Environmental risk evaluation report: Tricresyl phosphate (CAS no. 1330-785) [Internet]. Bristol (UK): UK Environmental Agency. [cited 2013 June 6] Available from: <http://a0768b4a8a31e106d8b0-50dc802554eb38a24458b98ff72d550b.r19.cf3.rackcdn.com/scho0809bquj-e-e.pdf>

UNEP Publications. 1998. Triethyl Phosphate Case No.: 78-40-0. SIDS Initial Assessment Report. For SIAM 5, Organisation for Economic Co-operation and Development (OECD), Geneva, Switzerland, pp. 1–18 (October). [cited in van der Veen and de Boer 2012].

[US CPSC] US Consumer Product Safety Commission. 1998. Post-hearing comments of the Upholstered Furniture Action Council on the toxicity of flame retardants chemical treatments for upholstery fabrics. Washington (DC). Available from: <http://www.cpsc.gov/PageFiles/80024/uphlfsn2.pdf>

[US EPA] US Environmental Protection Agency. 1993. Wildlife Exposure Factors Handbook. Washington (DC): US EPA, Office of Research and Development

[US EPA] US Environmental Protection Agency. 2010. HPV Chemical Hazard Characterizations, Screening-level hazard characterization, Phosphoric acid, trimethylphenyl ester [Internet]. Washington (DC): U.S. EPA, Office of Pollution Prevention and Toxics. [cited 2013 June 6] Available from: [http://iaspub.epa.gov/oppthpv/hpv\\_hc\\_characterization.get\\_report](http://iaspub.epa.gov/oppthpv/hpv_hc_characterization.get_report)

[US FDA] US Food and Drug Administration. 2006. Total Diet Study Market Baskets 1991-3 through 2003-4. College Park (MD): Center for Food Safety and Applied Nutrition. Available from: <http://www.fda.gov/downloads/Food/FoodScienceResearch/TotalDietStudy/UCM184304.pdf>

[US FDA] US Food and Drug Administration. 2014. Total Diet Study. [Internet]. Silver Spring (MD): US Food and Drug Administration. Available from: <http://www.fda.gov/Food/FoodScienceResearch/TotalDietStudy/default.htm>

[US FWS] US Fish and Wildlife Service. 1980. Handbook of Acute Toxicity of Chemicals to Fish and Aquatic Invertebrates. [Internet]. Washington (DC): US Government Printing Office. p. 79. [cited 2013 June 6]. Available from: <http://www.cerc.usgs.gov/pubs/center/pdfDocs/90301.pdf>

Van den Eede N, Dirtu AC, Neels H, Covaci A. 2011. Analytical developments and preliminary assessment of human exposure to organophosphate flame retardants from indoor dust. *Environ Int* 37(2):454–461.

Van den Eede N, Dirtu AC, Ali N, Neels H, Covaci A. 2012. Multi-residue method for the determination of brominated and organophosphate flame retardants in indoor dust. *Talanta* 89:292–300

van der Veen I, de Boer J. 2012. Phosphorus flame retardants: Properties, production, environmental occurrence, toxicity and analysis. *Chemosphere*: 88:1119-1153.

van den Dikkenberg RP, Canton HH, Mathijssen-Spiekman LAM, Roghair CJ. 1989. Usefulness of *Gasterosteus aculeatus* – the three-spined stickleback – as a test organism in routine toxicity tests. Report 718625003, Rijksinstituut Voor Volksgezondheid en Milieuhygiene, Biltoven, the Netherlands, 28.

van Netten C. 2008. Design of a small personal air monitor and its application in aircraft. *Sci Total Environ* 407:1206–1210.

Veith GD, Defoe DL, Bergstedt BV. 1979. Measuring and estimating the bioconcentration factor of chemicals in fish. *J Fish Res Board Can* 36:1040–1048.

Wakabayashi, A. 1980. Environmental pollution caused by organophosphoric fireproofing plasticizers. Annual Report Tokyo Metropolitan Research Institute of



Environmental Protection 11:110–113 (in Japanese) [cited in IPCS 1990].

Wang X-W, Liu J-F, Yin Y-G. 2011. Development of an ultra-high-performance liquid chromatography–tandem mass spectrometry method for high throughput determination of organophosphorus flame retardants in environmental water. *J Chromatogr A* 1218:6705– 6711.

Weil, ED. 1993. Flame retardants (Phosphorus). *Kirk-Othmer Encyclopedia of Chemical Technology*, Volume 10, Fourth Edition, pp 976-998. John Wiley and Sons, Inc., 1993. [cited in UK EA 2009].

Wensing M, Uhde E, Salthammer T. 2005. Plastics additives in the indoor environment – flame retardants and plasticizers. *Sci Total Environ* 339:19 – 40.

Westat, Inc. 1987. National Usage Survey of Household Cleaning Products. Prepared for U.S. EPA, Office of Toxic Substances. EPA Contract No. 68-02-42431987. WHO. 1998. EHC 209: Flame Retardants: Tris-(Chloropropyl)Phosphate and Tris-(2-Chloroethyl)phosphate, Geneva, Switzerland. [cited in van der Veen and de Boer 2012].

WHO. 1990. Flame retardants: Tricresyl phosphate. *Environmental Health Criteria* 110. World Health Organization, Geneva.

Wildlife International Ltd. 2002. Technical information and safety data sheet for Kronitex TCP [cited in UK EA 2009].

Wong PTS, Chau YK. 1984. Structure-toxicity of triaryl phosphates in freshwater algae. *Sci Total Environ* 32:157-165.

Woudneh MB, Benskin JP, Wang G, Grace R, Hamilton MC, Cosgrove JR. 2015. Quantitative determination of 13 organophosphorous flame retardants and plasticizers in a wastewater treatment system by high performance liquid chromatography tandem mass spectrometry. *J Chromatography A* 1400:149-155.

Yasuda H. 1980. Concentration of organic phosphorus pesticides in the atmosphere above the Dogo plain and Ozu basin. *J Chem Soc Jpn* 1980(4): 645–653 (in Japanese). [cited in WHO 1990]

## Appendix A: Half-life and physical and chemical property values used in Level III fugacity modelling for Phosphoric acid, tris(methylphenyl) ester) (CAS RN 1330-78-5)

Half-life and physical and chemical property values used in Level III fugacity modelling for Phosphoric acid, tris(methylphenyl) ester) (CAS RN 1330-78-5)

Environmental Media	Half-Life (hours)	Reference
Air	18.74	EPI Suite 4.10 2012
Water <sup>a</sup>	1029	EPI Suite 4.10 2012
Soil <sup>a</sup>	1029	EPI Suite 4.10 2012
Sediment	4116	EPI Suite 4.10 2012
Molar mass	368.37 g/mol	
Data temperature	25 °C	
Water solubility	0.36 mg/L	Saeger et al. 1979
Vapour pressure	6.6 x 10 <sup>-5</sup> Pa (at 25 °C)	UK EA 2009 (extrapolated)
Log K <sub>ow</sub>	5.11	Saeger et al. 1979
Melting point	-33°C	US EPA 2010 (Midwest Research Institute, 1977)
Log K <sub>aw</sub>	-4.564	Calculated from the Henry's Law to K <sub>aw</sub> conversion and Scale.xls <sup>b</sup>
K <sub>aw</sub>	2.729 x 10 <sup>-5</sup>	
Henry's Law Constant	0.0675 Pa-m <sup>3</sup> /mol	Calculated from the Henry's Law to K <sub>aw</sub> conversion and Scale.xls <sup>c</sup>
Log K <sub>oc</sub>	3.5253	KOCWIN v2.00 2010 <sup>d</sup>
K <sub>oc</sub>	3351.97	
Log K <sub>oa</sub>	9.591	KOAWIN v. 1.10 2010 <sup>e</sup>
K <sub>oa</sub>	3.90 x 10 <sup>9</sup>	

<sup>a</sup> Half-life values for water, soil, and sediment are scaled 1:1:4, respectively (i.e. the sediment half-life is four times that of water) based on the Boethling extrapolation approach (Boethling et al. 1995) as recommended by Environment and Climate Change Canada (2003).

