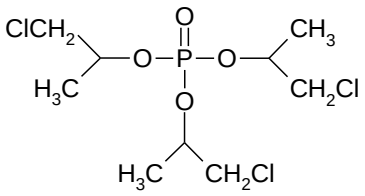
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	13674-84-5
Chemical Name	TRIS(2-CHLORO-1-METHYLETHYL) PHOSPHATE (TCPP)
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Physical-Chemical Properties

TCPP is a liquid at room temperature, has a melting point of less than -20˚C and a boiling point of 288˚C. TCPP has a relative density of 1.288 at 20˚C, a vapour pressure (measured) of 1.4 x 10^{-3} Pa at 25˚C and water solubility of 1080 mg/l at 20˚C. The log k_{ow} is 2.68. It is of low volatility (vapour pressure 1.4x10^{-3} Pa at 25°C).

Human Health

The metabolic fate of ^{14}C labelled TCPP was examined in rats following oral administration. Absorption was extensive (about 80%) and rapid (blood Tmax 0.5-2 hours). Distribution of radioactivity to tissues was rapid and widespread, but actual tissue levels of radioactivity were low and approximately 97-99% of dose was excreted within 7-8 days. Excreted material was <2% parent compound, indicating extensive metabolism. Most radioactivity appeared in the urine but about 20% appeared in the faeces, some of which reflected biliary excretion/enterohepatic recirculation. Metabolites identified in urine and faeces, in order of abundance, were o,o-[Bis(1-chloro-2-propyl)]-o-(2-propionic acid)phosphate, bis(1-chloro-2-propyl)monophosphoric acid and 1-chloro-2-propanol. An *in vitro* dermal study with TCPP using human skin membranes determined that the total absorption was 23%. A second study, mimicking handling of flexible PUR foam containing TCPP, determined that approximately 40% was absorbed by skin. Toxicokinetic data for the inhalational route of exposure were not available.

The acute oral LD_{50} (rat) ranged between 632 mg/kg bw and 4200 mg/kg b, with the majority of values less that 2000 mg/kg bw. Clinical signs of systemic toxicity noted in all studies included ataxia, hunched posture, lethargy, laboured respiration, increased salivation, partially closed eyelids, body tremors, clonic/tonic convulsions, pilo-erection, ptosis, loss of righting reflex, and red-brown staining around the mouth. The dermal LD_{50} (rat) following occluded contact for 24 hours, is greater than 2000 mg/kg bw. The 4 hour LC_{50} (rat) is greater than 4.6 mg/L. Clinical signs following inhalation exposure included mild lethargy, matted fur, acute bodyweight depression and convulsions. There was no evidence of inhibited plasma acetylcholinesterase or brain neurotoxic esterase enzyme levels in a delayed neurotoxicity study in hens. The findings on microscopic examination in that study were comparable between negative controls and TCPP treated hens.

Skin and eye irritation studies demonstrated that TCPP did not induce more than slight irritation. TCPP is not corrosive. Data on respiratory irritation were not available, but a few signs seen in several acute inhalation studies suggested that TCPP may be a mild respiratory tract irritant.

No evidence of skin sensitisation was found in a guinea pig maximisation test with TCPP and in a local lymph node assay in mice. TCPP is considered to be a non-sensitiser. Repeat dose toxicity data are available. In a thirteen week dietary study, broadly compliant with OECD Guideline 408, in which groups of 20 male and 20 female rats were fed diets containing 0, 800, 2500, 7500 or 20000 ppm TCPP, corresponding to mean substance intake values of 0, 52, 160, 481 or 1349 mg/kg bw/day, respectively, for males and 0, 62, 171, 570 or 1745 mg/kg bw/day, respectively, for females. A LOAEL of 800 ppm (52 mg/kg bw/day), the lowest tested

concentration, was derived for males based on an increase in absolute and relative liver weights, accompanied by mild thyroid follicular cell hyperplasia. A NOAEL of 2500 ppm (171 mg/kg bw/day) was derived for females based on increased absolute and relative liver weights. Other treatment related findings included a significant increase in absolute and relative liver weights in females at 570 and 1745 mg/kg bw/day, a reduction in mean body weight and periportal hepatocyte swelling in animals at the highest doses, 1349 mg/kg bw/day in males and 1745 mg/kg bw/day in females, and a significant increase in kidney weight in males at 481 and 1349 mg/kg bw/day.

In a 28-day oral gavage study in rats, broadly compliant with OECD Guideline 407, the liver was identified as the target organ. Increased absolute and relative liver weights were observed in males and females at the highest dose (1000 mg/kg bw/day), accompanied by hepatocyte hypertrophy in all high-dose males.A significant decrease in ALAT activity was also observed in high-dose males and females. Based on liver weight changes, accompanied by hepatocyte hypertrophy and changes in ALAT in high dose animals, a NOAEL of 100 mg/kg bw/day (mid dose) was derived.

