TRIS[2-CHLORO-1-(CHLOROMETHYL)ETHYL] PHOSPHATE (TDCP)

CAS No: 13674-87-8

EINECS No: 237-159-2

SUMMARY RISK ASSESSMENT REPORT

Final report of May 2008

Ireland (lead) and United Kingdom

Rapporteur for the risk assessment of TDCP 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-(chloromethyl)ethyl] phosphate (TDCP) 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

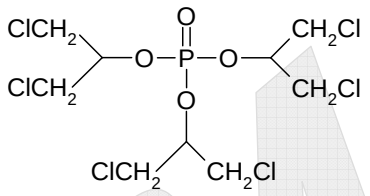
1 GENERAL SUBSTANCE INFORMATION

TDCP 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:	13674-87-8
EINECS Number:	237-159-2
IUPAC Name:	Tris[2-chloro-1-(chloromethyl)ethyl] phosphate
Synonyms	2-Propanol, 1,3-dichloro-, phosphate (3:1)
	Tris(1,3-dichloro-2-propyl) phosphate
	Tris(1-chloromethyl-2-chloroethyl) phosphate
	1,3-Dichloro-2-propanol phosphate (3:1)
	Phosphoric acid, tris(1,3-dichloro-2-propyl)ester
	TDCP: this common acronym is used throughout this report

Structural formula



1.2 PURITY/IMPURITIES, ADDITIVES

Tris[2-chloro-1-(chloromethyl)ethyl] phosphate (hereafter referred to as TDCP) is commercially available at a typical purity of 93–99.9% (w/w). The impurity profile differs between suppliers but the impurity content is low.

1.3 PHYSICO-CHEMICAL PROPERTIES

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

[2] The others being TCPP (CAS no. 13674-84-5) and V6 (CAS no. 38051-10-4).

Table 1.1 Identification and physico-chemical properties of TDCP

Property	Value
CAS number	13674-87-8
Molecular Formula	$C_9H_{15}Cl_6O_4P$
SMILES notation	O=P(OC(CCl)CCl)(OC(CCl)CCl)OC(CCl)CCl
Molecular Weight	430.91
Physical state at ntp	Liquid
Melting point	<-20°C (measured, commercial product composite sample)
Boiling point	~ 326°C (decomposes) (measured, commercial product composite sample)
Relative density	1.513 at 20°C (measured, commercial product composite sample)
Vapour pressure	5.6 x 10^{-6} Pa at 25°C (measured, commercial product composite sample)
Surface tension	No study available, but not expected to exhibit surface activity
Water solubility	18.1 mg/l at 20°C (measured, commercial product composite sample)
Partition coefficient n-octanol/water (K_{ow})	log K_{ow} = 3.69 (measured, commercial product composite sample)
Flash point	No closed cup result is available. Read-across from TCPP suggests that the result is likely to be above 245°C
Autoflammability (autoignition temperature)	513°C (measured, commercial product)
Flammability	Not expected to be flammable.
Explosive properties	Not expected to be explosive.
Oxidizing properties	Not expected to be oxidising.
Viscosity	1,800 cP at 25°C (measured, commercial product)
Henry's law constant	1.24 x 10^{-04} Pa.m^3/mol at 25°C (by calculation from vapour pressure and water solubility)

1.4 CLASSIFICATION

Classification for the environment (N, R51-53) was agreed at EU level in 2005[3].

It was agreed to classify TDCP as Carc. Cat 3; R40 in 2005[4].

The classification for effects on fertility and developmental toxicity are not yet agreed. Based on the information available, it is considered that there is no concern for effects on male fertility or developmental toxicity and therefore, no classification for these endpoints is proposed.

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
[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

2 GENERAL INFORMATION ON EXPOSURE

TDCP is used in the European Union (EU) as a flame retardant additive for polyurethane at typical loadings of ~ 3% w/w. The main use of the treated polyurethane is in flexible foams for the automotive industry. A smaller but still significant amount is used in flexible foams for furniture. A number of other minor confidential uses have been identified (<15% of the supply volume).

Less than 10,000 tonnes of TDCP were produced at one site in Germany and one in the UK in 2000, and both producers exported some substance. Overall the EU is a net exporter of finished articles. Therefore somewhat less than 10,000 tonnes of TDCP were consumed in the EU in 2000. Consumption levels have stabilised in recent years; this risk assessment represents a realistic upper limit of EU supply.

