

FOREWORD

INTRODUCTION

TRIPHENYL PHOSPHATE

CAS N°: 115-86-6

SIDS Initial Assessment Report

For

SIAM 15

Boston, Massachusetts; 22 – 25 October 2002

- 1. Chemical Name:** Triphenyl phosphate
- 2. CAS Number:** 115-86-6
- 3. Sponsor Country:** Germany
Contact Point:
BMU (Bundesministerium für Umwelt, Naturschutz und
Reaktorsicherheit)
Contact person: Prof. Dr. Ulrich Schlottmann
Postfach 12 06 29
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- 4. Shared Partnership with:**
- 5. Roles/Responsibilities of the Partners:**
 - Name of industry sponsor /consortium Bayer AG, Germany
Contact person:
Dr. Burkhardt Stock
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 - Process used see next page
- 6. Sponsorship History**
 - How was the chemical or category brought into the OECD HPV Chemicals Programme? by ICCA-Initiative
- 7. Review Process Prior to the SIAM:** last literature search (update):
17 May 2002 (Human Health): databases medline, topline;
search profile CAS-No. and special search terms
27 May 2002 (Ecotoxicology): databases CA, biosis; search
profile CAS-No. and special search terms
- 8. Quality check process:** As basis for the SIDS-Dossier the IUCLID was used. All data
have been checked and validated by BUA.
- 9. Date of Submission:** 20 August 2002
- 10. Date of last Update:**

11. Comments:

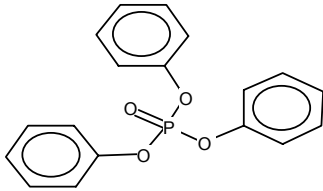
OECD/ICCA - The BUA* Peer Review Process

Qualified BUA personnel (toxicologists, ecotoxicologists) perform a quality control on the full SIDS dossier submitted by industry. This quality control process follows internal BUA guidelines/instructions for the OECD/ICCA peer review process and includes:

- a full (or update) literature search to verify completeness of data provided by industry in the IUCLID/HEDSET
 - Review of data and assessment of the quality of data
 - Review of data evaluation
 - Check of adequacy of selection process for key studies for OECD endpoints, and, where relevant, for non-OECD endpoints by checking original reports/publications
 - Review of key study description according robust summaries requirements; completeness and correctness is checked against original reports/publications (if original reports are missing: reliability (4), i.e. reliability not assignable)
 - Review of validity of structure-activity relationships
 - Review of full SIDS dossier (including SIAR, SIAP and proposal for conclusion and recommendation for further work)
- In case of data gaps, review of testing plan or rationale for not testing

* BUA (GDCh-Beratergremium für Altstoffe): Advisory Committee on Existing Chemicals of the Association of German Chemists (GDCh)

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	115-86-6
Chemical Name	Triphenyl phosphate
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR**Human Health**

Triphenyl-phosphate (TPP) is degraded by hydrolysis in rat liver homogenate to diphenyl-phosphate as the major metabolite. Acute toxicity after oral and dermal administration is very low: acute oral administration in rats, mice, rabbits and guinea pigs produced LD50 values in a range of 3000 to above 20 000 mg/kg bw. Only one study in mice with limited documentation gave a value of 1320 mg/kg bw. After dermal application an LD50 of above 7900 mg/kg bw was established in rabbits. No valid studies are available regarding the inhalation of triphenyl phosphate. Triphenyl phosphate is not irritant to the skin. The irritation potential of triphenyl phosphate on the mucous membrane of the eye is very low. No animal data regarding skin sensitisation are available. There are few human case reports showing evidence of skin sensitisation. The incidence of skin sensitisation is very low.

Based on the available data the toxicity after repeated oral treatment of rats with triphenyl phosphate was low. A 35 day study using doses of up to 350 mg/kg bw/day produced a slight depression of body weight gain and an increase of liver weights at the highest dose. An estimated dose of ~ 70 mg/kg bw/day was without any effect. Three studies for 4 month with doses of up to 1% in the diet (~ 700 mg/kg bw/day) confirmed the effect on growth. Whereas in two studies body weight gain was depressed only at the highest dose of 1 %, in another study a decrease was observed even at 0.5 %. The general well being as well as neurotoxic or immunotoxic parameters were not affected in all dose groups. Therefore the overall NOEL for these studies is 161 mg/kg bw/day due to reduced body weight gain. The low toxicity was confirmed also after dermal exposure of 100 and 1000 mg/kg bw/day in rabbits for 15 days without any sign of toxicity besides a depression of acetylcholinesterase as the only dose related effect. The toxicological relevance of this effect is hard to evaluate since quantitative data as well as the purity of the test material are not available.

Neurotoxicity is a potential adverse effect of many organophosphates. In available studies in hens and cats pure triphenyl phosphate did not induce immediate nor delayed neuropathy. The findings of a decreased activity of choline esterase and paralysis predominantly in cats in older studies indicating a neurotoxic potential were not reproduced in later studies and may be due to contamination of the tested samples by other organophosphorus esters. At the high doses of triphenyl phosphate used even small concentrations of impurities might have sufficient activity.

Tests for gene mutations in bacterial as well as yeast and mammalian cells did not reveal any sign of mutagenicity. An UDS-test in syrian hamster fibroblast cells showed no genotoxic effect. There is no test concerning chromosomal aberration.

There are no findings indicating any adverse effects on fertility or the development of the fetus up to the highest tested dose level of 1% in the diet (~ 700 mg/kg bw/day) in the rat treated for 4 months during gametogenesis prior to mating and throughout mating and gestation.

The mouse lung adenoma assay gave no indication of a carcinogenic potential.

Environment

Triphenyl phosphate has a solubility in water between 0.2 mg/l (river water) and 1.9 mg/l (distilled water) at 20 °C, a vapour pressure of 0.000835 Pa at 25 °C and a log Kow of 4.6. According to a Mackay Level I model calculation, triphenyl phosphate is mainly distributed to soil (43.9 %) and sediment (41.0 %), and to a lesser extent to water (14.3 %) and air (0.7 %). Triphenyl phosphate is hardly volatile from aqueous solution (calculated Henry constant: 0.018 - 0.036 Pa · m³/mol). The substance is strongly adsorbed to soil and sediment (measured Koc-values in the range of 2514 – 3561). In the atmosphere rapid degradation of triphenyl phosphate via indirect photolysis occurs ($t_{1/2\text{air}}$: ca. 12 h). While triphenyl phosphate is relatively stable under neutral and acidic conditions ($t_{1/2}$ = 19 d at pH 7; $t_{1/2}$ > 28 d at pH 5), it undergoes hydrolysis under alkaline conditions ($t_{1/2}$ = 7.5 d at pH 8.2; $t_{1/2}$ = 1.3 d at pH 9.5). In soil DT₅₀ for primary degradation is 37 and 21 days under aerobic and anaerobic test conditions, respectively. Triphenyl phosphate is readily biodegradable (83 - 94% degradation after 28 d). Under anaerobic conditions with river sediment ca. 90 % triphenyl phosphate were primary degraded after 40 days of incubation. Mineralisation was about 22 % after 40 days. Measured bioconcentration factors in fish were in the range of 110 - 144, indicating a moderate bioaccumulation potential. As the BCF values are related to the parent compound, there is no information on possible accumulation of stable metabolites. BCFs for *Lemna minor* and *Typha sp.* are stated to be < 50. As the substance was found in dolphins collected in the Gulf of Mexico, accumulation via the food chain may occur.

The acute toxicity has been determined for fish (*Oncorhynchus mykiss*: 96 h-LC₅₀ = 0.4 mg/l) and invertebrates (*Mysidopsis bahia*: 96 h-EC₅₀ > 0.18 - 0.32 mg/l, *Daphnia magna*: 48 h-EC₅₀ = 1.0 mg/l). In tests with algae (*Selenastrum capricornutum*, *Scenedesmus subspicatus*, *Chlorella vulgaris*) NOEC values in the range of 0.25 - 2.5 mg/l were obtained after exposure periods of 96 h. In long term tests with fish (*Oncorhynchus mykiss*) a 30 d - EC10 of 0.037 mg/l was found. A PNECaqua = 0.74 µg/l is derived from the aforementioned long term NOEC using an assessment factor of 50.

Exposure

The world wide (excluding East Europe) production of triphenyl phosphate is estimated to about 20 000 to 30 000 tonnes by approx. 15 producers in the year 2000. Major application areas for triphenyl phosphate are the use as a flame retardant in PVC (about 50 %) where it has also plasticizing properties, but also as a flame retardant in other polymers (about 22 %) and printed circuit boards (about 11 %), and in photographic films (about 7 %). Minor areas (about 10 %) are covered by the use of triphenyl phosphate in hydraulic liquids (main area), and adhesives, inks, and coatings (minor area).

RECOMMENDATION

Human Health: The chemical is currently of low priority for further work.

Environment: The chemical is a candidate for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health: The chemical is currently of low priority for further work based on a low hazard potential.

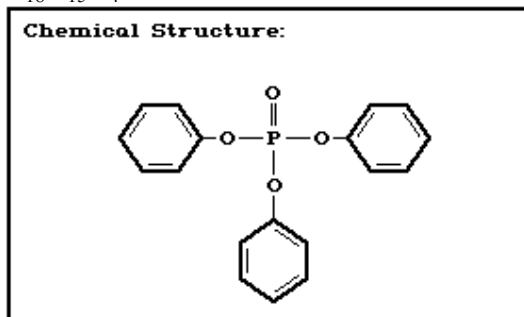
Environment: Triphenyl phosphate has a wide dispersive use as flame retardant. Environmental releases are likely to occur during production, during the use as flame retardant e.g. in polymer applications as well as during the service life and the disposal of products containing the substance. Also accidental spill and leakage of hydraulic liquids in different application areas can be a source of environmental release. However, no exposure information is available, except for the production at the sponsor company. Triphenyl phosphate is highly toxic to aquatic organisms (LC50 < 1 mg/l for fish, PNECaqua = 0.74 µg/l) and has a potential to accumulate in biota. Therefore, an exposure assessment and, if then indicated, an environmental risk assessment is recommended. Environmental exposure during production at the Sponsor company is adequately controlled.

SIDS Initial Assessment Report

1 IDENTITY

1.1 Identification of the Substance

CAS Number: 115-86-6
 IUPAC Name: Triphenyl phosphate / TPP
 Molecular Formula: $C_{18}H_{15}O_4P$
 Structural Formula:



Molecular Weight:

Synonyms:

Phosphoric acid, triphenyl ester

1.2 Purity/Impurities/Additives

The purity of the substance is given with $\geq 99.6\%$ w/w (Bayer AG, 2002a).

1.3 Physico-Chemical properties

Triphenyl phosphate is a solid substance at room temperature with a melting point of about 48 - 50 °C and a boiling point of 245 °C (at 14.6 hPa) (Merck Index, 1996). With a density of 1.2055 g/cm³ at 50 °C triphenyl phosphate is heavier than water (Lide, 1995). The vapour pressure has been measured and extrapolated to 25 °C with 0.000835 Pa (Dobry and Keller, 1957). Log K_{ow} is measured with 4.6 (Saeger et al., 1979).

In older literature, triphenyl phosphate is said to be insoluble in water. The substance's solubility has been determined taking several testing options into account:

distilled water:	1.9 mg/l at 20 °C	(Saeger et al., 1979)
buffered dist. water (pH 4.5 - 9.5):	1.4 - 1.6 mg/l at 21 °C	(Howard and Deo, 1979)
lake/river water (pH 7.8 - 8.2):	0.2 - 0.3 mg/l at 21 °C	(Howard and Deo, 1979)
seawater (pH 7.6 - 8)	0.1 - 0.6 mg/l at 15 °C	(Hill and Morgan, 1988)

Triphenyl phosphate shows pH dependent hydrolysis to diphenyl phosphate and phenol (Howard and Deo, 1979) in distilled water:

pH 5:	$t_{1/2} > 28$ d at 25 °C	(Mayer et al., 1981)
pH 7:	$t_{1/2} = 19$ d at 25 °C	(Mayer et al., 1981)
pH 8.2:	$t_{1/2} = 7.5$ d at 21 °C	(Howard and Deo, 1979)
pH 9:	$t_{1/2} = 3$ d at 25 °C	(Mayer et al., 1981)
pH 9.5:	$t_{1/2} = 1.3$ d at 21 °C	(Howard and Deo, 1979)

2 GENERAL INFORMATION ON EXPOSURE

Triphenyl phosphate is manufactured by an endothermic reaction of phenol with phosphorus oxychloride. Subsequent distillation leads to purification of triphenyl phosphate (Bayer AG, 2002a).

Environmental Releases

Releases into the environment may occur during production of triphenyl phosphate, during its use as a flame retardant in polymer and other applications as well as during the service life and waste disposal of products containing triphenyl phosphate as flame retardant. Also accidental spill and leakage of hydraulic liquids in different application areas can be a source of environmental contamination

Readily available information on exposure from production of the chemical in the sponsor country at Bayer AG is stated in the following.

Waste water leaving the production facility is lead into an industrial biological waste water treatment plant (WWTP). Triphenyl phosphate is monitored daily at the outlet of the WWTP with a routine determination limit. No triphenyl phosphate had been detected with the determination limit of 20 µg/l. As worst case for the receiving water a PEC of < 0.03 µg/l is calculated, taking the determination limit of 20 µg/l, the dilution factor (700), and the 10 percentile of the receiving river low flow (1050 m³/s) into account. Sewage sludge from the industrial WWTP is burnt. Thus there is no emission to the geosphere by sludge application. The exhaust from production of triphenyl phosphate is connected to filters as well as air washers. Thus during normal operation no triphenyl phosphate is emitted. Following the last Official Emission Declaration in 2000 less than 25 kg/a triphenyl phosphate were emitted into the atmosphere (Bayer AG, 2002a).

No data about releases at other production or processing/application sites or from products during their life-cycle are available.

Monitoring

Monitoring data of indoor air sampling at residential and public buildings showed triphenyl phosphate concentrations of 0.1 µg/m³ at maximum in Sweden (Carlsson et al. 1997), Germany (Hansen et al. 2001), and Japan (Otake et al. 2001).

Triphenyl phosphate was found in the inlet and outlet of a wastewater treatment plant and in several sampling sites in the Delaware river, which was the receiving water of effluent (Sheldon and Hites 1979). Highest concentrations were measured in the sewage treatment plant inlet (16 µg/l) and in its outlet (2 µg/l), indicating a > 85 % elimination during wastewater treatment. The concentrations measured in samples from several sites in the vicinity of the outlet were consistent with the effluent being the major source of triphenyl phosphate in the Delaware in this sampling area. Drinking water made from contaminated river water (0.2 µg/l) without activated carbon filtration contained traces of triphenyl phosphate (0.03 µg/l).

Fish, water, and sediments were sampled in several industrialized and non-industrialized areas of the USA (Mayer et al. 1981). Triphenyl phosphate was detected in

- 32 of 63 water samples (limit of detection 0.1 µg/l; concentrations in water up to 7.9 µg/l). The geometric mean of triphenyl phosphate concentrations in water (calculated using one half of detection limit for samples reported as non-detectable) was 0.12 µg/l
- 13 of 40 sediment samples (limit of detection 0.01 µg/g; concentrations in sediment up to 4 µg/g)
- 16 of 82 fish (limit of detection 0.1 µg/g; concentrations in fish up to 0.6 µg/g).

Streams in the USA have been monitored at sampling sites susceptible to contamination e.g. downstream of intense urbanization and livestock production in 1999 and 2000. Triphenyl phosphate was found in 14.1 % of 85 samples with a median = 0.040 µg/l and a maximum value of 0.22 µg/l (Kolpin et al. 2002).

Less recent sampling of river Ruhr in Germany at 20 sites from well to mouth into river Rhine showed triphenyl phosphate concentrations up to 0.280 µg/l (region with heavy industry and mining). In different small tributaries of the river Ruhr mean concentrations of 0.4 µg/l were found. In a small creek which was dominated by the outflow of a sewage treatment plant, 2 µg/l were found. In the canal Emscher (Germany) concentrations up to 3.4 µg/l were measured. This sewer cannot be regarded as natural stream. Before entering the river Rhine the Emscher water is lead through a sewage treatment plant. No measured data from the outlet of this sewage treatment plant are available. In groundwater of the Dortmund waterworks area no triphenyl phosphate could be detected (limit of detection 1 ng/l) (Lenhart and Lemm 1993).

In the effluent from one out of three large wastewater treatment plants examined in Sweden (treating both domestic and industrial wastewater), triphenyl phosphate was found in a concentration of 3 µg/l (Paxéus, 1996).

2.1 Production Volumes and Use Pattern

Production volume

The world wide (excluding East Europe) production of triphenyl phosphate is estimated to about 20 000 to 30 000 tons by app. 15 producers in year 2000. Thereof about 25 % is estimated to be produced in West Europe, about 40 % is estimated to be produced in the USA, and about 35 % is estimated to be produced in Asia. There is no information about production and use in East European countries.

Use

Triphenyl phosphate is known as a product with manifold fields of applications regarding its qualities in particular as a flame retardant.

Major application areas for triphenyl phosphate are the use as a flame retardant in PVC (about 50 %) where it has also plasticizing properties, but also as a flame retardant in polymers (about 22 %) and printed circuit boards (about 11 %), and in photographic films (about 7 %).

Minor areas (about 10 %) are covered by the use of triphenyl phosphate in hydraulic liquids (main area), and adhesives, inks, and coatings (minor area).

In Denmark, 10 products containing 0 - 2 % triphenyl phosphate had been registered amounting to a total of about 6 t/a triphenyl phosphate. They were allocated to a wide variety of industry groups as indicated already above. Of the 10 products four were registered with consumer relevance, all belonging to the industry group 'paints, laquers and varnishes' with a total of < 1 t/a (Danish Product Register 2002).

In Switzerland, altogether 82 products containing triphenyl phosphate had been registered, among them 4 products classified in the group 'consumers'. These consumer products were allocated to wood protection agents, adhesives and fillers, metal polishers, and detergents/soaps. 52 of the 78 products used professionally belong to the category lubricants/heat transport media, the remaining products are scattered to the categories indicated already above. Two fungicide products contain traces/impurities of triphenyl phosphate (0 - 0.1 %) (Swiss Product Register 2002).

According to the Swedish Product Register (2002) triphenyl phosphate is contained in 30 products with a total quantity of 84 t/a. None of these products is available to consumers.

In the Norwegian Product Register (2002) 11 products containing a total quantity of 25 t are registered.

2.2 Environmental Exposure and Fate

2.2.1 Calculated overall distribution pattern

The environmental distribution of triphenyl phosphate was calculated according to the Mackay Level I model taking into account a vapour pressure of 8.35×10^{-4} Pa, a water solubility of 1.9 mg/l, and a log K_{ow} of 4.6. Corresponding to this calculation, triphenyl phosphate is mainly distributed in the following manner: to soil with 43.9 %, to sediment with 41.0 %, to water with 14.3 %, to air with 0.7 %, to suspended matter with 0.07 %, and to biota with 0.03 % (Bayer AG, 2002b). Based on water solubility (1.9 mg/l) and vapour pressures (1.6×10^{-4} – 1.07×10^{-3} Pa) Henry's law constants in the range of 0.018 – 0.036 Pa · m³/mol were calculated (Boethling and Cooper, 1985). According to the criteria of Thomas (1990) these values indicate hardly any volatilisation from an aqueous solution.

2.2.2 Stability in Water

In several experiments with buffered distilled water and unbuffered natural waters, the kinetics of triphenyl phosphate hydrolysis was investigated. Half-lives of 1.3 and 7.5 days were found in buffered distilled water at pH 9.3 and 8.2, respectively. Half-lives in natural waters were found to be 1.1 – 2.0 days at pH 8.2. Reported hydrolysis products were diphenyl phosphate and phenol (mentioned in the analytical procedure only). Further hydrolysis of diphenyl phosphate was considered much slower as monophenyl phosphate was not found in these experiments, and diphenyl phosphate was considered stable under alkaline conditions with reference to an older paper (Howard and Deo, 1979).

2.2.3 Biodegradation

In a test on ready biodegradability (modified MITI I Test which corresponds to OECD guideline 301C) 83 - 94 % of the applied triphenyl phosphate were biodegraded after 28 days of incubation (CITI, 1992). Therefore, the substance can be classified as readily biodegradable.

In a test simulating an aerobic sewage treatment plant, conducted according to OECD guideline 303A, a mean elimination rate of 93.8 % after 20 days was determined, using an initial concentration of 5 mg/l. The adaptation phase was 14 days. Less than 1 % of the applied TTP was found in the sludge (Ciba-Geigy, 1982).

Triphenyl phosphate was also shown to be biodegraded under anaerobic conditions (N₂ purged respirometer flasks) with river sediment. Primary degradation amounted to 31.1 % after 3 days and 87.9 % after 40 days. CO₂ evolution showing ultimate degradation was 0.8 % after 3 days and 21.9 % after 40 days of incubation. However, the authors concluded due to the high CO₂ evolution that incubations probably were not strictly anaerobic (Muir et al., 1989).

The stability of triphenyl phosphate in German BBA standard soil 2.2 (loamy sand) was investigated with radiolabelled triphenyl phosphate (5 mg/kg) under aerobic and anaerobic conditions. In both cases degradation of the test substance was observed with DT₅₀-values of 37 and 21 days, respectively. After a period of 101 days in the aerobic experiment 26.6 % of the applied

radioactivity was extractable from the soil whereas 26.4 % remained bound. 48.3 % of the applied radioactivity was recovered as the final degradation product CO₂. The soil extracts were analysed by HPLC and TLC. The amount of triphenyl phosphate decreased steadily and accounted for 46.6 % of that applied after 32 days. Degradation slowed down and 101 days post-treatment 20.2 % of the applied test substance was recovered unchanged. Under anaerobic conditions 35.8 % of the applied radioactivity was extractable after 102 days of incubation while 24 % remained bound. 40.4 % of the applied radioactivity was recovered as the final degradation product CO₂. At the end of exposure 31.4 % of the applied test substance remained unchanged. In experiments with heat sterilized soil ca. 85 % of the applied radiolabelled triphenyl phosphate was recovered after 101 days of incubation; diphenyl phosphate was detected as a degradation product (7.1 % after 13 days; 1.4 % after 101 days); unknown degradation products were not detected and carbon dioxide release was < 0.1 %. (Anderson et al. 1993).

Distribution in sewage treatment plant

According to the model Simpletreat (EU TGD) the following distribution in sewage treatment plants can be estimated for triphenyl phosphate (readily biodegradable $k = 1 \text{ h}^{-1}$, $\log K_{OW} = 4.6$, Henry: 0.02 - 0.04):

air	0 %
sludge	63 %
water	6.7 %
degraded	30.3 %
removal	93.3 %

This estimate is rather consistent with the data of Sheldon and Hites (1979) from a wastewater treatment plant in the vicinity of the Delaware river. This wastewater treatment plant eliminated > 85 % of the incoming triphenyl phosphate (see chapt. 2, Monitoring).

Similarly, 92 % triphenyl phosphate was eliminated by a wastewater treatment plant of Osaka City, Japan. Triphenyl phosphate influx concentration was 0.054 - 2.12 µg/l (mean 0.241 µg/l), and effluent concentration 0.005 - 0.082 µg/l (mean 0.019 µg/l) (Fukushima and Kawai, 1986).

2.2.4 Bioaccumulation

In a continuous flow through test (0.01 mg/l triphenyl phosphate) with *Oryzias latipes* and an exposure period of 18 days a bioconcentration factor (BCF) of 144 (whole body) was determined. As the uptake of triphenyl phosphate in fish increased gradually till day 18 of exposure, it is not clear whether equilibrium was reached. The biological half-life in fish tissue was reported to be 1.2 h (Sasaki et al., 1982). In a static test with *Carassius auratus* a BCF of 110 (whole body) was determined after 72 h of exposure to 0.25 mg/l triphenyl phosphate (Sasaki et al., 1981). Also for this study it is unclear whether equilibrium was reached. In an insufficiently documented study with fry of *Oncorhynchus mykiss* (previously *Salmo gairdneri*), Mayer et al. (1981) found a BCF of 271 (BCF range: 132 – 364).

In another insufficiently documented study, the distribution of ¹⁴C-labelled triphenyl phosphate was followed within artificial ponds containing duckweed (*Lemna minor*), cattail (*Typha sp.*), and fish (*Pimephales promelas*), over a time period of 105 days (data reported for the first 10 days). Although no reliable data on accumulation of triphenyl phosphate can be derived from this study,

BCFs for *Lemna minor* and *Typha sp.* were stated to be < 50 (duckweed 43, cattail < 1), and 68 - 160 for *Pimephales promelas* (Muir et al., 1982).

As the BCFs are related to the parent compound, there is no information on possible accumulation of stable metabolites. The experimentally obtained BCF value is supported by the SRC-BCFWIN v2.14 (2000) (Bayer AG, 2002b) estimation with a correction factor for phosphate ester chemicals. The calculated BCF value for fish is 113.3. On the basis of the experimental results a moderate bioaccumulation potential for triphenyl phosphate can be assumed.

In 1990 dolphins (*Tursiops truncatus*) were collected during an unusual mortality event in the Gulf of Mexico. The cause of death could not be identified. For gathering background information on organic chemicals, metals and selenium, blubber of the dead dolphins had been analyzed. Several substances, among them triphenyl phosphate, were detected in the blubber. For sucklings a mean triphenyl phosphate content of 863 ng/g lipid (range: 17 – 3790 ng/g lipid) was found, in immature animals the mean concentration was 68 ng/g lipid (range: 19 – 244) and in adult females the mean concentration was 30 ng/g lipid (range: 19 – 42). The mean triphenyl phosphate concentration in adult males from different locations was in the range of 25 – 56 ng/g lipid with single values in the range of 15 – 142 ng/g lipid (Kuehl and Haebler, 1995).

These findings indicate that although triphenyl phosphate is not persistent in the environment, an accumulation via the food chain may occur.

2.2.5 Other Information on Environmental Fate

Behaviour in natural waters with sediment:

In an experiment with pond (silt clay: 3.7 % organic carbon), river (silty: 2.3 % organic carbon), and sand sediment (0.1 % organic carbon), spiking of the sediment with 50 and 500 µg ¹⁴C-triphenyl phosphate/kg showed that after 2 days of equilibration, 79 -89 % of the radioactivity remained in the sediment (Muir et al. 1983).

Fairchild et al. (1987) treated a stream ecosystem (50 m total length, with two pools) with triphenyl phosphate -contaminated sediment (locally obtained topsoil; 0.7 % organic carbon; triphenyl phosphate application by spraying of triphenyl phosphate solved in acetone on soil). The contaminated sediment was added once a week to the stream of well water, according to the experimental design in increasing amounts of triphenyl phosphate, beginning at 55 mg/kg and doubled each week up to a load of 2100 mg/kg (measured concentrations). During addition of triphenyl phosphate-contaminated sediment, a water flow of 40 l/s ran through the ecosystem half of which was discharged and replaced by fresh water. Already within the first hours after sediment addition the concentration of triphenyl phosphate has decreased to about 25 % of the concentration present in the applied topsoil. No ageing after application of triphenyl phosphate on the soil as a slurry was allowed. The authors discuss that biological degradation, desorption, and dilution were probably important factors in the loss of triphenyl phosphate from water and sediments during that study.

Behaviour in soil:

Anderson et al. (1993) investigated the adsorption behaviour of radiolabelled triphenyl phosphate in three soil types in experiments carried out in accordance with a method recommended by the US-EPA. They determined soil sorption coefficients (K_{OC}) of 2514, 2756, and 3561 with silty clay, silt loam, and loamy sand (organic carbon content: 0.64 - 2.60 %), indicating a strong to very strong sorption potential to the organic matter of soil according to the criteria of Blume (1990). Depending on the soil properties, partial degradation of triphenyl phosphate by hydrolysis was observed during the equilibrium period (equilibrium was reached after 48 hours). Maximum abiotic degradation

occurred in silty clay. Diphenyl phosphate was identified as main degradation product. Due to the partial degradation of triphenyl phosphate during the experiment the data obtained describe both the behaviour of the test substance itself and of the abiotic degradation product diphenyl phosphate.

Triphenyl phosphate in soil has been shown to be degraded by microorganisms with DT_{50} of 37 and 21 days both, under aerobic and anaerobic conditions respectively (see section 'Biodegradability of triphenyl phosphate').

Behaviour in air:

A calculation on the indirect photolysis shows the following result: Triphenyl phosphate entering the atmosphere is expected to rapidly be photodegraded by reaction with hydroxyl radicals. The calculated half-life $t_{1/2}$ via AOPWIN, v 1.90 is approx. 12 hours assuming an atmospheric OH radical concentration of 1.5×10^6 molecules/cm³ (Bayer AG, 2002b).

2.3 Human Exposure

2.3.1 Occupational Exposure

Occupational exposure to triphenyl phosphate is most likely to occur through inhalation and dermal contact.

Workplace

In Germany the Board on Dangerous Substances (AGS) has decided to adopt (with revision) the ILO exposure limit of the Netherlands for triphenyl phosphate with 3 mg/m³ for the inhalable fraction (8 h time-weighted average). This exposure limit is laid down in German Technical Guidance TRGS 900.

At Bayer AG, triphenyl phosphate is produced in a closed system. Investigations on triphenyl phosphate at the workplace have been performed according to German Technical Guidance TRGS 402. This includes a survey in the working area for possible exposition at different work situations and subsequent control measurements. To protect workers from exposure to triphenyl phosphate at workplace, several different precautionary and protective measures are taken. These measures include engineering controls, periodical personal training according to German Technical Guidance TRGS 555 including signature of the workmen, and appropriate personal protection equipment prescribed in detail for different work situations (e.g. during maintenance and repair work).

Workplace measurements (8 h total shift, time-weighted average) have been carried out at the Bayer production site and were below 3 mg/m³.

Down-stream users of triphenyl phosphate are informed by way of a material safety data sheet about safe handling of the substance.

The German exposure limit value is in accordance with the other European countries' limit values. Additionally, in the UK there is a short term limit value of 6 mg/m³ over a 15 min period (RTECS, 2004). In the USA there is a NIOSH (1997) recommended exposure limit (REL) of 3 mg/m³ for up to a 10 hour workday during a 40-hour workweek.

2.3.2 Consumer Exposure

As cited in chapter 2 triphenyl phosphate has been monitored by indoor air sampling at residential and public buildings. Ambient air showed triphenyl phosphate concentrations up to 0.1 µg/m³ in

Sweden, Germany, and Japan. For further information see chapt. 2 of this report: 'General Information on Exposure'.

Trialkyl and triaryl phosphates were surveyed in United Kingdom total diet samples. The total phosphates levels (tributyl phosphate, triphenyl phosphate, trioctyl phosphate) ranged from (mean) 0.05 mg/kg for beverages to 0.2 mg/kg for unspecified meat products and 0.25 mg/kg for offal. The mean daily intake for these products was calculated to be approximately 0.1 mg/d. However, the triphenyl phosphate level was not reported (Gilbert et al. 1986).

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

Only one valid study on the metabolism of triphenyl phosphate was found in the literature (Sasaki et al. 1984). Triphenyl phosphate was incubated with rat liver microsomal without NADPH and soluble fractions and found by gaschromatography that triphenyl phosphate was decomposed to diphenyl-phosphate as the major metabolite. Therefore, arylesterase in the microsomes contributes to triphenyl phosphate metabolism. The metabolic reactions were inhibited almost completely by SKF-525A and carbon monoxide in the absence of NADPH whereas KCN, NaN₃, dipyrindyl and EDTA showed little effect. Therefore, mixed function oxidase system in the microsomes plays a central role in the metabolism of triphenyl phosphate.

Conclusion: Triphenyl phosphate is degraded by hydrolysis in rat liver homogenate to diphenyl phosphate as the major metabolite.

3.1.2 Acute Toxicity

Toxicity studies were performed mainly in rats and hens, but mice, rabbits, cats and guinea pigs also were used, however no guideline study is available. Nevertheless, the acute toxicity can be evaluated from the available evidence.

There are a number of studies using intraperitoneal, subcutaneous and intramuscular injection. The valid among these studies confirm the low level of toxicity. These routes of administration are not considered relevant for triphenyl phosphate exposure in man and are therefore not included. There are sufficient data on toxicity via oral and dermal routes.

Studies in Animals

Inhalation

No valid studies are available regarding the acute inhalation of triphenyl phosphate.

Dermal

Two dermal toxicity studies were performed in 1976 and 1977.

2 groups of 5 albino rabbits were treated each with a dose of 10 000 mg/kg bw on either intact or abraded skin; no adverse effects nor mortality were observed (no further details reported). The LD₅₀ was above 10 000 mg/kg bw (FMC 1975).

Johannsen et al. (1977) occlusively applied undiluted triphenyl phosphate to the intact dorsal skin of male and female New Zealand White rabbits for 24 hours. The LD₅₀ was above the maximum dose

of 7900 mg/kg bw after 14 days of observation, after which they were sacrificed and subjected to gross autopsy (no further detail reported).

Conclusion: The toxicity of triphenyl phosphate after dermal application is very low with an LD₅₀ of above 7900 mg/kg bw in rabbits.

Oral

In 1976 a limit test in 5 male, 5 female Wistar rats was reported. Animals were treated by intragastric intubation of an aqueous suspension using a single dose of 20 000 mg/kg bw. The animals were observed daily for 14 days following administration of the test material. No mortality was observed. Sporadic visceral hemorrhages at necropsy were the only effects (FMC Industrial Chemical Division, 1975).

In a study by Ciba-Geigy (1954) groups of 5 male and female rats were treated with up to 5000 mg/kg bw triphenyl phosphate and observed for 8 days. Animals showed neither symptoms nor mortality. Houghton and Company (1962) determined for rats a LD₅₀ from over 6400 mg/kg bw.

Sutton et al. (1960) reported an experiment using a dose of 3000 mg/kg bw in male rats leading to no treatment related mortality nor any clinical signs of toxicity at all.

The acute study in rats by Johannsen et al. (1977) employed doses up to 15 800 mg/kg bw in male and female Sprague-Dawley rats and gave a LD₅₀ of 10 800 mg/kg bw after 14 days of observation.

In mice only 2 reliable studies are available. In a study by Ciba-Geigy (1954) groups of 5 male and female mice were treated with up to 5000 mg/kg bw triphenyl phosphate and observed for 8 days. Animals showed slight stupor for an unspecified time, but none of them died.

Sutton et al. (1960) reported an experiment using a dose of 3000 mg/kg bw in male mice leading to no mortality nor any clinical signs of toxicity at all. The partial inhibition of choline esterase activity in the whole blood was interpreted as a sign of absorption of triphenyl phosphate although a causal correlation was not proven. Choline esterase activity was reduced after doses of 10 to 500 mg/kg bw to 87.1 to 30.4 % of control. No cholinergic or other symptoms were reported.

A number of other less well documented studies in rats, mice, guinea pigs, hens (see 3.1.8.3) and rabbits confirmed the low level of toxicity and found the LD₅₀ values to be greater than the maximum doses of 3000 to 12 500 mg/kg bw (Sutton, 1960; Ciba-Geigy, 1954; 1980; 1981; Henschler, 1958; Houghton and Company, 1962; Johannsen, 1972; Smith et al., 1932).

Conclusion: After acute oral administration in rats, mice, rabbits and guinea pigs the LD₅₀ values are in a range above 3000 to above 20 000 mg/kg bw. This is far above the limit dose (2000 mg/kg bw.) applied in modern studies, which indicates a low level of toxicity after oral administration. Only 1 study in mice with limited documentation gave a value of 1320 mg/kg bw. Non-limit tests (i.e. those with doses above 2000 mg/kg) generally demonstrate low toxicity with LD₅₀s greater than 5000 mg/kg bw.

Conclusion

There is a low level of acute toxicity after oral and dermal administration.