<sup>b</sup> using empirical Ws = 0.36 mg/L and VP=6.6E-05 Pa at 25 °C as input

<sup>c</sup> using empirical Ws=0.36 mg/L and VP=6.6E-05 Pa at 25 °C as input

<sup>d</sup> with inputs of log K<sub>ow</sub>=5.11+MP=-33°C+Ws=0.36 mg/L

<sup>e</sup> log K<sub>ow</sub>=5.11+MP=-33°C+VP=3.5E+05 Pa+Ws=0.3 mg/L

## Appendix B: Ecological risk quotient analysis of TCP

### Summary of data used in the ecological risk quotient analysis of TCP

Parameters	Pelagic organisms	Soil organisms	Fish-consuming wildlife (Mink) <sup>h</sup>	Fish-consuming wildlife (River Otter) <sup>h</sup>
<b>Predicted exposure concentration (PEC)</b>	7.27 x 10 <sup>-8</sup> to 2.70 x 10 <sup>-6</sup> mg/L	0.045 mg/kg-bw/day <sup>c</sup> (TDI; standardized to 2% OC)	0.0010 mg/kg-bw/day (TDI)	0.0008 mg/kg-bw/day (TDI)
<b>Critical toxicity value (CTV)</b>	0.0013 mg/L <sup>a</sup>	5.3 mg/kg-bw/day <sup>d</sup>	5.3 mg/kg-bw/day <sup>d</sup>	5.3 mg/kg-bw/day <sup>d</sup>
<b>Application factor</b>	3 <sup>b</sup>	10 <sup>e</sup>	10 <sup>e</sup>	10 <sup>e</sup>
<b>Predicted no-effects concentration (PNEC)</b>	0.00043 mg/L	1.259 mg/kg-bw/day <sup>f</sup> (TRV)	0.39 mg/kg-bw/day <sup>f</sup> (TRV)	0.237 mg/kg-bw/day <sup>f</sup> (TRV)
<b>Risk quotient (PEC/PNEC)</b>	0.0002 to 0.006	0.036 <sup>g</sup>	0.0026 <sup>g</sup>	0.0032 <sup>g</sup>

Notes:

<sup>a</sup> Van den Dikkenberg et al. (1989) (also cited in UK EA 2009) 0.0013 mg/L for 35-day EC<sub>50</sub> for early life stage (after 4-week-old fish stage) mortality.

<sup>b</sup> Application factor of 3 for species sensitivity would be 3 because, although there are a lot of data, the chronic data only covers two categories: vertebrates and invertebrates (not primary producers). Therefore, the AF = 1 x 3 = 3.

<sup>c</sup> BASL4

Due to the lack of measured data, PEC was calculated using the BASL4 model (BASL4 2011). To examine potential impacts from long-term application, an application time period of 10 consecutive years was considered. The calculation considered a maximum application rate of 8300 kg dw/ha per year (based on the highest existing provincial regulatory limit) with a mixing depth of 0.1 m (default value for BASL4) and a soil density of 1487 kg/m<sup>3</sup> (default value for BASL4). The maximum biosolid concentration for TCP in Canada based on exposure analysis was 0.44 mg/kg. The figure of 0.44 mg/kg dw was used as the Csludge in the calculation. Soil half-life = 42.87 days.

This generates a mammal uptake rate, at the maximum of the last year of data (0.061 mg/kg-bw/day at 2.7% OC),

which can be compared to a toxic reference intake value. After standardizing to 2% OC, the TDI is 0.045 mg/kg-bw/day.

<sup>d</sup> Geomean of NOAEL and LOAEL values (geomean of 4 mg/kg-bw/day and 7 mg/kg-bw/day) from NTP (1994).

<sup>e</sup> To derive the wildlife PNEC for TCP, an application factor of 10 is applied to the TRV to account for extrapolation from laboratory to field conditions.

<sup>f</sup> TRV – total reference value

Due to the lack of data for wildlife species, the CTV is based on a Wildlife Toxicity Reference Value (TRV) (Sample et al. 1996), determined from the Wildlife Exposure Model, where potential effects in rodents for TCP (NTP 1994) are normalized to typical body weight of Mink, *Mustela vison*, a surrogate wildlife species:

$$TRV = MATC_{ts} \times (BW_{ts}/BW_{fs})$$

where:

TRV<sub>e</sub> = total reference value (mg/kg-bw/day)

MATC<sub>ts</sub> = maximum allowable toxicant concentration for test species (mg/kg-bw/day), MATC= Geomean of NOAEL and LOAEL for test species. A LOAEL of 7 mg/kg-bw/d and NOAEL of 4 mg/kg-bw/d (NTP 1994), were selected to determine a TRV for the evaluation of potential effects in wildlife. This endpoint was considered relevant, based upon a 2-year feed study in female rats (see Health Assessment Section (NTP 1994))

BW<sub>ts</sub> = mean body weight of test species (kg); BW<sub>ts</sub> = 0.32 kg (mean for NOAEL and LOAEL rat weight, NTP 1994)

(the body weights of female rats started with a mean of 91 g (91, 91, 92, 90 g for four respective different concentrations of TCP in feeds) in the first week of the study, and ended with a mean of 320 g (315, 320, 332, 313 g for four respective different concentrations of TCP in feeds) in the 104<sup>th</sup> week of the study.)

BW<sub>fs</sub> = body weight of focal species (kg) = weight = density/volume = (1 g/cm<sup>3</sup>) x (10 cm<sup>3</sup>) = 10 g = 0.01 kg; = 0.01 (Shrew) (US EPA 1993).

<sup>g</sup> Risk Quotient = TDI/TRV

<sup>h</sup> Wildlife Exposure Model and Toxicity Equations

The wildlife exposure is based on Total Daily Intake (TDI) for Mink (*Mustela vison*) and River Otter (*Lontra canadensis*) consuming fish, determined from Wildlife Exposure Model (US EPA 1993), where

$$TDI = [FMR (C_i \times ED \times P_i / GE_i \times AE_i) + (C_s \times IR_s) + (C_w \times IR_w)] \times P_t$$

where:

- TDI = total daily intake (mg/kg-bw/day)
- FMR = free-living metabolic rate of wildlife receptor of interest; In this assessment, it is assumed FMR = 235 kcal/kg-bw/day for Mink and 179 kcal/kg-bw/day for River Otter.
- C<sub>i</sub> = concentration of contaminant in the i<sup>th</sup> prey species (mg/kg) = C<sub>w</sub> x BCF; determined as C<sub>i</sub> = 0.0056 mg/kg-bw (default), representing highest published TCP concentration in Canadian fish sample (northern pike liver) (Houde et al. 2014)
- P<sub>i</sub> = proportion of the i<sup>th</sup> prey species in the diet (unitless); 0.85 for Mink and 0.84 for River Otter
- To be conservative it is assumed that approximately up to 100% of the diet of Mink and River Otter is fish: P<sub>i</sub> = 1.0
- GE<sub>i</sub> = gross energy of the i<sup>th</sup> prey species (850 kcal/kg prey) 5th percentile used for conservative value; GE<sub>i</sub> = 1177
- AE<sub>i</sub> = assimilation efficiency of the i<sup>th</sup> prey species by the wildlife receptor; AE<sub>i</sub> = 0.94 (Mink and River Otter). Default value
- C<sub>s</sub> = concentration of contaminant in the sediments (mg/kg dw); It is assumed that TCP exposure via sediment is negligible; C<sub>s</sub> = 0
- IR<sub>s</sub> = intake rate of sediments (kg dw/kg-bw/day); It is calculated that incidental sediment ingestion is zero IR<sub>s</sub> = 0.006 (Mink), 0.001 (River Otter)

- $C_w$  = concentration of contaminant in the water (mg/L); 2.7 ng/L, which is the highest measured total TCP concentration from exposure analysis, was selected to represent a potential regional water concentration (exposure section);  $C_w = 2.7 \times 10^{-6}$  mg/L for both Mink and River Otter.
- $IR_w$  = intake rate of water (L/day); Assumed to be 10%;  $IR_w = 0.1064$  (Mink), 0.642 (River Otter)
- $P_t$  = proportion of the time the receptor spends in the contaminated area.  $P_t = 1$  (Mink and River Otter)

A description and definition of each variable in the above equation can be found in US EPA (1993).

Due to the lack of data for wildlife species, the CTV is based on a Wildlife Toxicity Reference Value (TRV) (Sample et al. 1996), determined from the Wildlife Exposure Model, where potential effects in rodents for TCP (NTP 1994) are normalized to typical body weight of Mink, *Mustela vison*, a surrogate wildlife species:

$$TRV_s = MATC_{ts} \times (BW_{ts}/BW_{fs})$$

where:

$TRV_e$  = total reference value (mg/kg-bw/day)

$MATC_{ts}$  = maximum allowable toxicant concentration for test species (mg/kg-bw/day),  $MATC$  = Geomean of NOAEL and LOAEL for test species. A LOAEL of 7 mg/kg-bw/d and NOAEL of 4 mg/kg-bw/d (NTP 1994), were selected to determine a TRV for the evaluation of potential effects in wildlife. This endpoint was considered relevant, based upon a 2-year feed study in female rats (see Health Assessment Section (NTP 1994))

$BW_{ts}$  = mean body weight of test species (kg);  $BW_{ts} = 0.32$  kg (mean for NOAEL and LOAEL rat weight, NTP 1994)

(the body weights of female rats started with a mean of 91 g (91, 91, 92, 90 g for four respective different concentrations of TCP in feeds) in the first week of the study, and ended with a mean of 320 g (315, 320, 332, 313 g for four respective different concentrations of TCP in feeds) in the 104<sup>th</sup> week of the study)

$BW_{fs}$  = body weight of focal species (kg); =1.08 (Mink); 7.98 (River Otter) (US EPA 1993)

