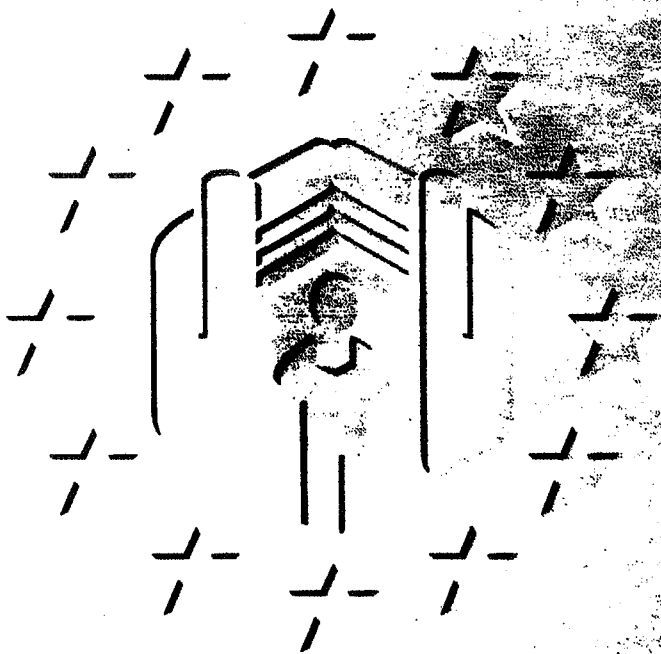




EUROPEAN COMMISSION

Occupational exposure limits

Recommendations
of the
Scientific Expert
Group
1991-92



Health and safety

Report
EUR 15091 EN

4-methylpentan-2-one

8-hour TWA: 20 ppm (83 mg/m³)
STEL (15 minutes): 50 ppm (208 mg/m³)
Additional classification: —

Substance identification

4-methylpentan-2-one (CH₃)₂CHCH₂COCH₃
Synonyms: Methyl isobutyl ketone, MIBK, hexone, isopropyl acetone
Einecs No: 203-550-1
EEC No: 606-004-00-4; Classification: F; R11
CAS No: 108-10-1
MWt: 100.16
Conversion factor (20°C, 101 kPa): 4.16 mg/m³ = 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 melting-point of -80°C, boiling-point of 115.8°C and a vapour pressure of 1.33 kPa at 30°C which leads to a saturation concentration of 40 g/m³ 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/m³). MIBK is a high-volume industrial solvent with a production rate in the European Community greater than 1 000 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 Wigaeus Hjelm, that a limit value could be recommended.

MIBK shows a low acute toxicity by oral administration to animals (rats, mice; LD50 > 2 000 mg/kg). A mouse LC50 value of 18 100 ppm (75 296 mg/m³) 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/m³) showed effects on the kidney at 100 ppm (416 mg/m³) in rats after 14 days' continuous exposure (enhanced kidney weight, reversible hyaline droplet toxic tubular nephrosis). First indications of central nervous system (CNS)

effects (extended reaction time) have been shown by exposing a small number (four) of baboons to 50 ppm (208 mg/m³) MIBK for seven days.

No long-term animal studies, nor studies on mutagenicity are reported. However, MIBK has been selected for testing in Salmonella by the National Toxicology Program in 1989.

Tests on reproductive toxicity with rats and mice showed no exposure-related embryotoxicity or malformations at exposure levels up to 1 000 ppm (4 160 mg/m³).

Investigation of occupational exposure to MIBK at 80 to 500 ppm (333 to 2 080 mg/m³), for 20 to 30 minutes a day, for three to 12 months) was reported by Linari with a follow-up by Armeli five years later when exposure had diminished to 50 to 105 ppm (208 to 437 mg/m³). 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). Sixteen workers experienced neurasthenic symptoms. The follow-up of 14 workers five years later with lower exposure showed a lowered, but still existing, prevalence of neurasthenia (4 out of 14) and irritative symptoms (2 out of 14).

The most recent study (Wigaeus 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 two hours at 2.4, 24 and 48 ppm (10, 100 and 200 mg/m³). 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 Armeli 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/m³), were considered to be an adequate basis for setting the limits. The recommended 8-hour TWA is 20 ppm (83 mg/m³). A STEL (15 minutes) of 50 ppm (208 mg/m³) 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

Armeli, G., Linari, F. and Martorano, G. (1968) 'Rilievi clinici ed ematochimici in operai esposti all'azione di un chetone superiore (MIBK) ripetuti a distanza di cinque anni', *Lav. Umato* 20, pp. 418-423.

Hagberg, M. (1988) 'Methyl isobutyl ketone', in Heimberger, G. and Lundberg, P. (eds) *Criteria documents from the Nordic Expert Group, Arbete och Halsä*, 33, pp. 53-76.

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.*, pp. 226-239.

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, pp. 19-26.