DRAFT SCREENING REPORT

AN ASSESSMENT OF WHETHER THE USE OF TCEP, TCPP and TDCP IN ARTICLES SHOULD BE RESTRICTED

SUBSTANCE NAMES (IUPAC):

tris(2-chloroethyl) phosphate (TCEP)

tris(2-chloro-1-methylethyl) phosphate (TCPP)

Reaction mass of tris(2-chloropropyl) phosphate and tris(2-chloro-1-methylethyl) phosphate and Phosphoric acid, bis(2-chloro-1-methylethyl) 2-chloropropyl ester and Phosphoric acid, 2-chloro-1-methylethyl bis(2-chloropropyl) ester (TCPP)

tris[2-chloro-1-(chloromethyl)ethyl] phosphate (TDCP)

EC NUMBERS: 204-118-5; 237-158-7; (-); 237-159-2

CAS NUMBERS: 115-96-8; 13674-84-5; (-); 13674-87-8

DOSSIER SUBMITTER: EUROPEAN CHEMICALS AGENCY

Contact: maarten.roggeman@echa.europa.eu

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Preface

The preparation of this screening report was initiated on the basis of Article 69(2) of the REACH Regulation that requires ECHA to consider whether the use of tris(2-chloroethyl) phosphate (TCEP) in articles poses a risk to human health or the environment that is not adequately controlled[1]. The intrinsic property for which TCEP is included in Annex XIV is toxic for reproduction (Article 57c). The screening report also covers the carcinogenic properties of TCEP since it is considered to be a critical endpoint in risk assessment.

Moreover, tris(2-chloro-1-methylethyl) phosphate (TCPP) and tris[2-chloro-1-(chloromethyl)ethyl] phosphate (TDCP) were identified as substances with similar properties and uses to TCEP and were therefore also included in the scope of the current screening report.

The screening report builds on the (Draft) EU Risk Assessment Reports for TCEP, TCPP and TDCP (EU RAR 2008a,b and EU RAR 2009) and the RMOA activities carried out by the Danish EPA on these substances (Danish EPA 2016a,b).

Disclaimer: the results and conclusions in the current report are the result of a screening assessment and may therefore be amended in light of further information and assessment in the case a restriction proposal would be developed by ECHA.

[1] This requirement applies after the sunset date. The sunset date of TCEP was 21 August 2015.

Summary

The screening assessment identified a risk for children from exposure to the flame retardants TCEP, TCPP and TDCP in flexible polyurethane (PUR) foams in childcare articles and residential furniture. Therefore, ECHA recommends that a restriction proposal is prepared.

TCEP, TCPP and TDCP belong to the family of organophosphate flame retardants (OPFRs). TCPP and TDCP are used amongst others as flame retardants in flexible PUR foams in articles such as baby mattresses, car safety seats, baby slings, and residential upholstered furniture[2]. TCPP is an all-round flame retardant for all types of flexible PUR foams with a registered volume under REACH of 10 000-100 000 tonnes/year. The registered volume of TDCP under REACH is 1 000 – 10 000 tonnes per year. TDCP is more expensive and is used mainly for automotive applications. TCEP is currently not used as flame retardant for flexible PUR foams in the EU, but may be present as an impurity in other commercial flame retardants or in imported articles.

The critical effect for risk assessment is carcinogenicity. The mode of action is not known but appears not to be mediated by genotoxicity. Therefore, a threshold mode of action is assumed in the current screening report and DNELs have been derived. DNELs have been derived for reproductive toxicity as well. The mode(s) of action of the three OPFRs and other endpoints such as neurotoxicity may need to be assessed if a restriction dossier is prepared.

The exposure assessment in this screening report is targeted to the exposure of infants to TCEP, TCPP and TDCP in flexible PUR foam in childcare articles and in residential upholstered furniture. The article types considered to be 'reference articles' for the risk assessment are baby mattresses, safety seats, baby slings and sofas. The three OPFRs may also be used in other articles such as pushchairs, prams, carry cots, high seats, and baby changing mats.

Migration data for TCEP, TCPP and TDCP from textile and foam samples of two baby slings, one baby mattress and four car safety seats were used for estimating the exposure from mouthing and from dermal contact. Dermal exposure appears to be the main route of exposure, followed by exposure from mouthing. Other routes or sources of exposure are negligible in comparison.

Based on the screening assessment, a risk for carcinogenicity from exposure of infants is identified for all three OPFRs and for all four reference article types, with the exception of TCPP in car safety seats (RCR of 0.5) and TDCP in baby slings (RCR of 0.4). The highest risk was identified for baby mattresses with RCRs of 27-125. The high risk level for baby mattresses is explained by a large contact surface area and a long duration of contact. A risk for reproductive effects from TCEP and TCPP in mattresses is furthermore identified.

[2] In this screening report, 'upholstered furniture' is considered to be furniture to sit on with soft comfortable covering such as sofas, armchairs and chairs.

Since the screening assessment identified a risk for children from exposure to TCEP, TCPP and TDCP in flexible polyurethane (PUR) foams in childcare articles and residential furniture, ECHA recommends an Annex XV restriction dossier is prepared. As the scope of such a restriction proposal is outside the scope of Article 69(2) in terms of the inclusion of TDCP and TCPP and the inherent properties other than reproductive toxicity, a request from the Commission will be needed to initiate the preparation of the report.

If a restriction report is prepared, exposure from other uses and article groups may need further consideration. In addition, other exposure populations, such as adults, may be considered.

SCREENING REPORT

1. The problem identified

Article 69(2) of REACH requires ECHA to consider whether the use if a substance on Annex XIV of REACH (Authorisation list) in Articles poses a risk to human health or the environment that is not adequately controlled. If the risk is not adequately controlled the Agency shall prepare an Annex XV dossier. TCEP was included on the candidate list (13/01/2010; ED/68/2009) and included into Annex XIV of REACH (Commission Regulation (EU) No 125/2012) with a sunset date of 21 August 2015. In making its assessment for TCEP, ECHA has identified two other substances (TCPP and TDCP) that have similar uses and are structurally and toxicologically similar. Therefore, ECHA proposes to consider these three substances as a group (see section 1.2.2). This screening report therefore considers the three substances together. Any further action on these three substances, however, would require a request from the Commission as only TCEP is included on Annex XIV to REACH.

The screening assessment identified a risk for children from exposure to TCEP, TCPP and TDCP in polyurethane (PUR) foams in childcare articles[3] and furniture. TCEP, TCPP and TDCP belong to the family of organophosphate flame retardants (OPFRs). TCEP, TCPP and TDCP are referred to as "the three OPFRs" in this report. TCPP and TDCP are used inside and outside the EU as flame retardants in articles such as baby mattresses, car safety seats, baby slings, and residential upholstered furniture. TCEP is currently not used as flame retardant for flexible PUR foams in the EU, but may be present as an impurity in other commercial flame retardants, such as TCPP, TDCP, V6 and V66, or in imported articles (ECHA 2010a; Danish EPA 2016a)[4]. In the cases where TCEP is present in such articles (currently the evidence is limited), TCEP also may lead to a risk in infants.

If a restriction report is prepared, exposure from other uses and article groups may need further consideration. In addition, other exposure populations may be considered, for example, the restriction on TCEP, TCCP and TDCP introduced in Commission Directive 2014/79/EU amending the Toys Directive, only applies to toys intended for children younger than 3 years or those toys intended to be placed in the mouth by older children[5]. As another

[3] The EU Commission defined childcare articles ""*any product intended to facilitate sleep, relaxation, hygiene, the feeding of children or sucking on the part of children". It is the Commission's interpretation that the entry in Annex XVII covers the accessible parts of articles such as push chairs, car seats and bike seats which are intended to facilitate sleep and relaxation during transport."* (ECHA 2017).

[4] E.g., sample B18A in Danish EPA (2015) contained 4 700 mg/kg TCEP (0.5% w/w). This sample also contained 16 300 mg/kg TCPP as well as 13 000 mg/kg TDCP.

[5] In case a restriction would be proposed, electrical and electronic equipment should not be excluded from the scope since there is no restriction of the OPFRs under the RoHS Directive (Directive

example, the EU RAR (2008a) for TCPP assessed a reasonable worst case exposure of 241 µg/kg bw/day to adult consumers from the use of 1-K foams for the DIY filling of e.g. cavities of walls which is close to the DNEL for carcinogenicity and reproductive toxicity. Although most consumers would not regularly be spraying foam, such exposure levels during pregnancy may be of concern to reproductive toxicity where a critical exposure window may be present.

The date of the last literature search for the EU Risk Assessments for TCPP, TDCP and presumably[6] also TCEP was in 2007. A search on Pubmed on 25/05/2017 revealed over 100 new publications on TCEP[7], 50 new publications on TCPP[8], and 140 new publications on TDCP[9]. The screening of the available literature and assessment of new information in light of the information at the time of the EU Risk Assessments will be required when an Annex XV dossier is prepared. Even though some of the publications returned by the Pubmed search are overlapping and some can be anticipated to be of little added value to the assessment, the literature review will be fairly resource intensive.

2011/65/EU of the European Parliament and of the Council of 8 June 2011 on the restriction of the use of certain hazardous substances in electrical and electronic equipment).

[6] The date of the last literature search is stated to be 28/05/2007 related to human health in the draft EU RAR for TCPP and TDCP. Presumably the date is the same for TCEP (not stated).

[7] Using the search "TCEP OR tris(2-chloroethyl) phosphate OR 115-96-8 OR Tris(2-chloroethyl) orthophosphate OR Tris(beta-chloroethyl) phosphate OR Tris-2-chloroethyl phosphate".

[8] Using the search "tcpp OR tris (2-chloro-1-methylethyl) phosphate OR tris (2-chloro-1-methylethyl) phosphate OR 911-815-4 OR 13674-84-5 OR tris (chloropropyl) phosphate OR tris (beta-chloropropyl) phosphate OR tris (2-chloroisopropyl) phosphate OR tris (2-chloroisopropyl) phosphate OR tcipp OR tris (1-chloro-2-propyl) phosphate OR tris (2-chloroisopropyl) phosphate"

[9] Using the search TDCP OR tris[2-chloro-1-(chloromethyl)ethyl] phosphate OR 13674-87-8 OR tris (1,3-dichloropropyl-2) phosphate OR Tris(1,3-dichloro-2-propyl) phosphate OR TDCPP OR TDCIPP

1.1. Status and outcome of regulatory activities

Table 1 presents an overview of the status and outcome of regulatory activities related to TCEP, TCPP and TDCP in the EU and in the US.

Table 1 Overview of the status and outcome of regulatory activities related to TCEP, TCPP and TDCP

Process	TCEP	TCPP	TDCP
EU Risk Assessment	Final EU Risk Assessment report of 2009 Conclusions workers: Current exposure levels (inhalation and dermal contact) are too high for all occupational exposure scenarios. Conclusions consumers: Risk reduction measures are required for babies with respect to the scenario sucking on toys taking into consideration the carcinogenic properties of the substance and the effects after repeated oral administration. Conclusions environment: No need for action but "A potential risk in future cannot be excluded if production and/or use volumes were to increase as a consequence of actions on other flame retardants. Therefore, it is recommended to monitor that the downtrend in use of TCEP is not reversed in future."	Draft EU Risk Assessment report of 2008. Transitional report of 2008. Conclusions workers: Need for action based on dermal exposure during manufacturing, for fertility and developmental toxicity concerns. Conclusions consumers: No need for action. Conclusions environment: No need for action. It meets the screening criteria for P or vP but lacks any significant bioaccumulation potential.	Draft EU Risk Assessment report of 2008. Transitional report of 2008. Need for further information on female fertility. Conclusions workers: Need for action based on dermal exposure during the manufacturing, production of flexible PUR foam – slabstock, and production of flexible PUR foam – moulded in relation to repeated dose toxicity and carcinogenicity. Conclusions consumers: No need for action. Conclusions environment: No need for action. It meets the screening criteria for P or vP.
Toys Directive	Limit of 5 mg/kg (0.0005% w/w) of TCEP, TCPP and TDCP in toys intended for children under 36 months and in toys intended to be put in the mouth (Commission Directive 2014/79/EU).	Limit of 5 mg/kg (0.0005% w/w) of TCEP, TCPP and TDCP in toys intended for children under 36 months and in toys intended to be put in the mouth (Commission Directive 2014/79/EU).	Limit of 5 mg/kg (0.0005% w/w) of TCEP, TCPP and TDCP in toys intended for children under 36 months and in toys intended to be put in the mouth (Commission

Process	TCEP	TCPP	TDCP
			Directive 2014/79/EU).
Harmonised classification	Yes (carcinogenicity & reprotoxicity)	No. No carcinogenicity study available. The Draft EU Risk Assessment report concluded that there is sufficient information to support a qualitative read-across to address the hazard and risk assessment but a quantitative read-across approach was not considered sufficiently robust for the purpose of classification and labelling. The Draft EU Risk Assessment report considered classification to be a borderline case between classification as Repro Cat 3, R62 for fertility and developmental toxicity and no classification for effects on fertility.	Yes (carcinogenicity): The classification dates from 2005 i.e. before final EU RAR (the manufacturers had voluntarily classified TDCP as a category 3 carcinogen). Regarding reproductive toxicity, the classification for effects on fertility and developmental toxicity were not yet agreed. The Draft EU Risk Assessment report noted that there is a data gap for female fertility. A conclusion (i) "on hold" is drawn for the endpoint of female fertility.
On Annex XIV and Candidate List?	Yes	No	No
Registration	No	10 000 - 100 000 tonnes per year	1 000 – 10 000 tonnes per year
Dossier compliance check	No	Compliance check decision requesting pre-natal developmental toxicity study in the rabbit and information regarding the name and identification of the constituents of the substance. The registrant is required to submit the information by 28 March 2018.	No
Substance evaluation		TCPP is included on the CoRAP for evaluation by DK in 2018 with several	Included on the CoRAP for evaluation by DE in 2019 with as