Risk Quotient =  $TDI/TRV$

## Appendix C: Weight of Evidence in the Ecological Risk Assessment

Major lines of evidence and weight assigned in the ecological risk assessment on TCP

Evidence	Data uncertainty <sup>a</sup>	Strength of inference <sup>b</sup>	Relevance / Impact <sup>c</sup>	Weight assigned <sup>d</sup>	Comment
Physical and chemical properties	High	Low	Low	Low	Used as input for fate (EQC model, persistence, BCF, BAF models), effects, exposure and risk quotients models (modelled BAF)
Persistence	High	Low	Low	Low	Does not meet persistence criteria
Bio-accumulation	High	Low	Low	Low	Model estimates; not support of meeting bioaccumulation regulation
Effects (PNEC, TRV)	Moderate – High	Low–Moderate	Low–Moderate	Low–Moderate (+)	Empirical data, BASAL4 model used and wildlife model used
Exposure analysis (PEC, TDI)	Moderate–High	Low–Moderate	Low–Moderate	Low–Moderate (++)	Empirical data, BASAL4 model used and wildlife model used
Risk	High	Low	Low	Low	Model estimates only; not support of meeting 64 (a) or (b)

<sup>a</sup> Considers data quality, quantity and consistency

<sup>b</sup> Ability to infer truth from the data given the level of uncertainty and power of the data

<sup>c</sup> Describes how relevant the data are scientifically and to this regulatory assessment

<sup>d</sup> Final weight assigned to a line of evidence which is a function of the outcomes assigned to the Strength of Inference and Relevancy

## Appendix D: Upper-bounding estimates of daily intake (µg/kg-bw/d) of TCP by various age groups within the general population of Canada

Route of exposure	0–6 mo <sup>a</sup> Breastfed <sup>b</sup>	0–6 mo Formula-fed <sup>c</sup>	0–6 mo Not Formula-fed <sup>d</sup>	0.5–4 yr <sup>e</sup>	5–11 yr <sup>f</sup>	12–19 yr <sup>g</sup>	20–59 yr <sup>h</sup>	≥60 yr <sup>i</sup>
Ambient air <sup>j</sup>	3.5E-06	3.5E-06	3.5E-06	7.5E-06	5.8E-06	3.3E-06	2.9E-06	2.5E-06
Indoor air <sup>k</sup>	2.5E-05	2.5E-05	2.5E-05	5.3E-05	4.1E-05	2.3E-05	2.0E-05	1.7E-05
Drinking water <sup>l</sup>	N/A	6.4E-03	2.4E-03	2.7E-03	2.1E-03	1.2E-03	1.3E-03	1.3E-03
Food <sup>m</sup>	1.3E-02	NI	NI	4.7E-03	3.8E-03	2.2E-03	2.1E-03	1.3E-03
Dust <sup>n</sup>	9.0E-02	9.0E-02	9.0E-02	4.7E-02	1.8E-02	6.6E-04	6.2E-04	6.1E-04
Soil <sup>o</sup>	0.0E+00	0.0E+00	0.0E+00	2.7E-07	2.0E-07	7.1E-09	6.8E-09	6.3E-09
<b>Total intake</b>	<b>1.0E-01</b>	<b>9.6E-02</b>	<b>9.2E-02</b>	<b>5.4E-02</b>	<b>2.4E-02</b>	<b>4.1E-03</b>	<b>4.0E-03</b>	<b>3.3E-03</b>

Abbreviations: N/A, not applicable; NI, data not identified in the literature; mo, months; yr, years.

<sup>a</sup> Assumed to weigh 7.5 kg, to breathe 2.1 m<sup>3</sup> of air per day (Health Canada 1998), and to ingest 38 and 0 mg of dust and soil per day, respectively (Wilson et al. 2013).

<sup>b</sup> Exclusively for breastfed infants, assumed to consume 0.742 L of breast milk per day, and breast milk is assumed to be the only dietary source. No monitoring of TCP in breast milk in Canada was identified. The concentration for whole breast milk of 0.13 µg/L was based on a reported 3.7 ng/g lipid x 3.4% (lipid content of breast milk) x 1.03 g/mL (density of breast milk) identified in 69 samples of human breast milk collected in 1997 in Sweden (Sundkvist et al. 2010).

<sup>c</sup> Exclusively for formula-fed infants, assumed to drink 0.8 L of water per day (Health Canada 1998), where water is used to reconstitute formula. No monitoring data on TBB and TBPH in formula were identified; therefore dietary intakes are only those from water. See footnote on drinking water for details.

<sup>d</sup> Exclusively for not-formula-fed infants, assumed to drink 0.7 L of water per day (Health Canada 1998), and approximately 50% of non-formula-fed infants are introduced to solid foods by 4 months of age, and 90% by 6 months of age (NHW 1990).

<sup>e</sup> Assumed to weigh 15.5 kg, to breathe 9.3 m<sup>3</sup> of air per day, to drink 0.7 L of water per day, to consume 54.7 g of fish per day (Health Canada 1998), and to ingest 41 and 14 mg of dust and soil per day, respectively (Wilson et al. 2013).

<sup>f</sup> Assumed to weigh 31.0 kg, to breathe 14.5 m<sup>3</sup> of air per day, to drink 1.1 L of water per day, to consume 89.8 g of fish per day (Health Canada 1998), and to ingest 31 and 21 mg of dust and soil per day, respectively (Wilson et al. 2013).

<sup>g</sup> Assumed to weigh 59.4 kg, to breathe 15.8 m<sup>3</sup> of air per day, to drink 1.2 L of water per day, to consume 97.3 g of fish per day (Health Canada 1998), and to ingest 2.2 and 1.4 mg of dust and soil per day, respectively (Wilson et al. 2013).

<sup>h</sup> Assumed to weigh 70.9 kg, to breathe 16.2 m<sup>3</sup> of air per day, to drink 1.5 L of water per day, to consume 111.7 g of fish per day (Health Canada 1998), and to ingest 2.5 and 1.6 mg of dust and soil per day, respectively (Wilson et al. 2013).

<sup>i</sup> Assumed to weigh 72.0 kg, to breathe 14.3 m<sup>3</sup> of air per day, to drink 1.6 L of water per day, to consume 72.9 g of fish per day (Health Canada 1998), and to ingest 2.5 and 1.5 mg of dust and soil per day, respectively (Wilson et al. 2013).

<sup>j</sup> No monitoring data of ambient air were identified. The detection limit for air concentration of 1 ng/m<sup>3</sup> for Swedish households (Staaf and Östman 2005) was selected for deriving upper-bounding estimates of daily intake for ambient air exposure. Canadians are assumed to spend 3 hours outdoors each day (Health Canada 1998).

<sup>k</sup> The detection limit for air concentration of 1 ng/m<sup>3</sup> for Swedish households (Staaf and Östman 2005) was selected for deriving upper-bounding estimates of daily intake for indoor air exposure. Canadians are assumed to spend 21 hours indoors each day (Health Canada 1998).

<sup>l</sup> The detection limit of 60 ng/L from the City of Toronto (2003) municipal monitoring program was selected for deriving upper-bounding estimates of daily intake for drinking water exposure.

<sup>m</sup> No monitoring data on marketed foods in Canada were identified; however environmental fish and shellfish data were available. The TCP concentration of 1.32 µg/kg wet weight (based on a reported maximum TCP concentration of 110 µg/kg lipid x 1.2% lipid content) in mussels collected in 2007 in Sweden (Sundkvist et al. 2010) was selected for deriving upper-bounding estimates of daily intake for exposure to all fish-related food items in the Fish food group. Amounts of foods consumed on a daily basis by each age group over 12 food groups were obtained from the 1970–1972 Nutrition Canada Survey (Health Canada 1998).

<sup>n</sup> The 95<sup>th</sup> percentile concentration of TCP (17 700 ng/g) from the baseline study based on samples collected from the Canadian House Dust Study (Kubwabo et al. 2014) was selected for deriving upper-bounding estimates of daily intake for dust exposure.

<sup>o</sup> No appropriate or relevant soil and sediment studies on TCP monitoring in North America were identified. The soil maximum predicted environmental concentration (PEC) of 300 ng/g dw (0.0003 mg/kg dw) was selected for deriving upper-bounding estimates of daily intake for soil exposure.



