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Environmental risk evaluation report: Tricresyl phosphate (CAS no. 1330-78-5)

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Steve Killeen

Head of Science

Executive summary

An environmental risk assessment has been carried out for tricresyl phosphate (CAS no. 1330-78-5) on the basis of available information and using the methods of a European Technical Guidance Document. This substance is mainly used in Europe in PVC, polyurethanes, adhesives, pigment dispersions, as an additive in lubricants and in photographic film.

Potential risks are identified for most or all areas of use for surface water (fresh and marine), sediment (fresh and marine) and soil compartments.

Emission estimates are based on information from a number of generic sources, including emission scenario documents and other risk assessments, so they could be refined with more specific information for the substance itself. However some of the risk characterisation ratios are high and it is unlikely that such information will be sufficient to remove all of the risks identified.

The assessment could also be refined by performing toxicity tests. No testing on freshwater organisms is indicated. Testing on sediment and terrestrial organisms would allow the assessments for these compartments to be refined. In each case it is likely that three long term-studies would be required. The actual need for testing is closely linked with that for the other triaryl and alkyl/aryl phosphates considered as part of this project. A suggested testing strategy for the group as a whole is outlined in a separate overview document.

The risks to waste water treatment plant, the air compartment, secondary poisoning and humans exposed through the environment are low for production and all uses of tricresyl phosphate. In addition, a low risk to surface water and sediment is identified from regional sources.

Tricresyl phosphate does not meet the criteria for a persistent, bioaccumulative and toxic (PBT) or very persistent and very bioaccumulative (vPvB) substance.

Introduction

This report is one of a series of evaluations covering a group of related substances that represent the major aryl phosphate ester products used in Europe:

Triphenyl phosphate
Trixylenyl phosphate
Tricresyl phosphate
Cresyl diphenyl phosphate
Tris(isopropylphenyl) phosphate
Isopropylphenyl diphenyl phosphate
Tertbutylphenyl diphenyl phosphate
2-Ethylhexyl diphenyl phosphate
Isodecyl diphenyl phosphate
Tetraphenyl resorcinol diphosphate

A further substance is known to be commercially available, but it has already been assessed under the Notification of New Substances (NONS) Regulations. Information is also available on some (possibly obsolete) triaryl phosphates that are not thought to be supplied in the EU. This information is summarised in Annex A, but the risks from these products have not been assessed. Information for the group as a whole has also been used in this assessment, where appropriate, to fill any gaps in the database for this particular substance. Annex B discusses the read-across of data between the various phosphate esters considered.

This group was highlighted for assessment during preliminary work for a review of flame retardants (eventually published as Environment Agency 2003), particularly because they are potential replacements for other flame retardants that have already been identified as a risk to health or the environment. Regulators need to understand the potential consequences of such market switches before substantial replacement takes place. These assessments are not intended to provide a basis for comparison between the different aryl phosphates themselves; such a comparison would require consideration of a wider range of factors than are included here (such as human health risks, efficacy, recycling potential and costs). The assessments have been produced as part of the UK Coordinated Chemical Risk Management Programme (UKCCRMP) (http://www.defra.gov.uk/environment/chemicals/ukrisk.htm).

The methodology used in the report follows that given in an EU Technical Guidance Document (TGD)[1] for risk assessment of existing substances. The scientific work was mainly carried out by the Building Research Establishment Ltd (BRE), under contract to the Environment Agency. The review of mammalian toxicity data for the assessment of non-compartment specific effects was carried out by the Institute of Environment and Health, under contract to the Department for Environment, Food and Rural Affairs (Defra).

[1] This document has recently been replaced by similar guidance for the REACH Regulation.

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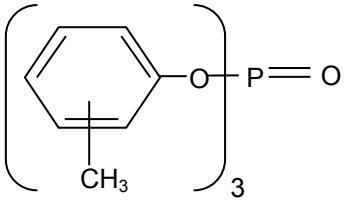
1 General substance information

1.1 Identification of the substance

This assessment considers the following commercial substance.

CAS No:	1330-78-5
EINECS No:	215-548-8
EINECS Name:	Tris(methylphenyl) phosphate
Common Name:	Tricresyl phosphate
Molecular formula:	$C_{21}H_{21}O_4P$
Molecular weight:	368.37 g/mol
Structural formula:	



The CAS numbers for the individual (non-commercial) isomers of tricresyl phosphate are as follows (WHO 1990):

Tri-*o*-cresyl phosphate	CAS No: 78-30-8
Tri-*m*-cresyl phosphate	CAS No: 563-04-2
Tri-*p*-cresyl phosphate	CAS No: 78-32-0

Other names, abbreviations, tradenames and registered trademarks for this substance include the following:

Tricresol phosphate
Tritolyl phosphate
Phosphoric acid, tris(methylphenyl) ester
Phosphoric acid, tricresyl ester
Phosphoric acid, tritolyl ester
TCP
PX-917®
Celluflex 179C®
Disflamoll TKP®
Kronitex TCP®
Kronitex R®
Phosflex Lindol®
Pliabrac TCP®
Santicizer 140®
Pliabrac 521®

Phosflex 179®
Kolflex 5050®

Some of the tradenames and trademarks may refer to older products no longer supplied to the EU, or to products produced outside the EU, but these are included in the report as they are sometimes referred to in the open literature.

The common name tricresyl phosphate will be used in this assessment.

1.2 Purity/impurity, additives

1.2.1 Purity/impurities

The commercial product is a relatively pure mixture of *meta*- and *para*-isomers (Weil 1993, Saeger *et al.* 1979). The amount of *ortho*-isomers present is minimised due to the known toxicity of this component (Merck Index 1996).

David and Sieber (1999) indicated that the main components present in a commercial tricresyl phosphate product were tri-*m*-cresyl phosphate, bis-*m,p*-cresyl phosphate and bis-*p,m*-cresyl phosphate.

Bayer (2002) report that a commercial tricresyl phosphate contained 65 to 70 per cent tricresyl phosphates (mixtures of *meta*- and *para*-isomers (the *ortho*-isomer content is below 0.05 per cent)) with 0.5 per cent triphenyl phosphate. The amounts of free phenol and cresol in the product are below 0.05 per cent.

Ofstad and Sletten (1985) determined the composition of a commercial tricresyl phosphate. The product was reported to contain a maximum of 0.03 per cent free phenolic compounds and a maximum of 0.01 per cent water. The acidity, as orthophosphoric acid, was a maximum of 0.01 per cent. A total of 21 different triaryl phosphate components were found to be present in the product, with tricresyl phosphates accounting for 36 per cent, triphenyl phosphate accounting for 25 per cent, trixylenyl phosphate accounting for 20 per cent, diphenyl cresyl phosphate accounting for four per cent, phenyl dicresyl phosphate accounting for three per cent and other aryl phosphates accounting for the remaining 12 per cent of the total.

1.2.2 Additives

Additives are not thought to be present in the commercially supplied products, although some aryl phosphate ester products are sometimes supplied as blends with other (halogenated) flame retardants.

1.3 Physico-chemical properties

Detailed test reports were not available for review, and so the validity of many of the reported values for physico-chemical properties is not always clear.

1.3.1 Physical state (at normal temperature and pressure)

The commercial substance is a clear, colourless to slightly yellow liquid (Ashford 1994, Bayer 2002, Great Lakes Chemical Corporation 2002, WHO 1990).

The physical state of the pure isomers of tricresyl phosphate ranges from a colourless liquid (tri-*o*-cresyl phosphate) to a colourless semi-solid (tri-*m*-cresyl phosphate) to a colourless crystalline solid (tri-*p*-cresyl phosphate) (WHO 1990).

1.3.2 Melting point

The substance does not have a distinct melting point. A pour point of -30°C (Ashford 1994) and -28°C (Merck Index 1996) has been reported. Bayer (2002) gives a pour point of -30°C for a commercial tricresyl phosphate determined using the ISO 3016 method. IUCLID (1998) gives a pour point range of -40 to -30°C for tricresyl phosphate.

WHO (1990) reports the melting point of commercial tricresyl phosphate to be -33°C. The same reference gives melting points for pure isomers of 11°C for tri-*o*-cresyl phosphate, 26°C for tri-*m*-cresyl phosphate and 77-78°C for tri-*p*-cresyl phosphate.

A melting/pour point of -30°C is assumed in this assessment.

1.3.3 Boiling point

The boiling point of tricresyl phosphate is reported to be 266-272°C at 1.3 kPa pressure (Ashford 1994). Merck Index (1996) reports a similar boiling point of ~265°C at 10 mmHg (1.33 kPa).

Bayer (2002) gives a boiling point of 245°C at 500 Pa for a commercial tricresyl phosphate determined using the DIN 53 171 method (a similar value of 240-250°C is reported in IUCLID (1998)) and Great Lakes Chemical Corporation gives the boiling point of another tricresyl phosphate product as above 300°C at 101,325 Pa.

The decomposition temperature of tricresyl phosphate is above 300°C (Great Lakes Chemical Corporation 2002).

WHO (1990) gives details of the boiling points of the pure isomers of tricresyl phosphates. The values reported are 410°C at 760 mmHg (101,325 Pa) for tri-*o*-cresyl phosphate, 260°C at 15 mmHg (2,000 Pa) for tri-*m*-cresyl phosphate and 244°C at 3.5 mmHg (467 Pa) for tri-*p*-cresyl phosphate.

IUCLID (2001) gives a boiling point of 241-255°C at 0.533 hPa (53.3 Pa) for a commercial product. The same range is reported in Boethling and Cooper (1985) and Muir (1984) but the pressure for the determination is given as 4 mmHg (533 Pa). It is presumed that the value given in IUCLID (2001) is in error as a pressure of 533 Pa is more in line with the other data available. Boethling and Cooper (1985) also report a boiling point of 265°C at 5 mmHg (667 Pa) for a commercial product.

A boiling point of above 300°C at atmospheric pressure is assumed for the commercial product here

1.3.4 Density

The density of the substance is given as 1,160 kg/m^3 at 20°C (Ashford 1994). Merck Index (1996) gives a relative density of 1.16 at 25°C. Shankwalkar and Cruz (1994)

and Playne and Smith (1983) reported relative densities of 1.17 and 1.16 respectively at 20°C for tricresyl phosphate. Bayer (2002) reports a density of 1.18 g/cm^3 at 20°C for a commercial tricresyl phosphate determined using the DIN 51 757 method and Great Lakes Chemical Corporation (2002) report a relative density of 1.1 at 20°C and 1.17 at 25°C for another commercial tricresyl phosphate product.

WHO (1990) reports relative densities (temperature not given) for pure tricresyl phosphate isomers of 1.1955 for tri-*o*-cresyl phosphate, 1.150 for tri-*m*-cresyl phosphate and 1.237 for tri-*p*-cresyl phosphate.

A relative density of 1.16 to 1.17 at 20°C will be assumed in the assessment.

1.3.5 Vapour pressure

The vapour pressure at ambient temperature is an important physico-chemical property for use in environmental risk assessment, as it is used to estimate both the distribution of a substance in the environment and the volatile releases from products.

Little reliable data appear to be available for tricresyl phosphate at temperatures around 20-25°C. However, information on boiling points at reduced pressure (see Section 1.3.3) is available.

Great Lakes Chemical Corporation (2002) give a vapour pressure of 0.033 mmHg (4.39 Pa) at 150°C for a commercial product. IUCLID (1998) gives a vapour pressure of 0.00001 hPa (0.001 Pa) at 46°C for a commercial tricresyl phosphate. A further vapour pressure of 0.0044 hPa (0.44 Pa) at 150°C is given in IUCLID (2001). Boethling and Cooper (1985) report a vapour pressure of 1.4×10^{-6} mmHg (1.87×10^{-4} Pa) at 30°C from an unpublished study. Muir (1984) gives further vapour pressures for the commercial product as below 0.02 mmHg (2.7 Pa) at 150°C and 0.29 mmHg (38.7 Pa) at 200°C.

The vapour pressure or reduced pressure boiling point of a pure substance is related to the temperature within a limited temperature range according to the simplified Clapeyron-Clausius equation:

$$\log(\text{vapour pressure}) = [\Delta H_v/2.3RT] + \text{constant}$$

where vapour pressure is in Pa
ΔH_v = heat of vapourization in J/mol
R = the universal gas constant 8.314 J/mol K
T = temperature in K

Figure 1.1 shows a plot of log (vapour pressure or reduced pressure (Pa)) against 1/(temperature or boiling point (K)) for the data available for the commercial tricresyl phosphate products. The following regression equation is derived from the plot.

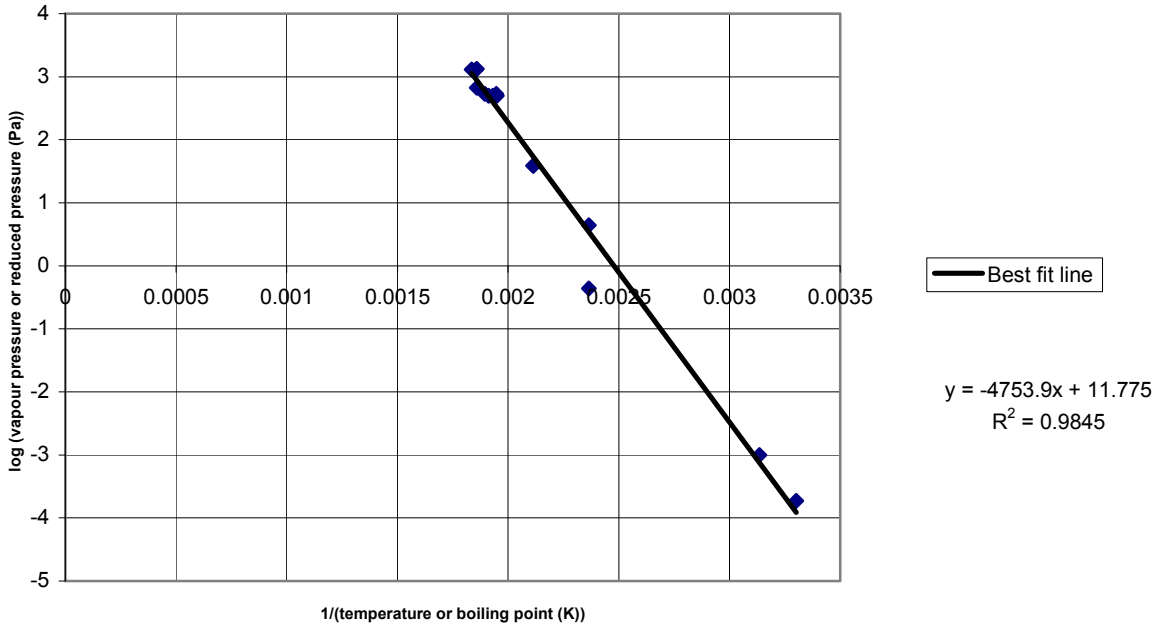
$$\log(\text{vapour pressure (Pa)}) = [-4753.9 \times 1/(\text{temperature (K)})] + 11.775$$

The value of ΔH_v for tricresyl diphenyl phosphate can be estimated as -90,905 J/mol.

Using this equation, the vapour pressure of tricresyl phosphate is estimated to be 3.5×10^{-5} Pa at 20°C, 6.6×10^{-5} Pa at 25°C, 3.4 Pa at 150°C and 53 Pa at 200°C.

The Clapeyron-Clausius equation should strictly speaking be applied only to data obtained with pure substances. For tricresyl phosphate, the boiling point data have been obtained with commercial products which consist of a mixture of several isomers of tricresyl phosphate. This introduces some uncertainty into the estimates. The value for ΔH_v may vary with temperature and so could introduce further errors in extrapolating the data obtained at elevated temperatures to ambient temperatures.

Figure 1.1 Plot of log (vapour pressure or reduced pressure (Pa)) against 1/(temperature or boiling point (K)) for tricresyl phosphate



Assuming that the pure isomers of tricresyl phosphate have the same ΔH_v as estimated above for the commercial product, it is possible to estimate the following vapour pressures for pure isomers using the boiling points given in Section 1.3.3:

Tri-*o*-cresyl phosphate	5.5×10^{-5} Pa at 20°C
Tri-*m*-cresyl phosphate	9.9×10^{-5} Pa at 20°C
Tri-*p*-cresyl phosphate	4.4×10^{-5} Pa at 20°C

The value at 20°C for tri-*o*-cresyl phosphate is in line with the data reported by Dobry and Keller (1957) who estimated the vapour pressure at 20°C to be 8.4×10^{-7} Pa for purified tri-*m*-cresyl phosphate and 1.2×10^{-4} Pa at 25°C for pure tri-*o*-cresyl phosphate, extrapolated from data obtained at elevated temperatures. Two of the pure isomers are solids at 20°C (tri-*m*-cresyl phosphate and tri-*p*-cresyl phosphate) and so the vapour pressure estimated for these two substances is for the sub-cooled liquid.

WHO (1990) reports a further estimate for the vapour pressure of tricresyl phosphate of 1×10^{-4} mmHg (0.0133 Pa) at 20°C, but this figure seems to be out of line with other data.

A vapour pressure (at 25°C) of 2.6×10^{-8} mmHg (3.4×10^{-6} Pa) can be estimated for tricresyl phosphate from its structure using the Syracuse Research Corporation MPBPWIN (version 1.28) software (modified Grain method). Boethling and Cooper (1985) estimated a vapour pressure at 25°C of 9.4×10^{-7} to 2.3×10^{-6} mmHg (1.3×10^{-4} to 3.1×10^{-4} Pa) from the boiling point of tricresyl phosphate (Grain method).

A vapour pressure of 3.5×10^{-5} Pa at 20°C and 6.6×10^{-5} Pa at 25°C, as obtained from the above analysis of available data, is used in this assessment for tricresyl phosphate.

1.3.6 Water solubility

The substance is reported to be practically insoluble in water (Ashford 1994). Merck Index gives the water solubility as below 0.002 per cent (0.02 g/l) at 85°C but indicates that the substance is miscible with all common organic solvents.

Saeger *et al.* (1979) determined the solubility of a tricresyl phosphate using a shake flask method. The substance used was a commercial product consisting mainly of a mixture of isomers of tricresyl phosphate. In the experiment, 25 ml of the phosphate ester was added to 500 ml of purified water and shaken for 48 hours. The solution was then allowed to stand for one week in the dark before the aqueous phase was centrifuged at 20,000 g for one hour to remove droplets of undissolved substance. The aqueous phase was then extracted twice with methylene dichloride and the extracts were analysed for the commercial product by a gas chromatography method (the centrifugation/extraction/analysis steps were carried out in duplicate and gave a mean relative average deviation of 13 per cent). The solubility of the substance tested (as the commercial product) was determined to be 0.36 mg/l at room temperature.

WHO (1990) reports a similar water solubility of 0.34 mg/l for commercial tricresyl phosphate.

IUCLID (1998) reports a further water solubility of 0.0034 g/l (3.4 mg/l) for tricresyl phosphate at 20°C.

Hollifield (1979) estimated a water solubility for tri-*p*-cresyl phosphate of 0.074 mg/l at 24°C using a nephelometric technique. The method involved dissolving the substance in a water miscible solvent (ethanol or acetone) and measuring the turbidity of dilutions of increasing amounts of this solution in water. A turbidity curve was then constructed and extrapolation of this curve to the blank value provided an estimate of the water solubility of the substance.

Ofstad and Sletten (1985) determined the water solubility of a commercial tricresyl phosphate product using the OECD 105 column elution method using two different flow rates at 25°C. The analytical method was able to distinguish between the main components of the product and the water solubility was determined to be 3.1 mg/l (sum of all components), 0.34 mg/l for the tricresyl phosphate component (all isomers), 2.1 mg/l for the triphenyl phosphate component and 0.11 mg/l for the trixylenyl phosphate component (all isomers). The value obtained in this study for tricresyl phosphate agrees well with that determined above by Saeger *et al.* (1979).

A water solubility of around 0.018 mg/l can be estimated for tricresyl phosphate using the Syracuse Research Corporation WSKOW version 1.30 software (the estimate is based on an estimated log K_{ow} of 6.34).

A water solubility of 0.36 mg/l is used in this assessment for tricresyl phosphate.

1.3.7 Octanol-water partition coefficient (log K_{ow})

The octanol-water partition coefficient of a tricresyl phosphate has been determined using a shake flask method (Saeger *et al.* 1979). The substance used was a commercial product consisting mainly of a mixture of isomers of tricresyl phosphate. In the study the substance was dissolved in n-octanol (at least two concentrations were tested between 100 mg/kg and 10,000 mg/kg) and 100 ml of this solution was shaken with 500 ml of purified water for 48 hours in the dark. The mixture was then allowed to stand for seven days in the dark before the concentration in the water phase (based on the sum of the major components of the product found in the gas chromatography trace) was determined (as only small amounts of the test substance were found to

partition into the water phase, the concentration of the substance in the n-octanol phase was taken to be the starting concentration). The K_{ow} obtained was determined to be 128,000 (log K_{ow} = 5.11).

Renberg *et al.* (1980) determined the octanol-water partition coefficient for a tricresyl phosphate (the same substance as used by Saeger *et al.* 1979 above) using a high performance thin layer chromatography (HPTLC) method. Two main components of the substance were evident using the method and the partition coefficients determined (log values) for these components were 4.30 and 4.65. The mean value obtained for all components was 4.51. These measured values are in reasonable agreement with the values estimated above.

A log K_{ow} value of 5.1-5.3 has been reported for tricresyl phosphate (Bengtsson *et al.* 1986). The value was from an unpublished source.

IUCLID (2001) and Boethling and Cooper (1985) report a log K_{ow} of 5.93 of tricresyl phosphate from an unpublished source.

Veith *et al.* (1979) reported a log K_{ow} value for tricresyl phosphate of 3.42. The value was possibly estimated using a high performance liquid chromatography (HPLC) method but few other details are available.

A log K_{ow} of 6.34 can be estimated for tricresyl phosphate from its structure using the Syracuse Research Corporation Log K_{ow} (version 1.60) software.

A log K_{ow} of 5.11 as determined by Saeger *et al.* (1979) will be used in the assessment.

1.3.8 Hazardous physico-chemical properties

The flash point (closed cup) is given as 410°C (Merck Index 1996). Bayer (2002) reports a flash point (open cup) for a commercial tricresyl phosphate of above 230°C determined by the ISO 2592/DIN 51376 method and Great Lakes Chemical Corporation (2002) report a similar flash point of above 220°C for another commercial product. IUCLID (2001) gives a flash point (closed cup) of 225°C for tricresyl phosphate. WHO (1990) reports a flash point of 257°C for tricresyl phosphate.

The ignition temperature is reported to be above 500°C for a commercial tricresyl phosphate determined by the DIN 51794 method (Bayer 2002) and Great Lakes Chemical Corporation (2002) and IUCLID (2001) give an ignition temperature of 607°C for another commercial product.

The explosive limits for tricresyl phosphate have not been determined (Bayer 2002).

No information could be located on the oxidising properties of this substance.

1.3.9 Other relevant physico-chemical properties

Henry's law constant

A Henry's law constant of 5.35×10^{-8} atm m^3/mol (0.0054 Pa m^3/mol) at 25°C can be estimated for tricresyl phosphate from the chemical structure (bond contribution method) using the Syracuse Research Corporation HENRYWIN (version 3.00) software.

Muir *et al.* (1985) measured the Henry's law constant for ^{14}C-labelled tri-*m*-cresyl phosphate using a gas sparging technique. The test was carried out at 25°C using a

one-litre water column containing between 10 and 100 μg/l of the test substance. The column was sparged with nitrogen at a flow rate of 200 ml/min for up to 46 hours and the amount of the test substance present in the gas was determined at various time intervals. A mean Henry's law constant of 8.38 Pa m^3/mol was determined from the slope of the first order volatilisation curve. The purity of the substance tested was not given in the paper, but it was indicated that the substance was synthesised from ^{14}C-labelled *m*-cresol. As ^{14}C measurements were used to determine the amounts of the test substance volatilised in this study, the presence of any ^{14}C impurity more volatile than the tricresyl phosphate could have adversely affected the results of this test.

It is also possible to estimate the Henry's law constant for tricresyl phosphate from the water solubility (0.36 mg/l) and vapour pressure (3.5×10^{-5} Pa at 20°C and 6.6×10^{-5} at 25°C). Using these data, the Henry's law constant is estimated to be 0.036 Pa m^3/mol at 20°C and 0.068 Pa m^3/mol at 25°C. This value is used in the assessment here as it is consistent with the available water solubility and vapour pressure data.

Thermal decomposition

Christos *et al.* (1997) investigated the products formed from the thermal decomposition of tricresyl phosphate and tri-*p*-cresyl phosphate in sealed systems at 370°C. The decomposition seen was only around 0.2 to 0.8 per cent and the major products formed were found to be phenol (1.17-1.59 mg/g) and cresols (up to 0.039 mg/g). Other products identified included carbon monoxide, carbon dioxide, methane, water, unidentified C_2-C_{10} species, benzene, toluene, C_2- and C_3-benzenes, methanol, ethanol, C_4-alcohols, acetaldehyde, isobutylraldehyde, acetone, methyl ethyl ketone, cyclopenanone, 3,4,7-trimethyl-1-indanone, methyl-*p*-cresyl ether, dimethoxy methane, *p*-dioxane, acetic acid and n-butyl formate.

1.3.10 Summary of physico-chemical properties

The physico-chemical properties of tricresyl phosphate are summarised in Table 1.1 Most of the data has been obtained with commercial products and so some of the properties may vary depending on the actual composition of the product.

Table 1.1 Summary of environmentally relevant physico-chemical properties for tricresyl phosphate

Property	Value
Melting point	-30°C (pour point)
Boiling point (at atmospheric pressure)	>300°C
Relative density	1.16-1.17 at 20°C
Vapour pressure	3.5×10^{-5} Pa at 20°C and 6.6×10^{-5} Pa at 25°C
Water solubility	0.36 mg/l at room temperature
Octanol-water partition coefficient (log value)	5.11
Henry's law constant	0.036 Pa m^3/mol at 20°C and 0.068 Pa m^3/mol at 25°C

For the purposes of this assessment, the commercial substance is considered to behave as a single substance in the environment.

2 General information on exposure

2.1 Production

Tricresyl phosphate is made by the reaction of a mixture of *meta*- and *para*-cresol with phosphorus oxychloride (Ashford 1994). As noted in Section 1, the amount of any *ortho*-cresol present is minimised. There are two known European production sites (including Chemtura (formerly Great Lakes), UK) and one additional European supplier. Information on production volume and market size is therefore confidential. It is possible that other companies may supply this substance, but no further information is available for this report.

2.2 Use

2.2.1 General introduction

Trialkyl phosphate flame retardants were first commercialised in the early twentieth century for use in flammable plastics such as cellulose nitrate and later for cellulose acetate (Weil 1993). Use in cellulose products is still significant, but the largest area of application is now in plasticized vinyl polymers. The main applications of these products are in wire and cable insulation, connectors, automotive interiors, vinyl moisture barriers, furniture upholstery, conveyor belts (for mining) and vinyl foams.

In addition to their use as flame retardants in polymer systems, triaryl phosphates are also used as fire-resistant hydraulic fluids, lubricants and lubricant additives (Weil 1993). Small amounts are also reported to be used as non-flammable dispersing media for peroxide catalysts.

2.2.2 Uses of tricresyl phosphate

The substance is used as a flame retardant in flexible PVC, cellulose nitrate, ethylcellulose coatings, lacquers, adhesives and various rubber products (Weil 1993, Ashford 1994). The flame-retarded products are used in applications such as vinyl tarpaulins, mine conveyor belts, air ducts, cable insulation and vinyl films.

The substance is also used as an extreme pressure additive in lubricants, as a fire-resistant hydraulic fluid and a petrol/diesel fuel antipreignition additive. Other reported uses include as a clarifying agent in casein polymer production (Ashford 1994).

Hydraulic fluid formulations containing tricresyl phosphate and/or triphenyl phosphate as the major component have been used by the United States Airforce since the 1970s (David and Seiber 1999).

Information on the sales of tricresyl phosphate into the EU has been provided by the relevant supplier companies for the year 2005. The major current uses are in PVC, polyurethanes, adhesives, pigment dispersions, as an additive in lubricants and in photographic film.

3 Environmental exposure

This assessment has been prepared in accordance with the principles of Council Regulation (EEC) 793/93 (the Existing Substances Regulation or ESR)[2] and the methods laid down in Commission Regulation (EC) 1488/94[3] , which is supported by a technical guidance document or 'TGD' (EC 2003). The European Union System for the Evaluation of Substances (EUSES) computer program[4] (v2.0.3) implements the TGD models. The EUSES output file for this assessment is confidential because of the information it contains on tonnage and use pattern.

The assessment is generic, representing a *realistic worst case approach* for a hypothetical environment that broadly reflects average European conditions. It uses a number of assumptions (such as a fixed river dilution level), and further details can be found in the TGD. The assessment is based on estimated sales figures for Europe and some site-specific information. Since these are confidential, the calculations are presented in the Confidential Annex, but they are discussed qualitatively in the report as appropriate.

3.1 Environmental fate and distribution

3.1.1 Degradation

Abiotic degradation

Atmospheric photooxidation

A rate constant for reaction of tricresyl phosphate with atmospheric hydroxyl radicals of 1.4×10^{-11} cm^3/molecule s can be estimated from its structure using the Syracuse Research Corporation AOP (version 1.86) software. This program implements the method recommended in the TGD for estimating the rate constant.

Using an atmospheric hydroxyl radical concentration of 5×10^5 molecules/cm^3, a half-life for the reaction in air is estimated to be 27.5 hours.

Hydrolysis

Wolfe (1980) developed linear free energy relationships to estimate the rate constants for neutral and alkaline hydrolysis of triaryl phosphates using the available published information on hydrolysis. Under alkaline conditions, the second order reaction rate constant for hydrolysis was found to correlate with the sum of the Hammett (σ) substituent constants for the aryl substituents and the following equation was derived.

$$\log k = 1.40 \times \sigma - 0.47$$

where k = second order rate constant for hydrolysis at 30°C (l/mol s)
σ = sum of Hammet substituent constants

[2] O.J. No L 084, 05/04/1993 p. 0001–0075.
[3] O.J. No L 161, 29/06/1994 p. 0003–0011.
[4] Available from the European Chemicals Bureau, http://ecb.jrc.ec.europa.eu/.

For tricresyl phosphate, σ = -0.069 (*meta*-) or -0.17 (*para*-) and so the second order hydrolysis rate constant is 0.20-0.27 l/mol s. Using this value the hydrolysis half-life at any alkaline pH can be estimated. For example, at pH 8 the concentration of hydroxyl anions present is 10^{-6} mol/l and so the pseudo first-order hydrolysis reaction rate constant for triphenyl phosphate at this pH is around $2.0\text{-}2.7\times10^{-7}$ s^{-1}. This is equivalent to a hydrolysis half-life of around 30 to 40 days.

For hydrolysis under neutral conditions, the following equation was derived.

$$\log k = -0.95 \times pKa - 1.20$$

where k = first order rate constant for neutral hydrolysis at 25°C (s^{-1})
pKa = $-\log_{10}$ {acid dissociation constant for the phenolic leaving group)

For tricresyl phosphate, the pKa of the leaving phenol group is around 10.2 (*ortho*-), 10.01 (*meta*-) and 10.17 (*para*-). This leads to an estimated value for the rate constant for the neutral hydrolysis of around 1×10^{-11} to 2×10^{-11} s^{-1} and an estimated half-life for neutral hydrolysis of 1,100 to 2,200 years. The alkaline reaction will also take place at pH 7, with a half life of 300 to 400 days.

Great Lakes Chemical Corporation (2003) indicate that hydrolysis of aryl phosphates can also occur under acidic conditions and packages are usually added to hydraulic fluids to delay the onset of hydrolysis during the service life of the products. The standard test for such fluids is the 'coke bottle' test. In this test, the fluid is placed in a coke bottle with distilled water (sometimes with catalytic metals such as copper) and the degradation is followed by the increase in acidity (the initial hydrolysis product would be diaryl phosphates (diesters of phosphoric acid), which are acidic). The rate of hydrolysis in such a test generally increases as the acidity increases during the test. However, although this indicates that hydrolysis of aryl phosphates can occur at acidic pHs, the autocatalysis seen in the test as a result of the formation of acidic products (resulting in an increase in acidity) is unlikely to occur in the environment owing to its natural buffering capacity.

Hydrolysis of the *ortho*-, *meta*- and *para*- isomers of tricresyl phosphate, and also a commercial tricresyl phosphate product in natural water (Lake Ontario (pH 8.2)) has been studied by Howard and Deo (1979). Saturated solutions of the test substances were prepared by shaking an excess of the substance with the natural water for two hours, followed by filtration (11 μm) to remove the undissolved material. The concentration of the tricresyl phosphate in solution was then determined; the solution was incubated at 21°C and the concentration of the test substance present was determined at various time periods. The experiments all showed a lag period of around two days prior to the onset of degradation of the tricresyl phosphate. After this lag phase, the tricresyl phosphate was found to be degraded rapidly (half-life around two to five days), with the rate of degradation found to increase in the order *para*- to *meta*- to *ortho*- amongst the isomers (the rate of degradation of the *para*-isomer was similar to that of triphenyl phosphate under similar conditions). The commercial tricresyl phosphate product tested was also found to degrade rapidly (again after a lag period of two days). Given the initial lag phase prior to degradation, microbial degradation rather than hydrolysis was probably the dominant degradation process occurring in these samples (although the water samples were filtered prior to use, the size of the filter used (11 μm) was chosen so as not to remove microorganisms from the water).

