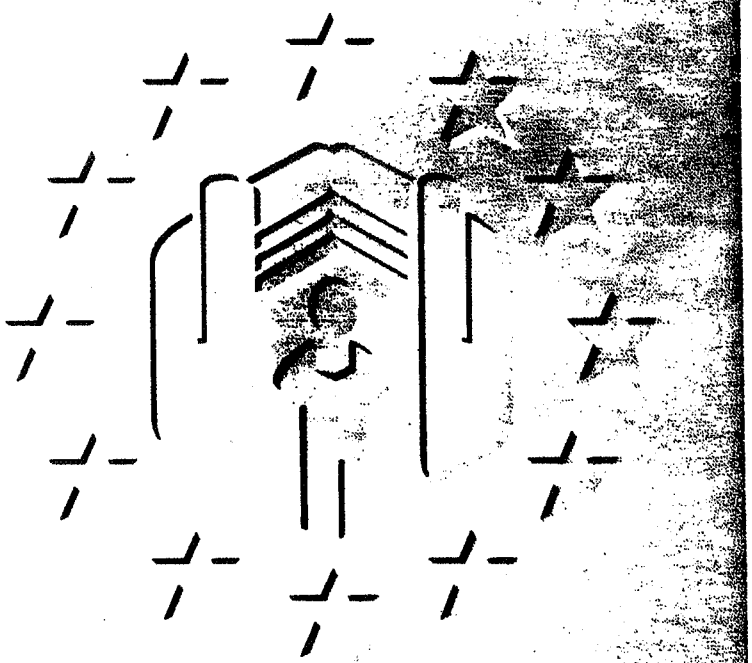
EUROPEAN COMMISSION

Occupational exposure limits

Recommendations of the Scientific Expert Group 1991-92



Health and safety

Report
EUR 15091 EN

Heptan-3-one

8-hour TWA:	20 ppm (95 mg/m^3)
STEL:	—
Additional classification:	—

Substance identification

Heptan-3-one	$CH_3CH_2CO(CH_2)_3CH_3$
Synonyms:	3-heptanone, ethyl butyl ketone, EBK
Einecs No:	203-388-1
EEC No:	606-003-00-9; Classification: R10 Xn; R20 Xi; R36
CAS No:	106-35-4
MWt:	114.2
Conversion factor (20°C, 101 kPa):	4.75 mg/m^3 = 1 ppm

Occurrence/use

Heptan-3-one is a colourless, flammable liquid with a strong fruity odour. It has a melting-point of – 39°C, a boiling-point of 148.5°C, a vapour pressure of 0.2 kPa at 25°C and a saturation concentration in air of 0.18% by volume. Heptan-3-one is a medium-volume solvent with a production rate less than 1 000 tonnes per annum in the European Community. It is used as a solvent for nitrocellulose and polyvinyl resins.

Health significance

The SEG discussed and reviewed heptan-3-one on the basis of the health-risk assessment carried out by the Dutch Expert Committee for Occupational Standards together with the additional information given by a member of the group.

The SEG considered the experimental data available to be limited, especially with respect to the almost complete lack of human data.

The data on acute toxicity via inhalation are incomplete. However, on the basis of LC10 values for rats, heptan-3-one showed greater toxicity than heptan-2-one (LC10 of 2 000 ppm (9 500 mg/m^3) for four hours compared with an LC10 value of 4 000 ppm (19 000 mg/m^3) for four hours).

Although the principal non-systemic hazards reported to be associated with exposure to ketone vapours are irritative effects on the eyes and the upper respiratory airways, no data for heptan-3-one are reported.

From the three reported subchronic animal studies on the nervous system with different routes of application (drinking water, gavage, inhalation), the inhalation study of Katz et al. (1980) on rats at 700 ppm (3 325 mg/m^3), 72 hours a week for 24 weeks, is considered to be the key study and has neurotoxicity as the critical effect. From these data it may be concluded that the NOAEL in respect of the neurotoxicity of heptan-3-one in rats is about 1 258 mg/kg/day, or 700 ppm (3 325 mg/m^3) based on a test for 24 weeks in inhaled air. This is well in line with the estimated NOAELs of 1 000 mg/kg/day by other routes of application (Homan and Maronpot, 1978; O'Donoghue et al., 1984).

The available data suggest that heptan-3-one is more neurotoxic than heptan-2-one. This may be due to the different neurotoxicity of the metabolites reported (2,5-heptanedione from heptan-3-one and 2,6-heptanedione from heptan-2-one).

No data with respect to chronic exposure, mutagenicity, carcinogenicity and reproductive toxicity are available.

The only human data available showed no irritation of heptan-3-one to human skin (25 volunteers) after 48 hours under an occlusive patch at a concentration of 4% in petrolatum.

Recommendation

The subchronic inhalation study in rats reported by Katz, establishing a NOAEL of 700 ppm, was considered to be an adequate basis for setting the limit. Because of the limited data, the SEG agreed that a safety factor of 20 should be used together with rounding down to comply with the SEG 'preferred value approach' to setting limits. The recommended 8-hour TWA is 20 ppm (95 mg/m^3). No STEL was considered to be necessary.

At the level recommended no measurement difficulties are foreseen.

Key bibliography

Dutch Expert Committee for Occupational Standards and Nordic Expert Group (1989) 'Basis for an occupational health standard 7/8-carbon chain aliphatic monoketones', Wibowo, A. A. E., *Arbete och Halsä*, pp. 1-45.

Homan, E. R. and Maronpot R. R. (1978) 'Neurotoxic evaluation of some aliphatic ketones', *Toxicol. Appl. Pharmacol.*, 45, p. 312.

Katz, G. V., O'Donoghue, J. L., Divincenzo, G. D. and Terhaar, C. J. (1980) 'Comparative neurotoxicity and metabolism of ethyl n-butyl ketone and methyl n-butyl ketone in rats', *Toxicol. Appl. Pharmacol.*, 52, pp. 153-158.

O'Donoghue, J. L., Krasavage, W. J., Divincenzo, G. D. and Katz, G. V. (1984) `Further studies on ketone neurotoxicity and interactions', *Toxicol. Appl. Pharmacol.*, 72, pp. 201-209.