## Appendix E: Environmental monitoring data

Table E-1. Monitoring of TCP in indoor air

Location	Country	n	DL (ng/m <sup>3</sup> )	Concentration (ng/m <sup>3</sup> )	Reference
Electronics stores	Switzerland	5	0.41	ND to 0.21	Hartmann et al. 2004
Furniture stores	Switzerland	2	0.41	ND	Hartmann et al. 2004
Offices	Switzerland	4	0.41	ND to 0.37	Hartmann et al. 2004
Theatre	Switzerland	1	0.41	2.1	Hartmann et al. 2004
Homes	Sweden	50	1	<DL	Staafl and Östman 2005
Various indoor environments (e.g. bicycle store, carpet store, clothing store, health care facilities, bakery, carpet store)	Sweden	50	1	<DL	Staafl and Östman 2005
Car	Sweden	5	1	<DL	Staafl and Östman 2005
Bus	Sweden	10	1	<DL	Staafl and Östman 2005
Subway car	Sweden	5	1	<DL	Staafl and Östman 2005
Car garage	Sweden	5	1	<DL	Staafl and Östman 2005
Bus garage	Sweden	5	1	<DL	Staafl and Östman 2005
Subway car garage	Sweden	5	1	<DL	Staafl and Östman 2005
Aircraft			4.5	Flight A: 108 Flight B: 36	Van Nette 2009

Abbreviations: ND, not detected; DL, detection limit; LOQ, limit of quantification

**Table E-2. Monitoring of TCP in household dust**

Location	Sample type	Sampling year	n	Median (range) (ng/g)	Reference
Various locations, Canada	Vacuum Cleaner	2007–08	818	4860 (<30–295 0000)	Kubwabo et al. 2014
Various locations, Canada	Vacuum cleaner —Fresh dust	2007–2010	134	2600 (80–62000)	Fan et al. 2014
Various locations, Canada	Vacuum cleaner —House dust	2007–2010	134	990 (50–75000)	Fan et al. 2014
California, USA	Living area surfaces	2006	16	1000 (330– 400)	Dodson et al. 2012
California, USA	Living area surfaces	2011	16	680 (180–10 000)	Dodson et al. 2012
NS, Germany	Vacuum cleaner	NS	65	2200 (NS–36 000)	Kersten and Reich 2003 <sup>a</sup>
Urban area, Germany	Carpet and floor	2010–2011	10	94 (mean) (<40 to 240)	Brommer et al. 2012
Iasi, Romania	Carpet	2010	47	500 (<50 to 5500)	Dirtu et al. 2012
Urban area, Belgium	Carpet and floor	2008	33	240	Van den Eede et al. 2011
NS, Belgium	Vacuum cleaner	2006–2010	6	106 (29–1 110)	Van den Eede et al. 2012 <sup>b</sup>
NS, Spain	Vacuum cleaner	2006	1	89 (only value)	Van den Eede et al. 2012 <sup>b</sup>
NS, Romania	Vacuum cleaner	2007	3	430 (86–2 350)	Van den Eede et al. 2012 <sup>c</sup>
Various locations, New	Carpet and floor	2008	34	120 (<50 to 3 760)	Ali et al. 2012

Location	Sample type	Sampling year	n	Median (range) (ng/g)	Reference
Zealand					
Various locations, New Zealand	Mattress	2008	16	157 (<50 to 2 155)	Ali et al. 2012
Malate, Philippines	Vacuum cleaner	2008	17	18 (<0.27 to 25)	Kim et al. 2013
Payatas, Philippines	Vacuum cleaner	2008	20	7.7 (<0.27 to 140)	Kim et al. 2013

Abbreviations: NS, not specified; DL, detection limit

Notes:

a. Cited in Wensing et al. 2005.

b. Only raw data available. Calculated values.

**Table E-3. Monitoring of TCP in drinking water**

Location	Sample type	Sampling year	Sample size	Mean [range] (ng/L)	Reference
Toronto, ON, Canada	Drinking water	2000	10	: [ND]	City of Toronto 2000
				<i>m</i> -TCP: [ND]	
				<i>p</i> -TCP: [ND]	
Toronto, ON, Canada	Drinking water	2001	19	: [ND]	City of Toronto 2001
				<i>m</i> -TCP: [ND]	
				<i>p</i> -TCP: [ND]	
Toronto, ON, Canada	Drinking water	2002	19	: [ND]	City of Toronto 2002
				<i>m</i> -TCP: [ND]	
				<i>p</i> -TCP: [ND]	
Toronto, ON, Canada	Drinking water	2003	14	: [ND]	City of Toronto 2003
				<i>m</i> -TCP: [ND]	
				<i>p</i> -TCP: [ND]	
Ontario DWTPs, Canada	Drinking water	1978	12	[ND to 0.3]	Lebel et al. 1981
Various locations, Canada	Drinking Water	1979	60	[ND to 4.3]	Williams and Lebel 1981
Various locations,	Drinking water	1980	12	[0.4–1.8]	Williams et al. 1982

Location	Sample type	Sampling year	Sample size	Mean [range] (ng/L)	Reference
Canada					
Rome, Italy	Drinking water	2006	6	[ND]	Bacaloni et al. 2007

Abbreviations: ND, not detected

**Table E-4. Foods from the U.S. Total Diet Studies (TDS)**

Food type	Location	Country	Sampling year	n	Concentration (ng/g)	Reference
All other food types	Various locations	USA	1991 to 2002	>15 000	ND	(US FDA (2006))
Bread	Various locations	USA	2003	44	2.05 (mean) (ND-90) DF= 2%	US FDA (2013c)
All other food types	Various locations	USA	2004 to 2005		ND	US FDA (2013b)

**Table E-5. Monitoring of TCP in biota**

Food type	Location	Sampling year	n	Conc. (range) (ng/g lipid)	Conc. (range) (ng/g wet wt.)	Reference
Sturgeon	Columbia River, USA	NS	NS	40		Lombardo and Egry 1979 <sup>b</sup>
NS	near TAP manufacturing site, USA	NS	NS	(2–5)		Muir 1984 <sup>b</sup>
Herring (marine)	Baltic Proper, Sweden	2007	4 (72 P)	<0.4	<0.010	Sundkvist et al. 2010
Perch (marine)	Holmon and Kvadofjarden, Sweden	2007	2 (10 P)	22 (20-23)	0.095 (0.082-0.1)	Sundkvist et al. 2010
Mussels (marine)	Sweden	2007	30	110	1.32	Sundkvist et al. 2010
Mussels (marine)	Sweden	2007	11	11	0.13	Sundkvist et al. 2010
Eelpout (marine)	Fjallbacka, Sweden	2007	5	19	0.11	Sundkvist et al. 2010

Food type	Location	Sampling year	n	Conc. (range) (ng/g lipid)	Conc. (range) (ng/g wet wt.)	Reference
Salmon (marine)	Bothnian Bay, Sweden	2005	5	1.8	0.16	Sundkvist et al. 2010
Perch (fw)	Background locations, Sweden	2007	7 (60 pooled)	18 (<2.1 to 43)	0.07 (0.01-0.13)	Sundkvist et al. 2010
Perch (fw)	Near sources, Sweden	2007	3 (27 P)	24 (22–137)	0.10 (0.10–0.20)	Sundkvist et al. 2010
NS	Various locations, Japan	1993	75	(63 – 82)		MOE Japan 2003
NS	Various locations, Japan	1978	93	ND		MOE Japan 2003
NS	Various locations, Japan	1975	96	ND		MOE Japan 2003
Fish and shellfish	Seto Inland Sea, Japan	1980	41	(1–19)		Kenmotsu et al. 1981 <sup>b</sup>

Abbreviations: ND, not detected

**Table E-6. TCP Monitoring in breast milk from Sweden**

Food Type	Location	Spl year	n	Conc. (range) (ng/g lipid)	Conc. (range) (ng/g wet wt.)	Reference
Breast milk	Uppsala	1997	69 (P)	3.7	0.126	Sundkvist et al. 2010
Breast milk	Uppsala	1998	90 (P)	3.0	0.102	Sundkvist et al. 2010
Breast milk	Uppsala	2006	50 (P)	<0.1	<0.003	Sundkvist et al. 2010
Breast milk	Lycksele	2003	39 (P)	<0.2	<0.008	Sundkvist et al. 2010
Breast milk	Lund	2003	37 (P)	<0.2	<0.008	Sundkvist et al. 2010
Breast milk	Umeå	2007	1	1.7	0.019	Sundkvist et al. 2010

Abbreviations: ND, not detected; P, pooled;

## Appendix F: Exposure estimates of TCP from manufactured items

Based on the available information, dermal exposure intakes were estimated for direct contact with furniture upholstery with TCP backcoating for young children and adults (Table F-1). The exposure estimates presented below are considered upper-bounding based on conservative assumptions. Note that these products are included based on the assumption of their use in Canada as these uses were only identified in U.S. or international information sources.

$$\text{Intake} = [\text{SA} \times \text{SCF} \times \text{M} \times \text{ED}] / \text{BW}$$

**Table F-1. Parameters for intake estimates from dermal contact with furniture**

Symbol	Description	Value
SA <sup>a</sup>	Surface area of skin contact	357 cm <sup>2</sup> (Toddler) 1395 cm <sup>2</sup> (Adult)
SCF <sup>b</sup>	Skin contact factor	0.13
M <sup>c</sup>	Migration rate	2.17 × 10 <sup>-4</sup> mg/cm <sup>2</sup> /h (TCEP) 5.6 × 10 <sup>-5</sup> mg/cm <sup>2</sup> /h (TDCPP)
ED <sup>d</sup>	Exposure duration	1 hr (Toddler) 6 hr (Adult)
BW <sup>e</sup>	Body weight	15.5 kg (Toddler) 70.9 kg (Adult)
Intake	Intake estimate	1.7 × 10 <sup>-4</sup> to 6.5 × 10 <sup>-4</sup> mg/kg-bw/d (Toddler) 8.6 × 10 <sup>-4</sup> to 3.3 × 10 <sup>-3</sup> mg/kg-bw/d (Adult)

<sup>a</sup> For this scenario, it is assumed that an individual is wearing shorts and a t-shirt. The surface area of exposure is based on exposure to a fraction of the lower limbs. The surface area of the lower limbs (Health Canada 1995) was multiplied by one third to account for the triangular shape of limbs, where only one side is directly in contact with upholstered furniture (CPSC 2006b).<sup>b</sup> No TCP-specific skin contact factor, i.e. the fraction of substance on a surface adhering to skin, was identified in the literature. As such, a value of 0.13, an average of multiple substances (i.e. malathion, glyphosate, permethrin and TRIS [tris-(2,3-dibromopropyl) phosphate]) to various textiles in wet and dry simulations (US CPSC 2006), was selected.