3.1.3 Irritation

Skin Irritation

Studies in Animals

The skin irritation potential of triphenyl phosphate was determined in a study according to international standards (Bayer AG, 1990; OECD 404). Three rabbits were treated for 4 hours by occlusively applying 500 mg of moistened test substance to the clipped dorsal skin (2 x 3 cm) and observed daily for 14 days. Erythema and edema formation were evaluated. No signs of irritation were detected. The irritation index was 0.0.

The findings are confirmed by other studies carried out between 1960 and 1983 (FMC, 1975; Ciba-Geigy, 1983a; Sutton et al., 1960; Antonyuk, 1969, 1974)

Conclusion: triphenyl phosphate does not possess an irritation potential on the skin.

Eye Irritation

Studies in Animals

The irritation potential of triphenyl phosphate on mucous membranes of the rabbit eye was determined by Märtns according to OECD Guideline 405 in 1990. The treated eyes were rinsed 24 hours after instillation. No sign of irritation was detected (Bayer AG, 1990).

Similar findings were recorded in a study according to US regulations (16 CFR 1500.42). employing 4 hours treatment without rinse in 6 rabbits (group 1) and rinsing after 4 seconds in 3 additional rabbits (group 2). In group 1 conjunctival effects were observed in all six animals. These effects cleared during the 72-hour- observation period. In group 2 no ocular effects were observed in any of the three animals. The material was found mildly and transiently irritating when not washed out (FMC, 1975).

A minimal irritating potential of triphenyl phosphate in 6 New Zealand White rabbits was also found in another -study according to US regulations. 100 mg of the test compound were instilled into the conjunctival sac of the left eye. The eyelids were then held closed for 1 second. After 30 seconds the compound was flushed out of the eyes of three of the rabbits. Very slight reactions were seen in 2/3 washed and 3/3 unwashed eyes 1 hour after compound application. The reactions were less severe at 24 hours although all washed and unwashed eyes were affected. 3/3 washed eyes and 1/3 unwashed eyes were normal at 48 hours, 1 unwashed eye at 27 hours and the remaining unwashed eye at day 6. Slight opacity and damage to the surface epithelium was seen in 1 unwashed eye at 24 hours. This was no longer present at 48 hours minimal irritating potential of triphenyl phosphate in New Zealand White rabbits was found (highest score 7; score 0 - 10 minimally irritant) (Ciba-Geigy, 1983b).

Conclusion

The irritation potential of triphenyl phosphate on the mucous membrane of the eye is very low.

3.1.4 Sensitisation

Studies in Animals

No animal data are available regarding the sensitisation potential of triphenyl phosphate.

Studies in Humans

Single human cases have been reported with allergic dermatitis from triphenyl phosphate through the years (Andersen, 1977; Berkhoff, 1938; Carlsen et al., 1986; Hjorth, 1964; Pegum, 1966; Spirig, 1995).

Among the 23 192 patients patch tested from 1950 to 1962, positive reactions to cellulose acetate film containing 7 to 10 % triphenyl phosphate and 3 to 4 % phthalic esters occurred in 15 (0.065 %). The sensitivity to cellulose acetate film was analysed in only two cases, in both of which the sensitizer was found to be triphenyl phosphate. In the others it may have been either triphenyl phosphate or the phthalic ester (Hjorth, 1964).

Tarvainen tested 343 patients and found none reacting to triphenyl phosphate (Tarvainen, 1995).

This low incidence was confirmed by another study (Kanerva et al., 1997; 1999), which tested 174 patients and revealed only irritation reactions in 1 patient, but no sensitisation.

Kayser and Schlede (BgVV, 2001) also concluded that there are only scarce indications of a contact sensitising action.

Conclusion

No animal data regarding skin sensitisation are available. There are few human case reports showing evidence of skin sensitisation. The incidence of skin sensitisation is very low.

3.1.5 Repeated Dose Toxicity

Studies in Animals

Rats were treated by dietary administration of triphenyl phosphate for 35 days. Three groups of 5 male animals of the Holtzman strain per group were employed. Doses were 0 (control), 0.5 and 5.0 % (estimated doses: ~ 350 - 3500 mg/kg bw/day) in the diet at the start. The high dose animals refused food and lost weight. Therefore the dose was reduced to 0.1 % after three days. Parameters recorded were clinical observations, body weights (3 times/week), food consumption, and hematology (hemoglobin content, cell volume, red cell count, total and differential white cell count). At the end of the treatment period 2/5 rats were kept for a further 14 day recovery period. All animals were killed and subjected to gross necropsy. Organ weights (kidneys and livers) were recorded (no further examinations - clinical chemistry, histopathology, urinalysis - reported).

Treatment caused a slight depression of body weight gain and an increase of liver weights at a level of 0.5 % (estimated dose: ~ 350 mg/kg bw/day) in the diet. No findings were recorded in clinical observation, haemoglobin content, cell volume, red cell count, total and differential white cell count and at necropsy. A concentration of 0.1 % in the diet (estimated dose: ~ 70 mg/kg bw/day) was without any effect (= NOEL) (Sutton et al., 1960).

Two four months studies were conducted in rats to determine possible effects on the immune or the nervous system. (0, 0.25, 0.5, 0.75, and 1 % of triphenyl phosphate in the diet corresponding to doses of about 0, 161, 345, 517 and 711 mg/kg bw/day). The animals were observed for clinical symptoms. Body weights and food consumption were recorded weekly. The neurotoxicity was assessed in open field, accelerating rotarod, forelimb grip strength and negative geotaxis examinations. These parameters were determined 4 times at the end of each month of treatment. Immunotoxicity was assessed by measurements of the weights of lymphoid organs, immunohistochemical evaluation of spleen, thymus, lymph nodes, and the humoral response to antigens.

Only limited data are reported and a number of standard parameters of repeated dose toxicity is missing, e.g. organ weight measurement and histopathology of organs other than lymphoid organs (spleen, thymus, lymph nodes) as well as haematology and clinical chemistry other than serum proteins. Nevertheless, the studies show that triphenyl phosphate did not interfere with the general well being and behavior of the animals at levels of up to 1 % in the diet for 4 months. At the dose levels of 0.5 to 1 % a slight but statistically significant reduction of growth rate was detected as the only change in one of the two studies (Sobotka et al., 1986), whereas an reduced growths rate was recorded at the 1 % dose level in the other study (Hinton et al., 1987), leading to NOEL's of 161 or 517 mg/kg bw/day. The studies are described in detail under Chapter 3.1.8.

In a study on fertility and developmental toxicity in Sprague-Dawley rats dietary doses of 0, 0.25, 0.50, 0.75, 1.0 % corresponding to 0, 166, 341, 516 or 690 mg/kg bw/day were administered to forty males and forty females per group for 4 months and during mating and gestation. The animals were treated further throughout mating and gestation and killed at day 20 of gestation. There was no evidence of general toxicity or reproductive toxicity after exposure to the chemical. The NOEL given by the authors for male and female fertility, maternal toxicity, and developmental toxicity was 1 % in the diet (690 mg/kg bw/day) (for more detail. see chapter 3.1.7; Welsh et al., 1987).

The toxicity of triphenyl phosphate after repeated dermal exposure was determined in rabbits. Ten male and 10 female animals per group were treated on clipped, intact (half of the animals) and abraded skin (half of the animals), five times per week for three weeks with doses of 0, 100 and 1000 mg/kg bw/day under open conditions. Ingestion was prevented by means of a collar. Triphenyl phosphate was applied as a 50 % solution in ethanol. The application volume was 0.2 or 2 ml/kg bw/day. Control animals were treated with 1 ml/kg bw of distilled water.

The findings detected at the site of treatment as well as all other parameters (mortality, clinical symptoms, body weight, hematology, clin. chemistry, necropsy, organ weights, histopathology of > 30 tissues (including reproductive organs and nervous system)) were not different from control animals. The only treatment related effect was a depression of acetyl cholinesterase in plasma, erythrocytes and brain of triphenyl phosphate treated rabbits. No clinical or histological correlate was found. No quantitative data are reported for this endpoint. This effect is not considered as of toxicological relevance. (Monsanto, 1979).

Conclusion

Based on the available data, the toxicity after repeated treatment of rats or rabbits with triphenyl phosphate is low. The majority of the available studies did not report a wide variety of parameters, but taken together the studies using dietary doses of up to 711 mg/kg bw/day or dermal doses of up to 1000 mg/kg bw/day cover clinical observations, body weight gain, food consumption, haematology, clinical chemistry, organ weights as well as histopathology. After 5 weeks of treatment a slight depression of body weight gain and an increase of liver weights at a level of 0.5 % (estimated dose: ~ 350 mg/kg bw/day) were seen. A concentration of 0.1 % (estimated dose: ~ 70 mg/kg bw/day) in the diet was without any effect.

Limited studies with treatment for 4 month at dose levels of up to 1 % in the diet (~ 711 mg/kg bw/day) confirm this effect on growth. The general well being, immune and nervous systems were not affected. The NOEL was 161 mg/kg bw/day due to reduced body weight gain with \geq 345 mg/kg bw/day in one of the two studies. A subchronic study on developmental toxicity and fertility revealed a NOEL for male and female fertility and maternal toxicity of 1 % in the diet (690 mg/kg bw/day). The low general toxicity was confirmed also after dermal exposure of 100 or 1000 mg/kg bw in rabbits for 15 days without any sign of toxicity besides an unquantified depression of acetylcholinesterase as the only dose related effect. The overall NOEL is 161 mg/kg bw/day.

3.1.6 Mutagenicity

Gene Mutation

The potential of triphenyl phosphate to induce gene mutations was examined in the Ames test (Monsanto, 1978a) without any signs of mutagenicity in *S. typhimurium* TA 98, TA 100, TA1535, TA1537, TA1538 and *S. cerevisiae* D4 with and without metabolic activation by S-9-mix from Aroclor-induced adult male Sprague-Dawley rats. The range of concentrations was 1 to 1000 µg/plate.

Similarly Zeiger found no mutagenicity in *S. typhimurium* TA 98, TA 100, TA 1535, TA 1537, TA 1538 with and without activation by S9 mix from aroclor 1254 treated rat livers. Bacteria were perincubated for 20 minutes at 37 °C. Experiments were performed in triplicate and repeated. Positive and negative controls were included. Test concentrations and cytotoxicity were not reported (Zeiger, 1987)

These results were supported by Kimmerle in *S. typhimurium* TA98 and TA100, at concentrations of 0 to 5000 µg/plate, with and without metabolic activation. (Kimmerle, 1984).

The mouse lymphoma test in L5178Y cells with (6.25 – 75 µg/ml) and without (3.13 – 50 µg/ml) metabolic activation showed no effects (Monsanto, 1978b).

Conclusion

Tests for gene mutations in bacterial as well as yeast and mammalian cells did not reveal any sign of mutagenicity.

Cytogenetic effects

Unscheduled DNA synthesis was examined by Schmuck (1989) in syrian hamster fibroblast cells at concentrations of 0.05 to 10 x 10⁻⁵ M. After 5 hours incubation without activation in the presence of 3H-thymidine. Triphenyl phosphate showed no genotoxic effect. (No further details given).

No other studies regarding cytogenetic effects are available

Conclusion

An UDS-test in syrian hamster fibroblast cells showed no genotoxic effect. There is no test concerning chromosomal aberration.

3.1.7 Carcinogenicity

There are no long term carcinogenicity bioassays available. Male Strain A/St mice (20 animals/group, these animals show a very high sensitivity to carcinogens resulting in short latency periods and high tumor rates) were treated by intraperitoneal injection with 20 (18 doses), 40 (3 doses) or 80 mg/kg bw (single dose) of triphenyl phosphate (purity: 95 - 99.9 %) 3 times a week and observed for further 18 weeks. Afterwards lungs were examined for adenomas.

The survival rate was 18/20 in the 20 mg/ bw group, 3/20 in the 40 mg/kg bw group and 12/ 20 in the 80 mg/kg bw group.

Adenomas were seen only in the 80 mg/kg bw group with no significant increase of incidence (Theiss et al. 1977).

Conclusion

There are no long term carcinogenicity bioassays available. The strain-A-mouse lung adenoma assay gave no indication of a carcinogenic potential.

3.1.8 Toxicity for Reproduction

Fertility and developmental toxicity were examined in a dietary study in Sprague-Dawley rats at doses of 0, 0.25, 0.50, 0.75, 1.0 % corresponding to 0, 166, 341, 516 or 690 mg/kg bw/day. Forty males and 40 females per group were treated for 3 months and mated afterwards. Animals were treated further throughout mating and gestation and killed at day 20 of gestation (Welsh et al., 1987).

Studies in Animals

Effects on Fertility

The study included treatment of males and females for three months prior to mating throughout gametogenesis and during mating and gestation. No significant differences were recorded in the number of corpora lutea, implants, implantation efficiency, viable fetuses and the number of early or late deaths between treated and control rats. No significant signs of parental toxicity were detected. As there was no effect on the litter size (indirectly measured by the number of viable fetuses and implants) and both sexes were treated in the study, these findings indicate that fertility is not adversely affected by triphenyl phosphate in male and female rats. The NOEL was 690 mg/kg bw (Welsh et al., 1987).

In a dermal repeated dose toxicity study in rabbits there was no effect on the reproductive organs up to the highest dose of 1000 mg/kg bw (see chapter 3.1.5 for more detail; Monsanto, 1979).

Conclusion: fertility is not adversely affected by triphenyl phosphate in male and female rats up to the highest tested dose of 690 mg/kg bw daily after treatment during 3-4 months prior to mating and throughout mating and gestation.

Developmental Toxicity

Neither maternal toxicity nor changes in the types or numbers of anomalies in the fetuses were detected. All treated groups had significantly more fetuses with moderate hydronephrosis than the control group. In the opinion of the authors, the high baseline incidence exhibited in the control group and lack of a clear dose-related response make the biological significance of this finding unclear. There were also significantly more fetuses in the treated groups with moderately enlarged ureters in the region adjacent to the kidney than in the controls. Again, the incidence was not related to dose since a greater proportion of fetuses were affected in the lower dose levels than in two high levels. The average number of fetuses having at least two soft-tissue variations was significantly higher in the 0.25, 0.50 and 0.75 but not the 1 % triphenyl phosphate groups than in the control group. The 1 % group was only slightly, non-significantly higher than the control. The number of litters with fetuses having at least two soft-tissue variations was significantly greater only in the 0.5 and 0.75 % groups. The authors concluded that there was no evidence of bioaccumulation or increased reproductive toxicity after exposure to the chemical.

The NOEL given by the authors for male and female fertility, maternal toxicity, and developmental toxicity was 1 % in the diet (690 mg/kg bw/day) (Welsh et al., 1987).

Conclusion: No signs of developmental toxicity were seen up to the highest tested dose of 690 mg/kg bw/day daily in the rat.

Conclusion

There are no findings indicating adverse effects on fertility or the development of the fetus up to the highest tested dose of 690 mg/kg bw daily in the rat treated for 4 months during gametogenesis prior to mating and throughout mating and until day 20 of gestation.

3.1.9 Immunotoxicity

Five groups of 10 male and 10 female Sprague-Dawley rats were fed diets containing 0, 0.25, 0.5, 0.75, and 1 % of triphenyl phosphate for 120 days. The animals were observed for clinical symptoms. Body weights and food consumption were recorded weekly. Blood samples were analysed for total protein and by electrophoresis of plasma proteins. Immunotoxicity was assessed by measurements of the weights of lymphoid organs, immuno-histochemical evaluation of spleen, thymus, lymph nodes, and the humoral response to antigens.

At the 1% dose level reduced growth rate was detected. There were no significant differences between immunized and non-immunized animals. The weights of lymphoid organs (spleen, thymus,) varied in a non-dose-dependent way. No significant changes were found in these organs and lymph nodes by histopathologic examination and no significant alterations of serum protein were detected. Electrophoresis revealed increased levels of alpha- and beta-globulin in male or female rats but effects were similar at all dose levels, relative to the control group. Only non-dose-dependent variation was found in the humoral immune response to sheep red blood cells in female rats. (Hinton et al., 1987).

Conclusion: In a non-validated assay no effects were observed in a range of parameters of immune function in rats receiving oral doses up to ~ 700 mg/kg bw/day (1 %). The NOEL for immunotoxicity was 1 % (~ 700 mg/kg bw) of triphenyl phosphate in the diet and 0.75 % (~ 517 mg/kg bw) for all effects due to a slight reduction of body weight gain at the highest dose level. The significance of these results with respect to humans is not fully clear.

3.1.10 Neurotoxicity

Neurotoxicity is a potential adverse effect of many organophosphates. Some organo-phosphates also induce delayed neurotoxicity. Therefore triphenyl phosphate was tested for neurotoxicity in vivo and in vitro. It is recognized that the rat is a poor model for such delayed effects compared to the hen. Therefore the hen is, according to OECD guideline 418 (acute exposure), the standard test system to detect these effects.

There are several reports of the investigation of triphenyl phosphate for such effects. The endpoints determined were the inhibition of choline esterases, neuropathy target esterase (NTE) and clinical observations in hens and cats and a functional observational battery in rats during subchronic exposure.

The earliest results regarding triphenyl phosphate were those being reported by Smith et al. in 1932, who treated 4 hens orally with doses of 500 to 2000 mg/kg bw without any effects.

These findings were confirmed by Hine et al. in 1956 at an oral dose of 1000 mg/kg bw. Animals were observed for their ability to walk for 14 to 36 days. Cholinesterase was determined in plasma, brain, and spinal cord. Microscopic sections were examined from brain, spinal cord, and sciatic nerve.

The birds did not show signs of paralysis and no histologic changes were detected. Cholinesterase activity was reduced to 39 to 65 % in plasma depending on the substrate.

In 1958 Henschler and Bayer described an experiment in hens using oral doses of up to 10 000 mg/kg bw triphenyl phosphate (delivered in 2 - 3 days) in olive oil without any effect during the observation period.

Other authors (Aldridge and Barnes 1961) also found no sign of neurotoxicity after an oral dose of 500 mg/kg bw in hens after 3 weeks of observation, although they found a reduction of cholinesterase in blood of 60 %.

The low acute oral toxicity of pure triphenyl phosphate in hens is confirmed by later studies. In 1977 Johannsen et al. treated 9 hens twice daily with 5000 mg/kg bw for 3 days and after an interval of 18 days for another 3 days. (total: 60 g/kg bw). Animals were sacrificed on day 42. Neither behavioural nor histological changes of nerve tissue were detected in any of the animals.

Swallow and Bradley did not detect any adverse effects in hybrid Rhode Island Red x Light Sussex hens treated orally with 12000 (Ciba-Geigy, 1980) or 2000, 3000, 5000, 8000, or 12 500 mg/kg bw (Ciba-Geigy, 1981a) and observed for 2 to 3 weeks. No symptoms nor alterations at necropsy were noticed.

The activity of CHE was determined in a number of studies. Hine et al (1956) found a severe depression of plasma CHE (without signs of paralysis) in hens, which was confirmed by Sutton et al. (1960) in mice after oral, intraperitoneal or inhalative administration and by Aldridge and Barnes (1961) in hens.

Sutton also reported that choline esterase activity was reduced after doses of 10 to 500 mg/kg bw in mouse whole blood to 87.1 to 30.4 % of control. No cholinergic or other symptoms were reported. The partial inhibition of choline esterase activity in the whole blood was interpreted as a sign of absorption of triphenyl phosphate although a causal correlation was not proven.

Sutton et al. (1960) described further experiments in rats, mice, and guinea pigs using single doses of 3000 mg/kg bw in male and female animals leading to no mortality nor any clinical signs of toxicity at all. Additionally Sutton et al. (1960) found inhibitory effects in human blood in vitro. At a concentration of 6×10^{-5} Mol/l effects were most pronounced in human erythrocytes, human plasma and mouse whole blood with residual activities of 21, 40 or 57 %, resp. (unspecified duration of incubation). At a concentration of 6×10^{-7} Mol/l no inhibition was recorded.

Neuropathy target esterase, an enzyme involved in the development of delayed neuropathy after organophosphate exposure in animals, was determined by Johnson (1975a, 1975b) in hen brain homogenate. Johnson (1975b) found a structure activity relationship (SAR) in a large series of organophosphorus compounds that indicates no neurotoxic potential for triphenyl phosphate. This SAR was confirmed by Johannsen et al. (1977).

Padilla et al. (1987) also found that triphenyl phosphate did not inhibit NTE in vitro in the microsomal fraction of rat brain and spinal cord tissues at concentrations of 1 to 10 μ M after 20 minutes of incubation. At 100 μ M NTE was inhibited to about 60 %, while positive control (diisopropyl-fluoro-phosphate) showed complete inhibition below 10 μ M.

Most of these studies were performed in hens, as this is the species of choice for organophosphate induced neuropathy, or in cats, as this species seems to be exceptionally sensitive to triphenyl phosphate. The major fault of many of these studies is that there are no reports of the purity of the tested samples. As these studies were performed before about 1970 one has to assume that in many cases the samples were contaminated by other phosphoric acid esters due to the synthetic processes used in those years (Bayer AG, 2002c).

Only one study employed high purity triphenyl phosphate (zone refined, 99.99 %) (Wills et al., 1979) Two cats each were injected once subcutaneously with doses of 400, 700 mg/kg bw. One cat received 1000 mg/kg bw and 2 additional cats were employed as controls.

At 400 mg/kg bw one cat stayed without findings, while the other lost weight (31 %) before recovering within 3 months. No signs of unusual weakness or ataxia were seen.

At 700 mg/kg bw both animals became anorexic with watery diarrhea and prostration within several days. Histology of various organs revealed generalized vascular damage with perivascular edema in many tissues. The epithelial lining of the colon was lost. The livers showed fatty change and sinusoidal dilation. No changes were seen in the kidneys.

Sections from 11 levels of the nervous system from cortex to peripheral nerve were examined and did not provide any evidence of axon degeneration, demyelination or any other pathological change.

The cat given 1000 mg/kg bw became anorexic within one week, was unable to rise from the floor 3 weeks after treatment, when it was killed. It had lost 48 % of its original weight. Sections of nervous tissue did not show any evidence of neuronal damage.

In a 4 month study in rats Sobotka et al. determined the influence of dietary treatment with triphenyl phosphate at levels of 0, 0.25, 0.5, 0.75, and 1 %, corresponding to 161 to 711 mg/kg bw, on the nervous system of male rats (10 per group). In addition to standard clinical observations the neurotoxicity was assessed in open field, accelerating rotarod, forelimb grip strength and negative geotaxis examinations. These parameters were determined 4 times at the end of each month of treatment. Additionally body weights and food consumption were recorded weekly.

No adverse effects were noted in any of the neurotoxicity parameters. Body weights were dose dependently reduced at 0.5 and 1 % triphenyl phosphate (Sobotka et al., 1986).

Conclusion

Neurotoxicity is a potential adverse effect of many organophosphates. In available studies in hens and cats pure triphenyl phosphate does not induce immediate nor delayed neuropathy. Although the rat is a poor model for delayed neurotoxic effects, the absence of neurotoxicity after 4 months of treatment confirms the findings in other species. The findings of a decreased activity of choline esterase and paralysis predominantly in cats in older studies indicating a neurotoxic potential were not reproduced in later studies and may be due to contamination of the tested samples by other organophosphorus esters. At the high doses of triphenyl phosphate used even small concentrations of impurities might have sufficient activity.

3.1.11 Cytotoxicity

Saboori et al. (1991) and Mandel et al. (1989) reported that triphenyl phosphate efficiently inhibits the non-specific esterase activity of human monocytes in vitro. This effect was discovered incidentally during hematologic investigations in triphenyl phosphate-exposed workers and not associated with any detectable health effect. There was no effect of triphenyl phosphate on the number and function of monocytes in a group of 38 workers similarly exposed to triphenyl phosphate and investigated by Emmett et al. (1985). The acetyl choline esterase of erythrocytes was depressed only marginally in these workers.

Conclusion: Triphenyl phosphate inhibits the unspecific esterase of human monocytes.

3.2 Initial Assessment for Human Health

Triphenyl-phosphate is degraded by hydrolysis in rat liver homogenate to diphenyl-phosphate as the major metabolite. There is a low level of acute toxicity after oral and dermal administration. After acute oral administration in rats, mice, rabbits and guinea pigs the LD₅₀ values are in a range above 3000 to above 20 000 mg/kg bw. This is far above the limit dose (2000 mg/kg bw.) applied in modern studies, which indicates a low level of toxicity after oral administration. Only 1 study in mice with limited documentation gave a value of 1320 mg/kg bw. Non-limit tests (i.e. those with doses above 2000 mg/kg bw) generally demonstrate low toxicity with LD₅₀s greater than 5000 mg/kg bw. The toxicity of triphenyl phosphate after dermal application is very low with an LD₅₀ of above 7900 mg/kg bw in rabbits. No valid studies are available regarding the acute inhalation of triphenyl phosphate. Triphenyl phosphate does not possess an irritation potential on the skin. The irritation potential of triphenyl phosphate on the mucous membrane of the eye is very low.

No animal data regarding skin sensitisation are available. There are few human case reports showing evidence of skin sensitisation. The incidence of skin sensitisation is very low.

Based on the available data, the toxicity after repeated treatment of rats or rabbits with triphenyl phosphate is low. The majority of the available studies did not report a wide variety of parameters, but taken together the studies using dietary doses of up to 711 mg/kg bw /day or dermal doses of up to 1000 mg/kg bw/day cover clinical observations, body weight gain, food consumption, haematology, clinical chemistry, organ weights as well as histopathology. After 5 weeks of treatment a slight depression of body weight gain and an increase of liver weights at a level of 0.5 % (estimated dose: ~ 350 mg/kg bw/day) were seen. A concentration of 0.1 % (estimated dose: ~ 70 mg/kg bw/day) in the diet was without any effect.

Limited studies with treatment for 4 month at dose levels of up to 1 % in the diet (~ 711 mg/kg bw) confirm this effect on growth. The general well being, immune and nervous systems were not affected. The NOAEL was 161 mg/kg bw due to reduced body weight gain with \geq 345 mg/kg bw/day in one of the two studies. A subchronic study on developmental toxicity and fertility revealed a NOEL for male and female fertility and maternal toxicity of 1% in the diet (690 mg/kg bw/day). The low toxicity was confirmed also after dermal exposure of 100 or 1000 mg/kg bw/day in rabbits for 15 days without any sign of toxicity besides an unquantified depression of acetylcholinesterase as the only dose related effect.

Tests for gene mutations in bacterial as well as yeast and mammalian cells did not reveal any sign of mutagenicity. An UDS-test in syrian hamster fibroblast cells showed no mutagenic effect. There is no test concerning chromosomal aberration.

There are no findings indicating any adverse effects on fertility or the development of the fetus up to the highest tested dose of 690 mg/kg bw daily in the rat treated for 4 months during gametogenesis prior to mating and throughout mating and until day 20 of gestation.

There are no long term carcinogenicity bioassays available. The strain-A-mouse lung adenoma assay gave no indication of a carcinogenic potential

The treatment of rats for 4 month did not influence a range of parameters of immune function in rats receiving oral doses up to ~ 700 mg/kg bw/day (1 %). The NOEL for immuno-toxicity was 1 % of triphenyl phosphate (~ 700 mg/kg bw/day) in the diet and 0.75 % (~ 517 mg/kg bw/day) for all effects due to a slight reduction of body weight gain at the highest dose level. The significance of these results with respect to humans is not fully clear.

Neurotoxicity is a potential adverse effect of many organophosphates. In available studies in hens and cats pure triphenyl phosphate does not induce immediate nor delayed neuropathy. Although the rat is a poor model for delayed neurotoxic effects, the absence of neurotoxicity after 4 months of treatment confirms the findings in other species. The findings of a decreased activity of choline esterase and paralysis predominantly in cats in older studies indicating a neurotoxic potential were not reproduced in later studies and may be due to contamination of the tested samples by other organophosphorus esters. At the high doses of triphenyl phosphate used even small concentrations of impurities might have sufficient activity. Triphenyl phosphate inhibits the unspecific esterase of human monocytes.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

For the effects assessment on aquatic organisms the low water solubility of triphenyl phosphate (0.2 to 1.9 mg/l at room temperature, see chapt. 1), its adsorption potential, and its rapid abiotic and biotic decomposition in aqueous solution to various degradation products (see chapt. 2.1) have to be taken into account, particularly in tests with longer exposure periods.

Due to the instability, the aquatic effects data cover not only the toxicity of triphenyl phosphate but also the toxicity of the degradation products.

Out of the multitude of acute tests performed with triphenyl phosphate and fish, daphnia, and algae, only those tests were chosen for the aquatic hazard assessment that were performed to today's standard testing guidelines or showed sufficient reliable results for organism groups other than fish, daphnia, and algae.

A test on the acute toxicity of triphenyl phosphate to fish was conducted according to OECD guideline 203. Static exposure of *Oncorhynchus mykiss* for 96 hours resulted in a LC₅₀ value of 0.85 mg/l (nominal concentration) (Ciba-Geigy, 1981b).

Several acute fish tests were performed according to the U.S. guideline EPA-660/3-75-009. (Mayer et al., 1981) reports static test results with 96 h-LC₅₀ values of 0.4 mg/l for *Oncorhynchus mykiss* and $> 0.32 < 0.56$ mg/l for the marine species *Cyprinodon variegatus* (both nominal concentrations).

In a long-term flow through tests with sac fry stage of *Oncorhynchus mykiss* a 90 d-NOEC ≥ 0.0014 mg/l based on measured triphenyl phosphate concentrations was determined for the endpoints eye cataract, vertebral collagen amount, survival, and growth (Mayer et al., 1981). In another test with analytic control, a 30 d-LOEC of 0.055 mg/l was determined for the development of sac fry stage of *Oncorhynchus mykiss* regarding the endpoints length and weight (Sitthichaikasem, 1978). From the test raw data an EC₁₀ of 0.037 mg/l was calculated, equipollent to the NOEC (EU TGD, 1996).

In a 30 day flow-through test with *Pimephales promelas* the highest applied triphenyl phosphate concentration of 0.23 mg/l (measured conc.) reduced the survival of fry significantly. However no effects on egg hatchability, eyes, or growth were noted with triphenyl phosphate concentrations up to the highest concentration tested of 0.23 mg/l. For survival the authors report a NOEC of 0.087 mg/l and a LOEC of 0.23 mg/l (Mayer et al., 1981).

A test on the acute toxicity of triphenyl phosphate to *Daphnia magna* was conducted according to the US guideline EPA-660/3-75-009. Static exposure for 96 hours resulted in a LC₅₀ value of 1.0 mg/l (nominal concentration) (Mayer et al., 1981).

Lower effective concentrations were found for another crustacean, *Mysidopsis bahia*, in a test on the acute toxicity as well conducted according to US guideline EPA-660/3-75-009. Static exposure for 96 hours resulted in a LC₅₀ value of > 0.18 < 0.32 mg/l (nominal concentration) (Mayer et al., 1981).

No long-term study on *Daphnia magna* or other aquatic invertebrates is available.

The toxicity of triphenyl phosphate was investigated to algae with different growth media (Bolds basal medium = BBM, OECD and US-EPA media). In a test according to OECD guideline 201 (modified) *Selenastrum capricornutum* as well as *Scenedesmus subspicatus* showed 72 h-LOEC values on growth of 0.5 mg/l with BBM, 1.0 mg/l with OECD medium, and 5.0 mg/l with EPA medium. *Chlorella vulgaris* did not show any effect at 5.0 mg/l growing on any of the media. All values are based on nominal concentrations. Since the focal point of this test was the difference in influence of growth media on algae growth, no EC₀ values are reported (Millington et al., 1988). Due to the only slight effect (< 20 %) shown in the figures, NOECs are derived for this test, applying a factor of 2 on the LOEC (EU TGD 1996). Thus the 72 h-NOEC for *Chlorella vulgaris* is determined with 2.5 mg/l, and for *Selenastrum capricornutum* as well as *Scenedesmus subspicatus* with 0.25 to 2.5 mg/l, depending on the growth medium used.

Derivation of the PNECaqua

The lowest available long-term value, the NOEC of 0.037 mg/l, found in a test with *Oncorhynchus mykiss* is used for the derivation of PNECaqua. Since valid long-term tests with species from two trophic levels (fish and algae) are available, an assessment factor of 50 is applied, resulting in a PNECaqua of 0.74 µg/l.

Toxicity to Microorganisms

For the toxicity of triphenyl phosphate on microorganisms 24 h-EC₀ values of 200 mg/l (each) were reported for *Escherichia coli* and *Pseudomonas fluorescens* (Bayer AG, 1978; test protocols are no longer available). Since the biodegradability of triphenyl phosphate showed a result of 83 - 94 % after 28 d of incubation with 30 mg/l sludge and 100 mg/l triphenyl phosphate in a test on ready biodegradability, there is no significant effect of triphenyl phosphate in the low concentration range expected.

4.2 Terrestrial Effects

No data available.

4.3 Other Environmental Effects

No valid data available.

4.4 Initial Assessment for the Environment

Triphenyl phosphate has a solubility in water between 0.2 mg/l (river water) and 1.9 mg/l (distilled water) at 20 °C, a vapour pressure of 0.000835 Pa at 25 °C and a log K_{OW} of 4.6. According to a Mackay Level I model calculation, triphenyl phosphate is mainly distributed to soil (43.9 %) and sediment (41.0 %), and to a lesser extent to water (14.3 %) and air (0.7 %). Triphenyl phosphate is hardly volatile from aqueous solution (calculated Henry constant: 0.018 - 0.036 Pa m³/mol). The substance is strongly absorbed to soil and sediment (measured K_{oc}-values in the range of 2514 - 3561). In the atmosphere rapid degradation of triphenyl phosphate via indirect photolysis occurs (t_{1/2air} = ca. 12 h). While triphenyl phosphate is relatively stable under neutral and acidic conditions

($t_{1/2} = 19$ d at pH 7; $t_{1/2} > 28$ d at pH 5), it undergoes hydrolysis under alkaline conditions ($t_{1/2} = 7.5$ d at pH 8.2; $t_{1/2} = 1.3$ d at pH 9.5). In soil half-lives for primary degradation of 37 and 21 days were determined under aerobic and anaerobic test conditions, respectively. Triphenyl phosphate is readily biodegradable (83 - 94 % degradation after 28 d). Under anaerobic conditions with river sediment ca. 90 % triphenyl phosphate were primary degraded after 40 days of incubation. Mineralisation was about 22 % after 40 days. Measured bioconcentration factors in fish were in the range of 110 to 144, indicating a moderate bioaccumulation potential. As the BCF values were related to the parent compound, there is no information on possible accumulation of stable metabolites. BCFs for *Lemna minor* and *Typha sp.* are stated to be < 50 . As the substance was found in dolphins collected in the Gulf of Mexico, accumulation via the food chain may occur.

The acute toxicity has been determined for fish (*Oncorhynchus mykiss*: 96 h-LC₅₀ > 0.4 mg/l) and invertebrates (*Mysidopsis bahia*: 96 h-EC₅₀ $> 0.18 - 0.32$ mg/l, *Daphnia magna*: 48 h-EC₅₀ = 1.0 mg/l). In tests with algae (*Selenastrum capricornutum*, *Scenedesmus subspicatus*, *Chlorella vulgaris*) NOEC values in the range of 0.25 to 2.5 mg/l were obtained after exposure periods of 96 h. In a long term test with fish (*Oncorhynchus mykiss*) a 30 d-NOEC of 0.037 mg/l was found. A PNEC_{aqua} of 0.74 µg/l is derived from the aforementioned long-term NOEC using an assessment factor of 50.

