TRIS(2-CHLORO-1-METHYLETHYL) PHOSPHATE (TCPP)

CAS No: 13674-84-5

EINECS No: 237-158-7

SUMMARY RISK ASSESSMENT REPORT

Final report of May 2008

Ireland (lead) and United Kingdom

Rapporteur for the risk assessment of TCPP is Ireland (lead) and United Kingdom. The environmental exposure and property review was undertaken under contract to the rapporteur by Peter Fisk Associates. The human health exposure review was undertaken under contract to the rapporteur by Workplace Environment Solutions Ltd.

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PREFACE

The report provides the environmental risk assessment of the substance tris(2-chloro-1-methylethyl) phosphate (TCPP) in the frame of Council Regulation (EEC) No. 793/93 on the evaluation and control of the risks of existing substances. For detailed information on the risk assessment principles and procedures followed, the underlying data and the literature references, the reader is referred to the original risk assessment report that can be obtained from the European Chemicals Bureau[1]. The present summary report should preferably not be used for citation purposes.

[1] European Chemicals Bureau – Existing Chemicals – http://ecb.jrc.it

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EUSES calculations can be viewed as part of the report at the website of the European Chemicals Bureau: http://ecb.jrc.it

TABLES

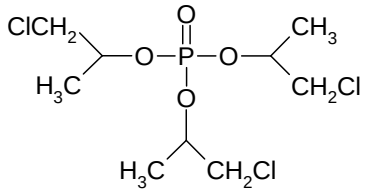
1 GENERAL SUBSTANCE INFORMATION

TCPP is one of three chloroalkyl phosphate substances[2] that have undergone risk assessment in parallel due to their similar use pattern.

1.1 IDENTIFICATION OF THE SUBSTANCE

CAS Number:	13674-84-5
EINECS Number:	237-158-7
IUPAC Name:	Tris(2-chloro-1-methylethyl) phosphate
Synonyms	2-Propanol, 1-chloro, phosphate (3:1)
	Tris(monochloroisopropyl) phosphate (TMCP)
	Tris(2-chloroisopropyl) phosphate (TCIP)
	Phosphoric acid, tris(2-chloro-1-methylethyl) ester
	Tris(beta-chloroisopropyl) phosphate
	1-Chloro-2-propanol phosphate (3:1)
	TCPP: this common acronym is used throughout this report

Structural formula



1.2 PURITY/IMPURITIES, ADDITIVES

Tris(2-chloro-1-methylethyl) phosphate (hereafter referred to as TCPP) is a reaction product containing a mixture of stereoisomers. The individual isomers are not marketed separately. The main isomer (50-85% w/w) is the tris(1-chloro-2-propyl) form. The CAS number 13674-84-5 is used for this structure and also for the commercial substance. A typical purity (total of the four key isomers) is >97.9% (w/w). The impurity profile is specific to each manufacturer.

1.3 PHYSICO-CHEMICAL PROPERTIES

General substance information and physicochemical properties are shown in Table 1.1.

[2] The others being TDCP (CAS no. 13674-87-8) and V6 (CAS no. 38051-10-4).

Table 1.1 Identification and physico-chemical properties of TCPP

Property	Value
CAS number	13674-84-5
Molecular Formula	$C_9H_{18}Cl_3O_4P$
SMILES notation	O=P(OC(CCl)C)(OC(CCl)C)OC(CCl)C
Molecular Weight	327.57
Physical state	Liquid
Melting point	<-20°C (measured, commercial product composite sample)
Boiling point	~ 288°C (decomposes) (measured, commercial product composite sample)
Relative density	1.288 at 20°C (measured, commercial product composite sample)
Vapour pressure	1.4 x 10^{-3} Pa at 25°C (measured, commercial product composite sample)
Surface tension	No study available, but not expected to exhibit surface activity
Water solubility	1,080 mg/l at 20°C (measured, commercial product composite sample)
Partition coefficient n-octanol/water (K_{ow})	log K_{ow} 2.68 (measured, commercial product composite sample)
Flash point	No flash up to 245°C, then decomposes (closed cup; measured)
Autoflammability	>400°C (measured)
Flammability	Not expected to be flammable.
Explosive properties	Not expected to be explosive.
Oxidizing properties	Not expected to be oxidising.
Viscosity (kinematic viscosity)	68.5 cP at 20°C (measured)
Henry's law constant	3.96 x 10^{-4} Pa m^3/mol at 25°C (by calculation from vapour pressure and water solubility)