<sup>c</sup> No TCP-specific migration rates were identified in the literature. Therefore a range in migration rates based on other organophosphate flame retardants were selected. The migration rate of 2.17 × 10<sup>-4</sup> mg/cm<sup>2</sup>/h for TCEP from furniture textiles is based on an unpublished study by Bruckert et al. (1990) reported in the TCEP EU RAR (2009). The migration rate of 5.6 × 10<sup>-5</sup> mg/cm<sup>2</sup>/hr for TDCPP were used to estimate dermal exposures based on migration studies of treated furniture foam by TNO Quality of Life (EU RAR 2008) and the U.S. CPSC (US CPSC 2005), respectively. The U.S. CPSC built a furniture miniseat mock-up consisting of a block of foam covered with cotton fabric and attached to plywood. The miniseat was wetted with a saline solution to mimic sweat, with pressure applied to imitate the action of sitting. The migration rate of 5.6 × 10<sup>-5</sup> mg/cm<sup>2</sup>/hr for TDCPP was determined based on the reported maximum daily amount extracted (8 µg) onto the filter (5-cm diameter) over the course of the migration testing period (6 hours) (US CPSC 2005).

<sup>d</sup> Exposure duration for sitting was adjusted from durations reported in CPSC (2006) for leisurely sitting.  
<sup>e</sup> Health Canada (1998).

## Appendix G: TCP in oils in engine oils, lubricants and fluids

Table G-1. Concentrations of TCP in engine oils, lubricants and fluids

Product	Total TCP	o-TCP	m-TCP	p-TCP	Reference	Notes
Power steering fluid	0.2%	NR	NR	NR	Environment and Climate Change Canada 2013	
Automobile engine oil	NR	2.2–2.9 mg/g	1.9–2.3 mg/g	ND	Takimoto et al. 1999	Measured in Japan
Motorcycle engine oil	NR	1.7–7.3 mg/g	1.5–6.8 mg/g	ND	Takimoto et al. 1999	Measured in Japan
Aircraft turbine oil	NR	13–150 mg/L	NR	NR	De Nola et al. 2008	
Aircraft turbine oil	2-3%	NR	NR	NR	De Nola et al. 2008	From product MSDS
Aircraft turbine oil	NR	<50 mg/kg	NR	NR	De Nola et al. 2008	
Aircraft Turbine oil	NR	<LOQ	~ 2.5%	NR	De Nola et al. 2011	
Aircraft turbine oil	NR	20–40 µg/L	NR	NR	De Nola et al. 2011	Manufactured after 2001
Aircraft turbine oil	1-5%	NR	NR	NR	Solbu et al. 2007	From MSDS
Aircraft turbine oil	32 mg/g	NR	NR	NR	Solbu et al. 2010	New oil
Aircraft turbine oil	21.8 mg/g	NR	NR	NR	Solbu et al. 2010	10 year-old oil
Aircraft turbine oil	3%	NR	NR	NR	van Netten 2008	
Aircraft turbine oil	3%	NR	NR	NR	Winder and Balouet 2002; Michaelis 2002	Amount in Mobil Jet Oil II
Hydraulic fluid	NR	0.5% by weight	NR	NR	ATSDR 1997	
Lubricating oil	NR	2%	42%	31%	WHO 1990	Measured in 1975
Refrigeration lubricant	NR	1–2%	NR	NR	HPD 2011	Automotive air conditioning

						refrigerant
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Abbreviations: NR = not reported; ND = not detected; LOQ = limit of quantitation



## Dermal exposure from oils

Direct skin contact with oils can result in dermal exposure to TCP used in various oils and other fluids. Of all the potential uses of TCP in oils and other fluids, the selected product considered was power steering fluid based on confirmation of this use in Canada (Environment and Climate Change Canada 2013). The exposure event for an adult filling the power steering fluid reservoir of a vehicle is not expected to occur frequently (likely 2 to 4 times per year), and thus was estimated on a per event and acute or short-term basis. The exposure estimates presented below are based on conservative assumptions.

$$\text{Intake} = [\text{SA} \times \text{FT} \times \rho \times \text{WF}] / \text{BW}$$

**Table G-2. Exposure factors for power steering fluid dermal scenario**

Symbol	Description	Value	Reference
SA	Surface area of finger tips (cm <sup>2</sup> )	6	Versar handbook thin film, instant application scenario (Westat 1987)
FT	Thickness of oil film on hand (cm)	1.59×10 <sup>-2</sup>	Versar handbook thin film, instant application scenario (Westat 1987)
r	Density of product (g/cm <sup>3</sup> )	0.88	Versar handbook thin film, instant application scenario (Westat 1987)
WF	TCP Weight fraction	0.002	Environment and Climate Change Canada (2013–2014)
BW	Body weight	70.9 kg (Adult)	Health Canada (1998)
Intake	Intake (ug/kg-bw)	2.4	

## Appendix H: Summary of health effects information for TCP

Table H-1. Studies in experimental animals and cells

Endpoint	Lowest effect levels <sup>1</sup> /Results
Acute toxicity	<p><b>Lowest oral LD<sub>50</sub> (mouse)</b> = 3900 mg/kg-bw (Izmerov, 1982 cited in IPCS 1990)</p> <p><b>Lowest dermal LC<sub>50</sub> (cat)</b> = 1500 mg/kg (Abou-Donia et al. 1980 cited in IPCS 1990)</p> <p><b>Lowest inhalation LC<sub>50</sub> (rat)</b> &gt;5.2 mg/L (Stauffer Chemical Co. 1979 cited in ECB 2001)</p> <p><b>Oral LOAEL (rat)</b> = 2000 mg/kg-bw based on significant inhibition of serum, erythrocyte and brain cholinesterase activity observed in female Sprague Dawley rats exposed to TCP (a mixture containing at least 20 organophosphates including 0.4%, 19.5% <i>m</i>-TCP and 2.4% <i>p</i>-TCP), via gavage, in a single dose of 2000 mg/kg-bw (Mobil 1987))</p> <p>[<b>Additional studies:</b> FMC Corporation 1975 cited in IUCLID 2001; Johanssen et al. (1977); Marhold 1972 cited in IPCS 1990; Stauffer Chemical Co.1988 cited in IPCS 1990; EPA 2010.</p>
Irritation/ Sensitization	<p><b>Negative in Draize skin test (EPA guideline):</b> Six albino rabbits had TCP (100%) applied on the intact left side of the back and the abraded right side of the back. The areas were wrapped in surgical gauze for 24 hours, after which the gauze was removed and the skin was observed for irritation. Erythema was observed in the abraded skin of one animal at 24 hours. The erythema was gone at the 72-hour observation. None of the animals showed edema at either the abraded or unabraded (intact) application areas. Thus TCP did not cause skin irritation in this test (Food and Drug Research Lab. Inc. 1975a cited in ECB 2001).</p> <p><b>Negative in Draize eye test (EPA guideline):</b> Nine rabbits received 0.1 ml of undiluted TCP on their right eyes. The eyes of 6 rabbits remained unwashed during the observation period while the eyes of 3 rabbits were washed 4 seconds after application. All eyes were examined at 24, 48 and 72 hours after exposure and again after 7 days. The eyes were scored according to the Draize method. Conjunctival effects were observed at 24 hours in two of the six rabbits with unwashed eyes, which cleared by 48 hours. No ocular effects were observed in the eyes of rabbits whose eyes were washed 4 seconds after application. The laboratory reports that, on the basis of these results, TCP is not an eye irritant (Food and Drug Research Lab. Inc. 1975b cited in ECB 2001).</p>