David and Seiber (1999) carried out a number of experiments investigating the abiotic degradation of tricresyl phosphate water and soil-water slurries. The substance tested was a commercial tricresyl phosphate (mixture of isomers, the three main isomers identified as tri-*meta*-cresyl phosphate, bis-*m*,*p*-cresyl phosphate and bis-*p*,*m*-cresyl phosphate), tri-*m*-cresyl phosphate (purity 93 per cent), tri-*p*-cresyl phosphate (purity not given) or tri-*o*-cresyl phosphate (purity not given). Sodium perborate was used in

some of the experiments as a source of the hydrogen peroxide anion HOO^-, which is known to attack the phosphorus centre of phosphate esters at a rate ten to 100 times that of the hydroxyl ion under alkaline conditions.

The hydrolysis studies in water were carried out by adding 1 ml of a solution of the phosphate ester under consideration to 1 to 2 litres of deionized tap water. The initial concentration present was then measured (the initial concentration was always below the water solubility of the substance) and the degradation reaction was started by adding either Na_2CO_3 directly to the test vessel to give a 0.007 M solution (pH 10.7) or $NaBO_3$ to give a 0.03 M solution (pH 10.3). The hydrolysis was then followed by analysing samples of the water at various time points for the disappearance of the starting phosphate ester. Each experiment was carried out in triplicate. The half-life for hydrolysis in the experiments with Na_2CO_3 (hydroxyl ion acting as the nucleophile) was found to be 200 minutes for the mixed tricresyl phosphate isomers, 280 minutes for tri-*o*-cresyl phosphate and 670 minutes for tri-*p*-cresyl phosphate. The corresponding half-lives in the experiments with $NaBO_3$ (HOO^- acting as nucleophile) were 70 minutes of the mixed tricresyl phosphate isomers, 87 minutes for tri-*o*-cresyl phosphate and 27 minutes of tri-*p*-cresyl phosphate.

The soil used in the soil-slurry experiments was a loamy sand soil consisting of 82 per cent sand, ten per cent silt and eight per cent clay with an organic matter content of 0.3-0.35 per cent and a water content of below three per cent. The soil was spiked with a mixture of organophosphate chemicals, including triphenyl phosphate, tributyl phosphate and a mixture of tricresyl phosphate isomers to give a total concentration of 50-100 mg/kg. The soil-water slurries were prepared by adding 2 grams of the spiked soil to 100 ml of dionized tap water and shaking for 72 hours. After this equilibration period, the degradation experiments were started by adding a solution of Na_2CO_3 (to give a final concentration of 0.007 M and a pH of 10.4) or $NaBO_3$ (to give a final concentration of 0.03 M and a pH of 10.1). Controls at pH 6.8 were also run. The slurries were then shaken for between four and 408 hours and the concentrations of test substances were determined at various intervals. Each experiment was carried out in duplicate. Degradation of the phosphate esters did not fit either a first- or second-order kinetic model. The results were best explained in terms of the rate-limiting step being desorption of the phosphate esters from the solid phase, followed by a rapid hydrolysis of the desorbed substance. The time for 90 per cent degradation was estimated on the basis of this model to be 535 hours for tri-*o*-cresyl phosphate, 26 hours for tri-*m*-cresyl phosphate, 24 hours for bis-*m*,*p*-cresyl phosphate and 13 hours for bis-*p*,*m*-cresyl phosphate in experiments with $NaBO_3$. The amount of tricresyl phosphate remaining after ten days was determined to be 13 per cent for tri-*o*-cresyl phosphate and one per cent for the mixed tricresyl phosphate isomers in the $NaBO_3$ experiments, 26 per cent for tri-*o*-cresyl phosphate and 12 per cent for the mixed tricresyl phosphate isomers in the $NaCO_3$ experiments and 80 per cent for tri-*o*-cresyl phosphate and 74 per cent for the mixed isomers in water at pH 6.8.

The hydrolysis of a commercial synthetic oil containing a large proportion of tricresyl phosphate isomers was studied by Wagemann *et al*. (1974) and Wagemann (1975). The product consisted of around 75 per cent tricresyl phosphate (mainly *meta*- and *para*-isomers), 18 per cent trixylenyl phosphate and seven per cent other phosphates (including triphenyl phosphate, tri(ethylphenyl) phosphate and tri(trimethylphenyl) phosphate). The cresol concentration in a saturated solution of the synthetic oil in sterile demineralised water at 22°C was found to reach 112 μg/l after 30 days indicating that hydrolysis was occurring. The pH was also found to decrease with time to pH 5.6, indicating formation of an acidic species. The rate of the hydrolysis reaction in sterile river water was determined at 25°C under a variety of conditions (presence and absence of sediment and presence and absence of light). The hydrolysis reaction was monitored by determining the amount of molybdate reactive phosphate formed (most probably orthophosphate) during the course of the experiment. The reaction in

sterile river water appeared to stop during periods of darkness (such as weekends where the solution were kept in a dark laboratory). It is not clear if this effect was a consequence of the method used to measure the extent of the hydrolysis reaction or whether the hydrolysis truly needed the presence of light to occur. The presence of sediment at 1 g/l had little effect on the rate of reaction. Based on the results, a hydrolysis half-life of around 96 days was obtained. The actual pH of the solution during this test is unknown.

Photolysis

IUCLID (1998) reports the results of studies of Ishikawa *et al.* (1985a) showing that 90 to 100 per cent degradation of tricresyl phosphate occurred within one hour using ultraviolet (UV) light.

Further photolysis experiments using UV radiation were carried out by Ishikawa *et al.* (1992). In these experiments, tricresyl phosphate was added to 100 ml of water and was dissolved/dispersed by ultrasonication for one hour. The solution was then mixed with 1,900 ml of water (giving a final concentration of around 0.1 mg/l) for 30 minutes. After adjustment to the desired pH with HCl or NaOH, the solution was then irradiated with a 15 W low-pressure mercury lamp and samples were collected from the solution periodically and analysed for the presence of tricresyl phosphate. The disappearance of tricresyl phosphate from the system was found to be rapid and follow first order kinetics. The rate constant for the degradation was above 20 h^{-1} at pH 3 and above 15 h^{-1} at pH 10 (corresponding to half-lives of less than two minutes at pH 3 and less than three minutes at pH 10). Further experiments were carried out using higher concentrations of the test substance (3×10^{-4} mol/l = 0.1 g/l) in order to identify the photodecomposition products. These experiments were carried out in both water without pH adjustment and in water with an initial pH of 12. The products formed were identified as phosphoric acid and phenolic compounds (only found in the pH 12 experiment). The yield of phenolic compounds after three hours irradiation under the alkaline conditions was found to be around two per cent and the phenolic compounds were found to be decomposed by further irradiation. Under more acidic conditions, the decomposition of phenol was thought to be more rapid than its formation.

Muir (1984) and Boethling and Cooper (1985) reported that tricresyl phosphate gave some diaryl products when irradiated using a medium pressure mercury arc lamp in ethanol (concentration 0.02 M). The products formed included dimethylbiphenyl (31-57 per cent yield) and mono-cresyl phosphate (2 to 10 per cent yield).

Biodegradation

Dearden and Cronin (1996) reported the result of a MITI I ready biodegradation test with both tri-*o*-cresyl phosphate and tri-*p*-cresyl phosphate. The degradation, as determined by biological oxygen demand (BOD) at the end of the study, was 28 per cent for the *ortho*- isomer and 37 per cent for the *para*- isomer. No experimental details of the specific test were given.

Bayer (2002) and IUCLID (1998) report that 80 per cent degradation of a commercial tricresyl phosphate was obtained after 28 days in a modified MITI I test using domestic sewage as inoculum. The concentration of the test substance used was 100 mg/l. Further details of this test are unpublished. Based on these results, the substance can be considered readily biodegradable but it is not clear if the 10-day window was met.

Saeger *et al.* (1979) determined the biodegradation of a tricresyl phosphate using various test systems. The substance used was a commercial product consisting mainly of a mixture of isomers of tricresyl phosphate. The first test investigated the primary

degradation of the test substance using a river die-away method. The water used in the test was settled Mississippi River water. The test substance (at a concentration of 1 mg/l) was added to the water and the test vessels (bottles) were sealed with a foil-lined cap and stored in the dark at room temperature. Sterile control solutions (containing the same concentration of test substance) and positive control solutions (containing linear alkyl benzene sulphonate) were also run. At various times during the study, a bottle was removed and the amount of the phosphate ester present was determined (the gas chromatographic method used analysed the sum of the major components present in the test substance). The results showed that the test substance underwent primary degradation in the test system with complete degradation in less than seven days. No significant degradation was seen in the sterile controls.

The second part of the study investigated the primary degradation of the test substance using a semi-continuous activated sludge (SCAS) unit. The method used was based on the Soap and Detergent Association procedure (Soap and Detergent Association 1965 and 1969). The activated sludge used in the test was of domestic origin and the vessels used in the test had an operating volume of 1.5 litres. The test substance was added to the unit at a rate of either 3 or 13 mg/l per 24-hour cycle. The units were operated for a period of four weeks and samples of the mixed liquor were removed at weekly intervals and the concentration of the phosphate ester present was determined. The results indicated an equilibrium removal rate of greater than 97 per cent at 3 mg/l and greater than 99 per cent at 13 mg/l in the test system. In addition, in order to investigate the loss by volatilisation the off-gases were passed through a series of scrubbers. No significant loss by volatilisation (below 0.5 per cent per cycle) of the phosphate ester was seen in the experiment.

The final part of the study investigated the ultimate mineralisation of the test substance using a degradation method based on the modified Sturm method. An acclimated bacterial seed was prepared by incubation of 100 ml of settled supernatant from a SCAS unit with 20 mg of one of eleven phosphate esters (including the test substance), 50 mg of yeast extract and 900 ml of standard biological oxygen demand (BOD) water for 14 days in the dark at room temperature. At the end of the incubation period, a combined acclimated seed was prepared by mixing samples from each acclimation bottle and this was used as seed for the inherent biodegradation test. In the test, 500 ml of the composite seed was added to 5,500 ml of BOD water and the substance was then added to the bottle (initial concentration 26.4 mg/l). During the test, CO_2-free air was continually bubbled through each bottle and the CO_2 evolved from the system was determined. Control bottles (receiving no test substance) were also run. The amount of CO_2 evolved from the control bottles was around 10-15 per cent of that of the bottles containing the test substance and the results were corrected for this background CO_2 level. The CO_2 evolved from the test substance (expressed as a percentage of the maximum theoretical amount) was 79 per cent after seven days, 82 per cent after 28 days and 86 per cent after 48 days. Therefore the substance can be considered at least inherently biodegradable based on the results of this test.

WHO (1990) reports that several old (1960s) SCAS studies showed a high level of degradation (around 99 per cent) over a 24-hour period at a feed level of 3 to 13 mg/l.

IUCLID (1998) reports that Ishikawa *et al.* (1985a) found around 60 per cent degradation of tricresyl phosphate after two days using unacclimated activated sludge and around 90 per cent degradation after two days using acclimated activated sludge.

Ku and Alvarez (1982) investigated the biodegradation of ^{14}C-labelled tri-*p*-cresyl phosphate (labelled on the methyl group) in a model sewage sludge system using activated sludge of domestic origin. The test substance was added to the system at 1 mg/l and the activated sludge (1.8 mg dry cells/ml) was incubated at 21°C with skimmed milk (0.5 g/l) as an energy source. Air, at a flow rate of 28 ml/minute, was continuously provided to the test system. At the end of the 24-hour incubation period,

around 70-80 per cent of the tri-*p*-cresyl phosphate added to the system was found to have been degraded (based on parent compound analysis), with the remainder associated with the sludge solids. The extent of mineralisation was, however, relatively low over the test period at around 2.4 per cent; $^{14}CO_2$ formation was observed. The major metabolite found in the sludge was *p*-hydroxybenzoic acid and two unstable, ether extractable metabolites were also found to be present (these were not identified). The half-life for tri-*p*-cresyl phosphate in the system was around 7.5 hours.

Boethling and Cooper (1985) report the results of an unpublished study using tri-*o*-cresyl phosphate and a commercial tricresyl phosphate. In this study, activated sludge mixed liquor was acclimated to progressively higher concentrations of the test substance. At the start of the test, the acclimated liquor was diluted 1:10 with a mineral salts medium and the test substance was added as the sole source of carbon. The initial concentrations used were 271 mg/l for tri-*o*-cresyl phosphate and 524 mg/l for the commercial tricresyl phosphate and the substances were 98 per cent and 87 per cent degraded respectively within seven days. The same report indicates that tri-*o*-cresyl phosphate was found to be extensively degraded in a river die-away test over seven days (97 per cent degraded in seven days). The half-life for commercial tricresyl phosphate in the river die-away test was around three days.

Xing and Raetz (2001) showed that tricresyl phosphate, as part of a contaminated ground water (contaminated with phenols and benzene, toluene, ethylbenzene and xylene (BTEX)), was effectively biodegraded using a bench-scale pressurised fluidised bed reactor. The reactor was initially seeded with mixed phenol-degrading bacteria. The system was found to degrade tricresyl phosphate from an influent concentration of 2,500 μg/l to an effluent concentration of below 40 μg/l (above 98 per cent removal).

The effect of temperature and redox potential on the degradation of several phosphate esters, including tri-*m*-cresyl phosphate, in two natural sediments was investigated by Muir *et al.* (1989). The tri-*m*-cresyl phosphate tested was ^{14}C-labelled mixed with purified non-labelled tri-*m*-cresyl phosphate. The sediment samples used in the study were collected from a eutrophic farm pond and the Red River, Winnipeg (both samples were from agricultural areas remote from industry). The pond sediment consisted of 75 per cent clay, 24 per cent silt and one per cent sand and had an organic carbon content of 3.7 per cent and a pH of 7.6 and the river sediment consisted of 48 per cent clay, seven per cent sand and 43 per cent silt and had an organic carbon content of 2.3 per cent and a pH of 7.7.

The aerobic sediment experiments were carried out using loosely capped flasks (static test) or in respirometer flasks with air flowing through the system (1-2 ml/minute). The sediments incubated under anaerobic conditions (in respirometer flasks under a nitrogen flow (1-2 ml/minute)) were amended with one per cent by weight of microcrystalline cellulose to provide an additional source of carbon. The degradation experiments were carried out using around 10 g (dry weight) of sediment in dechlorinated water (sediment:water ratios of either 1:10 (static test) or 1:20 (respirometer flask)). Each sediment sample was pre-incubated for 21 days at the intended experimental temperature prior to the addition of the test substance. The concentration tested was either 0.1 mg/l (static test) or 0.05 mg/l (respirometer flasks) and the substance was added as 0.1 ml of a solution in acetone. All experiments were carried out in duplicate for up to 64 days and sterile controls were also run to investigate the abiotic degradation of tri-*m*-cresyl phosphate under the conditions used. The aerobic experiments were incubated with a 16:8 hours light:dark photoperiod (using low intensity light) whereas the anaerobic experiments were incubated in darkness. The microbial biomass present in the test systems was between 9×10^6 to 32×10^6 colony forming units (CFU)/g in the experiments with river sediments. The microbial biomass present in the aerobic pond respirometer sediments was found to decline from 42×10^6 CFU/g to 0.3 CFU/g over the 64-day period. The total microbial

biomass (aerobic and facultative anaerobic heterotrophs) present in the N_2-purged respirometer experiments was 5.3×10^6 CFU/g after 3 to 8 days and 24×10^6 after 30 to 40 days, but the number of strict anaerobes present was around eight to 40 times less, and so the incubations were not strictly anaerobic. The results of the experiments are summarised in Table 3.1.

The results show extensive degradation of tri-*m*-cresyl phosphate in the study. Initially, most of the tri-*m*-cresyl phosphate added to the system adsorbed onto the sediment phase but by the end of the experiment the amount of extractable radioactivity associated with the sediment phase had decreased substantially. Detailed analysis of the sediment extracts indicated that the major portion of the extractable radioactivity was as unchanged tri-*m*-cresyl phosphate, with low levels of degradation products, including di-*m*-cresyl phosphate, also present.

Pickard *et al.* (1975) studied the biodegradation of a commercial triaryl phosphate product, along with triphenyl phosphate, trixylenyl phosphate and tri-*o*-cresyl phosphate by mixed bacterial populations. The actual composition of the commercial product was not given but it was reported that the following mixture of phenolic compounds was used to manufacture the product: 2.6 per cent phenol, 0.5 per cent *ortho*-cresol, 13.6 per cent *meta*- and *para*-cresol, 0.6 per cent 2-ethylphenol, 22.3 per cent 2,4- and 2,5-xylenol, 49.2 per cent mixed xylenols, 8.6 per cent 3,4-xylenol, 1.3 per cent C_6-C_9 phenolics and 1.4 per cent trimethyl phenol. Based on this starting mixture the commercial product would be a mixture of trixylenyl phosphate and tricresyl phosphates, along with other mixed triaryl phosphates. The purity of the triphenyl phosphate, trixylenyl phosphate and tri-*o*-cresyl phosphate used was not reported.

The microbial cultures used in the study were obtained by enrichment (using 0.1 per cent solutions of the commercial product) of a mud sample from a lake that had been used as a seaplane base and that was rich in oil-utilizing microorganisms. The enriched mixed microbial cultures were capable of growing on the commercial product, tri-*o*-cresyl phosphate and trixylenyl phosphate as sole source of carbon, but grew only poorly when triphenyl phosphate was used as the sole carbon source.

Hattori *et al.* (1981, cited in WHO 1990) investigated the degradation of tricresyl phosphate in river water and sea water from Osaka, Japan. The substance was tested at an initial concentration of 1 mg/l. Tricresyl phosphate was found to degrade rapidly in river water after a lag period of one to two days, and was almost completely degraded within five days. No degradation was seen over 15 days in heat sterilised river water indicating that the degradation seen was due mainly to biotic processes. In contrast to this, tricresyl phosphate was found to degrade only slowly in sea water.

Boethling and Cooper (1985) estimated that the removal of tricresyl phosphate during biological waste water treatment at a production plant in the United States was 96 per cent, based on the average concentration in waste water (6.23 mg/l) and the average concentration in effluent from the treatment plant (0.23 mg/l). The removal was thought to be due to biodegradation since air stripping was not thought to be an important removal mechanism, and sludge wastage was not practiced at the facility. However, it was also indicated that the results of this study should be treated with caution as the recoveries found for the effluent samples were generally much lower than found for the waste water samples (27 per cent overall versus 89 per cent overall). Thus, the concentrations in the effluent may have been higher than indicated (and hence the removal lower than indicated).

Table 3.1 Effect of temperature and redox potential on degradation of ^{14}C-tri-*m*-cresyl phosphate in sediments

Test system	Sediment	Temp.	Time (days)	Amount of ^{14}C present (% of applied)							Estimated half-life[c] (days)
				Sediment – extractable[a]	Sediment – non-extractable	Water – extractable[b]	Water – non-extractable	CO_2	Total	Percent of total as parent compound	
Aerobic static test system	Pond	25°C	0.25	89.2	3.7	2.3	n/a		95.2		3.2±1.4
			64	6.1	22.2	0.7	3.2		32.3		
		10°C	0.25	57.3	6.6	0.9	12.4		77.2		4.1±0.7
			64	10.8	16.0	0.5	1.8		29.1		
		2°C	0.25	122.3	3.0	1.4	n/a		126.7		16.3±8.8
			6	102.6	1.7	1.5	n/a		105.8		
	River	25°C	0.25	89.0	0.6	0.8	1.7		92.1		10.1±1.1
			40	61.0	8.4	<0.1	13.3		82.7		
Aerobic respirometer	Pond	25									
	River	25	3	85.3	2.6	7.8	n/a	0.1	95.7	85.3	
			40	50.7	15.7	10.4	n/a	14.5	98.4	22.6	
Anaerobic respirometer	River	25°C	3	92.8	1.3	6.5	n/a	0.1	100.7	54.5	
			40	60.2	7.7	14.1	n/a	13.8	95.8	31.2	
Autoclaved sample (aerobic static test system)	Pond	25°C	64	80.8	3.1	1.2	3.1		88.2		

Source: Muir *et al.* (1989).

Notes: a) Extracted with aqueous methanol to recover undegraded phosphate ester and any diaryl phosphate degradation products.
b) Extracted with dichloromethane to recover undegraded phosphate ester.
c) Half-life estimated based on the data obtained over days 0-6 for pond sediment and days 0-10 for river sediment. The half-life refers to the disappearance of the parent compound from the sediment phase.

Boethling and Cooper (1985) indicates that unpublished work by Shelton and Tiedje (1981) found no evidence for biodegradation under anaerobic conditions of tri-*m*-cresyl phosphate over eight weeks using 1:10 dilutions of primary anaerobic sludge. The method used determined the amount of methane formed in the system.

Summary of environmental degradation

Abiotic degradation

The available information indicates that tricresyl phosphate undergoes hydrolysis and the rate of this hydrolysis increases with increasing pH. Based on the data available for other triaryl phosphates (for example, see the risk evaluation report for triphenyl phosphate in this series) the products from the hydrolysis reaction are likely to be cresol and dicresyl phosphate, which is likely to be more stable to hydrolysis than the parent compound. The available information indicates that the hydrolysis reaction is only likely to be rapid at very high pH (for example, the estimated half-life at 25°C is 1,100 to 2,200 days at pH 7 and 30 to 40 days at pH 8) or low pH. Since the pH in the environment is generally outside the range where rapid hydrolysis would be expected, and since other biotic removal mechanisms are likely to be much more important than hydrolysis for tricresyl phosphate at lower pH, the rate of hydrolysis of tricresyl phosphate will be assumed to be zero in this assessment. However, in some acidic or alkaline environments, hydrolysis could become significant and so the effect of inclusion of a hydrolysis rate on the predicted concentrations is considered in Annex C.

Several studies have shown that tricresyl phosphate can undergo photolytic degradation using UV radiation. However, as the amount of UV radiation reaching the Earth's surface is small, the significance of these studies to the behaviour in the environment is limited. For the purposes of this assessment, the rate of photolysis of tricresyl phosphate will be assumed to be zero.

Atmospheric photo-oxidation of tricresyl phosphate is predicted to occur with a half-life of around 27.5 hours. This reaction will be taken into account in the risk assessment.

In summary, the abiotic degradation rates constants and half-lives assumed in the assessment are as follows. The importance of inclusion of hydrolysis to the overall conclusions of the risk assessment is considered further in Annex C.

Hydrolysis	$khyd_{water}$ = 0 d^{-1}	half-life = infinite
Photolysis	$kphoto_{water}$ = 0 d^{-1}	half-life = infinite
Atmospheric photooxidation	k_{OH} = 1.4×10^{-11} cm^3/molecule s	half-life = 27.5 h

Biodegradation

The most likely pathway for biodegradation of aryl phosphates is the initial hydrolysis of the phosphate ester to form orthophosphate and corresponding phenolic compounds or alcohols, which then themselves undergo further biodegradation (Saeger *et al.* 1979).

Many studies have shown that tricresyl phosphate degrades rapidly in a variety of aerobic test systems. In standard tests, tricresyl phosphate can be considered to be readily biodegradable, but it is not clear if the 10-day window is met.

The recommended biodegradation half-lives for sewage treatment, surface water, sediment and soil from the TGD for tricresyl phosphate (assuming it is readily biodegradable but not meeting the 10-day window or readily biodegradable meeting the 10-day window), with a Kp_{soil} of 94 l/kg (see Section 3.1.2), are summarised below.

	Not meeting 10-day window	Meeting 10-day window
STP	half-life = 2.3 hours	half-life = 0.7 hours
Surface water	half-life = 50 days	half-life = 15 days
Soil	half-life = 300 days	half-life = 30 days
Sediment	half-life = 3,000 days	half-life = 300 days

The available screening studies with which to compare these data are limited in that most of them have measured primary degradation rather than mineralisation. However, the available river die-away studies generally show very rapid primary degradation (half-life less than seven days), and primary degradation half-lives of 3 to 16 days have been measured in sediment-water systems. Given that the intermediate product of primary degradation is likely to be cresol, which is itself expected to under go further rapid mineralisation (for example, the IUCLID database indicates that *o*-cresol, *m*-cresol and *p*-cresol can all be considered readily biodegradable), it is probable that the default half-life of 15 days for water is more appropriate for tricresyl phosphate than the longer default half-life of 50 days. Therefore, it is proposed that the default half-lives obtained assuming the 10-day window is met are used in the risk assessment, as these appear to be in reasonable agreement with the available data for surface water at least.

For sediment, the TGD recommends that the default rate constant should be ten times lower than that for soil to reflect the fact that the deeper sediment layers are anaerobic (this calculation assumes that degradation under anaerobic conditions does not occur). The available data for tricresyl phosphate under anaerobic conditions are conflicting in this respect, with one study (Muir *et al.* 1989) apparently showing a similar rate of degradation in river sediment under aerobic and anaerobic conditions (although the conditions in this test may not have been strictly anaerobic) and another study (Shelton and Tiedje 1981) showing no mineralisation to methane under anaerobic conditions. Therefore, for this assessment, it is assumed that the overall rate of mineralisation in sediment will be one tenth of that in soil (as recommended in the TGD) to reflect the fact that mineralisation under anaerobic conditions could be much lower than under aerobic conditions for this substance.

In summary, the following biodegradation rate constants and half-lives will be used in the assessment.

STP	$k = 1\ h^{-1}$	half-life = 0.7 hours
Surface water	$k = 4.7\times10^{-2}\ d^{-1}$	half-life = 15 days
Sediment	$k = 2.3\times10^{-3}\ d^{-1}$	half-life = 300 days
Soil	$k = 2.3\times10^{-2}\ d^{-1}$	half-life = 30 days

Although the phenolic part of triaryl phosphate will undergo mineralisation, orthophosphate/phosphoric acid will also be produced as a result of degradation. The fate, behaviour and effects of this substance are beyond the scope of this assessment.

3.1.2 Environmental partitioning

Adsorption

Hoke *et al.* (1993) determined the levels of tricresyl phosphate in sediment and sediment pore water of sediment samples collected from the Grand Calumet River (field study). The results are summarised in Table 3.2. From the data presented it is possible to estimate the approximate value for the K_{oc} for tricresyl phosphate of around 1,618 l/kg. However, this value is estimated from field data (as opposed to being determined in a well-defined laboratory study) and should be treated with caution.

Table 3.2 K_{oc} values estimated from field data

Organic carbon content of sediment sample	Tricresyl phosphate concentration		Estimated K_{oc} value (l/kg)
	Sediment (mg/kg dry weight)	Pore water (mg/l)	
28.1%	1.95	0.0129	538
4.4%	1.13	0.0115	2,233
7.2%	0.57	0.0226	350
12.5%	0.09	0.0003	2,400
14.3%	1.00	0.0025	2,797
15.9%	1.14	0.0046	1,559
14.7%	1.34	0.0056	1,628
22.3%	0.22	0.0005	1,973
18.8%	3.40	0.0068	2,660
13.4%	0.05	0.0097	38
		Mean	1,618 $\pm$ 993

Source: Hoke *et al.* (1993).

Kenmotsu *et al.* (1980, cited in WHO 1990) determined an adsorption coefficient of 420 l/kg for tricresyl phosphate in marine sediment. The organic carbon content of the sediment was not given.

A K_{oc} value of 2.37×10^4 l/kg can be estimated for tricresyl phosphate from its structure using the Syracuse Research Corporation PCKOC version 1.63 software which employs a molecular connectivity index method.

Chapter 4 of the TGD recommends the following equation for estimating K_{oc} from log K_{ow} for phosphates:

$$\log K_{oc} = 0.49 \log K_{ow} + 1.17$$

Using this equation for tricresyl phosphate (log K_{ow} of 5.11) results in an estimated K_{oc} value of 4,720 l/kg. This value is in reasonable agreement (within a factor of three) with the values estimated from the field data of Hoke *et al.* (1993). A K_{oc} value of 4,720 l/kg is assumed in the assessment. The resulting partition coefficients for soil and sediment calculated using the methods given in the TGD are shown below.

K_{oc}	4,720 l/kg		
Kp_{susp}	472 l/kg	$K_{susp\text{-}water}$	119 m^3/m^3
Kp_{sed}	236 l/kg	$K_{sed\text{-}water}$	119 m^3/m^3
Kp_{soi}	94.4 l/kg	$K_{soil\text{-}water}$	142 m^3/m^3

These values will be used in the risk assessment.

Volatilisation

Muir *et al.* (1985) carried out experiments investigating the volatilisation from and distribution in an artificial pond (15-17 m^2 area and 0.5 m depth) over a total of 360 days. The substance tested was ^{14}C-labelled tri-*m*-cresyl phosphate which was added to give an initial water concentration of 50 μg/l. The paper estimated (using a two-resistance model) that the potential cumulative losses by volatilisation accounted for a total of around 10 per cent of the total radioactivity added by day 21. The results of the study are summarised in Table 3.3. The half-life of the substance in the water and

sediment phase was estimated to be 0.57 and 39 days respectively based on parent compound analysis.

Table 3.3 Distribution of ^{14}C-labelled tri-m-cresyl phosphate in an artificial pond

Time	Distribution (as percentage of initial amount applied)			
	Water	Sediment	Air[a]	Biota
1 hour	82.4	-		-
18 hours	23.1	77.7	5.7	1.3
7 days	10.3	55.1	9.0	0.3
21 days	8.2	41.8	9.8	<0.1
105 days	<2.0	32.3	-	-
360 days	-	30.5	-	-

Source: Muir *et al.* (1985).
Notes: a) Values for air represent theoretical cumulative total using a two-resistance model.

The Henry's law constant for tricresyl phosphate is estimated to be 0.068 Pa m^3/mol at 25°C. This indicates that volatilisation from water is likely to be limited.

Fugacity modelling

The potential environmental distribution of tricresyl phosphate has been studied using a generic level III fugacity model. The model used was a four-compartment model (EQC version 1.01, May 1997) that has been circulated for use within the Organisation for Economic Cooperation and Development (OECD) High Production Volume (HPV) programme. The model was run four times with a nominal release rate of 1,000 kg/hour initially entering the air, soil or water compartments in different proportions. The physico-chemical properties used and the results of the modelling exercise are shown in

Table 3.4.

The results of the model show that only a very small amount of the tricresyl phosphate released to the environment will be in the air compartment at steady state. When the substance is released to air it distributes mainly to the soil compartment, presumably by atmospheric deposition. When it is released to soil, the substance generally remains in the soil, with only a small fraction distributing to the water and sediment compartments. When released to water, the substance is likely to distribute between the water and sediment phases at steady state.

Table 3.4 Results of generic level III fugacity model for tricresyl phosphate

Input data	Value				
Vapour pressure	3.5×10^{-5} Pa at 20°C				
Water solubility	0.36 mg/l				
Henry's law constant	0.036 Pa m^3/mol at 20°C				
Log K_{ow}	5.11				
Atmospheric half-life	27.5 hours				
Half-life in water	15 days				
Half-life in soil	30 days				
Half-life in sediment	300 days				
Emission rate	**Model results at steady state**				
	Amount in air	**Amount in soil**	**Amount in water**	**Amount in sediment**	**Overall residence time/ persistence**
1,000 kg/hour to air 1,000 kg/hour to soil 1,000 kg/hour to water	0.63%	54.3%	12.3%	32.8%	36.5 days
1,000 kg/hour to air 0 kg/hour to soil 0 kg/hour to water	3.67%	85.8%	2.94%	7.87%	18.8 days
0 kg/hour to air 1,000 kg/hour to soil 0 kg/hour to water	6.0×10^{-5}%	99.97%	9.2×10^{-3}%	0.025%	43.3 days
0 kg/hour to air 0 kg/hour to soil 1,000 kg/hour to water	1.5×10^{-3}%	0.036%	27.2%	72.8%	47.3 days

The behaviour of tricresyl phosphate during waste water treatment was estimated using the EUSES model. Using a degradation rate constant of 1 h^{-1} (see Section 3.1.1), a K_{oc} of 4,720 l/kg (see above) and a vapour pressure of 6.6×10^{-5} Pa at 25°C (see Section 1.3.5), the following behaviour was predicted.

Degraded	62.8%
Adsorbed to sludge	27.5%
Volatilised to air	0.02%
To effluent	9.64%

These figures are used in predicted environmental concentration (PEC) calculations.

3.1.3 Bioaccumulation and metabolism

Measured data

Uptake from water

The bioconcentration of a commercial triaryl phosphate product in bleak (*Alburnus alburnus*) has been investigated (Bengtsson *et al.* 1986). The substance tested contained triphenyl phosphate, cresyl diphenyl phosphate (two main components), tricresyl phosphate (three main components) and trixylenyl phosphate (three main

components). The tests were carried out using a flow-though system with natural brackish water (7‰ salinity) at 10°C. The fish used in the test had an average weight of five grams (53 fish were used in 60 litres of water) and were fed twice daily (once daily at weekends) with a 0.25 g portion of commercial food. The pH of the water was 7.6 to 7.9 and the dissolved oxygen concentration remained above 90 per cent of saturation throughout the study. The experiment consisted of a 14-day uptake period where the fish were exposed to a nominal concentration of 50 μg/l of the triaryl phosphate product and this was followed by a 14-day depuration period in clean flowing water. Samples of both fish (three fish per sample time except at day 14 and 28 when five groups of three fish were sampled) and water were analysed for the concentrations of the main components (as determined by gas chromatographic analysis) of the triaryl phosphate product on days 0, 1, 2, 4, 7, 14, 17, 18, 21 and 28 of the experiment. No mortality or abnormal behaviour was seen in the fish during the experiment. Steady state was found to have been reached within the 14-day exposure period (steady state was actually attained within two days) for triphenyl phosphate, the cresyl diphenyl phosphate components and two of the tricresyl phosphate components of the mixture. Steady state bioconcentration fators (BCFs) were determined as 400 l/kg, 100 to 220 l/kg and 800 l/kg for these components respectively. For the other components, steady state was approached, but had not been reached by the end of the 14-day period and non-steady state BCFs estimated at 14 days were 400 for the remaining tricresyl phosphate component and 1,300 to 1,900 for the three trixylenyl phosphate components. All components were found to be rapidly eliminated from the fish, with a depuration half-life of four days or less. Triphenyl phosphate, cresyl diphenyl phosphate and tricresyl phosphate components were almost completely eliminated from the fish within 14 days but trixylenyl phosphate components were still evident in the fish after 14 days.

