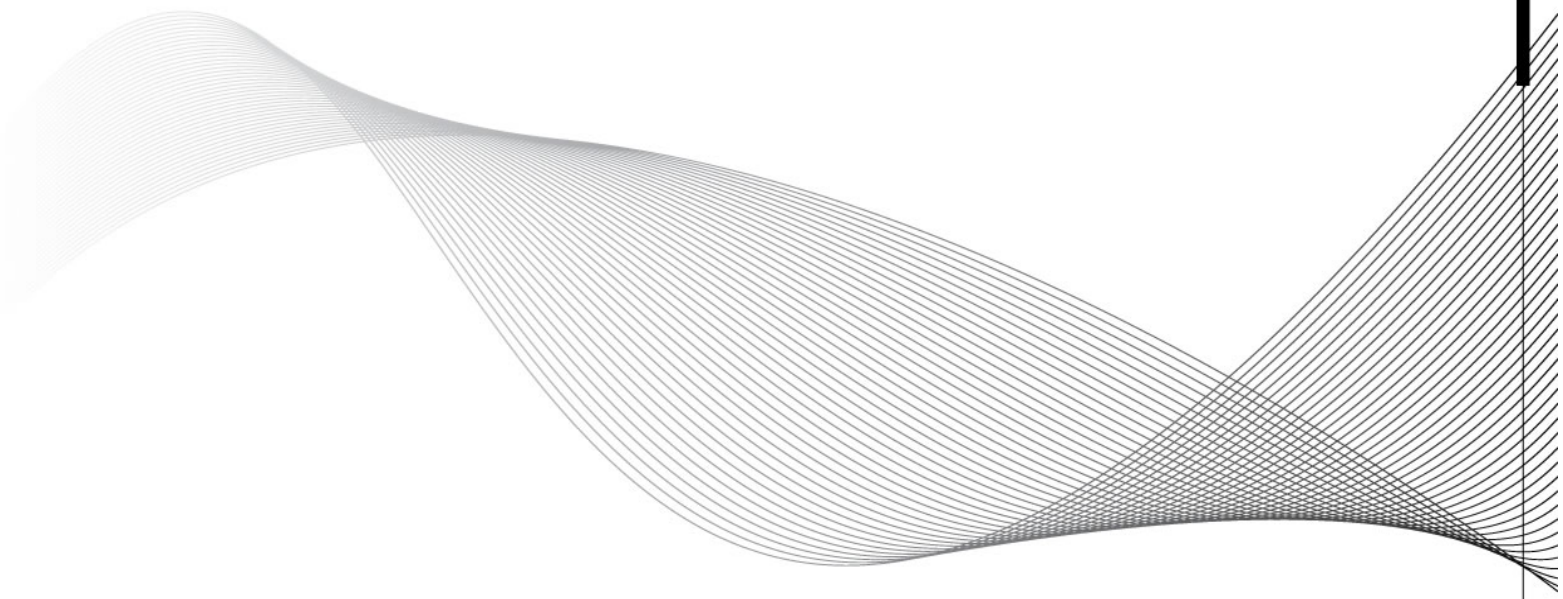
Social Europe



Recommendation from the Scientific Committee on Occupational Exposure Limits for tetraethylsilicate

SCOEL/SUM/64

July 2008

European Commission

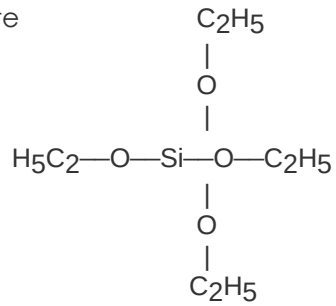
Table of Contents

Recommendation from the Scientific Committee on Occupational Exposure Limits for Tetraethylsilicate

8 hour TWA:	5 ppm (44 mg/m^3)
STEL (15 mins) :	(see Recommendation)
Notation:	(see Recommendation)

SUBSTANCE

Tetraethylsilicate



Synonyms : ethyl orthosilicate; ethyl silicate; tetraethoxysilane; tetraethyl orthosilicate; silicic acid tetraethyl ester
EINECS N° : 201-083-8
Annex I Index No: 014-005-00-0
EU Classification : R: 10 Flammable
Xn; R20 Harmful by inhalation.
Xi; R36/37 Irritating to eyes and respiratory system.
-
CAS N° : 78-10-4
MWt : 208.3

Conversion factor (20°C, 101 kPa) : 8.66 mg/m^3 = 1 ppm

1. OCCURRENCE/USE

Tetraethyl silicate is a colourless, flammable liquid with a characteristic penetrating odour. It has a MPt of -77°C, a BPt of 165.5 °C and a vapour pressure of 0.143 kPa at 20°C. The vapour density is 7.2 times that of air. The odour threshold is about 85 ppm (736 mg/m^3).