Endpoint	Lowest effect levels <sup>1</sup> /Results
	<p><b>Positive in Local Lymph Node Assay (OECD guideline):</b> Twenty female CBA/J Rj mice were allocated to five groups of four animals each: – three groups received the appropriate formulation of Kronitex TCP at concentrations of 100% (undiluted), 50% and 25% (w/v), – the negative control group received acetone olive oil (AOO) and – the positive control group received 25% <math>\alpha</math>-Hexylcinnamaldehyde (HCA) in AOO. The solutions of the test item were applied on the dorsal surface of ears of experimental animals (25 <math>\mu</math>l/ear) for three consecutive days (Days 1, 2 and 3). There was no treatment on Days 4, 5 and 6. On Day 6, the cell proliferation in the local lymph nodes was measured by incorporation of tritiated methyl thymidine (3HTdR) and the values obtained were used to calculate stimulation indices (SI). No mortality, systemic toxicity or local irritation was observed during the study. No treatment-related effects were observed on animal body weights in any treated groups. Stimulation index values of the test item were 3.7, 3.4 and 5.7 at treatment concentrations of 100% (undiluted), 50% and 25% (w/v), respectively. <math>\alpha</math>-Hexylcinnamaldehyde (25% (w/v) dissolved in AOO) was used as a positive control to demonstrate the appropriate performance of the assay. A significant lymphoproliferative response (stimulation index value of 17.2) was noted for the positive control chemical and this result confirmed the validity of the assay. In conclusion, under the conditions of the present assay Kronitex TCP, tested in a suitable vehicle, was shown to have sensitization potential (sensitizer) in the Local Lymph Node Assay (LAB Research Ltd. 2010)</p>
Short-term toxicity	<p><b>Lowest oral LOAEL (mouse)</b> = 360 mg/kg-bw /day based on decreased hindlimb grip strength observed in male mice. B6C3F1 mice (10 per sex per dose) were exposed to TCP (containing 79% tricresyl phosphate esters including 21% tri-m-cresyl phosphate, 4% tri-p-cresyl phosphate, &lt; 0.1% tri-o-cresyl phosphate, and other unidentified tricresyl phosphate esters; plus 18% of dicresyl phosphate esters), via gavage, at 0, 360, 730, 1450, 2900 mg/kg-bw /day in corn oil or 5800 mg/kg-bw /day (neat) for 13 or 14 days in a 16-day period. A significant reduction of hindlimb grip strengths was also observed at 730 mg/kg-bw/day in males and females, at 1450 in males and at 5800 mg/kg-bw/day in males and females; a significant reduction of forelimb grip strengths was observed at 1450 mg/kg-bw/day in males and at 5800 mg/kg-bw/day in females on day 14 of the study. Five males and all females receiving 1450 mg/kg-bw/day, all mice receiving 2900 mg/kg-bw/day, and four males and one female receiving 5800 mg/kg-bw/day died before the end of the study. Final mean body weights of male mice receiving 1450 or 5800 mg/kg-bw/day were significantly lower than controls. Final mean bodyweight of female mice receiving 360, 730 or 5800 mg/kg-bw/day were significantly greater than controls. Multifocal necrosis of the mandibular lymph node, spleen and thymus were observed primarily in</p>

Endpoint	Lowest effect levels <sup>1</sup> /Results
	<p>mice receiving 2900 and 5800 mg/kg-bw/day (NTP 1994).</p> <p><b>Oral LOAEL (rat)</b> = 1450 mg/kg-bw /day based on reduced body weight in a dose-related manner in male and female F344/N rats (10 per sex per dose) exposed to TCP (containing 79% tricresyl phosphate esters including 21% tri-m-cresyl phosphate, 4% tri-p-cresyl phosphate, &lt; 0.1% tri-o-cresyl phosphate, and other unidentified tricresyl phosphate esters; plus 18% of dicresyl phosphate esters), via gavage, at 0, 360, 730, 1450, 2900 or 5800 mg/kg-bw /day, for 13 or 14 doses in a 16-day period. One female receiving 1450 mg/kg-bw/day, and five males and eight females receiving 2900 mg/kg-bw/day died before the end of the study. Final mean bodyweight of rats receiving 1450 mg/kg-bw/day or higher doses were significantly lower than controls. Necrosis of the mandibular lymph node, spleen and thymus were observed primarily at 2900 and 5800 mg/kg-bw/day in males and females. Diffuse aspermatogenesis was observed in males at 2900 and 5800 mg/kg-bw/day. Significant reduction of forelimb grip strengths were observed in females at 1450 mg/kg-bw/day and higher doses, and in males at 2900 and 5800 mg/kg-bw/day. Significant reduction in hindlimb grip strengths were observed in males at 2900 and 5800 mg/kg-bw/day, and in females at 5800 mg/kg-bw/day (NTP 1994).</p> <p><b>Lowest dermal LOAEL (rat)</b> = 500 mg/kg-bw /day based on reduced serum cholinesterase observed in female Sprague-Dawley rats (5/dose) exposed to TCP (3% in jet engine oil) via dermal application to the shaved skin at 0, 500 or 1000 mg/kg-bw /day, for a total of 20 exposures over four weeks. Clinical signs of hypersensitivity, such as increased motor activity, were observed at 1000 mg/kg-bw/day. Serum cholinesterase was significantly (p&lt;0.05) reduced in all exposed rats (Mobil 1990a).</p> <p><b>[Additional studies:</b> Foster D. Snell Inc. 1976 cited in ECB 2001; Oishi et al. 1982; Chapin et al. 1988; Kinkead et al. 1990, 1993; Banerjee et al. 1992; Freudenthal et al. 1993; NTP 1994; Mackerer et al. 1999]</p> <p>No inhalation studies were identified.</p>
Sub-chronic toxicity	<p><b>Lowest oral LOAEL (rat)</b> = 50 mg/kg-bw /day based on cytoplasmic vacuolization of the adrenal cortex observed in Fisher 344/N rats (10 per sex per dose) exposed to TCP in a mixed isomer preparation (containing 79% tricresyl phosphate esters including 21% tri-m-cresyl phosphate, 4% tri-p-cresyl phosphate, &lt; 0.1% tri-o-cresyl phosphate, and other unidentified tricresyl phosphate esters; plus 18% of dicresyl phosphate</p>

Endpoint	Lowest effect levels <sup>1</sup> /Results
	<p>esters), via gavage, at 0, 50, 100, 200, 400 or 800 mg/kg-bw /day in corn oil, 5 days per week, for 13 weeks. No mortalities were observed. Final mean body weights of males were significantly lower than controls at 200 mg/kg-bw/day and higher doses. Cytoplasmic vacuolization of the adrenal cortex was observed in both sexes at all dose groups with severity increasing with dose. Ovarian interstitial cell hypertrophy was observed in all treated females. Atrophy of seminiferous tubules was observed in male rats at 400 mg/kg-day and higher doses. There were no biologically significant changes in neurobehavioral parameters. (NTP 1994).</p> <p><b>Lowest oral LOAEL (mouse)</b> = 50 mg/kg-bw /day based on cytoplasmic vacuolization of the adrenal cortex observed in B6C3F1 mice (10 per sex per dose) exposed to TCP in a mixed isomer preparation (containing 79% tricresyl phosphate esters including 21% tri-m-cresyl phosphate, 4% tri-p-cresyl phosphate, &lt; 0.1% tri-o-cresyl phosphate, and other unidentified tricresyl phosphate esters; plus 18% of dicresyl phosphate esters), via gavage, at 0, 50, 100, 200, 400 or 800 mg/kg-bw /day in corn oil, 5 days per week, for 13 weeks. No mortalities were observed. Final mean body weights were significantly decreased in males at 200 mg/kg-bw/day and higher doses and in females at 400 mg/kg-day and higher doses. Cytoplasmic vacuolization of the adrenal cortex was observed in both sexes of all treated groups in a dose-dependent manner. Ovarian interstitial cell hypertrophy was observed in all treated females. Multifocal degeneration of the spinal cord was observed at 100 mg/kg-day and higher doses in both sexes; and multifocal degeneration of the sciatic nerve was observed at 200 mg/kg-bw/day in males and at 100 mg/kg-bw/day in females. Significantly decreased forelimb grip strength was observed at 200 and higher doses in males and at 400 mg/kg-bw/day in females. Significantly decreased hindlimb grip strength was observed at 200 mg/kg-bw/day and higher doses in both sexes (NTP 1994).</p> <p><b>Other studies:</b></p> <p><b>Oral LOAEL (rat)</b> = 55 or 65 mg/kg-bw /day (males or females males respectively) based on cytoplasmic vacuolization of the adrenal cortex observed in males, and hyperplasia of ovarian interstitial cells in females. Fisher 344/N rats (10 per sex per dose) were exposed to TCP (containing 79% tricresyl phosphate esters including 21% tri-m-cresyl phosphate, 4% tri-p-cresyl phosphate, &lt; 0.1% tri-o-cresyl phosphate, and other unidentified tricresyl phosphate esters; plus 18% of dicresyl phosphate esters) in feed at 0, 900, 1700, 3300, 6600 or 13 000 ppm (approximately 0, 55, 120, 220, 430, or 750 mg/kg-bw/day for males and</p>