The bioconcentration of tricresyl phosphate (no information on purity; a ^{14}C-labelled substance was possibly used) in fathead minnows (*Pimephales promelas*) was studied over 32 days using a flow-through system at 25°C (Veith *et al.* 1979). The water used in the test was lake water with a hardness of 45.5 mg/l as $CaCO_3$ and a pH of 7.49. The dissolved oxygen concentration in the test remained above 5 mg/l throughout the test. A cosolvent (acetone, no information on concentration) was used in the test and the concentration of tricresyl phosphate in the test tank was verified by daily measurements. The mean exposure concentration was 31.6 μg/l. The test used a total of 30 adult (six-month old) fish and five fish were removed after 2, 4, 8, 16, 24 and 32 days of exposure and analysed for the concentrations of tricresyl phosphate present. The BCF determined after 32-days exposure was 165 l/kg. It is not entirely clear from this paper if the measured concentrations are based on ^{14}C measurements or parent compound measurements.

Muir *et al.* (1983) investigated the bioconcentration of ^{14}C-labelled tri-*p*-cresyl phosphate and ^{14}C-labelled tri-*m*-cresyl phosphate (radiochemical purity of both was above 98 per cent; mixed with unlabelled triphenyl phosphate) by both rainbow trout (*Oncorhynchus mykiss*) and fathead minnows (*Pimephales promelas*). The fish (mean weight 0.75 g for rainbow trout (loading density 3.0 g/l) and 2.5 g for fathead minnows (loading density 7.2 g/l)) were exposed in glass aquaria containing 10 litres of dechlorinated, carbon-filtered tap water at 10°C. The fish were acclimated to the aquaria for 16 hours prior to the addition of the test substance at either 5 μg/l or 50 μg/l (the test substance was added as a solution in acetone (0.05 to 0.4 ml added to each aquaria)). Fish (three at each sampling point) were removed from the aquaria at various times (1, 3, 6, 12 and 24 hours) during the exposure period for analysis of the concentration of radiolabel. At the end of the 24-hour exposure period, the remaining fish were removed, placed in a 40-litre tank with a continuous flow of water and depurated for up to 432 hours (fish were sampled after 12, 24, 48, 96, 144, 240 and 432 hours of depuration). In addition, the concentration of radiolabel present in the water phase was determined during the exposure part of the experiment. In some

cases, concentrations of the test substance present were also determined by parent compound analysis (gas chromatography using an N-P detector).

During the exposure part of the test, the concentration of the test substance in water decreased with time as a result of uptake in the fish. This decrease was more marked for fathead minnows than for rainbow trout due to the higher loading used for fathead minnow. For trout, steady-state concentration was not reached within the 24-hour exposure period but the concentrations in fathead minnows generally reached a maximum, steady-state value within 12 hours of exposure. Depuration of the test substance was found to be biphasic for tri-*m*-cresyl phosphate, especially with rainbow trout, with a more rapid depuration seen over the first six days on transfer to clean water, but was better described by a single exponential decay for tri-*p*-cresyl phosphate. The kinetic data and bioconcentration factors determined from the data are summarised in Table 3.5. The authors also estimated BCF values of 310 ± 52 l/kg and 462 ± 3 l/kg for rainbow trout and fathead minnows respectively for tri-*m*-cresyl phosphate and 770 ± 24 and 709 ± 76 respectively for tri-*p*-cresyl phosphate based on the estimated amount of untransformed tricresyl phosphate present in the fish.

Table 3.5 Uptake and elimination of ^{14}C-labelled tricresyl phosphate in rainbow trout and fathead minnow

Species	Substance	Exposure concentration (µg/l)		Uptake rate constant (initial rate method) (hour^{-1})[a]	Depuration rate constant (hour^{-1})[a]		Bioconcentration factor (BCF)		
		0 h	24 h		0-144 hour	0-432 hour	b	c	d
Rainbow trout	Tri-p-cresyl phosphate	5.8[e]	2.8	25.8±15.6	0.0104 ±0.0040	0.0106 ±0.0036	2,768 ±641	1,420 ±42	1,466 ±138
		52.5	14.0	21.8±13.0	0.0096 ±0.0044	0.0133 ±0.0045			
	Tri-m-cresyl phosphate	4.4[e]	2.0	28.8±17.3	0.0242 ±0.0091	0.0115 ±0.0042	1,162 ±313	784 ±82	1,102 ±137
		40.0	17.5	24.0±14.4	0.0229 ±0.0094	0.0149 ±0.0053			
Fathead minnow	Tri-p-cresyl phosphate	4.3	0.7	25.9±13.0	0.0096 ±0.0039	0.0070 ±0.0024	2,199 ±227	928 ±78	588 ±129
		46.5	6.9	7.8±3.9	0.0077 ±0.0035	0.0095 ±0.0032			
	Tri-m-cresyl phosphate	3.8	0.6	18.2±9.2	0.0147 ±0.0055	0.0085 ±0.0032	1,653 ±232	596 ±103	385 ±92
		43.8	8.8	12.2±6.2	0.0117 ±0.0049	0.0101 ±0.0035			

Source: Muir *et al.* (1983).

Notes:
a) Uptake and depuration data calculated based on ^{14}C measurements. The ± values are the 95 per cent confidence limits.
b) BCF determined using initial rate method for uptake rate constant.
c) BCF determined using the method of Zitko (1980) to take account of the decrease in exposure concentration with time.
d) BCF determined using BIOFAC computer program. Values calculated by this method are not considered reliable as the method requires the exposure concentration to remain constant during the test.
e) Values determined after one hour.

The accumulation of a commercial product that contained a significant amount of tricresyl phosphate has been studied in rainbow trout in an outdoor flow-through system (Lockhart *et al.* 1975, Wagemann *et al.* 1974, Wagemann 1975). The substance tested consisted of two per cent tri-*o*-cresyl phosphate, 42 per cent tri-*m*-cresyl phosphate, 31 per cent tri-*p*-cresyl phosphate, 18 per cent tris-(dimethylphenyl)

phosphates, six per cent tris-(ethylphenyl) phosphates and one per cent other phosphates (including triphenyl phosphate and tris-(trimethylphenyl) phosphates). The tests were carried out using yearling rainbow trout in three-metre diameter tanks receiving the test substance in inflowing water (10 l/min). The mean concentration of the test substance in the inflow was 0.9 mg/l as determined by total P analysis. At the end of the four-month exposure period, six fish were analysed for the concentration of test substance in the muscle and gut (digestive tract with pyloric caeca and associated adipose deposits). The analytical method used determined the concentrations of *meta*- and *para*-cresols in hydrolysed fish samples and the concentration of the commercial substance was calculated from these data using the measured yield of these cresols from hydrolysis of IMOL S-140. Thus, the method provided an indirect estimate of the total concentration of aryl phosphate esters present. Mean concentrations found in the white muscle samples and gut of fish after four months of exposure were 9.05 ± 1.90 mg/kg wet weight and 152 ± 38 mg/kg wet weight. Based on these data, BCF values of 10 for muscle and 169 for gut can be estimated. Effects were seen on the feeding rate during this study (see Section 4.1.1) and, although the fish were reported to still be growing in this study, it is not clear what effect this reduced feeding may have had on the lipid content of the fish and uptake of the test substance. Therefore, the results of this study are considered to be less reliable than those from other studies.

Boethling and Cooper (1985) report that unpublished studies by Metcalf (1976) showed that tri-*p*-cresyl phosphate accumulated in several aquatic organisms tested using model ecosystems. Ecological magnification factors of 320,000 for alga (*Oedogonium* sp.), 28,000 for snail (*Physa* sp.), 3,700 for mosquito (*Culex* sp.), 3,700 for fish (*Gambusia* sp.) and 2,900 for *Daphnia* sp. were reported. The actual basis behind these factors is unknown.

Sitthichaikasem (1978) carried out a bioconcentration study using ^{14}C-labelled tri-*p*-cresyl phosphate with bluegill (*Lepomis macrochirus*). The experiment was carried out using an intermittent flow-through system. The fish (mean weight 0.64 g, mean length 36.4 mm) were equilibrated to the test system (40 fish per tank, two tanks for the uptake study and one for the depuration study, each tank containing 45 litres of water at 22°C, flow-through system providing seven to eight water volumes per day) for two days prior to addition of the test substance (nominal concentration 0.15 μg/l). No control tanks (without the test substance) appear to have been run in this study. The actual concentration of the test substance in water was analysed twice per week over the four-week exposure period. During the test, fish were fed daily with *Daphnia magna* (at a rate of five per cent of body weight). *Daphnia magna* used for feeding were held in the test water for 24 hours prior to feeding to the fish and so would have acted as a source of exposure to the test substance for the fish as the *Daphnia magna* themselves would be expected to have accumulated some test substance from solution during this holding period (the actual concentration of the test substance in *Daphnia magna* was determined to be around 100 μg/kg after 24 hours exposure on day 20). No mortalities occurred during the test and mean concentrations in water and fish and estimated BCF values (all based on ^{14}C determinations) are summarised in Table 3.6. The mean BCF value determined was 1,589 l/kg. Owing to the method of feeding used in this study, the results probably reflect uptake via both water and food and so may overestimate the true BCF (via water alone) for this substance. Elimination experiments (28 days in clean water) showed a two-stage elimination of the test substance. The first stage showed rapid elimination of the radiolabel over the first three days, with little or no further elimination until day seven. From day seven onwards, elimination of the radiolabel occurred at a slower rate with a half-life of around 39 days. By day 28 of the elimination period the total body burden of the radiolabel had fallen to around 32 μg/kg.

Muir *et al.* (1985) determined the uptake of ^{14}C-labelled tri-*m*-cresyl phosphate by *Pimephales promelas* in an artificial pond. The pond was 15-17 m^2 in area, with a depth

of 0.5 m, and the substance was added to the pond water to give an initial concentration of 50 μg/l. The maximum concentration of ^{14}C in the fish was determined eight hours after addition of the test substance to the pond and an approximate BCF of 348 l/kg was reported at this time. After this time, the concentration of the test substance in fish declined, reflecting the decline in the concentration in the water phase in the experimental pond. The same study also investigated uptake of the test substance by invertebrate (*Chironomus tentans*) larvae. The larvae were found to accumulate ^{14}C, via pore water or from the sediment itself, and the maximum concentration found in the organism was 6.7 mg/kg at day 70. The authors estimated concentration factors (based on the measured concentration of the tri-*m*-cresyl phosphate present in sediment) of 21 at day 49, with the factor generally being above 10 over days 21 to 70. As the exposure concentration in water in this study was not maintained, the BCFs are difficult to interpret in terms of steady-state values.

Table 3.6 Uptake of ^{14}C-labelled tri-*p*-cresyl phosphate by bluegill

Expo-sure time	Replicate 1			Replicate 2			Combined replicate 1+2		
	Water conc[a] (μg/l)	Fish conc. (μg/kg)	BCF (l/kg)	Water conc[a] (μg/l)	Fish conc. (μg/kg)	BCF (l/kg)	Water conc[a] (μg/l)	Fish conc. (μg/kg)	BCF (l/kg)
7 days	0.1184	206.4	1,743	0.1171	190.6	1,628	0.1181	198.5	1,681
14 days	0.1373	242.8	1,768	0.1404	211.4	1,506	0.1389	227.1	1,635
21 days	0.1355	220.3	1,626	0.1316	221.1	1,680	0.1336	221.2	1,656
28 days	0.1449	190.3	1,343	0.1527	219.7	1,439	0.1488	205.0	1,378

Source: Sitthichaikasem (1978).
Notes: a) Average concentration measured over the time period.

Uptake from food

A long-term dietary accumulation study with a commercial triaryl phosphate product was carried out with minnows (*Phoxinus phoxinus*) (Bengtsson *et al.* 1986). The substance tested contained triphenyl phosphate, cresyl diphenyl phosphate (two main components), tricresyl phosphate (three main components) and trixylenyl phosphate (three main components). The test was carried out using a flow-through system with six groups of 30 fish (average body weight 1.9 g), each in 50 litres of natural brackish water (7‰ salinity). The test was started in January and was carried out for 163 days (although the resulting concentrations in fish were determined after four months only). The water temperature followed natural seasonal fluctuations (3.6-4.5°C from January to April, 7°C by end of April, 13°C by end of May and 12.3-15.5°C from June until the end of the experiment). Dissolved oxygen concentration in the test was always above 90 per cent of saturation and the pH of the water was 7.7 to 8.0. Five concentrations of the test substance were used (100, 300, 1,000, 3,000 and 10,000 mg/kg food) plus a control using uncontaminated food was run. The food used was a commercial fish food which was spiked by adding the triaryl phosphate as a solution in acetone and evaporating off the solvent. The fish were given two 0.25 g portions of food per day. The total amount of food given to the fish by four months of the experiment was two grams per fish. No mortalities or abnormal behaviour were seen in any of the fish, and all food given to the fish was eaten. Concentrations of the various components of the fish after four months exposure are shown in Table 3.7. Overall, only around 0.017 to 0.14 per cent of the total amount of the test substance fed to fish was found to be

present in the fish at the end of the study. Bioaccumulation factors, based on the estimated concentrations in fish and in food, are all very much less than one.

Uptake from soil

The uptake of pure tri-*p*-cresyl phosphate was studied in soybean plants (Casterline Jr *et al.* 1985). The soil used in the test was sterilised before use and consisted of 73 per cent sand, 17 per cent silt, eight per cent clay and two per cent organic matter. The test substance was added to the surface of the dry soil as a solution in acetone and once the solvent had evaporated, the soil was thoroughly mixed to give a tri-*p*-cresyl phosphate concentration of 10 mg/kg. The treated soil was then placed in pots (two kg per pot) and was covered with a 2 cm deep layer of untreated soil into which the seeds were added. The resulting plants were harvested after 90 days of growth had occurred and the stems, leaves, pods and seeds were analysed for the presence of tri-*p*-cresyl phosphate and any metabolites by a gas chromatographic method. The results of the tissue analysis are shown in Table 3.8. The study found that around 70 per cent of the tri-*p*-cresyl phosphate had disappeared from the soil by day 90 of the study and was found to have been taken up into the various tissues of the plant. The amount of tri-*p*-cresyl phosphate present in the plant tissues at day 90 was around 33.8 μg, which corresponded to 0.17 per cent of the amount of chemical initially applied to the soil.

Table 3.7 Concentrations in minnows after four months of exposure to contaminated food

Food concentration	Total concentration in fish (mg/kg fresh weight)			
	Triphenyl phosphate	Cresyl diphenyl phosphate (sum of two components)	Tricresyl phosphate (sum of three components)	Trixylenyl phosphate (sum of three components)
Control	0.005	Not detected	0.005	Not detected
100 mg/kg	0.030	0.023	0.053	0.094
300 mg/kg	0.020	0.016	0.085	0.47
1,000 mg/kg	0.225	0.019	0.225	0.896
3,000 mg/kg	0.12	0.016	0.88	2.01
10,000 mg/kg	0.73	0.043	1.39	2.05

Table 3.8 Uptake and metabolism of tri-*p*-cresyl phosphate by soybean plants after 90 days

Plant part	Weight of plant part (g fresh weight)	Concentration of tri-*p*-cresyl phosphate (μg/g fresh weight)	Total amount of tri-*p*-cresyl phosphate (μg)
Seed	3.0	<0.0001	
Pod	5.4	0.09	0.5
Leaf	7.2	1.14	8.2
Stem	4.0	6.28	25.1
Total shoot	19.6	1.72	33.8

Source: Casterline Jr *et al.* (1985).

Calculated data

For the terrestrial food chain, the TGD requires a BCF for earthworms. No experimental data are available for this endpoint and so an earthworm BCF value is estimated using the following equation given in the TGD:

$$BCF_{earthworm} = 0.84 + 0.012\ K_{ow}/RHO_{earthworm}$$

where $RHO_{earthworm}$ = density of the earthworm = 1 kg/l
K_{ow} = octanol-water partition coefficient

Using a log K_{ow} value of 5.11, the $BCF_{earthworm}$ is estimated as 1,547 l/kg. This value is used in the assessment, though the reliability of this estimate is unknown.

Summary of accumulation

Several studies show bioconcentration of tricresyl phosphate in fish. Some studies are limited in their usefulness for this risk assessment, given that the concentration was not maintained adequately during the study (and so the resulting BCF does not represent a steady-state value) or the result was based on ^{14}C measurements (and so may lead to an overestimate of the actual bioconcentration factor of tricresyl phosphate if extensive metabolism was occurring in the fish), or effects on feeding/growth were seen (the actual effect of this on the BCF is unclear but it does add some uncertainty to the interpretation of the data). The available values are summarised in Table 3.9.

From Table 3.9 it can be seen that when the more reliable data based on parent compound analysis are considered, the BCF is generally around 310 to 800 l/kg. Higher values (up to 2,768 l/kg) have been determined based on ^{14}C measurements but this study found the BCF based on parent compound to be around 310 to 770 l/kg. The difference between the values obtained by ^{14}C and parent compound measurements reflects the relatively rapid metabolism of tricresyl phosphate in fish. Metabolites of tricresyl phosphate are generally rapidly excreted from fish.

The log K_{ow} value of tricresyl phosphate is 5.11. Using the methods recommended in the Technical Guidance Document, a BCF for fish of 4,400 l/kg is estimated. This value is higher than those determined in the more reliable studies.

A BCF of 800 l/kg is used in this risk assessment for tricresyl phosphate.

In addition to a BCF, the revised TGD also requires a biomagnification factor (BMF) to be taken into account. For tricresyl phosphate, the default BMF would be one based on the BCF values determined above. This is consistent with the available feeding study which showed that bioaccumulation from food was low.

Tricresyl phosphate has also been shown to be taken up by plants from soil. However, the available data do not allow a concentration or uptake factor to be estimated.

Using a log K_{ow} value of 5.11 and methods outlined in the TGD, the $BCF_{earthworm}$ is estimated as 1,547 l/kg.

Table 3.9 Summary of bioconcentration factors for tricresyl phosphate

BCF (l/kg)	Species	Comment	Rel.	Reference
400-800	*Alburnus alburnus*	Fourteen-day flow-through study in brackish water. Investigated the three main tricresyl phosphate components of a commercial mixture. Steady state was reached for two of these (BCF 800) and steady state was approached for the third component (BCF 400). Values based on parent compound measurements.	2	Bengtsson *et al.* 1986
3,700 (units unclear)	*Gambusia sp.*	The result is an "ecological magnification factor" from a model ecosystem. The basis behind this factor is unknown.	4	Metcalf 1976
1,589	*Lepomis macrochirus*	Four-week study using an intermittent-flow method. BCF based on ^{14}C measurements. The result probably reflects uptake from both water and food and so is not a true BCF value.	2	Sitthichaik-asem 1978
784-2,768	*Oncorhynchus mykiss*	A 24-hour study based on ^{14}C measurements. The concentration in water was found to decrease with time and so the BCF was estimated using the initial rate method and a method that takes this decrease into account. The BCF based on parent compound was 310-770 l/kg. Values are for the isomers tri-p-cresyl phosphate and tri-m-cresyl phosphate.	2	Muir *et al*. 1983
10 (muscle) 169 (gut)	*Oncorhynchus mykiss*	Four-month outdoor flow-through study. The commercial product tested contained several triaryl phosphates. The analytical method used determined the concentrations of *meta*- and *para*-cresols after hydrolysis of the samples and so provides only an indirect measure of the amount of parent compound present. Effects on feeding were reported to be seen in this study.	3	Lockhart *et al.* 1975, Wagemann *et al.* 1974, Wagemann 1975
165	*Pimephales promelas*	A 32-day flow-through study. Not clear if value is based on ^{14}C or parent compound measurements.	2	Veith *et al*. 1979
596-2,199	*Pimephales promelas*	A 24-hour study based on ^{14}C measurements. The concentration in water was found to decrease with time and so the BCF was estimated using the initial rate method and a method that takes this decrease into account. The BCF based on parent compound was 462-709 l/kg. Values are for the isomers tri-p-cresyl phosphate and tri-m-cresyl phosphate.	2	Muir *et al*. 1983
348	*Pimephales promelas*	Pond study. The concentration in water was found to decline rapidly. The maximum BCF based on ^{14}C measurements was determined eight hours after addition of the test substance to the pond.	3	Muir *et al.* 1985

Notes: Rel. = Reliability; 1) Valid without restrictions; 2) Valid with restrictions; 3) Not valid; 4) Insufficient information.

3.2 Environmental releases

3.2.1 General discussion

Releases from the production and use of tricresyl phosphate were estimated using a number of sources such as default methods from the TGD, the Emission Scenario Document on plastics additives (OECD 2004a) the Emission Scenario Document (ESD) on lubricants (OECD 2004b) and scenarios developed under the Existing Substances Regulation for other substances with similar uses. In the absence of

specific information on the substance, the ESDs and scenarios for other substances are considered to be a reasonable basis for emission estimation; TGD default values are intended for use as realistic worst case values in the absence of other data. Hence, estimates from these sources will have some degree of uncertainty. The actual calculations are considered confidential as they are based on confidential production and use figures.

The producers of tricresyl phosphate provided information on the amounts used by representative large customers, and this was used in the local estimates.

3.2.2 Releases from production

Releases from production sites were estimated from specific information provided by the producing companies. The results are included in Table 3.11.

3.2.3 Releases from use (processing)

PVC

Emissions from the use in PVC were estimated using the methods outlined in the ESD on plastics additives (OECD 2004a). The ESD provides methods for estimating the releases from three stages:

- handling of raw materials;
- compounding – the blending into the polymer of additives;
- conversion – the forming of the polymer into finished articles.

The first two stages are assumed to always take place together. There are companies which compound the plastics and then sell them on to converters, so separate calculations are carried out for the two as well as for the case where compounding and conversion take place together. Emission factors in the ESD are derived from information on a model substance, di(2-ethylhexyl)phthalate (DEHP), and are modified according to the relative properties of this substance and the substance of interest. The main property affecting emissions is the vapour pressure of the substance. Tricresyl phosphate has a lower vapour pressure than DEHP at the processing temperatures, and is classed as of low volatility according to the criteria in the ESD[5]. The ESD also uses the particle size or form of the substance in estimating the possible releases from raw materials handling. Tricresyl phosphate is a liquid (Section 1.3.1).

The emission factors derived using the ESD methods are:

- Compounding (including raw materials handling): 0.001 per cent to air, 0.011 per cent to waste water.
- Conversion: 0.005 per cent to air, 0.005 per cent to waste water.

Photo film, pigment dispersions and polyurethane

Methods from the ESD are also used for these materials. For these, the emission factors are:

[5] 'Low volatility' is used in comparison to DEHP which is of 'medium volatility'. All phosphate esters assessed in this series have vapour pressures considered low for organic substances.

- Compounding (including raw materials handling): 0.001 per cent to air, 0.011 per cent to waste water
- Conversion: 0.001 per cent to air, 0.001 per cent to waste water (for pigment dispersions, conversion losses are assumed to be covered by those from the plastics into which they are included, so the conversion factor is zero).

Lubricants

Emissions from the use of the substance in lubricants (from the blending step) were estimated using the methods outlined in the ESD on lubricants (OECD 2004b). Estimates were made for use as an additive in lubricants. The estimated emissions to air from lubricant blending are very low. The emission factor for releases to water from blending is 1.2×10^{-5} kg/tonne lubricant.

3.2.4 Releases over lifetime of products

Tricresyl phosphate is used in products that are expected to have extended service lives (more than one year). These may therefore act as sources of emissions to the environment. Possible losses from PVC and other polymeric materials through leaching and volatilisation are considered in this section. A limited amount of information relevant to the release of tricresyl phosphate is available, and is included here, but estimates are based on the methods outlined in the Emission Scenario Document (OECD 2004a) and also take into account the approaches used in the risk assessment of other substances (for example, the risk assessment on medium-chain chlorinated paraffins carried out under the Existing Substances Regulation (ECB 2005)). The approach taken also considers the release of polymer particulates (waste remaining in the environment) over the lifetime of products and at disposal as appropriate; this is based on the treatment of this area in other risk assessments such as that on medium-chain chlorinated paraffins.

In the absence of information on the types of polymeric materials in which the pigment dispersions are used, a release of five per cent to cover the service life and losses on disposal (see below) is assumed.

For lubricants, the nature of usage means that only losses to air are likely. These are estimated from data supplied by industry, and the overall emissions are included in Table 3.11.

Leaching loss

No information appears to be available on the leaching of tricresyl phosphate from products.

Factors from the ESD on plastics additives are used in the assessment for emissions from PVC products. Compared to the model substance DEHP in the ESD, tricresyl phosphate is classed as a medium solubility substance, and so the factor is increased by a factor of five to account for this. The factor is 0.25 per cent over the lifetime of the product for indoor use, and 7.25 per cent for outdoor use of products. For adhesives, a factor of 0.75 per cent over the lifetime of use is assumed.

Photographic film and polyurethane articles are considered not to come into contact with water on a regular basis and so emissions to water from these uses are considered to be negligible.

Volatile loss

The stability of, and volatile loss from, several commercial aryl and alkyl/aryl phosphate products has been studied using a combination of differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA) under both a nitrogen atmosphere (Shankwalkar and Cruz 1994) and an oxygen atmosphere (Shankwalkar and Placek 1992). The results of the studies are summarised in Table 3.10.

Results under a nitrogen atmosphere show that triaryl phosphates start to decompose at temperatures of around 310-350°C, whereas alkyl diphenyl phosphates start to decompose at a temperature of around 260°C. The decomposition temperatures under an oxygen atmosphere are significantly lower. For all the substances tested, significant weight loss occurred at temperatures below that at which decomposition starts, indicating a loss of the substance by volatilisation at elevated temperatures.

Table 3.10 Thermal degradation temperature and weight loss of aryl and alkyl/aryl phosphates

Phosphate ester	Experiments under an oxygen atmosphere				Experiments under a nitrogen atmosphere		
	Start of thermal degradation	1% weight loss	5% weight loss	10% weight loss	Start of thermal degradation	5% weight loss	10% weight loss
Triphenyl phosphate	>400°C	188°C	236°C	252°C			
Tricresyl phosphate	215°C	184°C	255°C	252°C	333°C	272°C	306°C
Trixylenyl phosphate	210°C	224°C	268°C	286°C	311°C	276°C	302°C
Isopropyl-phenyl diphenyl phosphate[a]	210-215°C	200-218°C	239-265°C	263-288°C	311-314°C	264-282°C	293-307°C
Tertbutyl-phenyl diphenyl phosphate[a]	295-305°C	213-234°C	262-277°C	280-295°C	338-347°C	274-278°C	305-306°C
2-Ethylhexyl diphenyl phosphate	200°C	90°C	220°C	229°C	257°C	226°C	231°C
Isodecyl diphenyl phosphate	165°C	93°C	213°C	235°C	264°C	233°C	246°C

Notes: a) Data for three (nitrogen atmosphere) or four (oxygen atmosphere) different grades.

The weight loss on heating a 10 mg sample of a commercial tricresyl phosphate at a rate of 10°C per minute under nitrogen atmosphere has been determined as five per cent at 222°C, ten per cent at 239°C, 50 per cent at 289°C and 95 per cent at 323°C by thermogravimetric analysis (Great Lakes Chemical Corporation 2002).

These data do not allow emission factors for the service life to be estimated. Factors from the ESD on plastics additives are used, as applied in the risk assessment of medium-chain chlorinated paraffins. These are applied to articles from PVC and polyurethane, and to adhesives. Volatile losses from products occur at ambient temperatures, and at these temperatures tricresyl phosphate is considered to have a similar vapour pressure to DEHP, the reference compound. The appropriate factor from

the ESD is therefore that for medium volatility substances or 0.05 per cent over the lifetime of the product. An exception to this is where the use is in thin films, where a higher value of two per cent over the lifetime was used. For photo films, the thin film factor was used but assuming only limited exposure to air over the lifetime (see the assessment on triphenyl phosphate). The emission factor used was 0.079 per cent over the lifetime.

Waste in the environment

This considers the loss of substance in particles of plastic material from articles in use. The approach is the same as that used in the risk assessment for medium-chain chlorinated paraffins. For use in PVC and adhesives, a loss of two per cent of the material over the lifetime of the products or articles is assumed, together with a further two per cent loss on disposal at the end of the service life. For the other uses, no waste generation during the lifetime is assumed, but two per cent loss on disposal is assumed for polyurethane. Losses on disposal of photo films are considered to be negligible. In the calculations, the substance in these particles is assumed to be available in the environment; this is likely to be an overestimate, but there are no actual data to indicate how much may be available.

3.2.5 Summary of environmental releases

Estimated environmental releases of tricresyl phosphate are summarised in Table 3.11.

Table 3.11 Summary of estimated environmental releases of tricresyl phosphate

Life cycle stage		Local (kg/day)			Regional (kg/year)			Continental (kg/year)		
		Air	Water	Soil	Air	Water[a]	Soil	Air	Water[a]	Soil
Production			1.6 2			54 to surface water[b]			32 to surface water[b]	
Pigment dispersion	Raw materials handling and compounding	0.025	0.075							
	In service losses/waste in the environment				0.1	24.9 to surface water[b]	75	0.9	224 to surface water[b]	675
Adhesives	In service losses				0.15	60.7 to surface water[b]		1.35	546 to surface water[b]	
	Waste in the environment				0.01	2.7 to surface water[b]	8.0	0.10	23.9 to surface water[b]	72.0
Lubricant additive	Blending	3.38×10^{-9}	3.33×10^{-4}		1.8×10^{-7}	0.02		4.2×10^{-7}	0.04	
	Losses in-use				14,000			126,000		
PVC – 1	Raw materials handling and compounding	8.3×10^{-3}	0.09							
	Conversion	0.04	0.04							
	Raw materials handling, compounding and conversion	0.05	0.13		c	c		c	c	
	In service losses				626	77.5		5,636	698	
	Waste in the environment[d]				0.61	151 to surface water	454	5.45	1,358 to surface water	4,089

Table 3.11 continued.

Life cycle stage		Local (kg/day)			Regional (kg/year)			Continental (kg/year)		
		Air	**Water**	**Soil**	**Air**	**Water[a]**	**Soil**	**Air**	**Water[a]**	**Soil**
PVC – 2	Raw materials handling and compounding	1.0×10^{-3}	0.011							
	Conversion	1.0×10^{-3}	1.0×10^{-3}							
	Raw materials handling, compounding and conversion	2.0×10^{-3}	0.012		c	c		c	c	
	In service losses				0.1	14.5		0.9	131	
	Waste in the environment[d]				7.6×10^{-3}	1.9 to surface water	5.7	0.07	17 to surface water	51
Photographic films	Raw materials handling and compounding	5.0×10^{-3}	0.055							
	Conversion	5.0×10^{-3}	5.0×10^{-3}							
	Raw materials handling, compounding and conversion	0.01	0.06		c	c		c	c	
	In service losses				15.5			140		
	Waste in the environment[d]									

Table 3.11 continued.

Life cycle stage		Local (kg/day)			Regional (kg/year)			Continental (kg/year)		
		Air	**Water**	**Soil**	**Air**	**Water[a]**	**Soil**	**Air**	**Water[a]**	**Soil**
Polyurethane	Raw materials handling and compounding	5.0×10^{-3}	0.055							
	Conversion	5.0×10^{-3}	5.0×10^{-3}							
	Raw materials handling, compounding and conversion	0.01	0.06		c	c		c	c	
	In service losses				4.65			41.9		
	Waste in the environment[d]				0.19	46.3 to surface water	139	1.67	417 to surface water	1,255
Miscellaneous					149	23.1 + 65.8 to surface water	156	1,340	208 + 592 to surface water	1,407
Total					14,819	581	840	133,225	4,274	7,556

Notes: a) Regional and continental emissions to water are split 80:20 between wastewater treatment and direct discharge to surface water, except where noted.
b) Emissions calculated from site-specific data, after wastewater treatment (sludges from production sites are incinerated, calculating the values after treatment allows this to be reflected in the emission estimates).
c) Values for individual steps are confidential, but are included in the total figure.
d) Releases as waste in the environment are assumed to go directly to surface water.

3.3 Environmental concentrations

3.3.1 Aquatic environment (surface water, sediment and wastewater treatment plant)

Calculation of PECs

PECs for surface water, waste water treatment and sediment were estimated with the EUSES program using the data summarised in the previous sections as input. The concentrations predicted for water and sediment are shown in Table 3.12.

Table 3.12 Summary of predicted local concentrations for the aquatic compartment

Scenario		PEC_{local}			
		Microorganisms in sewage treatment plant (mg/l)	**Surface water - emission episode (μg/l)**	**Surface water - annual average (μg/l)**	**Sediment (mg/kg wet weight)**
Production of tricresyl phosphate		3.67×10^{-3} and 1.0	0.10 and 0.02	0.09 and 0.02	0.01 and 2.48×10^{-3}
Lubricant additive	Lubricant blending	1.6×10^{-5}	7.34×10^{-3}	6.58×10^{-3}	7.59×10^{-4}
Adhesives		negligible	negligible	negligible	negligible
PVC – 1	Compounding	4.39×10^{-3}	0.44	0.36	0.05
	Conversion	1.93×10^{-3}	0.20	0.16	0.02
	Combined compounding and conversion	6.26×10^{-3}	0.63	0.52	0.06
PVC – 2	Compounding	5.3×10^{-4}	0.06	5.89×10^{-3}	6.04×10^{-3}
	Conversion	4.82×10^{-5}	0.01	0.01	1.09×10^{-3}
	Combined compounding and conversion	5.78×10^{-4}	0.06	0.05	6.53×10^{-3}
Photo-graphic film	Compounding	2.65×10^{-3}	0.27	0.22	0.03
	Conversion	2.41×10^{-4}	0.03	0.03	3.07×10^{-3}
	Combined compounding and conversion	2.89×10^{-3}	0.29	0.24	0.03
Poly-urethane	Compounding	2.65×10^{-3}	0.27	0.02	0.03
	Conversion	2.41×10^{-4}	0.03	6.73×10^{-3}	3.07×10^{-3}
	Combined compounding and conversion	2.89×10^{-3}	0.29	0.02	0.03
Pigment dispersions	Production of dispersions	3.61×10^{-3}	0.37	0.3	0.04

The predicted regional concentrations are 5.75×10^{-3} μg/l for surface water and 6.1×10^{-4} mg/kg wet weight for sediment.