Process	TCEP	TCPP	TDCP
		justifications, including suspected carcinogenic, suspected reprotoxic and suspected PBT/vPvB.	justification potential endocrine disruptor (for the environment).
RMOA	RMOA by DK for group (TCEP,TCPP & TDCP)	RMOA by DK for group (TCEP,TCPP & TDCP) RMOA by DK for TCPP	RMOA by DK for group (TCEP,TCPP & TDCP)
US NTP		The US National Toxicology Programme is performing a battery of studies: – cancer studies in rats and mice. Final results possibly available by May 2018. – 90 day studies in rat and mice. Preliminary results available – prenatal developmental toxicity study in rat. Preliminary results available. – Genetic toxicity studies. Results available. – Preliminary Toxicokinetic Study: report drafting stage – GD 6 - PND 127 Immunotoxicity (Dosed-Feed): running	

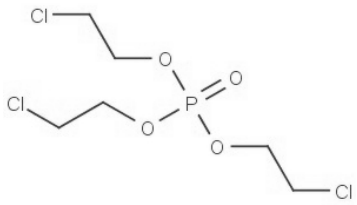
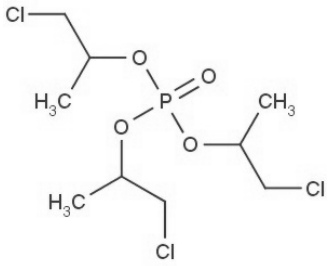
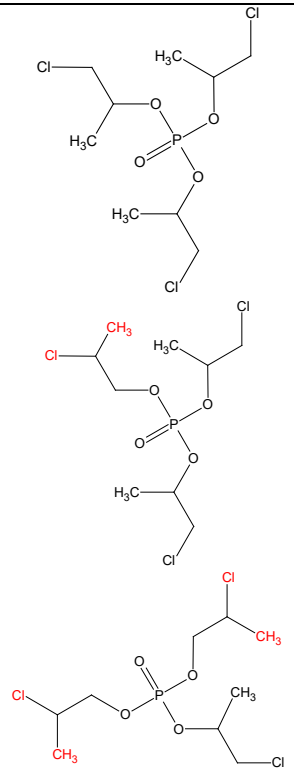
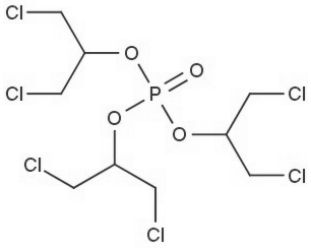
Note: on-going activities are marked **orange**.

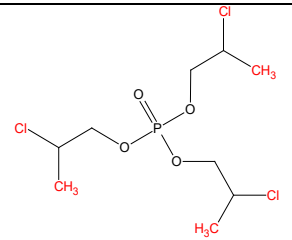
1.2. Hazard, exposure/emissions and risk

1.2.1. Identity of the substances, and physical and chemical properties

Table 2 Identity of the substances, and physical and chemical properties

	TCEP	TCPP*		TDCP
Regulatory process name (IUPAC name)	tris(2-chloroethyl) phosphate	tris(2-chloro-1-methylethyl) phosphate	Reaction mass of tris(2-chloropropyl) phosphate and tris(2-chloro-1-methylethyl) phosphate and Phosphoric acid, bis(2-chloro-1-methylethyl) 2-chloropropyl ester and Phosphoric acid, 2-chloro-1-methylethyl bis(2-chloropropyl) ester	tris[2-chloro-1-(chloromethyl)ethyl] phosphate
EC Number	204-118-5	237-158-7	/	237-159-2
CAS Number	115-96-8	13674-84-5	/	13674-87-8
Other names	TCEP Ethanol, 2-chloro-, phosphate (3:1) Tris(2-chloroethyl) orthophosphate Tris-2-chloroethyl phosphate Tris(beta-chloroethyl) phosphate	TCPP TCIPP TCIP Tris(Chloropropyl)phosphate 2-Propanol, 1-chloro-, phosphate (3:1) (9CI) Tris-(β-chloropropyl)-phosphate Tris(2-chloroisopropyl)phosphate tris (2-chloroisopropyl) phosphate tris (1-chloro-2-propyl) phosphate	TCPP Antiblaze 81 Antiblaze 85 Antiblaze TCPP Antiblaze TMCP Daming Technology Taizhou Xin`an WSFR-TCPP SikaSense®-3460/92 FYROL PCF LO Fyrol PCF Levagard PP Lupragen TCPP	TDCP TDCPP TDCIPP tris (1,3-dichloropropyl-2) phosphate Tris(1,3-dichloro-2-propyl) phosphate Fyrol FR-2

	TCEP	**TCPP***		**TDCP**
		Tris(monochloroisopropyl) phosphate (TMCP) Phosphoric acid, tris(2-chloro-1-methylethyl) ester		
Molecular weight	285.48 g/mol	327.57 g/mol	327.57 g/mol	430.905 g/mol
Molecular formula	C6H12Cl3O4P	C9H18Cl3O4P	C9H18Cl3O4P	C9H15Cl6O4P
Structural formula				

	TCEP	TCPP*		TDCP
				
Physical state	liquid at 20 °C (EU RAR 2009)	Liquid (EU RAR 2008a)	liquid **	liquid at 20 °C and 101.3 kPa (ECHA 2010b)
Melting point	< -70 °C (EU RAR 2009)	<-20°C (EU RAR 2008a)	< -20 °C **	<-20°C (ECHA 2010b)
Boiling point	decomposition at 320 °C at 1013 hPa (EU RAR 2009)	Ca. 288°C (decomp.) (EU RAR 2008a)	288 °C at 101.42 kPa (with decomposition)**	Ca. 326°C (decomp.) (ECHA 2010b)
Relative density	1.4193 g/cm^3 at 25 °C	1.288 at 20°C (EU RAR 2008a)	1.29 at 20°C**	1.513 at 20°C (ECHA 2010b)
Vapour pressure	43 Pa at 136.9 °C 1.14 x 10^{-3} Pa at 20 °C (extrapolated) (EU RAR 2009)	1.4 x 10^{-3} Pa at 25°C (EU RAR 2008a)	1.4 x 10^{-3} Pa at 25°C **	5.6 x 10^{-6} Pa at 25°C (ECHA 2010b)
Water solubility	7820 mg/l at 20 °C (EU RAR 2009)	1080 mg/l at 20°C (EU RAR 2008a)	1080 mg/l at 20°C at pH 5.5 **	18.1 mg/l at 20°C (ECHA 2010b)
Partition coefficient n-octanol/water (logPow)	1.78 (EU RAR 2009)	2.68±0.36 (EU RAR 2008a)	2.68 at 30°C at pH 7.1 **	3.69±0.36 (ECHA 2010b)
Notes		Composition reported in EU RAR (2008a): Tris(2-chloro-1-methylethyl) phosphate (EINECS 237-158-7; CAS 13674-84-5; 50-85% w/w content)	This is a multi-constituent substance, includes structural isomers and stereoisomers as described by the structural formulae included in this table. The same isomers have been	

	TCEP	TCPP*		TDCP
		Bis(1-chloro-2-propyl)-2-chloropropyl phosphate (CAS 76025-08-6 ; 15-40% w/w content) Bis(2-chloropropyl)-1-chloro-2-propyl phosphate (CAS 76649-15-5 ; <15% w/w content) Tris(2-chloropropyl) phosphate (EINECS 228-150-4 ; CAS 6145-73-9 ; <1% w/w content)	reported for the substance tris(2-chloro-1-methylethyl) phosphate with EC entry 237-158-7*.	

******Information as reported in the registration dossier and disseminated on the ECHA web-site.

***Note on substance identity of TCPP**

Registration dossiers for TCPP have been submitted using the identifiers:

- Reaction mass of tris(2-chloropropyl) phosphate and tris(2-chloro-1-methylethyl) phosphate and Phosphoric acid, bis(2-chloro-1-methylethyl) 2-chloropropyl ester and Phosphoric acid, 2-chloro-1-methylethyl bis(2-chloropropyl) ester; and
- tris(2-chloro-1-methylethyl) phosphate (EC 237-158-7).

All registrations submitted using EC entry 237-158-7 have been inactivated.

TCPP consists of different structural isomers, each structural isomer shows stereochemistry. Therefore the composition of this substance includes numerous constituents: structural isomers and stereoisomers.

The table reports the compositional information based on the information disseminated on the ECHA website from the registration dossiers for these substances. Although the structural formulae for these constituents therefore are reported in this table only in the column for the substance *"Reaction mass of tris(2-chloropropyl) phosphate and tris(2-chloro-1-methylethyl) phosphate and Phosphoric acid, bis(2-chloro-1-methylethyl) 2-chloropropyl ester and Phosphoric acid, 2-chloro-1-methylethyl bis(2-chloropropyl) ester"*, the same isomers are reported in the EU RAR (2008a) in the compositional information for substance tris(2-chloro-1-methylethyl) phosphate (EC 237-158-7). Additional information on test materials and isomeric composition of this substance is included in the EU RAR (2008a).

Based on the available information, it is concluded that in practise the actual substances placed on the market are and have been largely the same among the different registrants (albeit concentration levels of the constituents may vary somewhat among the different registrants) and that the substances were merely identified in a different way in the past by registrants.

As mentioned in Table 1, the identity of the currently registered substance is challenged in a compliance check decision and thus, the identifiers for the registered substance may change in the future.

1.2.2. Justification for grouping

The use pattern of TCEP, TCPP and TDCP is similar: they are used as flame retardant in polyurethane foam (PUR). TCPP and TDCP are commonly found together in articles (Danish EPA 2016b).

The structure of the three substances are similar and can be grouped as chlorinated phosphate ester flame retardants (CPE FRs, a sub-group of the OPFRs family). Also, the physicochemical properties between TCEP and TCPP are rather similar. However, the differences in molecular weight, vapour pressure, water solubility, and the partition coefficient of TCEP and TDCP are substantial. The similarity between TDCP and TCPP is stronger than between TDCP and TCEP, still, water solubility and vapour pressure of TDCP and TCPP differ with several orders of magnitude.

Grouping with other organophosphate substances was considered but was not found necessary or justified. For example, tris(2-butoxyethyl) phosphate (TBOEP, CAS No 78-51-3) has a much longer side chain and is not a chlorinated organophosphate.

Grouping would be consistent with the recent amendment of the Toy Safety Directive (Directive 2009/48/EC) that introduced a limit of 5 mg/kg (0.0005% w/w) of TCEP, TCPP and TDCP in toys intended for children under 36 months and in toys intended to be put in the mouth. The Directive 2014/79/EU amending the Toys Safety Directive referred to the opinion of SCHER (2012) to motivate the grouping approach. SCHER (2012) considered that there is sufficient information from the structures, physical-chemical properties, toxicokinetics and mutagenic profiles of TCEP, TDCP and TCPP to support a qualitative read-across, indicating a potential concern for carcinogenicity for TCPP by a non-genotoxic mechanism. The read-across implies, according to SCHER (2012), that considerations given for TCEP could be applied to its halogenated alternatives as well, if used in toy manufacturing.

1.2.3. Classification and labelling

Table 3 Harmonised classification and labelling of the four phthalates

Substance	Classification and labelling according to the CLP Regulation[10]	
	Hazard class and category codes	**Hazard statement codes**
TCEP	Carc. 2 Repr. 1B Acute Tox. 4 Aquatic Chronic 2	H351 "Suspected of causing cancer" H360F "May damage fertility" H302 "Harmful if swallowed" H411 "Toxic to aquatic life with long lasting effects"
TCPP	none	none
TDCP	Carc. 2	H351 "Suspected of causing cancer"

Classification of TDCP for the environment (N, R51-53, toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment) was agreed at EU level in 2005 (EU RAR 2008b). This was based on the lowest acute E(L)C50 of 1.1 mg/l (fish) and the lack of ready biodegradability. However, it appears that the agreed classification has not resulted in a harmonised classification of TDCP for its environmental properties. However, the classification provided by companies to ECHA in REACH registrations identifies that this substance is very toxic to aquatic life with long lasting effects.

1.2.4. Hazard assessment

The hazard assessment in the screening document is based in the conclusions of the EU Risk Assessments.

1.2.4.1. Toxicokinetics (absorption, metabolism, distribution and elimination)

1.2.4.1.1. TCEP

The EU RAR (2009) summarised the available information on toxicokinetics, metabolism and distribution as follows:

> "No toxicokinetic data on TCEP have been reported for humans. The substance is well absorbed (> 90% of the dose) and distributed in rats after oral administration. Higher concentrations were found in liver and kidney up to 24h after administration. An enterohepatic circulation is supposed to occur. Elimination from plasma and red blood cells occurred biphasic with a half-life of 3 and 3.4 hours in the beginning and 1.8 and 10.8 days in the second phase. Metabolism and elimination are the same after single and repeated application.

[10] Regulation (EC) No 1272/2008 on the classification, labelling and packaging of substances and mixtures.

Metabolites in urine were identical in rats and mice. Main metabolites were bis(2-chloroethyl) carboxymethylphosphate, bis (2-chloroethyl)hydrogen phosphate and bis(2-chloroethyl) -2-hydroxyethyl-phosphate glucuronide. In the risk characterisation, the rates of oral, dermal, and inhalation absorption are assumed to be 100%."