5 RECOMMENDATIONS

Environment:

The chemical is a candidate for further work. Triphenyl phosphate has a wide dispersive use as flame retardant. Environmental releases are likely to occur during production, during the use as flame retardant e.g. in polymer applications as well as during the service life and the disposal of products containing the substance. Also accidental spill and leakage of hydraulic liquids in different application areas can be a source of environmental release. However, no exposure information is available, except for the production at the sponsor company. Triphenyl phosphate is highly toxic to aquatic organisms (LC₅₀ < 1 mg/l for fish, PNEC_{aqua} = 0.74 µg/l) and has a potential to accumulate in biota. Therefore, an exposure assessment and, if then indicated, an environmental risk assessment is recommended. Environmental exposure during production at the sponsor company is adequately controlled.

Human Health:

The chemical is currently of low priority for further work because of its low hazard potential.

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I U C L I D

Data Set

Existing Chemical	: ID: 115-86-6
CAS No.	: 115-86-6
EINECS Name	: triphenyl phosphate
EC No.	: 204-112-2
TSCA Name	: Phosphoric acid, triphenyl ester
Molecular Formula	: C ₁₈ H ₁₅ O ₄ P
Producer related part	
Company	: Bayer AG
Creation date	: 15.01.2001
Substance related part	
Company	: Bayer AG
Creation date	: 15.01.2001
Status	:
Memo	: AKTUELL / ICCA (Bayer Datensatz aus 1992 und ECB-Datensatz gemergt)
Printing date	: 05.09.2005
Revision date	:
Date of last update	: 05.09.2005
Number of pages	: 124
Chapter (profile)	: Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	: Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	: Flags: without flag, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION**1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR****1.0.3 IDENTITY OF RECIPIENTS****1.0.4 DETAILS ON CATEGORY/TEMPLATE****1.1.0 SUBSTANCE IDENTIFICATION**

IUPAC Name :
Smiles Code : O=P(Oc(cccc1)c1)(Oc(cccc2)c2)Oc(cccc3)c3
Molecular formula : C₁₈H₁₅O₄P
Molecular weight : 326.29
Petrol class :

Flag : Critical study for SIDS endpoint
10.11.2004

(1)

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type :
Substance type : organic
Physical status : solid
Purity : >= 99.6 % w/w
Colour :
Odour :

Flag : Critical study for SIDS endpoint
07.05.2002

1.1.2 SPECTRA**1.2 SYNONYMS AND TRADENAMES****TPP**

Flag : Critical study for SIDS endpoint
10.11.2004

Phosphoric acid, triphenyl ester

10.11.2004

(1)

1.3 IMPURITIES

Remark : <= 0.4 % water, phenol, other esters
Flag : Critical study for SIDS endpoint
 07.05.2002

1.4 ADDITIVES**1.5 TOTAL QUANTITY****1.6.1 LABELLING**

Labelling : provisionally by manufacturer/importer
Specific limits :
Symbols : N, , ,
Nota : , ,
R-Phrases : (50/53) Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
S-Phrases : (61) Avoid release to the environment. Refer to special instructions/Safety data sets

Flag : Critical study for SIDS endpoint
 18.03.2002

1.6.2 CLASSIFICATION

Classified : provisionally by manufacturer/importer
Class of danger :
R-Phrases : (50/53) Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
Specific limits :

Flag : Critical study for SIDS endpoint
 07.05.2002

1.6.3 PACKAGING**1.7 USE PATTERN**

Type of use : industrial
Category : Polymers industry

Flag : Critical study for SIDS endpoint
 07.05.2002

Type of use : type
Category : Use resulting in inclusion into or onto matrix

Flag : Critical study for SIDS endpoint
 03.05.2002

Type of use : use
Category : Flame retardants and fire preventing agents

Flag : Critical study for SIDS endpoint
 07.05.2002

Type of use : use
Category : other: Plasticisers

Flag : Critical study for SIDS endpoint
 07.05.2002

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit : other: TRGS 900 (DE)
Limit value : 3 mg/m³

Flag : Critical study for SIDS endpoint
 07.05.2002

Type of limit : TLV (US)
Limit value : 3 mg/m³

Short term exposure limit value
Limit value : 9 mg/m³
Time schedule :
Frequency : 3 times

Remark : length of exposure: no more than a total of 30 min during a workday

Flag : Critical study for SIDS endpoint
 07.05.2002

Type of limit : OES (UK)
Limit value : 3 mg/m³

Short term exposure limit value
Limit value : 6 mg/m³
Time schedule : 10 minute(s)
Frequency : 1 times

Flag : Critical study for SIDS endpoint
 08.12.2004

(2)

1.8.2 ACCEPTABLE RESIDUES LEVELS

1. GENERAL INFORMATION

ID: 115-86-6

DATE: 20.08.2002

1.8.3 WATER POLLUTION

Classified by : KBwS (DE)
Labelled by :
Class of danger : 2 (water polluting)

Remark : WGK-Identification-Nr. 1232
Flag : Critical study for SIDS endpoint
 07.05.2002

1.8.4 MAJOR ACCIDENT HAZARDS

Legislation :
Substance listed : no
No. in Seveso directive :

Flag : Critical study for SIDS endpoint
 07.05.2002

1.8.5 AIR POLLUTION

Classified by : other: No classification
Labelled by :
Number :
Class of danger :

Flag : Critical study for SIDS endpoint
 07.05.2002

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES**1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS**

Type : degradation product
CAS-No : 108-95-2
EC-No : 203-632-7
EINECS-Name : phenol
IUCLID Chapter :

Remark : IUCLID Chapter 3.1.2 and 3.1.3
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
 14.12.2004 (3) (4)

Type : degradation product
CAS-No : 838-85-7
EC-No : 212-657-2
EINECS-Name : diphenyl hydrogen phosphate
IUCLID Chapter :

Remark : IUCLID Chapter 3.1.2 and 3.1.3
Flag : Critical study for SIDS endpoint
 14.12.2004 (3) (4)

1. GENERAL INFORMATION

ID: 115-86-6

DATE: 20.08.2002

Type : degradation product
CAS-No : 124-38-9
EC-No : 204-696-9
EINECS-Name : carbon dioxide
IUCLID Chapter :

Remark : IUCLID Chapter 3.1.3 and 3.5
Flag : Critical study for SIDS endpoint
14.12.2004

(3) (5)

1.9.2 COMPONENTS**1.10 SOURCE OF EXPOSURE**

Remark : TPP is manufactured from phosphous oxychloride and phenol. TPP is used as a plasticizer for polymers and its use results in inclusion into the polymer matrix. Exposure of the general population to TPP through normal use can be regarded as minimal.

Flag : Critical study for SIDS endpoint
10.11.2004

(6)

1.11 ADDITIONAL REMARKS**1.12 LAST LITERATURE SEARCH**

Type of search : Internal and External
Chapters covered :
Date of search :

Remark : Environmental aspects and ecotoxicology: May 2002
Toxicology: December 2000
CAS number search in external and internal databases, e.g. HSDB, Aquire, Biosis, Embase, Toxline, Scisearch.

Flag : Critical study for SIDS endpoint
01.08.2002

1.13 REVIEWS

2.1 MELTING POINT

Value	:	= 49 - 50 °C	
Remark	:	Method in handbook not reported	
Reliability	:	(2) valid with restrictions Data from peer-reviewed handbook or collection of data	
Flag	:	Critical study for SIDS endpoint	
14.12.2004			(7) (6)
Value	:	= 50.5 °C	
Remark	:	Method in handbook not reported	
Reliability	:	(2) valid with restrictions Data from peer-reviewed handbook or collection of data	
14.12.2004			(8)
Value	:	48 - 50 °C	
Remark	:	Method in safety data sheet not reported	
Reliability	:	(4) not assignable Manufacturer data without proof	
14.12.2004			(9)
Value	:	= 50 °C	
Remark	:	Method in handbook not reported	
Reliability	:	(4) not assignable Data from non-peer-reviewed handbook or collection of data	
14.12.2004			(10)

2.2 BOILING POINT

Value	:	= 245 °C at 14.6 hPa	
Decomposition	:		
Method	:	other: no data	
Year	:		
GLP	:		
Test substance	:		
Reliability	:	(2) valid with restrictions Data from peer-reviewed handbook or collection of data	
Flag	:	Critical study for SIDS endpoint	
14.12.2004			(8) (7)
Value	:	= 220 °C at 6.6 hPa	
Decomposition	:		
Method	:	other: no data	
Year	:		
GLP	:		
Test substance	:		
Remark	:	Method not reported	
Reliability	:	(2) valid with restrictions Data from handbook or collection of data	
14.12.2004			(6)

Value : 220 °C at 5 hPa

Remark : Method in safety data sheet not reported

Reliability : (4) not assignable
Manufacturer data without proof

14.12.2004 (9)

Value : 245 °C at 14.6

Decomposition :

Method : other: no data

Year : 1996

GLP :

Test substance :

Reliability : (4) not assignable
Data from non-peer-reviewed handbook or collection of data

14.12.2004 (10)

2.3 DENSITY

Type : relative density

Value : = 1.2055 g/cm³ at 50 °C

Remark : It is assumed that the density is reported at 50 °C since the substance is melted at that temperature. The melt is the form which is often used for transport

Reliability : (2) valid with restrictions
Data from peer-reviewed handbook or collection of data

Flag : Critical study for SIDS endpoint

14.12.2004 (8)

Type : relative density

Value : 1.205 g/cm³ at 50 °C

Remark : Determination according to DIN 51757

Reliability : (4) not assignable
Manufacturer data without proof

Flag : Critical study for SIDS endpoint

14.12.2004 (9)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : = .00000835 hPa at 25 °C

Decomposition :

Method : other (calculated)

Year : 1957

GLP :

Test substance :

Remark : extrapolated from measured data by the Clausius-Clapeyron equation

Reliability : (2) valid with restrictions
Accepted calculation method

Flag : Critical study for SIDS endpoint

14.12.2004 (11)

2. PHYSICO-CHEMICAL DATA

ID: 115-86-6

DATE: 20.08.2002

Method	:	other (measured)	
Year	:	1979	
GLP	:	no	
Test substance	:		
Remark	:	experimentally determined by partitioning between water and 1-octanol in a closed bottle at room temperature	
Test condition	:	Measured by preparing at least 2 concentrations (100 ppm - 1%) TPP in 100 ml 1-octanol. This was added to 500 ml water and shaken for 48 hours. Mixture was allowed to stand for 1 week in dark. Aliquots were drained and extracted with methylene chloride and analyzed.	
Reliability	:	(2) valid with restrictions Basic data given	
Flag	:	Critical study for SIDS endpoint	(5)
14.12.2004			
Partition coefficient	:	octanol-water	
Log₁₀ K_{ow}	:	= 4.76 at °C	
pH value	:		
Method	:	other (measured)	
Year	:	1981	
GLP	:		
Test substance	:		
Test condition	:	50 mg added to separatory funnel containing 50 ml octanol (saturated with water) and 50 ml distilled water. The funnel was shaken for 2 h. Aliquots of the aqueous phase were extracted three times with hexane and analysed by GC. Quantity in organic phase was calculated from the triphenyl phosphate in water.	
Reliability	:	(2) valid with restrictions Basic data given	
14.12.2004			(14)
Partition coefficient	:	octanol-water	
Log₁₀ K_{ow}	:	= 4.59 at °C	
pH value	:		
Remark	:	experimentally determined, method not reported	
Reliability	:	(2) valid with restrictions Data from peer-reviewed handbook or collection of data	
14.12.2004			(15)
Partition coefficient	:	octanol-water	
Log₁₀ K_{ow}	:	4.7 at °C	
pH value	:		
Method	:	other (calculated): SRC-KOWWIN v1.66 (2000)	
Year	:	2002	
GLP	:		
Test substance	:		
Reliability	:	(4) not assignable Manufacturer data without proof	
14.12.2004			(16)
Partition coefficient	:	octanol-water	
Log₁₀ K_{ow}	:	= 4.59 at °C	
pH value	:		
Reliability	:	(4) not assignable Data from non-peer-reviewed handbook or collection of data	

2. PHYSICO-CHEMICAL DATA

ID: 115-86-6

DATE: 20.08.2002

14.12.2004 (10)

Partition coefficient : octanol-water
Log pow : 4.62 at °C
pH value :
Method : other (measured)
Year : 1981
GLP : no
Test substance :

Remark : The authors of the study report that they determined Kow experimentally with the method of Saeger VW, Hicks O, Kaley RG, Michael PR, Mieure JP, Tucker ES (1979) Environmental Fate of Selected Phosphate Esters. Environ Sci Technol 13: 840 - 844. Both groups obtained exactly the same value.

Reliability : (2) valid with restrictions
 Basic data given

14.12.2004 (17)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in Value : Water
 : at °C
pH value concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method : other: Shaking excess amounts of TPP with water for 2 h at room temp., filtering off undissolved TPP with 2 µm filter, methylation and analysis with GC/flame photometric detector
Year : 1979
GLP :
Test substance :

Result : at room temperature (21 °C)

1. Test: Buffered distilled water, pH 4.5 - 9.5
 solubility: 1.4 - 1.6 mg/l

2. Test: Lake/River water, pH 7.8 - 8.2
 solubility: 0.2 - 0.3 mg/l

Reliability : (2) valid with restrictions
 Basic data given

Flag : Critical study for SIDS endpoint

14.12.2004 (4)

Solubility in Value : Water
 : = 1.9 mg/l at 20 °C
pH value concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :

2. PHYSICO-CHEMICAL DATA

ID: 115-86-6

DATE: 20.08.2002

Method	:	other: Agitating excess TPP in purified water (Milli-Q water purif. system) for 48 h, standing for 1 week to permit phase separation in the dark, centrifugation and extraction of water phase with dichloromethane. Analysis with GC/FID	
Year	:	1979	
GLP	:	no	
Test substance	:		
Test condition	:	Room temperature (in SIAR assumed to be 20 °C)	
Reliability	:	(2) valid with restrictions Basic data given	
Flag	:	Critical study for SIDS endpoint	(5)
14.12.2004			
Solubility in Value	:	Water 1.9 mg/l at 25 °C	
pH value concentration	:	at °C	
Temperature effects	:		
Examine different pol.	:		
pKa	:	at 25 °C	
Description	:		
Stable	:		
Deg. product	:		
Method	:	other: see test condition	
Year	:	1981	
GLP	:		
Test substance	:		
Test condition	:	25 ml ester was added to 500 ml water, agitated for 48 h and left standing in dark for 1 week. Aqueous phase was centrifuged and extracted twice for 1 h. Extracts were analyzed. pH of water was not reported. Performed at room temperature.	
Reliability	:	(2) valid with restrictions Basic data given	
Flag	:	Critical study for SIDS endpoint	(17)
14.12.2004			
Solubility in Value	:	Water < .1 - .6 mg/l at 15 °C	
pH value concentration	:	7.6 - 8 at °C	
Temperature effects	:		
Examine different pol.	:		
pKa	:	at 25 °C	
Description	:		
Stable	:		
Deg. product	:		
Method	:		
Year	:	1988	
GLP	:	no	
Test substance	:	other TS: technical grade TPP (Ciba-Geigy DVP 438)	
Method Result	:	Measurements of solubility of TPP in seawater (pH 8.1) During incubation for acute toxicity tests of TPP on Brown Shrimp (Crangon crangon), the substance was added to seawater under constant stirring. Still after several days and at concentrations as low as 0.25 mg/l precipitates were observed. The following analytical TPP-concentrations were determined after adding 2.5 mg/l of the substance to seawater:	

Time (h): 6 24 30 48 54 72 78 96
 mg/l: 0.14 0.44 <0.1 <0.1 <0.1 <0.1 0.16 <0.1

These results demonstrate that TPP is dissolved very slowly. After 4 d the limit of solubility (approx. 2 mg/l) is not reached. From the data it seems doubtful that the limit of solubility ever will be reached since degradation may start to play an important role in natural water.

Test condition	:	Solubility in seawater tested since use of seawater was essential for performance of acute toxicity test with Brown Shrimp (<i>Crangon crangon</i>) - Temperature nominal 15 °C, range during test 14.6-16.2 °C	
Reliability	:	(2) valid with restrictions Basic data given	
Flag 14.12.2004	:	Critical study for SIDS endpoint	(18)
Solubility in Value	:	Water .75 mg/l at 25 °C	
pH value concentration	:	at °C	
Temperature effects	:		
Examine different pol.	:		
pKa	:	at 25 °C	
Description	:		
Stable	:		
Deg. product	:		
Method	:	OECD Guide-line 105	
Year	:	1985	
GLP	:	no data	
Test substance	:	other TS: TPP (Pilabrac 521)	
Remark	:	Cited according to ECB IUCLID	
Reliability 14.12.2004	:	(4) not assignable Literature not available	(19)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Value	:	> 230 °C	
Type	:		
Method	:	other: DIN 51376	
Year	:		
GLP	:		
Test substance	:		
Reliability 14.12.2004	:	(4) not assignable Manufacturer data without proof	(9)

2.8 AUTO FLAMMABILITY

Value	:	> 500 °C at
Method	:	other: DIN 51794
Year	:	
GLP	:	
Test substance	:	

Reliability : (4) not assignable
Manufacturer data without proof

14.12.2004

(9)

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	air	
Light source	:		
Light spectrum	:	nm	
Relative intensity	:	based on intensity of sunlight	
INDIRECT PHOTOLYSIS			
Sensitizer	:	OH	
Conc. of sensitizer	:	1500000 molecule/cm ³	
Rate constant	:	.000000000108423 cm ³ /(molecule*sec)	
Degradation	:	50 % after 11.8 hour(s)	
Deg. product	:		
Method	:	other (calculated): AOPWIN, v.1.90	
Year	:	2001	
GLP	:		
Test substance	:		
Remark	:	the calculated t1/2 is based on the assumption of 12h light-cycle/d and a concentration of 1.5x10E6 OH/cm3	
Reliability	:	(2) valid with restrictions generally accepted calculation method	
Flag	:	Critical study for SIDS endpoint	
07.05.2002			(20)
Type	:	water	
Light source	:	other: low-pressure mercury lamp	
Light spectrum	:	254 nm	
Relative intensity	:	based on intensity of sunlight	
Conc. of substance	:	.1 mg/l at °C	
Deg. product	:		
Method	:		
Year	:	1991	
GLP	:	no data	
Test substance	:	other TS: commercial TPP purified by zone refining; purity checked by GC.	
Method	:	Photolysis in static reactor: Irradiation of a TPP-solution in distilled water with a mercury lamp, analysis of samples by GC (packed column) - FID. Phosphoric acid was analyzed by the Ascorbic Acid Method (APHA et al., 1975), phenols by the 4-Aminoantipyrine Method (Environmental Health Bureau 1978).	
Result	:	Disappearance of 0.1 mg/l TPP at pH3 and pH10 resp. caused by irradiation was shown within minutes.	
		TPP degradation without pH adjustment at pH 3.4 after 6 h irradiation: 100 % TPP degraded, 60 % of theoretical phosphate found, no phenol found.	
		TPP degradation with initial pH 12 after 6 h irradiation: 100 % TPP degraded, 60 % of theoretical phosphate found, 9 % of theoretical phenol found. The produced phenol was further decomposed by irradiation.	
		Degradation products di- and monophenyl phosphate were not determined in neither of the tests.	
Test condition	:	Degradation at alkaline pH may involve the hydrolysis with NaOH. Solution of TPP in 100 ml distilled water for 1 h by ultrasonication, dilution with 1.9 l distilled water; withdrawal of samples during irradiation.	
		Irradiation with the following confirmed wavelength: 254 nm (6.640-6.800 mW/cm ²), 297 nm (0.140-0.143 mW/cm ²), 365 nm (0.153-0.158 mW/cm ²).	

3. ENVIRONMENTAL FATE AND PATHWAYS

ID: 115-86-6

DATE: 20.08.2002

Reliability	:	(2) valid with restrictions Acceptable, well-documented publication which meets basic scientific principles	
Flag 24.07.2002	:	Critical study for SIDS endpoint	(21)
Type	:	other: methanol	
Light source	:	other: mercury lamp	
Light spectrum	:	267.5 nm	
Relative intensity	:	based on intensity of sunlight	
Deg. product	:		
Method	:		
Year	:	1985	
GLP	:		
Test substance	:		
Remark	:	0.1 mg/l triphenyl phosphate in methanol was exposed to UV light to examine the degradation of TPP. With a low pressure mercury lamp 100 % were degraded after 1 hour, with a high pressure mercury lamp 100 % were degraded after 20 minutes. Reference in Japanese, cited according to English translation	
Reliability 14.12.2004	:	(2) valid with restrictions Basic data given: comparable to guideline	(22)
Type	:	water	
Light source	:	other: low-pressure mercury lamp	
Light spectrum	:	254 nm	
Relative intensity	:	based on intensity of sunlight	
DIRECT PHOTOLYSIS	:		
Half-life t_{1/2}	:		
Degradation	:	% after	
Quantum yield	:	.29	
Deg. product	:		
Method	:	other (calculated)	
Year	:	1994	
GLP	:	no data	
Test substance	:	other TS: > 97%	
Remark	:	Measured quantum yield 0.29 according to the authors at 254 nm with a mercury lamp for triphenyl phosphate. the quantum yield was calculated from the rate of light absorption and the rate of disappearance of the substance; control samples stored in the dark (< 10 h) showed no concentration change; analysis was conducted via LC/UV	
Test condition	:	mery-go-round sample rack; concentration of TS: 1.5-3 mg/l; irradiation was performed until > 75% of TS was degraded; fenitrothion as reference compound	
Reliability 24.07.2002	:	(2) valid with restrictions Basic data given, study meets generally accepted scientific principles	(23)
Type	:	water	
Light source	:		
Light spectrum	:	nm	
Relative intensity	:	based on intensity of sunlight	
Result	:	Test of UV light absorption of TPP in aqueous solution with a low pressure mercury lamp at 254 nm: E = 644 (logE = 2.81). No absorption at 313 nm.	

Reliability	:	(2) valid with restrictions No guideline study, but sound and well documented study	
Flag	:	Critical study for SIDS endpoint	
24.07.2002			(23)
Type	:	other: methanol	
Light source	:		
Light spectrum	:	nm	
Relative intensity	:	based on intensity of sunlight	
Result	:	Test of UV light absorption of TPP in methanol with a low pressure mercury lamp at 254 nm: 714 (logE = 2.85). No absorption at 313 nm.	
Reliability	:	(2) valid with restrictions No guideline study, but sound and well documented study	
24.07.2002			(23)
Result	:	Test of TPP in ethanol Wavelength of maximum absorption: 261 nm: E = 957 (logE = 2.981)	
24.07.2002			(24)
Result	:	Test of TPP in hexane Wavelengths of maximum absorption: 256 nm: E = 960 262 nm: E = 1180 268 nm: E = 910	
24.07.2002			(25)

3.1.2 STABILITY IN WATER

Type	:	abiotic	
t1/2 pH4	:	at °C	
t1/2 pH7	:	= 19 day(s) at 25 °C	
t1/2 pH9	:	= 3 day(s) at 25 °C	
t1/2 pH 5	:	> 28 day(s) at 25 °C	
Deg. product	:		
Method	:	other	
Year	:	1981	
GLP	:	no data	
Test substance	:	no data	
Remark	:	Hydrolysis products not measured.	
Test condition	:	Initial triphenyl phosphate concentration: 50 µg/l , solubilizing agent: methanol Test with pH 5: 0.05 M buffered solution with potassium acid phthalate/sodium hydroxide Test with pH 7: 0.05 M buffered solution with potassium and disodium orthophosphate Test with pH 9: 0.05 M buffered solution with boric acid/sodium hydroxide	
Reliability	:	(2) valid with restrictions study in accordance with generally accepted scientific principles and described in sufficient detail	
Flag	:	Critical study for SIDS endpoint	
14.12.2004			(17)
Type	:	abiotic	

3. ENVIRONMENTAL FATE AND PATHWAYS

ID: 115-86-6

DATE: 20.08.2002

t1/2 pH4 : at °C
t1/2 pH7 : at °C
t1/2 pH9 : at °C
Deg. product :
Method :
Year : 1979
GLP : no
Test substance : other TS: Aldrich Chemical Co., purity not reported
Deg. products : 108-95-2 203-632-7 phenol
 838-85-7 212-657-2 diphenyl hydrogen phosphate

Method : Analyses were performed by GC/flame photometric detector after extraction with diethylether and derivatisation of free OH groups with diazomethane. Recovery of TPP was 90-100 %.
Remark : In all cases the authors used TPP saturated solutions, obtained by excess amounts of TPP shaken in water for 2 hours and than filtered (11 micron filter).
Result : Triphenyl phosphate showed different behaviour in distilled water and natural waters referring to solubility (see chapt. 2.6.1) as well as to hydrolysis.

Hydrolysis of TPP was found to be much faster under alkaline conditions than in neutral or acid solution:

Distilled water:

with adjusted pH values at 21 °C:

pH 4.5 (1): t1/2 = too slow for reliable measurement

pH 6.7 (2): t1/2 = too slow for reliable measurement

pH 8.2 (3): t1/2 = 7.5 days

pH 9.5 (4): t1/2 = 1.3 days

pH adjustment at the test with dist. water by:

(1) HCl

(2) dist. water

(3) sodium/disodium phosphate buffer

(4) boric acid/sodium hydroxide

River and lake water:

with natural buffer, without pH control at 21 °C:

pH 7.8 to pH 8.2: very little degradation for the first two days, thereafter rapid loss at a rate that is faster than in distilled water at comparable pH.

Reported hydrolysis products were diphenyl phosphate and phenol (the later is mentioned in the analytical procedure only). Further hydrolysis of diphenyl phosphate was considered much slower as monophenyl phosphate was not found in these experiments, and diphenyl phosphate was considered stable under alkaline conditions with reference to an older paper.

Reliability : (2) valid with restrictions
 study well documented, meets generally accepted scientific principles

Flag : Critical study for SIDS endpoint

14.12.2004

(4)

Type : biotic
t1/2 pH4 : at °C
t1/2 pH7 : at °C
t1/2 pH9 : at °C
Deg. product :
Method :
Year :

3. ENVIRONMENTAL FATE AND PATHWAYS

ID: 115-86-6

DATE: 20.08.2002

- GLP** : no data
Test substance : other TS: purity 98 %
- Method** : Outdoor experimental stream including two pools and 50 m total length at National Fisheries Contaminant Research Center. Addition of soil once a week with increasing TPP amounts over the time. Test on TPP content in stream sediment and in the water outflow.
- Result** : Monitoring of TPP concentrations: in soil (before added), sediment x days after addition of treated soil, water (at outflow):

TPP concentrations in soil before added to stream:

Week in soil(mg/kg)

1	55.2
2	92.4
3	233.8
4	451.8
5	841.9
6	2099.1

TPP concentrations measured in sediment:

after 0

d	1 d	3 d	7 d	14 d		
week	Sediment (mg TTP/kg sediment)t(1/2) TPP					
1	--	--	--	--	--	--
2	--	--	--	--	--	--
3	33.1	34.8	0.5	0.2	--	0.9 d
4	128.3	99.2	11.0	4.0	--	1.1 d
5	197.1	156.7	85.9	32.2	--	2.7 d
6	688.1	627.3	264.2	30.8	10.9	2.0 d

[-- : not measured]

TPP concentration measured in stream (µg/l):

Week	Water-Outflow 2 h after soil add.	Water-Outflow 96 h after soil add.	Interstitial water at riffle	Interstitial water at pool
1	27.9	0.4	--	--
2	109.7	0.4	--	--
3	70.4	0.3	--	--
4	184.6	0.7	0.0	0.7
5	75.7	0.6	25.0	11.8
6	2105.2	2.4	33.2	10.5
7	--	0.7	21.5	19.5
10	--	0.2	0.7	0.4
18	--	0.0	0.5	0.1

[-- : not measured]

The authors discuss that biological degradation, desorption, and dilution were probably important factors in the loss of TPP from water and sediments during that study, which resulted in relative low exposure to the contaminant.

- Test condition** : Water used: Well water,
 pH at inlet and outlet: 7.31 - 8.04
 Sediment used: locally obtained topsoil, 0.70 % organic C, 5 % sand, 77 % silt, 18 % clay.

Application of TPP to stream: Spraying of acetone solubilized TPP on soil. 24 h adsorption time and volatilization of acetone. The soil added to the stream was treated with TPP each week for 6 weeks with increasing amounts of TPP, beginning at 50 mg/kg and doubled each week to a high of 1600 mg/kg. The treated soil was flushed into the circulation water once

		a week. The TPP contaminated soil was added during a water flow of 40 l/s for 4 hours, half of which was discharged at the end of the stream and replaced by fresh water.	
Reliability	:	(3) invalid Method not validated; well-documented publication	
Flag	:	Critical study for SIDS endpoint	
02.08.2002			(26)
Type	:	abiotic	
t1/2 pH4	:	at °C	
t1/2 pH7	:	at °C	
t1/2 pH9	:	at °C	
Degradation	:	= 100 % after 10 minute(s) at pH 13 and °C	
Deg. product	:		
Method	:	other: Purified water was adjusted stepwise for pH using HCl or NaOH. TPP was added so that final concentration was 0.1 mg/l. Flask was stored in dark at 20 °C.	
Year	:	1985	
GLP	:	no data	
Test substance	:	no data	
Remark	:	Reference in Japanese, cited according to English translation	
Reliability	:	(3) invalid Documentation insufficient for assessment	
11.11.2004			(22)
Type	:	abiotic	
t1/2 pH4	:	at °C	
t1/2 pH7	:	at °C	
t1/2 pH9	:	at °C	
Deg. product	:		
Method	:		
Year	:	1980	
GLP	:	no data	
Test substance	:	no data	
Result	:	second-order alkaline hydrolysis rate constant: 2.7 x 10E-1 M-1 x sec-1	
Reliability	:	(4) not assignable Original data cited are not available (unpublished data by the author)	
18.07.2002			(27)

3.1.3 STABILITY IN SOIL

Type	:	other: laboratory, aerobic test system
Radiolabel	:	yes
Concentration	:	5 mg/kg
Soil temperature	:	20 °C
Soil humidity	:	40 other: % of max. water capacity
Soil classification	:	other: BBA standard soil 2.2 (loamy sand)
Year	:	
Content of clay	:	%
Content of silt	:	%
Content of sand	:	%
Organic carbon	:	2.2 %
pH	:	
Cation exch. capacity	:	
Microbial biomass	:	373 other: mg microbial carbon/kg soil (dw)
Dissipation time	:	
DT50	:	37 day(s)

DT90	:	
Dissipation	:	% after
Deg. product	:	
Method	:	
Year	:	
GLP	:	no data
Test substance	:	other TS: 98.4 % radioactive purity
Deg. products	:	124-38-9 204-696-9 carbon dioxide 838-85-7 212-657-2 diphenyl hydrogen phosphate
Remark	:	Control: In the heat-sterilized soil mainly unchanged TS was recovered within the 101 days of incubation, which indicates that the degradation of TPP in soil is mainly due to microbial action. Only 1.4 % of the applied radioactivity accounted to diphenylphosphate after 101 days.
Result	:	After 101 days allocation of the applied radioactivity: 48.3 % as CO ₂ , 26.4 % non-extractable from soil, 26.6 % extractable from soil. The amount of CO ₂ formed increased steadily during the whole incubation time, whereas the amount of non-extractable residues increased steadily and then slowed down after an incubation time of 32 days. Only 0.2 % of the applied radioactivity accounted to diphenylphosphate after 101 days.
Test condition	:	Aerobic test system Incubation in the dark, solvent for aliquot application: acetonitrile, CO ₂ and volatiles were trapped in glass wool soaked with paraffin oil and soda lime resp.
Reliability	:	(2) valid with restrictions Acceptable, well-documented publication/study report which meets basic scientific principles
Flag	:	Critical study for SIDS endpoint
11.01.2005		(3)
Type	:	other: laboratory, anaerobic test system
Radiolabel	:	yes
Concentration	:	5 mg/kg
Soil temperature	:	20 °C
Soil humidity	:	40 other: % of max. water capacity
Soil classification	:	other: BBA standard soil 2.2 (loamy sand)
Year	:	
Content of clay	:	%
Content of silt	:	%
Content of sand	:	%
Organic carbon	:	2.2 %
pH	:	
Cation exch. capacity	:	
Microbial biomass	:	373 other: mg microbial carbon/kg soil (dw)
Dissipation time	:	
DT50	:	21 day(s)
DT90	:	
Dissipation	:	% after
Deg. product	:	
Method	:	
Year	:	
GLP	:	no data
Test substance	:	other TS: 98.4 % radioactive purity
Deg. products	:	108-95-2 203-632-7 phenol 124-38-9 204-696-9 carbon dioxide 838-85-7 212-657-2 diphenyl hydrogen phosphate
Result	:	After 102 days allocation of the applied radioactivity: 40.4 % as CO ₂ , 6.3 % volatiles, 35.8 % extractable from soil, 24.04 % non-extractable from soil by methane/water (9:1). The amount of CO ₂ formed, increased steadily during the whole incubation time. The amount of non-extractable residues

	increased faster during the first days and slowed down to a steadily slow increase. Only 0.5 % of the applied radioactivity accounted to diphenylphosphate and 1.6 % to phenol after 102 days.	
Test condition	: Anaerobic test system Incubation in the dark, solvent for aliquot application: acetonitrile. CO ₂ was adsorbed on soda lime, organic volatiles were passed over CuO at 900 °C and measured as CO ₂ .	
Reliability	: (2) valid with restrictions Acceptable, well-documented publication/study report which meets basic scientific principles	
Flag 11.01.2005	: Critical study for SIDS endpoint	(3)