Predicted concentrations were also calculated for the marine environment, using the EUSES program. These are included in Table 3.13. Note that production is not included in this table; the production sites do not discharge to the marine environment.

Table 3.13 Summary of predicted local concentrations for the marine compartment

Scenario		PEC_{local}		
		Marine water - emission episode (μg/l)	**Marine water - annual average (μg/l)**	**Marine sediment (mg/kg wet wt.)**
Lubricant additive	Blending of lubricant	2.2×10^{-3}	1.42×10^{-3}	2.27×10^{-4}
Adhesives		negligible	negligible	negligible
PVC – 1	Compounding Conversion Combined compounding and conversion	0.45 0.2 0.64	0.37 0.16 0.53	0.05 0.02 0.07
PVC – 2	Compounding Conversion Combined compounding and conversion	0.06 5.51×10^{-3} 0.06	7.0×10^{-4} 5.51×10^{-3} 0.05	5.7×10^{-3} 5.7×10^{-4} 6.22×10^{-3}
Photo-graphic film	Compounding Conversion Combined compounding and conversion	0.27 0.03 0.3	0.23 0.02 0.25	0.03 2.62×10^{-3} 0.03
Poly-urethane	Compounding Conversion Combined compounding and conversion	0.27 0.03 0.3	0.01 1.57×10^{-3} 0.01	0.03 2.62×10^{-3} 0.03
Pigment dispersions	Production of dispersions	0.37	0.31	0.04

Measured levels in water and sediment

Water

Tricresyl phosphate was monitored in England and Wales over the period November 2007 to April 2008 as part of the Environment Agency's Targeted Risk Based Monitoring (TRBM) initiative. Six samples were collected at approximately weekly intervals from 15 paired WWTP effluent/receiving water sites across all eight Environment Agency Regions. The site selection criteria are not specified – it is likely that most are reasonably large WWTP with mixed industrial/household influent.

There were no positive detections of tricresyl phosphate in any sample, at a detection limit of 0.05 μg/l.

Measured levels of tricresyl phosphate in water from other countries are summarised in Table 3.14.

Table 3.14 Summary of measured levels in water

Location	Comment	Measured level (μg/l)	Reference
Waste water from triaryl phosphate production plant, USA	Sampled in 1980.	6,230 waste water 230 effluent water	Boethling and Cooper 1985
Sewage treatment plants, Japan	Detected in 2 out of 6 influent samples. Not detected in effluent samples. Detection limit 0.06 μg/l.	0.36-0.78 influent ND effluent	Ishikawa *et al.* 1985c
Influent of Barcelona primary treatment plants	Detection limit 0.6 ng/l.	Detected	Valls *et al.* 1990
Factory effluents, Japan	Detected in 2 effluent samples from 1 out of 9 chemical factories sampled. Not detected in effluents from 3 food factories, 2 steel factories, 3 metal factories or 8 other factories. Detection limit was 0.06 μg/l.	0.4-0.58	Ishikawa *et al.* 1985c
Domestic effluent, Japan	Detected in 2 out of 8 samples. Detection limit 0.06 μg/l.	0.2-0.4	Ishikawa *et al.* 1985c
Domestic sewage treatment plants, Denmark	Detected in 5 out of 45 influent samples (detection limit 0.02 μg/l), detected in 1 out of 45 effluent samples (detection limit 0.02-0.08 μg/l) and detected in 3 out of 15 sewage sludge samples (detection limit 50-100 μg/kg dry weight).	Influent – mean 0.07 Effluent 0.53 Sewage sludge mean 613 μg/kg dry wt.	Miljøstyrelsen 2002a
River water near triaryl phosphate manufacturing plants and large user of hydraulic fluids, United States	Detection limit 10 μg/l.	ND	Boethling and Cooper 1985
Industrial areas of United States	Not detected in 4 samples from Saginaw River, 4 samples from Baltimore Harbour, 3 samples from Detroit River, 4 samples from Delaware River and 7 samples from Kanawha River. Detection limit 0.1-0.5 μg/l.	ND	Boethling and Cooper 1985
River water, Aarhus, Denmark	Sampled in 1997-1998. Detection limit 0.2 μg/l. Not detected in 4 samples from 2 rivers.	ND	Boutrup *et al.* 1998
Kanawha river water, USA	Sampled in 1978.	20	Boethling and Cooper 1985
River water, Kitakyushu City, Japan	Detected in 3 out of 16 samples. Detection limit 0.02 μg/l.	0.067-0.259	Ishikawa *et al.* 1985b
	Detected in 2 out of 14 samples. Detection limit 0.02 μg/l.	0.067-0.160	Ishikawa *et al.* 1985c
River water, Japan	Long-term monitoring program.	generally <0.5 μg/l	Fukushima *et al.* 1982

Table 3.14 continued.

Location	Comment	Measured level (μg/l)	Reference
Surface water, Japan	Not detected in 100 samples in 1975 (detection limit 0.05-1.5 μg/l) and not detected in 114 samples in 1978 (detection limit 0.005-2.5 μg/l).	ND	Environment Agency Japan 1996
River water, Osaka, Japan	Detected in 11 out of 13 samples.	0.1-9.5	Kawai *et al.* 1978, cited WHO 1990
River water, Tokyo, Japan	Not detected in 12 samples. Detection limit 50 μg/l.	ND	Wakabayashi 1980, cited WHO 1990
Eastern Lake Superior, United States	Not detected in 4 samples. Detection limit 0.1-0.5 μg/l.	ND	Boethling and Cooper 1985
Sea water, of Besos river estuary, Spain	Detection limit 0.05 ng/l.	ND	Valls *et al.* 1990
Sea water, Tokyo, Japan	Not detected in 3 samples. Detection limit 50 μg/l.	ND	Wakabayashi 1980, cited WHO 1990
Sea water, Kitakyushu City, Japan	Not detected in 9 samples. Detection limit 0.02 μg/l.	ND	Ishikawa *et al.* 1985b
Drinking water, Canada	Samples from 29 municipalities. Detected in 7 out of 58 samples taken.	ND-0.0043	Williams and LeBel 1981
Drinking water, Canada	Samples from 12 municipalities, Great Lakes area. Detected in 6/24 samples taken.	ND-0.0018	Williams *et al.* 1982
Drinking water, Canada	Samples from 6 water treatment plants in Eastern Ontario. Detected in 1 out of 12 samples.	ND-0.0003	Lebel *et al.* 1981
Contaminated groundwater		500-2,600	Xing and Raetz 2001

Notes: ND – Not detected.

Boethling and Cooper (1985) reported that tricresyl phosphate was not detected (detection limit 10 μg/l) in water samples collected near to an aryl phosphate production site and a large user of hydraulic fluids in the United States.

Ishikawa *et al.* (1985b) found tricresyl phosphate to be present at a concentration of 0.067-0.259 μg/l in three out of sixteen river water samples from Kitakyushu City, Japan. Tricresyl phosphate was not detected in nine samples of seawater from the area. The detection limit of the method used was 0.010 μg/l. Similarly, Ishikawa *et al.* (1985c) found tricresyl phosphate to be present in two out of fourteen river water samples at 0.067-0.160 μg/l from the same area (these may be a subset of the same samples reported in Ishikawa *et al.* 1985b). The detection limit for the Ishikawa *et al.* (1985c) study was 0.02 μg/l.

Ishikawa *et al.* (1985c) found tricresyl phosphate to be present in two out of six influent samples from five sewage treatment plants in Japan at a concentration of 360-780 ng/l. The substance was not found in effluent samples from the plants (detection limit 60 ng/l). The substance was also detected in two out of eight samples of domestic effluent at a concentration of 200-400 ng/l (detection limit 60 ng/l) and in one out of four

influent samples of a night soil treatment facility (the original paper is in Japanese and so it is not clear exactly what this refers to), but was not detected (detection limit 60 ng/l) in effluent from the facility.

Ishikawa *et al.* (1985c) also analysed factory effluents for the presence of tricresyl phosphate. The detection limit of the analytical method used was 60 ng/l. Triphenyl phosphate was not detected in effluents from three food factories, two steel factories, three metal factories, or eight factories classified as other industries. However, it was detected in two effluent samples from one out of the nine chemical factories sampled at 400-580 ng/l.

A survey of the levels of triaryl phosphates in Canadian drinking water was carried out (Williams and LeBel 1981). Drinking water samples (sampled over a 24-hour period) were collected from 29 municipalities during August-September and again during November-December. In general, higher levels were found in drinking water associated with river sources rather than lake sources and groundwater sources. Overall, tricresyl phosphate was detected (detection limit around 0.05 ng/l) in only seven of the 58 samples taken at a concentration of up to 4.3 ng/l.

LeBel *et al.* (1981) reported that tricresyl phosphate was present at a concentration of 0.3 ng/l in one out of twelve samples of drinking water collected in 1978 from six water treatment plants in Eastern Ontario, Canada.

The levels of tricresyl phosphate in drinking water samples from twelve Great Lakes municipalities were determined (Williams *et al.* 1982). The samples were collected over a 24-hour period during January 1980 and again in July/August 1980. Tricresyl phosphate was detected (detection limit not stated) in six out of 24 samples taken at a concentration of 0.4-1.8 ng/l.

Tricresyl phosphate was found to be present in waste water samples (influent of the Barcelona primary treatment plant) but not seawater (collected 1.5 km offshore of the Besos river estuary) collected in 1987 (Valls *et al.* 1990). The detection limit of the method used was around 0.6 ng/l for waste water and 0.05 ng/l for seawater.

Boutrup *et al.* (1998) determined the levels of tricresyl phosphate in freshwater river samples collected from the Country of Aarhus, Denmark in 1997-1998. The detection limit of the method used was around 0.2 μg/l and tricresyl phosphate was not detected in the four samples investigated from two rivers (Giber Å River and Møddebro bœk stream). The water was sampled over a 24-hour period on each occasion.

Two surveys of the levels of tricresyl phosphate in surface waters from all over Japan were carried out by Environment Agency Japan (1996). The substance was not detected in 100 samples analysed in 1975 (detection limit in the range 0.05-1.5 μg/l) and was not detected in 114 samples analysed in 1978 (detection limit in the range 0.005-2.5 μg/l).

A survey of the levels of tricresyl phosphate in influent, effluent and sewage treatment sludge from municipal waste water treatment plants in Denmark was carried out (Miljøstyrelsen 2002a). For each sewage treatment plant, around four individual samples of influent or effluent were collected and the mean concentration of tricresyl phosphate was determined for each treatment plant and the overall mean and fifth and 95th percentiles were calculated for the total population of waste water treatment plants using the mean value for each individual plant (in calculating overall statistics, if the concentration in more than half of the samples was above the limit of detection, the non-detected results were assumed to be half the detection limit: where more than half the samples were below the detection limit, the overall mean was calculated only from results above the detection limit). The detection limit for tricresyl phosphate was 0.02 μg/l in the influent samples, 0.02 to 0.08 μg/l in the effluent samples and 50 to100 μg/kg dry weight in the sewage sludge samples. In total, 45 influent samples and

45 effluent samples were analysed from twelve waste water treatment plants. In the influent samples, tricresyl phosphate was found at a concentration above the detection limit in five samples with the mean, fifth percentile and 95th percentile concentrations being determined as 0.07, 0.03 and 0.13 μg/l respectively. In the effluent samples, tricresyl phosphate was found to be present at a concentration above the detection limit in only one sample at 0.53 μg/l. For the sewage sludge, a total of 15 samples were analysed, and tricresyl phosphate was found to be present at concentrations above the detection limit in three of these. The mean, fifth percentile and 95th percentile concentrations found were 613, 256 and 1,120 μg/kg dry weight respectively.

Xing and Raetz (2001) reported a tricresyl concentration of 500 to 2,600 μg/l in contaminated groundwater.

Boethling and Cooper (1985) reported the results of an early 1980s survey of the levels of tricresyl phosphate in surface water in the United States. Tricresyl phosphate was not found (detection limit 0.1-0.5 μg/l) in four samples from Saginaw River (industrialised area), four samples from Baltimore Harbour (industrialised area), three samples from Detroit River (industrialised area), four samples from Delaware River (industrialised area near to aryl phosphate manufacturer), seven samples from Kanawha River (industrialised area near to aryl phosphate manufacturer) and four samples from Eastern Lake Superior (remote area). An earlier study (1978) reported in Boethling and Cooper (1985) found tricresyl phosphate at a concentration of 20 μg/l in the Kanawha River. The same authors also report that tricresyl phosphate was present at 6,230 μg/l in waste water from a triaryl phosphate production plant, and the concentration in the effluent from the site after treatment was 230 μg/l. These samples were collected in 1980.

Fukushima *et al.* (1992) summarised the results of a long-term monitoring program for triphenyl phosphate and tricresyl phosphate in the Yodo River basin, Lake Biwa, Yodo River and rivers in Osaka City, Japan. The program started in 1976 and water samples were generally collected seasonally or semi-annually, with more recent samples from the Yamato River and Osaka Bay collected during 1989 and 1990. Occurrences of both triphenyl phosphate and tricresyl phosphate were generally limited to highly polluted areas and were more often associated with suspended sediments and sediments rather than the water phase. The concentrations found were generally below 0.5 μg/l.

Further studies from Japan report that tricresyl phosphate was present in eleven out of thirteen samples of river water from Osake (Kawai *et al.* 1978, cited in WHO 1990) and was not detected (detection limit 50 μg/l) in twelve samples of river water and three samples of sea water from Tokyo (Wakabayashi 1980, cited in WHO 1990).

Sediment

Levels of tricresyl phosphate in sediment are summarised in Table 3.15.

Boethling and Cooper (1985) report the results of monitoring studies carried out in the late 1970s near an aryl phosphate production site in the United States. The substances included in the studies were triphenyl phosphate, tricresyl phosphate, isopropylphenyl diphenyl phosphate and aryl phosphates with molecular weights above 410 (which included trixylenyl phosphate and di-(isopropylphenyl) phenyl phosphate). The concentration of total aryl phosphates found in the sediment was 229 mg/kg at the outfall and 4.4 mg/kg at a location eight miles downstream from the outfall. A further twelve sediment samples were also analysed and were found to contain total aryl phosphate concentrations of 0.07 to 1,032 mg/kg. As a result of these findings, a more comprehensive survey was undertaken. This found total aryl phosphate concentrations of 7 to 6,320 mg/kg at locations less than 100 yards downstream of the plant. Levels further downstream were much lower, but concentrations above 1 mg/kg were found in

some samples ten miles downstream. The report indicates that the actual concentration present in the sediments could have been much higher than indicated by these data, as the analytical recovery from spiked sediment was around six per cent. The mixed aryl phosphates with molecular weights above 452 were thought to be present at the highest concentrations and triphenyl phosphate was thought to be present at the lowest concentrations in these samples.

Table 3.15 Summary of levels of tricresyl phosphate in sediment

Location	Comment	Measured level	Reference
Near to aryl phosphate production site, United States	Samples collected in late 1970s. Results given as total triaryl phosphate.	Up to 6,320 mg/kg as total triaryl phosphate.	Boethling and Cooper 1985
Industrial areas, United States	Samples collected in early 1980s. Not detected in 4 samples from Saginaw River, detected in 2 out of 3 samples from Baltimore Harbour, detected in 2 out of 2 samples from Detroit River, not detected in 2 samples from Delaware River and not detected in 6 samples from Kanawha River. Detection limit 0.2 mg/kg.	Detected in 4 out of 17 samples at 0.23-1.3 mg/kg.	Boethling and Cooper 1985
Baltimore harbour, United States	Samples collected in 1983.	Detected in 3 out of 4 samples at 0.4-0.6 mg/kg.	Boethling and Cooper 1985
Mouth of Detroit River, United States	Samples collected in 1983.	Detected in 2 out of 2 samples at 0.23-1.3 mg/kg.	Boethling and Cooper 1985
Grand Calumet River, United States	Industrial area. Samples collected in 1988-1990.	Detected in 10 out of 10 samples at 0.05-3.4 mg/kg dry wt. Mean level 1.1 mg/kg dry wt.	Hoke *et al.* 1993
Freshwater sediment, Aarhus, Denmark	Collected in 1997-1998. Detection limit 0.010 mg/kg dry weight.	Detected in 1 out of 5 lake sediments at 12 μg/kg dry wt. Not detected in five river sediments.	Boutrup *et al.* 1998
River samples from Tokyo, Japan		Detected in 9 out of 10 samples at 0.007-0.37 mg/kg.	Wakabayashi 1980, cited WHO 1990
Japan	Samples from all over Japan collected in 1975 or 1978. Detection limit 0.25-300 μg/kg dry weight.	Detected in 1 out of 100 samples in 1975 at 0.15 mg/kg dry wt. Detected in 3 out of 114 samples at 1.06-2.16 mg/kg dry wt.	Environment Agency Japan 1996
Eastern Lake Superior, United States	Remote area. Samples collected in early 1980s. Detection limit 0.2 mg/kg.	Not detected in 2 samples.	Boethling and Cooper 1985
Besos river estuary and 4 km offshore	Samples collected in 1987.	Not detected.	Valls *et al.* 1990

Table 3.15 continued.

Location	Comment	Measured level	Reference
Marine sediment, Aarhus, Denmark	Collected in 1997-1998. Detection limit 0.010 mg/kg dry weight.	Not detected in 6 samples.	Boutrup *et al.* 1988
Marine sediment, Jutland, Denmark	Detection limit 0.010 mg/kg dry weight.	Not detected in 15 samples.	Glob 1998
Marine sediment, Vejle, Denmark	Detection limit 0.010 mg/kg dry weight.	Detected in 1 out of 15 samples at 59 μg/kg dry wt.	Glob 1998
Marine sediment, Fyn, Denmark	Detection limit 0.010 mg/kg dry weight.	Detected in 2 out of 38 samples at 0.033-0.14 mg/kg dry wt.	Glob 1998
Marine sediment, Denmark	Samples were taken in harbours and more open marine areas in 1999 or 2000. Detection limit 0.035 mg/kg dry weight.	Detected at 0.37 mg/kg dry wt in 1 out of 12 harbour samples. Not detected in open marine areas.	Miljøstyrelsen 2002b
Marine sediment, Tokyo, Japan		Detected in 1 out of 3 samples at 0.004 mg/kg.	Wakabayashi 1980, cited WHO 1990
Marine sediment, Kitakyushu City, Japan	Detection limit 0.010 mg/kg.	Not detected in 9 samples.	Ishikawa *et al.* 1985b

Boethling and Cooper (1985) reported the results of a later (early 1980s) survey of the levels of tricresyl phosphate in sediments from the United States. Tricresyl phosphate was not found (detection limit 0.2 mg/kg) in four samples from Saginaw River (industrialised area), but was present at 0.4-0.6 mg/kg in two out of three samples from Baltimore Harbour (industrialised area), at 0.23-1.3 mg/kg in two out of two samples from Detroit River (industrialised area) and was not present in two samples from Delaware River (industrialised area near to aryl phosphate manufacturer), six samples from Kanawha River (industrialised area near to aryl phosphate manufacturer) or two samples from Eastern Lake Superior (remote area).

Boutrup *et al.* (1998) determined the levels of tricresyl phosphate in freshwater and marine water sediments collected from the County of Aarhus, Denmark in 1997-1998. The detection limit of the method used was around 10 μg/kg dry weight and tricresyl phosphate was found in one out of five freshwater lake sediments at 12 μg/kg dry weight, but was not detected in five river sediments nor in six marine sediments.

A further study of the levels of tricresyl phosphate in marine sediments from around Denmark was carried out by Glob (1998). The detection limit of the method used was 10 μg/kg dry weight and tricresyl phosphate was not detected in 15 samples from the County of Southern Jutland, was detected in one out of 15 samples from the County of Vejle at 59 μg/kg dry weight and was detected in two out of 38 samples from the County of Fyn at 33-140 μg/kg dry weight.

Miljøstyrelsen (2002b) reported the results of further surveys for the levels of tricresyl phosphate in marine sediments from around Denmark. These surveys found that

tricresyl phosphate was not detected (detection limit 35 μg/kg dry weight) in twelve harbour sediments collected in 1999, was present at a concentration of 370 μg/kg dry weight in one of five harbour sediments collected in 2000 but was not detected in more open marine areas (Nibe Bredning, Kattegat, Øresund, Smålandsfarvandet and Mecklenburg Bugt). In addition, another survey found no tricresyl phosphate in harbour sediments (detection limit was again 35 μg/kg dry weight).

Hoke *et al.* (1993) determined the levels of tricresyl phosphate in sediment and sediment pore water from the Grand Calumet River, Indiana (industrialised area). In all, ten composite sediment samples were collected during 1988-1990 and tricresyl phosphate was found in all ten sediment samples, and also the pore water extracted from the sediment. The concentration of tricresyl phosphate found in the sediment samples was 0.05-3.4 mg/kg dry weight (mean level was 1.1 mg/kg dry weight) and the concentration found in the pore water was 0.3-22.6 μg/l (mean 7.7 μg/l).

Tricresyl phosphate was found not to be present in sediment samples collected from the Besos river estuary or 4 km offshore the river mouth, in 1987 (Valls *et al.* 1990).

Boethling and Cooper (1985) reported that tricresyl phosphate was present at a concentration of 400-600 μg/kg in three out of four sediment samples collected from Baltimore Harbour and at 230 to 1,300 μg/kg in two out of two sediment samples from the mouth of the Detroit River. The samples were collected in 1983.

Two surveys of the levels of tricresyl phosphate in sediments from all over Japan were carried out by Environment Agency Japan (1996). The substance was detected in one out of 100 samples analysed in 1975 at a concentration of 150 μg/kg dry weight (the detection limit was in the range two to 50 µg/kg dry weight). In the second survey carried out in 1978, tricresyl phosphate was detected in three out of 114 samples at a concentration of 1.06-2.16 mg/kg dry weight (the detection limit was in the range 0.25-300 μg/kg dry weight).

Wakabayashi (1980, cited in WHO 1990) found tricresyl phosphate in nine out of ten river sediment samples from Tokyo, Japan, at a concentration of 7 to 370 μg/kg, and in one out of three marine sediments from the area at a concentration of 4 μg/kg.

Ishikawa *et al.* (1985b) found that tricresyl phosphate was not present in nine samples of marine sediment collected near to Kitakyushu City, Japan. The detection limit of the method used was 10 μg/kg.

Comparison of measured levels with predicted levels

The available data show elevated levels of tricresyl phosphate in surface water and sediments near to sources of release, with levels in more remote regions generally much lower (often below the limit of detection of the method used). The higher levels measured are of the same order of magnitude as those calculated for some uses. However, many of the more elevated levels were determined in the late 1970s or the early 1980s and it is not known if these levels would be typical of the current situation. A general survey performed by the Environment Agency in 2008 failed to detect the substance in any sample of WWTP effluent or river water at a detection limit of 0.05 µg/l, although the scope of the study was limited. The predicted concentrations will be used in the risk characterisation.

3.3.2 Terrestrial compartment

Calculation of PECs

PECs for the soil compartment were estimated using EUSES 2.0.3 and are summarised in Table 3.16.

The estimated regional concentrations for the soil compartment are summarised below.

$PEC_{regional}$ = 2.36×10^{-5} mg/kg wet weight for agricultural soil
= 2.83×10^{-4} μg/l for pore water of agricultural soil
= 9.14×10^{-5} mg/kg wet weight for natural soil
= 3.8×10^{-4} mg/kg wet weight for industrial soil

Table 3.16 Summary of predicted local concentrations for the air and terrestrial compartments

Scenario		PEC_{local}			
		Annual average conc. in air (mg/m^3)	**Agricultural soil – 30 day average (mg/kg wet wt.)**	**Agricultural soil – 180 day average (mg/kg wet wt.)**	**Ground-water under agricultural soil (μg/l)**
Production of tricresyl phosphate		5.17×10^{-7} and 4.34×10^{-7}	9.15×10^{-5a}	9.15×10^{-5a}	1.1×10^{-3a}
Adhesives		negligible	negligible	negligible	negligible
Lubricant additive	Lubricant blending	4.34×10^{-7}	2.14×10^{-4}	1.32×10^{-4}	1.58×10^{-3}
PVC – 1	Compounding	2.33×10^{-6}	0.03	0.01	0.13
	Conversion	9.57×10^{-6}	0.01	4.96×10^{-3}	0.06
	Combined compounding and conversion	1.19×10^{-5}	0.05	0.02	0.19
PVC – 2	Compounding	4.35×10^{-7}	4.15×10^{-3}	1.42×10^{-3}	0.02
	Conversion	7.12×10^{-7}	4.61×10^{-4}	2.13×10^{-4}	2.56×10^{-3}
	Combined compounding and conversion	8.91×10^{-7}	4.52×10^{-3}	1.55×10^{-3}	0.02
Photo-graphic film	Compounding	1.58×10^{-6}	0.02	6.75×10^{-3}	0.08
	Conversion	1.58×10^{-6}	1.94×10^{-3}	7.0×10^{-4}	8.39×10^{-3}
	Combined compounding and conversion	2.72×10^{-6}	0.02	7.36×10^{-3}	0.09
Poly-urethane	Compounding	4.91×10^{-7}	0.02	6.75×10^{-3}	0.08
	Conversion	4.91×10^{-7}	1.94×10^{-3}	6.97×10^{-4}	8.36×10^{-3}
	Combined compounding and conversion	5.48×10^{-7}	0.02	7.36×10^{-3}	0.09
Pigment dispersions	Production of dispersions	6.15×10^{-6}	0.03	9.19×10^{-3}	0.11

Notes: a) Sludge from the production sites is not applied to agricultural land.

Measured levels

Boethling and Cooper (1985) reported that tricresyl phosphate was present at a concentration of 1,000-4,000 μg/kg in all four soil samples collected near to a production plant in the United States in 1979. The area sampled was reported to be subject to spills. Tricresyl phosphate was not found in soil at another production plant or in soil from an aryl phosphate formulations site or three aryl phosphate user sites (two steel works and a PVC processor).

Boethling and Cooper (1985) reported that tricresyl phosphate was not detected (detection limit 0.1 mg/kg) in soil samples collected near to an aryl phosphate production site and a large user of hydraulic fluids in the United States.

Boethling and Cooper (1985) report the results of monitoring studies carried out in the late 1970s near to an aryl phosphate production site in the United States. The substances included in the studies were triphenyl phosphate, tricresyl phosphate, isopropylphenyl diphenyl phosphate and aryl phosphates with molecular weights above 410 (which included trixylenyl phosphate and di-(isopropylphenyl) phenyl phosphate). The concentration of total aryl phosphates found in a soil sample collected from the plant yard was 26,550 mg/kg. This sample was collected in an area subject to frequent spills. The total aryl phosphate concentration found in river bank soil (collected from an area known to have received discarded soil from the plant yard) was 37 mg/kg.

David and Seiber (1996) found tricresyl phosphate at a total concentration of around 53-59 mg/kg in soil from a US air force base contaminated with hydraulic fluids.

Naturvårdsverket (2006) reported the analysis of snow samples taken from an airport in Sweden. In a sample from the aircraft parking area, the concentration found was 10,000 ng/kg, while in two samples from a runway the average concentration was 850 ng/kg. The substance was found in aircraft oils at the airport, as expected from the use pattern.

Comparison of measured levels with predicted levels

Available monitoring data for soil concern mainly spills of the substance onto soil at sites of use. PECs are calculated based on aerial deposition and application of sewage sludge and so are not directly comparable with these measured data. The predicted levels are used in the risk characterisation.

3.3.3 Air compartment

Calculation of PECs

Concentrations of tricresyl phosphate in air were estimated using EUSES. The PECs calculated are summarised in Table 3.16.

The predicted regional concentration in air is 4.34×10^{-7} mg/m^3.

Measured levels

Boethling and Cooper (1985) reported that tricresyl phosphate was not detected (detection limit 2 μg/m^3) in air samples collected near to an aryl phosphate production site and a large user of hydraulic fluids in the United States.

Boethling and Cooper also report the results of a more extensive investigation of the levels of tricresyl phosphate in air close to two aryl phosphate producer sites, an aryl phosphate formulation site, and three user sites (two steel works and a PVC processor). Tricresyl phosphate was found in air from the production sites at a concentration of 0.01-2 ng/m^3 but was not detected in air from formulation or user sites.

Hansen *et al.* (2000) carried out a study to determine the concentration of *para*-tricresyl phosphate in air and dust in six schools and two kindergartens where building materials containing organophosphate chemicals (in particular tris(2-chloroethyl) phosphate) were thought to be used. The sampling was carried out in accordance with VDI 4300 B1.8 (dust) and VDI 4300 B1.1 (indoor air). The level of *para*-tricresyl phosphate in dust was below 0.5 mg/kg. The concentrations in indoor air were below 0.01 μg/m^3. The concentration of *para*-tricresyl phosphate in outdoor and indoor air from other buildings where contamination was not suspected was found to be below 0.01 μg/m^3.

Yashuda (1980, cited in WHO 1990) determined the concentrations of tricresyl phosphate in air over the eastern Seto Inland Sea, the Dogo Plain and the Ozu Basin in Japan. The levels found were in the range 11.5 to 21.4 ng/m^3 in samples from heavily industrialised cities (Fukuyama, Akashi and Osaka), 26.7 to 70.3 ng/m^3 in urban air from Matsuyama but were below the detection limit in agricultural areas.

Comparison of measured levels with predicted levels

The available measured data indicate that tricresyl phosphate is present in air only at very low concentrations. The level in air at production sites has been reported up to 2 ng/m^3 (2×10^{-6} mg/m^3) in the United States and up to 11-70 ng/m^3 ($1\text{-}7\times10^{-5}$ mg/m^3) in industrial and urban air from Japan. These measured levels are of a comparable order of magnitude to the predicted levels near sources. The predicted levels are considered in the risk assessment.

3.3.4 Non-compartment specific exposure relevant for the food chain

Predicted concentrations in biota and food

Predicted concentrations of tricresyl phosphate in fish and earthworms are shown in Table 3.17 and predicted concentrations in prey species for marine food chains are also included. The predicted concentrations in food for human consumption are shown in Table 3.18. The concentrations were calculated using EUSES 2.0.3.

Measured levels in biota and food

Two surveys of the levels of tricresyl phosphate in fish from all over Japan were carried out by Environment Agency Japan (1996). The substance was not detected in any of the 96 samples analysed in 1975 (detection limit was in the range 20 to 250 μg/kg wet weight) and was not detected in any of the 93 samples analysed in 1978 (detection limit was in the range 0.25-150 μg/kg).

Kenmotsu *et al.* (1981, cited in WHO 1990) found tricresyl phosphate to be present in four out of 41 fish and shell fish samples from Seto Inland Sea, Japan. The concentrations found ranged between one and 19 μg/kg.

Muir (1984) found tricresyl phosphate in fish near a triaryl phosphate manufacturing plant in the United States at a concentration of 2-5 μg/kg. Lombardo and Egry (1979) found tricresyl phosphate at a concentration of 40 μg/kg in sturgeon from the Columbia River, USA, from an area downstream of several metal processing plants.

Boethling and Cooper (1985) reported that tricresyl phosphate was present at a concentration of 1,000-20,000 μg/kg in all four vegetation samples collected near a production plant in the United States in 1979. The levels in air and soil in the area were 0.01-0.05 ng/m^3 and 1,000-4,000 μg/kg respectively.

Gilbert *et al.* (1986) carried out a survey of the levels of total trialkyl and triaryl phosphates, including triphenyl phosphate, in composite total diet samples (representing 15 commodity food types) representing an average adult diet for eight regions of the United Kingdom. The mean total dietary intake of total organic phosphates was estimated to be 0.072-0.105 mg/day. In general, the highest concentrations of total phosphate esters (total triaryl and trialkyl) were in offal and nuts (these food groups have only a low relative importance in diet). Tricresyl phosphate was found to occur only in minor amounts in isolated samples.

Table 3.17 Summary of predicted local concentrations for secondary poisoning

Scenario		Predicted concentration			
		Fish (mg/kg)	**Earthworms (mg/kg)**	**Marine fish (mg/kg)**	**Marine top predators (mg/kg)**
Production of tricresyl phosphate		0.04 and 0.01	9.65×10^{-4}[a]	not applicable	not applicable
Adhesives		negligible	negligible	negligible	negligible
Lubricant additive	Lubricant blending	4.93×10^{-3}	1.3×10^{-3}	7.85×10^{-4}	5.06×10^{-4}
PVC – 1	Compounding	0.15	0.09	0.15	0.03
	Conversion	0.07	0.04	0.07	0.01
	Combined compounding and conversion	0.21	0.13	0.21	0.04
PVC – 2	Compounding	4.65×10^{-3}	0.01	4.96×10^{-4}	4.49×10^{-4}
	Conversion	6.51×10^{-3}	1.99×10^{-3}	2.42×10^{-3}	8.34×10^{-4}
	Combined compounding and conversion	0.02	0.01	0.02	4.35×10^{-3}
Photographic film	Compounding	0.09	0.06	0.09	0.02
	Conversion	0.01	6.06×10^{-3}	8.6×10^{-3}	2.07×10^{-3}
	Combined compounding and conversion	0.10	0.06	0.10	0.02
Polyurethane	Compounding	8.92×10^{-3}	0.06	4.93×10^{-3}	1.33×10^{-3}
	Conversion	4.99×10^{-3}	6.04×10^{-3}	8.45×10^{-4}	5.18×10^{-4}
	Combined compounding and conversion	9.32×10^{-3}	0.06	5.33×10^{-3}	1.42×10^{-3}
Pigment disp.	Production of disp.	0.12	0.08	0.12	0.02

Notes: a) Sludge from the production sites is not applied to agricultural land.

