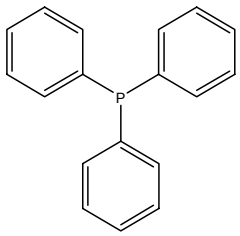
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	603-35-0
Chemical Name	Triphenylphosphine
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Toxicokinetics, metabolism, and distribution of triphenylphosphine have not been studied *in vivo*. According to the results from toxicity studies with experimental animals it can be deduced that triphenylphosphine may be absorbed to some extent after inhalation as well as after oral application, depending on the vehicle employed and/or particle size.

In rats, the 4-hr LC_{50} of triphenylphosphine was determined to be 12 500 mg/m^3 (whole-body exposure). Clinical signs were typical of respiratory irritation. The dermal LD_{50} was > 2500 mg/kg bw in rats, and > 4000 mg/kg bw in rabbits; no systemic toxicity or local irritation was noted. The oral LD_{50} of triphenylphosphine in rats was dependent on the vehicle used and ranged from 700 mg/kg bw (in olive oil) to > 6400 mg/kg bw (in aqueous suspension). In mice, the oral LD_{50} of triphenylphosphine (in olive oil) was 1000 mg/kg bw. Hyperexcitability, followed by atony and transient ataxia were the most prominent toxic signs in rabbits and dogs at sublethal oral doses. In a hen acute delayed neurotoxicity study (US EPA 163) neuropathological changes in the spinal cord and in the sciatic nerve, without clinical signs of neurotoxicity were found at oral doses of 1500 mg/kg bw and above; ataxia was observed at 6000 mg/kg bw. Neurotoxicity was also induced in ferrets after subcutaneous injection of 250 mg/kg bw triphenylphosphine without affecting the neuropathy target esterase (NTE) and acetylcholine esterase (AChE) activities.

Occlusive exposure of a 50 % suspension of triphenylphosphine in ethanol for 20 hours was very slightly irritating to the skin of rabbits. One drop of a 10 % solution of triphenylphosphine in olive oil induced very slight eye irritation in rabbits; 50 mg of the solid substance was irritating. Triphenylphosphine was a skin sensitizer in guinea pigs (Directive 84/449/EEC, B.6).

In rats mild respiratory irritation was the only effect after 2 weeks of inhalation exposure to 2,400 mg/m^3. In a 5-week inhalation study on dogs, clinical signs of neurological impairment, ataxia, and pathological changes in the cervical and lumbar spinal cord were found after exposures to 28 mg/m^3 (NOAEL: 9.7 mg/m^3).
A NOAEL of 6 mg/kg bw/day was found in a 3-month gavage study on rats (OECD TG 408). At 60 mg/kg bw/day changes indicative of liver enzyme induction (decrease in plasma prothrombin time, and a slight increase in liver weight in females and, in both sexes, centrilobular hepatocyte hypertrophy) were found. There were no clinical signs of neurotoxicity up to and including 120 mg/kg bw/day. In dogs, oral doses of 5 mg/kg bw/day, 2 - 5 days/week, induced ataxia, in a 5-week study; 10 or 20 mg/kg bw/day induced axonal degeneration in the spinal cord (NOAEL: 1 mg/kg bw/day). Triphenylphosphine induced severe nervous system disorder also in rabbits at oral doses 100 mg/kg bw/day (lowest tested dose).

Triphenylphosphine was not mutagenic in *Salmonella typhimurium* TA98, TA100, TA1535, and TA1537 in the presence and absence of metabolic activation system. In studies with limited validity no mutagenic activity was

detected in *Salmonella typhimurium* TA102 and *Escherichia coli* strains, both in the presence and absence of metabolic activation systems. It was also tested negative in the rec assay in *Bacillus subtilis*, and did not induce chromosomal aberrations in an *in vitro* micronucleus test with Chinese Hamster Lung cells. *In vivo*, triphenylphosphine did not induce micronuclei in bone marrow cells of mice treated intraperitoneally on four consecutive days with doses of up to 80 % of the 4-day LD_{50} value. Overall, triphenylphosphine showed no mutagenic activity *in vitro* and no clastogenic activity *in vitro* or *in vivo*.

There are no data available as to the carcinogenic potential of triphenylphosphine.

Triphenylphosphine had no effects on reproductive organ weights in a 3-months oral repeat dose toxicity study on rats according to OECD TG 408 (NOAEL: 120 mg/kg bw/day; highest dose tested). No adverse developmental effects were seen in a study performed in accordance with OECD TG 414 on Wistar rats (NOAEL, maternal toxicity: 30 mg/kg bw/day; NOAEL, developmental toxicity: 90 mg/kg bw/day = highest dose tested).

Environment

Triphenylphosphine is an organic solid with a melting point of 80.5 °C, a boiling point of 377.5 °C, and a relative density of 1.194 (at 25 °C). The calculated vapor pressure is 1.4×10^{-5} hPa at 25 °C. Water solubility has been measured (2 studies) to be in the range of 0.09 mg/l to ≤ 0.165 mg/l at 22 – 25 °C. A pH of 6.8 – 7.2 is reported for an aqueous solution of 0.09 mg/l at 25 °C. The log K_{OW} was measured as 5.69, and calculated as 5.02. The Henry's Law constant was calculated as 2.289×10^{-3} Pa x m^3/mole (25 °C), the soil adsorption coefficient log K_{OC} as 5.65.

