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SEG/SUM/7
1991

Recommendation from Scientific Expert Group

on Occupational Exposure Limits

for Heptan-2-one

8 hour TWA	:	50 ppm (238 mg/m^3)
STEL	:	-
Additional classification	:	-

Substance identification:

Heptan-2-one

Synonyms : 2-Heptanone, methyl n-amylketone, MAK, methyl pentyl ketone

$CH_3CO(CH_2)_4CH_3$

EINECS N° : 203-767-1

EEC N° : 606-024-00-3 Classification: R10 Xn; R22

CAS N° : 110-43-0

MWt : 114.2

Conversion factor (20°C, 101kPa) : 4.75 mg/m^3 = 1 ppm

Occurrence/use:

Heptan-2-one is a colourless liquid with low volatility and a penetrating fruity odour. It has a MPt of -26.9°C, a BPt of 150.6°C, a vapour pressure of 0.2kPa and an odour threshold of about 0.02 ppm (0.1 mg/m^3).

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 1000 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. 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: 1670-2400 mg/kg). No LC50 values are reported, but in rats a LC10 value of 4000 ppm/4h (19000 mg/m^3) 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 (4250 mg/m^3) for 15mins 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 (43-428 mg/m^3) to protect from irritation. From the reported subchronic studies on different species (rats, monkeys) by different routes (oral, inhalation) with different effects (kidney, liver, cardio-pulmonary system, nervous system) the studies of Lynch (1981) and Johnson (1978) are regarded as key studies for the evaluation because of the route of exposure (inhalation), and the length of studies (9-10 months).

From these studies an overall NOAEL of about 1000 ppm (4750 mg/m^3) 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 (2000 ppm, 9500 mg/m^3).

Recommendation:

The animal studies of Lynch and Johnson, establishing a NOAEL of 1000 ppm (4750 mg/m^3) 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/m^3). This value is in line with the range of recommended limit values 9-90 ppm (43-428 mg/m^3) derived from the RD50 value by the method of Kane. No STEL was considered necessary.

At the level recommended, no measurement difficulties are foreseen.

Bibliography:

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

Dutch Expert Committee for Occupational Standards (1989): Basis for an Occupational Health Standard for 7/8-carbon chain aliphatic monoketones. A. A. E. Wibowo, Arbete och Halsä, p1-45.

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. Hyg. Ass. J. 39, 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. Hyg. Ass. J. 40, 207-229.

Lynch, D.W., Lewis, T.R., Moorman, W.J., Plotnick, W.B. et al. (1981). Inhalation toxicity of methyl n-amylketone (2-heptanone) in rats and monkeys. Toxicol. Appl. Pharmacol. 58, 341-352.