3 ENVIRONMENT

3.1 ENVIRONMENTAL EXPOSURE

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

- TDCP is expected to degrade in the atmosphere by reaction with hydroxyl radicals, with an estimated half-life of 21.3 hours.
- TDCP biodegrades very slowly in sludge and soil and does not readily hydrolyse ($t_{1/2}$ >1 year in neutral conditions at ambient temperature). No definitive conclusion can be reached regarding inherent biodegradability on the basis of the existing data set.
- It is moderately adsorbing to organic matter based on measured log K_{oc} of 1,780, and it has a low tendency to volatilise from water, based on Henry's Law constant of 1.24×10^{-4} Pa.m^3/mol.
- TDCP has a low potential to bioaccumulate in fish (the measured bioconcentration factor (BCF) is 0.3-89 in various test systems).

Fugacity modelling suggests that if TDCP 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 low.

The predicted fate in waste water treatment plant (WWTP) is: 82.1% to water; 17.9% 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. For all life cycle stages concerning 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 flexible foam and other articles containing TDCP however, available data suggest that releases of TDCP via landfill leachate are negligible.

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 TDCP. 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 EU Risk Assessment Technical Guidance Document (TGD), and these are given in Table 3.1.

Table 3.1 Summary of PECs for TDCP

Media	Release source (local PECs shown as min. – max. ranges)		
	Production	Downstream use stages	Regional sources
Surface water (mg/l)	3.4E-05 – 3.2E-04	2.2E-05 – 0.041	2.2E-05
Sediment (mg/kg wwt)	0.0014 – 0.013	8.8E-04 – 1.6	1.4E-03
WWTP final effluent (mg/l)	0.0012 – 0.030	0 – 0.41	-
Soil (mg/kg wwt)	0.001 – 0.01	0.001 – 3.1	1.2E-03
Air (mg/m^3)	1.4 E-08 – 7.8E-08	1.5E-08 – 7.6E-05	1.4E-08
Secondary poisoning (mg/kg)	0.001 – 0.01	0.001 – 2.8	-
Marine water (mg/l)	1.7E-05 – 3E-04	2.2E-06 – 0.005	2.2E-06
Marine sediment (mg/kg wwt)	6.6E-04 – 0.012	8.8E-05 – 0.20	1.2E-04
Marine secondary poisoning (mg/kg)	1.2E-04 – 0.0018	1.0E-04 – 0.033	-

Extensive monitoring data are available, particularly for freshwaters and sediments. 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 1.1 mg/l for rainbow trout (*Oncorhynchus mykiss*), a 48-hour EC_{50} of 3.8 mg/l for the invertebrate *Daphnia magna*, and a 72-hour E_rC_{50} and E_bC_{50} of 4.6 mg/l and 2.8 mg/l respectively for the alga *Pseudokirchneriella subcapitata*. Two chronic test results are also available: the 21-day NOEC for *D. magna* reproduction is 0.5 mg/l. The 72-hour E_rC_{10} and 72-hour NOEC for growth rate for *P. subcapitata* are 2.3 mg/l and 1.2 mg/l respectively.

In the acute tests fish were marginally more susceptible to TDCP than *D. magna* and two species of algae. Given the similarity in acute susceptibility of the three taxa, further testing to determine a threshold concentration for chronic effects in fish could not be justified on animal welfare grounds.

A $PNEC_{aquatic}$ of 0.01 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 0.001 mg/l.

Sediment

28-day toxicity tests with three species of sediment-dwelling invertebrates (the midge *Chironomus riparius*, the oligochaete *Lumbriculus variegatus* and the amphipod *Hyallela azteca*) were performed. *C. riparius* was most sensitive, giving a NOEC of 8.8 mg/kg dry weight in sediment containing 5.3% total organic carbon. This is equivalent to a NOEC of 8.3 mg/kg dry weight (1.8 mg/kg wet weight) when corrected to the TGD organic matter default content.

A $PNEC_{sediment}$ of 0.18 mg/kg wet weight is derived by applying an assessment factor of 10 to the corrected NOEC. (This is supported by the $PNEC_{sediment}$ of 0.395 mg/kg wet weight derived from the $PNEC_{aquatic}$ using the equilibrium partitioning approach.)

No measured data are currently available for marine sediment organisms. A $PNEC_{marine\ sediment}$ of 0.036 mg/kg wet weight has been by dividing the corrected *C. riparius* NOEC by an assessment factor of 50.