1.4 CLASSIFICATION

A classification of not dangerous for the environment (not classified) was agreed at EU level in 2005[3].

TCPP is classified as R22 (harmful if swallowed). The classification for carcinogenicity and reproductive toxicity are not yet agreed. Based on the information available, no classification for carcinogenicity is proposed. TCPP is considered a borderline case for classification for effects on fertility (Repro Cat 3 R62 / no classification) and developmental toxicity (Repro. Cat 3 R63 / no classification).

The classification and labelling proposal for TDCP will be considered by the Risk Assessment Committee (RAC) in due course.

[3] Commission Working Group on the Classification and Labelling of Dangerous Substances Meeting on Environmental Effects of Existing Chemicals, Pesticides & New Chemicals September 28-30, 2005

2 GENERAL INFORMATION ON EXPOSURE

TCPP is used in the European Union (EU) as a flame retardant additive for polyurethane at typical loadings of ~ 8-10% w/w. The main use of the treated polyurethane is in rigid foams for construction applications. A smaller but still significant amount is used in flexible foams for furniture. A number of other minor confidential uses have been identified (<2.5% of the supply volume).

36,000 tonnes of TCPP were produced at three sites in Germany and one in the UK in 2000. There was both import of TCPP to the EU from a non-EU producer and also some export in 2000, with an overall net import of ~ 2,000 tonnes. EU consumption remained stable between 1999 and 2003 – the supply tonnage used in the risk assessment represents the upper limit of sales over this period. There is some import of treated goods (furniture, canned foams and finished goods containing TCPP in rebonded foam). Over 40,000 tonnes of TCPP were consumed in the EU in 2000.

TCPP is one of the main substances to have replaced tris(chloroethyl) phosphate (TCEP, CAS number 115-96-8) in Europe. TCEP has also been assessed in the ESR process.

3 ENVIRONMENT

3.1 ENVIRONMENTAL EXPOSURE

The environmental fate and behaviour of TCPP is characterised by the following properties:

- TCPP is expected to degrade in the atmosphere by reaction with hydroxyl radicals, with an estimated half-life of 8.6 hours.
- TCPP is inherently biodegradable, though not fulfilling the criteria of the EU Risk Assessment Technical Guidance Document (TGD) for degradation in the waste water treatment plant (WWTP). There is some evidence of microbial acclimation, which suggests that removal at some industrial sites could be higher than modelled in the risk assessment. TCPP does not not readily hydrolyse ($t_{1/2}$ >1 year in neutral conditions at ambient temperature).
- It does not adsorb significantly to organic matter, based on an estimated log K_{oc} of 174, and has a low tendency to volatilise from water, based on a Henry's Law constant 3.96 x 10^{-4} Pa.m^3/mol.
- TCPP has a low potential to bioaccumulate in fish (the measured bioconcentration factor (BCF) is 0.8-4.6).

Fugacity modelling suggests that if TCPP were released to air, it would mostly precipitate to soil; if released to water or soil, it would mostly remain in the compartment of release. There is relatively little movement between soil and water, because transfer via the air compartment is very slow. In water, the modelled adsorption to sediment is very low.

The predicted fate in WWTP is: 97.9% to water; 2.1% adsorbed to sewage sludge; 0% to air; and 0% degraded.

