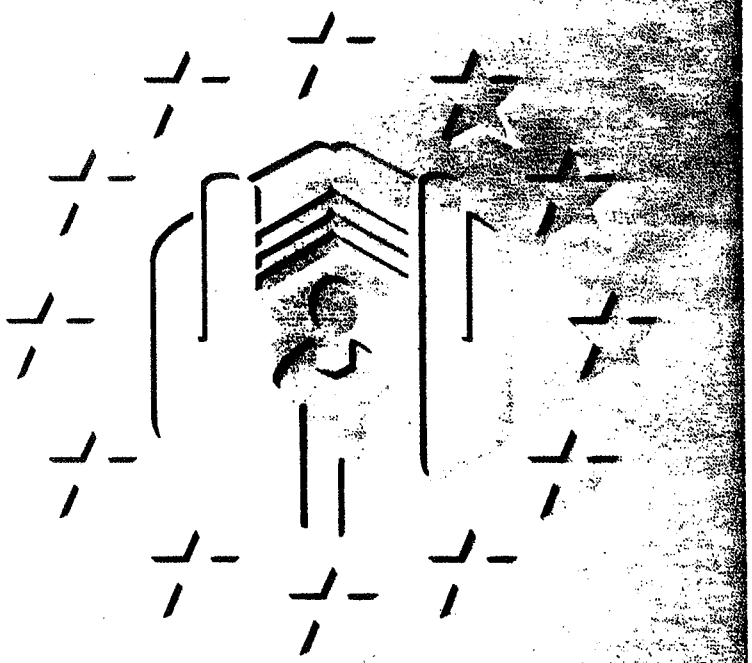
EUROPEAN COMMISSION

Occupational exposure limits

Recommendations of the Scientific Expert Group 1991-92



Health and safety

Report
EUR 15091 EN

Heptan-2-one

8-hour TWA: 50 ppm (238 mg/m³)
STEL: —
Additional classification: —

Substance identification

Heptan-2-one	$CH_3CO(CH_2)_4CH_3$
Synonyms:	2-heptanone, methyl n-amyl ketone, MAK, methyl pentyl ketone
Einecs No:	203-767-1
EEC No:	606-024-00-3; Classification: R10Xn; R22
CAS No:	110-43-0
MWt:	114.2
Conversion factor (20°C, 101 kPa):	4.75 mg/m³ = 1 ppm

Occurrence/use

Heptan-2-one is a colourless liquid with low volatility and a penetrating fruity odour. It has a melting-point of −26.9°C, a boiling-point of 150.6°C, a vapour pressure of 0.2 kPa and an odour threshold of about 0.02 ppm (0.1 mg/m³).

Heptan-2-one occurs naturally in oil of cloves and in Ceylon cinnamon oil. It is a medium volume solvent with a production volume less than 1 000 tonnes per annum in the European Community. It is used as a solvent in synthetic resin finishes and lacquers, and as a flavouring agent.

Health significance

The SEG reviewed and discussed the document from the Dutch Expert Committee for Occupational Standards. The health assessment as carried out by this group was considered to be adequate. The reported animal data are regarded to be limited but sufficient for an evaluation. An almost complete lack of human data was stated.

Heptan-2-one shows a relatively low acute toxicity by oral administration to animals (rats, mice, LD50: 1 670 to 2 400 mg/kg). No LC50 values are reported, but in rats an LC10 value of 4 000 ppm/4h (19 000 mg/m³) has been determined.

The acute irritation potential on the upper respiratory airway has been investigated in mice (De Ceaurriz et al., 1984). In measuring the decrease of the respiratory rate an RD50 value of 895 ppm (4 250 mg/m³) for 15 minutes has been determined. On this basis, using the model

of Kane et al. (1979), the occupational exposure limit value should be between 9 and 90 ppm (43 to 428 mg/m³) to protect from irritation. From the reported subchronic studies on different species (rats, monkeys) by different routes (oral, inhalation) with different effects (kidney, liver, cardiopulmonary system, nervous system) the studies of Lynch et al. (1981) and Johnson et al. (1978) are regarded as key studies for the evaluation because of the route of exposure (inhalation) and the length of studies (nine to 10 months).

From these studies, an overall NOAEL of about 1 000 ppm (4 750 mg/m³) can be established. The critical effects are irritation of the upper respiratory tract and systemic effects on the nervous system, liver and kidneys.

Observations in man are scarce. The reports of peripheral neuropathy in man after sniffing lacquer thinners are difficult to interpret due to the multitude of chemicals present (3-heptanone, n-hexane, toluene, xylene, nitropropane). In a sensitization study on human volunteers, 2-heptanone showed no positive reaction.

No data on mutagenicity and carcinogenicity are available.

Reproduction toxicity cannot be evaluated because the studies reported have been performed at maternal toxic exposure levels (2 000 ppm, 9 500 mg/m³).

Recommendation

The animal studies of Lynch and Johnson, establishing a NOAEL of 1 000 ppm (4 750 mg/m³), were considered to be an adequate basis for setting the exposure limit. Because of the lack of human data and the limited animal data, the SEG considered it appropriate to use a safety factor of 20. The recommended 8-hour TWA is 50 ppm (238 mg/m³). This value is in line with the range of recommended limit values of 9 to 90 ppm (43 to 428 mg/m³) derived from the RD50 value by the method of Kane. No STEL was considered necessary.

At the level recommended no measurement difficulties are foreseen.

Key bibliography

De Ceaurriz, J., Micillino, J. C., Marignac, B., Bonnet, P., Muller, J. and Guenier, J. P. (1984) 'Quantitative evaluation of sensory irritating and neurobehavioural properties of aliphatic ketones in mice', *Fd. Chem. Toxicol.*, 22, pp. 545-549.

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

Johnson, B. L., Setzer, J. S., Lewis, T. R. and Hornung, R. W. (1978) 'An electrodiagnostic study of the neurotoxicity of methyl n-amyl ketone', *Am. Ind. Hygiene. Ass. J.*, 39, pp. 866-872.

Kane, L. E., Barrow, C. S. and Alarie, Y. (1979) 'A short-term test to predict acceptable levels of exposure to airborne sensory irritants', *Am. Ind. Hygiene. Ass. J.*, 40, pp. 207-229.

Lynch, D. W., Lewis, T. R., Moorman, W. J., Plotnick, W. B. et al. (1981), 'Inhalation toxicity of methyl n-amyl ketone (2-heptanone) in rats and monkeys', *Toxicol. Appl. Pharmacol.*, 58, pp. 341-352.