Waste water treatment plant micro-organisms

An unbounded NOEC of 1,000 mg/l was obtained for WWTP micro-organisms (activated sludge). Dividing this by an assessment factor of 10 gives a $PNEC_{WWTP}$ of ≥ 100 mg/l.

Terrestrial compartment

Toxicity tests have been conducted with soil invertebrates (acute and chronic), plants (seedling emergence and growth test) and soil micro-organisms (nitrogen transformation) for TDCP. The 56-day NOEC for reproduction of 9.6 mg/kg soil dry weight with the earthworm *Eisenia foetida* is the lowest chronic result. This is equivalent to a NOEC of 3.3 mg/kg dry weight when corrected to the TGD organic matter default content.

A $PNEC_{soil}$ of 0.33 mg/kg soil dry weight (equivalent to 0.29 mg/kg soil wet weight) has been derived by dividing the corrected NOEC by an assessment factor of 10.

The $PNEC_{soil}$ derived by the equilibrium partitioning method from the $PNEC_{aquatic}$ is 0.32 mg/kg wet weight, which is very similar.

Atmosphere

No data are available on the toxicity of TDCP to plants or other organisms exposed via air. TDCP has been detected in the needles of pine trees (*Pinus ponderosa*), and no phytotoxic effects were apparent at the concentrations found.

The possibility of TDCP 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 <3.3 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. PEC/PNEC ratios are shown in Table 3.2. A ratio above 1 indicates a concern. Consequently there are:

- No identified risks to any compartment or end point from local or regional sources associated with production or the current uses.
- Potential risks to aquatic (including sediment) and terrestrial organisms, and possibly to predators from secondary poisoning, for a minor confidential use (C) but this is understood to be no longer relevant in Europe. If the use were to resume, it may be possible to refine the assessment for some of these end points with better data.

Table 3.2 Summary of PEC/PNEC ratios for TDCP

Media	Release source (local PEC/PNECs shown as maximum values)			
	Production	Downstream use stages (major)	Downstream use stages (minor)	Regional sources
Surface water	0.032	2.97E-03	**4.1**	0.0022
Sediment	0.070	6.49E-03	**8.9**	0.0076
WWTP	<0.003	<7.38E-06	<0.041	-
Soil	0.035	5.45E-03	**10.7**	0.0042
Secondary poisoning	>0.0030	>7.53E-04	>0.832	-
Marine water	0.30	3.13E-03	**5.0**	0.0022
Marine sediment	0.33	3.42E-03	**5.4**	0.0032
Marine secondary poisoning	>5.3E-04	>3.51E-05	>0.0098	-

3.3.1 PBT assessment

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

Areas of uncertainty in the environmental risk assessment

The availability of TDCP for release from foams is assumed to be limited. This uncertainty has been considered in a sensitivity analysis, and no additional risks are identified. The $PNEC_{oral}$ for secondary poisoning is effectively based on a limit value, which means that all the resulting PEC/PNEC ratios are presented as 'greater-than' values. However, due to TDCP'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 TDCP may occur during its manufacture and during the manufacture and cutting of polyurethane (PUR) foam. Inhalation of vapours and skin contact are the predominant routes of exposure.

The occupational exposure scenarios considered for TDCP are:

1. Manufacture of TDCP
2. Manufacture of flexible PUR foam
    a. slabstock foams
    b. moulded foams
3. *Cutting of flexible PUR foam
4. Production of foam granules and rebonded PUR foam
5. Manufacture of automotive parts

*Scenario 3 covers the cutting of foam by furniture manufacturers, where it occurs.

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 of RWC and typical exposure values for inhalation and dermal exposure for all scenarios taken forward for risk characterisation

Scenario	Inhalation exposure ($\mu g/m^3$)		Dermal exposure ($mg/cm^2/day$)		Dermal exposure area (cm^2)
	RWC	Typical	RWC	Typical	
1.Occupational exposure during manufacture of TDCP	5.6	2.8	0.1	5×10^{-2}	210
2a. Occupational exposure during manufacture of flexible PUR foam	5.1	0.62	7×10^{-2}	2×10^{-3}	420
2b. Occupational exposure during manufacture of moulded foam	4.8	0.63	7.5×10^{-2}	1.5×10^{-3}	420
3. Occupational exposure during cutting of flexible PUR foam	4.1	1.9	7.1×10^{-3}	9.8×10^{-4}	420
4. Occupational exposure during production of foam granules & rebonded foam	4.6	0.59	1.7×10^{-3}	5.5×10^{-4}	420
5. Occupational exposure during manufacture of automotive parts	4.6	1.9	7.1×10^{-3}	9.8×10^{-4}	420

Consumer exposure

Most of TDCP used in flexible foam is for the automotive industry, with some used in furniture. 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/m^3 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/m^3 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.