Comparison of measured levels with predicted levels

Available measured data show that tricresyl phosphate has been found in fish and shell fish, plants near to sources of release and also human diet. There are insufficient measured data to make a comparison with the predicted scenarios considered in this risk assessment. The predicted levels are used in the risk characterisation.

Table 3.18 Summary of predicted local concentrations in food for human consumption

Scenario		Concentration							
		Fish (mg/kg)	**Root crops (mg/kg)**	**Leaf crops (mg/kg)**	**Drinking water (mg/l)**	**Meat (mg/kg)**	**Milk (mg/kg)**	**Air (mg/m^3)**	**Total daily human intake (mg/kg bw/day)**
Production of tricresyl phosphate		0.07 and 0.02	1.12×10^{-3}	1.46×10^{-3} and 1.22×10^{-3}	2.33×10^{-5} and 5.18×10^{-6}	3.23×10^{-4} and 2.68×10^{-4}	1.02×10^{-4} and 8.49×10^{-5}	8.31×10^{-8}	1.57×10^{-4} and 5.64×10^{-5}
Adhesives		negligible	negligible	negligible	negligible	negligible	negligible	negligible	negligible
Lubricant additive	Lubricant blending	5.27×10^{-3}	1.62×10^{-3}	1.22×10^{-3}	1.65×10^{-6}	2.68×10^{-4}	8.47×10^{-5}	9.55×10^{-12}	4.05×10^{-5}
PVC – 1	Compounding	0.29	0.14	6.64×10^{-3}	1.33×10^{-4}	1.47×10^{-3}	4.66×10^{-4}	1.9×10^{-6}	1.35×10^{-3}
	Conversion	0.13	0.06	0.03	5.95×10^{-5}	5.91×10^{-3}	1.87×10^{-3}	9.14×10^{-6}	1.06×10^{-3}
	Combined compounding and conversion	0.41	0.20	0.03	1.9×10^{-4}	7.36×10^{-3}	2.33×10^{-3}	1.14×10^{-5}	2.38×10^{-3}
PVC – 2	Compounding	4.71×10^{-3}	0.02	1.23×10^{-3}	1.71×10^{-5}	2.73×10^{-4}	8.62×10^{-5}	7.62×10^{-10}	1.27×10^{-4}
	Conversion	8.42×10^{-3}	2.62×10^{-3}	2.0×10^{-3}	2.63×10^{-6}	4.39×10^{-4}	1.39×10^{-4}	2.78×10^{-7}	6.58×10^{-5}
	Combined compounding and conversion	0.04	0.02	2.52×10^{-3}	1.85×10^{-5}	5.54×10^{-4}	1.75×10^{-4}	4.57×10^{-7}	2.21×10^{-4}
Photo-graphic film	Compounding	0.18	0.08	4.49×10^{-3}	8.1×10^{-5}	9.94×10^{-4}	3.14×10^{-4}	1.14×10^{-6}	8.33×10^{-4}
	Conversion	0.02	8.59×10^{-3}	4.44×10^{-3}	8.39×10^{-6}	9.74×10^{-4}	3.08×10^{-4}	1.14×10^{-6}	
	Combined compounding and conversion	0.19	0.09	7.71×10^{-3}	8.83×10^{-5}	1.7×10^{-3}	5.38×10^{-4}	2.28×10^{-6}	9.6×10^{-4}

Table 3.18 continued.

Scenario		Concentration							
		Fish (mg/kg)	**Root crops (mg/kg)**	**Leaf crops (mg/kg)**	**Drinking water (mg/l)**	**Meat (mg/kg)**	**Milk (mg/kg)**	**Air (mg/m^3)**	**Total daily human intake (mg/kg bw/day)**
Poly-urethane	Compounding	0.01	0.08	1.43×10^{-3}	8.09×10^{-5}	3.25×10^{-4}	1.03×10^{-4}	5.71×10^{-8}	5.05×10^{-4}
	Conversion	5.38×10^{-3}	8.55×10^{-3}	1.39×10^{-3}	8.36×10^{-6}	3.05×10^{-4}	9.64×10^{-5}	5.71×10^{-8}	8.2×10^{-5}
	Combined compounding and conversion	0.01	0.09	1.6×10^{-3}	8.82×10^{-5}	3.63×10^{-4}	1.15×10^{-4}	1.14×10^{-7}	5.51×10^{-4}
Pigment dispersions	Production of dispersions	0.24	0.11	0.02	1.1×10^{-4}	3.82×10^{-3}	1.21×10^{-3}	5.71×10^{-6}	1.34×10^{-3}
Regional sources		4.6×10^{-3}	2.9×10^{-4}	1.22×10^{-3}	1.44×10^{-6}	2.68×10^{-4}	8.46×10^{-5}	4.34×10^{-7}	3.21×10^{-5}

4 Effects assessment: Hazard identification and dose (concentration) – response (effect) assessment

4.1 Aquatic compartment

The following sections review the available toxicity data for tricresyl phosphate with aquatic organisms. Where possible, a validity marking is given for each study (this appears in the summary tables within each section). The following validity markings have been used:

1. **Valid without restriction.** The test is carried out to internationally recognised protocols (or equivalent protocols) and all or most of the important experimental details are available.
2. **Use with care.** The test is carried out to internationally recognised protocols (or equivalent protocols) but some important experimental details are missing, or the method used, or endpoint studied, in the test means that interpretation of the results is not straightforward.
3. **Not valid.** There is a clear deficiency in the test that means the results cannot be considered valid.
4. **Not assignable.** Insufficient detail is available on the method used to allow a decision to be made on the validity of the study.

In terms of the risk assessment, toxicity data assigned a validity marking of one or two are considered to be of acceptable quality when deriving the predicted no effect concentration (PNEC).

Several of the tests are unpublished studies carried out by industry. It has not been possible to validate all of these tests within the scope of this report and these are assigned a validity marking of four unless it is clear that some aspects of the test invalidate the results (for these a validity marking of three is given). Studies given a validity marking of four have also been considered along with the studies assigned a validity marking of one and two when deriving the PNEC.

One important property when considering the aquatic toxicity data is water solubility. The water solubility of tricresyl phosphate is 0.36 mg/l. Several studies have been carried out at concentrations greater than this water solubility and, although this in itself does not necessarily invalidate the test (for example, cosolvents or solubility aids could have been used in the test to aid dispersion of the substance in the test media), this does introduce some uncertainty over the concentration to which the organisms were actually exposed in the test. In cases where it is clear that undissolved test substance was present in the test media, the tests have been marked as not valid.

4.1.1 Toxicity to fish

Short-term studies

Freshwater fish

The short-term toxicity of tricresyl phosphate to freshwater fish is summarised in Table 4.1.

The acute toxicity of tricresyl phosphate (no information on purity) to bluegill sunfish (*Lepomis macrochirus*) was determined by Dawson *et al.* (1977). The test system used was a static system and the report indicates that gentle aeration was applied when dissolved oxygen was depleted during the test (no information is given as to whether or not this occurred with the test with tricresyl phosphate). The 96-hour LC_{50} determined was 7,000 mg/l. Concentrations tested in this study are much greater than the water solubility of the substance, and the substance appears to have been added directly to the test vessel. It is therefore possible that the effects seen in this test were indirect effects caused by undissolved test substance rather than a direct toxic effect of the substance itself and so the test is considered invalid.

Yoshioka and Ose (1993) reported a 96-hour LC_{50} for red killifish (*Oryzias latipes*) of 6.7 mg/l for tricresyl phosphate. The test appears to have been carried out according to the OECD 203 test guideline (although this is not certain as the paper combined data from tests carried out by the authors with other literature data). This value is above the water solubility of the substance.

Lockhart *et al.* (1975), Wagemann *et al.* (1974) and Wagemann (1975) reported that a commercial product that contained a significant proportion of tricresyl phosphate was not acutely toxic to guppies (*Poecilia reticulata*) when exposed for 24 hours in water saturated with the test substance. The substance tested consisted of two per cent tri-*o*-cresyl phosphate, 42 per cent tri-*m*-cresyl phosphate, 31 per cent tri-*p*-cresyl phosphate, 18 per cent tris-(dimethylphenyl) phosphates, six per cent tris-(ethylphenyl) phosphates and one per cent other phosphates (including triphenyl phosphate and tris-(trimethylphenyl) phosphates). As the exposure concentration used in this test is not well defined, and the test was carried out over 24 hours only, the results cannot be considered fully valid.

Adema *et al.* (1983) reported the results of a OECD 203 acute toxicity test for tricresyl phosphate (no information on purity) with the guppy (*Poecilia reticulata*). Only a summary of the results is available and the 96-hour LC_{50} was reported to be 4 mg/l. This value is again above the water solubility of the substance.

Sitthichaikasem (1978) carried out an acute toxicity test using tri-*p*-cresyl phosphate with bluegill (*Lepomis macrochirus*). The test was carried out using a static system and the 96-hour LC_{50} was reported to be above100 mg/l. The study also determined an EC_{50} value based on the appearance of hemorrhagic areas around the gills and behavioural effects. The 96-hour EC_{50} was again above 100 mg/l. Therefore, based on this study, tri-*p*-cresyl phosphate showed little or no effects on bluegills over short-term exposure. The concentrations used in this test are well above the water solubility of tricresyl phosphate and so the results of this test are best interpreted in terms of the substance showing no effects at water solubility.

Table 4.1 Short-term toxicity of tricresyl phosphate to freshwater fish

Species	Test guide-line	Number of animals/ treatment	Age/ size	Co-solvent	Concs. tested	N or M	Test conditions						Endpoint	Control resp.	Effect conc.	Reference	Val.
							Media	Temp.	Hard.	pH	Static/ flow	D.O.					
Brachydanio rerio						N							Mortality Mortality, behave. & appear.		96h-LC_{50} = >1.0 mg/l 96h-NOEC = 0.18 mg/l	van den Dikken-berg *et al*. 1989	4
Ictalurus punctatus	USEPA 1975		1.3 g					12°C	44	7.4	Flow		Mortality		96h-LC_{50} = 0.80 mg/l	Mayer and Ellersieck 1986	3
Jordanella floridae						N							Mortality Mortality, behave. & appear.		96h-LC_{50} = 5.0 mg/l 96h-NOEC = 1.0 mg/l	van den Dikken-berg *et al.* 1989	2
Gasterosteus aculeatus		10, each in duplicate, in one litre water	4-5 week		0.1-1 mg/l. The highest and lowest concs. were at the start of the test. These were 87% of nominal.	M		19°C	11.7	8.2	Semi-static		Mortality Mortality, behave. & appear.		96h-LC_{50} = 0.44 mg/l 96h-EC_{50} = 0.17 mg/l 96h-NOEC = 0.16 mg/l	van den Dikken-berg *et al.* 1989	2

Table 4.1 continued.

Species	Test guide-line	Number of animals/ treatment	Age/ size	Co-solvent	Concs. tested	N or M	Test conditions						Endpoint	Control resp.	Effect conc.	Reference	Val.
							Media	Temp.	Hard.	pH	Static/ flow	D.O.					
Lepomis macrochirus		Loading was <1 g/l.	33-75 mm	Direct addition of the test substance.	3,200, 5,000, 7,900 and 10,000 mg/l plus control.	N	Well water	23°C	55	7.6-7.9	Static		Mortality	1.3% Mortality overall.	96h-LC_{50} = 7,000 mg/l	Dawson *et al.* 1977	3
	USEPA 1975		0.6 g					12°C	44	7.4	Flow		Mortality		96h-LC_{50} = 0.15 mg/l	Mayer and Ellersieck 1986	3
	USEPA 1975		0.6 g					12°C	314	7.6	Flow		Mortality		96h-LC_{50} = 0.082 mg/l	Mayer and Ellersieck 1986	3
	USEPA 1975	10 per treatment	0.02 g	Acetone	Log series of concs. plus control and solvent control	N	Recon water	22°C	40-48	7.0-7.2	Static		Mortality Hemorrh-agic areas		96h-LC_{50} >100 mg/l 96h-LC_{50} >100 mg/l	Sitthich-aikasem 1978	2
Oncorhyn-chus mykiss	USEPA 1975		0.23 g					12°C	44	7.4	Flow		Mortality		96h-LC_{50} = 0.26 mg/l	Mayer and Ellersieck 1986	2
	USEPA 1975		0.50 g					12°C	44	7.4	Flow		Mortality		96h-LC_{50} = 0.40 mg/l	Mayer and Ellersieck 1986	2
	USEPA 1975	10		Yes	0.56, 1.0, 1.8, 3.2 and 5.6 mg/l plus control plus solvent control	N			42	7.4			Mortality	100% survival	96h-LC_{50} = 0.75 mg/l	IUCLID 2001	4

Table 4.1 continued.

Species	Test guide-line	Number of animals/ treatment	Age/ size	Co-solvent	Concs. tested	N or M	Test conditions						Endpoint	Control resp.	Effect conc.	Reference	Val.
							Media	Temp.	Hard.	pH	Static/ flow	D.O.					
Oryzias latipes	OECD 203	10 per treatment in 2 litres		DMSO or a dispers. HCO-40) may have been used.	5 concs. spaced by a factor of 1.8 plus control and/or solvent control		Tap water (dech-lorin-ated)	20°C	40	7.2		>60 %	Mortality		96h-LC_{50} = 6.7 mg/l	Yoshioka and Ose 1993	2
						N							Mortality		96h-LC_{50} = 4.9 mg/l	van den Dikken-berg *et al.* 1989	2
													Mortality, behave. & appear.		96h-NOEC = 1.8 mg/l		
Perca flavescens	USEPA 1975							12	242	7.4	Flow		Mortality		96h-LC_{50} = 0.50 mg/l	Mayer and Ellersieck 1986	2/3
Pimephales promelas		10			10, 18, 32, 56 and 100 mg/l	N			44	7.23	Static		Mortality		96h-LC_{50} >100 mg/l	IUCLID 2001	4
Poecilia retuculata			7-9 day old	No	Saturated solution used.	N					Static		Mortality		No mort. over 24 hours in saturated solution	Lockhart *et al.* 1975	3
	OECD 203, The Nether-lands 1980		4 week old			N							Mortality		96h-LC_{50} = 4.0 mg/l	Adema *et al.* 1983	2
															96h-NOEC = 1.0 mg/l		
						N							Mortality		96h-LC_{50} = 5.5 mg/l	van den Dikken-berg *et al*. 1989	2
													Mortality, behav. & appear.		96h-NOEC = 1.0 mg/l		

Notes: N = Nominal concentration. M = Measured concentration. Temp. = Temperature. Hard. = Water hardness as mg $CaCO_3$/l. D.O. = Dissolved oxygen (mg O_2/l or per cent saturation). Val. = Validity rating (see Section 4.1): 1) Valid without restriction; 2) Use with care; 3) Not valid; 4) Not assignable.

Mayer and Ellersieck (1986) report 96-hour LC_{50} values for tricresyl phosphate of 0.26 and 0.40 mg/l with rainbow trout (*Oncorhynchus mykiss*), 0.80 mg/l with channel catfish (*Ictalurus punctatus*), 0.082 and 0.15 mg/l with bluegill (*Lepomis macrochirus*) and 0.70 mg/l with yellow perch (*Perca flavescens*). These data are from unpublished studies in the United States and the authors of the report consider the data to be valid. However, all these tests were reportedly carried out at 12°C. According to the current OECD 203 test guidelines, this temperature is only appropriate for rainbow trout and so the data for the other species should be treated with caution (the recommended temperature for bluegill is 21-25°C; yellow perch and channel catfish are not included in the OECD 203 guideline but the recommended temperature for channel catfish in the OECD 210 guideline is 26°C; the appropriate temperature for testing yellow perch is unclear). The results obtained in this test are below or close to the solubility limit of the substance.

Van den Dikkenberg *et al.* (1989) investigated the toxicity of tricresyl phosphate to the three spined stickleback (*Gasterosteus aculeatus*). The 96-hour LC_{50} value obtained was 0.44 mg/l based on measured concentrations. This is close to the solubility limit of the substance. The study also determined a 96-hour no observed effect concentration (NOEC) of 0.17 mg/l based on mortality, behaviour and appearance.

The study by van den Dikkenberg *et al.* (1989) also reports the results of other toxicity studies carried out by Adema *et al.* (1981) with guppy (*Poecilia reticulata*), zebrafish (*Brachydanio rerio*), flagfish (*Jordanella floridae*) and red killifish (*Oryzias latipes*). The 96-hour LC_{50} values determined were 5.5 mg/l for *P. reticulata* (based on nominal concentrations), above 1.0 mg/l for *B. rerio* (based on nominal concentrations), 5.0 mg/l for *J. floridae* (based on nominal concentrations) and 4.9 mg/l for *O. latipes* (based on nominal concentrations). As well as mortality, the studies also determined NOECs taking into account mortality, behaviour and appearance. The NOECs for these endpoints were 1.0 mg/l for *P. reticulata*, 0.18 mg/l for *B. rerio*, 1.0 mg/l for *J. floridae* and 1.8 mg/l for *O. latipes.* LC_{50}s for *P. reticulata*, *B. rerio, J. floridae* and *O. latipes* were all above the water solubility of the test substance.

IUCLID (2001) gives the results of further unpublished acute toxicity studies with tricresyl phosphate. The 96-hour LC_{50} values determined were above100 mg/l (two out of ten fish died at 100 mg/l) with fathead minnows (*Pimephales promelas*) and 0.75 mg/l for rainbow trout (*Oncorhynchus mykiss*). Again the results of these tests, particularly with *P. promelas*, are above the water solubility of the test substance.

A fish 96-hour LC_{50} and a 14-day LC_{50} of 1.21 and 0.97 mg/l respectively were estimated for tricresyl phosphate from the log K_{ow} value of 5.11 using the USEPA ECOSAR (version 0.99h) software.

Using the methods given in the TGD, a 96-hour LC_{50} of 0.47 mg/l can be estimated using the equation for polar narcosis (recommended for esters) and a log K_{ow} of 5.11. This is in good agreement with data in the studies carried out by Mayer and Ellersieck.

Marine fish

The short-term toxicity of tricresyl phosphate to marine fish is summarised in Table 4.2.

Table 4.2 Short-term toxicity of tricresyl phosphate to marine fish

Species	Test guide-line	Number of animals/ treatment	Age/ size	Cosolvent	Concs. tested	N or M	Test conditions						Endpoint	Control resp.	Effect conc.	Ref.	Val.
							Media	Temp.	Sal.	pH	Static/ flow	D.O.					
Menidia beryllina		Loading <1 g/l.	40-100 mm	Direct addition of the test substance.	1,800, 3,200, 5,600 and 10,000 mg/l plus control.	N	Artificial seawater	20°C			Static		Mortality	3% Mortality overall.	96h-LC_{50} = 8,700 mg/l	Dawson *et al.* 1977	3

Notes:
N = Nominal concentration.
M = Measured concentration.
Temp. = Temperature.
Sal. = Water salinity (given as parts per thousand (‰)).
D.O. = Dissolved oxygen (given as mg O_2/l or per cent saturation).
Val. = Validity rating (see Section 4.1): 1) Valid without restriction; 2) Use with care; 3) Not valid; 4) Not assignable.

The acute toxicity of tricresyl phosphate (no information on purity) to tidewater silverside (*Menidia beryllina*) was determined by Dawson *et al.* (1977). The test system used was a static system and continuous aeration was applied during the test. The 96-hour LC_{50} determined was 8,700 mg/l. Concentrations tested in this study were much greater than the water solubility of the substance, and the substance appears to have been added directly to the test vessel. It is therefore possible that the effects seen in this test were indirect effects due to undissolved test substance rather than a direct toxic effect of the substance itself and so the test is considered invalid.

Long-term studies

The long-term toxicity of tricresyl phosphate to freshwater fish is summarised in Table 4.3.

Adema *et al.* (1983) reported the results of a 4-week growth and mortality test for tricresyl phosphate (no information on purity) with the guppy (*Poecilia reticulata*) and a 6-week embryo-larval study for flagfish (*Jordanella floridae*). Only a summary of the results is available and the NOECs determined were 1.0 mg/l for *P. reticulata* and 0.01 mg/l for *J. floridae*. The same results are also reported in van den Dikkenberg *et al*. (1989) and Adema *et al.* (1981). In addition, van den Dikkenberg *et al.* (1989) gives the results of further embryo-larval studies carried out by Adema *et al.* (1981) with zebrafish (*Brachydanio rerio*) and medaka (*Oryzias latipes*). The overall NOECs determined for these species were 0.0056 mg/l for *B. rerio* and 0.01 mg/l for *O. latipes.*

Van den Dikkenberg *et al.* (1989) investigated the toxicity of tricresyl phosphate to the embryo-larval stages of three spined stickleback (*Gasterosteus aculeatus*). The test was carried out using a semi-static system (renewal three times per week) with 25 organisms per treatment. The eggs used in the test were less than six hours old at the start of the test. The endpoints determined included mortality, effects on the embryonic stage, sublethal effects and growth. The 35-day NOECs reported from the study (nominal values) were 1 μg/l for mortality, 1 μg/l for mortality and sublethal effects (excluding growth), 3.2 μg/l for sublethal effects on the embryonic stage and delayed time of hatching and 0.32 μg/l for growth. The 35-day LC_{50} was 1.7 μg/l.

The long-term toxicity of a commercial product that contained a significant proportion of tricresyl phosphate to rainbow trout (*Oncorhynchus mykiss*) has been determined over a four-month period (Lockhart *et al.* 1975, Wagemann *et al.* 1974, Wagemann 1975). The substance tested consisted of two per cent tri-*o*-cresyl phosphate, 42 per cent tri-*m*-cresyl phosphate, 31 per cent tri-*p*-cresyl phosphate, 18 per cent tris-(dimethylphenyl) phosphates, six per cent tris-(ethylphenyl) phosphates and one per cent other phosphates (including triphenyl phosphate and tris-(trimethylphenyl) phosphates). The test was carried out using yearling trout in a three-metre diameter outdoor pool. Water containing the test substance was supplied at a flow-rate of 10 l/min. The average concentration of the test substance in the water inflow was 0.9 mg/l over the experimental period. Both lethal and sub-lethal effects on the fish were investigated during this study. The fish were found to feed at a reduced rate compared to that in control tanks (eleven in total) after eight days of exposure, and the exposed fish completely rejected floating pellets after 14 days of the experiment. However, the exposed fish still continued to grow during the experiment and it was thought that feeding of the exposed fish may have continued unobserved on sunken food pellets. Biochemical changes (including elevated lactate dehydrogenase (LDH) and glutamic oxalacetic transaminase (GOT)) were noted in blood serum of the exposed fish after 16 days of exposure (July) and these changes became more marked by November. After four months exposure, the exposed fish showed internal discolouring of tissues and enlarged livers compared with the control fish.

Table 4.3 Long-term toxicity of tricresyl phosphate to freshwater fish

Species	Test guide-line	Number of animals/ treatment	Age/ size	Co-solvent	Concs. tested	N or M	Test conditions						Endpoint	Control resp.	Effect conc.	Ref.	Val.
							Media	Temp.	Hard.	pH	Static/ flow	D.O.					
Brachydanio rerio			Embryo-larval			N							Mortality, growth and sublethal effects		NOEC = 0.0056 mg/l	Adema *et al.* 1981, van den Dikken-berg *et al.* 1989	2
													Embryonic development and time to hatch		NOEC = 0.32 mg/l		
Gasterosteus aculeatus	Adema *et al.* 1981	25 in 1 litre (eggs) or 2 litres (fish)	Less than six hour eggs			N		19°C	11.7	8.2	Semi-static		Mortality		35d-LC_{50} = 0.0017 mg/l 35d-NOEC = 0.0010 mg/l	van den Dikken-berg *et al*. 1989	2
													Mortality and sublethal effects (excluding growth)		35d-EC_{50} = 0.0013 mg/l 35d-NOEC = 0.0010 mg/l		
													Embryo stage		35d-NOEC = 0.0032 mg/l		
													Growth		35d-NOEC = 0.00032 mg/l		

Table 4.3 continued.

Species	Test guide-line	Number of animals/ treatment	Age/ size	Co-solvent	Concs. tested	N or M	Test conditions						Endpoint	Control resp.	Effect conc.	Ref.	Val.
							Media	Temp.	Hard.	pH	Static/ flow	D.O.					
Jordanella floridae	OECD 210, The Nether lands 1980		Embryo-larval			N							Mortality, growth, behaviour and colour Egg-larval development and time to hatch		6 week NOEC = 0.01 mg/l NOEC = 1.0 mg/l	Adema *et al.* 1983, van den Dikken-berg *et al.* 1989, Adema *et al.* 1981	2
Oncoryhn-chus mykiss			Year-ling		0.9 mg/l plus controls	M					Flow		Sublethal effects		Sublethal effects seen at 0.9 mg/l over 4 months	Lockhart *et al.* 1975	2
Oryzias latipes						N							Mortality and growth Embryonic development and time to hatch		NOEC = 0.01 mg/l NOEC = 0.032 mg/l	van den Dikken-berg *et al.* 1989, Adema *et al.* 1981	2
Poecilia reticulate	OECD 204; The Nether lands 1980												Mortality, growth, swimming behaviour, colour		4 week NOEC = 1.0 mg/l	Adema *et al.* 1983	2

Notes: N = Nominal concentration. M_f = Measured concentration in filtered (0.45 μm) solution. M_u = Measured concentration in unfiltered solution.
M = Measured concentration (not clear if solution was filtered or unfiltered). Temp. = Temperature. Hard. = Water hardness (given as mg $CaCO_3$/l). D.O. = Dissolved oxygen (given as mg O_2/l or per cent saturation). Val. = Validity rating (see Section 4.1): 1) Valid without restriction, 2) Use with care, 3) Not valid, 4) Not assignable.

The USEPA ECOSAR program (version 0.99h) predicts a long-term no effect concentration of 0.057 mg/l. This is of the same order of magnitude as a number of the measured NOEC values, but is significantly higher than the lowest values measured with *Gasterosteus aculeatus*.

No data are available on the long-term toxicity of tricresyl phosphate to marine fish.

4.1.2 Toxicity to aquatic invertebrates

Short-term studies

The short-term toxicity of tricresyl phosphate to freshwater aquatic invertebrates is summarised in Table 4.4.

Adema *et al.* (1983) reported the results of an OECD 202 acute toxicity test for tricresyl phosphate (no information on purity) with *Daphnia magna*. Only a summary of the results is available and the 48-hour EC_{50} was reported to be 5.6 mg/l. This value is above the water solubility of the substance.

IUCLID (2001) reports the results of an unpublished acute toxicity test for tricresyl phosphate with *Daphnia magna*. The 48-hour EC_{50} in this study was 0.27 mg/l.

Using the methods given in the TGD a 48-hour EC_{50} of 0.82 mg/l can be estimated for *Daphnia magna* using the equation for polar narcosis (recommended for esters) and a log K_{ow} of 5.11. This is in reasonable agreement with the data available. The USEPA ECOSAR program (version 0.99h) predicts a value of 0.43 mg/l for the same endpoint.

No data are available on the short-term toxicity of tricresyl phosphate to marine invertebrates.

Long-term studies

The long-term toxicity of tricresyl phosphate to freshwater invertebrates is summarised in Table 4.5.

Adema *et al.* (1983) reported the results of an OECD 202 reproduction test for tricresyl phosphate (no information on purity) with *Daphnia magna*. Only a summary of the results is available and the 21-day NOEC was reported to be 0.1 mg/l.

There are no data available on the long-term toxicity of tricresyl phosphate to marine invertebrates.

4.1.3 Toxicity to algae

The toxicity of tricresyl phosphate to fresh water algae is summarised in Table 4.6.

Table 4.4 Short-term toxicity of tricresyl phosphate to freshwater invertebrates

Species	Test guide-line	Number of animals/ treatment	Age/ size	Co-solvent	Concs. tested	N or M	Test conditions						End-point	Control resp.	Effect conc.	Ref.	Val.
							Media	Temp.	Hard.	pH	Static/ flow	D.O.					
Daphnia magna	OECD 202; The Nether lands 1980												Immob. mortality		48h-EC_{50} = 5.6 mg/l 48h-NOEC = 0.18 mg/l	Adema *et al.* 1983	2
		Five per replicate, three replicates per treatment (four for controls)		Acetone	0.06, 0.10, 0.18, 0.32 and 0.56 mg/l plus control and solvent control	N					Static		Immob. mortality	0% immob. mortality	48h-EC_{50} = 0.27 mg/l 48h-NOEC = 0.10 mg/l	IUCLID 2001	4

Notes:
N = Nominal concentration.
M = Measured concentration.
Hard. = Water hardness (given as mg $CaCO_3$/l).
Temp. = Temperature.
Val. = Validity rating (see Section 4.1): 1) Valid without restriction; 2) Use with care; 3) Not valid; 4) Not assignable.

Table 4.5 Long-term toxicity of tricresyl phosphate to freshwater invertebrates

Species	Test guide-line	Number of animals/ treatment	Age/ size	Co-solvent	Concs. tested	N or M	Test conditions						End-point	Control resp.	Effect conc.	Ref.	Val.
							Media	Temp.	Hard.	pH	Static/ flow	D.O.					
Daphnia magna	OECD 202; The Nether-lands 1980												Mortality and repro.		21d-NOEC = 0.1 mg/l	Adema *et al.* 1983	2

Notes:
N = Nominal concentration.
M = Measured concentration.
Temp. = Temperature.
Hard. = Water hardness (given as mg $CaCO_3$/l).
D.O. = Dissolved oxygen (given as mg O_2/l or per cent saturation).
Val. = Validity rating (see Section 4.1): 1) Valid without restriction; 2) Use with care; 3) Not valid; 4) Not assignable.

Table 4.6 Toxicity of tricresyl phosphate to freshwater algae

Species	Test guide-line	Initial inoculum conc.	Co-solvent	Concs. tested	N or M	Test conditions				Endpoint	Control resp.	Effect concentration	Ref.	Val.
						Media	Temp.	Hard.	pH					
Ankistrodesmus falcatus		4.7×10^4 cells/ml	Acetone at ≤0.05%.	Solvent control and dark control ran.	N	CHU-10 medium	20°C			Primary production (uptake of ^{14}C)	Uptake in dark control was <5% of total seen in solvent control.	4h-IC_{50} = 2.5 mg/l (*ortho*- isomer) 4h-IC_{50} >5 mg/l (*meta*- isomer) 4h-IC_{50} >5 mg/l (*para*- isomer)	Wong and Chau 1984	2
Scenedesmus pannonicus	OECD 201; The Nether-lands 1980				N					Growth		96h-EC_{50} = 1.5 mg/l 96h-NOEC = 0.32 mg/l	Adema *et al.* 1993	2
Scenedesmus quadricauda		4.7×10^4 cells/ml	Acetone at ≤0.05%.	Solvent control and dark control ran.	N	CHU-10 medium	20°C			Primary production (uptake of ^{14}C)	Uptake in dark control was <5% of total seen in solvent control.	4h-IC_{50} = 4.2 mg/l (*ortho*- isomer) 4h-IC_{50} >5 mg/l (*meta*- isomer) 4h-IC_{50} >5 mg/l (*para*- isomer)	Wong and Chau 1984	2
Natural algal community			Acetone at ≤0.05%.	Solvent control and dark control also ran.	N	CHU-10 medium	20°C			Primary production (uptake of ^{14}C)	Uptake in dark control was <5% of total seen in solvent control.	4h-IC_{50} = 1.7 mg/l (*ortho*- isomer) 4h-IC_{50} = 4.1 (*meta*- isomer) 4h-IC_{50} >5 mg/l (*para*- isomer)3	Wong and Chau 1984	2

Notes: N = Nominal concentration.
M = Measured concentration.
Temp. = Temperature.
Hard. = Water hardness (given as mg $CaCO_3$/l).
Val. = Validity rating (see Section 4.1): 1) Valid without restriction; 2) Use with care; 3) Not valid; 4) Not assignable.

Wong and Chau (1984) carried out studies to investigate the toxicity of the *ortho-*, *meta-* and *para-*tricresyl phosphate isomers (no information on purity) to algae. The experiments investigated the effects on the primary production (as measured by ^{14}C-uptake from ^{14}C-carbonate) in cultures of *Scenedesmus quadricauda* and *Ankistrodesmus falcatus* over a four-hour period. Tests were carried out by inoculating 13.9 ml of growth medium with one ml of algal cell culture (7×10^5 cells/ml giving an initial inoculum concentration of 4.7×10^4 cells/ml in the test solution; algal cells were in the logarithmic growth phase) and incubating for 24 hours with the test substance. The test substance was added as a solution in acetone (final acetone concentration in the test solution was below 0.05 per cent and an acetone control was also run at this concentration). After the initial 24-hour incubation, 0.1 ml of a sodium ^{14}C-carbonate solution was added and the solution was incubated for a further four hours. At the end of four hours, the amount of radioactivity taken up by the cells (corrected for the uptake in dark controls) was determined and the concentration causing a 50 per cent reduction in primary production (IC_{50}) was determined to be 2.5 mg/l (*ortho-)* and above 5 mg/l (*meta-* and *para-* isomers) for *A. falcatus* and 4.2 mg/l (*ortho-*) and above 5 mg/l (*meta-* and *para-* isomers) for *S. quadricauda*. A similar experiment using phytoplankton from Lake Ontaria yielded a four-hour IC_{50} of 1.70 mg/l, 4.10 mg/l and above 5.0 mg/l for the *ortho-*, *meta-* and *para-* isomers respectively. These results are all above the water solubility of tricresyl phosphate.