Tetraethyl silicate is used in the production of weatherproof and acid proof mortar, in heat- and chemical resistant paints, and other coatings and as a chemical intermediate in the production of organic silicon compounds. It is obtained from the reaction of chlorosilanes with ethanol.

2. Health significance

There are no available data relating to pharmacokinetics or metabolism of tetraethyl silicate.

Oral doses of 111, 223, and 333 mg/day (about 1300, 2600, 3900 mg/kg bw/day) for up to 4 days resulted in significant reduction of body weight, increase of mortality and acute onset of renal failure in F344 rats at the two highest doses. In all dose groups, silicate accumulation in the stomach glands and the muscle layer of the forestomach and glandular stomach were observed as well as acute tubular necrosis, accumulation of silicates, and superficial necrotizing papillitis in the kidneys. In the renal pelvis and bladder, there was urothelial simple hyperplasia, focal erosion of the mucosa, edema, and inflammation. These acute toxic changes were dose and time dependent, significant sex differences were not observed. The microscopic changes in the urothelium were similar to those observed following administration of high doses of sodium saccharin to male rats in which urinary silicate precipitate and crystals form (Okamura et al., 1992).

The histopathological features and mechanism of tetraethyl silicate toxicity in the kidney of mice were investigated in a light and electron microscopy study, which included energy dispersive X-ray microanalysis. A single dose of tetraethyl silicate was given to mice as intraperitoneal injection of approximately 1670 mg/kg body weight. Renal injury was considered to be the most probable cause of death due to acute tubular necrosis, a dense deposit of silicon over the microvilli of dead tubular epithelial cells, an abundant aggregation of hydroxyapatite crystals containing calcium in the cytoplasm and mitochondria of the dead tubular epithelial cells, and abundant myelinosomes and some hydroxyapatite crystals in the cytoplasm of viable proximal convoluted tubule epithelial cells. It was speculated that silicon compounds may bind to the plasma membranes of the proximal convoluted tubule epithelial cell microvilli and damage or interfere with membrane calcium channels. The resulting calcium ion imbalance may play a role in the subsequent progression of acute tubular necrosis by TEOS (Yamazaki et al., 1992).

Acute inhalation exposure of tetraethyl silicate to rats at 949 ppm (8218 mg/m^3) for 8h produced strong irritation of the eyes, nose and lungs and was lethal to some animals (Rowe *et al*., 1948). Exposure of groups of 10 mice to 1000 ppm (8669 mg/m^3) tetraethyl silicate for 1, 2, 4 and 8 hours resulted in 0, 1, 1, and 6 lethalities, respectively (Nakashima *et al.*, 1994). Acute tubular necrosis, acute splenic atrophy and necrosis of the olfactory epithelium were observed in all dead mice.

In rats, subacute inhalation of 400 ppm (3464 mg/m^3), 7h/d for 30d, resulted in some deaths and lung, liver and kidney damage in the survivors. Less pronounced effects were seen at 128 ppm (1108 mg/m^3) (Rowe *et al.*, 1948).

Following exposure of mice to 200 ppm (1732 mg/m^3) tetraethylsilicate for 6 h/day, 5 days/week for 2 or 4 weeks, tubular interstitial necrosis was seen in most animals and infiltration of polymorphonuclear neutrophils was observed in the nasal mucosa of all mice killed 1 day after completion of the exposure period (Nakashima *et al.*, 1994).

Exposure of mice to 50 or 100 ppm tetraethyl silicate for 6 h/day, 5 days/week, for 2 or 4 weeks resulted in tubulo-interstitial nephritis in mice exposed to 100 ppm. No kidney lesions or renal function changes were observed in mice exposed to 50 ppm. However, histopathological changes (submucosal infiltration of neutrophilic leukocytes) were detected in the nasal mucosa of mice exposed to 50 ppm (7/10 mice after 2 weeks exposure and 10/10 mice after 4 weeks exposure) and 100 ppm (10/10 mice after 2 and 4 weeks exposure); in control mice these changes were not observed (Omae et al., 1995).