1.2.4.1.2. TCPP

The Draft EU Risk Assessment (EU RAR 2008a) summarised the available information on toxicokinetics, metabolism and distribution regarding as follows:

"After oral administration, there were indications of <100% absorption, when oral and i.v. dosing were compared. It is quite difficult to estimate the percent oral absorption. However, it appears from the available information that oral absorption is at least 75%, and may be slightly higher (based on the Minegishi data, and supported by the Stauffer data). Therefore, 80% oral absorption will be taken forward to risk characterisation.

After oral administration, Cmax in plasma was reached in 0.5 to 2 hours and 5.7 hours in tissues. Tissue radioactivity concentrations were dose and administration route-dependent (oral and intravenous). Although tissue/blood ratios over 7 days were > 1 for liver, kidney, lung and adipose tissue, absolute concentrations were low and the bioaccumulation potential was considered minimal. TCPP is extensively metabolised and accounted for <2% of urinary or faecal radioactivity after oral administration. Metabolites identified in urine and faeces, in order of abundance, were 0,0-[Bis(1-chloro-2-propyl)]-0-(2-propionic acid)phosphate, bis(1-chloro-2-propyl)monophosphoric acid and 1-chloro-2-propanol. Elimination of TCPP from plasma and tissues was biphasic. The average terminal plasma t½ was 48.7 hours. The longest tissue t½ was recorded in adipose tissue (up to 103.4 hours). Urinary and faecal excretion of radioactivity was dose and administration route-dependent (oral and intravenous), and occurred quite rapidly. The observed biliary/faecal excretion ratio is indicative of enterohepatic recirculation. In a separate in vitro comparative metabolism study with ^{14}C-TCPP, TCEP and TDCP, TCPP was metabolised to TCPP was metabolised to 89 and 61% respectively in rat liver S9 mix and liver slices. An in vitro percutaneous absorption study using human skin membranes was conducted to determine the absorption following topical application of [^{14}C]-TCPP. The skin membranes were exposed to TCPP for 8 hours, mimicking a normal working day. The mean total absorption was 22.7 %, 13.6 % and 3.7 %, for doses 0.002, 0.1 and 1 mg/cm^2, respectively. The total absorption value of 23% is taken forward to risk characterisation for scenarios where there is exposure to "neat" TCPP. A second in vitro study was conducted to determine the percentage of TCPP absorbed across the skin resulting from manual handling of flexible PUR foam containing TCPP. The skin membranes were exposed to the target concentrations of TCPP in artificial sweat for a period of 8 hours, mimicking a normal working day. It was

> determined that the total mean absorptions were 33.3% and 38.1% for the low and high doses of TCPP respectively. Therefore, with respect to risk characterisation, 40% dermal absorption will be taken forward for those scenarios where there is exposure due to handling of foam containing TCPP, i.e. Scenario 3 "Cutting of flexible PUR foam", Scenario 4 "Production of rebounded PUR foam" and Scenario 8 "Use of rigid PUR foam".
>
> No toxicokinetic data is available for the inhalation routes at present. For this route, and in line with the TGD, 100% absorption is assumed."

The US National Toxicology Programme performed a preliminary toxicokinetic study in the rat with TCPP (CAS No. 13674-84-5). The results are not yet available, for the status see https://ntp.niehs.nih.gov/testing/status/agents/ts-m20263.html.

1.2.4.1.3. TDCP

The Draft EU Risk Assessment (EU RAR 2008b) summarised the available information on toxicokinetics, metabolism and distribution as follows:

> "TDCP was well absorbed by the oral route of exposure and based on available studies, 100 % absorption will be assumed. In accordance with the default values given in the TGD, 100 % absorption via the inhalation route will also be assumed. An in vitro percutaneous absorption study using human skin membranes was conducted to determine the absorption following topical application of [^{14}C]-TDCP. The skin membranes were exposed to TDCP for 8 hours, mimicking a normal working day. The mean total absorption was 15.4 %, 10.69 % and 6.0 %, for doses 0.003, 0.01 and 0.12 mg/cm^2, respectively. A value of 15 % dermal absorption is taken forward to risk characterisation for exposure scenarios where there is potential exposure to "neat" TDCP and 30 % dermal absorption is assumed for scenarios 3, 4 and 5, where there is exposure due to handling of foam containing TDCP.
>
> Distribution studies showed highest levels in the liver and kidney and lung following oral, dermal and i.v. administration. Tissue concentrations of either the parent compound or metabolites were always low due to rapid excretion. Rapid and extensive (essentially 100 %) oxidative metabolism, mainly to the metabolite bis (1,3-dichloro-2-propyl) phosphate (BDCP almost 70% of metabolites), occurred. Excretion was mainly via the urine (approx 50 %), but also occurred via faeces and expired air.
>
> Elimination was rapid and so no accumulation in the body is expected."

1.2.4.1.4. Summary of Toxicokinetics

Table 4 summarises the absorption assumption taken forward in the risk assessment.

Table 4 Absorption of TCEP, TCPP and TDCP

	Oral	Dermal	Inhalation
TCEP	100%	50%	100%
TCPP	80%	40%	100%
TDCP	100%	30%	100%

1.2.4.2. Toxicity to reproduction

1.2.4.2.1. TCEP

The EU RAR (2009) summarised the available information on reproductive toxicity as follows:

> "Tris(2-chloroethyl)phosphate treatment revealed significant impairment of fertility for both sexes during continuous breeding and for two successive generations in mice. Reproductive failure was observed at daily doses of 700 mg/kg bw with at best and no more than 3 litters produced and with no pups surviving from the last litter produced. The findings were essentially confirmed from the results of a separate cross over mating trial in mice at the same dose level. The reproductive system of male mice appeared to be more sensitive to tris(2-chloroethyl)phosphate treatment as evidenced by less successive reproduction of treated males in comparison to treated females and further by significant male reproductive organ weight reduction and sperm parameter impairment in mice of two different strains. Based on a statistically significant reduction of the number of litters produced by the F0 generation, reduced pregnancy and fertility indices in the F1 generation, and statistically significantly reduced litter size in both the F0 and the F1 generations a NOAEL/fertility of 175 mg/kg bw/d was derived from the study in CD-1 mice with oral administration (Gulati and Chapin, 1991).
>
> A firm conclusion on developmental toxicity is hampered by poor reporting of rather old data as only a summary report and a reporting from a screening assay are available. However, it appears, that tris(2-chloroethyl)phosphate has no embryo-/fetotoxic or specific teratogenic properties in mice and rats even at maternally toxic doses. A NOAEL/developmental toxicity of 200 mg/kg bw/d and a NOAEL/maternal toxicity of 100 mg/kg bw/d was derived from a study with rats with oral administration (Kawashima et al., 1983).
>
> Based on the available animal data tris(2-chloroethyl)phosphate is identified as a reproductive toxicant with a significant toxic potential adverse to fertility. Treatment of mice resulted in significant impairment of reproductive success of both sexes and of male reproductive organs and of sperm parameters. Therefore, tris(2-chloroethyl)phosphate will be classified and labeled as reproductive toxicant Cat. 2, R60. No significant toxicity to embryo-/fetal development has been revealed from tris(2-chloroethyl)phosphate treatment of pregnant rats."

1.2.4.2.2. TCPP

The Draft EU Risk Assessment (EU RAR 2008a) summarised the available information on reproductive toxicity as follows:

> "In a two-generation reproductive toxicity study with TCPP, there were no treatment related effects in pre-coital time, mating index, female fecundity index, male and female fertility index, duration of gestation and post-implantation loss. There was no effect on sperm parameters at necropsy. In females, the length of the longest oestrus cycle and the mean number of cycles per animal were statistically significantly increased in high dose animals of both generations. A decrease in uterus weight was observed in all dosed females in F0 and in high dose females in F1. Effects were also noted on pituitary weights, significant in high dose females of both generations. A LOAEL of 99 mg/kg is derived for effects on fertility. This is based on effects on the effect on uterus weight seen in all dosed females in F0 and high dose females in F1.
>
> From the same study, a LOAEL of 99 mg/kg is derived for developmental toxicity. This is based on a treatment related effect on the number of runts observed in all TCPP-treated groups of the F0 generation.
>
> In a separate study, no treatment-related effects on foetal mortality, implantation number, resorption or foetal weight were observed following treatment of pregnant dams with TCPP. Cervical ribs and missing 13th ribs were noted at a low incidence in all treatment groups, but not in the control group. However, as a specific rib count undertaken in the 2-generation study did not reveal an increase in this effect, it is concluded that this is not toxicologically significant. Weaning rate and rearing condition were unaffected by treatment and there was no evidence of any abnormality."

Regarding classification, the EU RAR (2008a) noted that all organ weight changes occurred in the absence of any histopathological changes, and it is accepted that uterine weight can fluctuate during the oestrus cycle. Therefore, the effects observed may be due to normal variation in cycling females. Based on the above, the EU RAR (2008a) considered the classification to be a borderline case between classification as Repro Cat 3 and no classification for effects on fertility. However, for risk assessment the conclusion was different: *"While the effects on the uterus weight and oestrus cycle may be due to normal variation or weight loss, overall, based on a weight of evidence approach, it cannot be excluded that TCPP has an effect on uterus weight. This effect on the uterus was also observed in all dosed females in the preliminary study. Although the effects on the uterus occurred in the absence of histopathological changes, the magnitude of the decrease in uterus weight in the dosed animals is sufficient to be considered as significant. In addition, the mean number of cycles per animal are decreased and the length of the longest oestrus cycle are statistically increased in high dose animals of both generations, indicating a possible treatment related effect on the oestrus cycle. Therefore, a LOAEL of 99 mg/kg, based on effects on uterus weight, is derived for effects on fertility and this figure is taken forward to risk characterisation for this endpoint."*

The EU RAR (2008a) considered it is possible that TCPP has an effect on the developing pups but considered classification to be a borderline case between classification as Repro Cat 3 and no classification for developmental toxicity. Ireland submitted a CLH proposal to conclude that there is no sufficient evidence to classify. This dossier was subsequently withdrawn following the decision that RAC would not review classification proposals for "no classification". It is listed on the registry of withdrawn Harmonised Classification and Labelling intentions on ECHAs website (for TCPP with CAS No. 13674-84-5).

Test data are available for the rat from an oral two-generation reproduction toxicity study and from a preliminary range finding study (one-generation reproductive toxicity study). However, since data from a second species was missing and not waived by the registrants, ECHA requested the registrants to perform a pre-natal developmental toxicity study in the rabbit in a compliance check decision (ECHA 2016c). The registrant is required to submit the information by 28 March 2018. The US National Toxicology Programme has performed a dose range finding prenatal developmental toxicity study and a prenatal developmental toxicity study in rat with TCPP. Depending on the results from this testing, the registrant may provide arguments to waive the need to perform the prenatal developmental toxicity study in the rabbit.

TCPP is included on the CoRAP for evaluation in 2018 with several justifications, including suspected reprotoxic properties.

The preliminary results of the US NTP dose range finding (about 15 days, gavage, Harlan Sprague-Dawley rats, dose levels: 0, 300, 650, or 1,000 mg/kg/day) and prenatal developmental toxicity studies in rat (GD 6 to GD 20, gavage, Harlan Sprague-Dawley rats, dose levels 0, 162.5, 325, or 650 mg/kg/day) are available on https://ntp.niehs.nih.gov/results/path/tablelistings/longterm/tr500599/tr_tcpp/index.html#DART. The results will still undergo pathology peer review before the final scores will be available.

1.2.4.2.3. TDCP

The Draft EU Risk Assessment (EU RAR 2008b) summarised the available information on reproductive toxicity as follows:

> "With regard to effects upon fertility, no information is available in humans.
>
> A negative result was obtained in a fertility study carried out in male rabbits in which animals were dosed daily with concentrations of TDCP up to 200 mg/kg/day for twelve weeks and then mated with two females during the last week of treatment. Mating, fertility, pregnancy parameters, sperm analysis and the male reproductive tract were unaffected by treatment.
>
> In a 2-year carcinogenicity study in rats, an evaluation was made of the male reproductive system. Only control and high dose animals were evaluated at 12 months, and no significant differences were noted at this time point. Effects

were noted in the testes, epididymis and seminal vesicles in all animals at 24 months, with a trend for higher incidence in the treated groups.

As described in section 4.1.2.8.1, an increase in interstitial cell tumours of the testes in the mid and high dose males at the 12 and 24 months was observed in this study. Therefore, it is possible that the effects observed on the testes may be secondary to an effect of the Leydig cell tumours. It should also be considered that the effects noted in the male reproductive system are only observed in animals at 24 months and, therefore, may be secondary to the natural ageing process of rats rather than a specific effect on the male reproductive system.

In addition to these points, as indicated above, no effect on the male reproductive system and no effects on fertility were observed in the fertility study in male rabbits. Therefore, based on a weight of evidence, it is considered that there is no concern for male fertility.

No evaluation of the female reproductive system was included in the 2-year carcinogenicity study with TDCP. In reproductive toxicity studies with the structurally similar substances, TCEP and TDCP, inconsistent effects were observed on the female reproductive system. Therefore, it is not considered appropriate to read-across from data on either substance to address the possible effects of TCPP on female fertility. Therefore, it is considered that there is a data gap for female fertility.

In relation to developmental effects, there are no data available in humans. In a developmental study in rats, a dose of 400 mg/kg/day significantly increased the rate of resorptions compared to controls. At this high dose there was also evidence of retarded skeletal development. All of this was accompanied by significant maternal toxicity at this high dose. There was no evidence of embryotoxicity in the absence of maternal effects. The NOAEL for developmental toxicity was 100 mg/kg/day, based on the statistically significant increased resorptions and the decreased foetal viability index at 400 mg/kg/day.

In a second developmental study on rats, the highest dose of 400 mg/kg/day resulted in the deaths of 11 out of 15 of the dams with a reduction in live foetuses and a significantly high incidence of foetal deaths. No observations were noted at 200 mg/kg/day.