Emissions at the manufacturing stage have been estimated using site-specific data from the producer companies. Emissions from formulation sites (systems houses and formulators of one-component foams) have been estimated based on defaults from the plastics additives Emission Scenario Document and using site-specific assessment as appropriate, though it is noted that there is evidence that releases to air might be very much lower when best practice is followed.. For all life cycle stages concerning processing or storage of polyurethane foams, emission estimates are based on modelling work performed for the purposes of this assessment. Emissions from the confidential minor uses are based on estimates from relevant Emission Scenario Documents, read-across from relevant published risk assessments, site-specific information and WWTP details in some instances. Emissions arising from key recycling applications have also been assessed. Disposal to landfill is considered likely to be the most significant route of disposal of foam and other articles containing TCPP. A limited amount of TCPP monitoring data has provided a generic worst case release from landfill leachate. This makes a contribution of ~ 7% to the total regional releases of TCPP to waste water.

The major emissions from industry are expected to occur to surface water. Emissions to air are also significant from point sources and over the service life of articles containing TCPP. At the regional level, total emissions to air are predicted to be significantly higher than to water, mainly as a result of volatilisation from polymer products over their service life. There

are no direct emissions to soil, but sewage sludge application and aerial deposition are predicted to be routes of release to soil.

3.1.1 Predicted Environmental Concentrations (PECs)

Concentrations in fresh and marine waters and sediments, air, soil, and biota were estimated according to the methods in the TGD, and these are given in Table 3.1.

Table 3.1 Summary of PECs for TCPP

Media	Release source (local PECs shown as min. – max. ranges)			
	Production	Formulation	Downstream use stages	Regional sources
Surface water (mg/l)	5.2E-04 – 0.011	5.0E-04 – 0.041	5.1E-04 – 0.25	5.0E-04
Sediment (mg/kg wwt)	0.0024 – 0.049	0.0023 – 0.19	0.0023 – 1.1	2.4E-03
WWTP final effluent (mg/l)	0.035 – 0.15	0.012 – 0.60	0 – 2.5	-
Soil (mg/kg wwt)	0.0058 – 0.015	0.0073 – 0.083	0.0058 – 0.31	2.7E-03
Air (mg/m^3)	1.4E-07 – 5.3E-07	4.0E-06 – 8.8E-04	1.4E-07 – 1.7E-04	1.4E-07
Secondary poisoning (mg/kg)	0.0014 – 0.016	0.0014 – 0.049	0.0014 – 0.059	-
Marine water (mg/l)	6.9E-05 – 0.0016	5.4E-05 – 0.0042	4.9E-05 – 0.025	4.9E-05
Marine sediment (mg/kg wwt)	3.2E-04 – 0.0071	2.5E-04 – 0.019	2.2E-04 – 0.11	2.2E-04
Marine secondary poisoning (mg/kg)	1.4E-04 – 0.0018	1.3E-04 – 0.0048	1.3E-04 – 0.006	-

Extensive monitoring data are available, particularly for freshwaters and sediments, but also for marine predators (cormorants and porpoise). The modelled concentrations are generally consistent with the measured values, especially at the regional scale, which suggests that the predicted release rates are not unreasonable.

3.2 EFFECTS ASSESSMENT

Surface water

The lowest effect values in short-term tests are a 96-h LC_{50} of 51 mg/l for fathead minnow (*Pimephales promelas*), a 48-hour EC_{50} of 131 mg/l for the invertebrate *Daphnia magna*, and a 72-hour E_rC_{50} and E_bC_{50} of 82 mg/l and 33 mg/l respectively for the alga *Pseudokirchneriella subcapitata*. Two chronic test results are also available: the 21-day NOEC for *D. magna* reproduction is 32 mg/l. The 72-hour E_rC_{10} and 72-hour NOEC for growth rate for *P. subcapitata* are 42 mg/l and 13 mg/l respectively.

A $PNEC_{aquatic}$ of 0.64 mg/l has been derived by dividing the *D. magna* NOEC by an assessment factor of 50. No measured data are available for marine organisms, so the $PNEC_{seawater}$ is a factor of 10 lower, at 0.064 mg/l.