Endpoint	Lowest effect levels <sup>1</sup> /Results
	<p>0, 65, 120, 230, 430, or 770 mg/kg-bw/day for females), 7 days per week, for 13 weeks. No mortalities were observed. Final mean body weights were significantly decreased at 430 mg/kg-bw/day and higher dose in males and at 230 mg/kg-bw/day and higher doses in females. There were no biologically significant changes in neurobehavioral parameters. Cytoplasmic vacuolization of the adrenal cortex was observed in all exposed groups of both sexes. Ovarian interstitial cell hypertrophy and inflammation of the ovarian interstitium were observed in all exposed female groups. Renal papillary edema and renal papillary necrosis were observed at 750 mg/kg-bw/day in males and at 430 mg/kg-bw/day and higher doses in females. Basophilic hypertrophy of the pituitary gland pars distalis and atrophy of the seminiferous tubules were observed at 430 mg/kg-bw/day and higher doses in males (NTP 1994).</p>
	<p><b>Oral LOAEL (mouse)</b> = 65 or 110 mg/kg-bw /day (females or males respectively) based on cytoplasmic vacuolization of the adrenal cortex observed in B6C3F1 mice exposed to TCP (containing 79% tricresyl phosphate esters including 21% tri-m-cresyl phosphate, 4% tri-p-cresyl phosphate, &lt; 0.1% tri-o-cresyl phosphate, and other unidentified tricresyl phosphate esters; plus 18% of dicresyl phosphate esters) in feed at 0, 250, 500, 1000, 2100 or 4200 ppm (approximately 45, 110, 180, 380, or 900 mg/kg b-w/day for males and 65, 130, 230, 530, or 1,050 mg/kg-bw/day for females), 7 days per week, for 13 weeks. No mortalities occurred. Mean body weights were decreased (significance not stated) at 900 mg/kg-bw/day in males, and at 530 mg/kg-bw/day and higher dose in females. Cytoplasmic vacuolization of the adrenal cortex was observed in all exposed groups except for the 45 mg/kg-bw/day males. Papillary hyperplasia of the gallbladder mucosa was observed at 110 mg/kg-bw/day and higher doses in males, and at 230 mg/kg-bw/day and higher doses in females. Renal tubule degeneration was observed in all males at 900 mg/kg-bw/day. Axonal degeneration was observed at 380 mg/kg-bw/day and higher doses in males, and at 230 mg/kg-bw/day and higher doses in females. Significant decreases in forelimb grip strength were observed at 380 and 530 mg/kg-bw/day in males and females, respectively (<math>p \leq 0.05</math>), and at 900 and 1050 mg/kg-bw/day in males and females, respectively (<math>p \leq 0.01</math>). Significant decreases in hindlimb grip strength were observed at 900 in males and at 530 mg/kg-bw/day and higher dose in females (<math>p \leq 0.01</math>). A NOAEL was identified at 45 mg/kg-bw/day for males (NTP 1994).</p> <p><b>Oral LOAEL (rat)</b> = 1000 mg/kg-bw /day based on hypertrophy of the adrenal cortex observed in Sprague-Dawley rats (5 per sex per dose) exposed to TCP in 5% gum arabic solution, via gavage, at 30, 100, 300 or 1000 mg/kg-bw/day, 6 days per week for 3 months. The control group</p>

Endpoint	Lowest effect levels <sup>1</sup> /Results
	<p>received a 5% gum arabic solution. Excessive salivation was observed at all doses immediately following gavage. All treatment groups showed a slight increase in liver weights. Other observations at 1000 mg/kg-bw/day included significant decreases in body weight gain and slight decreases in spleen, heart, and lung weights in males, and increase in adrenal gland weight in females (Sumitomo Chemical Company 1974 cited in ECB 2001).</p> <p><b>[Additional studies:</b> Saito et al. 1974, Haggerty et al. 1986 (abstract only), Irwin et al. (1987, abstract only), Freeman et al. (1988, abstract only), Daughtrey et al. (1996)—all cited in IPCS 1990]</p> <p>No dermal and inhalation studies were observed.</p>
Chronic toxicity/carcinogenicity	<p><b>Oral carcinogenicity in rats:</b> Fischer 344/N rats (95 per sex per group) were exposed to TCP (containing 79% tricresyl phosphate esters including 21% tri-m-cresyl phosphate, 4% tri-p-cresyl phosphate, &lt; 0.1% tri-o-cresyl phosphate, and other unidentified tricresyl phosphate esters; plus 18% of dicresyl phosphate esters) in feed at 0, 75, 150 or 300 ppm (approximately 0, 3, 6 or 13 mg/kg-bw/day for males and 0, 4, 7 or 15 mg/kg-bw/day for females) for 2 years. An additional group of rats received 600 ppm TCP in feed for 22 weeks and then received control feed. Rats were examined at 3, 9 and 15 months and 2 years into the study. There was no evidence of carcinogenic activity of TCP found in the exposed male and female rats (NTP 1994).</p> <p><b>Oral carcinogenicity in mice:</b> B6C3F1 mice (95 per sex per dose) were exposed to TCP (containing 79% tricresyl phosphate esters including 21% tri-m-cresyl phosphate, 4% tri-p-cresyl phosphate, &lt; 0.1% tri-o-cresyl phosphate, and other unidentified tricresyl phosphate esters; plus 18% of dicresyl phosphate esters) in feed at 0, 60, 125 or 250 ppm (approximately 0, 7, 13 or 27 mg/kg-bw/day in males and 0, 8, 18 or 37 mg/kg-bw/day in females) for 2 years. Mice were examined at 3, 9 and 15 months and 2 years into the study. There was no evidence of carcinogenic activity of TCP found in the exposed male and female mice (NTP 1994).</p> <p><b>Non-neoplastic effect</b></p> <p><b>Lowest oral LOAEL (rat)</b> = 7 (or 26) mg/kg-bw/day (females or males respectively) based on cytoplasmic vacuolization of the adrenal cortex observed in female rats. Fischer 344/N rats (95 per sex per group) were exposed to TCP (containing 79% tricresyl phosphate esters including 21% tri-m-cresyl phosphate, 4% tri-p-cresyl phosphate, &lt; 0.1% tri-o-cresyl phosphate, and other unidentified tricresyl phosphate esters; plus</p>

Endpoint	Lowest effect levels <sup>1</sup> /Results
	<p>18% of dicresyl phosphate esters) in feed at 0, 75, 150 or 300 ppm (approximately 0, 3, 6 or 13 mg/kg-bw/day in males and 0, 4, 7 or 15 mg/kg-bw/day in females) in feed for 2 years. An additional group of rats (95 per sex per dose) received diets containing 600 ppm TCP for 22 weeks and then received only control feed (approximately 26 mg/kg-bw/day for males and 30 mg/kg-bw/day for females). At 3, 9 and 15 months of exposure, up to 15 rats/sex/dose were necropsied and evaluated for histopathological lesions. No mortalities occurred. No effect on the final mean body weights was observed. Cytoplasmic vacuolization of the adrenal cortex was observed at 26 mg/kg-bw/day in males and at 7 mg/kg-bw/day and higher doses in females at 3 months. At 9 and 15 months, cytoplasmic vacuolization was observed primarily in females at 15 mg/kg-bw/day, with the incidence and severity significantly increased at the end of the study. Ovarian interstitial cell hyperplasia was observed in female rats at 15 mg/kg-bw/day and the incidence and severity were increased at the end of the study. A NOAEL was identified at 4 or 13 mg/kg-bw/day for females or males, respectively (NTP 1994).</p> <p><b>Oral LOAE L (mouse) = 7 (or 37) mg/kg-bw/day</b> (males or females respectively) based on ceroid pigmentation of the adrenal cortex observed in male mice. B6C3F1 mice (95 per sex per dose) were exposed to TCP (21% <i>m</i>-TCP, 4% <i>p</i>-TCP, &lt;0.1% and other unidentified tricresyl phosphate esters) in feed at 0, 60, 125 or 250 ppm (approximately 0, 7, 13 or 27 mg/kg-bw/day in males and 0, 8, 18 or 37 mg/kg-bw/day in females) for 2 years. Mice were examined at 3, 9 and 15 months and 2 years into the study. At 3, 9 and 15 months of exposure, up to 15 mice/sex/concentration were necropsied and evaluated for histopathological lesions. Body weights, survival and feed consumption of exposed groups were similar to that of controls. Ceroid pigmentation of the adrenal cortex was observed in all exposed groups throughout most of the 2-year study, except in 8 and 18 mg/kg-bw/day females at the 3-month necropsy. The severity was markedly increased in females at 37 mg/kg-bw/day. Increased incidence in clear cell foci, fatty change and ceroid pigmentation of the liver were observed in males at 13 mg/kg-bw/day and higher doses. A NOAEL was identified at 18 mg/kg-bw/day for females (NTP 1994).</p> <p>No dermal and inhalation studies were identified.</p>
Reproductive toxicity	<p><b>Lowest oral LOAEL (mouse) = 63 mg/kg-bw/day</b> based on decreased number of litters per pair of mice. Swiss CD-1 mice (20 per sex per dose for test group, 40 per sex for control group) were exposed to 0, 0.05, 0.1 or 0.2% of TCP (with &lt;0.1%) by weight (approximately 0, 63, 124, or 250 mg/kg-bw/day in feed, for 7 days prior to breeding and 98 days during the breeding. The study protocol comprised of a continuous breeding</p>