An overall NOAEL of 100 mg/kg/day can be derived for developmental toxicity based on the statistically significant increased resorptions and the decreased foetal viability index at 400 mg/kg/day seen in the first developmental study reported. This NOAEL is taken forward to risk characterisation in preference to the NOAEL of 200 mg/kg identified in the second study described, as only the abstract from the second study is available in English and therefore, full details of the study are not available to the Rapporteur.

> A NOAEL of 100 mg/kg/day is derived for maternal toxicity, based on the clinical signs of toxicity and statistically significant decrease in mean body weight noted in animals dosed at 400 mg/kg/day in the first study reported."

The classification for effects on fertility and developmental toxicity were not yet agreed at the time of the Draft EU Risk Assessment for TDCP. The Draft EU Risk Assessment report noted that no data is available on the effects on the possible effect of TDCP on female fertility and considered that there is a data gap for female fertility. A conclusion (i) "on hold" was drawn for the endpoint of female fertility. Based on the information available, the EU RAR considered that there is no concern for effects on male fertility or developmental toxicity and therefore no classification for these endpoints was proposed.

1.2.4.3. Carcinogenicity

1.2.4.3.1. TCEP

The EU RAR (2009) summarised the available information on carcinogenicity as follows:

> "From animal data it is obvious that there is a cancerogenic potential of tris(2-chloroethyl)phosphate. There are relevant guideline cancer studies using F344/N rats and B6C3F1 mice available (NTP 1991, Matthews 1993). In addition data of a diet study for 18 months using Scl:ddY mice comparable to guideline study with acceptable restrictions is available (Takada et al., 1989).
>
> Carcinogenic potential of tris(2-chloroethyl)phosphate in rats and mice was demonstrated for the oral route.
>
> Tris(2-chloroethyl)phosphate caused primarily benign tumors but also and malignant tumors in the kidney in F344/N rats (males and females) and also in male mice of two mouse strains (B6C3F1, Scl:ddY). Rats and mice of both strains developed a similar spectrum of tumor types in the kidneys. Additionally tumor development after tris(2-chloroethyl)phosphate treatment was seen in the liver of male in Scl:ddY mice, and in Harderian gland of B6C3F1 female mice, respectively. The data in the kidneys were considered to provide a clear evidence of tris(2-chloroethyl)phosphate induced carcinogenic activity in male Scl:ddY mice. Because of increased rates of renal proliferative lesions and of cell atypia in renal tubule epithelium which were observed in animals treated at ≥12 mg/kg bw/d, a NOAEL for kidney tumor formation could not established. Thus, for risk characterisation purposes a LOAEL of 12 mg/kg bw/d is brought forward for tumor formation.
>
> An increased incidence of renal tubular cell adenomas and carcinomas was observed in male and female F344/N rats at ≥44 mg/kg bw/d (below MTD); statistically significantly high incidences of tumors at 88 mg/kg bw/d (NTP 1991, Matthews 1993). In male B6C3F1 mice increased incidences of renal tubule cell neoplasms and of renal tubule cell hyperplasia were reported at 350

> mg/kg bw/d (below MTD). In addition, increased rates of cellular atypia of renal tubule epithelium cells such as karyomegaly were noted in both male and female mice given ≥175 mg/kg bw/d (NTP 1991, Matthews 1993). Dose-related increased incidence of tumors in the kidneys were also seen in male Scl:ddY mice fed diet concentrations of 300 mg/kg bw/d (below MTD) and above for 18 months. Also in male Scl:ddY mice statistically significantly high incidences of tumors (adenomas and carcinomas) in the liver were noted at 300 mg/kg bw/d (below MTD) and above. In female B6C3F1 mice marginally increased incidence of Harderian gland adenomas was seen at the lowest tested doses of 175 mg/kg bw/d and above (NTP 1991, Matthews 1993).
>
> No species-specific mode of action for tris(2-chloroethyl)phosphate carcinogenesis was identified.
>
> A reasonable threshold mechanism could not be identified for all tumors and tumor sites. Cytotoxicity was assumed as underlying mode of carcinogenesis in the kidney although indications on cytotoxicity, inflammation or the involvement of apoptosis are presently absent or not available. However, signs of increased proliferation and karyomegaly of renal tubule epithelial cells were seen in F344 rats of both sexes at ≥44 mg/kg bw/d and in male B6C3F1 mice at ≥175 mg/kg bw/d (NTP 1991, Matthews 1993) as hyperplasia and hypertrophy of the urinary tubule epithelium together with nuclei enlargement in male Scl:ddY mice fed at ≥12 mg/kg bw/d for 18 months (Takada et al., 1989). No other non-genotoxic mode of action was identified.
>
> Persistent cell damage and development of tumors was also discussed for non-genotoxic modes in the liver. In the study with Scl:ddY mice local necrosis, and vacuolation of liver cells were observed in all treatment groups (≥12 mg/kg bw/d). However, other non-genotoxic modes might be suspected, but not yet verified. A NOAEL for the cytotoxic effects was not established, and also not for cell proliferation mechanism.
>
> The carcinogenic effect of tris(2-chloroethyl)phosphate is thought to be related to nongenotoxic (epigenetic) mechanisms.
>
> According to the decision of the EU C&L WG tris(2-chloroethyl)phosphate will be classified as a carcinogen, category 3 and labelled as Harmful, Xn, R 40.”

Regarding the mode of action, the EU RAR (2009) concluded that there is no relevant evidence for mutagenicity of tris(2-chloroethyl)phosphate. There is no indication to assume that the tumours induced in rats and mice may be related to primary genotoxic effects. The existence of other/alternative (non-genotoxic) mechanisms is assumed. Any new information regarding the mode of action and the assumption of a threshold will need to be considered in the event a restriction report will be prepared.

1.2.4.3.2. TCPP

There are no carcinogenicity studies with TCPP available. The Draft EU Risk Assessment (EU RAR 2008a) summarised the available information on carcinogenicity toxicity as follows:

> "As discussed in section 4.1.2.7, TCPP, like TDCP and TCEP is not genotoxic in vivo. Based on the available repeat dose toxicity data for TCPP, supported by a qualitative read-across from TDCP and TCEP, there is a potential concern for carcinogenicity for TCPP by a nongenotoxic mechanism. No quantitative read-across can be performed since there are no insights into an underlying mode of action for TCEP and TDCP which would make a prediction on a relatively potency of TCPP possible. Therefore, as a reasonable worst case approach, a risk characterisation will be carried out for this end-point. It is proposed that the effects observed in the 90-day study for TCPP are taken as a starting point for risk characterisation. If these effects were to progress to cancer, they would do so by a non-genotoxic mechanism. Therefore, it is proposed that the LOAEL of 52 mg/kg/day, identified from the 90-day study with TCPP, should be used as a basis for risk characterisation of the carcinogenicity endpoint."

The effects observed in the 90-day study referred to in the citation above from the EU RAR (2008a) are increased absolute and relative liver weight, accompanied by mild thyroid follicular cell hyperplasia in males of all dose groups in a 90 day dietary study in the rat (Stauffer Chemical Co. 1981, as cited in the EU RAR 2008a). Only hepatocyte swelling (hypertrophy) in the high dose groups was seen as a histopathological finding related to the increased liver weight. The EU RAR (2008a) suggested that the effects on the thyroid in the male animals at all doses and the females at the highest dose could be secondary to altered liver metabolic activity. A LOAEL of 52 mg/kg bw/day was derived from this study.

To address the data gap resulting from the absence of a cancer bioassay, a qualitative read-across from TCEP and TDCP was presented in the Draft EU Risk Assessment (EU RAR 2008a). Following from the limitations of the read-across, the EU RAR (2008a) concluded that a quantitative read-across approach was not considered sufficiently robust for the purpose of classification and labelling. Ireland submitted a CLH proposal to conclude that there is no sufficient evidence to classify. This dossier was subsequently withdrawn following the decision that RAC would not review classification proposals for "no classification". It is listed on the registry of withdrawn Harmonised Classification and Labelling intentions on ECHAs website (for TCPP with CAS No. 13674-84-5).

The lead registrant for TCPP (EC No. 911-815-4) waived carcinogenicity data on the basis of structural similarity to TDCP and TCEP, referring also to the conclusions of the Draft EU Risk Assessment. The registrant proposed no classification for carcinogenicity.

The compliance check decision for TCPP (EC No. 911-815-4) does not require the registrant to perform a carcinogenicity study (ECHA 2016c). TCPP is included on the CoRAP for evaluation in 2018 with several justifications, including suspected carcinogenicity "As the EU-RAR concluded that a quantitative read-across approach was not considered sufficiently robust for the purpose of classification and labelling, further action needs to be considered.".

The US National Toxicology Programme completed TCPP cancer studies in rats and mice and is in the process of preparing the study reports, which will undergo a formal pathology review. The results may not be available before May 2018 (personal communication with NTP, 17 May 2017).

The preliminary results of the 90 day studies in rat and mice are published (https://ntp.niehs.nih.gov/results/path/tablelistings/longterm/tr500599/tr_tcpp/index.html#DART). The results will still undergo pathology peer review before the final scores will be available.

Genetic toxicity studies were performed as well by the US National Toxicology Programme with the following results (US NTP 2017):

- Micronucleus in B6C3F1 mice (G20263B): positive in the male, negative in the female
- Micronucleus in Harlan Sprague-Dawley rats (G20263): negative in both sexes
- Salmonella (815918): test result negative. Results reported in the EU RAR (2008a) as Zeiger et al. (1992)
- Salmonella (G20263C): test result negative

The abovementioned studies from US NTP and any other new information regarding the mode of action and the assumption of a threshold will need to be considered in the event a restriction report will be prepared.

1.2.4.3.3. TDCP

The Draft EU Risk Assessment (EU RAR 2008b) summarised the available information on carcinogenicity toxicity as follows:

> "In a 2-year carcinogenicity study, in which groups of 60 male and 60 females rats were fed diets containing TDCP to achieve dose levels of 0, 5, 20 and 80 mg/kg/day, there was a significant increase in the incidence of renal cortical adenomas in mid and high dose animals at 24 months. There was no increase at 12 months. The incidence of benign testicular interstitial cell tumours was also increased in the mid- and high-dose animals at both 12 and 24 months. Hepatocellular adenomas and adrenal cortical adenomas were statistically increased in the high dose animals at 24 months.
>
> In the testes, there was an increased incidence of Leydig cell tumours in the mid and high dose males at both 12 and 24 months. The mechanism by which TDCP induces such tumours is not known. It is reported that one non-genotoxic mode of action by which chemicals can induce such tumours is attributed to alterations in the Hypothalmus-Pituitary-Testis (HPT) Axis which results in elevated levels of luteinising hormone (LH). Increases in LH levels have been shown to be necessary for the induction of Leydig cell tumours through chronic stimulation of the Leydig cells. There are seven known non-genotoxic hormonal

mechanisms which have the potential to disrupt the HPT axis leading to Leydig cell tumour induction. Two of these modes of action are not considered of relevance to humans (GnRH antagonism and dopamine agonism) (Clegg et al., 1997). However, the other five mechanisms, (5 α- reductase inhibition, androgen receptor antagonism, inhibition of testosterone biosynthesis, aromatase inhibition and exogenous oestrogen agonism) have been considered to be potentially relevant to humans.

Overall, while the mode of action by which these tumours are induced cannot be identified, there may be some concern for man regarding their formation.

Regarding the derivation of a N(L)OAEL for carcinogenicity to take forward to risk characterisation, this is taken as a LOAEL at 5 mg/kg/day. This is based on the hyperplasia of the convoluted tubule epithelium with increased incidences observed in all treated male animals and in high dose females at 24 months (as outlined in the repeated dose toxicity section 4.1.2.6.1). Hyperplasia was observed from the lowest dose tested. Hyperplasia is often considered as a pre-neoplastic lesion, which can lead to tumour formation. The study report does not provide enough detailed information to conclude whether the hyperplasia observed following treatment with TDCP would progress to cancer or whether the tumours observed with TDCP arise through a different mechanism. However, it is not unreasonable to assume that the tumours have developed through hyperplastic changes.

There is some evidence to suggest that TDCP is mutagenic in vitro. However, in vivo mutagenicity studies were negative, indicating that, in vivo, TDCP is non-genotoxic. This indicates that TDCP may be assumed to be a threshold carcinogen.

TDCP is classified as Carc. Cat. 3 R40 "Limited evidence of a carcinogenic effect" based on the results of the above carcinogenicity study further supported by a non-genotoxic mode of action for carcinogenic effects for TDCP.

In a study carried out to look at the mortality experience of worker in a TDCP manufacturing plant, there was a higher than expected number of lung cancers among male workers. However, the report concluded that there was no evidence linking these lung cancers with exposure to TDCP. There were no other cancers observed."

In the event a restriction report will be prepared, any new information regarding the mode of action and the assumption of a threshold will need to be considered.