Sediment

There are no toxicity data for sediment-dwelling organisms. A $PNEC_{sediment}$ of 2.92 mg/kg wet weight has therefore been derived from the $PNEC_{aquatic}$ by equilibrium partitioning (the $PNEC_{marine\ sediment}$ is 0.292 mg/kg wet weight using the same approach).

WWTP micro-organisms

An IC_{50} of 784 mg/l was obtained for WWTP micro-organisms (activated sludge). Dividing this by an assessment factor of 100 gives a $PNEC_{WWTP}$ of 7.84 mg/l.

Terrestrial compartment

Toxicity tests have been conducted with soil invertebrates (acute and chronic) and plants (seedling emergence and growth test). The results of a test with soil micro-organisms (nitrogen transformation) for TDCP have been read across to TCPP (on the basis of similar physicochemical properties and lack of effects on WWTP micro-organisms).

The lowest NOEC is 17 mg/kg dry weight, for emergence of *Lactuca sativa* seedlings in the TCPP higher plant study. No correction for organic carbon content is necessary, so a $PNEC_{soil}$ of 1.7 mg/kg dry weight (equivalent to 1.5 mg/kg soil wet weight) has been derived by dividing this value by an assessment factor of 10.

Atmosphere

No data are available on the toxicity of TCPP to plants or other organisms exposed via air. The possibility of TCPP contributing to atmospheric effects such as global warming, ozone depletion and acid rain is likely to be very small.

Non compartment specific effects relevant for the food chain (secondary poisoning)

A $PNEC_{oral}$ of <11.6 mg/kg food has been derived from the available mammalian toxicity data.

3.3 RISK CHARACTERISATION

The risk characterisation is performed by comparing the PEC with the relevant PNEC for each environmental compartment/endpoint. A ratio above 1 indicates a concern. Consequently there are:

- No identified risks to the freshwater aquatic and sediment compartments or sewage micro-organisms from local sources associated with any life cycle stage;
- No identified risks to the soil compartment from local sources associated with any life cycle stage;
- No identified risks of biotic or abiotic effects on the atmosphere;
- No identified risks of secondary poisoning of predators (including marine predators) from local sources associated with any life cycle stage;
- No identified risks to the marine aquatic and sediment compartments from local sources associated with any life cycle stage.

3.3.1 PBT assessment

For the PBT assessment, TCPP can be considered to meet the screening criteria as persistent (P) or potentially very persistent (vP) based on its ultimate mineralisation. The available information on bioaccumulation shows that TCPP does not meet the B or vB criterion. The T criterion is not met.

Areas of uncertainty in the environmental risk assessment

The $PNEC_{oral}$ for secondary poisoning is effectively based on a limit value, which means that all the resulting PEC/PNEC ratios are 'greater than' values. However, due to TCPP's low bioaccumulation potential, it is reasonable to conclude that there are no risks. Significant tonnage increases are not expected in the near future.

4 HUMAN HEALTH

4.1 HUMAN HEALTH (TOXICITY)

4.1.1 Exposure assessment

Occupational exposure

Occupational exposure to TCPP may occur during its manufacture, and during the manufacture and cutting of flexible and rigid polyurethane (PUR) foam. Inhalation of vapours and liquid aerosols and skin contact are the predominant routes of exposure during manufacture of TCPP and manufacture of foam, while inhalation of dust and skin contact are thought to be the predominant routes of exposure during foam conversion and cutting of rigid foam.

The occupational exposure scenarios considered for TCPP are:

1. Manufacture of TCPP
2. Manufacture of flexible PUR foam
3. Cutting of flexible PUR foam
4. Production of foam granules and rebonded PUR foam
5. Formulation of systems and manufacture of spray foam
6. Use of spray foams
7. Manufacture of rigid PUR foam
8. Use of rigid PUR foam
9. Manufacture of one-component foams
10. Use of one-component foams

For each exposure scenario, the reasonable worst case (RWC) and typical inhalation and dermal exposures were calculated and these are summarised in **Table 4.1**, below.