3.2.1 MONITORING DATA

Type of measurement	: other: background and contaminated area	
Media	: air	
Concentration	: .000001 - .000094 µg/l	
Method	: GC/MS	
Result	: Before the short term studies 0.7 ng/m ³ triphenyl phosphate were found in the air of the larger office. 1 day after the installation of brand-new computer equipment 84 ng/m ³ triphenyl phosphate were found, which decreased to 39 ng/m ³ within 8 days. In the air of other offices without computer equipment also 0.7 ng/m ³ triphenyl phosphate were found. In the air of the smaller offices with brand-new computer equipment, the triphenyl phosphate level was 94 ng/m ³ after 1 day of computer installation. This level decreased to 10 ng/m ³ within 150 d	
Test condition	: - Air sampling via filter and 2 adsorbents in series, air flow rate 3 l/min, samples collected for 700 min - Short term emission studies were performed in an office with about 60 m ³ (fully enclosed) - Long term emission studies were performed in an office with about 25 m ³ (fully enclosed) - In the small offices brand-new PC equipment was placed which contained up to 10 % w/w triphenyl phosphate in the outer cover - GC (Varian 3400, Varian, Walnut Creek, CA) on DB-5 column, nitrogen-phosphorus-detector and split/splitless injector - GC/MS Varian 3400 plus Finnigan Incos 50 quadrupole mass spectrometer	
Test substance	: Triphenyl phosphate (used as a standard), purity > 98 % was purchased from Aldrich Chemicals, Germany	
Reliability	: (2) valid with restrictions Basic data given	
Flag 13.12.2004	: Critical study for SIDS endpoint	(28)
Type of measurement	: background concentration	
Media	: other: particulate matter and indoor air in private houses	
Concentration	: < .00001 µg/l	
Method	: GC/MS	
Remark	: Without clearly indicating the literature source, it is reported in a literature survey that the indoor air concentrations of triphenyl phosphate are 0.01-0.03 µg/m ³ . For drinking water, concentrations of triphenyl phosphate are reported to be 0.12 µg/l	
Result	: Indoor and outdoor triphenyl phosphate concentrations were below 0.01 µg/m ³ . Even in the air of several buildings which were thought to contain triphenyl phosphate containing materials, no triphenyl phosphate was	

	found. In particulate matter from public buildings, a maximum of 220 mg triphenyl phosphate/kg was measured, but all other results \leq 3 mg/kg	
Test condition	: - Particulate matter extraction with methylene chloride	
Reliability	: (2) valid with restrictions Secondary literature	
Flag 13.12.2004	: Critical study for SIDS endpoint	(29)
Type of measurement	: background concentration	
Media	: air	
Concentration	: \leq .00001 $\mu\text{g/l}$	
Method	: GC/MS	
Result	: Triphenyl phosphate was detectable (limit of detection 0.0012 $\mu\text{g/m}^3$) in 2 out of 6 houses tested. The concentration of triphenyl phosphate was 0.01 $\mu\text{g/m}^3$ in indoor air of both houses.	
Test condition	: - Air sampling via charcoal filter, 1 l/min, approximately 3 d collecting period, total sampling volume 4.3 m ³ - Extraction with toluene during ultrasonication - GC (Hewlett-Packard 6890) on HP-1 column (methyl siloxane), HP 7683 auto sampler, with He as the carrier gas - MS (HP 5973 MS) SIM mode - Triphenyl phosphate (obtained from Wako Pure Chemical, Japan) was used as a standard	
Reliability	: (2) valid with restrictions Basic data given	
Flag 11.01.2005	: Critical study for SIDS endpoint	(30)
Type of measurement	: other: contaminated and uncontaminated media	
Media	: other: several water samples	
Concentration	:	
Method	: GC/MS	
Method	: - Grab samples collected in glass bottles - Methylene chloride and hydrogen chloride added to suppress microbial activity, storage at about 0 °C in the dark - Solvent extraction - Liquid chromatography extraction - GC/MS in both electron impact and chemical ionization modes, MS selected ion monitoring and high resolution MS	
Remark	: Drinking water preparation by prechlorination, settling, coagulation (ferric chloride, aluminate, lime), disinfection, flocculation, rapid sand filtration, and chlorination	
Result	: Triphenyl phosphate was found at the following sampling sites ($\mu\text{g/l}$): - Sewage treatment plant (inlet): 16 - Sewage treatment plant (outlet): 2 - Delaware river mile 106 (2 miles upstream of the outlet, but tidal movement, and sewage treatment plant discharges travel about 7 miles upstream during high tide; tidal volume is about 1 order of magnitude larger than freshwater flow): 0.3 - Delaware river mile 108 (4 miles upstream of the outlet): 0.2 - Torredale drinking water treatment plant (river water inlet located 6 miles upstream of the outlet of the sewage treatment plant): 0.2 - Torredale drinking water treatment plant (drinking water): 0.03 - Delaware river mile 118 (14 miles upstream of the sewage treatment plant outlet, presumably no influence of the outlet): traces, not quantifiable	
Reliability	: (2) valid with restrictions Basic data given	
Flag 11.01.2005	: Critical study for SIDS endpoint	(31)

Type of measurement	:	other: Several industrialized and non-industrialized areas of the USA	
Media	:	other: Water, sediment, and fish	
Concentration	:		
Method	:		
Result	:	Triphenyl phosphate was detected in - 32 of 63 water samples (limit of detection 0.1 µg/l; concentrations in water up to 7.9 µg/l). The geometric mean of triphenyl phosphate concentrations in water (calculated using one half of detection limit for samples reported as non-detectable) was 0.12 µg/l. - 13 of 40 sediment samples (limit of detection 0.01 µg/g; concentrations in sediment up to 4 µg/g). - 16 of 82 fish (limit of detection 0.1 µg/g; concentrations in fish up to 0.6 µg/g).	
Test condition	:	Water, sediment, and fish samples were collected at 13 site in the USA - Water samples (900 ml) were obtained from the water column by moving sample tube opening on straight traverse line from bottom to surface at constant velocity - Sediment samples were obtained with Ponar and Student-Ekman grab samplers - 25 fish species were collected with gill nets and seine hauls - Sediment samples and fish were frozen immediately after sampling with dry ice and stored in a freezer (-23 °C) until analysis - Analysis according to Gledhill WE, Kaley RG, Adams WJ, Hicks O, Michael PR, Saeger VW (1980). Environ. Sci. Technol. 14, 301-305	
Reliability	:	(2) valid with restrictions Basic data given	
Flag 13.12.2004	:	Critical study for SIDS endpoint	(17)
Type of measurement	:	background concentration	
Media	:	surface water	
Concentration	:	<= .22 µg/l	
Method	:	GC/MS	
Result	:	Triphenyl phosphate was found in 14.1 % of 85 samples with a median = 0.040 µg/l and a maximum value of 0.22 µg/l	
Test condition	:	Streams in the USA have been monitored at 139 sampling sites susceptible to contamination e.g. downstream of intense urbanization and livestock production in 1999 and 2000 - 1 l water samples extracted by CLLE (continuous liquid-liquid extraction) using methylene chloride - analysis by GC/MS	
Reliability	:	(2) valid with restrictions Basic data given	
Flag 13.12.2004	:	Critical study for SIDS endpoint	(32)
Type of measurement	:	concentration at contaminated site	
Media	:	other: surface water, ground water	
Concentration	:		
Method	:	GC/MS	
Result	:	Triphenyl phosphate concentrations reached up to 0.280 µg/l in the river Ruhr (region with heavy industry and mining) in Germany. In different small tributaries of the river Ruhr mean concentrations of 0.4 µg/l were found. In a small creek which was dominated by the outflow of a sewage treatment plant, 2 µg/l were found. In the canal Emscher (Germany) concentrations up to 3.4 µg/l were measured. This sewer cannot be regarded as natural stream. Before entering the river Rhine the Emscher water is led through a	

		sewage treatment plant. No measured data from the outlet of this sewage treatment plant are available. In enriched groundwater of the Dortmund waterworks area no triphenyl phosphate could be detected (limit of detection 1 ng/l)	
Test condition	:	- The river Ruhr was sampled at 20 sites from well to mouth into river Rhine	
		- GC/MS (HP 5971A, Hewlett-Packard)	
Reliability	:	(2) valid with restrictions	
		Basic data given	
Flag	:	Critical study for SIDS endpoint	
11.01.2005			(33)
Type of measurement	:	concentration at contaminated site	
Media	:	other: wastewater treatment plant effluent	
Concentration	:	3 µg/l	
Method	:	GC/MS	
Result	:	137 organic compounds were identified in the effluents of three large Swedish wastewater treatment plants. In the effluent from one out of these three wastewater treatment plants, triphenyl phosphate was found in a concentration of 3 µg/l	
Test condition	:	- 3 Swedish wastewater treatment plants (treating both domestic and industrial wastewater) were sampled: -- Henricksdal serves central and Southern Stockholm with 580000 inhabitant equivalents (hydraulic retention time 5-6 h, solids retention time 2-3 d, food/microorganisms ratio 0.1 kg COD/ kg of suspended substance/day) -- GRYAAB serves Göteborg with 550000 inhabitant equivalents (hydraulic retention time 4.8 h, solids retention time 4.2 d, food/microorganisms ratio 0.56 kg COD/kg of suspended substance/day) -- Sjoelunda serves Malmö and its surroundings with 247000 inhabitant equivalents (hydraulic retention time 4 h, solids retention time 2-3 d, food/microorganisms ratio 0.2-0.3 kg COD/kg of suspended substance/day) - Sampling 1 week to one month in Dec. 1993 or Jan. 1994 - 1 sample per plant obtained by combining daily 2 l samples - Solid phase extraction - Analysis by GC (HP 5890, Hewlett/Packard) /MS (Incos 50, Finnigan MAT)	
Reliability	:	(2) valid with restrictions	
		Basic data given	
Flag	:	Critical study for SIDS endpoint	
13.12.2004			(34)
Type of measurement	:	other: food product monitoring	
Media	:	food	
Concentration	:		
Method	:	GC	
Method	:	Trialkyl and triaryl phosphates were surveyed in United Kingdom total diet samples - Solvent extraction - Liquid column clean up (with diatomite) - GC with phosphorus specific detection (alkali flame ionization detector) - Limit of detection 0.02 - 0.1 mg/kg (not further specified) - Recovery from several food products: 90 - 105 % as checked by spiking experiments	
Remark	:	It is not clear to what extend exposure to triphenyl phosphate occurred	
Result	:	The total phosphates levels (tributyl phosphate, triphenyl phosphate, trioctyl phosphate) ranged from (mean) 0.05 mg/kg for beverages to 0.02 for unspecified meat products and 0.25 for offal. The mean daily intake for	

these products was calculated to be approximately 0.1 mg/d. The triphenyl phosphate level was not reported

Reliability : (2) valid with restrictions
Basic data given

Flag : Critical study for SIDS endpoint

11.01.2005 (35)

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

3.3.2 DISTRIBUTION

Media : air - biota - sediment(s) - soil - water

Method : Calculation according Mackay, Level I

Year : 1991

Remark : Data used in calculation:
temperature (°C): 25
molar mass (g/mol): 326.29
vapor pressure (Pa): 8.35 x 10E-4
water solubility (g/m3): 1.90
log Kow: 4.59

Volumes in unit world (m3):
air: 6 000 000 000
water: 7 000 000
soil: 45 000
sediment: 21 000
susp. sediment: 35
biota (fish): 7

Result : Target compartments:
43.9 % soil
41.0 % sediment
14.3 % water
0.7 % air
0.07 % susp. sediment
0.03 % biota (fish)

Reliability : (2) valid with restrictions
generally accepted calculation method

Flag : Critical study for SIDS endpoint

14.12.2004 (36)

Media : water - soil

Method :

Year :

Remark : Depending on soil properties hydrolysis (main product: diphenyl phosphate) was observed during the equilibration period, hence the determined values include TPP as well as diphenyl phosphate. Maximum degradation occurred in silty clay.

Result : Adsorption constants:
Koc Kd
2514 16.09 silty clay
3561 79.05 loamy sand
2756 71.67 silt loam

	Desorption constants: Koc Kd 3363 21.52 silty clay 3501 77.72 loamy sand 2596 67.50 silt loam	
Test condition	: Study with [¹⁴ C]TPP, at 20 °C, three different soils. Soil characteristics: BBA standard soil 2.2 (loamy sand): 2.22% organic carbon; LUFA Speyer clay soil (silty clay): 0.64% organic carbon; soil Hoefchen (silt loam): 2.60% organic carbon; Test concentrations 50, 37.5, 25, and 5% of water solubility (1; 0.75; 0.5; 0.1 mg TPP/l). Adsorption/desorptions equilibrium was reached after 48 hours.	
Reliability	: (2) valid with restrictions Acceptable, well-documented publication/study report which meets basic scientific principles	
Flag 11.01.2005	: Critical study for SIDS endpoint	(3)
Media	: other: water - sediment	
Method	: other (measurement)	
Year	: 1983	
Result	: Mass balance (% radioactivity): in sediment in water 85 15 pond 88.7 11.3 river sediment 78.9 21.1 sand	
Test condition	: Study with [¹⁴ C]TPP, three different sediments, sediment-to-water ratio: 1:5; four replicates. Sediment characteristics: Sand (commercial silica: 0.1% organic carbon, pH 7.0), pond (silt clay: 3.7% organic carbon, pH 7.6) river (silty: 2.3% organic carbon, pH 7.7) Sediments, drained of excess water were spiked with TPP at 50 and 500 µg/kg concentrations by 10 or 100 µl stock solution. After mixing, the sediments were flooded with 250 ml dechlorinated tap water and gently aerated while allowed to equilibrate for 2 d.	
Reliability	: (2) valid with restrictions study well documented, meets generally accepted scientific principles	
Flag 02.08.2002	: Critical study for SIDS endpoint	(37)
Media	: water - soil	
Method	: other (measurement)	
Year	: 1991	
Result	: Kp for clay is not reported because of a high coefficient of variation (>= 50 %). The authors explain that some of this variability may be due to the lack of uniform distribution of TPP spiked to the clay surface. However the mean value clay Kp was about three times higher than that of topsoil. The low organic carbon content of the clay suggests that non-organic carbon sorptive interactions may have played a role.	
	Topsoil sediment/water partition coefficients (organic carbon content 1.1 %): Kp (24 h)= 112 +/- 26 (N=4; soil-phase separation by filtration) Kp (24 h)= 96 +/- 41 (N=3; soil-phase separation by centrifugation)	
Test condition	: Study with commercial TPP, at 25 °C, two different sediments (topsoil and clay).	

		100 µg TPP in acetone was spiked to 100 mg air-dried sediment and later 100 ml deionized water was added. 24 hours shaking for equilibrium. TPP residue analysis with GC/thermionic detector.	
		Sediment characteristics: - topsoil/loess (loamy sand): 1.12 % organic carbon - montmorillonite clay: 0.33 % organic carbon	
Reliability	:	(3) invalid Relevant methodological deficiencies	
14.12.2004			(38)
Media	:	water - soil	
Method	:		
Year	:		
Method	:	Calculation acc. to Kenaga & Goring 1981 using the water solubility (1.9 mg/l) and octanol-water partition coefficient ($4.2 \times 10E4$).	
Result	:	Calculated soil sorption coefficient $K_{oc} = 5500$	
Reliability	:	(2) valid with restrictions Accepted calculation method	
07.05.2002			(17)
Media	:	water - soil	
Method	:		
Year	:		
Method	:	Calculation acc. to Kenaga & Goring (eq. 4-5 in Lyman 1982) using the water solubility (1.9 mg/l).	
Result	:	Calculated soil sorption coefficient $K_{oc} = 3100$	
Reliability	:	(2) valid with restrictions Accepted calculation method	
07.05.2002			(12)
Media	:	water - air	
Method	:	other (calculation)	
Year	:	1985	
Result	:	Henry's law constant (25°C): $1.8 \times 10E-2 - 3.6 \times 10E-2$ Pa m ³ /mol (calculated from water solubility (1.9 mg/l) and vapor pressures ($1.6 \times 10E-4$, $2.0 \times 10E-4$, and $1.07 \times 10E-3$ Pa))	
Reliability	:	(2) valid with restrictions generally accepted calculation method	
Flag	:	Critical study for SIDS endpoint	
07.05.2002			(12)
Media	:	water - air	
Method	:	other (calculation)	
Year	:	2001	
Method	:	Calculation according to the Bond estimation method using HENRYWIN, v. 3.10	
Result	:	Henry's law constant (25°C): $4.03 \times 10E-3$ Pa m ³ /mol	
Reliability	:	(2) valid with restrictions generally accepted calculation method	
07.05.2002			(39)

3.4 MODE OF DEGRADATION IN ACTUAL USE**3.5 BIODEGRADATION**

Type : aerobic
Inoculum : activated sludge
Concentration : 100 mg/l related to Test substance related to
Contact time :
Degradation : 83 - 94 (\pm) % after 28 day(s)
Result : readily biodegradable
Deg. product :
Method : other: see remarks
Year : 1992
GLP : no data
Test substance : no data

Remark : The test was conducted in accordance with "Biodegradation test of chemical substance by microorganisms etc." stipulated in the Order Prescribing the Items of the Test Relating to the New Chemical Substance (1974, Order of the Prime Minister, the Minister of Health and Welfare, the Minister of International Trade and Industry No. 1). This guideline corresponds to "301C, Ready Biodegradability: Modified MITI Test (I)" stipulated in the OECD Guidelines for Testing of Chemicals (1981)

Test condition : sludge concentration: 30 mg/l
Reliability : (1) valid without restriction guideline study

Flag : Critical study for SIDS endpoint
 13.05.2002

(40)

Type : aerobic
Inoculum : activated sludge, domestic, adapted
Concentration : 18.3 mg/l related to Test substance related to
Contact time :
Degradation : 82 (\pm) % after 28 day(s)
Result :
Deg. product :
Method : other: modified Sturm Test (1973)
Year : 1979
GLP : no
Test substance : other TS: purity > 90 %
Deg. products : 124-38-9 204-696-9 carbon dioxide

Remark : Acclimated bacterial seed was prepared using a 14d Bunch-Chambers die-away with no transfer and 20 mg/l test substance.

Ultimate biodegradation was investigated via CO₂ measurement.

Test result also secondary cited by Mayer, F.L. et al., Aquatic Toxicology and Hazard Assessment, Fourth Conference. ASTM STP 737, D.R. Branson and K.L. Dickson, Eds., 103-123 (1981)

Result : Based on CO₂ evolution after 7 d: 61.9 % of the employed TPP was ultimately biodegraded.

Reliability : (2) valid with restrictions study well documented, meets generally accepted scientific principles

3. ENVIRONMENTAL FATE AND PATHWAYS

ID: 115-86-6

DATE: 20.08.2002

14.12.2004

(41) (5)

Type : aerobic
Inoculum : activated sludge, adapted
Concentration : 30 mg/l related to Test substance related to
Contact time :
Degradation : 77 (±) % after 28 day(s)
Result : other: with adapted activated sludge well and ultimately degradable
Deg. product :
Method : other: Monsanto Shake Flask Procedure (precursor to later Closed Bottle Test)
Year : 1975
GLP : no data
Test substance : no data
Deg. products : 124-38-9 204-696-9 carbon dioxide

Test condition : Acclimated bacterial seed (100 ml) is mixed with standard BOD water (400 ml). A weighed quantity of TPP (app. 15 mg) was added to the flasks. After aerating the medium with 70% oxygen in nitrogen a reservoir containing barium hydroxide is connected to the flasks. After sealing, the flasks were agitated on a rotary shaker in the dark at room temperature. At appointed intervals the CO₂ evolved was determined. The CO₂ evolution values were corrected by results obtained in the controls.

Reliability : (2) valid with restrictions study well documented, meets generally accepted scientific principles

14.12.2004

(41)

Type : aerobic
Inoculum : other: synthetic mixture of activated sludge, from sewage treatment plant, river, and garden soil, adapted
Concentration : 5 mg/l related to Test substance related to
Contact time :
Degradation : 93.8 (±) % after 20 day(s)
Result : inherently biodegradable
Deg. product :
Method : OECD Guide-line 303 A "Simulation Test - Aerobic Sewage Treatment: Coupled Unit Test"
Year : 1982
GLP : yes
Test substance : other TS: 100%

Remark : Test on elimination in sewage treatment plants
Result : The mean of the elimination rate was determined with 93.8 % of the initial TTP concentration. Less than 1 % of the total applied TTP was found in the sludge.

Test condition : preparation of stock solution: emulsifying of 125 mg TPP in 1 ml octanol, 0.25 ml Tween and 1 l bidistilled water and applying ultrasound during 30 s; average retention time: 3 h; temperature 23°C; adaptation: 14 d; pH: 7.4 - 8.2, measurement of dissolved oxygen (7.0 - 8.9 mg/l), DOC, and TS; analysis of sludge at the end of the test for accumulated TS

Reliability : (1) valid without restriction guideline study

Flag : Critical study for SIDS endpoint

19.07.2002

(42)

Type : aerobic

3. ENVIRONMENTAL FATE AND PATHWAYS

ID: 115-86-6

DATE: 20.08.2002

Inoculum	:	other: river water	
Concentration	:	1 mg/l related to Test substance related to	
Contact time	:		
Degradation	:	100 (±) % after 3 day(s)	
Result	:	inherently biodegradable	
Deg. product	:		
Method	:	other: River die-away test	
Year	:	1979	
GLP	:	no	
Test substance	:	other TS: purity >90 %	
Remark	:	Heat-sterilized control in order to confirm, degradation was due to biodegradation and no other physical or chemical phenomenon.	
		Test result also secondary cited by Mayer, F.L. et al., Aquatic Toxicology and Hazard Assessment, Fourth Conference. ASTM STP 737, D.R. Branson and K.L. Dickson, Eds., 103-123 (1981)	
Result	:	t1/2: 1.1 - 23 days, complete primary degradation after 2 - 4 days in river water.	
Test condition	:	Settled Mississippi River water and TPP were mixed in sealed bottles and stored in the dark at room temperature. The bottles were analyzed periodically for the residual ester. Primary degradation was monitored via GC analysis.	
Reliability	:	(2) valid with restrictions study well documented, meets generally accepted scientific principles	
18.07.2002			(41) (5)
Type	:	aerobic	
Inoculum	:	activated sludge, domestic	
Concentration	:	13 mg/l related to Test substance related to	
Contact time	:		
Degradation	:	93 (±11) % after 49 day(s)	
Result	:	inherently biodegradable	
Deg. product	:		
Method	:	other: Modif. Semicontinuous Activated Sludge (SCAS) Method based on the procedure of the Soap and Detergent Association (1969)	
Year	:	1979	
GLP	:	no data	
Test substance	:	other TS: purity > 90 %	
Remark	:	TPP was tested in two parallel tests with at addition rates of 3 and 13 mg/l per 24h cycle resp. For measuring primary degradation 50 ml samples of mixed liquor were withdrawn a few minutes after feeding and at the end of the 24h cycle. The samples were extracted with hexane, concentrated and analyzed via GC/FID. Sampling was carried out on a one-cycle-per-week basis for each ester. No significant volatility losses were observed.	
		Modification from SCAS protocol: domestic activated sludge.	
		Test result also secondary cited by Mayer, F.L. et al., Aquatic Toxicology and Hazard Assessment, Fourth Conference. ASTM STP 737, D.R. Branson and K.L. Dickson, Eds., 103-123 (1981)	
Result	:	Biodegradation at a feed rate of 3 mg/l per 24h cycle: 96 +/-2 % (test duration 84 d)	
		Biodegradation at a feed rate of 13 mg/l per 24h cycle:	

3. ENVIRONMENTAL FATE AND PATHWAYS

ID: 115-86-6

DATE: 20.08.2002

Reliability	: 93 +/-11 % (test duration 49 d) : (2) valid with restrictions study well documented, meets generally accepted scientific principles	
18.07.2002		(41) (5)
Type	: aerobic	
Inoculum	: other: river sediment	
Concentration	: .05 mg/l related to Test substance related to	
Deg. product	:	
Method	:	
Year	: 1989	
GLP	: no	
Test substance	: other TS: Eastman Chemicals, purity not reported	
Result	: Primary degradation of TPP: after 3 days: 43.3 % after 40 days: 86.9 % CO2 evolution after 3 days: 0.2 % 40 days: 17.4 % Unextractable radioactivity from sediment after 3 days: 8.8 % 40 days: 31.9 % Extractable radioactivity from sediment after 3 days: 85.9 % 40 days: 20.5 % Radioactivity from water after filtration of sediment 3 days: 35.2 % 40 days: 9.7 % Less than 1 % of the radioactivity was trapped in PU foams indicating that volatilisation was not an important pathway of loss of TPP.	
Test condition	: 14C-labeled TPP Experiments conducted in respirometer flasks with duplicate performance. River sediment: 48% clay, 7% sand, 43% silt, 2.3% organic carbon, pH 7.7 Sediment-water ratio 1:20 21 d pre-incubation without test substance at the intended incubation temperature of 25 °C. 14C-TPP applied as acetone solution to the water column.	
Reliability	: (2) valid with restrictions study well documented, meets generally accepted scientific principles	
Flag	: Critical study for SIDS endpoint	
18.07.2002		(43)
Type	: anaerobic	
Inoculum	: other: river sediment	
Concentration	: .05 mg/l related to Test substance related to	
Deg. product	:	
Method	:	
Year	: 1989	
GLP	: no	
Test substance	: other TS: Eastman Chemicals, purity not reported	
Deg. products	: 124-38-9 204-696-9 carbon dioxide	

Remark	:	The high CO ₂ evolution may reflect the fact that incubations were not strictly anaerobic.
Result	:	<p>Primary degradation of TPP: after 3 days: 31.1 % after 40 days: 89.7 %</p> <p>CO₂ evolution after 3 days: 0.8 % 40 days: 21.9 %</p> <p>Unextractable radioactivity from sediment after 3 days: 8.2 % 40 days: 20.1 %</p> <p>Extractable radioactivity from sediment after 3 days: 68.9 % 40 days: 19.5 %</p> <p>Radioactivity from water after filtration of sediment 3 days: 40.4 % 40 days: 25.7 %</p> <p>Less than 1 % of the radioactivity was trapped in PU foams indicating that volatilisation was not an important pathway of loss of TPP.</p>
Test condition	:	<p>14C-labeled TPP.</p> <p>Experiments conducted in respirometer flasks under nitrogen aeration in duplicate performance; 1 % crystalline cellulose as additional source of carbon.</p> <p>Characteristics of river sediment: 48% clay, 7% sand, 43% silt, 2.3% organic carbon, pH 7.7. Sediment water ratio: 1:20 21 d pre-incubation without test substance at the intended incubation temperature of 25°C TPP applied as acetone solution to the water column;</p>
Reliability	:	(2) valid with restrictions study well documented, meets generally accepted scientific principles
Flag 14.12.2004	:	Critical study for SIDS endpoint
Type	:	aerobic
Inoculum	:	other: test with river sediment and test with pond sediment
Concentration	:	.1 mg/l related to Test substance related to
Deg. product	:	
Method	:	
Year	:	1989
GLP	:	no
Test substance	:	other TS: Eastman Chemicals, purity not reported
Result	:	<p>Unextractable radioactivity from sediment + water after 64 d: 25 °C: 15.4 % test with pond sediment 10 °C: 15.4 % test with pond sediment 25 °C: 38.8 % test with river sediment</p> <p>Extractable radioactivity from sediment + water after 64 d: 25 °C: 3.5 % test with pond sediment 10 °C: 4.3 % test with pond sediment</p>

(43)

	25 °C: 26.4 % test with river sediment	
	CO2 and volatiles not trapped/measured.	
Test condition	: 14C-labeled TPP Experiments carried out in culture flasks under static conditions in duplicate performance. River sediment: 48% clay, 7% sand, 43% silt, 2.3% organic carbon, pH 7.7 Pond sediment: 75% clay, 24% silt, 1% sand, 3.7% organic carbon, pH 7.6 Sediment-water ratio 1:10; 21 d pre-incubation without test substance at the intended incubation temperature. Incubation temperatures: 25, 10, and 2°C. CO2 evolution not trapped. Application of TPP as acetone solution to water column.	
Reliability	: (2) valid with restrictions study well documented, meets generally accepted scientific principles	
18.07.2002		(43)
Type	: aerobic	
Inoculum	: activated sludge, domestic	
Contact time	:	
Degradation Result	: = 40 (±) % after 48 hour(s)	
Deg. product	:	
Method	:	
Year	: 1985	
GLP	:	
Test substance	: other TS: extra pure reagent from Tokyo Kasei Co., further purified	
Remark	: Reference in Japanese, cited according to English translation Test on primary degradation of seven organic phosphate esters in the same test vessel	
Test condition	: Inoculum: 2000 mg/l (fresh weight, MLSS); TPP: 0.1 mg/l;	
Reliability	: (2) valid with restrictions Basic data given	
11.11.2004		(22)
Type	:	
Inoculum	: activated sludge, domestic, adapted	
Contact time	:	
Degradation Result	: ca. 100 (±) % after 2 day(s)	
Deg. product	:	
Method	:	
Year	: 1985	
GLP	:	
Test substance	: other TS: extra pure reagent from Tokyo Kasei Co., further purified	
Remark	: Test of biodegradation after acclimation of municipal sludge with seven organic phosphate esters in the same test vessel	
Test condition	: Inoculum: 2000 mg/l (fresh weight, MLSS); TPP: 0.1 mg/l;	
Reliability	: (3) invalid Test not meaningful for statements on triphenyl phosphate as is, due to multiple test substances application per testing.	
11.11.2004		(22)

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Type	:	aerobic	
Inoculum	:	activated sludge, industrial, adapted	
Deg. product	:		
Method	:		
Year	:	1980	
GLP	:		
Test substance	:		
Remark	:	average TPP concentration in wastewater: 0.74 mg/l; average TPP concentration in effluent: 0.007 mg/l; average removal: 99%	
Reliability	:	(4) not assignable secondary literature (Original: Personal communication of FMC Corp. to US-EPA in 1980)	
13.05.2002			(12)
Type	:	aerobic	
Inoculum	:	activated sludge	
Contact time	:		
Degradation	:	92 (±) % after	
Result	:		
Deg. product	:		
Method	:		
Year	:	1986	
GLP	:		
Test substance	:		
Remark	:	elimination in purification plants	
Result	:	Triphenyl phosphate influx concentration was 0.054-2.12 µg/l (mean 0.241), effluent concentration 0.005-0.082 µg/l (mean 0.019), and elimination was 92 %.	
Test condition	:	Osaka City wastewater treatment efficiency for triphenyl phosphate determined in 1984.	
Reliability	:	(4) not assignable original reference in Japanese	
Flag	:	Critical study for SIDS endpoint	
14.12.2004			(44)
Type	:	aerobic	
Inoculum	:	predominantly domestic sewage	
Concentration	:	3 mg/l related to related to	
Contact time	:		
Degradation	:	> 70 (±) % after 30 day(s)	
Result	:		
Deg. product	:		
Method	:	other: "Geschlossener Flaschen-Test", precursor to later OECD Guide-line 301 D "Ready Degradability: Closed Bottle Test"	
Year	:	1978	
GLP	:		
Test substance	:		
Remark	:	Emulsified with Emulgator W	
Reliability	:	(4) not assignable values taken from data compilation	
15.05.2002			(45)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

Species	: Oryzias latipes (Fish, fresh water)	
Exposure period	: 18 day(s) at 25 °C	
Concentration	: .01 mg/l	
BCF	: 144	
Elimination	: yes	
Method	:	
Year	: 1982	
GLP	: no	
Test substance	: no data	
Remark	: the BCF values given are related to whole body	
Result	: TPP uptake in fish was rapid and increased gradually till day 18 of exposure (BCF after 2 d: ca. 60; after 18 d: 144). The authors suggest that this phenomenon is due to some alteration of metabolism or reduced biotransformation by the fish with increase of exposure time. After the fish were transferred to clean water, fast elimination occurred and TPP concentrations in fish body decreased to levels below the detection limit within 24 h. The biological half-life is given to 1.2 h.	
Test condition	: continuous flow-through test, 70-100 fish in aquarium tank (10 l); fish fed once a day; 3-4 fish were taken out at various intervals for analysis; after 18 d fish were transferred to clean water and reared for 1-2 d; measured concentration of TS: 0.009 - 0.01 mg/l; analytical monitoring: FPD-GC; solubilizing agent: acetone	
Reliability	: (2) valid with restrictions study well documented, meets generally accepted scientific principles	
Flag	: Critical study for SIDS endpoint	
13.05.2002		(46)
Species	: other: fish	
Exposure period	: at °C	
Concentration	:	
BCF	: 113.3	
Elimination	:	
Method	: other: calculation with SRC-BCFWIN v2.14 (2000)	
Year	:	
GLP	:	
Test substance	:	
Remark	: Estimation equation with a correction factor for phosphate ester substances	
Reliability	: (2) valid with restrictions Accepted calculation method	
Flag	: Critical study for SIDS endpoint	
29.07.2002		(47)
Species	: Carassius auratus (Fish, fresh water)	
Exposure period	: 72 hour(s) at 25 °C	
Concentration	: .25 mg/l	
BCF	: 110	
Elimination	:	
Method	:	
Year	: 1981	
GLP	: no data	
Test substance	: no data	
Result	: Goldfish took up TPP rapidly within the first 5 hours but at a very slow rate thereafter. The uptake kinetic has been described for	

	24 h: BCF = 150 48 h: BCF = 130 72 h: BCF = 110
Test condition	: Depuration has not been determined. : static test; 3-5 fish per beaker (2 l); at total 3-4 beakers were used (one served as control for stability of TS in water); fish weight: 0.8-2.8 g; fish not fed during the test; test solution not aerated; analysis of fish via GLC
Reliability	: (2) valid with restrictions study well documented, meets generally accepted scientific principles
Flag 16.05.2002	: Critical study for SIDS endpoint (14)
Species	: other: Tursiops truncatus
Exposure period	: at °C
Concentration	:
Elimination	:
Method	: other: analysis of blubber of animals died during unusual mortality events
Year	: 1995
GLP	: no
Test substance	: other TS: triphenyl phosphate, highest purity possible, supplied by Supelco Inc. (Bellafonte, PA) and/or Ultra scientific Inc. (North Kingstown, RI)
Method	: In 1990 dolphins (Tursiops truncatus) were collected during an unusual mortality event in the Gulf of Mexico. The cause of death could not be identified. For gathering background information on organic chemicals, metals and selenium, blubber of the dead dolphins had been analyzed
Remark	: It is likely that the unusual high triphenyl phosphate content of sucklings (6 animals) is due to a single outlayer: A range from 17 to 3790 ng/g lipid and a mean of 863 ng/g lipid was found. If these numbers are correct, one suckling had a concentration of 3790 ng/g lipid and all other animals contributed in average 278 ng/g lipid, or the second highest value possible was 1303 ng/g lipid.
Result	: Several substances, among them triphenyl phosphate, were detected in the blubber. For sucklings a mean triphenyl phosphate content of 863 ng/g lipid (range: 17 - 3790 ng/g lipid) was found, in immature animals the mean concentration was 68 ng/g lipid (range: 19 - 244) and in adult females the mean concentration was 30 ng/g lipid (range: 19 - 42). The mean triphenyl phosphate concentration in adult males from different locations was in the range of 25 - 56 ng/g lipid with single values in the range of 15 - 142 ng/g lipid. In general, substances which are thought to bioaccumulate (e.g. PCBs, DDT, DDE, polybrominated biphenyls, Mirex) were higher in adult males than in sucklings, but lower in adult females than in adult males.
Test condition	: - During unusual mortality events in the Gulf of Mexico, 6 suckling calves, 5 weaned calves, 5 adult females (4 of which were pregnant), 9 adult males were collected from the Gulf coast in 1990 (mostly from Texas). 2 adult pregnant females were collected in the Gulf of Mexico and a 26 year-old male dolphin, which had died after 20 years of captivity for was obtained from San Diego, CA. - Blubber extracted in high speed blender - Isolation of analytes by gel permeation chromatography - Quantification by electron impact GC/MS - Quality checks by reagent/solvent blanks, duplicates, analyte fortified samples
Reliability	: (2) valid with restrictions Basic data given
Flag	: Critical study for SIDS endpoint

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(48)

Species : *Oryzias latipes* (Fish, fresh water)
Exposure period : 72 hour(s) at 25 °C
Concentration : .25 mg/l
Elimination : yes
Method :
Year : 1981
GLP : no data
Test substance : no data

Result : The initial TPP concentration dropped below 50 % within the first 5 hours of exposition with killifish. The authors repeated the test with a TPP concentration of 0.3 mg/l, but as soon as killifish was inserted the TPP concentration dropped to the same extend as reported above. The TPP concentration in a controll beaker without fish remained stable during 72 hours. At a parallel test with *Carassius auratus* the required test substance concentration remained in the range of 100 to 80 % of the initial concentration. Thus the BCF cited by the authors of 250 is regarded as invalid.

Test condition : static test;
 10-20 fish in one beaker (2 l); at total 3-4 beakers were used (one served as control for stability of TS in water); test solution not aerated; analysis of fish via GLC

Reliability : (3) invalid
 study well documented and meets generally accepted scientific principles, but test substance concentration was not kept \geq 80 % of the initial concentration.