Adema *et al.* (1983) reported the results of an OECD 201 toxicity test for tricresyl phosphate (no information on purity) with the alga (*Scenedesmus pannonicus*). Only a summary of the results is available and the 96-hour EC_{50} and NOEC were reported to be 1.5 mg/l and 0.32 mg/l respectively. The EC_{50} from this study is above the water solubility of the test substance.

The USEPA ECOSAR program (version 0.99h) predicts a 96-hour EC_{50} of 0.108 mg/l and a long-term no effect concentration of 0.089 mg/l for green algae. These are somewhat lower values than those measured.

There are no data available on the toxicity of tricresyl phosphate to marine algae.

4.1.4 Toxicity to microorganisms

Playne and Smith (1983) investigated the toxicity of suspensions of tricresyl phosphate to anaerobic bacteria. The tests were carried out using a mixture of facultative anaerobes (30 per cent *Bacillus cereus*, seven per cent *B. coagulans*, seven per cent *B. pantothenticus*, six per cent *Pseudomonas aeroginosa*, 20 per cent *Lactobacillus plantarum* and 30 per cent *Coryne* sp.) supplied in freeze dried form. The inoculum used was prepared by adding 400 ml of water to 50 g of the bacteria and incubating at 35°C for one hour. The test was carried out by adding 10 ml of the bacterial inoculum to 30 ml of growth medium containing two grams of alfalfa as substrate and gassing the vessels with a 90 per cent N_2:10 per cent CO_2 atmosphere for ten minutes. The tricresyl phosphate was added to the test vessels by direct volume addition and the bottles were shaken and incubated at 35°C for 75 hours. The bottles were shaken twice per day and the gas production was determined at 12-hour intervals. Carbon dioxide was found to account for around 73 per cent of the total gas produced. The tricresyl phosphate was tested at concentrations of 0.25, 1.25, 2.50 and 25 µl/ml (290, 1,450, 2,900 and 29,000 mg/l). The total gas production in the alfalfa controls was around 100 ml, and the gas production in the treatments (expressed as a percentage of that in the alfalfa controls) was 86 per cent at 290 mg/l, 104 per cent at 1,450 mg/l, 94 per cent at 2,900 mg/l and 109 per cent at 29,000 mg/l). Therefore, little or no effect was seen on the anaerobic bacteria in this experiment.

Bayer (2002) and IUCLID (2000) report that an IC_{50} of above 10,000 mg/l was determined for a commercial tricresyl phosphate (Disflamoll TKP) in an unpublished activated sludge respiration inhibition test carried out in accordance with the OECD 209 method.

4.1.5 Toxicity to sediment organisms

There are no toxicity data available for tricresyl phosphate with sediment organisms.

4.1.6 Predicted no effect concentration (PNEC) for the aquatic compartment

Surface water

Acute toxicity data are available for fish, invertebrates and algae. The lowest results from the more reliable standard tests are a 96-hour LC_{50} of 0.26 mg/l for fish (*Oncorhynchus mykiss*), a 48-hour EC_{50} of 0.27 mg/l for *Daphnia magna* and a 96-hour EC_{50} of 1.5 mg/l for the alga *Scenedesmus pannonicus*. The algal result is above the water solubility of the test substance.

Long-term data are also available for fish, *Daphnia magna* and algae. The lowest NOECs obtained from the more reliable studies were a 6-week NOEC of 0.32 μg/l for embryo-larval mortality, growth and development with *Gasterosteus aculeatus*, a 21-day NOEC of 0.1 mg/l for mortality and reproduction of *Daphnia magna* and a 96-hour NOEC of 0.32 mg/l for algae (*Scenedesmus pannonicus*).

The PNEC is derived based on the available long-term data. As data are available for three different trophic levels, an assessment factor of 10 is appropriate. Thus applying this factor to the lowest NOEC of 0.32 μg/l for fish gives a $PNEC_{water}$ of 0.032 μg/l. As noted in Annex B, the lowest NOEC value for fish, as used above, is lower than the results found for other species with tricresyl phosphate. The result is considered to be valid and so is used in the derivation of the PNEC. If the results for this species were excluded, then the PNEC based on the data for other species would be around one order of magnitude higher.

There are no valid data available on marine species. A PNEC of 0.0032 μg/l can be calculated using the long-term freshwater data and an assessment factor of 100 according to the TGD.

Microorganisms

An IC_{50} of above 10,000 mg/l was determined for tricresyl phosphate in an activated sludge respiration inhibition test. According to the TGD, an assessment factor of 100 is appropriate for this type of test result, and so the $PNEC_{microorganisms}$ is estimated to be above 100 mg/l. Although the water solubility of the test substance was exceeded in this test, the actual solubility in pure water may not be relevant to the exposure of microorganisms during waste water treatment.

Sediment

No sediment toxicity data are available for tricresyl phosphate. In the absence of data, the equilibrium partitioning method can be used to estimate the PNEC.

$$PNEC_{sed} = \frac{K_{susp-water}}{RHO_{susp}} \times PNEC_{water} \times 1000$$

where $K_{susp-water}$ = suspended sediment-water partition coefficient = 119 m^3/m^3 (see Section 3.1.2).
RHO_{susp} = bulk density of suspended sediment = 1,150 kg/m^3.

Using a $PNEC_{water}$ of 0.032 μg/l, the $PNEC_{sed}$ is estimated as 0.0033 mg/kg wet weight.

As the log K_{ow} of this substance is above five, according to the TGD, the resulting PEC/PNEC ratios should be increased by a factor of 10 when using this PNEC to take into account the possibility of direct ingestion of sediment-bound substance.

For the marine sediment, the PNEC is calculated in the same way using the marine water PNEC from above; this gives a PNEC of 0.33 µg/kg wet weight. The ratios are increased by a factor of 10 as for the freshwater sediment.

4.2 Terrestrial compartment

A number of contact studies for tricresyl phosphate with insects are reported in WHO (1990). These data, however, cannot be used to derive a PNEC for the terrestrial (or aquatic or atmospheric) compartment and so are not included in this assessment.

In the absence of suitable data, the equilibrium partitioning method can be used to estimate the PNEC

$$PNEC_{soil} = \frac{K_{soil-water}}{RHO_{soil}} \times PNEC_{water} \times 1000$$

where $K_{soil-water}$ = soil-water partition coefficient = 142 m^3/m^3 (see Section 3.1.2).
RHO_{soil} = bulk density of wet soil = 1,700 kg/m^3.

Using a $PNEC_{water}$ of 0.032 μg/l, the $PNEC_{soil}$ is estimated as 0.0027 mg/kg wet weight.

As the log K_{ow} of this substance is above five, according to the TGD, the resulting PEC/PNEC ratios should be increased by a factor of 10 when using this PNEC to take into account the possibility of direct ingestion of soil-bound substance.

4.3 Atmosphere

WHO (1990) reports that Inden and Tachibana (1975, cited in IUCLID 2000) found that tricresyl phosphate emitted from vinyl film caused some leaf shrinkage on crops when covered by the film. The original paper is in Japanese and so it has not been possible to obtain further details of this study for this assessment.

No information is available on the toxicity of tricresyl phosphate to organisms exposed via air. The low vapour pressure of the substance means that volatilisation to the atmosphere is likely to be limited and the resulting concentrations are likely to be low. The possibility of tricresyl phosphate contributing to atmospheric effects such as global warming and acid rain is thus likely to be small. In addition, as the substance does not contain halogen atoms, it will not contribute to ozone depletion.

4.4 Mammalian toxicity

Several review documents are available on the toxicity of tricresyl phosphate (CAS 1330-78-5). The International Programme on Chemical Safety produced an Environmental Health Criteria document on this substance (IPCS 1990), and there is a US National Toxicology Program Technical Report on the toxicology and carcinogenesis of tricresyl phosphate in F334/N rats and B6C3F mice (NTP 1994). An IUCLID data set for tris(methylphenyl) phosphate was created in 1993 (updated 1998, published 1999, referenced here as IUCLID 1998) under the US Environmental Protection Agency's (EPA) High Production Volume (HPV) Challenge Programme, although this does not present Klimisch reliability scores for the quoted information sources. A further IUCLID data set on phosphoric acid, tris(methylphenyl ester) was prepared by Great Lakes Chemical corporation in 2001 (IUCLID 2001).

These documents constitute the principal sources of information used in this report, supplemented as appropriate by reference to a small number of primary studies. In some cases the data included in these sources are limited. Appendix 1 indicates a number of possible areas for clarification in the mammalian toxicity database.

Tricresyl phosphate comprises one or more of the isomers tri-*o*-cresyl phosphate, tri-*m*-cresyl phosphate and tri-*p*-cresyl phosphate. Studies on tricresyl phosphate have been conducted principally on the *ortho*-isomer or on mixed isomers.

4.4.1 Toxicokinetics, metabolism and distribution

The absorption, distribution, metabolism and elimination of organophosphates are critical to the delayed neuropathic effects caused by these compounds, and it is known that factors such as route of administration, sex, age and species/strain affect their metabolic fate and hence their subsequent toxic effects in animals and humans (IPCS 1990). A number of relevant experimental studies on tricresyl phosphate have been conducted, principally on the *ortho*-isomer.

Dermal absorption of tri-*o*-cresyl phosphate in humans appears to be at least an order of magnitude faster than in dogs: the rate of transfer of ^{32}P-labelled tri-*o*-cresyl phosphate across the abdominal skin of a dog administered a single dermal dose of 200mg/kg was estimated to be about 100 times less rapid than through intact human palm skin, based on urinary excretion and surface area considerations (Hodge and Sterner 1943, cited in IPCS 1990). Significant dermal absorption occurs in cats, as evidenced by a study in which 73 per cent of the tri-*o*-cresyl phosphate disappeared within 12 hours after [^{14}C]-tri-*o*-cresyl phosphate (50 mg/kg) was applied dermally to adult male cats (Nomeir and Abou-Donia 1984, 1986, cited in IPCS 1990).

Absorption by other routes has been less well studied. Gross and Grosse (1932, cited in IPCS 1990) reported that tri-*o*-cresyl phosphate given orally (0.1 g/kg in olive oil) was absorbed by rabbits [no further information provided], while studies by Kurebayashi *et al*. (1985, cited in IPCS 1990) indicated incomplete absorption of tri-*p*-cresyl phosphate from the intestine of rats after a single oral dose of [methyl-^{14}C]-tri-*p*-cresyl phosphate (7.8 or 89.6 mg/kg) in dimethyl sulfoxide. Much of the radioactivity was recovered in the faeces, principally as unchanged tri-*p*-cresyl phosphate.

There is no direct information on absorption via the inhalation route.

Studies in a number of species have shown that absorbed tri-*o*-cresyl phosphate is widely distributed in the body.

In cats given a single dermal dose of 50 mg [^{14}C]-tri-*o*-cresyl phosphate per kg, the compound reached its highest concentration in plasma at 12 hours and metabolites

attained maximum concentration between 24 and 48 hours. Parent tri-*o*-cresyl phosphate was the predominant compound in the brain, spinal cord and sciatic nerve, while metabolites were predominant in the liver, kidney and lung. Measuring total radioactivity one to 10 days post-exposure, the highest levels were found in the bile, gall bladder, urinary bladder, kidney and liver, with only low levels in the spinal chord and brain (Nomeir and Abou-Donia 1984, 1986, cited in IPCS 1990). In dogs, following a single dermal dose of 200 mg/kg, the radioactivity in the blood within 24 hours was equivalent to an average value of 80 µg/litre and was distributed throughout the visceral organs, muscle, brain and bone. Measured levels of radioactivity in tissues were in the following order: liver > blood > kidney > lung > muscle/spinal chord > brain and sciatic nerve (Hodge and Sterner 1943, cited in IPCS 1990).

In rats, the highest concentrations were found in adipose tissue, liver and kidney after oral administration of tri-*p*-cresyl phosphate (Kurebayashi *et al*. 1985, cited in IPCS 1990) and in liver, adipose tissue, epididymus, sciatic nerve, plasma and erythrocytes following daily dosing with tri-*o*-cresyl phosphate for ten days (Somkuti and Abou-Donia 1990, cited in IUCLID 2001). An oral study in chickens by Sharma and Watanabe (1974, cited in IPCS 1990) showed distribution of tri-*o*-cresyl phosphate to the liver (predominantly as metabolites) and the blood (predominantly unchanged tri-*o*-cresyl phosphate) while the highest concentrations occurred in bile, kidneys, liver and lung of hens given a single 50 mg oral dose of tri-*o*-cresyl phosphate. The active metabolite saligenin cyclic *o*-tolyl phosphate was the predominant compound found in excreta (Abou-Donia *et al.* 1990, cited in IUCLID 2001).

Studies in other species have indicated distribution to the gut and liver after intravenous injection of tri-*o*-cresyl phosphate into rabbits (Gross and Grosse 1932, cited in IPCS 1990).

Metabolism studies have been conducted in rats, rabbits, mice, cats and chickens. Tri-*o*-cresyl phosphate is metabolized via three pathways: 1) hydroxylation of one or more of the methyl groups (catalysed by the microsomal mixed-function oxidase system) which results in formation of mono- and di-hydroxymethyl tri-*o*-cresyl phosphate and o-hydroxybenzyl alcohol; 2) dearylation of the o-cresyl groups, resulting in the formation of *o*-cresyl, di-*o*-cresyl phosphate, *o*-cresyl phosphate and phosphoric acid; and 3) further oxidation of the hydroxymethyl to aldehyde and carboxylic acid. The oxidation reactions are most likely to be mediated by alcohol and alcohol dehydrogenase. The hydroxylation step results in hydroxymethyl tri-*o*-cresyl phosphate being cyclised to form saligenin cyclic *o*-tolyl phosphate (IPCS 1990).

Tri-*o*-cresyl phosphate and its metabolites are eliminated via the urine and faeces, together with small amounts in the expired air. In male cats given a single dermal dose of 50 mg/kg [^{14}C]-tri-*o*-cresyl phosphate, approximately 28 per cent of the applied dose was excreted in the urine and 20 per cent via the bile into the faeces within ten days. The disappearance of tri-*o*-cresyl phosphate and its metabolites from the plasma followed exponential kinetics. The estimated half-lives (in days) of tri-*o*-cresyl phosphate and its metabolites in this study were: tri-*o*-cresyl phosphate, 1.20; saligenin cyclic-*o*-tolyl phosphate, 2.47; di-*o*-cresyl phosphate, 4.50; *o*-cresyl phosphate, 4.30; *o*-cresol, 2.65; *o*-hydroxybenzyl alcohol, 14.0; *o*-hydroxy-benzaldehyde, 5.70; *o*-hydroxybenzoic acid, 6.00; and monohydroxymethyl tri-*o*-cresyl phosphate, 2.20. These were considered to reflect the rates of all processes involving the conversion, clearance and/or redistribution of these metabolites (Nomeir and Abou-Donia 1984, 1986, cited in IPCS 1990). Elimination via the bile has also been shown after intravenous injection into rabbits (Gross and Grosse 1932, cited in IPCS 1990) and intraperitoneal injection into rats (Myers *et al*. 1955, cited in IPCS 1990). After a single oral dose of [methyl-^{14}C]-tri-*p*-cresyl phosphate (7.8 or 89.6 mg/kg) in dimethyl sulfoxide to rats, about 90 per cent and 76 per cent, respectively, of the radioactivity was eliminated in the urine and faeces within 24 hours. At the lower dose level about

28 per cent of the dose was eliminated via the bile. The expiratory excretion as $^{14}CO_2$ over three days amounted to 18 per cent of the radioactivity. The authors suggested that the enterohepatic circulation and intestinal microflora play an important role in the degradation of tri-*p*-cresyl phosphate biliary metabolites (Kurebayashi *et al*. 1985, cited in IPCS 1990) while clearance of radioactivity was noted by four days after completion of a ten-day repeat dose study with tri-*o*-cresyl phosphate at 50 mg/kg (Somkuti and Abou-Donia 1990, cited in Great Lakes Chemical Corporation 2001). In hens receiving a single 50 mg oral dose of tri-*o*-cresyl phosphate, excretion was relatively slow, with about 47 per cent excreted in the first 12 hours and 99 per cent after five days (Abou-Donia *et al.* 1990, cited in IUCLID 2001).

In summary, toxicokinetics studies have been conducted principally on tri-*o*-cresyl phosphate, but also on tri-*p*-cresyl phosphate. There appear to be significant interspecies differences in dermal absorption of tri-*o*-cresyl phosphate, with absorption being greater in humans and cats, than in dogs. Quantitative data on absorption via other routes is scarce; it appears that tri-*o*-cresyl phosphate is readily absorbed via the gut in rabbits, but TCPC is mostly excreted unchanged when given orally to rats. Studies generally indicate that, once absorbed, tri-*o*-cresyl phosphate is widely distributed throughout the body, and may be metabolized via three pathways: 1) hydroxylation of one or more of the methyl groups which results in formation of mono- and di-hydroxymethyl tri-*o*-cresyl phosphate and *o*-hydroxybenzyl alcohol; 2) dearylation of the *o*-cresyl groups, resulting in the formation of *o*-cresyl, di-*o*-cresyl phosphate, *o*-cresyl phosphate and phosphoric acid; and 3) further oxidation of the hydroxymethyl to aldehyde and carboxylic acid. Tri-*o*-cresyl phosphate and its metabolites are eliminated mainly via the urine and faeces, together with small amounts in the expired air. Elimination via the bile has also been shown after intravenous injection. The estimated half-lives (in days) of tri-*o*-cresyl phosphate and its metabolites range from approximately one to 14 days. Enterohepatic circulation and intestinal microflora may play an important role in the degradation of tri-*p*-cresyl phosphate biliary metabolites. Elimination of tri-*o*-cresyl phosphate in hens is relatively slow and it has been suggested that that this may contribute to the particular sensitivity of this species. From the available data, it is not possible to confidently compare the toxicokinetics of the different tricresyl phosphate isomers, or to attempt inter-species extrapolations on toxicokinetic behaviour.

4.4.2 Acute toxicity

Information on the acute toxicity of tricresyl phosphate to humans is available from a number of poisoning incidents that have occurred throughout the world, mostly resulting from accidental or irresponsible contamination of foodstuffs, and tri-*o*-cresyl phosphate has been implicated as the responsible agent (IPCS 1990). In addition, a number of specific case reports of acute toxicity of tricresyl phosphate and/or tri-*o*-cresyl phosphate in humans have been described. There is a good amount of information available on the acute toxicity of tricresyl phosphate and its isomers from studies on experimental animals.

Animal data

Oral

The acute oral LD_{50} of tricresyl phosphate in different experimental animals is summarised in Table 4.7 below (taken from IPCS 1990).

The acute symptoms of intoxication are typical of organophosphorous poisoning. The most toxic compound appears to be tri-*o*-cresyl phosphate, and the acute toxicity of tricresyl phosphate depends on the relative proportions of the different isomers (IPCS 1990, Henschler 1958, cited in IUCLID 2001). Chickens appear to be the most sensitive and rats and mice the least sensitive species (IPCS 1990, and Bischoff 1977, cited in IUCLID 2001).

Other studies of acute toxicity by the oral route have been undertaken on guinea-pigs, pigs and sheep. Sheep given oral doses of 100, 200 or 400 mg/kg tri-*o*-cresyl phosphate exhibited acute intoxication characterised by diarrhoea, dehydration, metabolic acidosis and death within six days. Pigs dosed with 100 to 1,600 mg/kg tri-*o*-cresyl phosphate showed minimal signs of acute intoxication but developed severe signs of delayed neuropathy approximately 15 days after administration (Wilson *et al*. 1982, cited by IPCS 1990).

Table 4.7 Oral LD_{50} values for tricresyl phosphate and its isomers

Compound(s)	Species	LD_{50} (mg/kg)	Reference[6]
Tricresyl phosphate (mixed isomers)	Rat	5,190	Marhold 1972
	Rat	>4,640	Stauffer 1988[a]
	Rat	>15,800	Johannsen *et al.*1977
	Mouse	3,900	Izmerov 1982
	Chicken	>10,000	Johannsen *et al.* 1977
Tri-o-cresyl phosphate	Rat	8,400	Johannsen *et al.* 1977
	Rat	1,160	Veronesi *et al.* 1984
	Rabbit	3,700	Johannsen *et al.* 1977
	Chicken	500	Kimmerle and Loeser 1974
	Chicken	100-200	Smith *et al.* 1932
Tri-p-cresyl phosphate	Rabbit	>3,000	Smith *et al.* 1932
	Chicken	>1,000	Smith *et al.* 1932
Tri-m-cresyl phosphate	Rabbit	>3,000	Smith *et al.* 1932
	Chicken	>2,000	Smith *et al.* 1932

Notes: [a] Personal communication to the IPCS from Stauffer Chemical Company (1988) entitled: Test procedures and data summaries for t-butyl phenyl diphenyl phosphate, tricresyl phosphate, trixylenyl phosphate, mixed triaryl phosphate and isopropyl phenyl diphenyl.

Inhalation

Although the IPCS (1990) document provides no information on acute inhalation toxicity of tricresyl phosphate, a number of poorly reported (and therefore potentially unreliable) rat studies are detailed in IUCLID (1998). The reported LC_{50}s in these studies range from above 3.53 mg/ml (six-hour exposure) to above 200 mg/ml (one-hour exposure). No details are provided in this IUCLID document regarding GLP or guideline status of these studies. However, the IUCLID (2001) data set includes one study by Stauffer Chemical Company (1979), not listed in IUCLID (1998) that was conducted to EPA Guideline OTS 798.1150 and GLP, and is considered 'valid without

[6] Cited IPCS (1990).

restriction'. In this study, a group of ten male and ten females rats were exposed to an aerosol of the test material at a mean concentration of 5.2 mg/l for four hours, followed by a 14-day observation period; signs of a response to treatment were limited to reduced activity and ruffled fur immediately after exposure but all had recovered by the following day. At necropsy, foci were noted in the lungs of five of the exposed rats, but the acute inhalation LC_{50} (4 hours) was considered to be above 5.2 mg/l.

Dermal

The acute dermal LD_{50} of tricresyl phosphate in different species is summarised in Table 4.8 below (taken from IPCS 1990). No details are provided in the report regarding GLP or other aspects of the reliability of these studies.

In addition to these, the IUCLID (1998) dataset references other studies of unknown quality and reliability (Monsanto Chemical Company 1984, Stauffer Chemical Company 1977a, b, Bio-Test Laboratory 1975, MB Research Laboratory 1978, FMC Industrial Chemical Division 1978, Consumer Product Testing Company 1979, New York University 1951, Treon *et al*. 1955, Abou-Donia *et al*. 1980). Quoted LD_{50} values in these studies (all conducted in the rabbit) range from 3,700 to above 10,000 mg/kg bodyweight. IUCLID (2001) cites an acute dermal study in albino rabbits (Food and Drug Research Laboratories Inc. 1975a) conducted to EPA guideline OTS 798.1100 but not GLP, and considered 'valid without restriction', in which tricresyl phosphate was applied to the shaved backs of albino rabbits (both abraded and unabraded sites). Animals were observed for 14 days and the dermal LD_{50} value was determined as above 10,000 mg/kg. Thus, it appears from the limited data available that tricresyl phosphate is more toxic in the cat than the rabbit by the dermal route.

Table 4.8 Dermal LD_{50} values for tricresyl phosphate and its isomers

Compound(s)	Species	LD_{50} (mg/kg)	Reference
Tricresyl phosphate (mixed isomers)	Rabbit Cat	>7,900 1,500	Johannsen *et al.* (1977) Abou-Donia *et al.* (1980)

Other

In a subcutaneous injection study in the cat (Houghton and Co. data sheet and Patty's Industrial Hygiene and Toxicology 1978, cited in IUCLID 1998), an LD_{50} of above 1,000 mg/kg was stated for tri-*p*-cresyl phosphate.

Human data

There are a number of generally poorly documented case reports of toxic effects resulting from accidental and/or occupational ingestion of tricresyl phosphate or products containing this compound (such as Lefaux 1968, Goldstein *et al*. 1988, Pashkova 1989, Zilber *et al*. 1989, all cited in IUCLID 1998). In one such case, one mouthful of a lubricating oil containing tricresyl phosphate caused vomiting, diarrhoea, weakness, drowsiness, delayed cholinergic crisis and depressed nerve conduction velocity, with full recovery occurring within four weeks (Goldstein *et al*. 1988, cited in IUCLID 1998). In a poisoning event recorded by Staehelin (1941, cited in IPCS 1990), 80 or more young men in the Swiss army ingested food containing tri-*o*-cresyl phosphate. Toxic symptoms appeared in one man who ate food containing only 0.15 g tri-*o*-cresyl phosphate, and severe neurological disturbance developed in three men whose intake was 0.5-0.7 g, but in two other cases an intake of 1.5-2.0 g did not result in symptoms. A latent period of 3 to 28 days was observed for the 'delayed neurotoxicity' symptoms which then progressively appeared. The author concluded that individual susceptibility varies greatly.

Summary of acute toxicity

Information is available from human studies which indicate that initial symptoms of acute tricresyl phosphate poisoning are gastrointestinal, ranging from slight to severe nausea and vomiting, sometimes accompanied by abdominal pain and diarrhoea. These symptoms are usually transient, lasting from a few hours to a few days (IPCS 1990). Symptoms of delayed neurotoxicity may then appear after a three to 28-day lag. Initial neurological symptoms are sharp cramp-like pains in the calves, and numbness and tingling in the feet and sometimes the hands (Staehelin 1941, cited in IPCS 1990).

The oral LD_{50} of tricresyl phosphate and its isomers in experimental animals ranges from 100-200 mg/kg (tri-*o*-cresyl phosphate; chicken) to above 15,800 mg/kg (tricresyl phosphate mixed isomers; rat). Dermal studies indicate that tricresyl phosphate is more toxic in the cat (LD_{50}= 1,500 mg/kg) than in the rabbit (LD_{50}= >7,900 mg/kg). Although of questionable reliability, inhalation LC_{50}s for the rat ranging from above 3.53 (six-hour exposure) to more than 200 mg/ml (one-hour exposure) have been reported.

The acute toxicity of tricresyl phosphate appears to depend on the relative proportions of the different isomers and there is some experimental evidence to suggest that the most toxic isomer may be tri-*o*-cresyl phosphate and that it may give rise to the major neurotoxic effects observed. The toxicity of the commercial products may thus depend predominantly on the concentration of the *ortho*-isomer, although the mixed *o*-cresyl esters in these products are also toxic and have neurotoxic activities (IPCS 1990).

4.4.3 Irritation

According to IPCS (1990), no published information is available on skin and eye irritation. The IUCLID (1998) dataset does list information on irritation in experimental animals but these studies are considered unreliable. Two Draize tests in rabbits listed in the 2001 IUCLID (Food and Drug Research Laboratories 1975bc) that are considered valid conclude that tricresyl phosphate is not irritating to the skin or eye.

No human studies have been conducted but there is a fatal case report of a man being burnt on the body by splashes of tricresyl phosphate containing ten per cent free cresol (a known irritant), and also a human repeated patch test that showed signs of irritation (New York University 1951, cited in IUCLID 1998).

Skin

A human patch test listed in the IUCLID (1998) dataset (New York University 1951) describes a mild irritative skin reaction following exposure to test compound containing 12 per cent esterised *o*-cresol.

No GLP animal studies are available. Of the eight sources listed in the IUCLID (1998) data set[7] (Guess and Haberman 1968, Marhold 1986, Stauffer Chemical Company 1977a, b, Union Carbide 1964, Monsanto Chemical Company 1984, FMC Industrial Chemical Division 1976, 1978, MB Research Laboratory 1978), all but one gave a negative result for skin irritation. The exception was Union Carbide (1964, cited in RTECS 1991), which indicated ‘mild’ irritation. No details are provided in the IUCLID (1998) document regarding the GLP or guideline status of the implicated studies. The IUCLID (2001) document lists one study in rabbits (Draize test; semiocclusive dressing) (Food and Drug Research Laboratories 1975c) considered valid without restriction though not conducted to GLP, which concluded that tricresyl phosphate did not cause

[7] Some studies cited from multiple references, hence there are more than eight references here.

skin irritation when tricresyl phosphate was applied undiluted to abraded or unabraded skin under semiocclusive conditions.

Eye

Of the five eye irritation studies/data sources cited in the IUCLID (1998) dataset[8] (Marhold 1986, Stauffer Chemical Company 1977a, b, Monsanto Chemical Company 1984, Bio-Test Laboratory 1975, FMC Industrial Chemical Division 1976 and 1978, MB Research Laboratory 1978, New York University 1951), only one by Marhold (1986) gave a 'slightly irritating' result; the others concluded the test substance was 'not irritating'. No details are provided in the IUCLID (1998) document regarding the GLP or guideline status of these studies. IUCLID (2001) lists one study in rabbits (Food and Drug Research Laboratories 1975b) considered valid without restriction though not conducted to GLP, which concluded that tricresyl phosphate is not an eye irritant when applied as 0.1 ml of undiluted material.

Summary of irritation

No reliable information is available from human studies. A case study reporting burns on exposure to splashes is uninterpretable because the material to which the individual was exposed also contained free cresol, and similarly the human repeat patch test is unreliable because of uncertainties about the identity of the test compound.

The balance of evidence (notably from the two available reliable studies) suggests that tricresyl phosphate is not irritating to the skin or eye.

4.4.4 Corrosivity

No human studies have been conducted but there is a fatal case report of a man being burnt on the body by splashes of tricresyl phosphate also containing ten per cent free cresol, a known irritant.

The experimental studies that have investigated the potential of tricresyl phosphate to irritate the skin and eyes do not suggest irritant or corrosive properties. One poorly reported non-GLP study in the IUCLID (1998) data set (FMC Industrial Chemicals Division 1978) involved a single application of 0.5 ml to non-abraded skin under an occluded patch in six rabbits, with four- and 48-hour observations, and concluded that tricresyl phosphate is not corrosive.

4.4.5 Sensitisation

A number of human patch test studies are listed in the IUCLID (1998) data set and indicate that tricresyl phosphate has skin sensitization potential. For example, in a study of 230 patients with possible occupational dermatitis from the metallurgical industry, 2.6 per cent showed positive patch test results with tricresyl phosphate. In another study, described in IUCLID (1998) as a maximization test (E.I. DuPont Denemours Co. Inc, Clover Laboratory, 1982), a positive reaction was obtained in seven out of 23 subjects although there is uncertainty about test substance identity and no further details about the study are provided. A case report describing allergic contact dermatitis induced by contact with Band-Aid brand adhesive bandages (Norris

[8] Some studies cited from multiple references, hence there are more than five references here.

and Storrs 1990, cited in IUCLID 2001), mentions that tricresyl phosphate was an ingredient in the Band-Aid plastic. Two patients were patch tested with Band-Aid strips and with several components of the strip, but not tricresyl phosphate. The article mentions that tricresyl phosphate had caused allergic contact dermatitis in previous studies but provides no further information.

No animal studies on skin sensitization were identified, and no human or animal information on respiratory tract sensitisation is available.

4.4.6 Repeated-dose toxicity

Animal data

A number of animal studies have been conducted on tricresyl phosphate (for various mixtures of isomers).

A 28-day feeding study in which groups of ten male and ten female Sprague-Dawley rats received tricresyl phosphate at 0.1, 0.5 or 1.0 per cent in the diet (Foster D. Snell Inc.1976, cited in IUCLID 2001) caused mortality in all treatment groups, with 19 of the 20 animals in the high-dose group dying. No treatment-related lesions or changes in haematological or urinalysis parameters, and no effects on organ to bodyweight ratios, were observed in the low-dose group. The authors concluded that the no observed adverse effect level (NOAEL) was 0.1 per cent in the diet, although the fact that one animal died at this dose level gives rise to uncertainty about this conclusion.

IUCLID (2001) cites two oral gavage studies in rats. In the first study (Latendresse *et al*. 1994a), groups of only three male and three female Fischer F344 rats were given 0.4 g/kg/day for 20, 40 or 60 days. Diagnostic pathology revealed hypertrophy and cholesterol lipidosis of the adrenal cortex (both sexes) and of ovarian interstitial cells; these effects were progressive with duration of treatment. Decreased testicular weights and degeneration of the seminiferous tubules were detected in all nine male rats. In the second study (Sumitomo Chemical Company 1974) groups of five male and five female Sprague-Dawley rats received daily doses of 30, 100, 300 or 1,000 mg/kg/day tricresyl phosphate, six days per week, for three months. Other than excessive salivation in a few animals at all doses immediately following gavage, there were no clinical signs suggestive of mortality and there were no treatment-related deaths. Significant decrease in bodyweight gain was noted in high-dose male rats throughout the test and various changes in clinical chemistry were detected. All treatment groups showed a slight increase in liver weights and an increase in adrenal glands weight was seen in the top-dose females, with a slight decrease in spleen, heart and lung weights in the high-dose males. Hypertrophy of the adrenal cortex was observed in the 1,000 mg/kg/day group.

A three-month oral study, in which tricresyl phosphate containing 60-65 per cent tri-*m*-cresyl phosphate and 35-40 per cent tri-*p*-cresyl phosphate (suspended in water with five per cent gum arabic) was given to SD rats at 30, 100, 300 or 1,000 mg/kg, produced no notable histopathological changes (Saito *et al*. 1974, cited in IPCS 1990). The authors concluded that the sample of tricresyl phosphate used [containing little or no tri-*o*-cresyl phosphate] was of low short-term toxicity. However, Oishi *et al.* (1982, cited in IPCS 1990) reported a 9-week feeding study in which Wistar rats were fed a pellet diet containing a mixture of tricresyl phosphate isomers, of unspecified composition, at 5 g/kg diet and found increased absolute and relative liver weights with associated histopathological changes and, in the plasma, significantly increased total protein, urea, cholesterol and glutamate pyruvate transaminase. Chapin *et al*. (1988, cited in IPCS 1990) exposed male and female CD-1 mice to diets containing 0, 0.437,

0.875, 1.75, 3.5 or 7.0 per cent tricresyl phosphate (mixed isomers) for 14 days. No clinical signs were observed in the animals at doses up to 0.875 per cent but all animals in the groups given 1.75, 3.5 or 7.0 per cent exhibited piloerection, tremors and diarrhoea and were lethargic prior to death within the 14-day treatment period.