Table 4.1 Summary table of RWC and typical inhalation and dermal exposure values taken forward for risk characterisation

Scenario	Inhalation exposure (μg/m³)		Dermal exposure (mg/cm²/day)		Dermal exposure area (cm²)
	RWC	Typical	RWC	Typical	
1: Production of TCPP	25	12.5	1	0.1	210
2: Manufacture of flexible PUR foam	5.1	0.62	0.07	0.002	420
3: Cutting flexible foam	4.1	1.9	7.1×10^{-3}	9.8×10^{-4}	420
4: Production of foam granules & rebonded foam	4.6	0.59	1.7×10^{-3}	5.5×10^{-4}	420
5: Formulation of systems and manufacture of spray foams	5	2.5	0.11	0.05	420
6: Use of spray foams	187.5	25	0.23	0.12	420
7: Manufacture of rigid foam	150	20	6.5×10^{-2}	3.2×10^{-2}	210
8: Use of rigid foam	4.1	1.9	1.3×10^{-2}	6×10^{-3}	210
9: Manufacture of 1K foams	12.5	6.7	5.2×10^{-3}	1×10^{-3}	210
10 Use of 1K foams	5×10^{-3}	2.5×10^{-3}	1.9×10^{-3}	9.3×10^{-4}	420

Consumer exposure

Flexible PUR foam containing TCPP is used in upholstery and bedding. Consumers do not come in direct contact with these foams; the foam is only used in ways in which it is enclosed and therefore it is concluded that exposure to consumers is negligible. From the chamber tests that were performed on two other flame retardants, TCPP and TDCP, a RWC inhalation exposure value of 3.8 μg/m³ 24 hour TWA is determined. This is to allow for people, particularly elderly people, who spend a large proportion of their time indoors in a room with PU foam-containing furniture. A typical exposure value of 2.8 μg/m³ is used for risk characterisation, on the basis of a consumer spending 18 out of 24 hours in rooms where there is PU foam-containing furniture.

For dermal exposure, for the reasonable worst case exposure value is 0.0011 mg/kg. A value for a RWC oral ingestion for children has been taken from the risk assessment for TCEP of 0.2 μg/kg/day, assuming a bodyweight of 9.1 kg.

Consumers may also be exposed to TCPP in 1-K foams, available to the general public for the DIY filling of cavities. The RWC and typical inhalation exposures for this scenario are 5×10^{-3} and 2.5×10^{-3} mg/m³, respectively. The dermal exposure is estimated to be 174 μg/cm².

Consumer exposure from closed cell rigid foam used for insulation purposes is negligible and is not considered further in the risk assessment.

Humans exposed via the environment

The highest local total daily adult human intake of TCPP via the environment is estimated by the EUSES model to be 0.1 mg/kg/day. The exposure at regional level is estimated to be 2E-04 mg/kg/day.

Combined exposure

The combined exposure to TCPP has been calculated from consumer exposure and indirect exposure via the environment, by all routes of exposure (oral, dermal and inhalation). As the occupational exposure levels are significantly higher than the estimated exposure to consumers or indirect exposure via the environment, it is not considered necessary to include it in the combined exposure calculation.

The RWC exposures used in calculating the combined exposure are presented in **Table 4.2** below.

Table 4.2 Exposures taken into account for combined TCPP exposure estimate (excluding occupational exposure)

Source of exposure	Exposure
Consumer	
Release of TCPP from flexible polyurethane foam	
Inhalation	0.0038 mg/m^3
Dermal	0.0011 mg/kg
Use of 1-K foam	
Inhalation	0.005 mg/m^3
Dermal	174 µg/cm^2
Release of TCPP from closed cell right foam	Negligible
Man via the environment	
Local exposure	0.104 mg/kg/day*
Regional exposure	0.0002 mg/kg/day

*highest exposure scenario for local exposure (A1a: large systems houses)

4.1.2 Effects assessment

Toxicokinetics, metabolism and distribution

From the available information, oral absorption of TCPP is at least 75%, and therefore, 80% oral absorption will be taken forward to risk characterisation. Following oral administration, C_{max} in plasma and tissues was reached in 0.5 to 2 hours and 5.7 hours, respectively. Absolute concentrations in tissues were at 7 days post dosing, indicating low bioaccumulation potential. 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. Urinary and faecal excretion occurred quite rapidly. The observed biliary/faecal excretion ratio indicates 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 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 potential 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. Based on the results of this study, a value 40% dermal absorption will be taken forward for those scenarios where there is potential exposure due to handling of foam containing TCPP.