14.12.2004

(14)

Species : other: *Oncorhynchus mykiss*, fry (previously *Salmo gairdneri*)
Exposure period : 90 day(s) at °C
Concentration :
Elimination :
Method :
Year : 1981
GLP : no
Test substance : no data

Remark : Composite sample of rainbow trout fry (n=25; whole fish) were analysed on TPP (concentration of TPP used in the study: 0.12 µg/l)

Result : BCF average value: 271
 BCF range: 132 - 364

Reliability : (3) invalid
 insufficient documentation: no specification of lipid content of the fry
 divergence to standard test guidelines: use of larvae (usually higher lipid content than adults)

Flag : Critical study for SIDS endpoint

14.12.2004

(17)

Species : other: *Lemna minor*, *Typha spec.*, *Pimephales promelas*
Exposure period : 105 day(s) at °C
Concentration : 60 µg/l
Elimination : yes
Method : other: Artificial pond test
Year : 1982
GLP : no
Test substance : other TS: 14C TPP synthesized from 14C phenol, unlabelled TPP from Eastman Chemicals

Method : Artificial pond test with 14C-labeled TPP, applied once in the beginning of

- the test. Evaluation of the distribution of ¹⁴C within the test system, consisting of water, sediment, duckweed (*Lemna minor*), cattail (*Typha* sp.), and fish (*Pimephales promelas*) was followed over a time period of 105 days (data reported for the first 10 days).
- Result** : Since no substance specific analysis has been made, no CO₂ has been trapped, and the authors state themselves that there is a considerable error associated with the different compartment weights, this study is considered a first approach to the behaviour of TPP in the environment.
- Reliability** : Although no reliable data on accumulation of TPP can be derived from this study, BCFs for *Lemna minor* and *Typha* sp. were stated to be < 50 (duckweed 43, cattail < 1), and 68-160 for *Pimephales promelas*.
- Flag** : (4) not assignable
Documentation insufficient for assessment
- 13.01.2005 : Critical study for SIDS endpoint (49)
- Species** : other: fish
- Exposure period** : at °C
- Concentration** :
- Elimination** :
- Method** : other: calculated acc. to Veith et al. cited in Bysshe (1982) equation 5-2 at Lyman, W.J. et al., Handbook of chemical property estimation, p 5-1, New York
- Year** : 1985
- GLP** :
- Test substance** :
- Remark** : The measured BCF result of tricresylphosphate is cited with 165 (32 d, *Pimephales promelas*) in Bysshe 1982. This test result has been used besides 55 other chemicals for derivation of the above mentioned equation (log BCF = 0.85 log Kow - 0.7).
Calculation of the theoretical BCF of tricresylphosphate based on this equation and a measured log Kow of 5.1 comes to a BCF of 4300.
- Result** : Calculated BCF of 1800
- Reliability** : (3) invalid
Relevant methodological deficiencies
- 14.05.2002 (12)
- Species** : other: *Oncorhynchus mykiss* (previously *Salmo gairdneri*) and *Pimephales promelas*
- Exposure period** : at °C
- Concentration** :
- Elimination** :
- Method** :
- Year** : 1983
- GLP** :
- Test substance** :
- Result** : Measurements of the TPP concentration in the aquaria showed rapid and strong loss of the test substance within 24 h:
- Tests with *Oncorhynchus mykiss*:
Initial concentration of 50 µg/l was reduced to 47 % and initial concentration of 5 µg/l was reduced to 55 %.
- Tests with *Pimephales promelas*:
Initial concentration of 50 µg/l was reduced to 36 % and initial concentration of 5 µg/l was reduced to 22 %.
- Thus deduction of BCF values are not suitable according to today's testing standards.

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Test condition	: 14C-labeled TPP, Static test system, short-term exposures (24 h) to TPP concentrations of 5 and 50 µg/l at 10 °C. Test fish: <i>Oncorhynchus mykiss</i> and <i>Pimephales promelas</i> .	
Reliability	: (3) invalid Relevant methodological deficiencies	
02.08.2002		(50)
Species	: other: <i>Oncorhynchus mykiss</i> (previously <i>Salmo gairdneri</i>)	
Exposure period	: 24 hour(s) at 10 °C	
Concentration	: 50 µg/l	
Elimination	:	
Method	:	
Year	: 1980	
GLP	: no data	
Test substance	: other TS: >= 99%	
Method	: 14C-labeled TPP, Several tests with dechlorinated water and river water were performed with rainbow trout fry. The test waters showed pH values of 8.12 - 8.36. The fingerlings were exposed to TS for 24 h and then transferred to a tank with continuous flow of dechlorinated city water.	
Result	: Based on the best rate constants for uptake and clearance "worst case" estimates for bioaccumulation (related to whole fish) were calculated. No measured BCF values by comparison of TS concentration in fish and water are reported.	
Reliability	: (3) invalid Does not meet important criteria of today standard methods	
13.01.2005		(51)
Species	: other: <i>Pomacea canaliculata</i> Lamarck (Golden apple snail)	
Exposure period	: at °C	
Concentration	:	
Elimination	:	
Method	:	
Year	: 2000	
GLP	:	
Test substance	:	
Remark	: Calculation of a BCF of 4397 for snail, based on an equation of Chiou, C.T.: <i>Environ. Sci. Technol.</i> 19, 57-62 (1985) determined for fish. No information about the background for the deduction of the calculation.	
Reliability	: (3) invalid Documentation insufficient for assessment	
14.05.2002		(52)

3.8 ADDITIONAL REMARKS

Memo	: Bioavailability Test with <i>Chironomus tetans</i>
Method	: TPP (purity >98 %); <i>Chironomus tetans</i> larvae, 4th instar; Sediment: Pond (silty clay): 0% sand, 25% silt, 75 % clay, 3.7% organic carbon, pH 7.6 River (silty): 7% sand, 45% silt, 48% clay, 2.3% organic carbon, pH 7.7 Sand (commercial silica sand): 100% sand, 0% silt, 0 % clay, 0.1% organic carbon, pH 7.0

50 g wet weight sediment per jar was spiked with 50 and 500 µg/kg concentrations by addition of 10 or 100 µl of acetone solved stock solution. Addition of 250 ml dechlorinated tap water. Four replicates of each concentration, 2 days gently aeration before addition of larvae to allow equilibration of the sediment-water system.

Exposition of larvae in screened container suspended in the water or directly to the water where they established themselves in the sediment. Chemical analysis only by determination of radioactivity.

Indistinct report whether TPP was the only test substance in each jar or whether it was a mixture of several substances.

No explicit concentration data of larvae held in water column for comparative purposes.

Accumulation data in Fig.1 are interpreted as steady state at 24 h though after 96 h exposure an obvious decline of test substance concentration in the test organisms had occurred.

Reliability : (3) invalid
Documentation insufficient for assessment. Test results are based on 24 h exposure which is meant to be steady state. 96 h exposure data in Fig. 1 showed an obvious decline of test substance concentration in the test organisms.

16.05.2002 (37)

Memo : TPP from thermolysis of polymer powder

Method : Commercial polycarbonate and polyphenylene was ground to powder and placed into a thermobalance under reduced pressure in an air stream for thermogravimetric analysis. Thermolysis of the powder up to 250 °C and identification of the volatiles was achieved by a GC injection port directly connected to a GC-MS system.

Result : Heating a commercially polycarbonate specimen as powder (extremely high surface) showed weight loss beginning at 420 °C, whereas a commercially polyphenylene specimen as powder showed weight loss beginning at 190 °C. Injection molding temperatures for polycarbonate polymers are between 249 to 315 °C.

GC/MS analysis of vapours resulting from heating the polycarbonat powder and the polyphenylene powder to 250 °C yielded weight loss of 1 % and 8 % resp. and weight fractions of 0.05 % TPP and 3.6 % TPP resp. referring to the loss in weight.

Reliability : (3) invalid
Unrealistic test conditions

01.08.2002 (53)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	: static	
Species	: Oncorhynchus mykiss (Fish, fresh water)	
Exposure period	: 96 hour(s)	
Unit	: mg/l	
LC50	: .85	
Limit test	:	
Analytical monitoring	: no	
Method	: OECD Guide-line 203 "Fish, Acute Toxicity Test"	
Year	: 1981	
GLP	: no data	
Test substance	: other TS: 100%	
Result	: 95%-confidence interval 96 h LC50: 0.72-1.01 mg/l; all values relate to nominal concentration	
Test condition	: 10 fish per concentration and controls (blank/vehicle); fish length/weight (average): 49 mm/0.94 g, fish not fed during the test; temperature: ca. 15°C; test water: chlorinated tap water with hardness 172 mg/l CaCO ₃ ; pH 7.8 - 8.1; dissolved oxygen: 5.4-6.7 mg/l (at the end of the test) solubilizing agents: octanol (>0.004 ml/l), Tween 20 (>0.07 ml/l and ethyleneglycolmonomethylether (>0.02 ml/l); vehicle control;	
Reliability	: (2) valid with restrictions Comparable to guideline study with acceptable restrictions; no analytical control of TS	
Flag	: Critical study for SIDS endpoint	
29.07.2002		(54)
Type	: static	
Species	: Oncorhynchus mykiss (Fish, fresh water)	
Exposure period	: 96 hour(s)	
Unit	: mg/l	
LC50	: .4	
Limit test	:	
Analytical monitoring	: no data	
Method	: other: EPA 660/3-75-009: Method for acute toxicity tests with fish, macroinvertebrates and amphibians (1975)	
Year	: 1981	
GLP	: no	
Test substance	: no data	
Result	: 95% confidence limit 96h LC50: 0.28-0.50 mg/l	
Reliability	: (2) valid with restrictions study conducted acc. to national standard methods without detailed documentation (pH, dissolved oxygen, and water hardness of test medium not stated)	
Flag	: Critical study for SIDS endpoint	
17.05.2002		(17)
Type	: static	
Species	: Cyprinodon variegatus (Fish, estuary, marine)	
Exposure period	: 96 hour(s)	
Unit	: mg/l	
LC50	: > .32 - .56	
Limit test	:	
Analytical monitoring	: no data	
Method	: other: acc. to EPA 660/3-75-009: Methods for acute toxicity tests with fish, macroinvertebrates and amphibians (1975)	
Year	: 1981	
GLP	: no	

Test substance	: no data	
Reliability	: (2) valid with restrictions study conducted acc. to national standard methods without detailed documentation (pH, dissolved oxygen, and water hardness of test medium not stated)	
Flag 17.05.2002	: Critical study for SIDS endpoint	(17)
Type	: static	
Species	: Pimephales promelas (Fish, fresh water)	
Exposure period	: 96 hour(s)	
Unit	: mg/l	
LC50	: .66	
Limit test	:	
Analytical monitoring	: no data	
Method	: other: acc. to EPA 660/3-75-009: Method for acute toxicity tests with fish, macroinvertebrates and amphibians (1975)	
Year	: 1981	
GLP	: no	
Test substance	: no data	
Result	: 95% confidence limit 96h LC50: 0.53-0.80 mg/l	
Reliability	: (2) valid with restrictions study conducted acc. to national standard methods without detailed documentation (pH, dissolved oxygen, and hardness of test medium not stated)	
15.05.2002		(17)
Type	: static	
Species	: Carassius auratus (Fish, fresh water)	
Exposure period	: 96 hour(s)	
Unit	: mg/l	
LC50	: .7	
Limit test	:	
Analytical monitoring	: yes	
Method	: other	
Year	: 1981	
GLP	: no data	
Test substance	: no data	
Test condition	: 7-9 fish per concentration level, weight: 0.8-2.8 g; fish were not fed during the test; test solution: 25°C, not aerated, pH values of test medium not given, in control experiments stability of test substance during the exposure period is demonstrated	
Reliability	: (2) valid with restrictions study well documented, meets generally accepted scientific principles	
15.05.2002		(14)
Type	: static	
Species	: Lepomis macrochirus (Fish, fresh water)	
Exposure period	: 96 hour(s)	
Unit	: mg/l	
LC50	: = .78	
Limit test	:	
Analytical monitoring	: no	
Method	: other: acc. to US-EPA 660/3-75-009: Methods for acute toxicity tests with fish, macroinvertebrates and amphibians (1975)	
Year	: 1991	

GLP : no data
Test substance : other TS: 99%

Remark : During toxicity tests with sediment, neither montmorillonite clay nor topsoil adversely affected fish survival under the test conditions used (1 g soil/l). However, in the presence of montmorillonite and topsoil bioavailability of TPP was reduced indicated by numerically higher LC50 values.

Result : 95% confidence interval 96 h LC50: 0.47-1.04 mg/l (nominal)
Test condition : 10 fish (0.5-1.0 g each); temperature: 22°C; solubilizing agent: acetone

Reliability : (2) valid with restrictions
 test conducted in accordance to national standard methods. Detailed documentation of water characteristics given in an other publication, no detailed information on pH and dissolved oxygen for this test given.

15.05.2002 (38)

Type : static
Species : other: *Oncorhynchus mykiss*, fry
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : = .36
Limit test :
Analytical monitoring Method : no data
 other: acc. to standardized acute toxicity methods by US-EPA (Committee on methods for toxicity testing with aquatic organisms (1975))

Year : 1983
GLP : no
Test substance : other TS: 99%

Remark : 95% confidence interval LC50: 0.31-0.41 mg/l;
 EC50: 0.30 mg/l (cumulative effects of mortality, immobility, and loss of equilibrium)
 95% confidence interval EC50: 0.24-0.37 mg/l

Test condition : 10 fish (fry 12 days past the swim-up stage) per jar, average weight: 0.11 g, average total length: 24 mm

Reliability : (2) valid with restrictions
 test conducted in accordance with national standard methods without detailed documentation (pH, dissolved oxygen, and water hardness of test medium not stated)

31.07.2002 (55)

Type : static
Species : *Oryzias latipes* (Fish, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : 1.2
Limit test :
Analytical monitoring Method : yes
 other
Year : 1981
GLP : no data
Test substance : no data

Result : The authors determined a 96 h-LC50 = 1.2 mg/l for *Oryzias latipes*. Analytical monitoring with GLC analysis of the test water showed the TPP concentration to decline rapidly after insertion of the fish. This effect has not been observed with *Carassius auratus* in parallel testing by the authors. There is no evidence in the publication whether the concentration dropped due to absorption or pH relating alteration of TPP.

Test condition	: 7-9 fish per concentration level, weight of fish: 0.1-0.2 g; fish were not fed during the test; test solution: 25°C, not aerated, pH values of test medium not given.	
Reliability	: (2) valid with restrictions study well documented, meets generally accepted scientific principles	
		(14)
		31.07.2002
Type	: static	
Species	: Leuciscus idus (Fish, fresh water)	
Exposure period	: 48 hour(s)	
Unit	: mg/l	
Limit test	:	
Analytical monitoring	: no data	
Method	: other: Bestimmung der Wirkung von Wasserinhaltsstoffen auf Fische. DEV, L 15 (1979)	
Year	: 1979	
GLP	: no data	
Test substance	: no data	
Result	: Screening tests on toxicity of TPP without and with solubility promotor (with 10 fish each) 1st running: 10 mg/l TPP in water: after 1/2 hour = 0 death 10 mg/l TPP in water: after 14 hours = 10 death 2nd running: 10 mg/l TPP in water: after 1 hour = 10 death 5 mg/l TPP in water: after 48 hours = 0 death 3rd running: 3 mg/l TPP(+aceton) in water: after 2 hours = 10 death 1 mg/l TPP(+aceton) in water: after 14 hours = 10 death	
Test condition	: Test water acc. to German DIN 003842, part 15; room temperature; control with acetone (0.6 ml acetone/l water): no effect after 48 h.	
Reliability	: (4) not assignable Basic data given; the test is regarded valid for screening purposes.	
		(56)
		31.07.2002
Type	: static	
Species	: Lepomis macrochirus (Fish, fresh water)	
Exposure period	: 96 hour(s)	
Unit	: mg/l	
LC50	: 290	
Limit test	:	
Analytical monitoring	: no	
Method	: other	
Year	: 1975	
GLP	: no	
Test substance	: no data	
Remark	: The authors state: Many of the chemicals in the tests had limited water solubilities. The values given for the LC50 reflect the total amount of substance introduced into the water and not simply the soluble fraction of the substance. ... The results are an overall indication of expected toxicity of the chemicals should they be introduced into the water in a pure state under acute spill circumstances.	
Test condition	: fish length: 33-75 mm; fish not fed for 48 h prior to	

testing; dilution water: potable well water (pH 7.6-7.9, hardness: 55 mg/l as CaCO₃); temperature 23°C; aeration of test solution if necessary

Reliability : (3) invalid
Well-documented publication/study report with the aim of indicating an expected toxicity under acute spill circumstances. However, the study does not meet important criteria of today standard methods (e.g. test substance concentration at solubility threshold in water).

31.07.2002 (57)

Type : static
Species : Menidia beryllina (Fish, estuary, marine)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : 95
Limit test :
Analytical monitoring : no
Method : other
Year : 1975
GLP : no
Test substance : no data

Remark : The authors state:
Many of the chemicals in the tests had limited water solubilities. The values given for the LC50 reflect th total amount of substance introduced into the water and not simply the soluble fraction of the substance. ... The results are an overall indication of expected toxicity of the chemicals should they be introduced into the water in a pure state under acute spill circumstances.

Test condition : open test system; fish length: 40-100 mm; continuous aeration; dilution water: potable well water (pH 7.6-7.9, hardness: 55 mg/ l as CaCO₃); temperature: 20°C

Reliability : (3) invalid
Well-documented publication/study report with the aim of indicating an expected toxicity under acute spill circumstances. However, the study does not meet important criteria of today standard methods (e.g. test substance concentration at solubility threshold in water).

31.07.2002 (57)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type :
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC50 : 1
Analytical monitoring : no data
Method : other: US EPA 660/3-75-009: Method for acute toxicity tests with fish, macroinvertebrates and amphibians (1975)
Year : 1981
GLP : no
Test substance : no data

Result : 95% confidence limit 48h-EC50: 0.86-1.2 mg/l
Test condition : static test system
Reliability : (2) valid with restrictions
study conducted acc. to national standard methods without detailed documentation (pH of test medium not stated)

Flag : Critical study for SIDS endpoint

16.05.2002 (17)

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC50 : 1.35
Analytical monitoring : no
Method : other: acc. to US EPA-660/3-75-009: Methods for acute toxicity tests with fish, macroinvertebrates and amphibians (1975)
Year : 1981
GLP : no
Test substance : no data

Result : 95% confidence limits: 1.23-1.56 mg/l; all values relate to nominal concentrations
Test condition : 5 daphnids per vessel; 4 replicates; one control vessel; beakers covered with watch-glasses; temperature: 20°C; 16 h light/8 h darkness; at the end of the test: dissolved oxygen: 7.03-7.19 mg/l, pH 8.6; DMF as solubilizing agent (>1.5 ml/l); dilution water: reconstituted water
Reliability : (1) valid without restriction
test conducted acc. to national standard methods;
not clearly stated if vehicle control was performed
16.05.2002 (58)

Type : static
Species : Mysidopsis bahia (Crustacea)
Exposure period : 96 hour(s)
Unit : mg/l
Analytical monitoring : no data
Method : other: US-EPA 660/3-75-009: Methods for acute toxicity tests with fish, macroinvertebrates and amphibians (1975)
Year : 1981
GLP : no
Test substance : no data

Result : 96 hour LC50: > 0.18 < .32 mg/l
Reliability : (2) valid with restrictions
study conducted acc. to national standard method without detailed documentation (e.g. test conditions, use of vehicle)
Flag : Critical study for SIDS endpoint
29.07.2002 (17)

Type :
Species : other: Gammarus pseudolimnaeus (Scud)
Exposure period : 96 hour(s)
Unit : mg/l
EC50 : .25
Analytical monitoring : no
Method : other: acc. to EPA 660/3-75-009: Method for acute toxicity tests with fish, macroinvertebrates and amphibians (1975)
Year : 1975
GLP : no
Test substance : other TS: 99%

Result : 95% confidence interval 96 h EC50: 0.16-0.39 mg/l
Test condition : test animals: mid-instar, 60-90 days old; temperature: 17°C; solubilizing agent: acetone
Reliability : (2) valid with restrictions
study conducted acc. to national standard methods without

15.05.2002 detailed information on test conditions (38)

Type : semistatic
Species : Crangon crangon (Crustacea)
Exposure period : 96 hour(s)
Unit : mg/l
LC50 : .304
Analytical monitoring : yes
Method : other: test conducted acc. to the procedure outlined in Blackman et al. 1977: MAFF Directorate of Fisheries Research Technical Report 39
Year : 1988
GLP : yes
Test substance : other TS: technical grade TPP (Ciba Geigy DVP 438)

Remark : Analytical monitoring showed that up to 50 % of the TS was precipitated or lost from the test solution in all concentrations tested. LC50 values have been calculated based on measured concentrations

Result : 95% confidence interval 96 h LC50: 0.22-0.44 mg/l

Moult deaths at a maximum of 5 out of 20 animals are recorded for the seawater control (5/20), the solvent control (3/20), and the lowest test concentration (4/20). Moult deaths are not recorded as mortality according to the test rules of MAFF. Mortality shown in this test follows a dose related effect after 96 hours:

0.2 mg/l 3 deaths

0.5 mg/l 8 deaths

1.0 mg/l 18 deaths

2.0 mg/l 20 deaths

Test condition : test organisms: 20 animals per vessel, average weight/length: 0.57 g/36 mm;
renewal of test solution at 24 h intervals, continuous agitation;
filtered dilution water: seawater, salinity: 34.92-35 ‰; temperature: 14.5-15.7°C; dissolved oxygen: 7.0-7.6 mg/l; pH 7.8-8.1; solubilizing agent: acetone (1 ml/l); solvent and seawater controls

Reliability : (2) valid with restrictions
Test procedure according to national standards

06.12.2004 (59)

Type : semistatic
Species : Crangon crangon (Crustacea)
Exposure period : 96 hour(s)
Unit : mg/l
LC0 : > 2.5
Analytical monitoring : yes
Method : other: study conducted acc. to the procedure outlined in Blackman et al. 1977: MAFF Directorate of Fisheries Research Technical Report 39
Year : 1988
GLP : yes
Test substance : other TS: technical grade TPP (Ciba Geigy DVP 438)

Remark : There is no mortality shown in this test ascribable to the test substance. Moult deaths are recorded for the seawater control, and all test concentrations. Moult deaths are not recorded as mortality according to the test rules of MAFF.

The LC0 value is based on nominal concentration.

Analytical measurements indicate that at 1.0 and 2.5 mg/l

less than 20% of the TS was present after each 24 h of exposure and that in the lowest concentration (0.25 mg/l) up to 56 % of TS was present in solution; the temperature range is slightly outside the range recommended by the guideline (by 0.2°C)

Test condition : Test organisms: 20 animals per vessel, average weight/length: 0.61 g/36.8 mm; renewal of test solution every 24 h, continuous agitation; dilution water: seawater, salinity 34.9-34.98‰; temperature: 14.6-16.2°C; dissolved oxygen: 7.2-8.0 mg/l; pH: 7.6-8.0, no solubilizing agent; seawater control

Reliability : (3) invalid study well documented, but measured test substance concentration was < 20 % less than nominal.

08.12.2004 (18)

Type :
Species : other: Chironomus riparius (Midge)
Exposure period : 48 hour(s)
Unit : mg/l
EC50 : = .36
Analytical monitoring Method : no
 : other: acc. to EPA 660/3-75-009: Method for acute toxicity tests with fish, macroinvertebrates and amphibians (1975)
Year : 1981
GLP : no
Test substance : other TS: 99%

Remark : The presence of 1 g/l montmorillonite clay in the test vessels reduced the bioavailability of the TS: a five-fold greater nominal concentration was required to reach the 48 h-EC50 endpoint.

Result : 95% confidence interval 48 h EC50: 0.25-0.52 mg/l
Test condition : 10 test animals (4th-instar larvae); temperature: 22°C; solubilizing agent: acetone

Reliability : (2) valid with restrictions study conducted acc. to national standard methods without detailed information on test conditions

Flag : Critical study for SIDS endpoint
 15.05.2002 (38)

Type :
Species : Daphnia magna (Crustacea)
Exposure period : 24 hour(s)
Unit :
Method : other: Daphnien-Schwimmunfaehigkeits-Test, UBA-Verfahrensvorschlag Mai 1984, Bestimmung der Schwimmunfaehigkeit beim Wasserfloh Daphnia magna, EC0, EC50, EC100 24h, statisches System
Year : 1989
GLP :
Test substance :

Remark : The low solubility of triphenyl phosphate in water and a poor distribution of the test substance determined heterogen (no dose related) results in the pretest.

Toxic effects have to be expected at TS concentrations < 10 mg/l (direct weight).
Reliability : (4) not assignable Pretest raw data not available, but a statement why the acute toxicity test had not been realized.

15.05.2002 (60)

Type :
Species : other aquatic mollusc: Pomacea canaliculata Lamarck (Golden apple snail)
Exposure period : 72 hour(s)
Unit : mg/l
LC50 : 38.2
LC90 : 83.5
Analytical monitoring : yes
Method : other
Year : 2000
GLP : no data
Test substance : other TS: 98%

Remark : No information whether LC50 value is based on nominal or measured concentration.
 Since 6 different concentrations (10-250 mg/l = all far above water solubility) had been tested, the use of a dissolving agent for the TPP test is assumed.

Test condition : snails 35-40 days old; 30 snails/glas bottle; dilution water: pH 7.5, temperature: 26°C; 6 concentrations tested (10-250 mg/l), three replications

Reliability : (2) valid with restrictions
 study well documented, meets generally accepted scientific principles

Flag : Critical study for SIDS endpoint

16.05.2002

(52)

Type :
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC50 : 1
Method : other: Standard Practices for Conducting Acute Toxicity with Fishes, Macroinvertebrates, and Amphibians. (E 729-80), Annual Book of ASTM Standards, ASTM, 1-25 (1980)
Year : 1986
GLP :
Test substance :

Remark : diluting agent

Reliability : (4) not assignable
 original reference not available

15.05.2002

(61)

Type :
Species : other: Chironomus tentans (midge)
Exposure period : 48 hour(s)
Unit : mg/l
LC50 : = 1.6
Analytical monitoring : no
Method : other
Year : 1986
GLP : no
Test substance : no data

Remark : No data available on actual concentrations tested.

Reliability : (4) not assignable
 original reference not available

13.12.2001

(61)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : Selenastrum capricornutum (Algae)
Endpoint : growth rate
Exposure period : 72 hour(s)
Unit : mg/l
NOEC : .25 - 2.5
LOEC : .5 - 5
Limit test :
Analytical monitoring : no
Method : other: acc. to a OECD guideline 201: Alga, growth inhibition test (1984); modified
Year : 1988
GLP : no data
Test substance : no data

Remark : The influence of varying growth medium compositions on the toxicity of a test substance was investigated.

The authors do not state NOEC values. Due to the only slight effect shown in the figures demonstrating the LOEC growth graphs compared to the control, derived NOECs are given for this test, using the procedure cited in the Technical Guidance Document by the EU for Risk Assessments. There, LOEC values of 10 to 20 % effect are halved to derive a NOEC (LOEC/2 = NOEC)

Result : BBM-Medium: 72 h-LOEC = 0.5 mg/l
 OECD-Medium: 72 h-LOEC = 5 mg/l
 US-EPA-Medium: 72 h-LOEC = 1 mg/l
 Growth medium composition does affect the toxic values obtained in standard algal toxicity tests. The observed effects, however, were neither consistant nor predictable.

Test condition : Algal inoculum from actively growing axenic cultures (initial cell concentration: 10E4 cells/ml); algal growth media: Bolds basal medium (= BBM), OECD and EPA recommended media;
 TPP concentrations tested: 0.05, 0.1, 0.5, 1, and 5 mg/l;
 incubation at 22°C; constant illumination; solubilizing agent: acetone (<= 100 µl/l); experiments carried out in triplicate

Reliability : (2) valid with restrictions
 Test procedure acc. to standard guideline with acceptable modifications (pH of test media not stated)

Flag : Critical study for SIDS endpoint
 29.07.2002

(62)

Species : Scenedesmus subspicatus (Algae)
Endpoint : other: growth
Exposure period : 72 hour(s)
Unit : mg/l
NOEC : .25 - 2.5
LOEC : .5 - 5
Limit test :
Analytical monitoring : no
Method : other: acc. to OECD guideline 201: Alga, growth inhibition test (1984); modified
Year : 1988
GLP : no data
Test substance : no data

Remark : The influence of varying growth medium compositions on the

	toxicity of a test substance was investigated.
	The authors do not state NOEC values. Due to the only slight effect shown in the figures demonstrating the LOEC growth graphs compared to the control, derived NOECs are given for this test, using the procedure cited in the Technical Guidance Document by the EU for Risk Assessments. There, LOEC values of 10 to 20 % effect are halved to derive a NOEC (LOEC/2 = NOEC)
Result	: BBM-Medium: 72 h-LOEC = 0.5 mg/l OECD-Medium: 72 h-LOEC = 5 mg/l US-EPA-Medium: 72 h-LOEC = 1 mg/l
	Growth medium composition does affect the toxic values obtained in standard algal toxicity tests.
	The observed effects, however, were neither constant nor predictable.
Test condition	: Algal inoculum from actively growing axenic cultures (initial cell concentration: 10E4 cells/ml); algal growth media: Bold's basal medium (= BBM), OECD and EPA recommended media; TPP concentrations tested: 0.05, 0.1, 0.5, 1, and 5 mg/l; incubation at 22°C; constant illumination; solubilizing agent: acetone (<= 100 µl/l); experiments carried out in triplicate
Reliability	: (2) valid with restrictions test procedure acc. to standard guideline with acceptable modifications (pH of test media not stated)
29.07.2002	(62)
Species	: Chlorella vulgaris (Algae)
Endpoint	: other: growth
Exposure period	: 72 hour(s)
Unit	: mg/l
NOEC	: 2.5
LOEC	: 5
Limit test	:
Analytical monitoring	: no
Method	: other: acc. to OECD guideline 201: Alga, growth inhibition test; modified
Year	: 1988
GLP	: no data
Test substance	: no data
Remark	: The influence of varying growth medium compositions on the toxicity of a test substance was investigated.
	The authors do not state NOEC values. Due to the only slight effect shown in the figures demonstrating the LOEC growth graphs compared to the control, derived NOECs are given for this test, using the procedure cited in the Technical Guidance Document by the EU for Risk Assessments. There, LOEC values of 10 to 20 % effect are halved to derive a NOEC (LOEC/2 = NOEC)
Result	: Toxicity of TPP on C. vulgaris was not affected by the medium used:
	BBM-Medium: 72 h-LOEC = 5 mg/l OECD-Medium: 72 h-LOEC = 5 mg/l US-EPA-Medium: 72 h-LOEC = 5 mg/l
Test condition	: Algal inoculum from actively growing axenic cultures (initial cell concentration: 10E4 cells/ml); algal growth media: Bold's basal medium (= BBM), OECD and EPA recommended media; TPP concentrations tested: 0.05, 0.1, 0.5, 1, and 5 mg/l;

	incubation at 22°C; constant illumination; solubilizing agent: acetone (<= 100 µl/l); experiments carried out in triplicate	
Reliability	: (2) valid with restrictions test procedure acc. to standard guideline with acceptable modifications (pH of test media not stated)	
Flag 29.07.2002	: Critical study for SIDS endpoint	(62)
Species	: Selenastrum capricornutum (Algae)	
Endpoint	:	
Exposure period	: 96 hour(s)	
Unit	: mg/l	
EC50	: 2	
Limit test	:	
Analytical monitoring	: no data	
Method	: other: acc. to US EPA: Algal Assay Procedure: Bottle Test (1971)	
Year	: 1981	
GLP	: no	
Test substance	: no data	
Result	: 95% confidence interval 96h EC50: 0.6-4 mg/l	
Test condition	: static test system	
Reliability	: (2) valid with restrictions study conducted acc. to national standard methods without detailed documentation (pH of test medium not stated)	
10.01.2002		(17)
Species	: Ankistrodesmus falcatus (Algae)	
Endpoint	: other: reproduction (growth)	
Exposure period	: 22 day(s)	
Unit	: mg/l	
IC100	: >= 1	
Limit test	:	
Analytical monitoring	: no	
Method	: other	
Year	: 1984	
GLP	: no	
Test substance	: no data	
Result	: At 0.05 and 0.1 mg/l reproduction of the alga was stimulated; at 0.5 mg/l reproduction was decreased in comparison to the control; concentrations >= 1 mg/l completely inhibited algal reproduction.	
Test condition	: reproduction was determined spectrophotometrically	
Reliability	: (2) valid with restrictions study well documented, meets generally accepted scientific principles, without detailed documentation (pH of test medium not stated)	
29.07.2002		(63)
Species	: Ankistrodesmus falcatus (Algae)	
Endpoint	: other: primary productivity	
Exposure period	: 4 hour(s)	
Unit	: mg/l	
IC50	: .26	
Limit test	:	
Analytical monitoring	: no	
Method	: other	
Year	: 1984	
GLP	: no	
Test substance	: no data	

Remark : Primary productivity was measured by the amount of
14C-carbonate taken up by the algae over a 4 h period
Test condition : inoculum: cells from logarithmic phase of growth; incubation
at 20°C; pH 8; solubilizing agent: acetone; radioactivity
was measured via LSC
Reliability : (2) valid with restrictions
study well documented, meets generally accepted scientific
principles, without detailed documentation (pH of test medium not stated)
15.05.2002 (63)

Species : Scenedesmus quadricauda (Algae)
Endpoint : other: primary productivity
Exposure period : 4 hour(s)
Unit : mg/l
IC50 : .5
Limit test :
Analytical monitoring : no
Method : other
Year : 1984
GLP : no
Test substance : no data

Remark : Primary productivity was measured by the amount of
14C-carbonate taken up by algae over a 4 h period
Test condition : inoculum: logarithmic phase of growth; pH 8; solubilizing
agent: acetone; measurement of radioactivity via LSC
Reliability : (2) valid with restrictions
study well documented, meets generally accepted scientific
principles, without detailed documentation (pH of test medium not stated)
15.05.2002 (63)

Species : other aquatic plant: Lake Ontario phytoplankton
Endpoint : other: primary productivity
Exposure period : 4 hour(s)
Unit : mg/l
IC50 : .2
Limit test :
Analytical monitoring : no
Method : other
Year : 1984
GLP : no
Test substance : no data

Remark : Primary productivity was measured by the amount of
14C-carbonate taken up by algae over a 4 h period
Reliability : (2) valid with restrictions
study well documented, meets generally accepted scientific
principles, without detailed documentation (pH of test medium not stated)
15.05.2002 (63)

Species : Anabaena flos-aquae (Algae)
Endpoint : other: nitrogenase activity
Exposure period : 4 hour(s)
Unit :
Limit test :
Analytical monitoring : yes
Method : other: acetylene reduction technique acc. to Stratton & Corke (1979)
Year : 1984
GLP : no
Test substance : no data

Result : Addition of 0.1, 1.0 and 5.0 mg/l reduced nitrogenase activity of *A. flos-aquae* to 84, 77 and 68%, respectively

Reliability : (2) valid with restrictions
study well documented, meets generally accepted scientific principles, without detailed documentation (pH of test medium not stated)

15.05.2002 (63)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type : aquatic
Species : activated sludge
Exposure period : 28 day(s)
Unit : mg/l
NOEC : 100

Result : Since the biodegradability of TPP showed a result of 83 - 94 % after 28 d of incubation with 30 mg/l sludge and 100 mg/l TPP in a test on ready biodegradability, there is no significant effect of TPP in the low concentration range expected.