Endpoint	Lowest effect levels <sup>1</sup> /Results
	<p>phase of the F0 generation, a cross-over mating to determine the affected sex in the F0 animals, and evaluation of the fertility and performance of the last litter (F1) from the continuous breeding. A significant (<math>p &lt; 0.01</math>) decrease in the number of litters per pair was observed in a dose-dependent manner. The proportion of pups born live was significantly decreased at 250 mg/kg/day. In the crossover mating phase, control males were mated with the treated females, and control females were mated with treated males. Impaired fertility was observed in both males and females at 250 mg/kg/day, with a greater effect in females. There were dose-related changes in the adrenals for both sexes; and body weight was decreased in both males and females at the high dose. A significant (<math>p &lt; 0.05</math>) decrease in sperm motility was observed at 62.5 and 124 mg/kg-bw/day (250 mg/kg-bw/day not examined). Atrophy of seminiferous tubules, decreased testis and epididymal weights in F0 males were observed at 250 mg/kg-bw/day. Changes in the adrenals in F0 of both sexes were significant at 250 mg/kg-bw/day, and the effect was dose-dependent. The last litter born in the 98-day breeding phase was reared to age 74 days and then mated within the control and two of the treatment groups (0.0%, 0.05%, and 0.1% TCP: there were too few offspring in the 0.2% group). There was a decrease in the fertility index in the 0.1% TCP group, and a decreased proportion of liveborn and number of liveborn pups per litter. In the F1 males at necropsy, sperm concentration and morphology were normal at termination, although motility was decreased in both the 0.05% and the 0.1% groups compared to controls. These data show that TCP impaired fertility in both sexes of mice in the F0 generation and affected sperm motility at even the lowest dose in F1 males. (Chapin et al. 1988).</p> <p><b>Other studies:</b></p> <p><b>LOAEL</b> = 100 mg/kg-bw/day based on fetotoxicity, abnormal sperm morphology, histopathological changes in testes, epididymides. TCP (containing &lt; 9%) was administered to male Long Evans rats (12 per dose) at 0, 100 or 200 mg/kg-bw/day, and to females (24 per dose) and at 0, 200, or 400 mg/kg-bw/day in corn oil via gavage. Males were dosed for 56 days, and females for 14 days prior to breeding and throughout the 10-day breeding period. The 100 mg/kg-day males were mated with the 200 mg/kg-day females and the 200 mg/kg-day males were mated with the 400 mg/kg-day females. Dose-dependent abnormal sperm morphology was observed at all doses. Sperm concentration, motility and progressive movement were decreased at 200 mg/kg-day. Reduced epididymal weights, necrosis and degeneration of seminiferous tubules, hypospermia in the epididymis, and increase in degeneration and immature spermatids were also observed in males at 200 mg/kg/day. In</p>

Endpoint	Lowest effect levels <sup>1</sup> /Results
	<p>females, alteration of ovarian interstitial cells, increased number of follicles, and corpora lutea were observed at 200 mg/kg-bw/day and higher dose. Number of live-delivered pups was reduced at all doses. Reduced litter size was observed at 200 mg/kg-bw/d and higher dose in a dose-dependent manner (Carlton et al. 1987).</p> <p><b>[Additional studies:</b> Morrissey et al. 1988b cited in IPCS 1990; Mobil (1991e, 1992b); Imperial Oil (1991); Latendresse et al. (1994a,b)</p> <p>No dermal and inhalation studies were identified.</p>
Developmental toxicity	<p><b>Lowest oral LOAEL (rat)</b> = 20 mg/kg- bw/day based on significantly decreased mean fetal body weight. Female Sprague Dawley rats were exposed to TCP (composition unknown), via gavage, at 0, 20, 100, 400 or 750 mg/kg-bw /day from day 0 to 19 of gestation. Clinical observations included increased salivation at <math>\geq 100</math> mg/kg-bw/day and alopecia and unkempt appearance at <math>\geq 400</math> mg/kg-day. Fetal body weights were reduced (significance not stated) compared to control groups at all dose levels. Incomplete ossification was observed at 750 mg/kg-bw/day (US EPA 2010).</p> <p><b>[Additional studies:</b> Tocco et al. 1987 cited in IPCS 1990 and EA 2009; Mele and Jensh 1977 cited in IPCS 1990 and EA 2009]</p> <p>No dermal and inhalation studies were identified.</p>
Genotoxicity and related endpoints: <i>in vivo</i>	<p><b>Unscheduled DNA Synthesis</b></p> <p><b>Negative:</b> in male rats administered TCP by gavage (Mirsalis 1985 cited in EA 2009).</p>
Genotoxicity and related endpoints: <i>in vitro</i>	<p><b>Mutagenicity in bacteria</b></p> <p><b>Negative:</b> in <i>Salmonella typhimurium</i> TA 98, TA100, TA1535, TA1537, TA1538 with or without metabolic activation (Haworth et al. 1983 cited in NTP 1994 and EA 2009; Litto Bionetics Inc. 1979a cited in ECB 2001 and EA 2009).</p> <p><b>Chromosome aberration</b></p> <p><b>Negative:</b> in Chinese hamster ovary cells (CHO) with or without metabolic activation (NTP 1994).</p> <p><b>Negative:</b> in mouse lymphoma cell line with or without metabolic activation (Litto Bionetics Inc. 1979b cited in ECB 2001 and EA 2009).</p> <p><b>Ambiguous:</b> in mouse lymphoma L5178Y cells with or without</p>

Endpoint	Lowest effect levels <sup>1</sup> /Results
	<p>metabolic activation (Litto Bionetics Inc. 1979c cited in ECB 2001 and EA 2009).</p> <p><b>Positive:</b> in BALB/3T3 cell line without metabolic activation (Litto Bionetics Inc. 1979d cited in ECB 2001 and EA 2009).</p> <p><b>Sister chromatid exchange</b></p> <p><b>Negative:</b> in CHO with or without metabolic activation (NTP 1994 and EPA 2010).</p>

<sup>1</sup> LC<sub>50</sub>, median lethal concentration; LD<sub>50</sub>, median lethal dose; LOAEC, lowest-observed-adverse-effect concentration; LOAEL, lowest-observed-adverse-effect level; LOEL, lowest-observed-effect level

**Table H-2: Studies in humans**

Epidemiology studies	Results
Polyneuropathy	<p>Several human studies were identified.</p> <p>An outbreak of acute polyneuropathy in over 20 young females occurred in Sri Lanka during 1977–1978. The cause of the neuropathy was traced to TCP found as a contaminant in special cooking oil (gingili oil). Contamination probably occurred during transport of the oil in containers previously used for storing mineral oils (Senanayake and Jeyaratnam 1981, cited in IPCS 1990).</p> <p>In 1944, three cases of toxic polyneuropathy among workers who had worked for six to eight months in a plant manufacturing TCP in England were reported. Skin penetration and inhalation were thought to be the main causes of the occupational poisoning (Hunter et al. 1944).</p> <p>A high prevalence of polyneuropathy among shoe factory workers has been reported in Italy since 1958. The cause may be attributed to TCP (Cavalleri and Cosi, 1978). However, the cause-effect relationship has not been established. This polyneuropathy might have various aetiological factors (including <i>n</i>-hexane) or be produced by a combination of them (Leveque 1983 cited in IPCS 1990).</p>
	<p>A case of severe intoxication in a 4-year-old child following ingestion of a lubricant containing TCP (substitution pattern not known) was reported. The clinical findings were vomiting, diarrhoea, weakness, drowsiness,</p>

Epidemiology studies	Results
Irritation/ sensitization	<p>delayed cholinergic crisis, and depressed nerve velocity. But full recovery occurred within four weeks (Goldstein et al. 1988).</p> <p>A human repeated patch test showed signs of irritation (New York University 1951, cited in EA 2009).</p> <p>In a study of 230 patients with possible occupational dermatitis from the metallurgical industry, 2.6 % of them showed positive patch test results with TCP (EA 2009).</p> <p>A case report described allergic contact dermatitis induced by contacting Band-Aid brand adhesive bandages which contains TCP as an ingredient (Norris and Storrs 1990, cited in IUCLID 2001, EA 2009).</p> <p>A maximization test conducted dermally on male human subjects showed that TCP is a moderately strong sensitizer (Dupont, 1992). (stimulation index value of 17.2) was noted for the positive control chemical and this result confirmed the validity of the assay. In conclusion, under the conditions of the present assay Kronitex TCP, tested in a suitable vehicle, was shown to have sensitization potential (sensitizer) in the Local Lymph Node Assay (LAB Research Ltd. 2010)</p>

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