1.2.4.4. Other effects

Other endpoints may need to be assessed, notably:

- Neurotoxicity: the brain was identified as one of the main sites of toxicity in the EU RAR (2009) for TCEP with a NOAEL of 44 mg/kg bw/day in the rat based on hippocampal lesions. A rat study not included in the EU RAR (2009) was Tilson et al. (1990). The study gives further evidence for neurotoxicity (learning deficits and hippocampal cellular damage). This study needs to be considered in any evaluation of neurotoxicity.
- Endocrine effects (e.g., for TCPP https://www.ncbi.nlm.nih.gov/pubmed/24051214)

1.2.4.5. Derivation of DNELs

In accordance with ECHA guidance Chapter R.8, the following default assessment factors (AFs) were applied to the starting point:

- Interspecies differences: 2.5 for interspecies differences and an allometric scaling factor of 4 for rats and 7 for mice;
- Intraspecies differences: 10;
- Dose-response relationship:
    - The guidance foresees that in specific cases, for example when for carcinogenicity the mode of action for a presumed threshold carcinogen is not well understood, an extra AF can be applied. This is relevant to the case at hand, as a reasonable threshold mechanism could not be identified for all tumours and tumour sites and thus no clear threshold can be identified for tumour induction.
    - Moreover, the guidance suggests to use an AF between 3 and 10 for extrapolation from LOAEL to NAEL, with the AF of 10 for exceptional cases.
    - Therefore, an overall factor of 6 is used to account for the uncertainties related to the dose-response relationship for carcinogenicity. For reproductive toxicity an AF of 3 was deemed sufficient.
- Differences in duration of exposure: a default AF of 2 is to be applied for extrapolating from sub-chronic (90-day study) to chronic (relevant to DNEL derivation for TCPP only). The reasoning is that a) in general the experimental NOAEL will decrease with increasing exposure times and b) other and more serious adverse effects may appear with increasing exposure times.

SCHER (2012) used an overall AF of 900 to the LOAEL of 12 mg/kg bw/day to derive a 'provisional' TDI of 13 µg/kg bw/day for TCEP. In contrast to the approach in the current assessment, SCHER (2012) used an AF of 3 for the LOAEL to NAEL extrapolation but used an additional AF of 3 considering the abovementioned uncertainties. SCHER (2012) used an AF for interspecies of 10 for the mouse however.

When an Annex XV dossier is prepared, a BMD approach might be considered as a starting point for DNEL derivation.

Table 5 Overview of DNEL derivation for carcinogenicity

	NOAEL (mg/ kg bw/day)	LOAEL (mg/ kg bw/day)	Endpoint and study reference	AFs	Correction for absorption	DNEL internal dose (µg/ kg bw/day)
TCEP	/	12	Kidney lesions (hyperplasia and hypertrophy of the urinary tubule epithelium together with enlargement of the nuclei) in an 18-month oral carcinogenicity study in mice at this LOAEL (Takada et al. 1989). Clear evidence for carcinogenicity at higher dose levels at various organ sites (kidney in rats and mice, thyroid in rats and liver in mice).	2.5 x 7 x 10 x 6 = 1050	1	**11**
TCPP	/	52	Increased absolute and relative liver weight, accompanied by mild thyroid follicular cell hyperplasia in males of all dose groups in a 90 day dietary study in the rat (Stauffer Chemical Co. 1981, as cited in the EU RAR 2008a)	2.5 x 4 x 10 x 6 x 2 = 1200	0.8	**35**
TDCP	/	5	Increase in the incidence of hyperplasia of the convoluted tubule epithelium in male rats at all dose levels in a dietary two-year carcinogenicity study (Stauffer Chemical Company 1981a, as cited in the EU RAR 2008b). Increased renal cortical adenomas, benign testicular interstitial cell tumours, hepatocellular adenomas, adrenal cortical adenomas and Leydig cell tumours were observed at higher doses.	2.5 x 4 x 10 x 6 = 600	1	**8**

Table 6 Overview of DNEL derivation for reproductive toxicity

	NOAEL (mg/ kg bw/day)	LOAEL (mg/ kg bw/day)	Endpoint and study reference	AFs	Correction for absorption	DNEL internal dose (µg/ kg bw/day)
TCEP	175	350	A NOAEL for fertility of 175 mg/kg bw/day was derived from an oral gavage study in CD-1 mice (Gulati et al. 1991 as cited in EU RAR 2009), based on a statistically significant reduction of the number of litters produced by the F0 generation, reduced pregnancy and fertility indices in the F1 generation, and statistically significantly reduced litter size in both the F0 and the F1 generations. A firm conclusion on developmental toxicity is hampered by poor reporting of rather old study (Kawashima et al. 1983 as cited in EU RAR 2009).	2.5 x 7 x 10 = 175	1	**1000**
TCPP	/	99	A LOAEL of 99 mg/kg is derived for effects on fertility and developmental toxicity in a dietary 2-generation study in rats (TNO Quality of Life 2007 as cited in EU RAR 2008a). This is based on effects on the effect on uterus weight seen in all dosed females in F0 (99, 330 and 988 mg/kg bw/day) and high dose females in F1, and regarding developmental effects based on a treatment related effect on the number of runts observed in all TCPP-treated groups of the F0 generation.	2.5 x 4 x 10 x 3 = 300	0.8	**264**
TDCP	100	400	A NOAEL of 100 mg/kg/day was derived from a developmental toxicity study with oral gavage during GD 6-15 in rats (Stauffer Chemical Company 1978f as cited in EU RAR 2008b), based on the statistically significant increased resorptions and the decreased foetal viability index at 400 mg/kg/day.	2.5 x 4 x 10 = 100	1	**1000**

1.2.4.6. Uncertainties in the hazard assessment

Uncertainties were not characterised as part of this screening report, although the following points deserve attention.

Carcinogenicity

- Mode of action
- Relevance to humans
- No carcinogenicity study is available for TCPP. The basis for the LOAEL is based on hyperplasia seen in a 90 day dietary study in the rat.

Reproductive toxicity

- A firm conclusion on developmental toxicity is hampered by poor reporting of a rather old study for TCEP.
- There is a data gap for female fertility for TDCP.

Other effects

- Neurotoxicity appears to be a sensitive effect in TCEP. Studies with TDCP and TCPP in hens did not raise a concern for this endpoint.
- Registrants self-classified TDCP as very toxic to aquatic life with long lasting effects.

1.2.5. Exposure assessment

TCPP is the least-cost and most- employed of the main flame retardants used in flexible polyurethane (PUR) foams (Danish EPA 2016a). The registered volume under REACH is 10 000-100 000 t/y. TCPP is an all-round flame retardant for all types of flexible PUR foams (Danish EPA 2016a).

The registered volume of TDCP under REACH is 1 000 – 10 000 tonnes per year. TDCP is more expensive and is used mainly for automotive applications, where TDCP is preferred due to lower fogging potential (lower potential to form a thin film on the windshield) (Danish EPA 2016a).

TCEP is currently not used as flame retardant for flexible PUR foams in the EU (Danish EPA 2016a). There was a full joint registration for TCEP in the 1-10 tonnage band but this registration is inactive. Information given by industry in 2003 revealed that there has been no manufacture in Western Europe (EU15) since 2001/2002 (ECHA 2010a). However, TCEP

may be present as impurity in other flame retardants[11], and possibly in imported articles (Danish EPA 2016a).

Danish EPA (2016a) reports that TCPP and TDCP have been identified in one third to one half of the tested safety car seats, while TCEP was identified in a few of the safety car seats. The substances were also present in a significant portion of the tested baby slings, prams, carrycots and baby strollers, as well as in a few earphones and baby changing mats.

The exposure assessment in this screening report is targeted to the exposure of infants to TCEP, TCPP and TDCP in flexible PUR foam in childcare articles, such as baby mattresses, safety seats and baby slings (also known as baby carriers). Furthermore exposure of infants to TCEP, TCPP and TDCP in residential upholstered furniture, in particular sofas. The article types considered to be 'reference articles' for the risk assessment are baby mattresses, safety seats, baby slings and sofas. The three OPFRs may also be used in other articles such as pushchairs, prams, carry cots, high seats, and baby changing mats (Danish EPA 2016a). Furthermore, at least in the US, the three OPFRs occur also in sleep positioners, nursing pillows, rocking chairs, infant bath maths, and baby walkers (Stapelton et al. 2011 as reported in Danish EPA 2016a).

The age group targeted in the assessment are infants (i.e., children below 12 months old). The reference age will be assumed to be 3 to <6 months. The mean body weight from the US EPA Exposure Factors Handbook (US EPA 2011) is 7.4 kg for this age group and the inhalation rate 4.1 m^3/day. The mean surface areas are: 690 cm^2 for the head, 1360 cm^2 for the trunk, 520 cm^2 for the arms, 200 cm^2 for the hands, 780 cm^2 for the legs, and 250 cm^2 for the feet.

1.2.5.1. Migration rates

Danish EPA (2015) reported data for the migration of TCEP, TCPP and TDCP from textile and foam samples of 2 baby slings, 1 baby mattress and 4 car safety seats. These 7 products were selected for migration testing because they contained the highest concentrations out of 30 screened products (Table 7)

The samples were taken from areas "where children will have the most direct contact". This was explained as "most often this will be the zones near of the baby's face, where the child can suck on the textiles".

Samples of approximately 2.5 grams were placed in 50 ml of artificial sweat for a duration of 3 hours. Using the surface area of the samples, the migration rate on weight basis (mg/kg) was converted to a migration weight on surface area basis (mg/m^2). Assuming, a

[11] According to ECHA (2010a), TCEP is a reaction by-product in the manufacture of other commercial flame retardants in which TCEP is present as impurity (tris(2-chloro-1-methylethyl)phosphate (TCPP); tris[2-chloro-1-(chloromethyl)ethyl]phosphate (TDCP); 2,2-bis(chloromethyl)trimethylenebis(bis(2-hloroethyl)phosphate)]). Danish EPA (2016a) also states that it occurs at low levels in a flame retardant which has traditionally been traded under the name V6 or V66 (and may hence be present in articles).

constant migration rate over 3 hours, the migration rate was divided by 3 to obtain a migration rate per hour (mg/cm^2/hour).

The migration data from Danish EPA (2015) is used as a basis for the oral and dermal exposure of children to car safety seats, baby slings, mattresses and sofas. However, considering the limited number of migration data (n= 11 for 7 products), the Danish data is not considered to be representative for the Danish market, the EU market, and especially not for markets in the UK and Ireland.

A loading rate for TCEP is 10 % relative to the finished foam is sufficient to achieve a clear flame retardant effect (EU RAR 2009). For TCPP a loading rate in flexible PUR foams between 2.5% and 14% is reported, with two producers indicating an average loading rate of around 7% to 8% (EU RAR 2008a). For the current risk assessment, only migration data for samples with a concentration of the individual flame retardant above 0.1% w/w (1000 mg/kg) were considered relevant to assess exposure from articles with intentionally added OPFRs. Inclusion of lower concentrations would lead to underestimating exposure from intentional use. Concentrations below 0.1% w/w may result from an OPFR being present as an impurity in other commercial flame retardants, contamination of the sample or the article, from rebonding of foams[12], or possibly in some cases also a result of migration into the material from other layers.

The average of the migration data (not relevant for TCEP) was used further in risk assessment. Thus, it is assumed that the concentration and migration is not dependant on the type of article. This may be a simplification of the reality, but no information is available to distinguish between article groups and the data available is not considered representative for the tested article groups.

It is noted that the exposure estimates derived for TCEP may underestimate the reasonable worst case exposure since the single migration measurement used was from a sample with a concentration of 0.5% w/w. The average concentration in the samples used to derive the average migration rate for TCPP is 1.3% which is roughly 5-fold lower than the typical concentration indicated by industry sources. The average concentration in the samples used to derive the average migration rate for TCPP is 3.4% which is the closest to the expected concentration. The reasonable worst case exposure estimates for TCEP may be underestimated with an order of magnitude and the estimates for TCPP may be underestimated sever fold as well.

According to industry information, a small volume of TDCP is used for textile applications in the EU (Danish EPA 2016a). However, Danish EPA (2016a) did not find concrete examples of such uses. The data from Danish EPA (2015) found generally very low concentrations (max. 0.07% w/w) of the three OPFRs in textiles which are not indicative for intentional use. In contrast, a study by the Danish Consumer Council from 2013, as reported in Danish EPA (2015), found levels up to 1.9% w/w of TCPP and 1.48% w/w of TDCP in the textile

[12] According to Danish EPA (2016a), about 10% of the produced PUR foam ends up as production scrap from the cutting. It is common to mix scraps of FR and non-FR foam and the rebonded foam may therefore contain varying levels of mixed flame retardants.

cover of car safety seats and in textile pads up to 1.2 % w/w of TCPP and 5.6% w/w of TDCP. When a restriction report is developed, further information regarding the use of the OPFRs in textiles may become available.

Table 7 Migration data from Danish EPA (2015)

Product	**Concentration (mg/kg)**			**Migration (mg/cm²/h)**		
	TCEP	**TCPP**	**TDCP**	**TCEP**	**TCPP**	**TDCP**
Car safety seats (textile + foam)						
A3B	<LOD	**0.480%**	**2.110%**	<LOD	**2.10E-03**	**1.40E-03**
A4	<LOD	0.006%	**4.260%**	<LOD	3.67E-05	**1.57E-03**
A5A	<LOD	0.005%	**3.150%**	<LOD	1.07E-04	**5.00E-03**
A8A	0.084%	**1.810%**	**0.510%**	4.30E-03	**8.67E-03**	**6.67E-04**
Baby slings						
B12A (foam)	0.008%	**1.120%**	0.016%	3.67E-04	**2.37E-02**	<LOD
B18A (foam + felt)	**0.470%**	**1.630%**	**1.300%**	**2.07E-02**	**3.67E-02**	**2.20E-03**
Baby mattresses (foam)						
M24B	<LOD	<LOD	**8.970%**	<LOD	<LOD	**7.00E-03**
average	**0.5%**	**1.3%**	**3.4%**	**2.07E-02**	**1.78E-02**	**2.97E-03**

1.2.5.2. Oral exposure

Children may be orally exposed to TCEP, TCPP and TDCP via intake of dust, mouthing of articles or due to hand to mouth behaviour.