Reliability : (2) valid with restrictions
Conclusion from guideline study on biodegradability

Flag : Critical study for SIDS endpoint

09.05.2005 (40)

Type : aquatic
Species : *Escherichia coli* (Bacteria)
Exposure period : 24 hour(s)
Unit : mg/l
EC0 : 200
Method : other: Bestimmung der biologischen Schadwirkung toxischer Abwaesser gegen Bakterien. DEV, L 8 (1968) modifiziert

Year : 1978
GLP :
Test substance :

Reliability : (4) not assignable
original reference not available; results from data compilation

16.05.2002 (64)

Type : aquatic
Species : *Pseudomonas fluorescens* (Bacteria)
Exposure period : 24 hour(s)
Unit : mg/l
EC0 : 200
Method : other: Bestimmung der biologischen Schadwirkung toxischer Abwaesser gegen Bakterien. DEV, L 8 (1968) modifiziert

Year : 1978
GLP :
Test substance :

Reliability : (4) not assignable
original reference not available; results from data compilation

16.05.2002 (65)

4.5.1 CHRONIC TOXICITY TO FISH

Species : other: *Oncorhynchus mykiss*, sac fry (formerly *Salmo gairdneri*)
Endpoint : other: weight and length of young fish

Exposure period	:	30 day(s)
Unit	:	mg/l
NOEC	:	.037
LOEC	:	.055
Method	:	other: method used is based on US-EPA procedure 'Methods for acute toxicity tests with fish, macroinvertebrates, and amphibians; EPA-660/3-75-009 (1975)
Year	:	1978
GLP	:	no
Test substance	:	other TS: derived from Eastman Kodak Comp., no further information
Remark	:	This test started with 10 d old sac fry and lasted 30 days and is considered part of an Early Life Stage Test. No NOEC was obtained with the triphenyl phosphate concentrations tested. With the raw data given in the test protocol, an EC10 of 0.037 mg/l can be calculated, equipollent to NOEC according to the Technical Guidance Document by the EU for Risk Assessments. In a second test with the same conditions as described above, the test was started with 49 d old fingerlings and performed for another 30 days. The NOEC with the fingerlings concerning length and weight is given with 0.55 mg/l.
Test condition	:	Flow through test: Test with sac-fry 10 days old, average weight 0.081 g, and average length: 22.3 mm. Test with fingerling 45 days old, average weight 0.75 g, and average length: 41.2 mm. 30 fish per aquarium; temperature: 12°C; dilution water: oxygen saturated well water, pH 7.4/7.5, dissolved oxygen: 7.3-8.5 mg/l; hardness: 295/305 mg/l as CaCO ₃ , alkalinity: 255/260 mg/l as CaCO ₃ ; pH 7.4/7.5; solubilizing agent: acetone (concentration not given); one aquarium served as control for solvent; the numbers of dead and moribund fish were recorded daily TPP concentrations tested: 0.055, 0.090, 0.125, 0.16, 0.24, 0.31, 0.45 mg/l (nominal); highest concentration measured and used for estimation of the lower concentrations.
Reliability	:	(2) valid with restrictions study design based on national standard method; detailed documentation
Flag	:	Critical study for SIDS endpoint
02.08.2002		(66)
Species	:	other: Oncorhynchus mykiss, sac-fry
Endpoint	:	other: eye cataract, vertebral collagen amount, survival, growth
Exposure period	:	90 day(s)
Unit	:	mg/l
NOEC	:	>= .0014
Analytical monitoring	:	yes
Method	:	
Year	:	1981
GLP	:	no
Test substance	:	no data
Result	:	There was no effect concerning the endpoints eye cataract, vertebral collagen amount, growth, or survival with the highest TPP concentration tested. The highest measured TPP concentration in the flow through system was 0.0014 mg/l.
Test condition	:	flow-through system; rainbow trout sac fry; seven concentrations tested, dilution factor: 0.75; water characteristics: well water, hardness 272 mg/l, alkalinity 237 mg/l, pH 7.2, temperature: 12°C; solvent concentration < 0.05 ml/l;

	solvent control mortality was recorded daily; fish were weighed and measured (total length) after 15, 30, 45, 60, and 90 days of exposure	
Reliability	: (2) valid with restrictions study well documented, meets generally accepted scientific principles	
Flag 02.08.2002	: Critical study for SIDS endpoint	(17)
Species	: Pimephales promelas (Fish, fresh water)	
Endpoint	: other: hatchability, eye cataract, growth, and survival	
Exposure period	: 30 day(s)	
Unit	: mg/l	
NOEC	: .087	
LOEC	: .23	
Analytical monitoring	: yes	
Method	:	
Year	: 1981	
GLP	: no	
Test substance	: no data	
Result	: With the highest TPP concentration of 0.23 mg/l (measured conc.) survival of fry was significantly reduced. No effects on egg hatchability, eyes, or growth were noted with TPP concentrations 0.0028 to 0.23 mg/l.	
Test condition	: eggs and fry of fathead minnow were exposed to TPP in a flow-through diluter system; concentration measured analytically; water characteristics: well water, hardness 272 mg/l, alkalinity 237 mg/l, pH 7.2, temperature: 12°C; solvent concentration < 0.05 ml/l;	
Reliability	: (2) valid with restrictions study conducted acc. to national standard methods without detailed documentation	
Flag 02.08.2002	: Critical study for SIDS endpoint	(17)
Species	: other: Oncorhynchus mykiss, sac fry (formerly Salmo gairdneri)	
Endpoint	: other: lethal concentration	
Exposure period	: 4 day(s)	
Unit	: mg/l	
LC50	: .31	
Analytical monitoring	: no	
Method	: other: method used is based on US-EPA procedure 'Methods for acute toxicity tests with fish, macroinvertebrates, and amphibians; EPA-660/3-75-009 (1975)	
Year	: 1978	
GLP	: no	
Test substance	: other TS: derived from US-FDA, no further information	
Remark	: Though test duration was only 96 hours, this test with juveniles of rainbow trout is considered part of an Early Life Stage Test.	
Test condition	: Static test: 10 rainbow trout sac fries, 10 days old per jar, not fed during exposure; temperature: 12°C; dilution water: reconstituted soft water, pH 7.0-7.2, hardness: 40-48 mg/l as CaCO ₃ , alkalinity: 32-38 mg/l as CaCO ₃ ; solubilizing agent: acetone (concentration not given); one aquarium served as control for solvent; the numbers of dead and moribund (loss of equilibrium) fish were recorded daily	
Reliability	: TPP concentrations tested with sac fry: 0.18, 0.24, 0.32, 0.42, 0.56, 1.0 mg/l (nominal); (2) valid with restrictions study design based on national standard method; detailed documentation	

31.07.2002 (66)

Species : other: Oncorhynchus mykiss, fingerling (formerly Salmo gairdneri)
Endpoint : other: lethal concentration
Exposure period : 4 day(s)
Unit : mg/l
LC50 : .32
Analytical monitoring : no
Method : other: method used is based on US-EPA procedure 'Methods for acute toxicity tests with fish, macroinvertebrates, and amphibians; EPA-660/3-75-009 (1975)
Year : 1978
GLP : no
Test substance : other TS: derived from Eastman Kodak Comp., no further information

Remark : Though test duration was only 96 hours, this test with juveniles of rainbow trout is considered part of an Early Life Stage Test.

Test condition : Static test:
 10 rainbow trout fingerlings 49 days old per jar, not fed during exposure;
 temperature: 12°C; dilution water:
 reconstituted soft water, pH 7.0-7.2, hardness: 40-48 mg/l as CaCO₃, alkalinity: 32-38 mg/l as CaCO₃; solubilizing agent: acetone (concentration not given); one aquarium served as control for solvent; the numbers of dead and moribund (loss of equilibrium) fish were recorded daily

Reliability : (2) valid with restrictions
 study design based on national standard method; detailed documentation

31.07.2002 (66)

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

Species : other: insects
Endpoint : mortality
Exposure period :
Unit :
Method : other: acc. to Busvine (1962)
Year : 1967
GLP : no
Test substance : no data

Remark : no information given whether a control with the solubilizing agent was performed

Result : Musca domestica:
NOEC=4.3 µg/fly (normal strain);
NOEC=9.5 µg/fly (malathion resistant strain)

Chrysomya putoria:
NOEC= 1.5 µg/fly (normal strain);
NOEC= 3.05 µg/fly (malathion resistant strain)

Test condition : 20 flies were used; TPP was dissolved in dioctyl phthalate and applied to the insects by topically; tests conducted in duplicate

Reliability : (3) invalid
documentation insufficient

10.01.2002 (67)

4.7 BIOLOGICAL EFFECTS MONITORING

Memo : Outdoor experimental stream including two pools and 50 m total length at National Fisheries Contaminant Research Center.

Result : Monitoring of
Nutrient dynamics: no effect
Leaf decomposition: no effect
Benthic algal dynamics: no effect
Benthic invertebrates:
number, diversity no effect
Insect emerge: no effect
Bentic organisms, drift: effect, immediatly starting when soil with TPP conc. >= 400 mg/kg were added, thereafter sedation

Fish: no mortality in caged bluegills exposed for 96 h each week. After the treatments at 400, 800, and 1600 mg/kg, bluegills were visually examined and x-rayed for vertebral abnormalities known to occur after laboratory exposure to some arylphosphates. The findings of Mayer et al. 1981 were affirmed (see chapt. 4.5.1), no such sublethal effects were detected with TPP.

Test condition : Water used: Well water,
pH at inlet and outlet: 7.31 - 8.04
Sediment used: locally topsoil, 0.70 % organic C, 5 % sand, 77 % silt, 18 % clay.

Application of TTP to stream: Spraying of acetone solubilized TTP on soil. 24 h adsorption time and volatilization of acetone. Sediment added to the stream was treated each week for 6 weeks with increasing amounts of TPP, beginning at 50 mg/kg and doubled each week to a height of 1600 mg/kg. Treated soil was flushed into the circulation water once a week.

For single measured test substance concentrations see chapter 3.1.2 (Stability in Water) Fairchild et al. 1987.

Reliability : (2) valid with restrictions
study well documented, meets generally accepted scientific principles

Flag : Critical study for SIDS endpoint

02.08.2002 (26)

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

In Vitro/in vivo	:	In vitro
Type	:	Metabolism
Species	:	
Number of animals	:	
Males	:	
Females	:	
Doses	:	
Males	:	
Females	:	
Vehicle	:	
Method	:	other:
Year	:	
GLP	:	
Test substance	:	
Method	:	Test System: liver homogenates (male Wistar rat)
		Control: Yes, concurrent
		Method: Rat livers were removed and the microsomal and soluble fractions extracted. An ethanol solution of TPP at 0.0004 M was used as substrate to determine the extent of decomposition by the fractions with and without NADPH and other enzyme systems. Major metabolites resulting from TPP degradation were characterized using gas chromatography.
Result	:	TPP was easily decomposed by the microsomal fraction without NADPH . Therefore arylesterase in the microsomes contributes to TPP metabolism. The metabolic reactions were inhibited almost completely by SKF-525A and carbon monoxide in the absence of NADPH whereas KCN, NaN ₃ , dipyrldyl and EDTA showed little effect. Therefore mixed function oxidase system in the microsomes plays a central role in the metabolism of TPP. Diphenyl phosphate (DPP) was the only major metabolite of TPP, and DPP was not decomposed by the microsomes.
		Conclusion: TPP is degraded by hydrolysis in rat liver homogenate to diphenyl phosphate as the major product.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint
09.05.2005		(68)

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	> 20000 mg/kg bw
Species	:	rat
Strain	:	Wistar
Sex	:	male/female
Number of animals	:	10
Vehicle	:	water
Doses	:	20000 mg/kg
Method	:	
Year	:	1975
GLP	:	no data
Test substance	:	no data
Method	:	observation for 14 days after dosage

Result : PARAMETER: mortality, necropsy
: MORTALITY: none
: NECROPSY: sporadic visceral hemorrhage
Reliability : (2) valid with restrictions
: SHORT REPORT, main features of study design given
Flag : Critical study for SIDS endpoint
05.09.2005 (69)

Type : LD50
Value : > 5000 mg/kg bw
Species : rat
Strain : no data
Sex : male/female
Number of animals : 10
Vehicle : other: 20 % emulsion with gum arabic
Doses : 2500-5000 mg/kg
Method :
Year : 1954
GLP : no
Test substance : no data

Method : NUMBER: 5 rats/dose
: OBSERVATION: 8 days
: PARAMETERS: mortality, clin. symptoms
Result : MORTALITY:none
: SYMPTOMS: none
Reliability : (2) valid with restrictions
: short report, main features of study design given
Flag : Critical study for SIDS endpoint
04.07.2002 (70)

Type : LD50
Value : > 6400 mg/kg bw
Species : rat
Strain :
Sex : no data
Number of animals :
Vehicle : no data
Doses :
Method : other: no data
Year : 1962
GLP : no data
Test substance : no data

Reliability : (4) not assignable
: LD 50 only, no details
Flag : Critical study for SIDS endpoint
01.07.2002 (71)

Type : LD50
Value : 3800 mg/kg bw
Species : rat
Strain : no data
Sex : no data
Number of animals :
Vehicle : no data
Doses : 500 to 5000 mg/kg
Method :
Year : 1974
GLP : no data
Test substance : no data

Method	:	PARAMETERS: observation (at least 5 days), mortality, necropsy, clin. symptoms,	
Result	:	CLIN. SYMPTOMS: reduced mobility, untidiness, weakness MORTALITY: 4-5 days post dose NECROPSY: edema and hyperemia in the gut wall, tough-like consistency of liver and kidneys (autolysis?), congestion in meniges	
Reliability	:	(4) not assignable abstract only, no details of study design	
Flag 10.07.2002	:	Critical study for SIDS endpoint	(72) (73)
Type	:	LD50	
Value	:	= 3500 mg/kg bw	
Species	:	rat	
Strain	:		
Sex	:	no data	
Number of animals	:		
Vehicle	:	other: olive oil (25%)	
Doses	:		
Method	:		
Year	:	1957	
GLP	:	no data	
Test substance	:	no data	
Method	:	TPP was administered as a 25% solution in olive oil and rats were observed for 6 days for signs of toxicity. Average calculated from 143 experiments.	
Result	:	OBSERVATION: Signs of toxicity appeared after 6-8 hours and included tremor, reduced food intake, diarrhea in all animals. Impaired coordination was recorded above a dose of 3000 mg/kg MORTALITY: death occurred within 6 days	
Reliability	:	(3) invalid dose range and number of animals not given no test substance data; early study	
04.07.2002			(74)
Type	:	LD50	
Value	:	= 10800 mg/kg bw	
Species	:	rat	
Strain	:	Sprague-Dawley	
Sex	:	male/female	
Number of animals	:		
Vehicle	:	other: undiluted or in corn oil	
Doses	:		
Method	:		
Year	:	1977	
GLP	:	no data	
Test substance	:		
Method	:	Maximum dosage was 15.8 g/kg. OBSERVATION: 14 days postdose. PARAMETERS: observation, mortality The LD50 was calculated according to De Beer (1945)	
Test substance	:	"prepared from pure phenol"	
Reliability	:	(2) valid with restrictions Number of animals not stated; only few details described	
Flag 22.07.2002	:	Critical study for SIDS endpoint	(75)

Type : LDLo
Value : > 3000 mg/kg bw
Species : rat
Strain : other: Holtzman
Sex : male
Number of animals : 11
Vehicle : no data
Doses : 3000 mg/kg
Method :
Year : 1960
GLP : no data
Test substance :

Method : NUMBER OF ANIMALS: 11
PARAMETERS: mortality, observation (1 month), necropsy
Result : MORTALITY: 1/11
CLIN: SIGNS: only in the rat that died for an unspecified non-treatment-related reason
NECROPSY: no data
Test substance : eastman organic chemicals "practical grade"
Reliability : (2) valid with restrictions
vehicle for the oral treatment not clearly stated
few details reported
Flag : Critical study for SIDS endpoint
10.07.2002 (76)

Type : LD50
Value : > 5000 mg/kg bw
Species : mouse
Strain : no data
Sex : male/female
Number of animals : 10
Vehicle : other: gum arabic
Doses : 2500-5000 mg/kg
Method : other: 5 mice/ group were observed for 8 days
Year : 1954
GLP : no data
Test substance : no data

Method : PREPARATION: 20% in aqueous gum arabic
NUMBER OF ANIMALS: 5/group
PARAMETERS: observation, mortality
Result : OBSERVATION: slight stupor
MORTALITY: none
Reliability : (2) valid with restrictions
short report; few details reported
Flag : Critical study for SIDS endpoint
10.07.2002 (70)

Type : LD50
Value : = 1320 mg/kg bw
Species : mouse
Strain : no data
Sex : no data
Number of animals :
Vehicle : other: oil (not specified)
Doses : 500-5000 mg/kg.
Method :
Year : 1974
GLP : no data

Test substance	:	no data	
Result	:	OBSERVATION: weakness, reduced motility, untidiness, MORTALITY: no data NECROPSY: findings in deceased animals: dilation of digestive tract, edema and hyperemia of gut, tough-like consistency of liver and kidneys, congestion of meninges with focal hemorrhages	
Reliability	:	(4) not assignable Abstract only	
Flag 04.07.2002	:	Critical study for SIDS endpoint	(73)
Type	:	LD0	
Value	:	> 3000 mg/kg bw	
Species	:	mouse	
Strain	:	other: CF1	
Sex	:	male	
Number of animals	:	10	
Vehicle	:	no data	
Doses	:	3000 mg/kg	
Method	:		
Year	:	1960	
GLP	:	no data	
Test substance	:		
Method	:	PARAMETERS:observation (1 month), mortality	
Remark	:	It is not clear whether the results were obtained in one or several studies and how the test conditions differed/ were similar The postulated correlation between TPP exposure and ChE inhibition is not proven	
Result	:	No deaths occurred at this dosage level. The activity of cholinesterase in plasma was reduced in a dose dependent manner: 10 to 50 mg/kg : 87-88 % activity 100 mg/kg: 60,7 % 200 mg/kg: 53,9 % 500 mg/kg: 30,4 %	
Test substance	:	eastman organic chemicals "practical grade"	
Reliability	:	(2) valid with restrictions vehicle for the oral treatment not clearly stated, few details reported	
Flag 22.07.2002	:	Critical study for SIDS endpoint	(76)
Type	:	LDLo	
Value	:	= 3000 mg/kg bw	
Species	:	rabbit	
Strain	:		
Sex	:	no data	
Number of animals	:	4	
Vehicle	:	other: gum acacia	
Doses	:		
Method	:	other: TPP was suspended in gum acacia.	
Year	:	1932	
GLP	:	no data	
Test substance	:	other TS: technical grade	
Result	:	One rabbit died in 7 days, 3 survived. no demonstrable neurotoxic action	
Test substance	:	crystalline technical product, recrystallized twice, final product with sharp melting point, though lower than before recrystallization	

Reliability	: (4) not assignable scarce information on study design	
Flag 10.07.2002	: Critical study for SIDS endpoint	(77)
Type	: LDLo	
Value	: < 400 mg/kg bw	
Species	: cat	
Strain	:	
Sex	: no data	
Number of animals	: 10	
Vehicle	: other: olive oil	
Doses	:	
Method	: other	
Year	: 1957	
GLP	: no data	
Test substance	: no data	
Method	: Three cats were administered 2000 mg/kg TPP once and observed for 6 days postdose. 4 other animals received either 200, 300, 500 or 800 mg/kg twice on 2 days. A 3rd group received 500 and 1000 mg/kg by gavage in oil solution. All of these animals died. Necropsy did not show any alterations. Histology of liver kidneys, adrenal glands and nervous tissue showed signs of toxicity in these organs.	
Remark	: No further details	
Result	: The LDLo is 2x 200 mg/kg/day : Clinical signs: diarrhea, salivation, tremor, hyperreflexia in hind extremities, apathy. recovery of survivors in 9 days. MORTALITY: Two of the three cat of the high dose (2000mg/kg) died during observation period. All cats treated twice died. HISTOPATHOLOGY: corrosion in GI tract, signs of acute intoxication in liver, kidneys and adremnal glands slight changes in ganglial cell and the myelin sheeth of peripheral nerves (no details reported)	
Reliability	: (3) invalid no test substance data, single animals per dose, no details of study design, conflicting results (1 cat survived 2000 mg/kg, while 2x200 mg/kg was lethal) early study	
10.07.2002		(74)
Type	: LD0	
Value	: > 4000 mg/kg bw	
Species	: guinea pig	
Strain	: no data	
Sex	: male	
Number of animals	: 10	
Vehicle	: no data	
Doses	: 3000-4000 mg/kg	
Method	:	
Year	: 1960	
GLP	: no data	
Test substance	:	
Method	: 2 groups of 5 guinea pigs were administered TPP orally (3g/kg; 4g/kg) and	

	examined for signs of toxicity for one month.	
Result	: OBSERVATION: 1 month, no clinical signs observed	
Test substance	: "practical grade" Eastman Organic Chemicals	
Reliability	: (2) valid with restrictions few details about study design given	
Flag	: Critical study for SIDS endpoint	
22.07.2002		(76)
Type	: LD50	
Value	: > 2000 mg/kg bw	
Species	: hen	
Strain	: no data	
Sex	: no data	
Number of animals	:	
Vehicle	: no data	
Doses	:	
Method	:	
Year	: 1962	
GLP	: no data	
Test substance	: no data	
Remark	: LD 50 only; cited from: Industrial Hygiene and Toxicology, Vol:2; Toxicology, 2nd edition Interscience, N.Y. 1962	
Reliability	: (4) not assignable LD 50 only; no further data	
Flag	: Critical study for SIDS endpoint	
04.07.2002		(71)
Type	: LD0	
Value	: > 2000 mg/kg bw	
Species	: hen	
Strain	: no data	
Sex	: no data	
Number of animals	: 4	
Vehicle	: no data	
Doses	: 500-2000 mg/kg	
Method	:	
Year	: 1932	
GLP	: no data	
Test substance	:	
Method	: 4 hens; 500 to 2000 mg/kg parameters: observation	
Result	: No effects were observed.	
Test substance	: crystalline technical product , recrystallized twice, final product with sharp melting point, though lower than before recrystallization	
Reliability	: (4) not assignable few details of study design given, low animal number	
Flag	: Critical study for SIDS endpoint	
08.10.2002		(77)
Type	: LD0	
Value	: > 5000 mg/kg bw	
Species	: hen	
Strain	: no data	
Sex	: no data	
Number of animals	:	
Vehicle	: other: gelatine capsule	
Doses	: 5000 mg/kg	
Method	:	

Year	:	1977	
GLP	:	no data	
Test substance	:		
Method	:	hens (White Leghorn) were treated with 5g/kg of TPP in gelatine capsules and observed for 14 days; no further detail	
Result	:	No signs of toxicity were observed during the 14 days postdose.	
Test substance	:	TPP was "prepared from pure phenol"	
Reliability	:	(2) valid with restrictions only few details given	
Flag	:	Critical study for SIDS endpoint	(75)
10.07.2002			
Type	:	other	
Value	:	> 10000 mg/kg bw	
Species	:	hen	
Strain	:	no data	
Sex	:	no data	
Number of animals	:	2	
Vehicle	:	other: olive oil (1:4), in gelatine capsule	
Doses	:		
Method	:		
Year	:	1958	
GLP	:	no data	
Test substance	:	no data	
Method	:	Number of animals: 2 Treatment: 30 g/kg TPP were administered to hens over several days and they were observed for signs of neurotoxicity for up to 3 weeks. Parameters: clin. signs, mortality	
Result	:	Observation: no symptoms Mortality: none	
Reliability	:	(2) valid with restrictions few details, no clear description of treatment	
Flag	:	Critical study for SIDS endpoint	(78)
10.07.2002			
Type	:	other	
Value	:	> 500 mg/kg bw	
Species	:	hen	
Strain	:	no data	
Sex	:	no data	
Number of animals	:	4	
Vehicle	:	other: arachis oil	
Doses	:	500 mg/kg	
Method	:		
Year	:	1961	
GLP	:	no data	
Test substance	:	no data	
Method	:	Four hens were administered TPP by mouth one time at a dosage of 500 mg/kg and observed for at least 21 days for signs of neurotoxicity. Parameters: observation, cholin esterase activity	
Result	:	Observation: No signs of neurotoxicology were observed, during the 21 day observation period. Cholin esterase activity: inhibition of 60% (4 hens) after 24 hrs; in every case activity had returned to normal levels within 4 days	
Reliability	:	(2) valid with restrictions only few details of study design given	

Flag : Critical study for SIDS endpoint
10.07.2002 (79)

Type : other
Value : > 1000 mg/kg bw
Species : hen
Strain : other: White Leghorn
Sex : male
Number of animals : 2
Vehicle : other: undiluted
Doses : 1000 mg/kg
Method :
Year : 1956
GLP : no
Test substance :

Method : Two cockerels were administered TPP by gavage at a dosage of 1000 mg/kg one time. Animals were observed for at least 14 days for signs of neurotoxicity.

PARAMETERS: Observation, histology (brain, cord, sciatic nerve) acetyl cholinesterase (24 h)

Result : No signs of neurotoxicity developed in either cockerel. Choline esterase was depressed to 49% in plasma at 24 h. No effects in brain and slight effect in cord tissue. There was no histologic evidence of degeneration in the brain, cord, or sciatic nerves.
No further data

Test substance : the compounds were of 98% purity or greater

Reliability : (2) valid with restrictions
few details given; early study aiming at neurotoxicity not acute toxicity

Flag : Critical study for SIDS endpoint
10.07.2002 (80)

Type : other
Value : > 12000 mg/kg bw
Species : hen
Strain : other: Rhode Island Red x Light Sussex
Sex : female
Number of animals : 2
Vehicle : other: arachis oil (25 ml/kg)
Doses : 12000 mg/kg
Method :
Year : 1981
GLP :
Test substance : no data

Method : PARAMETERS: Observation for 21 days, necropsy

Result : Observation: no signs of neurotoxicity
Necropsy: no findings

Reliability : (2) valid with restrictions
full report, low animal number (2)

Flag : Critical study for SIDS endpoint
10.07.2002 (81)

Type : other: delayed neurotoxicity
Value : > 12500 mg/kg bw
Species : hen
Strain : other: Rhode Island Red x Light Sussex
Sex : female
Number of animals : 10
Vehicle : other: arachis oil
Doses : 2000-3000-5000-8000-12500 mg/kg

Method	:	
Year	:	1980
GLP	:	no data
Test substance	:	no data
Method	:	Five groups of two hens each were administered a single dose of triphenyl phosphate by gavage at dosage levels of 2, 3, 5, 8, 12.5 g/kg in arachis oil and observed for signs of neurotoxicity for 21 days. To attain the dosage levels listed above, different concentrations of the mixture had to be used. Parameters: Observation (21 days), necropsy
Result	:	There were no signs of toxicity observed either in-life or at necropsy in any hens on study. The NOEL was 12,500 mg/kg.
Reliability	:	(2) valid with restrictions full report, low animal number
Flag	:	Critical study for SIDS endpoint
04.07.2002		(82)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Value	:	> 200 mg/l
Species	:	rat
Strain	:	
Sex	:	male/female
Number of animals	:	10
Vehicle	:	no data
Doses	:	
Exposure time	:	1 hour(s)
Method	:	
Year	:	1975
GLP	:	no data
Test substance	:	no data
Method	:	dust inhalation according to 16 CFR 1500.3 DURATION: 1 hour PARAMETERS: observation (14 days), mortality
Remark	:	no further details
Result	:	MORTALITY: none OBSERVATION: no symptoms
Reliability	:	(4) not assignable short report; no data on(if) analysis of test atmosphere
04.07.2002		(69)
Type	:	other: Choline esterase determination
Value	:	
Species	:	mouse
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Exposure time	:	
Method	:	2 Doses, 3 exposure periods: (363 (6h); 757 mg/m ³ (2h and 4 h))
Result	:	None of the animals exhibited any colinergic signs or symptoms. No significant effects at 363 mg/m ³ (6h) and 757 mg/m ³ (4 h)

Reliability : significant effect at 757 mg/m³ (2h) but with questionable biological relevance
 : (3) invalid
 : inconsistent results (high dose: effect after 2 hours but not after 4 hour of exposure)
 : No results other than ChE inhibition reported (as "delta pH")
 08.10.2002 (76)

5.1.3 ACUTE DERMAL TOXICITY

Type : LD50
Value : > 10000 mg/kg bw
Species : rabbit
Strain : no data
Sex : no data
Number of animals : 10
Vehicle : no data
Doses : 10000 mg/kg
Method : other: as described in 16 CFR 1500.40
Year : 1976
GLP : no data
Test substance : no data

Method : 2 groups of 5 rabbits: treatment on intact or abraded skin
 PARAMETERS: mortality
Result : MORTALITY: none
Reliability : (2) valid with restrictions
 Short report, few details
Flag : Critical study for SIDS endpoint
 05.09.2005 (83)

Type : LDLo
Value : > 7900 mg/kg bw
Species : rabbit
Strain : New Zealand white
Sex : male/female
Number of animals :
Vehicle : other: undiluted
Doses :
Method :
Year : 1977
GLP : no data
Test substance : no data

Method : rabbits were administered TPP on the skin of the back for 24 hours under an occlusive patch. Residues were washed off.
 Rabbits were observed for 14 days postdose.
 PARAMETERS: mortality, observation, necropsy
Remark : no further details
Result : MORTALITY: no data
 OBSERVATION: no data
 NECROPSY: no data
Reliability : (2) valid with restrictions
 number of animals and dose range not stated, no other findings reported
Flag : Critical study for SIDS endpoint
 08.10.2002 (75)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

Type : LD50
Value : = 6900 mg/kg bw
Species : mouse
Strain : CD-1
Sex : male/female
Number of animals : 70
Vehicle : other: DMSO
Doses : 4500-5000-6000-7000-8000 mg/kg
Route of admin. : i.p.
Exposure time :
Method :
Year : 1989
GLP :
Test substance :

Method : PARAMETERS: observation, body weights, mortality, necropsy
Result : MORTALITY:

males (dose in mg/kg: x/n)
 4500 : 2/5
 5000 : 2/10
 6000 : 1/5
 7000 : 5/5
 8000 : 3/5
 females (dose in mg/kg: x/n)
 4500 : 2/5
 5000 : 4/10
 6000 : 1/5
 7000 : 1/5
 8000 : 3/5

OBSERVATION: unkempt appearance, soft stool, hypoactivity, yellow staining of the perineum and sunken sides while walking. All surviving mice gained or maintained weight during the study.

NECROPSY: findings were limited to 1 mouse with red, friable small intestines and hard white material in the abdominal cavities of many of the TPPA treated mice. This white material is presumed to be undissolved TPPA accompanied by inflammatory reaction.

Reliability : (2) valid with restrictions
 full report available; missing data on test material

04.07.2002

(84)

Type : LD0
Value : > 5000 mg/kg bw
Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 20
Vehicle : other: DMSO
Doses : 5000 mg/kg
Route of admin. : i.p.
Exposure time :
Method : according to Fifra guidelines (40 CFR 158.81-1)
Year : 1989
GLP : yes
Test substance : no data

Method : The main study contained 5 male and 5 female rats per group

	A DMSO-control was also used. PARAMETERS: observation (14 days), body weights (before dosing and weekly thereafter), mortality, necropsy	
Result	: Rangefinding evaluations were conducted on 5 groups (2/sex); : Though deaths occurred in the range finding study, these were attributed to the ethanol vehicle used at that stage and were not related to TPP. In the limit test no mortality occurred in any group. Clinical signs included unkempt appearance, bloated abdomen and wet perineum in TPP treated rats. No adverse signs were noted in the control group. All rats gained weight. Necropsy findings were limited to hard white material in the abdominal cavities of TPP treated rats, regarded as undissolved TPP	
Reliability	: (2) valid with restrictions full report available; missing data on test material	
04.07.2002		(85)
Type	: LD0	
Value	: = 200 mg/kg bw	
Species	: rabbit	
Strain	: no data	
Sex	: no data	
Number of animals	:	
Vehicle	: no data	
Doses	:	
Route of admin.	: i.p.	
Exposure time	:	
Method	: other: Rabbits were administered 200 mg/kg TPP intraperitoneally and examined for signs of toxicity. No details reported.	
Year	: 1943	
GLP	: no	
Test substance	: no data	
Method	: no data	
Result	: No deaths nor paralysis.	
Reliability	: (3) invalid original not available; number of animals not stated;	
10.07.2002		(86)
Type	: other:TDlo	
Value	: 200 mg/kg bw	
Species	: cat	
Strain	: no data	
Sex	: female	
Number of animals	: 6	
Vehicle	: other: 70 % W/V in 95 % v/v aq. ethanol	
Doses	:	
Route of admin.	: i.p.	
Exposure time	:	
Method	:	
Year	: 1960	
GLP	: no data	
Test substance	:	
Method	: PARAMETERS: observation (up to 50 days), mortality, necropsy	
Result	: The cat receiving 100 mg/kg, and one of the cats receiving 300 mg/kg showed no signs of any kind for 30 days postdose. The other cat receiving 300 mg/kg was found dead on day 3, due probably to a perforated ulcer unrelated to TPP administration.	

