

***Recommendation from the Scientific Expert Group  
on Occupational Exposure Limits  
for 5-Methylhexan-2-one***

8 hour TWA	:	20 ppm (95mg/m <sup>3</sup> )
STEL	:	
Additional classification	:	

Substance:

5-Methylhexan-2-one

Synonyms : Methylisoamylketone, MIAK, isopentylmethylketone

(CH3)2CH(CH2)2COCH3

EINECS N° : 203-737-8

EEC N° : 606-026-00-4      Classification: R10

CAS N° : 110-12-3

MWt : 114.2

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

Occurrence/use:

5-Methylhexan-2-one (MIAK) is a colourless liquid with a sharp but pleasant, sweet odour. It has a MPt of -73.9°C, a BPt of 144°C, a vapour pressure of 0.65 kPa at 20°C. The odour threshold concentration is reported to be about 0.01 ppm (0.05 mg/m<sup>3</sup>).

MIAK is a high volume solvent with a production rate greater than 1000 tonnes per annum in the European Community. It is used as a solvent for cellulose-esters, acrylics and copolymers

#### Health Significance:

The SEG reviewed and discussed the document from the Dutch Expert Committee. The reported experimental animal data are considered to be limited but sufficient for an evaluation. As with 2 heptanone there is an almost complete lack of human data. Methylisoamylketone show a relatively low acute toxicity by oral administration to animals (mice, rats, LD50 : 2540 - 4760 mg/kg). The LD50 value for dermal application to rabbits has been estimated to be 10 g/kg. No LC50 values are reported, but in rats a 4 hour LC10 value of 2000 ppm (9500 mg/m<sup>3</sup>) has been determined.

The acute irritation potential of MIAK on the upper respiratory airway has been investigated (De Ceaurriz *et al.* 1984). In measuring the decrease of the respiratory rate an RD50 value of 1222 ppm (5805 mg/m<sup>3</sup>) for 15 mins has been determined. Using the model of Kane *et al.* (1979), the Occupational Exposure Limit value should be between 12 and 120 ppm (57 and 570 mg/m<sup>3</sup>) to protect from irritation.

With methylisoamylketone only one subchronic inhalation study on rats has been reported (200, 1000 and 2000 ppm; 950, 4750 and 9500 mg/m<sup>3</sup>; 6 h/day, 5 days/week for 90 days). Decrease in aural response, lethargy and histological changes in the liver and kidney were observed at 1000 ppm (4750 mg/m<sup>3</sup>) and 2000 ppm (9500 mg/m<sup>3</sup>). From this study (Katz *et al.*, 1986) it may be deduced that the critical targets are the CNS, kidney and liver, and that the NOAEL is 200 ppm (950 mg/m<sup>3</sup>).

The only observation in man is that MIAK showed no positive reaction in a sensitization study on human volunteers.

No data are available on mutagenicity, carcinogenicity and reproduction toxicity.

#### Recommendation:

The SEG considered the health risk assessment as carried out by the Dutch expert Group adequate except for the size of the safety factor. The Katz study was considered to be an adequate basis for setting the limit. Although the Dutch Expert Group had used a safety factor of 4 (with respect to the available animal data and the similarities between MIAK and 2heptanone), the SEG considered it more appropriate to use a factor of 10 in view of the nature of the available toxicological information and in order to maintain consistency with the evaluation of other ketones.

The recommended 8 hour TWA value is 20 ppm (95 mg/m<sup>3</sup>). This value is also in line with the range of recommended limit values of 12-120 ppm (57-570 mg/m<sup>3</sup>) derived from the RD50 value to protect from irritation. No STEL was considered necessary.

At the level recommended, no measurement difficulties are foreseen.

*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.* 22 545-549

Dutch Expert Committee and Nordic Expert Group (1989). Basis for an Occupational Health Standard 7/8-Carbon chain aliphatic monoketones. A.A.E. Wibowo, *Arbete och Hals*, p. 1-45

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.

Katz, G. V., Renner, C. J. and Terhaar, C. J. (1986). Subchronic inhalation toxicity of methyl isoamylketone in rats. *Fund. Appl. Toxicol.* 6, 498-505.