No toxicokinetic data is available for the inhalation route and so 100% absorption is assumed.

Acute toxicity

From the available inhalation studies, in it is concluded that TCPP is of low toxicity via the inhalation route. Studies in rats indicated that TCPP is of moderate toxicity via the oral route, with LD_{50} values ranging from 632 mg/kg up to 4200 mg/kg, with the majority of values determined to be <2000 mg/kg. A NOAEL of 200 mg/kg was derived for acute oral toxicity. Based on the results of the studies, TCPP should be classified with R22, harmful if swallowed. Studies in rats and rabbits indicated that TCPP is of low toxicity via the dermal route with LD_{50} values of >2000mg/kg

Irritation

TCPP is non-irritant in the rabbit eye and skin. The lack of any substantial skin or eye irritation and the lack of irritation observed in the acute inhalation studies suggest that TCPP would be unlikely to produce significant respiratory tract irritation.

Corrosivity

Results from animal skin and eye irritation studies indicate that TCPP is not corrosive.

Sensitisation

Evidence from a guinea pig study as well as from a local lymph node assay, indicates that TCPP does not possess significant skin sensitisation potential. No information is available on the respiratory sensitisation potential of TCPP.

Repeated dose toxicity

In a 13-week study, rats were fed diets containing TCPP at concentrations up to 1349 mg/kg/day and 1745 mg/kg/day, for males and females respectively. The liver and thyroid were identified as the main target organs affected by TCPP. Effects observed included statistically significant increases in absolute and relative liver weights in males at all doses and females at the two highest doses, periportal hepatocyte swelling in high dose groups and mild thyroid follicular cell hyperplasia in males at all doses and females at the highest dose. A LOAEL of 52 mg/kg/day is derived from this study.

In 4-week study study in rats, the liver was identified as the target organ, with increased liver weight changes observed at 1000 mg/kg, accompanied by hepatocyte hypertrophy in all males of this group (and one 100 mg/kg male) and changes in ALAT activity. A two-week study in which rats were fed diets of TCPP at concentrations up to 1636 mg/kg/day for males and 1517 mg/kg/day for females showed no major clinical signs of toxicity.

In a 2-generation reproductive toxicity study in which rats were fed TCPP in the diet over two successive generations, the low-dose of 99 mg/kg for females is considered to be the LOAEL for parental toxicity. This is based on decreased body weight and food consumption seen in

mid and high dose parental animals and the effects on uterus weight seen in all dosed animals. For males, a NOAEL of approximately 85 mg/kg is derived for parental toxicity, based on decreased body weights, food consumption and organ weight changes observed at mid and high dose groups.

No data are available on inhalation and dermal repeated dose toxicity.

Mutagenicity

TCPP is not a bacterial cell mutagen and is not mutagenic in fungi. In mammalian cells, there is evidence of clastogenic activity *in vitro*, in the presence of metabolic activation. The results from *in vitro* UDS studies are considered to be equivocal.

In an *in vitro/in vivo* UDS assay, an equivocal result was achieved. *In vivo*, TCPP was not clastogenic in a mouse bone marrow micronucleus test and did not induce an increase in chromosomal aberrations in a rat bone marrow cytogenetics assay. An *in vivo* Comet assay in the rat liver was conducted and under the conditions of this study, TCPP did not induce DNA damage in the liver of rats treated with either 750 or 1500 mg/kg TCPP.

Overall, it is considered that TCPP is not genotoxic *in vivo*.