Additional studies on tricresyl phosphate have been conducted and reported by the National Toxicology Program (NTP 1994). These studies in F344/N rats and B6C3F1 mice used a mixed isomer preparation of 79 per cent tricresyl phosphate esters consisting of 21 per cent tri-*m*-cresyl phosphate, four per cent tri-*p*-cresyl phosphate and less than one per cent tri-*o*-cresyl phosphate (plus other unidentified tricresyl phosphate esters).

A 16-day oral study was conducted in which groups of ten male and ten female rats received tricresyl phosphate in corn oil by gavage at doses of 0, 360, 730, 1,450, 2,900 or 5,800 mg/kg bodyweight, five days per week for a total of 13 or 14 doses in a 16-day period. One female receiving 1,450 mg/kg and five males and eight females receiving 2,900 mg/kg died before the end of the study. Final mean bodyweights of animals receiving 1,450 mg/kg or more were significantly lower than controls. Necrosis of the mandibular lymph node, spleen and thymus occurred primarily in rats receiving 2,900 and 5,800 mg/kg. Diffuse aspermatogenesis occurred in male rats receiving 2,900 and 5,800 mg/mg (NTP 1994).

A similar 16-day oral study was conducted in mice. Groups of ten male and ten female animals received tricresyl phosphate in corn oil by gavage at doses of 0, 360, 730, 1,450, 2,900 or 5,800 mg/kg bodyweight, five days per week for a total of 13 or 14 doses in a 16-day period. Five males and all females that received 1,450 mg/kg, all mice that received 2,900 mg/kg, and four males and one female that received 5,800 mg/kg, died before the end of the study. Final mean bodyweights of male mice that received 1,450 or 5,800 mg/kg were significantly lower than controls. Final mean body weights of female mice that received 360, 730 or 5,800 mg/kg were significantly greater than that of controls. Necrosis of the mandibular lymph node, spleen and thymus occurred primarily in mice receiving 2,900 and 5,800 mg/kg (NTP 1994).

A 13-week oral study was conducted in which groups of ten male and ten female rats received tricresyl phosphate in corn oil by gavage at doses of 0, 50, 100, 200, 400 or 800 mg/kg bodyweight. All rats survived to the end of the study. Final mean bodyweights of male rats receiving 200 mg/kg or more were significantly lower than controls. Cytoplasmic vacuolation of the adrenal cortex occurred in all dosage groups and the severity increased with dose. Ovarian interstitial cell hypertrophy occurred in all dosed groups of females. Atrophy of the seminiferous tubules occurred in male rats that received 400 and 800 mg/kg (NTP 1994).

A similar 13-week oral study was conducted in mice. Groups of ten male and ten female animals received tricresyl phosphate in corn oil by gavage at doses of 0, 50, 100, 200, 400 or 800 mg/kg bodyweight. All mice survived to the end of the study. Final mean bodyweights of male mice receiving 200 mg/kg and of female mice receiving 400 or 800 mg/kg were significantly lower than controls. Cytoplasmic vacuolation of the adrenal cortex occurred in all dosed animals and the severity increased with dose. Ovarian interstitial cell hypertrophy was present in all dosed groups of females (NTP 1994).

A 13-week feeding study was conducted in which groups of ten male and ten female rats were fed diets containing 0, 900, 1,700, 3,300, 6,600 or 13,000 ppm tricresyl phosphate – estimated to deliver 0, 55, 120, 220, 430 or 750 mg/kg bodyweight (males) and 0, 65, 120, 230, 430 or 770 mg/kg bodyweight (females). All rats survived to the end of the study. Mean bodyweights of males and females receiving 6,600 and 13,000 ppm and females exposed to 13,000 ppm were significantly lower than controls during the first week of the study. Cytoplasmic vacuolation of the adrenal cortex

occurred in all groups of dosed animals. Hyperplasia of ovarian interstitial cells and inflammation of the ovarian interstitium occurred in all exposed groups of females. Renal papillary oedema and renal papillary necrosis occurred in males and females receiving 13,000 ppm and in females receiving 6600 ppm. Basophilic hypertrophy of the pituitary gland pars distalis and atrophy of the seminiferous tubules occurred in males receiving 6,600 and 13,000 ppm (NTP 1994).

A similar 13-week feeding study was conducted in mice. Groups of ten male and ten female mice were fed diets containing 0, 250, 500, 1,000, 2,100 or 4,200 ppm tricresyl phosphate – estimated to deliver 0, 45, 110, 180, 380 or 900 mg/kg bodyweight (males) and 0, 65, 130, 230, 530 or 1,050 mg/kg bodyweight (females). All mice survived to the end of the study. Mean bodyweights of males receiving 4,200 ppm and of females exposed to 2,100 and 4,200 ppm were lower than controls throughout the study. Cytoplasmic vacuolation of the adrenal cortex occurred in all groups of dosed animals with the exception of 250 ppm males. Papillary hyperplasia of the gallbladder mucosa occurred in male mice exposed to 500 ppm or more and in females exposed to 1,000 ppm or more. Renal tubule regeneration occurred in all 4,200 ppm male mice (NTP 1994).

Two-year feeding studies were also conducted (NTP 1994, see also Section 4.1.2.8). Groups of 95 male and 95 female rats were fed diets containing 0, 75, 150 or 300 ppm of tricresyl phosphate – estimated to deliver average daily doses of 0, 3, 6 or 13 mg/kg (males) and 0, 4, 7 or 15 mg/kg (females), respectively. An additional group of 95 male and 95 female rats were fed diets containing 600 ppm of tricresyl phosphate for 22 weeks and then received only control diet. After 3, 9, and 15 months exposure, up to 15 males and 15 females per group were evaluated for forelimb and hindlimb strength, then necropsied and evaluated for histopathological lesions (see Neurotoxicity section below). Survival of the exposed rats was similar to that of control animals and the final mean bodyweights of all exposed groups of male and female rats were similar to controls. Cytoplasmic vacuolation of the adrenal cortex occurred in 600 ppm males and 150, 300, and 600 ppm females at the 3-month interim evaluation. At 9 and 15 months, this lesion occurred only in female rats, primarily in the 300 ppm group. Cytoplasmic vacuolation of the adrenal cortex and ovarian interstitial cell hyperplasia occurred in female rats exposed to 300 ppm throughout the study and the incidence and severity of these lesions were increased at the end of the study.

In the two-year mouse study, groups of 95 male and 95 female mice were fed diets containing 0, 60, 125 or 250 ppm of tricresyl phosphate – estimated to deliver average daily doses of 0, 7, 13 or 27 mg/kg (males) and 0, 8, 18 or 37 mg/kg (females), respectively. After 3, 9, and 15 months exposure, up to 15 males and 15 females per group were evaluated for forelimb and hindlimb strength, then necropsied and evaluated for histopathological lesions (see Neurotoxicity section below). Survival of exposed mice was similar to that of control animals and the final mean bodyweights of all exposed groups of male and female mice were also similar to controls. Ceroid pigmentation of the adrenal cortex was noted in all groups of mice, including controls, from month nine of the two-year study. However, although females given 60 or 125 ppm and their controls were unaffected at the three-month interim evaluation, the change was noted in some animals from all treated male groups but not their controls, at the three-month time point. The severity of this change increased in female mice receiving 250 ppm and also, to a lesser extent, in those receiving 125 ppm from month nine onwards. Incidences of clear cell foci, fatty change and ceroid pigmentation of the liver were significantly increased in male mice receiving 125 or 250 ppm (NTP 1994).

Neurotoxicity

In an early article on phosphate ester neurotoxicity, Henschler (1958, cited in IUCLID 2001) described 'tricresyl phosphate poisoning' as related to peripheral neurotoxicity and identified the *ortho*-isomer, tri-*o*-cresyl phosphate, as the principal neurotoxic component. The article also details the degenerative changes that occur in response to different amounts of tri-*o*-cresyl phosphate present in tricresyl phosphate. Bischoff (1977, cited in IUCLID 2001) also reviewed the neurotoxicity of tri-*o*-cresyl phosphate and provided a detailed picture of the neurological and histological changes that occur, identifying the hen as a sensitive model with which to evaluate the neurotoxic potential of the phosphate esters.

In a study designed to investigate the effect of tricresyl phosphate on humoral and cell-mediated immune responses, groups of ten male Wistar rats were fed a standard laboratory diet containing 0 (control), 20, 50 or 100 ppm tricresyl phosphate (comprising technical grade 90 per cent mixture of *ortho*-, *para*- and *meta*-isomers) for six weeks (Banerjee *et al*. 1992). There were no signs of cholinergic or delayed neurotoxic effects during the study.

A number of studies by the NTP (described in the following paragraphs) have also investigated aspects of the neurotoxic potential of tricresyl phosphate using a mixed isomer preparation of 79 per cent tricresyl phosphate esters consisting of 21 per cent tri-*m*-cresyl phosphate, four per cent tri-*p*-cresyl phosphate and less than one per cent tri-*o*-cresyl phosphate (plus other unidentified tricresyl phosphate esters).

Hindlimb grip strength in male mice receiving 360 and 1,450 mg/kg and male and female mice that received 730 and 5,800 mg/kg in the NTP 16-day gavage study were significantly lower than those of the controls at the end of the study. However, the observed neurobehavioural changes in animals in the top three dose groups were not attributed by the authors to a direct neurotoxic response (NTP 1994).

In a 13-week oral study conducted in mice, groups of ten male and ten female animals received tricresyl phosphate in corn oil by gavage at doses of 0, 50, 100, 200, 400 or 800 mg/kg bodyweight. Hindlimb grip strength in male mice receiving 200 mg/kg or more was significantly lower than that of controls at the end of the study. Multifocal degeneration of the spinal cord occurred in males and females receiving 100 mg/kg or more, and multifocal degeneration of the sciatic nerve was observed in male mice receiving 200 mg/kg or more and in females dosed with 100 mg/kg or more (NTP 1994). However, an equivalent study in rats, in which groups of ten male and ten female rats similarly received tricresyl phosphate in corn oil by gavage at doses of 0, 50, 100, 200, 400 or 800 mg/kg bodyweight, revealed no evidence of neurotoxicity (NTP 1994).

In the 13-week feeding study in rats fed diets containing 0, 900, 1,700, 3,300, 6,600 or 13,000 ppm tricresyl phosphate – estimated to deliver 0, 55, 120, 220, 430 or 750 mg/kg bodyweight (males) and 0, 65, 120, 230, 430 or 770 mg/kg bodyweight (females) discussed above, no biologically significant changes in neurobehavioural parameters were noted. However, in a similar 13-week study in mice fed diets containing 0, 250, 500, 1,000, 2,100 or 4,200 ppm tricresyl phosphate (estimated to deliver 0, 45, 110, 180, 380 or 900 mg/kg bodyweight (males) and 0, 65, 130, 230, 530 or 1,050 mg/kg bodyweight (females)) changes in grip strength were noted in groups of animals receiving 2,100 or 4,200, although the significance of this finding was said, by the authors, to have been confounded by reduced bod weight of these animals, and axonal degeneration occurred in male and female mice exposed to 2,100 and 4,200 ppm and females exposed to 1,000 ppm (NTP 1994).

In the two-year feeding study in rats, animals were fed diets containing 0, 75, 150 or 300 ppm of tricresyl phosphate – estimated to deliver average daily doses of 0, 3, 6 or

13 mg/kg (males) and 0, 4, 7 or 15 mg/kg (females), respectively. An additional group of 95 male and 95 female rats were fed diets containing 600 ppm of tricresyl phosphate for 22 weeks and then received only control diet. After 3, 9, and 15 months exposure, up to 15 males and 15 females per group were evaluated for forelimb and hindlimb strength, then necropsied and evaluated for histopathological lesions. Hindlimb grip strengths in 300 ppm male rats and in males and females exposed to 600 ppm were significantly lower than controls at the 3-month interim evaluation, but no significant changes in neurobehavioural parameters were seen among any groups of rats at the 9- and 15- month evaluations (NTP 1994).

Similarly, in a two-year mouse dietary study at levels of 0, 60, 125 or 250 ppm of tricresyl phosphate – estimated to deliver average daily doses of 0, 7, 13 or 27 mg/kg (males) and 0, 8, 18 or 37 mg/kg (females), respectively, after 3, 9, and 15 months exposure, up to 15 males and 15 females per group were evaluated for forelimb and hindlimb strength, then necropsied and evaluated for histopathological lesions. Hindlimb grip strength in 250 ppm female mice was significantly lower than in controls at the 3-month interim evaluation, but no other neurobehavioural changes were noted (NTP 1994).

Thus, overall, studies in rodents have not definitively established the neurotoxicity of tricresyl phosphate, except in the presence of tri-*o*-cresyl phosphate, following repeated exposure for periods of up to two years.

A number of studies on the neurotoxicity of tricresyl phosphate in the hen are briefly noted in the IUCLID (1998) but details of test material and methodology employed, and status with regard to international guidelines and GLP, are inadequately reported so their robustness can not be assessed. In one paper, treatment with 0.21 mg/kg bw/d or 0.26 mg tri-*p*-cresyl phosphate/kg bw/d for 18 to 20 days was reported not to affect serum cholinesterase or cause signs of ataxia or paralysis, while five doses of 5,000 mg tri-*m*-cresyl phosphate or tri-*p*-cresyl phosphate/kg bw/ d given over ten days, also elicited no effect (Hine *et al*. 1943, cited in IUCLID 1998).

The summary of data presented in IPCS (1990) and the papers by Henschler (1958) and Bischoff (1977) - both cited in IUCLID (2001) - indicate that chickens are the most sensitive species and rats and mice the least sensitive species to the toxic effects of tricresyl phosphate. There is thus a basis for concluding that tri-*o*-cresyl phosphate is the most toxic of the tricresyl phosphate isomers and that its presence in tricresyl phosphate mixtures may be the principal agent responsible for the neurotoxic effects observed. The toxicity of commercial products will therefore depend predominantly on the concentration of the *ortho*-isomer, although it is recognised that mixed o-cresyl esters in these products are also toxic and can contribute to the neurotoxic action (IPCS 1990).

Immunotoxicity

In a study designed to investigate the effect of tricresyl phosphate on humoral and cell-mediated immune responses, groups of ten male Wistar rats were fed a standard laboratory diet containing 0 (control), 20, 50 or 100 ppm tricresyl phosphate (comprising technical grade 90 per cent mixture of *ortho*-, *para*- and *meta*-isomers) for six weeks (Banerjee *et al*. 1992). Suppression of humoral and cell-mediated immune response (investigated by measuring serum antibody titre and immunoglobulin concentrations following immunization with tetanus toxoid) occurred in a dose-dependent fashion. The authors concluded that tricresyl phosphate at 50 ppm in the diet caused immunotoxicity and that the immune system may be a sensitive target for tricresyl phosphate. However, these findings are of questionable toxicological significance and the conclusions must be interpreted with caution, especially in the absence of other published studies on the immunotoxicity of tricresyl phosphate.

Human data

As previously noted, poisoning incidents implicating tri-*o*-cresyl phosphate have occurred throughout the world, mostly through contamination of foodstuffs; there are also reports of occupational poisoning from repeated dermal exposure (IPCS 1990).

Oral

One of the largest poisoning incidents reported in IPCS (1990) involved 50,000 people in mid-western and south-western USA who had consumed an adulterated alcoholic beverage containing about two per cent tri-*o*-cresyl phosphate and consequently suffered paralysis characterised by bilateral foot- and wrist-drop (Morgan 1982, cited in IPCS 1990).

Dermal

Three cases of toxic polyneuropathy were detected amongst employees who had worked for six to eight months in a plant in England manufacturing tricresyl phosphate. Skin penetration and inhalation were thought to be the main routes of exposure (Hunter *et al*. 1944, cited in IPCS 1990). Other reports of poisoning involved percutaneous absorption of tri-*o*-cresyl phosphate following exposure in chemical plants IPCS 1990).

Inhalation

As noted above, cases of toxic polyneuropathy were detected amongst employees who had worked for six to eight months in a plant in England manufacturing tricresyl phosphate. Skin penetration and inhalation were thought to be the main routes of exposure (Hunter *et al*. 1944, cited in IPCS 1990).

The various symptoms of repeated tricresyl phosphate exposure in humans are well established and fully described (see IPCS 1990). Short-term signs include vomiting, abdominal pains and diarrhoea, while longer term symptoms (usually delayed) are neurological, frequently resulting in paralysis and pyramidal signs such as spasticity.

Summary and discussion of repeated-dose toxicity

It is well established that tricresyl phosphate is toxic. In particular, there is evidence to suggest that tri-*o*-cresyl phosphate, rather than the other isomers of tricresyl phosphate, is neurotoxic to humans and animals after repeated oral or dermal (and potentially also inhalation) exposure. While human case studies do not allow a lowest observed adverse effect level (LOAEL) to be derived, there is a good amount of informative and useful animal data.

A number of pathological changes have been observed following repeat dose exposure to tricresyl phosphate mixed isomers, including effects in the liver, lymph nodes, spleen and thymus, testis, seminiferous tubules, ovaries, adrenal, kidney, gall bladder, sciatic nerve and spinal cord. The LOAEL for any treatment-related effect (cytoplasmic vacuolation of the adrenal cortex) in the 13-week studies was 250 ppm in the feed (in mice; equivalent to 45 mg/kg/bw or 65 mg/kg/bw for males and females respectively). In the two-year NTP feeding studies, the LOAEL for any treatment-related effect (pigmentation of the adrenal cortex) was 60 ppm in the feed (in mice; equivalent to 7 mg/kg/bw or 8 mg/kg/bw for males and females respectively).

With regard to neurotoxicity and neurobehavioural changes, reduced hindlimb grip strength was seen in male mice receiving 200 mg/kg or more, in a 13-week gavage study with multifocal degeneration of the sciatic nerve observed in males receiving 200

mg/kg or more and in females dosed with 100 mg/kg or more. Axonal degeneration occurred in male and female mice exposed to 2,100 and 4,200 ppm (equivalent to 380 and 900 mg/kg bodyweight in males and 530 and 1050 mg/kg bodyweight in females) and in females exposed to 1,000 ppm (equivalent to 230 mg/kg bw) in a 13-week feeding study. The lowest observed effect level (LOEL) for neurotoxicity (multifocal degeneration of the sciatic nerve) is therefore 100 mg/kg bodyweightand the NOAEL is 50 mg/kg bodyweight.

It is known from acute studies that significant interspecies differences in the toxicity of tricresyl phosphate exist and, from the repeat dose studies, that the mouse is more sensitive than the rat. The interpretation and extrapolation of rat and mouse data to humans must therefore be undertaken with extreme caution.

Given the limited nature of the neurotoxicity dataset available, in particular the absence of robust studies in hens to inform on potential delayed neuropathy potential of the various isomeric forms – in particular *ortho*-, *meta*- and *para*-cresyls – the information is inadequate to fully characterise the neurotoxic potential of tricresyl phosphate.

4.4.7 Mutagenicity

Studies in vitro

Studies on the genetic toxicology of tricresyl phosphate (mixed isomer preparation of 79 per cent tricresyl phosphate esters consisting of 21 per cent tri-*m*-cresyl phosphate, four per cent tri-*p*-cresyl phosphate and less than one per cent tri-*o*-cresyl phosphate plus other unidentified tricresyl phosphate esters) have been reported by NTP (1994). In addition, IUCLID (2001) lists a number of *in vitro* tests that are described as valid.

Genetic mutations

Tricresyl phosphate (at 100 to 10,000 µg/plate) was tested for the induction of gene mutations in *Salmonella typhimurium* strains TA98, TA100, TA1535 and TA1537 with and without S9 metabolic activation (Haworth *et al*. 1983, cited in NTP 1994). No induction of gene mutations was observed in any of the four tester strains. Similarly, negative results were obtained in two *Salmonella typhimurium* reverse mutation studies conducted to EPA guideline OTS 796.5265 but not to GLP, that are both cited in IUCLID (2001) as Litton Bionetics Inc. (1979c) and a further unreferenced study.

Chromosomal effects

In cytogenicity tests with cultured Chinese hamster ovary cells, tricresyl phosphate did not induce sister chromatid exchange or chromosomal aberrations, with or without Aroclor 1254-induced rat liver S9. The highest concentration of tricresyl phosphate tested in all trials except the sister chromatid exchange tests was 5,000 µg/ml. In the sister chromatid exchange assay conducted in the absence of S9, the highest concentration of tricresyl phosphate for which results could be obtained was 16 µg/ml. No tricresyl phosphate-induced cell cycle delay was observed in either of the assays (NTP 1994).

A number of other poorly reported tests cited in IUCLID (1998) were negative, except for a transformation assay in SHE cells (without metabolic activation) which yielded a positive result.

Mouse lymphoma assays conducted to EPA OTS 798.5375 (Litton Bionetics Inc. 1979b) and to EPA OTS 798.5300 (Litton Bionetics Inc. 1979d), both described in

IUCLID (2001) produced negative (tested at concentrations up to 0.01 ul/ml) or 'ambiguous' (tested up to 62 nl/ml) results. An additional test (Litton Bionetics Inc. 1979a, cited in IUCLID 2001) conducted to EPA OTS 795.2850 using a BALB/3T3 cell line, gave a positive result at test concentrations up to 0.04 µl/ml, without metabolic activation.

Studies in vivo

There is one *in vivo* genotoxicity study listed in IUCLID (1998). This was an unscheduled DNA synthesis test conducted in male rats administered tricresyl phosphate by gavage that gave a negative result (Mirsalis 1985).

Summary of mutagenicity

There is no indication from the studies available that tricresyl phosphate is mutagenic.

4.4.8 Carcinogenicity

Two-year feeding studies were conducted in F344/N rats and B6C3F1 mice (NTP 1994) using a mixed isomer preparation of 79 per cent tricresyl phosphate esters consisting of 21 per cent tri-*m*-cresyl phosphate, four per cent tri-*p*-cresyl phosphate and less than one per cent tri-*o*-cresyl phosphate (plus other unidentified tricresyl phosphate esters).

Groups of 95 male and 95 female rats were fed diets containing 0, 75, 150 or 300 ppm of tricresyl phosphate – estimated to deliver average daily doses of 0, 3, 6 or 13 mg/kg (males) and 0, 4, 7 or 15 mg/kg (females), respectively. An additional group of 95 male and 95 female rats were fed diets containing 600 ppm of tricresyl phosphate for 22 weeks and then received only control diet. After 3, 9, and 15 months exposure, up to 15 males and 15 females per group were evaluated for forelimb and hindlimb strength, then necropsied and evaluated for histopathological lesions. Survival of the exposed rats was similar to that of control animals and the final mean bodyweights of all exposed groups of male and female rats were also similar to controls. There were no chemical-related increased incidences of neoplasms.

In the mouse study, groups of 95 male and 95 female mice were fed diets containing 0, 60, 125 or 250 ppm of tricresyl phosphate – estimated to deliver average daily doses of 0, 7, 13 or 27 mg/kg (males) and 0, 8, 18 or 37 mg/kg (females), respectively. After 3, 9, and 15 months exposure, up to 15 males and 15 females per group were evaluated for forelimb and hindlimb strength, then necropsied and evaluated for histopathological lesions. Survival of exposed mice was similar to that of control animals and the final mean bodyweights of all exposed groups of male and female mice were also similar to controls. There were no chemical-related increased incidences of neoplasms.

4.4.9 Toxicity to reproduction

A high quality reproductive toxicity study on tricresyl phosphate (mixed isomers) has been performed on Swiss (SD-1) mice using a continuous breeding protocol (Chapin *et al*. 1988). Tricresyl phosphate was mixed into the feed at 0, 0.05, 0.1 and 0.2 per cent by weight. The test material comprised 75 per cent of pure and/or mixed tri-*o*-cresyl phosphate, tri-*m*-cresyl phosphate and tri-*p*-cresyl phosphate, with the remainder composed of dicresyl phenyl and di- and tri-cresylxylyl phosphates. The protocol

comprised four related elements: a 14-day range-finding study; a 98-day continuous breeding phase of the F_0 generation; a cross-over mating to determine the affected sex in the F_0 animals; and the fertility and performance of the last litter (F_1) from the continuous breeding.

Other relevant and informative studies on tricresyl phosphate mixed isomers and/or tri-*o*-cresyl phosphate have been conducted by Somkuti *et al.* (1987a, b), Carlton *et al*. (1987), Mele and Jensh (1977) and Tocco *et al.* (1987) – all cited in IPCS 1990 – and by Latendresse *et al*. (1994b) and Chapin *et al*. (1990) – cited in IUCLID 2001.

Fertility and reproductive toxicity

In the Chapin *et al*. (1988) study, although the fertility index did not change, the number of litters per pair decreased in a dose-related fashion and the proportion of pups born alive, and their weight, was significantly decreased in the high-dose group. The cross-over mating trial showed impaired fertility in both males and females exposed to 0.2 per cent tricresyl phosphate, with a greater effect in females. Histopathology of the F_0 pairs revealed dose-related seminiferous tubule atrophy and decreased testis and epididymal weights in the high-dose males, while the female reproductive tract showed no histological changes. There were dose-related changes in the adrenals of both sexes and bodyweight was depressed in both sexes at the highest concentration. The last litter born in the 98-day breeding phase was reared to 74 days and then mated within the control and two of the treatment groups (0.05 per cent and 0.1 per cent tricresyl phosphate). A decrease in fertility was observed in the 0.1 per cent tricresyl phosphate group. In the F_1 males at necropsy, sperm concentration and morphology were normal at termination, although motility was decreased in both the 0.05 per cent and the 0.1 per cent groups compared to controls. Functional neurologic impairment was not observed at any time in this study. The results indicate that at the doses tested, the tricresyl phosphate mixture was generally toxic to male and female mice, and there were functional and structural effects in the male reproductive system and functional reproductive impairment in females.

Carlton *et al*. (1987, cited in IPCS 1990) examined the reproductive effects of tricresyl phosphate (mixed isomers; below nine per cent tri-*o*-cresyl phosphate) in Long-Evans rats. Male rats received 0, 100 or 200 mg/kg and female rats received 0, 200 or 400 mg/kg test substance administered in corn oil by gavage. The low-dose males were mated with low-dose females and the high-dose males with low-dose females. Males were dosed for 56 days and females for 14 days prior to breeding and throughout the breeding period, gestation and lactation. Sperm concentration, motility and progressive movement were decreased in the high-dose males, and there was a dose-dependent increase in abnormal sperm morphology. The number of females delivering live young was severely reduced by tricresyl phosphate exposure. Histological changes were observed in the testes and epididymides of the treated males and in the ovaries of treated females.

In studies by Somkuti *et al.* (1987a, cited in IPCS 1990) tri-*o*-cresyl phosphate was tested for effects on the male reproductive tract in male Fisher 344 rats. Animals were dosed daily for 63 days at dose levels ranging from 10 to 100 mg/kg/day. Enzymatic, hormonal and sperm motility, density and morphology investigations indicated that tri-*o*-cresyl phosphate interfered directly with spermatogenic processes and sperm motility rather than via androgenic mechanisms or decreased vitamin E availability, and showed the threshold dose for observable testicular toxicity to be 10-25 mg/kg per day. Pathological changes in the testes were seen at doses above 25 mg/kg/day and included PAS-positive droplets, immature germ cells and multinucleate giant cells.

Further study by these authors (1987b, cited in IPCS 1990) showed that tri-*o*-cresyl phosphate administered at a dose level of 150 mg/kg/day for 21 days produces irreversible testicular toxicity (as measured by a number of parameters including spermatogenesis and sperm motility).

The study by Latendresse *et al*. (1994a, cited in IUCLID 2001), on Fischer 344 rats, employed a modified continuous breeding protocol using a naïve control group (20 breeding pairs), a vehicle control group (40 breeding pairs) and a 0.4 g/kg tricresyl phosphate group (20 breeding pairs). Rats were dosed for seven days prior to being paired and then dosed for a 63-day breeding period and throughout a 28-day post breeding interval. A crossover mating occurred between treated and control rats just after the post-breeding phase to determine sex-specific effects of treatment. Repeated exposure to 0.4 g/kg tricresyl phosphate resulted in a significant decrease in fertility index and number of litters per fertile pair. The number of live pups was also decreased in the tricresyl phosphate groups when compared to the control groups. The crossover phase showed no effects on the reproductive efficiency of tricresyl phosphate treated female rats, but treated male rats produced no litters. These male rats had significantly decreased testicular and epididymal weights. Since only one dose was used, a NOAEL was not established.

Chapin *et al*. (1990, cited in IUCLID 2001) conducted an *in vitro* toxicity study on Sertoli and Leydig cells from male Sprague-Dawley rats to investigate further the effects of tri-*o*-cresyl phosphate on male fertility. Cultured Leydig cells were shown to metabolize tri-*o*-cresyl phosphate to the active saligenin cyclic metabolite. Tri-*o*-cresyl phosphate decreased testosterone secretion from Leydig cells. Co-culture studies showed that Leydig cells activate tri-*o*-cresyl phosphate to the saligenin cyclic metabolite which then inhibits neurotoxic esterase in the Sertoli cells – indicating that tri-*o*-cresyl phosphate can be activated directly by the testis, which may explain why the testis is a target organ for tri-*o*-cresyl phosphate toxicity.

Developmental toxicity

In the study by Chapin *et al*. (1988) the last litter born in the 98-day breeding phase was reared to 74 days and then mated within the control and two of the treatment groups (0.05 per cent and 0.1 per cent tricresyl phosphate). A decreased proportion of liveborn and reduced number of liveborn pups per litter was observed.

Tocco *et al*. (1987, cited in IPCS 1990) tested the teratogenicity of tri-*o*-cresyl phosphate in Long-Evans rats treated with 87.5, 175 and 350 mg/kg per day throughout organogenesis from gestation days six to 18. Maternal deaths were greater than controls only in the high-dose group. Numerous soft tissue and skeletal malformations were observed in control and tri-*o*-cresyl phosphate-treated groups, with no significant intergroup differences in the frequency of malformations between the treated and control animals.

In a study by Mele and Jensh (1977, cited in IPCS 1990) which was primarily designed to investigate effects of prenatal treatment with tri-*o*-cresyl phosphate on postnatal behaviour, no abnormalities were reported in foetuses from pregnant Wister rats treated with 500 or 750 mg/kg on the 18^{th} and 19^{th} days of gestation.

In the study by Carlton *et al*. (1987, cited in IPCS 1990) described above, litter size and pup viability were decreased in the high-dose (400 mg/kg) group but pup bodyweight and developmental landmarks were unaffected by tricresyl phosphate exposure.

In the study by Latendresse *et al*. (1994a, cited in IUCLID 2001) described above, repeated exposure to 0.4 g/kg tricresyl phosphate resulted in a significant decrease in numbers of live births when both parents were continuously treated. In the crossover

phase, this parameter was not affected when treated females were considered but untreated females mated with treated male rats produced no litters.

Summary of toxicity to reproduction

Tricresyl phosphate induces functional and structural effects in the male reproductive system and functional reproductive impairment in females. Effects on fertility were noted at doses of 0.1 per cent or more in the feed. Observed male gonad pathologies included seminiferous tubule atrophy and decreased testis and epididymal weights at 0.05 per cent and above, with sperm motility reduced in both the 0.05 per cent and 0.1 per cent tricresyl phosphate groups compared to controls (Chapin *et al*. 1988).

In the study by Carlton *et al*. (1987, cited in IPCS 1990), sperm concentration, motility, and progressive movement were decreased in the males given 200 mg/kg tricresyl phosphate, and a dose-dependent increase in abnormal sperm morphology was observed. The number of females delivering live young was severely reduced by exposure to 200 mg/kg tricresyl phosphate or more. Histological changes were observed in the testes and epididymides of the treated males and in the ovaries of treated females at 200 mg/kg tricresyl phosphate or more.

Tri-*o*-cresyl phosphate has been shown to interfere with spermatogenic processes and sperm motility. The threshold dose for observable testicular toxicity is 10-25 mg/kg per day for 63 days, with irreversible testicular toxicity occurring at 150 mg/kg per day for 21 days (Somkuti *et al*. 1987a, b, cited in IPCS 1990).

Apart from effects on numbers of liveborn pups (probably related to maternal toxicity), no treatment-related developmental effects have been observed in any of the reproductive toxicity studies reported above.

The LOAEL for reproductive toxicity of tricresyl phosphate appears to be 0.05 per cent in the feed or 100 mg/kg/day. The LOAEL for tri-*o*-cresyl phosphate has been measured as 10-25 mg/kg/day.

4.4.10 NOAEL and Margins of Safety (MOS) for assessment of human exposure via the environment

Three key aspects of the toxicity profile for tricresyl phosphate could be considered when establishing the basis for deriving a PNEC: 1) reproductive toxicity potential; 2) evidence of neurotoxic potential from various studies; or 3) evidence from the two-year carcinogenicity studies in rodents.

Although neurotoxicity has been identified in some studies, there is some evidence that this may be largely attributable to the *ortho*-isomer, tri-*o*-cresyl phosphate. In the absence, or at very low inclusion levels, of this isomer, there is no conclusive evidence of any significant neurotoxicity from repeated exposure. However, in the absence of data from avian guideline studies, a conclusion cannot be reached on the potential for delayed polyneuropathy of the individual *o*-cresyl esters that may occur in tricresyl phosphate mixtures. Hence, the currently available database on this endpoint is considered inadequate to permit derivation of a NOAEL.