Humans exposed via the environment

The highest local total daily intake of TDCP via the environment is estimated to be 0.0346 mg/kg/day. The exposure at regional level is estimated to be 1.52 x 10^{-5} mg/kg/day.

Combined exposure

The combined exposure to TDCP 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 TDCP 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
Man via the environment	
Local exposure	6.99 x 10^{-4} mg/kg/day
Regional exposure	1.52 x 10^{-5} mg/kg/day

4.1.2 Effects assessment

Toxicokinetics, metabolism and distribution

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 mean total absorption was 15.4 %, 10.69 % and 6.0 %, for doses 0.003, 0.01 and 0.12 mg/cm^2, respectively. Based on the results of this study, 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 those scenarios, where there is potential 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.

Acute toxicity

Studies in rats indicated that TDCP is of low acute toxicity via the oral and dermal routes of exposure, with LD_{50} values of >2000 mg/kg in both cases. An inhalation exposure study in rats yielded an LC_{50} value of >5.22 mg/l indicating that TDCP is of low acute toxicity following inhalation exposure.

Irritation

The available data indicate that TDCP produces only minimal dermal and eye irritation in animals following single exposure and any mild effects observed are fully reversible. The lack of any substantial skin or eye irritation and the lack of irritation observed in the acute inhalation studies suggest that TDCP would be unlikely to produce significant respiratory tract irritation.

Corrosivity

From the data presented on skin and eye irritation, TDCP has no corrosive potential.

Sensitisation

Evidence from a study in guinea pigs indicates that TDCP does not possess significant skin sensitisation potential. No information is available on the respiratory sensitisation potential of TDCP.

Repeated dose toxicity

In a 2-year carcinogenicity study, groups of 60 male and 60 female rats were fed diets containing TDCP at target doses of 0, 5, 20 and 80 mg/kg/day for 24 months. Significantly greater mortality was recorded for high dose males. There was a clear adverse effect on body weight in the 80 mg/kg/day groups throughout the study, with body weights at termination >20 % lower than controls. A significant reduction in red blood cell parameters was noted for high-dose animals. Absolute and relative kidney, liver and thyroid weights were also increased in mid- and high-dose animals. A LOAEL of 5 mg/kg/day is derived from the study. This is based on the hyperplasia, which is considered to be a pre-neoplastic lesion, observed in the kidneys in all treated groups and the testicular effects observed at this dose.

In a 90-day study to investigate the possible neurotoxicity of TDCP in hens, there was no evidence of TDCP induced delayed neurotoxicity. In an epidemiology study carried out in a TDCP manufacturing plant as an adjunct to a mortality study, no adverse health effects linked to TDCP exposure were determined.

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

Mutagenicity

In the Ames mutation assay, positive responses were observed following metabolic activation only. In mammalian cell studies, TDCP caused mutations in mouse lymphoma L5178Y cells in the presence of metabolic activation. TDCP also caused an increase in the occurrence of chromosomal aberrations in mouse lymphoma cells, again in the presence of metabolic activation. However, in a chromosomal aberration study in CHO cells, no increase in cells with chromosome aberrations or polyploidy were recorded.

In vivo, TDCP was not clastogenic in a mouse micronucleus assay and was found not to induce unscheduled DNA synthesis in. Negative results were also obtained in a second *in vivo* micronucleus assay and in an *in vivo*/*in vitro* urine mutagenicity assay.

Carcinogenicity

In a 2-year carcinogenicity study, there was a significant increase in the incidence of renal cortical adenomas and benign testicular interstitial cell tumours in the mid (20 mg/kg/day) and high (80 mg/kg/day)-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. There was also an increased incidence of hyperplasia of the convoluted tububle epithelium. 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. A LOAEL at 5 mg/kg/day is derived. This is based on an increased incidence of hyperplasia of the convoluted tubule epithelium observed in all treated male animals and in high dose females at 24 months. 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[5].

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.