In vitro, TCPP is not a bacterial mutagen and did not induce gene conversion in fungi. It did not cause DNA damage in hamster lung cells. The results of a mouse lymphoma cell assay indicated that TCPP was mutagenic in the presence of metabolic activation. A clear increase in the proportion of small colony mutants was also observed, suggesting that TCPP is a clastogen in the presence of metabolic activation in mammalian cells. TCPP did not induce unscheduled DNA synthesis in two assays but the result was considered equivocal in one other assay. TCPP induced transformed foci in BALB/3T3 cells. *In vivo*, TCPP tested negative in a mouse micronucleus test. A Comet assay indicated that TCPP did not induce DNA damage in rat liver. It is concluded that TCPP is non-genotoxic *in vivo*.

Carcinogenicity data were not available for TCPP. TCPP is structurally similar to two other chlorinated alkyl phosphate esters, TDCP and TCEP, both of which might be considered non-genotoxic carcinogens. It is considered that there is some information from the structures, physical-chemical properties, toxicokinetics and mutagenic profiles of TCEP, TDCP and TCPP to support a qualitative read-across for carcinogenicity. However, based on the available data, there are differences in the metabolism, target organs, the severity of the effects observed and the potency of the three substances, which indicate that a direct quantitative read-across for carcinogenicity from either TDCP or TCEP to TCPP may not be appropriate.

An oral two-generation reproduction toxicity study in rats was carried out in accordance with OECD Guideline 416. Animals administered 0, 1500, 5000 or 15000 mg/kg TCPP in the diet, corresponding to overall intake values of 0, 85, 293 or 925 mg/kg bw/day, respectively, for males and 0, 99, 330 or 988 mg/kg bw/day, respectively, for females. There were no treatment-related effects in pre-coital time, mating index, female fecundicity index, male and female fertility parameters, duration of gestation and post-implantation loss. An increase in oestrus cycle length and a decrease in uterus weight were observed in all dosed females of F0 generation and high dose females in F1 generation. The mean number of oestrus cycles was also increased in high dose animals of both generations. Effects were noted on ovarian weights in high dose females of F0. Absolute pituitary weights were decreased in high dose females in F0 and all dosed females in F1. It is noted that organ weight changes occurred in the absence of any histopathological changes, and it is accepted that uterine weight can fluctuate during oestrus cycle. Therefore the effects observed may possibly be due to normal variation in cycling females. In the same study, the number of live pups per litter was reduced on PND 1 at the high dose for pups born from the F0 generation and at the mid and high doses for pups born from the F1 generation. These effects correlate with a decrease in maternal body weight observed during the gestation period in these dose groups. There was a treatment related effect on the number of runts (defined as a pup with a weight less than the mean pup weight of the control group minus 2 standard deviations) observed in all TCPP-treated groups of the F0 generation on PND 1 and persisted to PND 21 in the mid- and high-dose groups. Increased numbers of runts in all dose groups of the F0 generation on PND 1 could indicate systemic toxicity to the pups *in utero*, although it is noted that no similar significant increase in the number of runts was observed in the F1 generation or in the preliminary study at PND 1. A LOAEL of 99 mg/kg bw/day was derived for developmental toxicity based on the increased number of runts seen in the F0 generation, which may be relatively precautionary as the effect on runts was not observed in both generations. A LOAEL of 99 mg/kg bw/day was derived for parental toxicity in females. This was based on a decrease in uterus weight in all dosed F0 females and decreased body weight and food consumption seen in mid- (330 mg/kg bw/day) and high-dose (988 mg/kg bw/day) females in both generations. For males, a NOAEL of 85 mg/kg bw/day was derived for parental toxicity, based on decreased body weights, food consumption and organ weight changes observed at mid- (293 mg/kg bw/day) and high-dose (925 mg/kg bw/day) males.

Environment

TCPP has a low adsorption capacity (K_{oc} is 174, by read across of the log K_{oc} - log K_{ow} relationship from the structurally-related substance TDCP, for which a reliable adsorption study has been conducted). TCPP has a

low potential to bioaccumulate in fish (measured BCF is 0.8-4.6).

Fugacity modelling shows that if released to air, most TCPP would be precipitated to soil (>90%) and some would pass to water (9%). If released to water, most (>99%) would remain in water. If applied to soil, most would remain in soil (>90%) though some would migrate to water (9%). There is little movement of TCPP between soil and water, because transfer via the air compartment is very slow.

TCPP is not readily biodegradable, showing 0-14% degradation over 28 days in two studies. It did, however, pass the criteria for inherent biodegradability under the conditions of a SCAS test and also those of a non-standard test method (in which, after a long acclimation period mineralisation occurred). Evidence of partial degradation was also seen in several other studies. While phosphate esters are known to be chemically susceptible to hydrolysis, TCPP is expected to have a half-life of at least one year under environmental conditions, based on a standard preliminary hydrolysis test. It is expected to degrade in the atmosphere by reaction with hydroxyl radicals and a half-life of 8.6 hours has been estimated (rate constant = 44.763×10^{-12} cm^3/molecule.sec).