Mouthing

Danish EPA (2016a) used the migration data presented in section 1.2.5.1 and assumed that the migration to artificial saliva would be the same to artificial sweat. The magnitude of the migration rate is expected to be driven by the specific sample and not so much by whether artificial saliva or artificial sweat was used in the experiment (both are aqueous media). This assumption was therefore supported in the current assessment.

The assumptions made by ECHA in the current assessment and by Danish EPA (2016a) are presented in Table 8. In addition, an oral absorption of 100% is applied for TDCP and TCEP and absorption of 80% is used for TCPP. ECHA assumed shorter daily mouthing durations as generally mattresses are flat and thus not thought to be mouthed extensively. Similarly, car seats (e.g., the belt pads) and baby slings are not considered to be mouthed for extensive periods of time on a daily basis. The mouthing estimate is also considered to encompass

exposure from hand-to-mouth contact. Overall, 10 minutes of mouthing per day for these articles appears reasonable.

It should be remarked that mattresses, safety seats and baby slings are covered with textile which may form a barrier to migration from the PUR to the mouth. However, since saliva easily wets both the textile and the PUR foam underneath it is not clear if the barrier is significant. No textile penetration factor was assumed for the mouthing scenario.

The key uncertainties to the oral exposure estimates are considered to result from the limited amount of available migration data and the significance of the textile barrier to the mouthing scenario.

Table 8 Assumptions made by ECHA and by Danish EPA (2016a) in the oral exposure assessment

Article	Age (months)		BW (kg)		Mouthing duration (min/day)		Mouthing surface area (cm^2)
	ECHA	Danish EPA	ECHA	Danish EPA	ECHA	Danish EPA	
car seats	3-6	6-12	7.4	9.2	10	30	10
baby slings	3-6	1-3	7.4	5.6	10	30	10
baby mattresses	3-6	3-6	7.4	7.4	10	30	10
sofas	3-6	3-6	7.4	7.4	10	Not considered	10

The calculated oral exposure from the articles analysed by Danish EPA (2015) is given in the tables below.

In comparison, Health Canada (2009) calculated an exposure of 40 µg/kg bw/day for infants (0–6 months old) and 20 µg/kg bw/day for toddlers (6 months to 4 years old) due to mouthing of foam cushion or furniture for 9 min/day containing TCEP at a concentration equivalent to TCEP's water solubility[13]. The exposure estimate is an order of magnitude higher than the levels calculated in Table 9. However, the exposure model used was different from the one applied in the current risk assessment and the resulting exposure values were considered overestimates.

[13] The assumptions were: water solubility (WS) of TCEP is 7820 mg/L, salivary flow rate in child's mouth (Vs) is 0.22 ml/min, convert L to mL (CF), fractional rate of extraction by saliva (FR) is 0.038, absorption factor by the oral route (AFo) is 0.5, exposure frequency mouthing behaviour (EFmouth) is 9 min/day (Environ 2003a, b), and body weight (BW) is 7.5 kg for infants and 15.5 for toddlers (Health Canada 1998). Dose = (7820 mg/L × 0.22 ml/min × 0.001 L/ml × 0.038 × 0.5 × 9 min/day) / 7.5 kg or 15.5 kg

Table 9 Oral exposure of infants to TCEP, TCPP and TDCP from mouthing car safety seats, baby slings, baby mattresses and sofas.

	Mouthing time	$A_{mouthing}$	BW	Migration	Textile penetration factor	$D_{der,\ external}$	F_{abs}	$D_{der,\ internal}$
	(min)	(cm^2)	(kg)	(mg/cm2/hour)		(µg/kg bw/day)		(µg/kg bw/day)
TCEP	10	10	7.4	2.07E-02	1	4.66E+00	1	4.7
TCPP	10	10	7.4	1.78E-02	1	4.01E+00	0.8	3.2
TDCP	10	10	7.4	2.97E-03	1	6.70E-01	1	0.7

Dust

The EU RAR (2009) for TCEP estimated a 95th and 99th percentile uptake of TCEP from dust ingestion due to hand to mouth behaviour of respectively 0.0015 and 0.0033 µg/kg bw/day for women and respectively 0.1 and 0.2 µg/kg bw/day for 1-3 year olds (modelled with @RISK-4.5 and assuming 20 and 100 mg/day as respectively, typical and upper limits of dust intake). The EU RAR (2009) used the 99th percentile for risk assessment (0.2 µg/kg bw/day). The EU RAR (2008a,b) for TCPP and TDCP used the value from the EU RAR (2009) for TCEP.

In the current screening assessment, the uptake of TCEP and TDCP from dust ingestion due to hand to mouth behaviour by infants is assumed to be the same as calculated by EU RAR (2009) for toddlers, i.e., it will be assumed to be **0.2 µg/kg bw/day** and **0.16 µg/kg bw/day** for TDCP (80% oral absorption).

Many studies on organophosphates in settled dust have been published since the latest literature search of the EU Risk Assessments. This literature requires review and may change the exposure estimates (e.g. Langer et al. 2016). Table 4 in Langer et al. (2016) suggests that the median value used in the EU Risk Assessment of 0.6 µg TCEP/g dust from Ingerowski et al. (2001) may be an order of magnitude lower than in recent studies. A restriction proposal may also need to revise the above assumption that the exposure used from toddlers can be used for infants. However, as shown in Table 12, the exposure contribution from dust appears to be very limited compared to other sources. Thus, resources dedicate to refining this assumption should be proportionate to the limited importance of this exposure source.

Drinking water

Exposure to TCEP from drinking water was calculated, starting from a content in drinking water of 52 ng/l, a consumption of 1-1.5 l/day and an average body weight of 7.5 kg, to be in the range of 0.007-0.01 µg/kg bw/day (SCHER 2012). In the current assessment, the exposure to TCEP from drinking water will be assumed to be **0.009 µg/kg bw/day** (3-6 months old).

1.2.5.3. Dermal exposure

Dermal exposure may occur from contact with furniture, childcare articles and house dust.

The Danish EPA (2016a) calculated the dermal exposure of TCEP, TDCP and TCPP from car safety seats, baby slings and baby mattresses. The data on migration to artificial sweat discussed in section 1.2.5.1 was used to estimate dermal exposure.

It should be remarked that mattresses, safety seats and baby slings are covered with textile which forms a barrier to migration from the PUR to the skin. Comparing one sample of textile of a carrycot (M24A) from Danish EPA (2015) and one sample of the foam underneath (sample M24B), it appeared that the concentration of TDCP in textile may be 1000 times lower than in the foam. This data is illustrative and cannot be considered representative. Importantly, sweat moistens both the textile and the foam that is in contact with it which will facilitate migration from the foam, via the textile to the skin. Thus, regardless of representativeness of this content measurement data, it would be inappropriate to apply a factor based on the content differences of the two materials to the migration rates. Overall, it appears to be reasonable to consider that the textile forms a barrier to migration by applying a textile penetration factor of 0.1 to the migration measurements from foam or foam+textile samples[14].

The assumptions made by ECHA in the current assessment and by Danish EPA (2016a) are presented in Table 10. In addition, a dermal absorption of 50% is applied for TCEP, 40% for TCPP, and 30% for TDCP. ECHA assumes a much longer time children sleep on a mattress than Danish EPA (2016a). The current assessment assumes that the contact time is 16 hours per day since newborns sleep about 16 hours per day[15] and may spend further time on the mattress while awake.

One out of the 10 mattresses samples by Danish EPA (2015) contained TDCP. While the sample containing TDCP was taken from a carrycot, there seems no reason to believe that mattresses for prams or (baby) beds could not contain TDCP. Indeed, Danish EPA (2016b) stated that *"Most brands offer mattresses in different sizes, so that there are models suitable for carrycots, prams and baby beds, respectively. The materials appear to be identical in the different size groups.".* Moreover, it is assumed that also TCPP is present in mattresses since TCPP is the least-cost and most-used flame retardant in PUR foams. This

[14] Similarly, applicants for authorisation of DEHP (AFA 2013) assumed a clothing penetration factor of 0.35 in the dermal exposure assessment of consumers and professionals to PVC articles such as rainwear, footwear, sleeping mats, air mattresses, upholstery, car seats, etc. This value was based on Driver et al. (2007) who concluded on a mean clothing penetration of 8 and 12% for patch and whole-body passive dosimeter samples included in the Environmental Protection Agency's Pesticide Handlers Exposure Database. The samples covered both solids and liquids.

[15] http://www.stanfordchildrens.org/en/topic/default%3Fid%3Dnewborn-sleep-patterns-90-P02632&sa=U&ei=58e3VM6CIIr5yATNnIGwAg&ved=0CG8QFjAT&usg=AFQjCNFvyKhlh5_8yFZvCBirEv-fTY56pQ

assumption is confirmed by Danish EPA (2016a)[16] and EU RAR (2008a)[17]. It cannot be excluded that also TCEP would be present in imported mattresses. Therefore, also exposure estimates for TCEP and TCPP in mattresses are provided in Table 11.

For sofas it is assumed that infants are in contact with the sofa with 25 % of the surface area of arms, hands, legs, feet and head for a daily duration of two hours and that sofas can contain TCEP, TCPP or TDCP.

The key uncertainties to the dermal exposure estimates are considered to result from the limited amount of available migration data and the significance of the textile barrier.

[16] Danish EPA (2016a) states that *"consultation revealed that both TCPP and TDCP are currently used as flame retardants in PUR foam for children's articles, such as pushchairs and baby mattresses"*.

[17] The EU RAR (2008a) states: "Most TCPP is used in rigid PUR foam (over 80%) mainly for construction applications. The remaining PUR applications are accounted for by flexible foam (over 17%), used in upholstery and bedding for the UK and Irish markets."

Table 10 Assumptions made by ECHA and by Danish EPA (2016a) in the dermal exposure assessment

Article	Age (months)		BW (kg)		Contact duration (h/day)		Contact surface	
	ECHA	Danish EPA	ECHA	Danish EPA	ECHA	Danish EPA	ECHA	Danish EPA
car seats	3-6	6-12	7.4	9.2	1	1	25% of arms, hands and legs: 375 cm^2	25% of arms, hand and legs: 445cm^2
baby slings	3-6	1-3	7.4	5.6	1	1	25% of the torso: 340 cm^2	25% of the torso: 295 cm^2
baby mattresses	3-6	3-6	7.4	7.4	16	3	25% of arms, hands, legs, feet and head: 610 cm^2	25% of the surface area of the body: 950 cm^2
sofas	3-6	3-6	7.4	7.4	2	Not considered	25% of arms, hands, legs, feet and head: 610 cm^2	Not considered

The calculated exposure based on the above assumptions is given for each of the three flame retardants in Table 11.

Table 11 Dermal exposure of infants to TCEP, TCPP and TDCP in car safety seats, baby slings, baby mattresses and sofas

	contact duration	A_{skin}	BW	Migration	Textile penetration factor	L_{der}	$D_{der,\ external}$	F_{abs}	$D_{der,\ internal}$
	(h)	(cm^2)	(kg)	(mg/cm2/hour)		(mg/cm^2)	(μg/kg bw/day)		(μg/kg bw/day)
TCEP									
Car safety seats	1	375	7.4	2.07E-02	0.1	2.07E-03	1.05E+02	0.5	52.4
Baby slings	1	340	7.4	2.07E-02	0.1	2.07E-03	9.51E+01	0.5	47.6
Baby mattresses	16	610	7.4	2.07E-02	0.1	3.31E-02	2.73E+03	0.5	1365.1
Sofas	2	610	7.4	2.07E-02	0.1	4.14E-03	3.41E+02	0.5	170.6
TCPP									
Car safety seats	1	375	7.4	1.78E-02	0.1	1.78E-03	9.02E+01	0.4	36.1
Baby slings	1	340	7.4	1.78E-02	0.1	1.78E-03	8.17E+01	0.4	32.7
Baby mattresses	16	610	7.4	1.78E-02	0.1	2.85E-02	2.35E+03	0.4	938.7
Sofas	2	610	7.4	1.78E-02	0.1	3.56E-03	2.93E+02	0.4	117.3
TDCP									
Car safety seats	1	375	7.4	2.97E-03	0.1	2.97E-04	1.51E+01	0.3	4.5
Baby slings	1	340	7.4	2.97E-03	0.1	2.97E-04	1.37E+01	0.3	4.1
Baby mattresses	16	610	7.4	2.97E-03	0.1	4.76E-03	3.92E+02	0.3	117.6
Sofas	2	610	7.4	2.97E-03	0.1	5.95E-04	4.90E+01	0.4	19.6

In comparison, the Draft EU Risk Assessments (EU RAR 2008a,b) considered it is reasonable to assume that dermal exposure to TCPP and TDCP will not exceed inhalation exposure and therefore the data on inhalation was used to estimate the reasonable worst case dermal exposure. According to EU RAR (2008a), most of the TCPP used in flexible foam is used in upholstery and bedding. EU RAR (2008a) reasoned that consumers do not come into direct contact with these foams and that therefore consumer exposure to TCPP from these foams is expected to be very low.

The EU RAR (2009) reported a migration of TCEP of 0.217 µg/cm2/h from upholstery containing 8 mg/cm² TCEP a dermal exposure estimate of 10 µg/kg bw/day for children with body weight 9.1 kg was taken forward in the EU RAR (2009)[18]. Using a lower body weight of 7.5 kg, SCHER (2012) estimated dermal exposure for 1-3 years old of 12.1 µg/kg bw/day. In comparison, the external dermal exposure estimate for TCEP from a sofa is calculated to be 531 µg/kg bw/day in the current assessment (44 times higher). However, the EU RAR/SCHER estimates did not appear to consider migration from PUR foam underneath the textile.

The Draft EU Risk Assessments for TCPP and TDCP did not specifically assess dermal exposure of children from furniture[19].