[5] 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 study in male rabbits, no effect fertility was observed. In a 2-year carcinogenicity study in rats, an evaluation was made of the male reproductive system. 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. There was an increase in interstitial cell tumours of the testes at the 12 and 24 months. The effects observed on the testes may be secondary to an effect of the Leydig cell tumours also seen in this study. 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, 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 a developmental study in rats, a significant increase in the rate of resorptions and evidence of retarded skeletal development was observed at the highest dose of 400 mg/kg/day. Significant maternal toxicity was also observed at this 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.

For maternal toxicity, a NOAEL of 100 mg/kg/day is derived, based on the clinical signs of toxicity and statistically significant decrease in mean body weight.

4.1.3 Risk characterisation

Workers

With respect to worker scenarios 1 (manufacture of TDCP), 2a (manufacture of flexible PUR foam – slabstock) and 2b (manufacture of flexible PUR foam – moulded), there is a concern for reasonable worse case dermal exposures for repeated dose toxicity and carcinogenicity. and therefore **conclusion (iii)** is drawn. There is no concern for the typical dermal exposures or inhalation exposure for these exposure scenarios.

There is a data gap with respect to effects on female fertility. In the chronic toxicity study with TDCP, a LOAEL of 5 mg/kg was derived for repeated dose toxicity and carcinogenicity. It is considered that the low LOAEL derived from this study and any risk for female fertility will be addressed within the risk characterisation for repeated dose toxicity and carcinogenicity. Therefore, a conclusion (i) “on hold” is drawn for effects on female fertility for all exposure scenarios.

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

Consumers

Conclusion (ii) is drawn for consumers for all exposure scenarios for all endpoints except effects on female fertility, for which a **conclusion (i) "on hold"** is drawn.

Humans exposed via the environment

For both local and regional exposures, **conclusion (ii)** is drawn for all endpoints, with the exception of effects on female fertility, for which a **conclusion (i) "on hold**" is drawn.

Combined exposure

There is no concern for combined exposure (consumer exposure and indirect exposure via the environment) and therefore **conclusion (ii)** is drawn for all endpoints.

4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

TDCP 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.

Conclusion (ii) applies at the regional scale in all compartments and to all current local life cycle stages. TDCP does not meet all of the PBT criteria (it meets the screening criteria for P or vP).

It is understood that the life cycle stages associated with Confidential Use C (i.e. C1a, C1b and C2) are no longer relevant in Europe, on the basis of industry information. Should it be the case that supply resumes in future, conclusion (i) or (iii) would apply for some compartments and some life cycle stages.

5.2 HUMAN HEALTH

5.2.1 Human health (toxicity)

Workers

Conclusion (i) There is a need for further information and/or testing.

A conclusion (i) "on hold" applies to effects on female fertility for all worker exposure scenarios.

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, mutagenicity, effects on male fertility and developmental toxicity.

Conclusion (ii) applies to typical dermal exposure and inhalation exposures, both reasonable worst case and typical, during the manufacture of TDCP (worker scenario 1), manufacture of flexible PUR foam – stabstock (worker scenario 2a), and manufacture of flexible PUR foam – moulded (worker scenario 2b) in relation to repeated dose toxicity and carcinogenicity.

Conclusion (ii) also applies to all other worker exposure scenarios (worker scenarios 3, 4 and 5) for both reasonable worst case and typical exposures in relation to repeated dose toxicity and carcinogenicity.

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 worst case dermal exposure during the manufacture of TDCP (worker scenario 1), manufacture of flexible PUR foam – stabstock (worker scenario 2a) and manufacture of flexible PUR foam – moulded (worker scenario 2b) in relation to repeated dose toxicity and carcinogenicity.

Consumers

Conclusion (i) There is a need for further information and/or testing.

A conclusion (i) "on hold" applies to effects on female fertility for all consumer exposures.

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 for the endpoints acute toxicity, irritation, sensitisation, repeated dose toxicity, mutagenicity, carcinogenicity, effects on male fertility and developmental toxicity.

Humans exposed via the environment

Conclusion (i) There is a need for further information and/or testing.

A conclusion (i) "on hold" applies to effects on female fertility for both regional and local exposures.

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 for the endpoints acute toxicity, irritation, sensitisation, repeated dose toxicity, mutagenicity, carcinogenicity, effects on male fertility and developmental toxicity.

Combined exposure

Conclusion (i) There is a need for further information and/or testing.

A conclusion (i) "on hold" applies to effects on female fertility for 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 for the endpoints acute toxicity, irritation, sensitisation, repeated dose toxicity, mutagenicity, carcinogenicity, effects on male fertility and developmental toxicity.

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.