Social Europe

Recommendation from the Scientific Committee for Occupational Exposure Limits for phosphine

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8 hour TWA	:	0.1 ppm (0.14 mg/m^3)
STEL (15 mins)	:	0.2 ppm (0.28 mg/m^3)
Additional classification	:	-

Substance:

Phosphine PH_3

Synonyms : Hydrogen phosphide, phosphorus trihydride, phosphane
EINECS N° : 232-260-8
EEC N° : -
Classification : -
CAS N° : 7803-51-2
MWt : 34
Conversion factor (20°C, 101 kPa) : 1.41 mg/m^3 = 1 ppm

1. Occurrence/use

Pure phosphine is a colourless odourless gas. It has a MPt of -133°C, a BPt of -88°C and a vapour pressure of 101 kPa at -87.5°C. The vapour density is 1.17 times that of air and it is explosive at concentrations above 1.6% in air. It also produces violent reactions when in contact with many other chemicals. Phosphine prepared by hydrolysis of magnesium or aluminium phosphide has a garlic-like odour due to impurities. The odour threshold is in the region of 0.5 ppm (0.7 mg/m^3).

Phosphine is extremely rare in nature, occurring transiently in marsh gas and other sites of anaerobic degradation of phosphorus-containing material. Atmospheric phosphine occurs mainly in emissions and effluents from industrial processes, from the use of phosphides as rodenticides and fumigants, and due to the action of water on phosphides present as impurities in industrial materials.

Phosphine is used as a fumigant for pest control and as a chemical intermediate in the synthesis of organophosphines and organic phosphonium derivatives. Organophosphines are used in oil additive and pharmaceutical applications. Phosphonium compounds are used in manufacture of polymers used in flame-retardent treatment of fabric. In addition to the above uses of phosphine, occupational exposure may occur in operations where phosphine is released (welding, metallurgy, manufacture of semi-conductors) and transport workers. Exposure patterns vary with applications, but maximum levels in the order of 1 - 8 ppm (1.4 - 11 mg/m^3) have been reported.

2. Health Significance

Phosphine is readily absorbed through the lungs, but information on dermal absorption is not available. It undergoes oxidative metabolism and is excreted in the urine as hypophosphite, phosphite and orthophosphate (Curry *et al*., 1959; Lam *et al.,* 1991).

Phosphine is a powerful reducing agent that reacts with oxygen to produce active oxygen species. Its high affinity for oxygen results in interactions with haemoproteins, such as the cytochromes of the respiratory chain and haemoglobin. These activities probably underly the toxicity of phosphine. *In vitro* studies have shown that exposure of human erythrocytes to phosphine at 1 ppm (1.4 mg/m^3) for 4 hours can result in the formation of Heinz bodies, a phenomenon related to oxidative degradation of haemoglobin (Potter *et al*., 1991).

The acute inhalation toxicity of phosphine is high, in both experimental animals and humans. Four-hour LC_{50} values of 11 ppm (15 mg/m^3) in rats and about 30 ppm (42 mg/m^3) in mice have been reported Waritz and Brown, 1975; Omae *et al*., 1996). A number of fatalities in humans have occurred on acute exposure, although the conditions were not known with any accuracy (Harger and Spoylar, 1958; Hallermann and Pribilla, 1959). Indian fumigation workers exposed to 0.17 - 2.11 ppm (0.25 - 2.95 mg/m^3) phosphine for 20-30 minutes experienced symptoms of respiratory irritation, headache, giddiness, lethargy, irritability, nausea and epigastric pain immediately after exposure (Misra *et al.,* 1988). Similar symptoms have been reported in shipyard workers exposed to about 1 ppm (1.4 mg/m^3) (Roaldsnes, 1982).

In repeated inhalation studies in animals, no clinical signs, changes in haematology, serum clinical chemistry or urinalysis, or pathological evidence of effects were observed in cats,

guinea pigs and rats exposed to 1 ppm (1.4 mg/m^3) phosphine for 4 - 6 h/d, 6 d/week over a 24 week period (Klimmer, 1969).

However, severe toxicity and deaths occurred at 5 ppm (7 mg/m^3) in the same series of studies. In another well-reported 90-day repeated inhalation study in rats, conducted in accordance with OECD guidelines and involving daily exposures to 0, 0.3, 1 or 3 ppm (0, 0.4, 1.0, 4.2 mg/m^3) phosphine for 6 hours, no differences between the test and control animals were seen at the lowest exposure level of 0.3 ppm (0.4 mg/m^3); the only changes observed at 1 ppm (1.4 mg/m^3), those of reductions in bodyweight gain and food intake, are of doubtful toxicological significance in the absence of other evidence of toxicity (Newton *et al*., 1993) In a very limited study of repeated inhalation exposure toxicity in mice there was evidence of a dose-related decrease in bodyweight gain at all concentrations used, from 0.3 to 4.5 ppm (0.4 to 6.5 mg/m^3) (Barbosa *et al*., 1994). The change was not statistically significant at 0.3 ppm (0.4 mg/m^3). Little useful information is available on the effects of long-term exposure in humans.

The genotoxicity profile of phosphine is uncertain, because of an absence of published standard assays for this substance. *In vitro*, evidence for some clastogenic activity has been obtained (Garry *et al.*, 1989). In animal genotoxicity studies *in vivo*, rats and mice exposed to phosphine at 5 ppm (7 mg/m^3) for 9 or 10 days showed no evidence of genotoxicity in peripheral lymphocytes, bone marrow or germ cells (Kligerman *et al.*, 1994). In another study in which mice were exposed to 0, 0.3, 1, or 4.5 ppm (0.4, 1.4 or 6.5 mg/m^3) phosphine for 6h/d, 5d/week for 13 weeks there was some evidence of an increase in the incidence of micronucleated peripheral erythrocytes and spleen lymphocytes at the end of the exposure period, at the highest dose only (close to the LD50 in this laboratory); no increases in micronuclei were seen in peripheral erythrocytes or skin keratinocytes in mice exposed similarly to 5.5 ppm (8 mg/m^3) phosphine for 2 weeks (Barbosa *et al*., 1994).

In humans, exposure to phosphine has been reported to produce an increased incidence of chromosomal aberrations in circulating lymphocytes of grain fumigators in USA (Garry *et al*., 1989, 1990). However, a similar type of study on such workers in Australia found no evidence of this effect (Barbosa and Bonin, 1994).

Overall, it appears that if phosphine does exhibit genotoxic potential it is expressed only at high doses and may be due to generation of active oxygen species within the cell (Garry *et al*., 1990). No carcinogenicity studies have been conducted on phosphine.

A standard developmental toxicity study in rats exposed to up to 5 ppm (7 mg/m^3) phosphine for 6h/d on days 6-15 of gestation produced no significant maternal or developmental effects (Newton *et al*., 1993).

Recommendation

The several repeated inhalation exposure studies in animals were considered to form the best basis for deriving suitable occupational exposure limits. There is some uncertainty about the overall NOAEL, as the cause of the bodyweight gain changes seen in rats and mice in the region of 0.3 to 1.0 ppm (0.4 to 1.4 mg/m^3) was not identified. In view of this uncertainty, the SCOEL recommends an 8 hour TWA of 0.1 ppm (1.4 mg/m^3). A STEL (15 mins) of 0.2 ppm (0.28 mg/m^3) is also recommended to limit peaks in exposure which could result in irritation.
No "skin" notation was considered necessary.
At the levels recommended, no measurement difficulties are foreseen.

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