Using a fugacity model (Mackay level I), triphenylphosphine is predicted to appear mainly in the soil compartment (96.3 %), with minor amounts in sediment (2.14 %), water (1.04 %), and air (0.45 %), and negligible amounts in biota (0.011 %). Due to the instability in aqueous solution the calculated distribution is only of theoretical interest and not relevant under environmental conditions.

The half-life for photodegradation was calculated as 2.7 days (24h-day, 0.5×10^6 OH/cm^3) and 22 hours (= 1.8 days based on a 12 hr-day and 1.5×10^6 OH/cm^3), respectively. Because of its structure, triphenylphosphine is not susceptible to hydrolysis. Triphenylphosphine dissolved in very highly diluted form as available under environmental conditions is oxidized to triphenylphosphine oxide.
The calculated bioconcentration factor (BCF) was 4801. At environmentally relevant low concentrations, triphenylphosphine will be oxidized to triphenylphosphine oxide, whose experimental log K_{OW} was 2.83. Using this log K_{OW} a BCF of 30 was calculated for triphenylphosphine oxide. Triphenylphosphine and triphenylphosphine oxide are not biodegradable as shown in tests according to OECD TG 301F (less than 20 % biodegradation within 28 days each).
Short-term tests with fish, invertebrates, and algae are available. All effect values for aquatic species and bacteria are above the water solubility of triphenylphosphine.
The lowest effect values (based on nominal concentrations) from valid short-term tests are:
Leuciscus idus: 96h-LC_{50} > 10 000 mg/l
Daphnia magna: 48h-EC_{50} > 5 mg/l (0.6 mg/l, if tested with a dispersant. For environmental conditions this test result is of limited relevance.)
Desmosdesmus subspicatus: 72h-$EC_{50\ \text{growth rate/biomass}}$ > 5 mg/l
For bacteria the lowest valid toxicity value determined was a 0.5 h-EC_{50} > 10 000 mg/l (nominal) for *Pseudomonas putida*.
Tests on terrestrial species are not available.

Exposure

In 2001, between 5000 and 7000 tonnes of triphenylphosphine were produced in Europe. The production volume for Asia (2001) ranged between 1000 and 3000 tonnes, and for the U.S. (2001) between 1000 and 3000 tonnes.

The three producers in Europe have confirmed that triphenylphosphine is produced and used at their sites in closed systems only. Furthermore by the producer in Germany worker exposure is limited by industrial hygiene controls and personal protective measures, regular workplace measurements are not conducted. Exposure could also occur during loading or unloading of tank trucks, railroad tankers, barges, and drums. Dedicated systems are typically used for loading and unloading purposes and procedures should be in place to prevent spills or leaks during transportation. To this end, triphenylphosphine is transported in sealed containers, almost exclusively in the form of pellets or flakes. This also minimizes dust and improves handling and processing. Within the manufacturing site of

the Sponsor country, triphenylphosphine is transported in pipelines. Workplace measurements from other production and processing sites are not available. There exist no occupational exposure limit values for triphenylphosphine.

Triphenylphosphine is used as chemical intermediate in chemical synthesis, mainly for the synthesis of complexing agents, reducing agents, process regulators, vitamins, and pharmaceuticals. It is the starting material for Wittig reactions (primarily for the synthesis of vitamins and pharmaceuticals), and is used as catalyst ligand in hydroformylation reactions of olefins (oxosynthesis).
Because of the high chemical reactivity of triphenylphosphine, its concentrations in end-products are not expected to exceed trace levels, and exposure of consumers is therefore considered negligible. The SPIN database lists no triphenylphosphine-containing preparations for consumer use on the Nordic market. In the Swiss product register no preparations are listed which are supposed to be used in products for consumers.
Paints containing less than 1 percent of triphenylphosphine are reported to be used by professsionals in Norway for ship repairs.
Releases of triphenylphosphine into the environment may occur during manufacturing and processing. At the only manufacturing and processing site in the Sponsor country emissions into the atmosphere are below 25 kg/year. In the waste water treatment plant effluent the concentration of triphenylphosphine as oxide is regularly measured at one production plant in Germany and reported to the responsible authority. As triphenylphosphine is transported in sealed containers, emissions during transport are not expected to occur.

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

Human Health: The chemical is a candidate for further work. The chemical possesses properties indicating a hazard (acute and chronic toxicity, neurotoxicity, and sensitization potential) for human health. Based on data presented by the Sponsor country (relating to production by 3 producers in Europe which accounts for 53 to 71% of global production and relating to the use pattern in several OECD countries) exposure of workers during manufacturing is anticipated to be low. Consumer exposure is anticipated to be negligible. As no regular workplace measurements are available, the Sponsor country will develop an occupational exposure limit value (OELV).

Environment: The chemical is of low priority for further work. The chemical has a low water solubility and does not show acute aquatic toxicity at the limit of solubility. For the chemical and its oxidation product no data on chronic toxicity is available. Based on data presented by the Sponsor country (relating to production by 3 producers in Europe which accounts for 53 to 71% of global production and relating to the use pattern in several OECD countries), exposure to the environment is anticipated to be low and therefore this chemical is currently of low priority for further work. Countries may desire to investigate any exposure scenarios that were not presented by the Sponsor country.