Recommendation from Scientific Expert Group

on Occupational Exposure Limits

for Heptan-3-one

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

Substance identification:

Heptan-3-one

Synonyms : 3-heptanone, ethylbutylketone, EBK

$CH_3CH_2CO(CH_2)_3CH_3$

EINECS N° : 203-388-1

EEC N° : 606-003-00-9 Classification: R10 Xn; R20 Xi; R36

CAS N° : 106-35-4

MWt : 114.2

Conversion factor (20°C, 101kPa) : 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 MPt of -39°C, a BPt of 148.5°C, a vapour pressure of 0.2kPa 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 1000 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 2000 ppm (9500 mg/m^3) for 4h compared with LC10 of 4000 ppm (19000 mg/m^3) for 4h).

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 3 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 (3325 mg/m^3), 72 h/week for 24 weeks, is considered to be the key study and 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 1258 mg/kg/day; or 700 ppm (3325 mg/m^3 based on a test for 24 weeks in inhaled air. This is well in line with the estimated NOAEL's of 1000 mg/kg/day by other routes of application (Homan and Maronpot, 1978; O'Donoghue *et al.*, 1984).

The available data suggests 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 48h under an occlusive patch at a concentration of 4% in petrolatum.

Recommendation:

The sub-chronic 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 base, 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.

Bibliography:

Dutch Expert Committee and Nordic Expert Group: Basis for an Occuptational Health Standard 7/8-Carbon chain aliphatic monoketones. A.A.E. Wibowo, Arbete och Halsä 1989: p. 1-45

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

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

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