Carcinogenicity

No carcinogenicity studies have been carried out with TCPP. The study of longest duration for TCPP is a 90-day dietary study in rats. Increased liver weights (both relative and absolute) were observed in males at 52 mg/kg and above, and periportal hepatocyte swelling was noted at highest dose (1349 mg/kg in males and 1745 mg/kg in females). In addition, mild follicular cell hyperplasia was noted in females at 1745 mg/kg and in all dosed males. In the kidney, vacuolation in females at highest dose was also observed. A slightly excessive fatty infiltration indicative of mild bone marrow hypoplasia was noted in three high dose females. The LOAEL of 52 mg/kg/day is based on increased liver weights observed in males. In the absence of carcinogenicity data, it cannot be excluded that the effects observed in this study with TCPP may progress to cancer. Therefore, as a reasonable worse case approach, this data is used in a quantitative way to carry out a risk characterisation for carcinogenicity.

This initial concern for carcinogenicity is further supported by the fact that TCPP is structurally similar to two other chlorinated alkyl phosphate esters, TDCP and TCEP. TDCP and TCEP are considered to be non-genotoxic carcinogens and have agreed classifications of Carc. Cat. 3; R40[4]). It is considered that there is sufficient information from the structures, physical-chemical properties, toxicokinetics and mutagenic profiles of TCPP and the structurally similar substances, TCEP and TDCP, to support a qualitative read-across for carcinogenicity. However, differences in the metabolism, target organs, the severity of the effects observed and the potency of the three substances indicates that a quantative read-across for carcinogenicity from either TDCP or TCEP may not be appropriate. 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.

[4] Commission Working Group on the Classification and Labelling of Dangerous Substances Meeting on the Health Effects of Pesticides, Existing Chemicals & new Chemicals, November 14-18, 2005,

Toxicity for reproduction

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 13^{th} 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.

4.1.3 Risk characterisation

Workers

With respect to worker scenario 1 (manufacture of TCPP), there is a concern for reasonable worst case dermal exposures for fertility and developmental toxicity and therefore **conclusion (iii)** is drawn. There is no concern for the typical dermal exposures or inhalation exposures for this exposure scenario.

A **conclusion (ii)** is drawn for all other worker exposure scenarios for all other endpoints.

Consumers

Conclusion (ii) is drawn for consumers for all exposure scenarios. This conclusion applies to all endpoints.

Humans exposed via the environment

Conclusion (ii) is drawn for both regional and local exposures for all endpoints.

Combined exposure

Conclusion (ii) is drawn for combined exposure for all endpoints.

4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

TCPP gives no reason for concern to human health in relation to its physico-chemical properties. There is no need for further information and/or testing **(conclusion (ii)).**

5 OVERALL CONCLUSIONS

5.1 ENVIRONMENT

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

This applies to all compartments for all local life cycle stages, and at the regional scale in all compartments. TCPP does not meet the PBT/vPvB criteria.

5.2 HUMAN HEALTH

5.2.1 Human health (toxicity)

Workers

Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Conclusion (iii) applies to reasonable worse case dermal exposure during the manufacture of TCPP (worker scenario 1) in relation to effects on fertility and developmental toxicity.

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to all worker exposure scenarios for the endpoints acute toxicity, irritation, sensitisation, repeated dose toxicity, mutagenicity and carcinogenicity.

Conclusion (ii) applies to typical dermal exposure and inhalation exposures, both reasonable worst case and typical, during the manufacture of TCPP (worker scenario 1) in relation to effects on fertility and developmental toxicity.

Conclusion (ii) applies to all other worker exposure scenarios (worker scenarios 2-10) for both reasonable worst case and typical exposures in relation to effects on fertility and developmental toxicity.

Consumers

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to all consumer exposure scenarios in relation to all toxicological endpoints.

Humans exposed via the environment

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to both regional and local exposures in relation to all toxicological endpoints.

Combined exposure

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to combined exposure in relation to all toxicological endpoints.

5.2.2 Human health (risks from physico-chemical properties)

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to all endpoints.