The EU RAR (2009) concluded that dermal exposure to TCEP from airborne dust was negligible due to the low concentrations of TCEP in dust (max. 0.1 µg/m³). However, dermal exposure from contact with house dust was considered for children and accounted for 0.018 µg/kg bw/day.

[18] Assuming a contact area of 1000 cm² (half of both forearms and hands), a four hour contact (e.g. during watching TV) an amount of ≈ 870 µg/event (= 0.217 µg/cm²/h * 4 h * 1000 cm²) was calculated. Assuming 100 events the yearly total amount of TCEP migrating from an upholstered armchair to the skin accounts for 87000 µg, resulting in an average exposure of ~ 3.9 µg/kg bw/day for adults. In analogy, using a smaller contact area of 380 cm² for 1-3 year old children, 330 µg/event can be calculated.

[19] The Draft EU Risk Assessments assumed a dermal exposure of 1.1 µg/kg bw/day for both TDCP and TCPP for adults (EU RAR 2008a,b). EU RAR (2008a,b) argued that in the absence of data on dermal exposure it is reasonable to assume that the dermal exposure will not exceed inhalation exposure. Therefore, the EU RAR (2008a,b) used the data on inhalation for dermal exposure as a reasonable worst case for adults. No separate estimate for children was taken forward for risk assessment.

1.2.5.4. Inhalation exposure

TCEP, TCPP and TDCP can be considered semivolatile organic compounds (SVOC)[20]. They appear in gaseous form in very limited amounts under normal conditions. Therefore, they are released primarily by abrasion and becomes part of the dust fraction (EU RAR 2009). However, Danish EPA (2016) stated that TDCP is preferred over TCPP due to lower fogging potential of the windshield of cars. TCPP and TCEP have practically the same vapour pressure (respectively, 1.4 x 10^{-3} Pa at 25°C and 1.14 x 10^{-3} Pa at 20°C). This statement would suggest that evaporation of TCEP and TCPP is significant. The vapour pressure of TDCP is 250 times lower than that of TCPP.

The EU RAR (2009) for TCEP estimated an inhalation exposure of 0.6 µg/m³. The value represents the 98th percentile of a large set of air concentration measurements from a study published in 2001. On the basis of this estimate, EU RAR (2009) derived respectively a 95th and 99th percentile of 0.07 and 0.96 µg/kg bw/day for inhalation exposure to TCEP for 3 year olds. EU RAR (2009) used the 99th percentiles for risk assessment. In the current screening assessment it is assumed that the inhalation exposure to TCEP for infants is the same as calculated by EU RAR (2009) for toddlers. The current screening assessment assumes a 95th percentile inhalation exposure to TCEP for infants of **0.07 µg/kg bw/day**. A restriction proposal may need to revise the above assumption that the exposure used from toddlers can be used for infants.

The draft EU RAR for TCPP reported that from a chamber simulation study the inhalation exposure to TCPP can be estimated to be 3.8 µg/m^3 (EU RAR 2008a). The results from a long-term aging trial on flexible PUR foam showed very good retention of TCPP and TDCP over time which appeared to challenge the chamber trials. As a typical case, a 2.8 µg/m^3 24hr TWA was used assuming that 18 out of 24 hours are spent in areas with PUR foam-containing furniture or other items. A reasonable worst case of 3.8 µg/m^3 was used in risk assessment and assumed consumers may spend 24h indoors (especially elderly), resulting in an inhalation exposure for adults of 1 µg/kg bw/day (assuming a 70 kg person inhales 20 m^3 of air per day and absorption is 100%). The EU RAR (2008a) did not assess the exposure to children specifically, but based on the reasonable worst case air concentration of 3.8 µg/m^3, the exposure to infants would be **2.1 µg/kg bw/day** (assuming a BW of 7.4 kg, inhalation rate of 4.1 m^3/day and that infants spend 24 hours indoors).

EU RAR (2008b) for TDCP used the same exposure estimates reading across from TCPP in the absence of substance specific air measurements, but noted that the estimate for TCPP is likely to be an over-estimate of exposure to TDCP.

[20] ThermoFisher (2017) defines the term "semi-volatile compounds" as: *"organic compounds that possess Henry's law constants (H) in the range of 10^{-5} - 3 x 10^{-7} atm x m^3/mol and demonstrate higher boiling points, usually greater than that of water with correspondingly low vapor pressure from 10^{-14} - 10^{-4} atm"* (the range of vapour pressure in atm converted to Pa gives approximately 4.1 x 10^{-9} – 41 Pa). The vapour pressures of TCEP, TCPP and TDCP fall well within the range of this definition.

1.2.5.5. Aggregated exposure

The aggregated exposure from all routes of exposure is presented in Table 12. To estimate the reasonable worst case exposure of infants to the three OPFRs, the article with the highest dermal exposure was used, i.e., mattresses.

The reasonable worst case aggregated exposure of estimate is driven by the dermal exposure and by exposure from mouthing. A possible restriction dossier may attempt to estimate the size of the population in the EU that may be exposed at these levels. This population would roughly correspond to the annual number of mattresses with the three OPFRs placed on the market multiplied by the service life of a mattress. A similar exercise may be performed to cover the other identified articles that lead to exposures above the DNEL (e.g., baby slings, car safety seats, sofas).

It is noted that the exposure to TCEP may be underestimated with an order of magnitude, see section 1.2.5.1.

Table 12 Aggregated internal exposure of infants to TCEP, TCPP and TDCP from different exposure routes

Routes of exposure		**Internal exposure (µg/kg bw/day)**		
		TCEP	**TCPP**	**TDCP**
Oral	Mouthing (mattress)	4.7	3.2	0.7
	Dust intake	0.2	0.16	0.2
	Drinking water	0.009	No data	No data
Dermal (mattress)		1365.1	938.7	117.6
Inhalation		0.07	2.1	2.1
Aggregated exposure		**1370.0**	**944.1**	**120.6**

The EU RAR (2009) estimated a total body burden for TCEP under reasonable worst case conditions of about 3 months up to 240 µg/kg bw/day (from sucking on toys, the other paths were considered to be negligible). The EU RAR (2009) did not consider exposure from mouthing of childcare articles and the above estimate did not consider the mouthing of toys. No specific exposure scenario for infants were considered in the draft EU RARs for TCPP or TDCP (EU RAR 2008a,b).

Representative human biomonitoring may provide important information about the aggregated exposure. The representativeness of the biomonitoring data depends on the size of the studies and the population covered by the studies (e.g., number of countries). Based on the screening exercise, it would appear that only a very limited number of biomonitoring data is available for organophosphates (e.g. Fromme et al. 2014; Cequier et al. 2015) and the results are reported as urinary concentrations. Fromme et al. (2014) stated that no quantitative information for back-calculating to oral exposure was available for the flame retardants and thus the data cannot be readily compared with the exposure values from

modelling. In addition, biomonitoring data for infants is unlikely to be available. It would thus appear that a possible restriction proposal will principally rely on exposure modelling.

1.2.6. Risk characterisation

Based on the screening assessment, a risk for carcinogenicity from exposure of infants is identified for all three OPFRs and for all four reference article types (Table 13), except TCPP in car safety seats and TDCP in baby slings. A risk for reproductive effects from TCEP and TCPP in mattresses is furthermore identified.

As can be seen from Table 15, a risk for carcinogenicity from aggregated exposure to TCEP, TCPP and TDCP in childcare articles and from other exposure sources has been identified. A risk for reproductive toxicity from aggregated exposure to TCEP and TCPP in childcare articles and from other exposure sources is expected.

There are uncertainties related to the limited migration data available. As mentioned in section 1.2.5.1, the fairly low concentrations in the sampled products may lead to underestimation of the reasonable worst case exposure estimates (for TCEP possibly with an order of magnitude and for TCPP several fold as well.

The second key uncertainty to the oral and dermal exposure estimates is related to the relevance of the textile barrier to migration (i.e., no textile barrier assumed for exposure from mouthing and a penetration factor of 0.1 for dermal exposure).

As mentioned in section 1, if a restriction report is prepared, risks from exposure to the three OPFRs for other populations, such as adults, or resulting from other uses and article groups may need further consideration. A restriction proposal will also need to attempt to determine a safe concentration level for OPFRs in childcare articles and residential furniture. The evidence currently available suggests that non-intentional uses may still lead to RCRs above 1.

Table 13 Risk characterisation ratios for carcinogenicity resulting from exposure to TCEP, TCPP and TDCP per category of reference article types

	TCEP			**TCPP**			**TDCP**		
	Mouthing	**Dermal contact**	**Sum**	**Mouthing**	**Dermal contact**	**Sum**	**Mouthing**	**Dermal contact**	**Sum**
Car safety seats	0.4	4.8	**5.2**	0.1	1.0	**1.1**	0.1	0.6	**0.6**
Baby slings	0.4	4.3	**4.7**	0.1	0.9	**1.0**	0.1	0.5	**0.6**
Baby mattresses	0.4	124.1	**124.5**	0.1	26.8	**26.9**	0.1	14.7	**14.8**
Sofas	0.4	15.5	**15.9**	0.1	3.4	**3.4**	0.1	2.5	**2.5**

Table 14 Risk characterisation ratios for reproductive toxicity resulting from exposure to TCEP, TCPP and TDCP per category of reference article types

	TCEP			**TCPP**			**TDCP**		
	Mouthing	**Dermal contact**	**Sum**	**Mouthing**	**Dermal contact**	**Sum**	**Mouthing**	**Dermal contact**	**Sum**
Car safety seats	0.0	0.1	**0.1**	0.0	0.1	**0.1**	0.0	0.0	**0.0**
Baby slings	0.0	0.0	**0.1**	0.0	0.1	**0.1**	0.0	0.0	**0.0**
Baby mattresses	0.0	1.4	**1.4**	0.0	3.6	**3.6**	0.0	0.1	**0.1**
Sofas	0.0	0.2	**0.2**	0.0	0.4	**0.5**	0.0	0.0	**0.0**

Table 15 Risk characterisation ratios for carcinogenicity resulting from aggregated exposure to TCEP, TCPP and TDCP

	Internal exposure (µg/kg bw/day)	**DNEL internal dose (µg/kg bw/day)**	**RCR**
TCEP	1370.0	11	**124.5**
TCPP	944.1	35	**27.0**
TDCP	120.6	8	**15.1**

Table 16 Risk characterisation ratios for reproductive toxicity resulting from aggregated exposure to TCEP, TCPP and TDCP

	Internal exposure (µg/kg bw/day)	**DNEL internal dose (µg/kg bw/day)**	**RCR**
TCEP	1370.0	1000	**1.4**
TCPP	944.1	264	**3.6**
TDCP	120.6	1000	**0.1**

Combined exposure

For simplicity, the current screening report did not assess the risks from combined exposure. However, considering the structural similarity and similarity of observed effects related to carcinogenicity, and since co-exposure to TCEP, TCPP and TDCP occurs (Danish EPA (2015), it would appear reasonable to consider risks from combined exposure to these chlorinated organophosphate flame retardants.

Although the mode of action for carcinogenicity is uncertain it appears to be a non-genotoxic mechanism that is highly likely to be the same for all three substances. This has also been the assumption in the past qualitative read-across. Currently no carcinogenicity study data is available for TCPP but will be available next year and at that point the basis for assessing risks from combined exposure can be reviewed.

The risks from combined exposure should only consider adding RCRs where co-exposure can occur and exposure assumptions are reasonable. Several products in Danish EPA (2015) (i.e., A3, A8 and B18) show significant concentrations of two or three of the OPFRs[21]. Since, the drivers of exposure are dermal and oral exposure from the three OPFRs in childcare articles, the risks from combined exposure from ingestion of dust and from inhalation exposure would appear to be negligible in comparison to dermal and oral exposure.

1.3. Justification for an EU wide restriction measure

A Union-wide action to address the risks associated with EU manufactured or imported articles containing TCEP, TCPP and TDCP is needed, with the following reasons:

- To ensure a harmonised high level of protection of human health and the environment across the Union.
  One of the primary reasons to act on a Union-wide basis is the cross-boundary human health problem. Although the percentage of the population of infants at risk would appear to be the largest in the UK and Ireland as a result of the national legislation regarding fire safety, the risk identified nevertheless exists in all EU countries since the flame retardants are present also in childcare articles and furniture placed on the market in the other Member States. A possible restriction proposal may attempt to characterise the population at risk in further detail.

- To ensure the free movement of goods within the Union.
  To support the internal market of substances, articles containing the three OPFRs need to circulate freely once on the EU market, which stresses the importance of an EU-wide action rather than action by individual Member States.

However, see RMO 2 in section 2.1 regarding a possible exemption for the UK and IE.

[21] This is 3 out of 7 products where the individual concentration was above 0.1% w/w, suggesting co-occurrence may be common for TCEP, TCPP and TDCP.