Valid measured toxicity data are available for three aquatic taxonomic groups. The lowest effect values in short-term tests are a 96-h LC_{50} of 51 mg/l for Fathead minnow (*Pimephales promelas*), a 48-hour EC_{50} of 131 mg/l for the invertebrate *Daphnia magna*, and a 72-hour E_rC_{50} and E_bC_{50} of 82 mg/l and 33 mg/l respectively for the alga *Pseudokirchneriella subcapitata*.

Two chronic test results are also available: the 21-day NOEC for *D. magna* reproduction is 32 mg/l. The 72-hour ErC_{10} and 72-hour NOEC for growth rate for *P. subcapitata* are 42 mg/l (95% confidence interval 36-50 mg/l) and 13 mg/l respectively. A $PNEC_{aquatic}$ of 0.64 mg/l has been derived by dividing the NOEC for *D. magna* by an assessment factor of 50. There are no data for sediment-dwelling organisms. An IC_{50} of 784 mg/l was obtained for wastewater treatment plant micro-organisms (activated sludge).

Data are also available for terrestrial organisms. A 14-day LC_{50} of 97 mg/kg and a 56-day NOEC of 53 mg/kg soil dry weight were determined in tests with the earthworm *Eisenia foetida*. A lowest NOEC of 17 mg/kg soil dry weight was determined for lettuce (*Lactuca.sativa*) in a 21-day post emergence test with three plant species that also included wheat (*Triticum aestivum*) and mustard (*Sinapis alba*). A 28-day NOEC of ≥128 mg/kg wet weight (no inhibition at the highest concentration tested) was determined for inhibition of nitrogen transformation by soil micro-organisms for the structurally related substance TDCP (CAS 13674-87-8). Due to the structural similarity of TDCP to TCPP, their similar physico-chemical properties and their lack of toxicity to WWTP micro-organisms, it is considered justifiable to read-across this NOEC from TDCP to TCPP.

Exposure

Total EU production of TCPP in the year 2008 was 46,000 tonnes, with production taking place in three sites in Germany and one site in the UK. A total of 12,500 tonnes of TCPP was exported from the EU in the year 2008. TCPP is used as an additive flame retardant mostly (~98%) in polyurethane or PUR. It is physically combined with the material being treated rather than chemically combined. The amount of flame retardant used in any given application depends on a number of factors such as the flame retardancy required for a given product, the effectiveness of the flame retardant and synergist within a given polymer system, the physical characteristics of the end product and the use to which the end product will be put. TCPP may be exported in its raw format, may be used in the manufacture of polyurethane (PUR) foam for use in the furniture and automotive industries or may be used in the manufacture of rigid foam for use in building applications. Additionally, a number of company-specific, low-tonnage minor uses have been identified. These are not described due to commercial sensitivity.

Occupational exposure to TCPP may occur during its manufacture, during the manufacture and cutting of flexible PUR foams, during the production of foam granules and rebonded PUR foam, and the manufacture and use of spray foam, rigid PUR foam and one-component foams. Inhalation of vapours and skin contact are the predominant routes of exposure. Oral exposure is not considered to be a significant route of exposure. Exposure of workers to TDCP via the inhalation route does not present a concern due to the presence of adequate controls, such as local exhaust ventilation. Dermal exposure during manufacture of TCPP and the manufacture of flexible PUR foams may present some concerns. It is considered that the exposure could be controlled by improved occupational hygiene practices e.g. wearing of personal protective equipment (e.g. gloves) and changing of contaminated gloves. Dermal exposures for other scenarios are controlled through the use of personal protective equipment.

The foam is only used in ways in which it is enclosed and therefore it is concluded that exposure to consumers is negligible.

TCPP concentrations in a wide range of environmental media and domestic/industrial locations have been reported. Emissions to the environment can occur to the atmosphere (by evaporation) and waste water. Sources of release include sites undertaking TCPP production; formulation of polyol (a PUR component) into 'systems'; manufacture of flexible and rigid foams; foam recycling ('rebonding' and 'loose-crumb'); manufacture of 'one-component' canned foams; and processing sites associated with the minor uses. Emissions to the environment could also occur from finished articles during their use and at disposal, via both evaporation and generation of small particles, due to weathering and wear. Leaching from landfill sites is considered possible, based on the physicochemical properties of TCPP. In the EU risk assessment, landfill leachate monitoring data from England and Wales are used to calculate the regional input into the environment.

RECOMMENDATIONS AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health

The chemical is currently of low priority for further work. The chemical possesses properties indicating a hazard for human health (acute oral toxicity and repeated dose toxicity [including effects on uterine weight]). However, based on the data presented by the Sponsor country the exposure situation at the workplace is controlled and adequate risk management measures are in place. Individual countries may wish to carry out their own exposure assessments, relevant for their own scenarios followed by a risk assessment.

Environment

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

Note: TCPP is one of four closely-related chlorinated phosphate ester flame retardants, all of which have undergone risk assessment in the EU. The other substances are: TDCP, CAS no. 13674-87-8; V6, CAS no. 38051-10-4; TCEP, CAS no. 115-96-8.The identified uses of TCPP do not lead to a concern for the environment in the EU. The human health risk assessment is still being conducted.