Subchronic exposure of rats, guinea pigs, rabbits and mice (7h/d for 90d) resulted in decreased kidney weights in mice only at 88 ppm (762 mg/m^3) and no effect at 50 ppm (433 mg/m^3) (Pozzani and Carpenter, 1951).

Tetraethyl silicate was not found to cause mutation or sister chromatid exchanges in Chinese Hamster Ovary cells, with or without metabolic activation, but induced unscheduled DNA synthesis in rat hepatocytes (Slesinski *et al.*, 1981)As this test is an indicator test which does not allow a conclusion about mutagenicity, whereas a test for mutagenicity in CHO cells was negative, the positive UDS test is insufficient to consider tetraethyl silicate to be genotoxic.

There are no data available relating to carcinogenicity or reproductive toxicology.

Few human data are available. In a study on volunteers exposed for a short (unspecified) time period to tetraethyl silicate at 250 ppm (2165 mg/m^3), eye and nose irritation were reported (Smyth and Seaton, 1940).

There are no reports on occupational exposure.

RECOMMENDATION

The database on tetraethylsilicate is poor, but an OEL based on nephrotoxicity may be derived.
The study of Pozzani and Carpenter (1951) and Omae et al. (1995) indicate a NOAEL of 50 ppm (433 mg/m^3) for kidney effects in mice. However, histopathological changes were still detected in the nasal mucosa of mice exposed to 50 and 100 ppm for 14 and 28 days (Omae et al., 1995). A NOAEL for local irritation could not be derived from this study.
Although mice are more sensitive to irritating effects than humans, due to the anatomy of their nasal cavity, the high incidence of the inflammatory effect seen at 50 ppm requires a sufficiently large difference between the NOEL and the OEL, resulting in an 8-hour TWA of 5 ppm (44 mg/m^3). A STEL is needed to prevent from irritation, but the database does not

allow deriving one. In any case, a two-fold default value for a STEL should not be exceeded.

No data for a "skin" notation are available.

At the levels recommended, no measurement difficulties are foreseen.

KEY BIBLIOGRAPHY

Henschler, D. (ed) (1990). Criteria document of occupational exposure limits: tetraethyl silicate (21.06.1990). VCH Weinheim.

Nakashima, H., Omae, K., Sakai, T., Yamazaki, K. and Sakurai, H. (1994). Acute and subchronic inhalation of tetraethoxysilane (TEOS) in mice. Arch Toxicol. 68, 277-283.

Okamura, T., Garland, E.M., Johnson, L.S., Cano, M., Johansson, S.L., Cohen, S.M. (1992) Acute urinary tract toxicity of tetraethylorthosilicate in rats. Fundam Appl Toxicol. 18: 425-441.

Omae, K., Nakashima, H., Takebayashi, T., Uemura, T., Ishizuka, C., Yamazaki, K., Sakurai, H. (1995). No-effect level of subacute tetraethoxysilane inhalation on the mouse kidney. Sangyo Eiseigaku Zasshi (J Occup Health). 37, 1-4.

Pozzani, U. C. and Carpenter, C. P. (1951). Response of rodents to repeated inhalation of vapors of tetraethyl orthosilicate. Arch. Ind. Hyg. Occup. Med. 4, 465-468.

Rowe, V. K., Spencer, H. C. and Bass, S. L. (1948). Toxicological studies on certain commercial silicones and hydrolyzable silane intermediates. J. Ind. Hyg. Toxicol. 30, 332-352.

Slesinski, R. S., Guzzie, P. J., Hengler, W. C. and Wagner, K. J. (1981). Tetraethyl orthosilicates: in vitro mutagenesis studies (3-battery test). NTIS/OTS 0000469-0.

Smyth, H. F. and Seaton, J. (1940). Acute response of guinea pigs and rats to inhalation of the vapors of tetraethyl orthosilicate (ethyl silicate). J. Ind. Hyg. Toxicol. 22, 288-296.

Yamazaki, K., Nakashima, H., Eyden, B.P., Sakai, T., Omae, K., Sakurai, H. (1992). Acute renal injury by tetraethyl orthosilicate in mice: ultrastructure, histochemistry and X-ray microanalysis. J Submicrosc Cytol Pathol. 24: 257-268.