		<p>The cat receiving 400 mg/kg developed paralysis on day 16 followed by depression, anorexia and weight loss (force feeding was necessary) and was killed.</p> <p>One of the two cats receiving 200 mg/kg developed paralysis on day 18 followed by anorexia and weight loss (force feeding was necessary), depression; it died on day 50 from a recurrent respiratory infection.</p> <p>The other cat receiving 200 mg/kg showed no symptoms and was killed on day 28.</p>	
		<p>The small number of animals used, i.p. route of exposure and questions of sample purity make these results difficult to interpret</p>	
Test substance	:	"Practical grade" Eastman Organic Chemicals	
Reliability	:	(3) invalid	
		mortality in individuals while no signs in others at the same dose;	
		no sign at a high (300 mg/kg) dose combined with mortality and severe signs at a lower dose (200 mg/kg)	
		2 of 6 cat died due to disease (ulcer, respir. infection)	
		animals possibly employed in several studies (pretreated)	
24.07.2002			(76)
Type	:	LD50	
Value	:	> 3000 mg/kg bw	
Species	:	mouse	
Strain	:	no data	
Sex	:	male	
Number of animals	:	10	
Vehicle	:	other: 70 % W/V in 95 % v/v aq. ethanol	
Doses	:	3000 mg/kg	
Route of admin.	:	s.c.	
Exposure time	:		
Method	:		
Year	:	1960	
GLP	:	no data	
Test substance	:		
Method	:	PARAMETERS: observation(1 month), mortality, necropsy	
Remark	:	no further detail	
Result	:	MORTALITY: none	
		OBSERVATION: no effects	
		NECROPSY: residual test substance found at site of treatment in 1/10 mice	
Test substance	:	"Practical grade" Eastman Organic Chemicals	
Reliability	:	(2) valid with restrictions	
		few data on study design reported	
10.07.2002			(76)
Type	:	LD50	
Value	:	100 - 200 mg/kg bw	
Species	:	cat	
Strain	:	no data	
Sex	:	no data	
Number of animals	:		
Vehicle	:	no data	
Doses	:		
Route of admin.	:	s.c.	
Exposure time	:		
Method	:		
Year	:	1989	
GLP	:	no data	
Test substance	:	no data	

Remark : no detail
Reliability : (4) not assignable
LD50 only
04.07.2002 (71)

Type : LD0
Value : > 3000 mg/kg bw
Species : rat
Strain : other: Holtzman
Sex : male
Number of animals : 10
Vehicle : other: 70 % W/V in 95 % v/v aq. ethanol
Doses : 3000 mg/kg
Route of admin. : s.c.
Exposure time :
Method :
Year : 1960
GLP : no data
Test substance :

Method : PARAMETERS: observation(1 month), mortality, necropsy
Remark : no further detail
Result : MORTALITY: none
OBSERVATION: no effects
NECROPSY: residual test substance found at site of treatment in 5/10 rats
Test substance : "Practical grade" Eastman Organic Chemicals
Reliability : (2) valid with restrictions
few data on study design reported
10.07.2002 (76)

Type : LD0
Value : >= 3000 mg/kg bw
Species : guinea pig
Strain : no data
Sex : male
Number of animals : 10
Vehicle : other: 70 % W/V in 95 % aq. ethanol
Doses : 3000 mg/kg
Route of admin. : s.c.
Exposure time :
Method :
Year : 1960
GLP : no data
Test substance :

Method : PARAMETERS: observation(1 month), mortality, necropsy
Result : MORTALITY: none
OBSERVATION: no effects
NECROPSY: residual test substance found at site of treatment in 4/10
guinea pigs
Test substance : "Practical grade" Eastman Organic Chemicals
Reliability : (2) valid with restrictions
few details on study design reported
10.07.2002 (76)

Type : LDLo
Value : > 1000 mg/kg bw
Species : cat
Strain : no data
Sex : no data

Number of animals	:	8
Vehicle	:	other: propylene glycol or corn oil
Doses	:	400-700-1000 mg/kg
Route of admin.	:	s.c.
Exposure time	:	
Method	:	
Year	:	1979
GLP	:	no
Test substance	:	
Method	:	Five cats were given a single s.c. dose of TPP (99.99% pure) dissolved in corn oil or propylene glycol and observed for signs of neurotoxicity for up to 3 months. One cat received 1000 mg/kg TPP in corn oil, and 2 received doses of 700 mg/kg TPP in corn oil, and 2 received doses of 400 mg/kg TPP in propylene glycol. Control cats (2) received injections of corn oil or propylene glycol. PARAMETERS: observation, mortality, necropsy
Remark	:	Conclusion: TPP is not neurotoxic in the cat. Earlier studies were complicated by the fact that TPP prepared from coal-tar sources containing impurities which are neurotoxic.
Result	:	All cats dosed except one receiving 400 mg/kg lost weight. The cat that lost weight after receiving 400 mg/kg (about 31% of its original body weight) showed no signs of unusual weakness or ataxia during the 5 weeks after dosing. It returned to about its original weight within 3 months and seemed to be normal in behavior and appearance. The other cat receiving 400 mg/kg never showed any signs of toxicity. The 2 cats given 700 mg/kg TPP became anorexic shortly after dosing and prostrate in 3-7 days after injection. One was found to have a perforated ulcer in the stomach, and both had hyperemic intestines. Microscopic examination showed no evidence of neuropathology, but did show generalized vascular damage with edema in many tissues, especially the colon. Blood samples showed that cholinesterase levels were similar to the controls. The cat receiving 1000 mg/kg became anorexic 1 week after injection and by 3 weeks was prostrate having lost 48% of its body weight. Sections of the brain and spinal cord did not reveal evidence of axon degeneration or demyelination of axons in any tract.
Test substance	:	zone-refined TPP (declared purity 99.99%)
Reliability	:	(2) valid with restrictions high purity of testmaterial (99,99%), sensitive species low animal number
10.07.2002		(87)
Type	:	LDLo
Value	:	>= 400 mg/kg bw
Species	:	cat
Strain	:	no data
Sex	:	no data
Number of animals	:	5
Vehicle	:	other: olive oil
Doses	:	200-400-800 mg/kg
Route of admin.	:	s.c.
Exposure time	:	
Method	:	other: See freetext
Year	:	1932

GLP	:	no data	
Test substance	:	no data	
Method	:	Three cats received single s.c. doses of 200 mg/kg TPP in olive oil. One cat received 400 mg/kg and another received 800 mg/kg TPP in olive oil.	
Result	:	PARAMETERS: observation (21 days), histopathology(CNS and selected peripheral nerves) MORTALITY: The cat receiving 800 mg/kg died on day 2; cat receiving 400 mg/kg died on day 5 OBSERVATION: 400 mg/kg: flaccid paresis and hyperexcitability; 200 mg/kg: muscular tremors, flaccid paresis and spastic gait shortly after dosing (sacrificed on days 10 (two cats) and 21 (1 cat)). HISTOPATHOLOGY: peripheral nerve degeneration in all cats.	
Reliability	:	(4) not assignable early study; few animals	
02.07.2002			(88)
Type	:	LDLo	
Value	:	= 500 - 1000 mg/kg bw	
Species	:	monkey	
Strain	:	no data	
Sex	:	no data	
Number of animals	:	2	
Vehicle	:	no data	
Doses	:	500-1000 MG/KG	
Route of admin.	:	s.c.	
Exposure time	:		
Method	:	other: One monkey was administered 1000 mg/kg TPP subcutaneously and observed until death. A second monkey was administered 500 mg/kg TPP s.c. and observed for 10 days.	
Year	:	1932	
GLP	:	no data	
Test substance	:	no data	
Method	:	PARAMETERS: observation, mortality, histopathology of nerves system	
Result	:	MORTALITY: 1 of 2 OBSERVATION: The monkey receiving 1000 mg/kg TPP died the next day following several hours of general prostration and flaccid paralysis of entire body. Monkey receiving 500 mg/kg showed no effects for 8 days when pronounced flaccid paralysis of the extremities developed. In the next two days the conditions progressed involving the upper extremities as well. This animal was killed. HISTOPATHOLOGY: peripheral nerve degeneration	
Reliability	:	(4) not assignable early study; no details on testsubstance and animals only 2 animals (1 per dose)	
02.07.2002			(88)
Type	:	other	
Value	:	> 500 mg/kg bw	
Species	:	other: hen	
Strain	:	other: leghorn	
Sex	:	male	

Number of animals : 2
Vehicle : other: undiluted
Doses : 500 mg/kg
Route of admin. : s.c.
Exposure time :
Method :
Year : 1956
GLP : no
Test substance :

Method : Two cockerels were administered TPP s.c. at a dosage of 500 mg/kg one time and observed for signs of neurotoxicity for at least 14 days.

Result : No signs of neurotoxicity developed in either cockerel. There was no histologic evidence of degeneration in the brain, cord, or sciatic nerves.

Test substance : 98% purity or greater

Reliability : (2) valid with restrictions
 early study
 few animals

10.07.2002

(80)

Type : other: LD
Value : 1000 mg/kg bw
Species : rabbit
Strain : no data
Sex : no data
Number of animals :
Vehicle : no data
Doses :
Route of admin. : s.c.
Exposure time :
Method : no data
Year : 1943
GLP : no data
Test substance : no data

Result : 1000 mg/kg: fatal after repeated administration

Reliability : (4) not assignable
 secondary citation,
 no details

10.07.2002

(86)

Type : LD0
Value : > 1000 mg/kg bw
Species : rabbit
Strain : no data
Sex : no data
Number of animals :
Vehicle : other: olive oil
Doses : 1000 mg/kg
Route of admin. : i.m.
Exposure time :
Method : no data
Year : 1932
GLP : no data
Test substance : no data

Result : No effects were noted

Test substance : crystalline technical product, Testmaterial of unknown purity twice recrystallized from conc. H₂SO₄ and benzene; sharp melting point melting point reduced by "purification";

Reliability : (4) not assignable
"Purification" reduced melting point;
no details of study design (unknown number of animals)
10.07.2002 (77)

Type : LD0
Value : = 200 mg/kg bw
Species : cat
Strain :
Sex : no data
Number of animals : 8
Vehicle : no data
Doses : 100 - 1000 mg/kg
Route of admin. : other
Exposure time :
Method :
Year : 1932
GLP : no data
Test substance : no data

Method : Eight cats were administered TPP by injection (route not mentioned) and observed for up to 30 days.
Dosages ranged from 100-1000 mg/kg.

Result : 100 mg/kg was considered to be the no effect level.
Minimum toxic dose was 200 mg/kg.
One cat given 200 mg/kg did not die but displayed signs of toxicity including hyperexcitability and tremors, spastic gait. On the 17th day generalized flaccid paralysis occurred.

Test substance : crystalline technical product, Testmaterial of unknown purity twice recrystallized from conc. H2SO4 and benzene; sharp melting point melting point reduced by "purification";

Reliability : (4) not assignable
early study,
low animal number
Purification reduced melting point;
findings not confirmed in later studies
Evaluation of this study is not possible due to omission of key details of study design.

10.07.2002 (77)

5.2.1 SKIN IRRITATION

Species : rabbit
Concentration : 500 mg
Exposure : Semioclusive
Exposure time : 4 hour(s)
Number of animals : 3
Vehicle : water
PDII :
Result : not irritating
Classification : not irritating
Method : OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year : 1990
GLP : yes
Test substance : other TS: 99.7 % Disflamoll TP

Method : The test material was moistened with water and applied under a semioclusive patch

Result : no signs of irritation appeared within 7 days

Reliability	: (1) valid without restriction guideline study, GLP, full report available	
Flag 10.07.2002	: Critical study for SIDS endpoint	(89)
Species	: rabbit	
Concentration	: 500 mg	
Exposure	: Semiocclusive	
Exposure time	: 24 hour(s)	
Number of animals	: 6	
Vehicle	:	
PDII	:	
Result	: not irritating	
Classification	: not irritating	
Method	: other: see remarks	
Year	: 1976	
GLP	: no data	
Test substance	: no data	
Method	: 6 adult rabbits, shaved back, intact or abraded skin, 500 mg, 24 hours exposure time, observations at 24 and 72 hours. PARAMETERS: erythema, edema	
Result	: Erythema: 0/6 rabbits (intact and abraded skin) Edema: 0/6 rabbits (intact and abraded skin)	
Reliability	: (2) valid with restrictions short report, main details presented	
Flag 05.09.2005	: Critical study for SIDS endpoint	(69)
Species	: rabbit	
Concentration	: 500 mg	
Exposure	: Occlusive	
Exposure time	: 24 hour(s)	
Number of animals	: 6	
Vehicle	:	
PDII	:	
Result	: not irritating	
Classification	: not irritating	
Method	: other: see remarks	
Year	: 1983	
GLP	: no data	
Test substance	: other TS: Triphenyl phosphate	
Method	: test in accordance with "Hazardous Substances regulations" under the U.S.A. Federal Hazardous Substances Labelling Act Sect. 191.11 (February 1965) Method: The test material was applied under two patches on the backs of six rabbits (3/sex), each receiving 1.0 ml/patch of a 50 mg/ml suspension. One site was intact and the other abraded skin. The patches were occluded for 24 hours and then removed. Resulting irritation was scored at 24 and 72 hours after patch removal. PARAMETERS: erythema, edema	
Result	: The material was not irritating to the backs of the rabbits at any interval evaluated ERYTHEMA: 0/6 EDEMA: 0/6	
Reliability	: (2) valid with restrictions guideline study, full report available,	

Flag	:	no data on purity of test substance	
10.07.2002	:	Critical study for SIDS endpoint	(90)
Species	:	rabbit	
Concentration	:	no data	
Exposure	:	no data	
Exposure time	:	no data	
Number of animals	:		
Vehicle	:		
PDII	:		
Result	:	not irritating	
Classification	:	not irritating	
Method	:		
Year	:	1968	
GLP	:	no data	
Test substance	:	no data	
Method	:	rabbit intradermal irritation test	
Result	:	no response	
Reliability	:	(4) not assignable	
		tabular report only	
		irrelevant route for local irritation	
02.07.2002			(91)
Species	:	mouse	
Concentration	:	70 % active substance	
Exposure	:	Semiocclusive	
Exposure time	:	72 hour(s)	
Number of animals	:	25	
Vehicle	:		
PDII	:		
Result	:	not irritating	
Classification	:	not irritating	
Method	:		
Year	:	1960	
GLP	:	no data	
Test substance	:	other TS: 70 % solved in alcohol	
Method	:	0.5 ml of a 70 % solution in alcohol; skin contact 24 to 72h.	
Test substance	:	"Practical grade" Eastman Organic Chemicals	
Reliability	:	(4) not assignable	
		no details of findings reported	
Flag	:	Critical study for SIDS endpoint	
10.07.2002			(76)
Species	:	rat	
Concentration	:	no data	
Exposure	:	no data	
Exposure time	:	4 hour(s)	
Number of animals	:		
Vehicle	:	other: oil	
PDII	:		
Result	:	not irritating	
Classification	:	not irritating	
Method	:	other: no data	
Year	:	1974	
GLP	:	no data	
Test substance	:	no data	

Method : rats were treated once as well as 6 times
Reliability : (4) not assignable
 Abstract only
Flag : Critical study for SIDS endpoint
 04.07.2002 (72) (73)

5.2.2 EYE IRRITATION

Species : rabbit
Concentration : 99.7 %
Dose : 70 other: mg
Exposure time : 24 hour(s)
Comment : rinsed after (see exposure time)
Number of animals : 3
Vehicle :
Result : not irritating
Classification : not irritating
Method : OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year : 1990
GLP : yes
Test substance : other TS: 99.7 % Disflamoll TP

Result : CORNEA: no findings
 IRIS: no findings
 CONJUNCTIVA: slight rednes(3/3; 1-24 h), slight swelling (1/3; 1 h),
 discharge (3/3; 1 h)

Reliability : (1) valid without restriction
 guideline study, GLP, full report available

Flag : Critical study for SIDS endpoint
 10.07.2002 (89)

Species : rabbit
Concentration : no data
Dose : 100 other: mg/eye
Exposure time : unspecified
Comment :
Number of animals : 9
Vehicle : none
Result : slightly irritating
Classification :
Method :
Year : 1976
GLP : no data
Test substance : no data

Method : in analogy to 16 CFR 1500.42.
 100 mg/animal,
 6 animals: unwashed eyes;
 3 animals: eyes washed 4 seconds after instillation, observation 24, 48 and
 72 hours after instillation; 7 days

Result : without wash: slightly irritating (redness grade 1 in 6/6; discharge in 4/6;
 complete recovery in 72 hours)
 with wash 4 seconds after instillation: not irritating (no response at all)

Reliability : (2) valid with restrictions
 short report
 individual findings reported

Flag : Critical study for SIDS endpoint
 05.09.2005 (69)

Species : rabbit
Concentration : no data
Dose : 100 other: mg
Exposure time : unspecified
Comment : other: rinsed after 30 seconds or not rinsed
Number of animals : 6
Vehicle : none
Result : slightly irritating
Classification : irritating
Method : other: See freetext
Year : 1983
GLP : no data
Test substance : no data

Method : test in accordance with "Hazardous Substances regulations" under the U.S.A. Federal Hazardous Substances Labelling Act Sect. 191.12 (February 1965)

100 mg of the test material were instilled into the conjunctival sac of the left eye of each of 6 animals (New Zealand White rabbits; 3/sex) and the eyelid was held closed for 1 second. After 30 seconds the material was flushed out of the eyes of three of the rabbits with approximately 200 ml warm water. Rabbits were examined at 1, 24, 48 and 72 hours post-dose, and daily up to 6 days to determine reversability of response.

Fluroscein was used to aid assessment of corneal damage.

Result : Signs of irritation were observed in all animals during the first 24 hours post-dose. Unwashed eyes returned to normal later than washed. All eyes had returned to normal by day 6. Triphenyl phosphate is considered a minimal eye irritant in this model.

Reliability : (2) valid with restrictions
 full report available
 guideline study
 no data on purity of test substance

Flag : Critical study for SIDS endpoint

08.10.2002

(92)

5.3 SENSITIZATION

Type : Guinea pig maximization test
Species : guinea pig
Concentration : 1st: Induction 5 % intracutaneous
 2nd: Induction 75 % occlusive epicutaneous
 3rd: Challenge 75 % occlusive epicutaneous
Number of animals : 10
Vehicle : peanut oil
Result : not sensitizing
Classification : not sensitizing
Method : OECD Guide-line 406 "Skin Sensitization"
Year : 2001
GLP : yes
Test substance :

Remark : positiv control: Mercaptobenzthiazole, 9/9 positive

Reliability : (1) valid without restriction
 conforming to current guideline and GLP

Flag : Critical study for SIDS endpoint

04.06.2003

(93)

Type : Patch-Test

Species	:	human	
Number of animals	:		
Vehicle	:		
Result	:		
Classification	:		
Method	:	other: 4 persons who tested positive to plastic discs standardly used in patch testing were tested for response to TPP (10% in acetone).	
Year	:	1964	
GLP	:	no	
Test substance	:	no data	
Method	:	retrospective evaluation of 23192 human patch tests	
Result	:	4 persons tested positive to TPP. Among 23,192 patients who were tested using plastic disc patches between 1950 and 1962 only 0.065% had shown positive reactions to the discs, a remarkably low figure in view of the many sources of contact with TPP.	
Reliability	:	(2) valid with restrictions case reports; no details about exposure concentrations and duration	
Flag	:	Critical study for SIDS endpoint	
03.07.2002			(94)
Type	:	Patch-Test	
Species	:	human	
Number of animals	:		
Vehicle	:		
Result	:	sensitizing	
Classification	:		
Method	:	other: A single person who responded positively to celluloid acetate film was patched with TPP.	
Year	:	1964	
GLP	:	no	
Test substance	:	no data	
Remark	:	Patient reacted to cellulose acetate film Person also tested positive to TPP patch.	
Reliability	:	(2) valid with restrictions case report; no details about exposure concentrations and duration	
Flag	:	Critical study for SIDS endpoint	
03.07.2002			(94)
Type	:	Patch-Test	
Species	:	human	
Number of animals	:		
Vehicle	:		
Result	:	sensitizing	
Classification	:		
Method	:	other: see free text	
Year	:		
GLP	:	no	
Test substance	:	no data	
Method	:	Case reports of individuals suffering from allergic dermatitis caused by TPP in spectacle frames or glue	
Result	:	1 Person each tested positive for sensitization to TPP.	
Reliability	:	(2) valid with restrictions case report no details about exposure concentrations and duration	
Flag	:	Critical study for SIDS endpoint	
03.07.2002			(95) (96)
Type	:	Patch-Test	

Species	:	human	
Concentration	:	1 ^{st.} : 5 % occlusive epicutaneous 2 ^{nd.} : 3 ^{rd.} :	
Number of animals	:		
Vehicle	:	petrolatum	
Result	:	not sensitizing	
Classification	:		
Method	:		
Year	:	1997	
GLP	:		
Test substance	:		
Method	:	retrospective evaluation of human patch tests	
Result	:	patients with suspected occupational dermatoses were patch-tested with a variety of plastic and glue allergens; in 174 patients no allergic reaction towards triphenyl phosphate was found; one person showed irritant reactions (=0.6%)	
Test condition	:	Patients were treated once with 2 days occlusive exposure and evaluated at 3 time points (day 2, 3, 4-6) thereafter. Reactions were scored according to ICDRG recommendations. No further details described.	
Reliability	:	(2) valid with restrictions case report no details about exposure concentrations and duration	
Flag	:	Critical study for SIDS endpoint	(97)
23.05.2005			
Type	:	Patch-Test	
Species	:	human	
Number of animals	:		
Vehicle	:		
Result	:	sensitizing	
Classification	:		
Method	:		
Year	:	1966	
GLP	:	no	
Test substance	:	no data	
Method	:	One person with multiple causes producing dermatitis was patched with TPP and other aryl phosphates.	
Result	:	Person tested positive to all patches.	
Reliability	:	(2) valid with restrictions case report no details about exposure concentrations and duration	
Flag	:	Critical study for SIDS endpoint	(98)
03.07.2002			
Type	:	Patch-Test	
Species	:	human	
Number of animals	:		
Vehicle	:		
Result	:	not sensitizing	
Classification	:		
Method	:		
Year	:	1977	
GLP	:	no	
Test substance	:	no data	
Method	:	One case is presented in which a person exhibiting a dermal response to	

	eye glass frame plastic was patched with a 1% TPP solution in water.	
Remark	: There was no response to the TPP patch.	
Reliability	: (2) valid with restrictions case report no details about exposure concentrations and duration	
Flag	: Critical study for SIDS endpoint	(99)
04.07.2002		
Type	: Patch-Test	
Species	: human	
Number of animals	:	
Vehicle	:	
Result	:	
Classification	:	
Method	:	
Year	: 1999	
GLP	:	
Test substance	:	
Method	: TPP at 5% ; no further data	
Result	: 1 of 358 patients tested reacted positive from 1991 to 1996; 3 of 358 showed irritation; no further data	
Reliability	: (2) valid with restrictions retrospective evaluation of human patch tests no details about exposure concentrations and duration	
Flag	: Critical study for SIDS endpoint	(100)
03.07.2002		
Type	: Patch-Test	
Species	: human	
Number of animals	:	
Vehicle	:	
Result	: not sensitizing	
Classification	:	
Method	:	
Year	: 1995	
GLP	:	
Test substance	:	
Method	: retrospective evaluation of human patch tests	
Result	: None of 343 patients reacted to TPP	
Reliability	: (2) valid with restrictions case reports no details about exposure concentrations and duration	
Flag	: Critical study for SIDS endpoint	(101)
03.07.2002		
Type	: Patch-Test	
Species	: human	
Number of animals	:	
Vehicle	:	
Result	: sensitizing	
Classification	:	
Method	:	
Year	: 1992	
GLP	:	
Test substance	:	
Remark	: concomittant positive reactions to paraben mix, cobalt chloride, potassium dichromate, and formaldehyde	
Reliability	: (4) not assignable	

03.07.2002 case report
only 1 patient
no details about exposure concentrations and duration (102)

Type : other: 2 case reports
Species : human
Number of animals :
Vehicle :
Result : not sensitizing
Classification :
Method :
Year :
GLP :
Test substance :

Method : Patch test with 0.5% TPP in Pet was negative
Reliability : (2) valid with restrictions
case reports
only 1 patient each
no details about exposure concentrations and duration

04.07.2002 (103) (104)

Type : other: Review
Species :

Result : There are only scarce indication of a sensitising potential. No data on experimental animals are available.
(5 references)

Reliability : (2) valid with restrictions
secondary review

Flag : Critical study for SIDS endpoint

29.07.2002 (105)

Type : other: case reports, review
Species :

Remark : Review on eyeglass allergic contact dermatitis: Triphenyl phosphate as a cause of allergic reactions

Reliability : (3) invalid
review, no details

04.07.2002 (106)

Type :
Species : human

Method : 1 patient
Result : Contact dermatitis after prolonged intense contact to a hearing aid
Reliability : (2) valid with restrictions
case report

Flag : Critical study for SIDS endpoint

10.07.2002 (107)

5.4 REPEATED DOSE TOXICITY

Type : Sub-chronic
Species : rat
Sex : male
Strain : Sprague-Dawley

Route of admin.	: oral feed
Exposure period	: 4 months
Frequency of treatm.	: daily
Post exposure period	: no
Doses	: 0.25, 0.5, 0.75 or 1 % in feed; = 161-345-517-711 mg/kg bw/day
Control group	: other: feed without TPP
Method	: other: 10 animals/group; behavioral test on all rats monthly
Year	: 1986
GLP	: no data
Test substance	:
Method	: DESIGN: male rats only, 10 animals/group 4 month dietary treatment, monthly tests, PARAMETERS: open field activity, accelerating rod, fore limb grip strength, negative geotaxis, body weight (weekly), food consumption (daily),
Remark	: Study aimed at neurotoxicity; few other endpoints examined
Result	: OBSERVATION: no signs of toxicity BEHAVIORAL TEST (monthly): no evidence of overt neurotoxicity. BODY WEIGHT GAIN: very slight depression at 0,5% TPP and above in the diet FOOD CONSUMPTION: no significant effect NOEL = 161 mg/kg bw/day
Test substance	: purity 98 %
Reliability	: (2) valid with restrictions only few standard endpoints examined; neurotoxicity study; no clin. pathology or histopathology
Flag	: Critical study for SIDS endpoint
03.08.2005	(108)
Type	: Sub-acute
Species	: rat
Sex	: male
Strain	: other: Holtzman
Route of admin.	: oral feed
Exposure period	: 35 d
Frequency of treatm.	: daily
Post exposure period	: no
Doses	: 0.1 or 0,5 % in feed (estimated dose: 70 - 350 mg/kg bw/day)
Control group	: yes, concurrent no treatment
Method	:
Year	: 1960
GLP	: no data
Test substance	: other TS: substance purity not known
Method	: DESIGN: 5 male rats/group, 2 treated(diet)/ 1 control group, 5 weeks treatment + 2 weeks recovery (3/5 rats) PARAMETERS: observation, body weight, food consumption, hematology (hemoglobin content, cell volume, red cell count, total and differential white cell count), body weights (3x/week), hematology, gross necropsy, organ weights (liver, kidney)
Remark	: The 0.1% group started with 5% but the dose was reduced after 3 days due to severely reduced food consumption
Result	: BODY WEIGHTS: slight depression in growth rate (0.5 % group) HEMATOLOGY: no change NECROPSY: no gross abnormalities ORGAN WEIGHTS: increase in liver weights (0.5 % group) NOEL 0.1 %

Test substance	:	"Practical grade" Eastman Organic Chemicals	
Reliability	:	(2) valid with restrictions early study, standard endpoints missing, no clin. chemistry or histopathology	
Flag	:	Critical study for SIDS endpoint	
03.08.2005			(76)
Type	:		
Species	:	rat	
Sex	:	no data	
Strain	:	no data	
Route of admin.	:	gavage	
Exposure period	:	3 months	
Frequency of treatm.	:	daily	
Post exposure period	:	none	
Doses	:	380, 1900 mg/kg bw/day	
Control group	:	no data specified	
NOAEL	:	= 1900 mg/kg bw	
Method	:		
Year	:	1974	
GLP	:	no	
Test substance	:	no data	
Method	:	DESIGN: 2 groups, gavage, high doses (0.1 or 0.5 x LD50) PARAMETERS: body weight, choline esterase (blood), organ weights,	
Result	:	No toxic effects observed	
Reliability	:	(4) not assignable abstract only; few experimental details	
03.08.2005			(73)
Type	:		
Species	:	rat	
Sex	:	male/female	
Strain	:	no data	
Route of admin.	:	other: oral	
Exposure period	:	2 months	
Frequency of treatm.	:	daily	
Post exposure period	:	no	
Doses	:	1000 mg/kg bw/day	
Control group	:	yes, concurrent vehicle	
Method	:	other: Parameters measured were body weight and food consumption. A necropsy was performed on all rats on study. The heart, lungs, kidneys, adrenal gland, intestines, brain, spine, peripheral nerves and muscle were examined histologically.	
Year	:	1957	
GLP	:	no	
Test substance	:	no data	
Method	:	DESIGN: 9 treated/3 control rats; 1000 mg/kg bw/day in 1 ml vegetable oil; restricted food; PARAMETERS: body weight(weekly), observation, mortality, necropsy, histopathology (heart, lung, kidneys, adrenals,spleen, GI tract, brain, spinal cord, peripheral nerv, muscle)	
Result	:	MORTALITY: Three rats died on the 14th day and one on the 25th day. OBSERVATION: All treated animals had reduced appetite and growth rate, neglected fur BODY WEIGHT: severely reduced body weight gain throughout the study NECROPSY: no pathologic findings HISTOPATHOLOGY: pyknotic or swollen ganglionic cells in the spinal cord with vacuole formation; vacuole formation in peripheral nerves. No changes were observed in the myelin sheaths.	

		effects in liver and kidneys (reduced glycogen storage, single cell necroses, hyaline casts, fatty degeneration in tubuli) are ascribed to the reduced general condition	
Reliability	:	(3) invalid early study; one dose level only, standard endpoints missing; not all observed parameters reported TS not characterised;	
03.08.2005			(74)
Type	:		
Species	:	rat	
Sex	:	male/female	
Strain	:	Sprague-Dawley	
Route of admin.	:	other: dietary	
Exposure period	:	120 days	
Frequency of treatm.	:	daily	
Post exposure period	:	no	
Doses	:	0.25, 0.5, 0.75, 1% of diet (estimated dose: 170-700 mg/kg bw/day)	
Control group	:	yes, concurrent no treatment	
LOAEL	:	= 1 %	
Method	:	other: Rats were dosed for 120 days and then tested for immunotoxicity response to sRBCs. Histopathology and clinical chemistry were performed.	
Year	:	1987	
GLP	:	no data	
Test substance	:		
Method	:	DESIGN: 10 male + 10 female rats/group; dietary treatment for 120 days, interim killing (day 60), 5 rats/group were immunized with sheep red cells (i.p.) beginning at days 60 and 67, PARAMETERS: body weight (weekly), food consumption (weekly), blood chemistry (hemolysin titers, serum collection, serum electrophoresis), organ weights (spleen, thymus), histopathology (spleen, thymus, lymphnodes)	
Remark Result	:	Study aimed at immunotoxicity; few other endpoints BODY WEIGHT: significant reduction of growth rate in males at 1% FOOD CONSUMPTION: temporary increase in males, decrease in females CLIN CHEMISTRY: increased levels of alpha- and beta- globulin only in female resp. male rats. Effects were not dose dependent but similar in all treated groups. ORGAN WEIGHT: no effects HISTOPATHOLOGY: expanded immunohistochemical evaluation with the humoral response to a T-lymphocyte dependent antigen (SRBC) and immunohistochemical evaluation of B- and T-lymphocyte regions of the spleen, thymus and lymph nodes was without effect. NOEL 0.75 %	
Test substance	:	98% pure "stable under the experimental conditions of the feeding study"	
Reliability	:	(2) valid with restrictions NON STANDARD TEST, aiming at immunotoxicity	
Flag	:	Critical study for SIDS endpoint	
03.08.2005			(109)
Type	:		
Species	:	rat	
Sex	:		
Strain	:	no data	
Route of admin.	:	unspecified	
Exposure period	:	3 month	
Frequency of treatm.	:	daily	

Post exposure period	:		
Doses	:	1925 mg/kg bw/day	
Control group	:	yes, concurrent vehicle	
Method	:		
Year	:	1969	
GLP	:		
Test substance	:		
Method	:	DESIGN: vehicle: oil (20%), dose: 1/2 LD50 PARAMETERS: choline esterase (2 h after treatment)	
Result	:	no further details Choline esterase reduced to 37% in blood 2 hours after treatment no further data	
Reliability	:	(4) not assignable report in russian; german abstract;	
03.08.2005			(72)
Type	:	Sub-acute	
Species	:	rabbit	
Sex	:	male/female	
Strain	:	New Zealand white	
Route of admin.	:	dermal	
Exposure period	:	3 x 5 days/week	
Frequency of treatm.	:		
Post exposure period	:	no	
Doses	:	100-1000 mg/kg bw/day	
Control group	:	yes, concurrent vehicle	
Method	:	DESIGN: 1 control + 2 dose groups; 10 animals/sex intact and abraded (2x weekly) skin VEHICLE: ethanol (conc. 50%);0,2-2 ml/kg APPLICATION: open, collar to prevent ingestion, 6 hours exposure/day PARAMETERS: observation (erythema, edema, atonia, desquamation, fissuring, eschar formation, exfoliation; daily) body weights, hematology (pretest and end: HCT,HB,RBC,WBC), clinical chemistry (pretest and end: GPT, alk. phosphatase, BUN, glc, Tot. Protein, albumin, Ca, inorg. phosphate), necropsy, organ weights (adrenals, ovaries/testes, spleen, thyroid/ parathyroid, kidneys, liver),acetyl cholinesterase (plasma, RBC, brain,) histopathology (high dose and control; >30 tissues)	
Result	:	CLIN.CHEMISTRY: decrease of acetylcholinesterase activity in plasma, erythrocytes and brain in males and females ALL OTHER PARAMETERS: comparable to control/ no effects 4 rabbits (not treated with TPP/control) died/were killed for non treatment related reasons	
Reliability	:	(2) valid with restrictions purity of test substance not stated, individual quantitative results not reported	
Flag	:	Critical study for SIDS endpoint	
03.08.2005			(110)

Type :
Species : rabbit
Sex : no data
Strain : no data
Route of admin. : oral unspecified
Exposure period : repeated
Frequency of treatm. : no data
Post exposure period : no data
Doses : 100 to 1000 mg/kg bw/day
Control group : other: no data
Method :
Year : 1968
GLP : no data
Test substance : no data

Method : no data
Result : kidney damage which clears up quickly
Reliability : (4) not assignable
 short summary only, no data on design and parameters

03.08.2005

(111)

Type :
Species : rabbit
Sex : no data
Strain : no data
Route of admin. : other: oral
Exposure period : repeated
Frequency of treatm. : no data
Post exposure period : no
Doses : 100-1000 mg/kg bw/day
Control group : no data specified
Method : other
Year : 1943
GLP : no
Test substance : no data

Method : no data
Result : No death or paralysis
Reliability : (4) not assignable
 original publication not available; no details given in
 Sutton et al. (1960)

03.08.2005

(86)

Type :
Species : cat
Sex : no data
Strain : no data
Route of admin. : gavage
Exposure period : 5 - 10 d
Frequency of treatm. : 1x/d
Post exposure period : no
Doses : 50 mg/kg bw/day
Control group : no
Method :
Year : 1957
GLP : no data
Test substance : no data

Method : DESIGN: 4 animals; gavage; 2% in aqueous tragacanth,
 PARAMETERS: observation, mortality, choline esterase

Result	: no further details : OBSERVATION: dyspnoe, weakness, decreased bodyweight, MORTALITY: all animals died within 10 days CHOLINE ESTERASE: activity 71, 68, 65 or 64 % of normal values,	
Reliability	: (4) not assignable early study; summary only; few animals	
03.08.2005		(112)
Type	:	
Species	: cat	
Sex	: no data	
Strain	: no data	
Route of admin.	: gavage	
Exposure period	: 2 days	
Frequency of treatm.	: daily	
Post exposure period	: no	
Doses	: 200-800 mg/kg bw/day	
Control group	: no	
Method	: other	
Year	: 1957	
GLP	: no	
Test substance	: no data	
Remark	: Results: Signs of toxicity observed were salivation, trembling, diarrhea; all animals died	
Reliability	: (3) invalid number of animals and dose range insufficient; early study	
03.08.2005		(74)
Type	:	
Species	: cat	
Sex	: no data	
Strain	: no data	
Route of admin.	: oral unspecified	
Exposure period	: 30x	
Frequency of treatm.	: 1x/d	
Post exposure period	: no	
Doses	: 10-25 mg/kg bw/day	
Control group	: no	
Method	:	
Year	: 1957	
GLP	: no data	
Test substance	: no data	
Method	: DESIGN: 2 animals/group; PARAMETERS: observation, mortality, choline esterase,	
Result	: no further details : OBSERVATION: no sign of toxicity at 10 mg/kg bw/day; weakness, prostration, laboured respiration, severe reduction of body weight at 25 mg/kg bw/day MORTALITY: 1/2 at 25 mg/kg bw/day (day 27)	
Reliability	: CHOLINE ESTERASE: cholinesterase activity 77 or 87 % of normal value (4) not assignable summary only; early study	
03.08.2005		(112)

Type	:	
Species	:	cat
Sex	:	no data
Strain	:	no data
Route of admin.	:	oral unspecified
Exposure period	:	8 d
Frequency of treatm.	:	1x/d
Post exposure period	:	up to 8 w
Doses	:	1, 5, 20, 50, 100, 250 mg/kg bw/d
Control group	:	no
Method	:	
Year	:	1957
GLP	:	no data
Test substance	:	no data
Method	:	DESIGN: vehicle: oil (food or gavage); 2-3 animals/group; PARAMETERS: observation, body weight, mortality, histopathology
Result	:	OBSERVATION: 1 mg/kg : only slight depression of body weight 5 mg/kg bw/day : apathy, low food consumption, death 20 mg/kg bw/day : low food consumption 50 - 250 mg/kg bw/day: apathy, tremors, dyspnoea, severely reduced general condition (diarrhea, salivation, neglected fur, weakness, unsteady motion), death MORTALITY: 0/2 at 1 mg/kg bw/day 1/2 at 5 mg/kg bw/day 0/2 at 20 mg/kg bw/day 2/2 at 50 mg/kg bw/day (killed) 2/2 at 100 mg/kg bw/day 3/3 at 250 mg/kg bw/day BODY WEIGHT: 5,(but not 20), 50, 100 and 250 mg/kg bw/day caused depression of body weight The histological signs of neurotoxicity, histological changes in liver, kidney and heart (due to fasting) cannot be assigned to individual treatment groups
Reliability	:	(4) not assignable early study standard endpoints missing histologic findings cannot be assigned to treatment groups; quality of test sample not known;
03.08.2005		(74)
Type	:	
Species	:	hen
Sex	:	female
Strain	:	other: Rhode Island Red x light Sussex
Route of admin.	:	gavage
Exposure period	:	5 d
Frequency of treatm.	:	daily
Post exposure period	:	21 d
Doses	:	5000 mg/kg bw/d as 50 % suspension in arachis oil
Control group	:	other: yes
Method	:	
Year	:	1982
GLP	:	no data
Test substance	:	other TS: Reomol TPP as 50 % suspension in arachis oil

Method : DESIGN: 6 hens; gavage in peanut oil (50% w/v suspension) daily for 5 consecutive days; observation for 21 days. Hens with symptoms were sacrificed as the study progressed.

