

*Recommendation from Scientific Expert Group  
on Occupational Exposure Limits  
for 4-Methylpentan-2-one*

8 hour TWA	:	20 ppm (83 mg/m <sup>3</sup> )
STEL (15 mins)	:	50 ppm (208 mg/m <sup>3</sup> )
Additional classification	:	-

Substance identification:

4-Methylpentan-2-one

Synonyms : Methylisobutylketone, MIBK, hexone, isopropylacetone



EINECS N° : 203-550-1

EEC N° : 606-004-00-4      Classification: F; R11

CAS N° : 108-10-1

MWt : 100.16

Conversion factor (20°C, 101kPa) : 4.16 mg/m<sup>3</sup> = 1 ppm

Occurrence/use:

At ambient temperatures 4-methylpentan-2-one (MIBK) is a colourless, flammable liquid with a characteristic sweet odour. It has a MPt of -80°C, BPt of 115.8°C, a vapour pressure of 1.33kPa at 30°C which leads to a saturation concentration of 40 g/m<sup>3</sup> at 25°C. The explosive limits are 1.4% and 7.6% by volume in air. The odour threshold is about 0.7 ppm (3 mg/m<sup>3</sup>).

MIBK is a high volume industrial solvent with a production rate in the European Community greater than 1000 tonnes per annum. It is mainly used as a solvent in glues, paints, and cleaners, but also as a solvent for some plastics and various fats, oils and waxes. Frequently, MIBK is used in combination with other solvents such as toluene.

Health Significance:

The SEG reviewed a criteria document elaborated by the Nordic Expert Group. Although the database was regarded as limited, the SEG came to the conclusion, after discussing the cited reports of Armeli and Linari, together with the recently published paper of Hjelm, that a limit value could be recommended.

MIBK shows a low acute toxicity by oral administration to animals (rats, mice ; LD50 > 2000 mg/kg). A mouse LC50 value of 18100 ppm (75296 mg/m<sup>3</sup>) for a 45 minute exposure period has been determined.

Subacute (14 days) and subchronic (90 days) studies on different species with exposure concentrations of 100 and 200 ppm (416 and 832 mg/m<sup>3</sup>) showed effects on the kidney at 100 ppm (416 mg/m<sup>3</sup>) in rats after 14 days continuous exposure (enhanced kidney weight, reversible hyaline droplet toxic tubular nephrosis). First indications of CNS effects (extended reaction time) have been shown by exposing a small number (4) of baboons to 50 ppm (208 mg/m<sup>3</sup>) MIBK for 7 days.

No long term animal studies, nor studies on mutagenicity are reported. However, MIBK has been selected for testing in Salmonella by NTP in 1989.

Tests on reproductive toxicity with rats and mice showed no exposure-related embryotoxicity or malformations at exposure levels up to 1000 ppm (4160 mg/m<sup>3</sup>).

Investigation of occupational exposure to MIBK at 80-500 ppm (333-2080 mg/m<sup>3</sup>), for 20 to 30

mins/day, for 3 to 12 months) was reported by Linari with a follow up by Armeli 5 years later when exposure had diminished to 50-105 ppm (208-437 mg/m<sup>3</sup>). With the higher exposure, a majority of the 19 workers exposed complained of nausea (17), vomiting (10), diarrhoea (6), irritation of eyes (17), and airways (13). 16 workers experienced neurasthenic symptoms. The follow up of 14 workers 5 years later with lower exposure showed a lowered, but still existing prevalence of neurasthenia (4/14) and irritative symptoms (2/14).

The most recent study (Hjelm, 1990) of the toxicokinetics reported similar irritative effects and CNS-symptoms in a small number (8) of human volunteers during inhalation exposure to MIBK for 2 hours at 2.4, 24 and 48 ppm (10, 100 and 200 mg/m<sup>3</sup>). However, the SEG agreed that the symptoms were subjective and decided that, in the absence of a dose-related response, the evidence for effects at these concentrations was not convincing. The Armali study was therefore used as the basis for setting the limits.

From the limited data available, irritation of the eyes, the nose, the upper respiratory tract and effects on the CNS are regarded to be the key effects/organs.

Recommendation:

The human data of Armeli, which showed effects just below 100 ppm (410 mg/m<sup>3</sup>), was considered to be an adequate basis for setting the limits. The recommended 8-hour TWA is 20 ppm (83 mg/m<sup>3</sup>). A STEL (15 mins) of 50 ppm (208 mg/m<sup>3</sup>) is also recommended.

The proposed limit values do not take account of possible interactions with other solvents (e.g. MEK, toluene) in combined exposure.

At the levels recommended no measurement difficulties are foreseen.

Key Bibliography:

Linari, F., Perelli, G. and Varese, D. (1964): Rilievi clinici ed ematochimici in operai esposti all'azione di un chetone superiore: metil-isobutil-chetone. Arch.Sci.-Med., 226-239.

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Hagberg M. (1988): Methylisobutyl Ketone. In: Heimbürger G. and P.Lundberg (eds), Criteria documents from the Nordic Expert Group. Arbete och Hälsa, 33, 53-76.

Wigaeus Hjelm, E., Hagberg, M., Iregren, A. and Löf, A. (1990): Exposure to methyl isobutyl ketone: toxicokinetics and occurrence of irritative and CNS symptoms in man. Int. Arch. occup. Environ. Health, 62, 19-26.