The key study relating to reproductive toxic effects (Chapin *et al*. 1988, cited in IUCLID 2001) is a continuous breeding study in which CD-1 mice were given 0, 0.05, 0.1 or 0.2 per cent tricresyl phosphate by weight in their diet, for seven days before being paired for a breeding period of 98 days (in which animals continued to be exposed to the test material in their diet). Reproductive parameters were recorded. At the end of the first breeding period, a crossover breeding study was conducted in which treated

males were mated with untreated (control) females, and *vice versa*. Tricresyl phosphate impaired fertility in both males and females at the highest dose, and reduced sperm motility at all doses. The NOAEL for females was 0.1 per cent tricresyl phosphate in the diet. However, a NOAEL for males could not be determined from this study, in which the lowest dose to produce an effect (on sperm motility) was 0.05 per cent (35 mg/kg bw/day) in the diet.

It is thus not possible to determine a definitive NOAEL for tricresyl phosphate for reproductive toxic potential because a NOAEL could not be established for both sexes for fertility. However, an overall margin of safety of 1,000 could be applied to the available LOAEL of 35 mg/kg bw/day for the protection of human health. This incorporates a factor of 10 for extrapolation from the LOAEL to a NOAEL, and factors of 10 for both inter- and intraspecies variation (with no factor for study duration). This would give an acceptable level of 0.035 mg/kg bw/day.

In the two-year mouse study (NTP 2004), groups of 95 male and 95 female mice were fed diets containing 0, 60, 125 or 250 ppm of tricresyl phosphate – estimated to deliver average daily doses of 0, 7, 13 or 27 mg/kg (males) and 0, 8, 18 or 37 mg/kg (females), respectively. Ceroid pigmentation of the adrenal cortex was noted for all groups of mice, including controls, throughout most of the two-year study. However, control mice and treated females receiving 60 or 125 ppm were not affected at the 3-month interim evaluation; the extent of the adrenal change appears to have been minor below 125 ppm. The incidence of clear cell foci, fatty change and ceroid pigmentation of the liver was significantly increased in male mice at 125 or 250 ppm, but not at 60 ppm.

While, under the TGD, the LOAEL for this study is therefore 60 ppm (adrenal changes, particularly in males, equivalent to 7 mg/kg bw/day), this is considered to probably represent a minor effect of uncertain significance to human health. It is therefore considered that a margin of safety of 100 would be appropriate, made up of factors of 10 for each of inter- and intraspecies variation, with no additional factor for extrapolation from LOAEL to NOAEL. No factor is needed for study duration. This would give an acceptable level of 0.07 mg/kg bw/day.

The more conservative of the two results is used here, that is, a LOAEL of 35 mg/kg bw/day with a margin of safety of 1,000. This is based on the assumption that current commercial products contain little if any *o*-cresol isomers.

4.4.11 Derivation of PNEC for secondary poisoning

Two LOAEL values are considered in the derivation of a margin of safety for the human health assessment. The same two values could form the basis of the PNEC for secondary poisoning. The LOAEL from the two-year mouse study is 7 mg/kg bw/day, equivalent to 60 ppm in food. The effects at this level, adrenal changes in males, are considered to be of relatively minor importance in humans and no additional factor to extrapolate to a NOAEL is used. The same approach is applied here; hence 60 ppm is taken as the NOEC. As this is a chronic study, an assessment factor of 30 is used, giving a PNEC of 2 mg/kg in food.

The LOAEL for reproductive effects is 0.05 per cent (500 ppm). For the human health assessment, a factor of 10 is applied to extrapolate from this to a NOAEL. Adopting the same approach here, a tentative NOEC of 50 ppm could be derived. This is also considered to be a chronic study; hence an assessment factor of 30 is appropriate, giving a PNEC of 1.7 mg/kg.

The lower of these two values, 1.7 mg/kg, is used in the risk characterisation for secondary poisoning.

4.5 Hazard classification

4.5.1 Classification for human health

Tricresyl phosphate is not currently included in Annex I of Directive 67/548/EEC. According to EU criteria, tricresyl phosphate should be classified as toxic by the oral route and harmful by the dermal and inhalation routes, and as a possible skin sensitizer.

According to the criteria of the EU, tricresyl phosphate also requires classification (Xn R48 – harmful) for specific organ system toxicity following repeated oral exposure as a LOAEL for adrenal pathology of 250 ppm in mice (equivalent to 45 mg/kg/bw or 65 mg/kg/bw for males and females, respectively) for 13 weeks and 60 ppm in mice (equivalent to 7 mg/kg/bw or 8 mg/kg/bw for males and females, respectively) for two years.

Tricresyl phosphate should also be classified as toxic to reproduction (Category 2) following repeated oral exposure, as tricresyl phosphate has been shown to induce functional and structural changes in the male reproductive system and functional reproductive impairment in females at doses of 0.1 per cent or more by diet.

According to EU criteria, tricresyl phosphate should not be classified as irritating or corrosive to the skin or eye, nor as mutagenic or a developmental toxicant.

There are no data to address effects via or during lactation. Therefore, it is not possible to make recommendations regarding classification for such effects.

4.5.2 Classification for the environment

Tricresyl phosphate is not currently included in Annex I of Directive 67/548/EEC. The current classification of tricresyl phosphate with regards to the environment is unclear. Some manufacturers do not appear to classify their products for environmental effects whereas some products appear to be classified as dangerous for the environment and with the following labelling:

N:	Dangerous for the environment.
R51/53:	Toxic to aquatic organisms. May cause long-term adverse effects in the aquatic environment.

The fish BCF for tricresyl phosphate is around 800 l/kg. Acute toxicity data are available for fish, invertebrates and algae. The lowest results from the more reliable standard tests are a 96-hour LC_{50} of 0.26 mg/l for fish (*Oncorhynchus mykiss*), a 48-hour EC_{50} of 0.27 mg/l for *Daphnia magna* and a 96-hour EC_{50} of 1.5 mg/l for the alga *Scenedesmus pannonicus*. The algal result is above the water solubility of the test substance. Based on these data the following classification is appropriate:

N:	Dangerous for the environment.
R50/53:	Very toxic to aquatic organisms. May cause long-term adverse effects in the aquatic environment.

4.6 PBT assessment

The criteria for persistence (P and vP), bioaccumulation potential (B and vB) and toxicity (T) included in the TGD are shown in Table 4.9.

Table 4.9 Criteria for identification of PBT and vPvB substances

Criterion	PBT criteria	vPvB criteria
P	Half-life above 60 days in marine water or above 40 days in freshwater* or half-life above 180 days in marine sediment or above 120 days in freshwater sediment*	Half-life above 60 days in marine water or freshwater or above 180 days in marine or freshwater sediment
B	BCF above 2,000	BCF above 5,000
T	Chronic NOEC below 0.01 mg/l or classification for certain human health end points, or endocrine-disrupting effects	Not applicable

Notes: * For the purpose of marine environment risk assessment, half-life data in freshwater and freshwater sediment can be overruled by data obtained in marine conditions.

Persistence: tricresyl phosphate is readily biodegradable (Section 3.1.1), which is considered equivalent to a half-life of less than 40 days in freshwater. Hence the substance does not meet the P criterion.

Bioconcentration: a value of 800 is selected from the available data in Section 3.1.3. Hence the substance does not meet the B criterion.

Toxicity: the lowest NOEC value from the available tests is 0.0032 mg/l; it may also be classifiable as a Category 2 reprotoxin. The substance therefore meets the T criterion.

The overall conclusion is that the substance meets the T criterion but does not meet the other two criteria, and so is not a PBT substance.

5 Risk characterisation

This section identifies the potential risks that tricresyl phosphate might pose for the freshwater and marine aquatic compartments, terrestrial compartment, air compartment and predatory organisms through secondary poisoning. The risk characterisation is performed by comparing the PECs with the PNECs to derive a risk characterisation ratio (RCR). An RCR of less than one implies that any risk resulting from that level of exposure is acceptable. An RCR above one implies a potential risk, and all such values are highlighted in bold in the following tables. Annex C considers the effect of a faster hydrolysis rate on the overall conclusions.

As discussed in Section 3.1.2, the adsorption potential of the substance (represented by the K_{oc}) is estimated, and this has a significant influence on its predicted partitioning behaviour in the environment. There is some evidence for triphenyl phosphate (see the risk evaluation report of that substance in this series) that the prediction method might underestimate the K_{oc} for this type of substance. On the other hand, test data for tricresyl phosphate suggest that the method may possibly overpredict the K_{oc}. A sensitivity analysis has been performed in Annex D, and this shows that a higher K_{oc} value would affect the conclusions, but not necessarily in a straightforward (or especially significant) way. Further testing for sediment sorption coefficient is suggested for triphenyl phosphate, and this could indicate a need for further studies with this substance.

5.1 Aquatic compartment

5.1.1 Surface water

A $PNEC_{water}$ of 0.032 μg/l is calculated for tricresyl phosphate. The resulting risk characterisation ratios are summarised in Table 5.1.

Table 5.1 Summary of risk characterisation ratios for surface water

Scenario		Predicted concentration (μg/l)	PEC/PNEC
Production of tricresyl phosphate		0.10 and 0.02	**3.03** and 0.75
Adhesives		negligible	negligible
Lubricant additive	Lubricant blending	7.34×10^{-3}	0.23
PVC – 1	Compounding	0.44	**13.8**
	Conversion	0.20	**6.16**
	Combined compounding and conversion	0.63	**19.6**
PVC – 2	Compounding	0.06	**1.82**
	Conversion	0.01	0.33
	Combined compounding and conversion	0.06	**1.97**
Photographic film	Compounding	0.27	**8.4**
	Conversion	0.03	0.93
	Combined compounding and conversion	0.29	**9.15**

Table 5.1 continued.

Scenario		Predicted concentration (μg/l)	PEC/PNEC
Polyurethane	Compounding	0.27	**8.4**
	Conversion	0.03	0.93
	Combined compounding and conversion	0.29	**9.15**
Pigment dispersions	Production of dispersions	0.36	**11.4**
Regional sources		5.75×10^{-3}	0.18

The PEC/PNEC ratios are above one for production of tricresyl phosphate at one site, for the combined compounding and conversion, and compounding steps in PVC, polyurethane and photographic film production, and for use in pigment dispersion. For one of the PVC scenarios, the conversion step is also above one. Further information is needed on process emissions to refine the PECs for these scenarios. The emission estimates are based on information for the industry area from the Emission Scenario Documents (OECD 2004a and 2004b) or from other risk assessments, so could be revised with more specific information for the substance itself.

The sensitivity analysis in Annex C suggests that a faster hydrolysis rate than assumed in this assessment would only have a small impact on surface water concentrations.

The PNEC for tricresyl phosphate is derived from a set of three long-term no effect concentrations and so will not be revised through further testing.

The risk to surface water from use in lubricants and at the regional level appears to be low.

5.1.2 Waste water treatment

The PNEC for waste water treatment processes is estimated to be above 100 mg/l. The resulting risk characterisation ratios are calculated to be below 0.01 for production and all uses of tricresyl phosphate. Therefore, they are not presented here.

Based on the risk characterisation ratios, no risk to waste water treatment plants would be expected from the production and use of tricresyl phosphate.

5.1.3 Sediment

The PNEC for sediment has been estimated as 0.0033 mg/kg wet weight. The resulting risk characterisation ratios, increased by a factor of 10 to take into account the possibility of direct ingestion of sediment-bound substance, are given in Table 5.2.

The PEC/PNEC ratios are above one for all local sources considered. Without the additional factor of 10 the results would be the same as for the water compartment and so most scenarios would still show a risk. The further information on exposure identified for the aquatic compartment would also have an influence on the sediment risk ratios.

The sediment PECs are relatively insensitive to the sediment degradation rate used (see Annex C).

Toxicity data for sediment organisms would allow a PNEC to be derived directly, and remove the need for the additional factor. It is likely that three long-term tests on

sediment organisms would be required. Both testing and better exposure information are likely to be needed to remove the risks that have been identified.

Based on the worst case assessment, there is also a risk to sediment from regional sources.

Table 5.2 Summary of risk characterisation ratios for sediment

Scenario		Predicted concentration (mg/kg wet wt)	PEC/PNEC
Production of tricresyl phosphate		0.01 and 2.48×10^{-3}	**30.3** and **7.49**
Adhesives		negligible	negligible
Lubricant additive	Lubricant blending	7.59×10^{-4}	**2.29**
PVC – 1	Compounding	0.05	**138**
	Conversion	0.02	**61.6**
	Combined compounding and conversion	0.06	**196**
PVC – 2	Compounding	6.04×10^{-3}	**18.2**
	Conversion	1.09×10^{-3}	**3.29**
	Combined compounding and conversion	6.53×10^{-3}	**19.7**
Photographic film	Compounding	0.03	**84**
	Conversion	3.07×10^{-3}	**9.27**
	Combined compounding and conversion	0.03	**91.5**
Polyurethane	Compounding	0.03	**84**
	Conversion	3.07×10^{-3}	**9.27**
	Combined compounding and conversion	0.03	**91.5**
Pigment dispersions	Production of dispersions	0.04	**114**
Regional sources		6.1×10^{-4}	**1.84**

5.2 Terrestrial compartment

The PNEC for soil is estimated to be 0.0027 mg/kg wet weight. The resulting risk characterisation ratios, increased by a factor of 10 to take into account the possibility of direct ingestion of sediment-bound substance, are summarised in Table 5.3.

The estimated risk characterisation ratios indicate a possible risk to soil from all local scenarios except for production of tricresyl phosphate and lubricant blending. The risk to agricultural soil and natural soil from regional sources appears to be low. However, a risk to industrial soil from regional sources has been identified.

Further information is needed on process emissions to refine the PECs for these scenarios as already noted for the aquatic compartment. Soil PECs are relatively insensitive to the soil degradation rate used (see Annex C).

The PNEC for soil is based on the equilibrium partitioning approach, and PEC/PNEC ratios have been increased by a factor of 10 to take into account the possibility of direct ingestion of soil-bound substance. Toxicity tests with soil organisms would allow the PNEC for this endpoint to be refined. As for sediment, testing on three species in long-term tests would probably be required. Note that many of the ratios above one would

remain above one without the application of the extra factor of ten, so a combination of effects and better exposure data would be needed to remove the risks identified.

Table 5.3 Summary of risk characterisation ratios for the terrestrial compartment

Scenario		Predicted concentration (mg/kg wet wt)	PEC/PNEC
Production of tricresyl phosphate		9.15×10^{-5}[a]	0.34
Adhesives		negligible	negligible
Lubricant additive	Lubricant blending	2.14×10^{-4}	0.80
PVC – 1	Compounding	0.03	**126**
	Conversion	0.01	**55.8**
	Combined compounding and conversion	0.05	**180**
PVC – 2	Compounding	4.15×10^{-3}	**15.6**
	Conversion	4.61×10^{-4}	**1.73**
	Combined compounding and conversion	4.52×10^{-3}	**16.9**
Photographic film	Compounding	0.02	**76.4**
	Conversion	1.94×10^{-3}	**7.27**
	Combined compounding and conversion	0.02	**83.4**
Polyurethane	Compounding	0.02	**76.4**
	Conversion	1.94×10^{-3}	**7.26**
	Combined compounding and conversion	0.02	**83.3**
Pigment dispersion	Production of dispersions	0.03	**104**
Regional sources	Agricultural soil	2.36×10^{-5}	0.09
	Natural soil	9.14×10^{-5}	0.34
	Industrial soil	3.8×10^{-4}	**1.41**

Notes: a) Sludge from the production site is not applied to agricultural soil.

5.3 Atmosphere

No information is available on the toxicity of tricresyl phosphate to plants and other organisms exposed via air. The low vapour pressure of the substance means that volatilisation to the atmosphere is likely to be limited and the resulting concentrations are likely to be low. The possibility of tricresyl phosphate contributing to atmospheric effects such as global warming and acid rain is likely to be small. In addition, as the substance does not contain halogen atoms, it will not contribute to ozone depletion.

5.4 Secondary poisoning

A PNEC for secondary poisoning of 1.7 mg/kg food is derived for tricresyl phosphate. The resulting risk characterisation ratios are summarised in Table 5.4.

Based on the risk characterisation ratios, no risk from secondary poisoning would be expected from the production and use of tricresyl phosphate. However, the PNEC for

secondary poisoning is considered provisional in the absence of reliable data on neurotoxicity.

Table 5.4 Summary of risk characterisation ratios for secondary poisoning

Scenario		Fish food chain		Earthworm food chain	
		PEC (mg/kg)	PEC/PNEC	PEC (mg/kg)	PEC/PNEC
Production of tricresyl phosphate		0.04 and 0.01	0.02 and <0.01	9.65×10^{-4}[a]	<0.01
Adhesives		negligible	negligible	negligible	negligible
Lubricant additive	Lubricant blending	4.93×10^{-3}	<0.01	1.3×10^{-3}	<0.01
PVC – 1	Compounding	0.15	0.09	0.09	0.06
	Conversion	0.07	0.04	0.04	0.03
	Combined compounding and conversion	0.21	0.13	0.13	0.08
PVC – 2	Compounding	4.65×10^{-3}	<0.01	0.01	<0.01
	Conversion	6.51×10^{-3}	<0.01	1.99×10^{-3}	<0.01
	Combined compounding and conversion	0.02	0.01	0.01	<0.01
Photographic film	Compounding	0.09	0.05	0.06	0.03
	Conversion	0.01	<0.01	6.06×10^{-3}	<0.01
	Combined compounding and conversion	0.1	0.06	0.06	0.04
Polyurethane	Compounding	8.92×10^{-3}	<0.01	0.06	0.03
	Conversion	4.99×10^{-3}	<0.01	6.04×10^{-3}	<0.01
	Combined compounding and conversion	9.23×10^{-3}	<0.01	0.06	0.04
Pigment dispersions	Production of dispersions	0.12	0.07	0.08	0.05

5.5 Risk characterisation for human exposure via the environment

A LOAEL of 35 mg/kg bw/day in rats was identified in Section 4.4.10 as the most appropriate value for use in this assessment. A margin of safety of at least 1,000 is considered necessary to provide sufficient reassurance against effects on human health with this result (see Section 4.4.10). The estimated human exposures via the environment were calculated in Section 3.3.4 and are included in Table 5.5 together with the resulting margins of safety.

Table 5.5 Margin of exposure

Scenario		Total daily human intake (mg/kg bw/day)	Margin of exposure
Production of tricresyl phosphate		1.57×10^{-4} and 5.64×10^{-5}	223,000 and 620,600
Adhesives		negligible	-
Lubricant additive	Lubricant blending	4.05×10^{-5}	864,200
PVC – 1	Combined compounding and conversion	2.38×10^{-3}	14,700
	Compounding	1.35×10^{-3}	25,930
	Conversion	1.06×10^{-3}	33,020
PVC – 2	Combined compounding and conversion	2.21×10^{-4}	158,400
	Compounding	1.27×10^{-4}	275,600
	Conversion	6.58×10^{-5}	531,900
Photographic film	Combined compounding and conversion	9.6×10^{-4}	36,460
	Compounding	8.33×10^{-4}	42,020
	Conversion	1.64×10^{-4}	21,300
Polyurethane	Combined compounding and conversion	5.51×10^{-4}	63,520
	Compounding	5.05×10^{-4}	69,310
	Conversion	8.2×10^{-5}	426,800
Pigment dispersions	Production of dispersions	1.34×10^{-3}	25,930
Regional sources		3.21×10^{-5}	1,090,000

All of the margins of safety are well above the required value, and so no risks are indicated for any scenario.

5.6 Marine risk assessment

Although a PEC/PNEC approach can be applied to the marine environment, there are additional concerns which may not be adequately addressed using the same methods as above. Chief among these concerns is the possibility that hazardous substances may accumulate in parts of the marine environment. The effects of such accumulation are unpredictable in the long term, and once such accumulation has occurred it may be practically difficult to reverse. The properties which lead to substances behaving in this way also lead to greater uncertainty in estimating exposures and/or effect concentrations, and so make a quantitative risk assessment more difficult. In order to identify substances which are likely to behave in this way, criteria have been developed relating to the persistence, accumulation and toxicity of the substance. The first part of the marine assessment is therefore a comparison of the properties of the substance with these criteria. This is presented in Section 4.6.

The PEC values for the marine assessment are presented in Sections 3.3.1 and 3.3.4. These have been calculated using EUSES. PNECs for marine aquatic species are included in Section 4.1.6. The PNEC for secondary poisoning for the marine environment is the same as that for the freshwater fish and terrestrial food chains (4.1.6). The resulting PEC/PNEC ratios are in Table 5.6.

Table 5.6 Summary of risk characterisation ratios for the marine compartment

Scenario		PEC/PNEC ratio			
		Local marine compartment	**Local marine sediment compartment**	**Fish-eating birds and mammals**	**Top predators**
Lubricant additive	Blending of lubricant	0.69	**6.87**	<0.01	<0.01
Adhesives		negligible	negligible	negligible	negligible
PVC – 1	Compounding	**141**	**1,410**	0.09	0.02
	Conversion	**62.2**	**622**	0.04	<0.01
	Combined compounding and conversion	**202**	**2,020**	0.13	0.03
PVC – 2	Compounding	**17.2**	**172**	<0.01	<0.01
	Conversion	**1.72**	**17.2**	<0.01	<0.01
	Combined compounding and conversion	**18.8**	**188**	0.01	<0.01
Photo-graphic film	Compounding	**85.5**	**855**	0.05	0.01
	Conversion	**7.93**	**79.3**	<0.01	<0.01
	Combined compounding and conversion	**93.3**	**933**	0.06	0.01
Poly-urethane	Compounding	**85.5**	**855**	<0.01	<0.01
	Conversion	**7.93**	**79.3**	<0.01	<0.01
	Combined compounding and conversion	**93.3**	**933**	<0.01	<0.01
Pigment dispersion	Production of dispersions	**117**	**1,170**	0.07	0.02

Risks are indicated for all scenarios for marine waters and marine sediments. The regional concentration in marine waters does not indicate a risk. Based on the worst case assessment, there is a risk to marine sediment from regional sources, although it the PEC/PNEC ratio is only slightly above one (1.04).

Further information on process emissions indicated for the freshwater environment would also help to refine these conclusions. More specifically for the marine assessment, information on whether any of these processes can be considered not to discharge to the marine environment, or if they only do so after effluent treatment (the calculations above assume a direct discharge to the marine environment without waste water treatment) would be useful.

Testing on freshwater organisms is not indicated for the freshwater assessment. Testing on sediment organisms would be of more value for the marine sediment assessment. There is also the possibility of testing on marine species, which would allow the assessment factor to be reduced.

The size of the PEC/PNEC ratios suggests that no one part of the further information requirements would be sufficient on its own to reduce the ratios to below one.

The marine food chain risks would need to be reassessed once more reliable information on neurotoxicity becomes available.

6 Conclusions

Tricresyl phosphate can enter the environment from its production and use, and from the use of articles made from materials containing it. Based on the available information, potential risks are identified for all of the life cycle steps for one or more of the protection goals. The overall conclusions are summarised in Table 6.1 in a simplified form. In particular, the different steps within the use of each material have been combined here, and risks are indicated for PVC provided at least one of the different uses shows a risk for the specific protection goal. Section 5 should be consulted for the detailed results.

Table 6.1 Summarised potential environmental risks identified for tricresyl phosphate

Life cycle stage	Surface water	Sediment	WWTP	Air	Soil	Aquatic food chain	Terrestrial food chain	Marine water	Marine sediment
Production	✸[a]	✸	-	-	-	-	-	-	-
Adhesives	-	-	-	-	✸	-	-	-	-
Lubricant additive	-	✸	-	-	✸	-	-	-	✸
PVC	✸	✸	-	-	✸	-	-	✸	✸
Photographic film	✸	✸	-	-	✸	-	-	✸	✸
Polyurethane	✸	✸	-	-	✸	-	-	✸	✸
Pigment dispersions	✸	✸	-	-	✸	-	-	✸	✸
Regional	-	-	-	-	-	-	-	-	-

Notes: a) for one site

There are no risks for humans exposed via the environment, and no risks for marine food chain exposure for any of the life cycle stages.

Some monitoring data are available which show elevated levels of tricresyl phosphate near to sources of release; however, these are mostly older data and cannot be related to current activities.

The potential risks that have been identified could be reassessed following additional work, in particular:

- Collation of further site and industry-specific information on releases of tricresyl phosphate from use in the different types of materials indicated. This work could include:
    - Improved description of practices at sites using tricresyl phosphate, to determine the realism of the emission estimates, ideally through surveys of representative sites.
    - Targeted monitoring to confirm or replace the calculated PEC values (especially in water, sediment and WWTP sludge). Further environmental monitoring for tricresyl phosphate is taking place in England and Wales, at one WWTP per Environment Agency region, in both final effluent and associated receiving waters (6 samples at 4 week intervals). The sites are different from those used in the previous monitoring exercise. Sampling is expected to take place from September 2008 until March 2009.

    - Information on the fate of sludges from sites using the substance.
    - Surveys to locate user sites, especially in relation to marine discharges.
- Long-term sediment and soil organism testing.
- Studies on the fate of the substance in WWTP (municipal and industrial).
- Clarification of some aspects of the mammalian toxicity data (see Appendix 1).

A possible risk to aquatic organisms is identified for one production site. This conclusion could be refined through the work indicated above, but it is considered more appropriate for the local control authorities to consider this outcome.

There may be opportunities to read across information and test results from this substance to the other aryl phosphates assessed in this group (and vice versa). Therefore the additional work indicated above should be considered in relation to that proposed for other members of the group. The overview document should be consulted for more information on this.

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8 Glossary of terms

Term	Description
Biochemical oxygen demand (BOD)	A measure of degradation potential
Bioconcentration factor (BCF)	A measure of chemical uptake, being the ratio between the concentration in an organism and the concentration in an environmental compartment (usually water)
CAS number (no.)	An identifying code number assigned to chemicals by the Chemical Abstract Services. The CAS number is a generally recognised identification reference for a chemical; a substance can have more than one such number
Inherently biodegradable	Some potential for environmental degradation to carbon dioxide and water, and so on, as measured by laboratory screening tests involving microorganisms
Lowest observed effect concentration (LOEC)	The lowest concentration in a toxicity test that gives rise to adverse effects (relative to a control)
Median effective concentration (EC_{50})	The concentration in a toxicity test at which a particular effect is observed in half of the organisms exposed for a specified time
Median lethal loading (LL_{50})	The loading of substance in a water-accommodated fraction that leads to death in half of the organisms exposed for a specified time
Median lethal concentration/dose (LC/D_{50})	The concentration in a toxicity test that can be expected to cause death in half of the organisms exposed for a specified time
No observed effect concentration (NOEC)	The highest concentration in a toxicity test that does not give rise to adverse effects (relative to a control)
Octanol-water partition coefficient (K_{ow})	This parameter gives an indication of the partitioning behaviour of a substance between water and lipid-containing materials such as cell membranes or organic matter in soils and sediments
Readily biodegradable	Rapid environmental degradation to carbon dioxide and water, and so on, as measured by laboratory screening tests involving microorganisms

9 Abbreviations

Acronym	Description
B	Bioaccumulation
BCF	Bioconcentration factor
BMF	Biomagnification factor
BOD	Biochemical oxygen demand
bw	Bodyweight
CAS	Chemical Abstract Services
CMR	Carcinogenic, mutagenic and toxic to reproduction
DEHP	Di(2-ethylhexylphthalate)
DIN	Deutsche Industrie Norm (German norm)
DSC	Differential scanning calorimetry
EC	European Communities
EC_{50}	Median effect concentration
EC_x	As EC_{50}, but for x% effect; x usually being 0, 10, or 100
ECB	European Chemicals Bureau
EEC	European Economic Communities
EINECS	European Inventory of Existing Commercial Chemical Substances – this lists all chemical substances that were supplied to the market prior to 18th September 1981
EPA	Environmental Protection Agency (USA)
ESD	Emission Scenario Document
ESR	The Existing Substances Regulation – Council Regulation (EEC) 793/93 on the evaluation and control of the risks of 'existing' substances.
EU	European Union
EUSES	European Union System for the Evaluation of Substances (software tool in support of the TGD on risk assessment)
HPLC	High performance liquid chromatography
HPTLC	High performance thin layer chromatography
HPV	High Production Volume (supply above 1,000 tonnes/year)
IUCLID	International Uniform Chemical Information Database: contains non-validated tonnage, use pattern, property and hazard information for chemicals, submitted by industry under the Existing Substances Regulation (ESR)
K_{oc}	Organic carbon normalised distribution coefficient
K_{ow}	Octanol-water partition coefficient
Kp	Solids-water partition coefficient
$L(E)C_{50}$	Median lethal (effect) concentration

LD_{50}	Median lethal dose
LL_{50}	Median lethal loading
LO(A)EL	Lowest observed (adverse) effect level
log K_{ow}	Log of the octanol-water partition coefficient (K_{ow})
NO(A)EL	No observed (adverse) effect level
NOEC	No observed effect concentration
n.t.p.	Normal temperature and pressure
NTP	US National Toxicology Program
OECD	Organisation for Economic Cooperation and Development
P	Persistent
PBT	Persistent, bioaccumulative and toxic
PEC	Predicted environmental concentration
pH	Logarithm (to the base 10) of the hydrogen ion concentration [H+]
pK_a	Logarithm (to the base 10) of the acid dissociation constant
PNEC	Predicted no effect concentration
ppm	Parts per million
SCAS	Semi-continuous activated sludge unit
STP	Sewage treatment plant
TCP	Tricresyl phosphate
TGA	Thermogravimetric analysis
TGD	Technical Guidance Document
USEPA	Environmental Protection Agency, USA
UV	Ultraviolet region of the electromagnetic spectrum
vB	Very bioaccumulative
vP	Very persistent
vPvB	Very persistent and very bioaccumulative
wt	Weight
wwt	Wet weight
WWTP	Wastewater treatment plant

10 Data collection and peer review process

This report has been produced using publicly available data gathered and assessed by the contractor for the Environment Agency. Additional information has been submitted voluntarily by member companies of the Phosphate Ester Flame Retardant Consortium (PEFRC, http://www.pefrcnet.org/), and the Environment Agency would like to thank them for their cooperation.

The Environment Agency has been keen to ensure that the data used in this report are as complete and accurate as possible. Original reports and literature articles for key studies were retrieved and assessed for reliability wherever possible (it is clearly indicated where this was not the case).

The main scientific literature search was performed in 2002, with some further limited searching to consider specific issues up to 2007.

Drafts of this report have been circulated to key stakeholders in UK and European Industry for comment on several occasions, as well as members of the UK and European chemical regulatory community in July 2007. The Advisory Committee on Hazardous Substances has also provided helpful comments as part of its own deliberations on this substance group (their last review was in September 2007).

In addition, certain technical aspects of the report were peer-reviewed by an independent expert group set up by the Environment Agency for this purpose in April 2007. The experts were:

- Dr Kay Fox (independent consultant);
- Dr Tamara Galloway (University of Plymouth).

Their comments have not been published but are available on request. All comments received have been addressed in the final report where appropriate.

The Institute for Environment and Health wrote the human health effects assessment, and this was peer-reviewed by colleagues at the Health and Safety Executive and Health Protection Agency.

Appendix 1 Points for clarification on mammalian toxicity data

The following points address uncertainties in the mammalian data (Section 4.4), and may lead to revision of the assessment of human exposure via the environment, and of the classification, if addressed.

- The information presented in the IUCLID files on the irritancy and sensitization potential of tricresyl phosphate is limited. In particular, further information relating to the composition of the material used in the human patch tests in IUCLID (1998), and any available experimental information that may inform on the sensitizing potential of this compound, would be useful.
- If available, any information on the actual isomeric composition of the test material used in the study by Banerjee *et al.* (1992) would be valuable, as would information on the intakes achieved in this study.
- Given the complexity of establishing the neurotoxic potential of the various isomers of tricresyl phosphate, further details on the hen neurotoxicity studies reported in IUCLID (1998), would be useful. In particular, there do not appear to be any robust data on the properties of substances containing both *ortho*- and *meta*- or *para*-cresyl residues within one phosphate ester. Consideration could also be given to undertaking mechanistic (*in vitro*) studies to confirm the relative neurotoxic potential of each isomer, and the doses at which they would be expected to exert such toxicity.
- The study reported on Page 18 of IUCLID (2001), in between the reports of study references 22 and 21, has no reference.
- For the study by Haworth *et al*. (1983, cited in NTP 1994), information on the isomeric composition of the test material used, and any information on the use (and results) of any positive controls employed in the *Salmonella typhimurium* assays would be helpful.
- For the 28-day feeding study in rats (see Ref 14 of IUCLID, 2001), further information on the case of death of the animals in the group given 0.1 per cent in the diet would help to justify that this is a NOEL level.
- In the study by Carlton *et al*. (1987, cited in IPCS 1990), please advise if any postnatal (lactation period) investigations were undertaken that might inform on the developmental toxicity potential of the test material.
- It is not clear whether the publication cited in IUCLID (1998) as Hine *et al.*, 1943, J. Pharmacol. Exp. Therap, 79, 227-236, is in fact Hine, C.H., Dunlap, M.K., Rice, E.G., Coursey, M.M., Gross, R.M. and Anderson, H.H. (1956) *The neurotoxicity and anticholinesterase properties of some substituted phenyl phosphates*. J. Pharmacol. Exp. Ther., 116, 227-236.
- Similarly, it is not clear whether the publication cited in IUCLID (1998) as Mirsalis, J. *et al.*, 1985, EnvMutag. 5, 482, is in fact Mirsalis, J., Tyson, K., Beck, J., Loh, E., Steinmetz, K., Contreras, C., Austere, L., Martin, S. and Spalding, J. (1983) *Induction of unscheduled DNA synthesis (UDS) in hepatocytes following in vitro and in vivo treatment* (Abstract No. Ef-5), Environ. Mutag., 5, 482.

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