1.4. Baseline

Manufacturing and use

The manufacturing and use in the EU is described in Danish EPA (2016a). The following are extracts from the study:

> ***"Application as flame retardants***
>
> *The three substances are additive flame retardants, i.e. they are physically combined with the material being treated, rather than being chemically combined. The amount of flame retardant used in any given application depends on a number of factors, such as the flame retardancy required for a given product; the effectiveness of the flame retardant and synergist within a given polymer system; the physical characteristics of the end product (e.g. colour, density, stability, etc.); and the use to which the end product will be put. Data provided by the producers of flexible foams in response to the EU Risk Assessment for TCPP indicates loading rates between 2.5% and 14%, with two of the producers indicating a loading rate of around 7% to 8% TCPP in average foams (ECB, 2008b).*
>
> ***Overall use of TCPP, TDCP and TCEP***
>
> *TCPP is the least-cost and most-used of the main flame retardants used in flexible polyurethane (PUR) foams. EU consumption was about 40,000 t/y in 2000 and the registered volume under REACH is in the 11,000-110,000 t/y range. TCPP is an all-round flame retardant for all types of flexible PUR foams. TDCP is more expensive and the total EU consumption is less than 10,000 t/y, being used mainly for automotive applications, where TDCP is preferred due to lower fogging potential (lower potential to form a thin film on the windshield). TCEP is currently not used as flame retardant for flexible PUR foams in the EU, but may be present at low levels in a flame retardant which has traditionally been traded under the name V6 or V66 (and may hence be present in articles).*
>
> ***Intentional use of the substances in children's articles***
>
> *None of the article manufacturers that provided inputs to the study acknowledge the use of TCEP in their products. Furthermore, some article manufacturers have added this substance to a black list of chemicals to be avoided. On the other hand, consultation revealed that both TCPP and TDCP are currently used as flame retardants in PUR foam for children's articles, such as pushchairs and baby mattresses. No examples of the use of the three chlorinated flame retardants in textiles were identified through the consultation.*
>
> *Manufacturers consulted claim that the main driver to use the flame retardants in children's articles is the UK fire safety regulations. In fact, all the manufacturers that confirmed use of one or more of the flame retardants are either UK-based or add the flame retardants only to those products des-tined for the UK and Irish market. They also all agreed that their preference was to*

not add these substances, claiming potential health risks and consumer concerns as the main reasons. According to consultees, PUR foam containing flame retardants has an inferior technical performance com-pared to standard non-FR foam, particularly regarding durability, comfort and smell. Cost is also listed as a reason for some products with high PUR foam content, with FR foam being around 15% more expensive than non-FR foam. In addition to these costs, non-UK manufacturers consulted suggest that complying with UK fire regulations implies significant logistical costs, linked to keeping separate stocks, production and distribution lines for products destined for the UK and Irish markets."

Baseline

A possible restriction proposal will define a "baseline" scenario, which describes the tonnages of TCEP, TCPP and TDCP estimated to be contained in articles[22] placed on the EU28 market in the absence of a restriction. The starting point would be the information on manufacturing and use described above, but as far as possible, the baseline should reflect the main factors impacting a projection of future tonnages in the relevant articles in scope of a possible restriction (e.g., childcare articles and furniture). These factors include foreseen regulatory changes in and outside the EU, any long term market forces influencing the use of the TCPP and TDCP in article manufacturing in EU28, and market forces influencing the import of articles containing TCEP, TCPP and TDCP to the EU.

2. Impact assessment

2.1. Risk management options

Section to be developed in case a restriction report is prepared. Some initial considerations regarding risk management options (RMOs) and combinations thereof that may be considered are as follows:

1. An EU-wide proposal to restrict TCEP, TCPP and TDCP in PUR foams in childcare articles and residential furniture. The concentration limit for such a restriction is discussed in section 2.5. The restriction may need to cover textiles as well (see section 1.2.5.1).

2. A restriction as in RMO 1, but exempting UK and Ireland (or giving these MSs the choice to opt-out under certain conditions). On the one hand, the population at risk from exposure to the three OPFRs would appear to be the largest in the UK & IE, but on the other hand, the chief share of the impacts of a possible restriction as in RMO 1 would be carried by these two Member States. Substitution costs of this RMO may be minimal: there may be some costs for UK and IE article manufacturers related to

[22] The type of articles will depend on the scope of a possible proposed restriction. On the basis of the assessment in the current screening report, the focus would be on tonnages in childcare articles and furniture.

logistics of separating products for markets with different requirements, but these may be partly offset by reduced production costs of non-FR PUR foams. The UK & IE would then be able to choose to have their own national restriction or to follow the EU-wide restriction.

3. Inclusion of toys for children older than three years in the scope of a restriction as in RMO 1 or 2. The OPFRs in toys for children older than three are not restricted by the current restriction under the Toys Directive, except for those toys that are intended to be placed in the mouth.

4. In addition to the three RMOs mentioned above, harmonised classification and labelling may be an appropriate action for TCPP. Depending on the outcome of the US National Toxicology Programme cancer studies for TCPP, a need for harmonised classification for carcinogenicity may need to be considered. A harmonised classification as Carc. 1B or Repro 1B would normally result in a restriction of TCPP in consumer mixtures and thereby address the potential concern with TCPP in 1-K foams for the DIY filling of cavities.

2.2. Restriction scenario(s)

Section to be developed in case a restriction report is prepared. A possible restriction proposal may propose to restrict TCEP, TCPP and TDCP in PUR foams in childcare articles and residential furniture. The concentration limit for such a restriction is discussed in section 2.5.

2.3. Economic impacts

Section to be developed in case a restriction report is prepared. Some initial considerations regarding substitution can be made here.

Of note is that addition of flame retardants is seen as a cost and a burden by the article manufacturers (n=7) consulted by Danish EPA (2016a). The main driver for their use being UK and Irish fire safety regulations (Danish EPA 2016a). The European Furniture Industries Confederation (EFIC) lodged a legal complaint with the European Commission against the UK and Irish Fire Safety Regulations[23], and supported a policy paper "The Case for Flame Retardant Free Furniture"[24]. EFIC considers there is growing evidence showing that many flame retardants are toxic to health and the environment and that the UK and Irish fire safety regulations represent a trade barrier inside the European Single Market.

PUR foams with FRs are around 15% more expensive than without FRs and their quality is inferior (lower technical performance regarding durability, comfort and smell) (Danish EPA 2016a). Moreover, non-UK article manufacturers claimed they are forced to have separate production lines for products destined for the UK and Irish markets. This then suggests that

[23] http://www.efic.eu/News.aspx?id=43

[24] http://www.efic.eu/News.aspx?id=25

non-EU article manufacturers do not add FRs to products destined for the EU market and that the products found on these markets with the three OPFRs come from the UK, Ireland or are imported from outside the EU. However, this information is based on a limited number of article manufacturers. The call for evidence on this screening report may provide further information on this matter.

Interestingly, the substitution costs of a possible restriction may therefore be minimal[25], except for the UK and Ireland where they may be significant. It is at this point in time unclear how the future relationship between the UK and the European Union may influence the need or not to factor in the costs (and benefits) for the UK.

For some childcare articles the UK fire safety regulations do not apply, e.g., baby carriers, slings and rucksack which are designed to be worn outdoors. It would appear that for these articles the presence of the flame retardants has no useful function and it might be assumed that therefore there are no substitution costs, on the contrary, there may be gains from substitution as the use of non-FR PUR is cheaper and the quality of the product increases.

The alternatives to the use of the three OPFRs in childcare articles was studied by Danish EPA (2016a) and summarised as follows:

> *"Alternatives to the substances*
>
> *Several chemical alternatives with a better environmental and health profile than the profiles for the chlorinated phosphorous FRs exist, as evaluated by US EPA Design for the Environment programme. In addition to the overall better score on key parameters as concerns PBT and CMR properties, reactive flame retardants and polymeric flame retardant alternatives are considered to result in lower levels of user exposure and lover releases to the environment compared to the three chlorinated phosphorous flame retardants (which are additive flame retardants).*
>
> *In particular, the alternatives have been developed for use in automotive applications where requirements for low fogging and low VOC emissions have been the driving forces for their development. In general, the available alternatives thus have better properties for these parameters. The lower fogging potential may also indicate a lower potential for evaporation of the substances from articles in use. The low levels of migration of reactive flame retardants has made these flame retardants attractive for foams marketed as "green", and the reactive flame retardants are in particular applied in PUR foams from bio-based polyols marketed as "green" for the US market.*
>
> *The applications of PUR foam using alternative flame retardants has mainly been for automotive applications and furniture complying with regulation in the USA. Limited experience with the use of the evaluated alternative flame*

[25] There may for example be costs for article manufacturers using rebounded PUR foam and recyclers of soft PUR foam, as well as substitution costs for companies outside the EU that may partially be transferred to the EU supply chain.

retardants for furniture complying with the UK fire safety regulations has been identified. For some dense foams, melamine (also used in combination with e.g. TCPP) can be used alone, but melamine is only applicable for a limited range of foams. None of the available alternatives can be used as a simple substitute for the chlorinated phosphorus flame retardants for all applications, but different alternatives may be needed for different foams. The use of the alternative flame retardants for children's articles for the UK market may be challenging and substantial R&D is needed. However, the manufacturers of alternative flame retardants contacted for this study have not indicated that it would be impossible to meet the requirement by using the alternative flame retardants. Time needed for R&D is indicated to be in the range of 3 months to one year for each application. It is estimated by one manufacturer of alternatives that, for a full transition, the build-up of additional capacities for alternatives may be necessary, and the time required for this would be 3-5 years.

The alternative flame retardants are substantially more expensive than the chlorinated phosphorous flame retardants and, even though lower loadings are necessary, additional costs in the 20-200% range have been indicated by manufacturers. More information on additional costs is provided in a confidential Annex for the Danish EPA only."

2.4. Human health and environmental impacts

Section to be developed in case a restriction report is prepared. The possible risks for increased cancer cases and possible other adverse health outcomes as a result of exposure to the three OPFRs will need to be assessed.

2.5. Other impacts, practicability and monitorability

Distributional impacts

On the one hand, the population at risk from exposure to the three OPFRs would appear to be the largest in the UK & IE, but on the other hand, the chief share of the impacts of a possible restriction as in RMO 1 would be carried by these two Member States. If benefits of a possible restriction outweigh the risks, the net benefits of a possible restriction to society will also be concentrated in the UK & IE.

Practicability and monitorability

Some initial considerations regarding a concentration limit for a potential restriction proposal can be made here. The concentration limit will affect the practicability and monitorability of possible restriction on the three OPFRs in PUR foams in childcare articles and residential furniture.

According to Danish EPA (2016a), most production sites in the EU produce both FR and non-FR grades of PUR foams which may lead to contamination. Moreover, the three OPFRs may be present as impurities in commercial FR mixtures (Danish EPA 2016a). Thus, if a limit value of 5 mg/kg (0.0005% w/w) is applied as in the restriction under the Toys Directive (Commission Directive 2014/79/EU), a contractual agreement that the substances are not intentionally added to the product would not ensure that the substances are not present above the limit value. This would impact compliance control costs for companies. From this perspective, a higher limit value such as 0.1% w/w would appear to be attractive.

A limit of 0.1% w/w would appear to prevent intentional use of the three OPFRs (except perhaps from rebondig). However, based on the information considered in the screening assessment, a limit value of 0.1 % w/w would not be sufficiently protective. From the perspective of risk reduction and harmonisation of limits with the Toys Directive, a limit value of 5 mg/kg (0.0005% w/w) may be the most suitable option.

A possible future restriction proposal should endeavour to optimise practicability while still achieving adequate control.

2.6. Proportionality (including comparison of options)

Section to be developed in case a restriction report is prepared.

3. Assumptions, uncertainties and sensitivities

Section to be developed in case a restriction report is prepared.

4. Conclusion

On the basis of Article 69(2) of the REACH Regulation, ECHA has developed a screening report considering whether the use of tris(2-chloroethyl) phosphate (TCEP) in articles poses a risk to human health or the environment that is not adequately controlled. The intrinsic property for which TCEP is included in Annex XIV is toxic for reproduction (Article 57c) but the screening report also covers the carcinogenic properties of TCEP since it is considered to be a critical endpoint in risk assessment.

In developing the screening report, tris(2-chloro-1-methylethyl) phosphate (TCPP) and tris[2-chloro-1-(chloromethyl)ethyl] phosphate (TDCP) were identified as substances with similar properties and uses to TCEP and were therefore also included in scope.

The screening assessment identified a risk for children from exposure to TCEP, TCPP and TDCP in flexible polyurethane (PUR) foams in childcare articles and residential furniture. Therefore, ECHA recommends an Annex XV restriction dossier is prepared. As the scope of such a restriction proposal is outside the scope of Article 69(2) in terms of the inclusion of TDCP and TCPP and the inherent properties other than reproductive toxicity, a request from the Commission will be needed to initiate the preparation of the report.

5. Abbreviations and acronyms

bw	body weight
CAS	Chemical Abstract Service
CPE FRs	chlorinated phosphate ester flame retardants
DfE	Design for the Environment Programme (US EPA programme)
DIY	Do It Yourself
Danish EPA	Danish Environmental Protection Agency
DNEL	Derived No-Effect Level
ECHA	European Chemicals Agency
EU RAR	European Union Risk Assessment Report
FR	flame retardant
LOAEL	Lowest Observed Adverse Effect Level
NAEL	No Adverse Effect Level
NOAEL	No-Observed Adverse Effect Level
OPFRs	organophosphate flame retardants
PUR	polyurethane (also known as PU)
RCR	Risk Characterisation Ratio
RMO	Risk Management Option
R&D	research and development
TCEP	tris(2-chloroethyl) phosphate
TCPP	tris(2-chloro-1-methylethyl) phosphate or "Reaction mass of tris(2-chloropropyl) phosphate and tris(2-chloro-1-methylethyl) phosphate and Phosphoric acid, bis(2-chloro-1-methylethyl) 2-chloropropyl ester and Phosphoric acid, 2-chloro-1-methylethyl bis(2-chloropropyl) ester"
TDCP	tris[2-chloro-1-(chloromethyl)ethyl] phosphate
US EPA	United States Environmental Protection Agency
US NTP	United States National Toxicology Programme

V6	commercial products of 2,2-bis(chloromethyl) trimethylene bis[bis(2chloroethyl)phosphate]
V66	commercial products of 2,2-bis(chloromethyl) trimethylene bis[bis(2chloroethyl)phosphate]
VOC	volatile organic carbon
1-K foam	one component foam (also known as 1K foam)

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