Result : PARAMETERS: observation, mortality, body weight, gross necropsy
: OBSERVATION:
lethargy, no evidence of anticholinesterase activity, marked loss of body weight

MORTALITY:
3/6 animals died + 2/6 killed in extremis

BODY WEIGHT: severe reduction

NECROPSY : not reported

Histopathology:
axonal degeneration in spinal cord in 2 treated and 1 control birds
questionable findings in the other control and 3 treated animals
The slides were re-evaluated in 1991 and none of the microscopic findings could be confirmed

Reliability : (3) invalid
Identical findings (axonal degeneration) in control and treated animals at similar incidence and severity
Evaluation of delayed neurotoxicity was confounded by systemic toxicity caused by the excessive dose (5x 5g/kg/day) and could not be confirmed by re-evaluation of slides in 1991
Standard endpoints missing
Identity/Purity of the commercial product tested not known

03.08.2005

(113) (114)

Type :
Species : hen
Sex : female
Strain : no data
Route of admin. : oral unspecified
Exposure period : 12 d
Frequency of treatm. : 1x/d
Post exposure period : no data
Doses : 2500 mg/kg bw/d
Control group : other: no data
Method :
Year : 1958
GLP : no data
Test substance : no data

Method : DESIGN: vehicle : olive oil (20%); total dose: 30000 mg/kg
PARAMETERS: observation

Result : OBSERVATION: no signs of neurotoxicity

Reliability : (4) not assignable
scarce details given; only 2 hens at 1 dose

08.07.2002

(78)

Type :
Species : hen
Sex : female
Strain : Leghorn
Route of admin. : other: oral
Exposure period : 6 days (days 1-3, 21-23)
Frequency of treatm. : twice/day

Post exposure period	:	treatment-free intervals: days 4 to20 and days 24-42
Doses	:	2 x 5000 mg/kg bw/day
Control group	:	
NOAEL	:	= 10000 mg/kg bw
Method	:	
Year	:	1977
GLP	:	no
Test substance	:	no data
 Method	:	 DESIGN: 9 birds/group; gavage; total dose 60000 mg/kg; twice daily treatment (5000 mg/kg each time) on days 1-3 and 21-23 vehicle: corn oil Dosing regime: 1-3 oral dose, twice daily 4-21 observation of abnormal behaviour 21-23 oral dose, twice daily 24-42 observation for normal behaviour 42 sacrifice, histopathology PARAMETERS: observation (42 days), body weights (days: 0, 21, 42), mortality, necropsy, histopathology
Result	:	OBSERVATION: no effects, neurotoxic response: 0/9 (number positive/number of birds) BODY WEIGHT: not reported MORTALITY: not reported NECROPSY: not reported HISTOPATHOLOGY: no effects
Reliability	:	(2) valid with restrictions non standard study, main features reported, standard endpoints missing, high dose, study aiming at neurotoxicity
03.08.2005		(75)
Type	:	
Species	:	other: cockerel
Sex	:	female
Strain	:	
Route of admin.	:	other: oral
Exposure period	:	no data
Frequency of treatm.	:	no data
Post exposure period	:	no data
Doses	:	500 mg/animal/dose, total dose 25,000 mg/animal
Control group	:	yes, concurrent vehicle
Method	:	other: 2 cockerels were dosed with up to 25 g pure TPP.
Year	:	1944
GLP	:	no
Test substance	:	no data
 Method	:	 DESIGN: 2 hens treated, 4 control PARAMETERS: observation, mortality
Result	:	OBSERVATION: No evidence of ill health was observed. MORTALITY: none
Reliability	:	(4) not assignable

Year	:	1983	
GLP	:	no data	
Test substance	:	no data	
Reliability	:	(4) not assignable Result only	
03.07.2002			(118)
Type	:	Bacterial gene mutation assay	
System of testing	:	E. coli strain Sd-4-73	
Test concentration	:	no data	
Cycotoxic concentr.	:		
Metabolic activation	:	without	
Result	:	negative	
Method	:	other: see free text	
Year	:	1958	
GLP	:	no data	
Test substance	:	no data	
Method	:	modified paper disk method (application of testsubstance as a microdrop or small crystal), change from streptomycin dependence to independence Strain: E. coli sd-4-73 no metabolic activation	
Reliability	:	(4) not assignable early report non standard test system, no defined dose/concentration	
10.07.2002			(119)
Type	:	Ames test	
System of testing	:	S. typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538	
Test concentration	:		
Cycotoxic concentr.	:		
Metabolic activation	:	with and without	
Result	:	negative	
Method	:		
Year	:	1987	
GLP	:	no data	
Test substance	:	other TS: vendor purity: 98+ %	
Method	:	S9 mix from aroclor 1254 treated rat livers perincubation for 20 minutes at 37 C experiments were performed in triplicate and repeated positive and negative control were included	
Reliability	:	test concentrations and cytotoxicity not reported (2) valid with restrictions Method described in detail test concentrations and cytotoxicity not reported Results of NTP;	
Flag	:	Critical study for SIDS endpoint	
04.07.2002			(120)
Type	:	Mouse lymphoma assay	
System of testing	:	L5178Y	
Test concentration	:	3.13 - 50 ug/ml (nonactivation); 6.25 - 75 ug/ml (activation)	
Cycotoxic concentr.	:	50 - 75 ug/ml, resp.	
Metabolic activation	:	with and without	
Result	:	negative	

Method	:		
Year	:	1978	
GLP	:	no data	
Test substance	:	no data	
Method	:	Scoring for mutation was based on selecting cells that had undergone forward mutation from a TK+/- to a TK-/- genotype by cloning them in soft agar with BrdU	
		pos. (EMS), solvent, and neg. controls included	
Reliability	:	(2) valid with restrictions detailed report, no purity data about test sample	
Flag	:	Critical study for SIDS endpoint	(116) (121)
10.07.2002			
Type	:	Ames test	
System of testing	:	TA 98, TA 100	
Test concentration	:	50ug - 5 mg	
Cycotoxic concentr.	:	> 5 mg	
Metabolic activation	:	with and without	
Result	:	negative	
Method	:		
Year	:	1984	
GLP	:	no	
Test substance	:		
Method	:	S9 mix from aroclor 1254 treated rats Plate test and preincubation test experiments in duplicate positive and negative controls included Vehicle: DMSO	
Test substance	:	specially synthesized, purified by distillation purity not stated or 99%	
Reliability	:	(2) valid with restrictions detailed description of methods; only 2 tester strains	
Flag	:	Critical study for SIDS endpoint	(122) (123)
10.07.2002			
Type	:	Unscheduled DNA synthesis	
System of testing	:	Syrian hamster embryonic fibroblast cells (SHE)	
Test concentration	:	0.1 - 10x E-5 M	
Cycotoxic concentr.	:		
Metabolic activation	:	without	
Result	:	negative	
Method	:		
Year	:	1989	
GLP	:		
Test substance	:	other TS: 99%	
Method	:	DESIGN: 5 hours incubation without activation in the presence of 3H-thymidin	
Reliability	:	(2) valid with restrictions detailed description of testsystem given	
Flag	:	Critical study for SIDS endpoint	(123)
10.07.2002			
Type	:	Micronucleus test in vitro	
System of testing	:	syrian hamster embryonic fibroblast Cells (SHE)	
Test concentration	:	10E-6 to 10E-4 M	
Cycotoxic concentr.	:	no data	

Metabolic activation	:		
Result	:	ambiguous	
Method	:		
Year	:	1989	
GLP	:		
Test substance	:		
Method	:	TEST SYSTEM: Syrian Hamster Embryonic (SHE) cells INCUBATION: 5h exposure + 6,12,18,24,30 h post exposure ACTIVATION: none EVALUATION: microscopy at 400x; 2000 cell per concentration (background: 14,45 +- 4,3 micronuclei/ 2000 cells)	
Result	:	slight (<2x) increase of micronuclei after 18 hours but not at 24 hours	
		18 h: (micronuclei/cells) control: 18+-4.9/2000 5x10E-5: 28.7+-4,0/2000 (smaller increases at all other concentrations)	
		24 h: (micronuclei/cells) control: 17.5+-2.1/2000 0.1x10E-5: 17.0+-4.5/2000 (larger decreases at all other concentrations)	
Reliability	:	(4) not assignable detailed description of testsystem given; equivocal response in a non-standard system	
10.07.2002			(123)
Type	:	Ames test	
System of testing	:	TA 1535, TA 100, TA 1537, TA 1538, TA 98	
Test concentration	:	0,1 ml/plate at 100%, 10%, 1%, 0.1% 0.01%,	
Cycotoxic concentr.	:		
Metabolic activation	:	with and without	
Result	:	negative	
Method	:		
Year	:		
GLP	:		
Test substance	:	other TS	
Remark	:	undiluted test substance caused precipitation	
Test substance	:	mixture containing 34% TPP, 43% t-butylphenyl-diphenyl-phosphate and 23% more highly substituted triphenyl phosphates	
Reliability	:	(3) invalid TPP only 34 % in mixture	
04.07.2002			(124)
Type	:	Ames test	
System of testing	:	TA 1535, TA 100, TA 1537, TA 1538, TA 98	
Test concentration	:	0,1 ml/plate at 10%, 1%, 0.1% 0.01%, 0.001%	
Cycotoxic concentr.	:		
Metabolic activation	:	with and without	
Result	:	negative	
Method	:		
Year	:		
GLP	:		
Test substance	:	other TS	
Test substance	:	mixture containing 19% TPP, 46 % t-butylphenyl-diphenyl-phosphate and 35 % more highly substituted triphenyl phosphates	
Reliability	:	(3) invalid TPP only 19 % in mixture	

04.07.2002

(125)

5.6 GENETIC TOXICITY 'IN VIVO'**5.7 CARCINOGENICITY**

Species : mouse
Sex : male
Strain : other: Strain A/St
Route of admin. : i.p.
Exposure period : up to 6 weeks
Frequency of treatm. : 3 times/week
Post exposure period : 18 to 24 weeks
Doses : 20, 40, 80 mg/kg
Result : negative
Control group : yes, concurrent vehicle
Method :
Year : 1977
GLP : no data
Test substance :

Method : DESIGN: Mouse Lung Adenoma Test
 i.p. injection
 pos.+ neg. control groups
 MTD tested

DOSE REGIMEN:

20 mice/group
 20 mg/kg: 18 injections/6 weeks
 40 mg/kg: 3 injections/1 week
 80 mg/kg: 1 injection

Result : Max. tolerated doses were determined in a preliminary study
 Survival:
 in the 20 mg/kg group that received 18 doses : 18/20;
 in the 40 mg/kg group that received 3 doses : 3/20;
 in the 80 mg/kg group that received 1 dose : 12/20.
 Adenomas were only seen in the 80 mg/kg group. There was no significant increase in the adenoma incidence in this test compared to neg. control
 pos. control (urethane) produced 19.6 tumors per mouse at 100% survival

Test substance : No other findings reported
Reliability : Purity of TPP was 95-99.9%
 : (2) valid with restrictions
 non-standard test
 main details on study design given
Flag : Critical study for SIDS endpoint

09.09.2004

(126)

5.8.1 TOXICITY TO FERTILITY

Type : One generation study
Species : rat
Sex : male/female
Strain : Sprague-Dawley
Route of admin. : oral feed
Exposure period : 91 days
Frequency of treatm. : daily

Premating exposure period

Male :
Female :
Duration of test : 3 months
No. of generation studies :
Doses : 0.25, 0.5, 0.75 or 1 % in feed (= 166, 341, 516, 690 mg/kg)
Control group : yes, concurrent no treatment
Method : other: see freetext
Year : 1987
GLP : no data
Test substance : other TS: purity: 98%

Method

: DESIGN:
Four treated groups plus an untreated control, each consisting of 40 rats/sex, were administered TPP in the diet for 91 days in a subchronic study.
At the completion of this study females were mated with males from the same group. All remained on the same diet as in the subchronic study until day 20 of gestation when dams were sacrificed.
DURATION:
Substance application from 4 weeks post weaning through mating and gestation.
PARAMETERS:
observation, body weight, food consumption, necropsy
Fetuses were examined for soft tissue (1/2 of litter) and skeletal malformations.

Remark

: purity: commercial grade
fertility and teratogenicity tested

Result

: OBSERVATION: no findings reported
FOOD CONSUMPTION: increased in pregnant dams (not dose-dependent)
BODY WEIGHT: decreased during pregnancy (non-significant)
NECROPSY: no significant differences in number of corpora lutea, implants, implantation efficiency, viable fetuses and number of early or late deaths.
As there was no effect on the litter size (indirectly measured by the number of viable fetuses and implants) and both sexes were treated in the study, these findings indicate that fertility is not adversely affected by TPP in male and female rats.
parental NOEL = 690 mg/kg bw

Reliability

: (2) valid with restrictions

Flag

: Critical study for SIDS endpoint

01.10.2002

(127)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species : rat
Sex : no data
Strain : Wistar
Route of admin. : oral feed
Exposure period : 6 month
Frequency of treatm. : daily
Duration of test : 6 month
Doses : 0,05-0,1-1 mg/animal (5-10-100 mg/?? diet)
Control group : other: no data
Method : other: no data
Year : 1968
GLP : no data
Test substance : no data

Method	:	PARAMETERS: body weight, impregnation, gestation, parturition, nursing no details given	
Result	:	normal growth, impregnation, gestation, parturition, and nursing no details given	
Reliability	:	(3) invalid short summary only; no methodological details doses low concentration of TPP in diet not clear	
10.07.2002			(111)
Species	:	rat	
Sex	:	male/female	
Strain	:	Sprague-Dawley	
Route of admin.	:	oral feed	
Exposure period	:	91 days	
Frequency of treatm.	:	daily	
Duration of test	:	3 months	
Doses	:	0.25, 0.5, 0.75 or 1 % in feed (= 166, 341, 516, 690 mg/kg)	
Control group	:	yes, concurrent no treatment	
NOAEL maternal tox.	:	>= 690 mg/kg bw	
NOAEL teratogen.	:	>= 690 mg/kg bw	
Method	:	other: see freetext	
Year	:	1987	
GLP	:	no data	
Test substance	:		
Method	:	DESIGN: Four treated groups plus an untreated control, each consisting of 40 rats/sex, were administered TPP in the diet for 91 days in a subchronic study. At the completion of this study females were mated with males from the same group. All remained on the same diet as in the subchronic study until day 20 of gestation when dams were sacrificed. DURATION: Substance application from 4 weeks post weaning through mating and gestation. PARAMETERS: observation, body weight, food consumption, necropsy Fetuses were examined for soft tissue (1/2 of litter) and skeletal malformations.	
Remark	:	purity: commercial grade fertility and teratogenicity tested	
Result	:	OBSERVATION: no findings reported FOOD CONSUMPTION: increased in pregnant dams (not dose- dependent) BODY WEIGHT: decreased during pregnancy (non-significant) NECROPSY: no significant differences in number of corpora lutea, implants, implantation efficiency, viable fetuses and number of early or late deaths. No increase in skeletal anomalies. Slight, non-dose- related increases in visceral variations ("All treated groups had significantly more fetuses with moderate hydroureter than the control group. However, the high baseline incidence exhibited in the control group and lack of a clear dose-related response make the biological significance of this finding unclear. There were also significantly more fetuses in the treated groups with moderately enlarged ureters in the region adjacent to the kidney than in the controls. Again, the incidence was not related to dose since a greater portion of fetuses were affected in the lower dose levels than in two high levels").	

Test substance : No signs of teratogenicity.
Reliability : purity: 98%
 : (2) valid with restrictions
 : detailed publication
Flag : Critical study for SIDS endpoint
 09.05.2005 (127)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

Type of experience : Human - Epidemiology

Method : TEST MATERIAL: aryl phosphate mixture containing
 30 % TPP, 40 % monoisopropylphenyl diphenylphosphate, 30 %
 triphenyl phosphate with 2 or more isopropyl substituents
 POPULATION: 38 male workers
 CONTROL GROUP: yes
 PARAMETERS:
 observation, hematology, serum immunoglobulins, acetylcholinesterase
 activity in red blood cells, plasmacholinesterase activity and lymphocyte
 neurotoxic esterase (NTE), activity of monocyte nonspecific surface
 esterase
 Three methods of measuring the monocyte count were used and results
 compared.

Remark : OBJECTIVE: Monocyte counts in man
 When an automated counting instrument using an esterase stain was
 employed to evaluate monocyte counts, there was an apparent decrease in
 count in the exposed workers. They were not depressed with manual
 counting or with an automated counter using a different staining method.

Result : hematologic parameters, serum immunoglobulins were normal,
 no signs of anergy, marginal depression of acetylcholinesterase activity in
 red blood cells, plasmacholinesterase activity and lymphocyte neurotoxic
 esterase (NTE) unaffected, transiently lowered activity of nonspecific
 surface monocyte esterase

The apparently depressed monocyte count was significantly
 associated with a mild reduction in erythrocyte cell
 acetylcholinesterase, but no reduction was seen in plasma
 pseudocholinesterase or lymphocyte neurotoxic esterase. The histology of
 the mumps reaction was similar in both control and treated groups of
 people. No anergy was seen with mumps or staphylococcal phage lysate
 hypersensitivity skin tests.

Reliability : (4) not assignable
 Testmaterial contained only 30 % TPP

Flag : Critical study for SIDS endpoint
 03.07.2002 (128)

Type of experience : Human - Epidemiology

Method : OBJECTIVE: Monocyte counts in man
 TEST MATERIAL: triaryl phosphate, unspecified
 POPULATION: 20 workers (14/6 m/f)
 CONTROL GROUP: yes
 PARAMETERS: blood monocyte non-specific esterase staining, monocyte

	number	
	Blood samples from these workers, a group of in-plant non-exposed workers, and a group of non-exposed people living in a neighborhood 50 miles away were collected and the monocyte nonspecific esterase measured using four different methods. Monocyte counts were done using four different techniques - two automated counting machines, the Technicon D-90 and the Technicon H-6000, and two manual methods, one using an esterase stain and one a Wright stain.	
Result	: decreased non-specific esterase staining in monocytes. Number of monocytes normal.	
	The average monocyte percentage for the triaryl phosphate exposure group was just over 4.0% compared to a value of 5.43% for the plant controls; they were significantly different. The Technicon D-90 reported decreased MNSE positivity as compared to the other methods.	
Reliability	: (4) not assignable	
	test substance not identified	
Flag	: Critical study for SIDS endpoint	
10.07.2002		(129)
Type of experience	: Human - Medical Data	
Method	: OBJECTIVE: health survey POPULATION: 11+32 men engaged in manufacture of TPP EXPOSURE: time weighted average of exposure to vapor and dust 3.5 mg/m3	
Remark	: The study was performed in 1960 and hygienic conditions should have been different from todays standards	
Result	: No dermatitis, no eye or respiratory tract irritation, no neurological diseases. In the laboratory examination, only the cholinesterase activity in red blood cells showed alteration. The overall health situation was unaffected.	
Reliability	: (2) valid with restrictions retrospective health survey	
03.07.2002		(76)
Type of experience	: other: Determination of exposure	
Remark	: OBJECTIVE: determination of exposure	
Result	: Triphenyl phosphate was found in human adipose tissue in all states of the USA	
03.07.2002		(130)
Type of experience	: other: Determination of exposure	
Remark	: Biomonitoring Species: human	
	Method: Samples of adipose tissue from the greater omentum were obtained at autopsies of people residing in six Ontario, Canada municipalities. Each was analyzed for presence of 13 trialkyl/aryl phosphates, including TPP.	
03.07.2002	No measurable TPP (detection limit 1 ng/g) was found in any fat samples.	(131)
Type of experience	: Human - Epidemiology	
Method	: This total diet study evaluated chemical contaminants in foods/diets eaten by 8 different age groups of people in the US. More than 200 foods were analyzed and an average diet was determined for 6-11 month olds, 2 year	

	olds, 14-16 year old males, 14-16 year old females, 25-30 year old females, 25-30 year old males, 60-65 year old males and 60-65 year old females. About 105 chemical contaminants were identified including TPP.	
Result	: The calculated intake of TPP in each of the 8 age groups, in mg/kg body weight/day was: 6-11 month olds - 0.3, 2 year olds - 4.4, 14-16 year old males - 1.2, 14-16 year old females - 1.6, 25-30 year old males - 1.6, 25-30 year old females - 0.8, 60-65 year old males - 0.5 and 60-65 year old females - 0.5.	
03.07.2002	These levels were considered safe.	(132) (133) (134)
Type of experience	: Human - Epidemiology	
Remark	: general toxicity, human	
Result	: The mean hours of work absences did correlated inversely with exposure The decrease of monocyte count based on esterase staining correlated with exposure but the total white cell count was increased at high exposure. Differences diappeared using two other methods of detection. Red blood cell cholinesterase was not influenced The rate of acute or chronic infection was not different between groups "Masses" and "pre malignant lesions" were not different Hematology revealed a statistically significant increase in lymphocytes No relevant neurologic findings were found	
Test substance	: mixture of 30% TPP, 40% mono-isopropyl-TPP, 30% di- and tri-isopropyl-TPP isomeres	
Reliability	: (2) valid with restrictions	
03.07.2002		(135)

5.11 ADDITIONAL REMARKS

Type	: adsorption	
Method	: metabolism, in vivo: rat, single i. p. injection of 300 mg of a commercial plasticizer containing 35 % TPP and several cresylphosphate isomeres: determination of TPP in the liver and blood after 4 h and 24 h determination of induction of microsomal cytochrome P-450 in the liver, pseudocholeline esterase in plasma, histopathology of caudal nerves	
Result	: metabolism, in vivo: TPP in the liver after 4 h 36.6±23.3 µg/g, after 24 h 1.8±1.9 µg/g; in blood: TPP after 4h: 0.7+-0.3 µg/g, 24 h not detectable induction of microsomal cytochrome P-450 in the liver, decrease of pseudocholeline esterase in plasma, swollen myelin sheaths in caudal nerves 2 weeks after injection of 300 mg/kg.	
Reliability	: (3) invalid Mixture cotaining only 35% TPP tested	
04.07.2002		(136)
Type	: Biochemical or cellular interactions	

Method	: 4 hens; 500 mg/kg bw; oral; blood was drawn 24 hr later and the activity of blood choline esterase determined	
Remark	: The authors state: "Solid esters were dissolved in arachis oil or, where this was not possible, in a mixture of tri-4-methylphosphate and tri-3-methylphenylphosphate (20:80 or 40:60)." Therefore it is not clear which vehicle was used and whether there was exposure to a mixture of phosphates. Birds were observed for at least 21 days after a single dose and evidence of ataxia sought.	
Result	: There was a decrease of 60% in blood cholinesterase activity. Activity had returned to normal levels within 4 days of an oral dose	
Reliability	: (2) valid with restrictions purity of test sample: not known possible exposure to a mixture of phosphate esters	
Flag 05.09.2005	: Critical study for SIDS endpoint	(79)
Type	: Biochemical or cellular interactions	
Method	: DESIGN: 5 male leghorn, oral, single dose, 1000 mg/kg bw, subcutaneous, single dose, 500 mg/kg PARAMETERS: observation, acetyl cholinesterase activity in plasma (24 h after treatment); histopathology fourteen to thirty-six days after administration (brain, spinal cord, sciatic nerve)	
Result	: OBSERVATION: no paralysis, ACETYL CHOLIN ESTERASE: severe depression (39-65%) of plasma cholinesterase 24 hrs after dosing depending on substrate used (acetylcholine, butyrylcholine, methacholine). There were no significant changes in spinal cord or brain choline esterases HISTOPATHOLOGY (NERVE TISSUE): no effects	
Test substance	: purity >=98%	
Reliability	: (2) valid with restrictions early study	
Flag 05.09.2005	: Critical study for SIDS endpoint	(80)
Type	: Biochemical or cellular interactions	
Result	: metabolism in vitro by carboxylesterase: TPP inactivates purified hog liver carboxylesterase in a time and dose dependent manner. Hydrolytic metabolite: phenol. metabolism in vitro by human monocytes: metabolites: phenol, phenolic metabolites (catechol, hydroquinone, 2,2-biphenol, 4,4-biphenol).	
Reliability 05.09.2005	: (4) not assignable	(137)
Type	: Biochemical or cellular interactions	
Method	: in vitro: inhibition of human serum cholinesterase	
Result	: fractions of residues from commercial hexane distillation inhibit cholinesterase	
Reliability	: (3) invalid mixtures of unknown composition tested	
31.08.2001		(138)
Type	: Biochemical or cellular interactions	
Result	: mouse, i.p.: 50-500 mg/kg bw single injection: blood cholinesterase inhibition (86.2 to 50.8 % of control	

	value).	
	mouse, oral: 10-500 mg/kg bw single application: blood cholinesterase inhibition (87.1 to 30.4 %).	
	mouse, inhalation: 363 - 757 mg/m ³ , 2-6h: no cholinergic symptoms, slight decrease in blood cholinesterase activity after 2 h at 757 mg/m ³ , but not at other concentration/ duration.	
	mouse, dermal: unknown dose, probably 0,5 ml/animal: slight decrease in whole blood cholinesterase activity.	
Test substance	: "Practical grade" Eastman Organic Chemicals	
Reliability	: (2) valid with restrictions Purity of TPP unknown, early study Cholinesterase was measured as indicator of absorption of TPP. A causal relation between TPP and the inhibition of cholinesterase in mice is not proven. It is possible that impurities are responsible. The authors build their case on SAR considerations. The results are equivocal: significant inhibition after 2 hours inhalation in mice, but not after 4 h at the same concentration (757 mg/m ³)	
Flag 05.09.2005	: Critical study for SIDS endpoint	(76)
Type	: Biochemical or cellular interactions	
Remark	: human blood, in vitro: concentration dependent inhibition of serum-and erythrocyte cholinesterase. At a concentration of 6 x 10E-5 Mol/L effects were most pronounced in human erythrocytes, human plasma and mouse whole blood with residual activities (activity expressed as per cent of controls delta pH per hour) of 21, 40 or 57 %, resp. (unspecified duration of incubation). At a concentration of 6 x 10E-7 Mol/L 85, 86 or 93 % resp.were recorded.	
Test substance	: "Practical grade" Eastman Organic Chemicals	
Reliability	: (2) valid with restrictions early study Cholinesterase was measured as indicator of absorption of TPP. A causal relation between TPP and the inhibition of cholinesterase is not proven. It is possible that impurities are responsible. The authors build their case on SAR considerations.	
Flag 05.09.2005	: Critical study for SIDS endpoint	(76)
Type	: Biochemical or cellular interactions	
Remark	: In an in-vitro estrogen receptor (ER) competitive-binding assay the IC ₅₀ (50% inhibition of receptor binding of labeled Estradiol) for triphenyl phosphate was larger than 1 x 10-4M. For 17β-Estradiol the IC ₅₀ was 8.99 x 10-10 M.	
Reliability	: (4) not assignable relevance to human health unknown	
05.09.2005		(139)
Type	: Biochemical or cellular interactions	
Method	: System of testing: human erythrocytes and plasma, chicken plasma Method: In vitro evaluation was performed of the ability of TPP to inhibit the cholinesterase activity of human erythrocytes and human and chicken plasma. No other details were available.	
Result	: TPP did not inhibit the cholinesterase in this in vitro system. Only fowl plasma was investigated.	
Reliability	: (2) valid with restrictions	

Flag 04.07.2002	<p>early study, : Critical study for SIDS endpoint</p>	(80)
Type	: Biochemical or cellular interactions	
Method	: System of testing: hen brain homogenate	
Result	<p>Method: A substrate dispersion made by dissolving TPP in dimethyl formamide and Triton X-100 was incubated with hen brain homogenate in which paraoxon-sensitive activity was completely inhibited. The inhibition of neurotoxic esterase (IC50) was measured as compared to a control, using phenyl phenylacetate or phenyl valerate as substrate.</p> <p>: TPP caused no significant inhibition of neurotoxic esterase at 100 uM, or at saturating concentration. At 100 mM TPP there was no significant inhibition of Mipafox- resistant activity in the brain homogenate.</p>	
Reliability Flag 08.07.2002	<p>: (2) valid with restrictions : Critical study for SIDS endpoint</p>	(140) (141)
Type	: Biochemical or cellular interactions	
Method	: 0.5 ml of a 70% solution of TPP in ethanol was applied to skins of mice for 24, 48 and 72 hours and blood was analyzed for blood cholinesterase level.	
Result	<p>: Cholinesterase levels were 0.86 (24 hours), 0.83 (48 hours), and 0.69 (72 hours) delta-pH (parameter of enzyme activity?) per hour. Control animals (ethanol only) showed an average delta-pH per hour of 0.80. Differences were not significant at 5% level</p>	
Test substance Reliability 05.09.2005	<p>TPP did pass through the skin in this vehicle : "Practical grade" Eastman Organic Chemicals : (4) not assignable Cholinesterase was measured as indicator of absorption of TPP. A causal relation between TPP and the inhibition of cholinesterase is not proven. It is possible that impurities are responsible. The authors build their case on SAR considerations.</p>	(76)
Type	: Biochemical or cellular interactions	
Remark Result	<p>: Inhibition of purified enzyme in vitro : TPP efficiently inhibits the human monocyte carboxylesterase in vitro Ki= 8x10E-9</p>	
Reliability Flag 08.07.2002	<p>: (2) valid with restrictions relevance for human health not known : Critical study for SIDS endpoint</p>	(142)
Type	: Biochemical or cellular interactions	
Method	: Determination of hemolysis in vitro Source of erthrocytes: white rabbit	
Result	: TPP shows hemolytic activity in vitro EC50 = 45uM EC20 = 31uM	
Reliability 08.10.2002	: (4) not assignable	(143)

Type : Biochemical or cellular interactions

Remark : OPIDN (organophosphorus-induced delayed neuropathy) is correlated only to inhibition above 80%

Result : TPP inhibits the NTE in neuronal cell lines C6 and N18 but the maximum effect remains below 80% inhibition

Reliability : (4) not assignable
relevance to human health not known

05.09.2005 (123)

Type : Biochemical or cellular interactions

Method : NTE (Neuro-toxic esterase) activity was determined in rat brain and spinal cord microsomes relative to positive control (di-isopropyl-phosphofluoridate) concentration: 1 to 100 uM

Remark : The authors use the abbreviation "TPP" for triphenyl phosphite. Purity of triphenyl phosphate: 98%.

Result : Triphenyl phosphate did not inhibit NTE in vitro in the microsomal fraction of rat brain and spinal cord tissues at concentrations of 1 to 10 µM after 20 minutes of incubation. At 100 µM NTE was inhibited to about 60 %, while positive control (diisopropyl-fluoro-phosphate) showed complete inhibition below 10µM.

Reliability : (2) valid with restrictions
relevance to human health not known
methods described in detail

Flag : Critical study for SIDS endpoint

05.09.2005 (144)

Type : Cytotoxicity

Method : Human cells, in vitro: proliferation of lymphocytes unaffected,

Result : inhibition of monocyte-antigen-presentation (20 - 60%)

Reliability : (4) not assignable
non standard test, relevance to human health not known

08.10.2002 (145)

Type : Cytotoxicity

Remark : Mouse fibroblasts and chick embryo cells: no cytotoxic effect,

Reliability : (3) invalid
concentration range not stated

04.07.2002 (91)

Type : Cytotoxicity

Method : System of testing: human KB and HEL-R66 cells, monkey Vero cells, dog MDCK cells.

Control: Yes

Result : Inhibition of growth by TPP was dose dependent in all cell lines. The ID50 of TPP in KB cells was 0.6 mM, HEL-R66 cells

<p>Reliability 08.10.2002</p>	<p>was 0.5 mM, in Vero cells was 0.4 mM and in MCDK cells was 0.5 mM. : (4) not assignable</p>	<p>(146)</p>
<p>Type</p>	<p>: Cytotoxicity</p>	
<p>Method</p>	<p>: System: chicken nerve cells Control: yes, concurrent</p>	
<p>Result</p>	<p>Method: Sympathetic dorsal root ganglia from 10-11 day old chick embryos were excised and placed in a depression of a microslide with the appropriate media. This was covered with a cover slip, inverted and incubated for 72 hours. Several dilutions of TPP were added, both with and without nerve growth factor (NGF), and after a 3 day incubation period nerve fibers, neurons and glial cells were observed by phase contrast microscopy and light microscopy. The concentration of the chemical at half maximum (50%) response, slope function and their respective 95% confidence intervals were calculated. : There was a dose related response in vacuolization, swelling, reduced or absent glial cells and nerve fibers, and degenerative changes therein. At concentrations of up to .01M slight to no toxic effects were observed for TPP.</p>	
<p>Reliability 08.10.2002</p>	<p>EC50 = >10E-2 M : (4) not assignable non standard test relevance to human health not known</p>	<p>(147)</p>
<p>Type</p>	<p>: Cytotoxicity</p>	
<p>Method</p>	<p>: SYSTEM: in vitro; peritoneal macrophages and spleen cells from C57Bl mice</p>	
<p>Result</p>	<p>ENDPOINTS: NK-cell activity; antibody dependent phagocytosis; TNF assay; lymphocyte blastogenesis; IgM sythesis; viability : macrophages: Phagocytosis: no effect TNF activity: no effect at 0.3 uM; dose related decrease up to 33.3 uM viability: 0.3 - 10 uM >= 86% ; 33.3 uM =73% ; 100uM =31%</p>	
<p>Test substance Reliability 08.10.2002</p>	<p>spleen cells: NK-activity: dose dependent decrease lymphocyte blastogenesis: no effect <=10 uM IgM secretion: dose dependent decrease : TPP, 98% pure : (4) not assignable non standard test</p>	<p>(148)</p>
<p>Type</p>	<p>: Cytotoxicity</p>	
<p>Remark Result</p>	<p>: no clear dose/effect relation : TPP reduces the neurite outgrowth of neuronal cell lines (C6 and N18 neuronal cells)</p>	
<p>Reliability 08.10.2002</p>	<p>: (4) not assignable non standard test, relevance to human health not known</p>	<p>(149) (123)</p>

Type	: Neurotoxicity	
Method	: SPECIES: cat, 8 animals, (2 low dose, 2 mid dose, 1 high dose, 3 control) ROUTE/DOSE: s.c., single dose; 400, 700 and 1000 mg/kg bw PARAMETERS: observation, necropsy, histopathology of nervous tissues (11 levels from brain to peripheral nerve, several stains)	
Result	: OBSERVATION: 400 mg/kg bw: no ataxia 700 mg/kg bw: weight loss, prostration, diarrhea 1000 mg/kg bw: weight loss, prostration, Histopathology (700 mg/kg): generalized vascular damage, perivascular edema, loss of colon epithelium, fatty change in the liver HISTOPATHOLOGY OF NERVOUS TISSUES: no axon degeneration or demyelination or any other pathological change at any dose level.	
Test substance	: purity 99.99 %	
Reliability	: (2) valid with restrictions high purity test substance, low animal number	
Flag	: Critical study for SIDS endpoint	
08.10.2002		(87)
Type	: other: Cytotoxicity / Metabolic Inhibition Test	
Method	: HeLa Cells: cytotoxicity in vitro,	
Result	: minimal inhibitory concentration 6 mg/ml	
Reliability	: (4) not assignable relevance to human health not known	
05.09.2005		(150)
Type	: other: Review	
Remark	: Review on organophosphate-induced delayed neurotoxicity of Triarylphosphates	
Reliability	: (4) not assignable	
08.10.2002		(151)
Type	: other: toxicity	
Result	: mouse, i.p.: 0.5 ml/ 20 g: no response, no death	
Reliability	: (4) not assignable no details of study design and parameters determined, purity of test sample not known. only result listed in table	
05.09.2005		(91)

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