Recommendation of the Scientific Committee for Occupational Exposure Limits for 2-butanone

Mac/2320
153-15

8-hour TWA: 200 ppm (600 mg/m³)
STEL (15 mins): 300 ppm
Additional classification: 'skin'

Substance identification

Butanone: $CH_3CH_2CHOCH_3$
Synonyms: methyl ethyl ketone, MEK, 2-butanone, methyl acetone
Einecs No: 201-159-0
EEC No: 606-002-00-3
Classification: F; R11 Xi: R36/37
CAS No: 78-93-3
MWt: 72.12
Conversion factor (20 °C, 101 kPa): 3.00 mg/m³ = 1 ppm

Occurrence/use

Butanone (MEK) is, at ambient temperature, a colourless, volatile, water-miscible, highly flammable liquid with a characteristic odour resembling that of acetone. It has a MPt of –87 °C, a BPt of 79.6 °C and a vapour pressure of 10.3 kPa at 20 °C which leads to a saturation concentration of 10 % (100 000 ppm) in air at 20 °C under normal conditions. The flash point is below 0 °C. The explosive limits are 1.8 % and 12 % by volume in air. The odour threshold varies between 2 and 83 ppm (6 and 250 mg/m³).

MEK occurs naturally in very small amounts, possibly as a result of fatty acid metabolism. MEK is a high volume industrial solvent with a production rate in the European Union greater than 1 000 tonnes per annum. MEK is mainly used as a solvent constituent of coatings, but also in extraction processes, in azeotropic separations and as an intermediate for the preparation of catalysts, flavours, antioxidants, perfumes and in the manufacture of ethyl-n-amylketone and MEK-peroxide. It is a solvent of abuse (sniffers).

Health significance

The SCOEL reviewed the document of the Dutch Expert Committee for Occupational Standards (1990). Taken together with a detailed analysis of the available human studies in workers and in volunteers, the SCOEL regarded the available data as sufficient to evaluate MEK.

MEK is rapidly absorbed through human skin. Quantitative data are not available, but it has been reported that MEK was detected in expired air three minutes after start of dermal exposure (Munies and Wurster, 1965; Wurster and Munies, 1965).

MEK shows a low oral (LD50: 2 400 to 5 600 mg/kg) and dermal (LD50: 13 000 mg/kg) acute toxicity in animals. Rat LCLo values have been determined as 4 000 ppm (12 000 mg/m³) with a two-hour exposure and 2 000 ppm (6 000 mg/m³) with a four-hour exposure.

In an interlaboratory test with topical application on rats, MEK was rated to be an eye irritant and not a skin irritant (Weil and Scala, 1971). No skin sensitising properties of MEK could be shown in the mouse ear swelling test (Gad, *et al.*, 1986). Dose-related behavioural changes have been shown in mice. IC50 values (50 % decrease in response times) have been estimated to be approximately 2 000 ppm (6 000 mg/m³) and 2 900 ppm (8 700 mg/m³) in separate studies (De Ceaurriz, *et al.*, 1983; Glowa and Dews, 1987).

Subchronic studies with a limited number of rats (12) continuously exposed for 24 h/day to 1 133 ppm (3 400 mg/m³) for between 55 days and 5 months showed no peripheral neurotoxicity. From these limited studies, a NOAEL of 1 133 ppm (3 400 mg/m³) could be concluded (Saida, *et al.*, 1976).

The subchronic inhalation study of Cavender, *et al.* (1983) on groups of 15 male and 15 female F344 rats, exposed to MEK at 0, 1250, 2 500, 5 000 ppm (0, 3 750, 7 500 and 15 000 mg/m³), 6h/day, 5 days/week for 90 days is regarded as the key animal study. There was a depression of mean body weight and a slight but significant increase in relative and absolute liver weight in the high dose group. The NOAEL was 2 500 ppm (7 500 mg/m³). At all applied concentrations no signs of upper respiratory irritation or neuropathological/pathological lesions could be detected.

Mutagenicity tests have been negative (Zeiger, *et al.*, 1992) with the single exception of the induction of aneuploidy in yeast at relatively high concentrations (3.5 % in the culture medium) (Zimmerman, *et al.*, 1985).

No study on carcinogenicity is available. The reproductive toxicity cannot be evaluated finally, but no significant embryotoxicity or teratogenic effect could be demonstrated in one study (rats) with exposures of from 400 to 3 000 ppm (1 200 to 9 000 mg/m³) MEK for 7h/day during the period of major organogenesis (Deacon, *et al.*, 1981).

Animal data show that MEK potentiates the neurotoxicity of methyl n-butylketone, ethyl butylketone (EBK) and n-hexane. Due to the varying concentrations in the mixture, NOAELs cannot be generally established.

According to Elkins (1951), exposure to MEK at and above 300 ppm (900 mg/m³) resulted in headaches, throat irritation and other symptoms of local irritative effects. However, this information is given without further references and thus cannot be substantiated. In an inadequately documented study involving 10 subjects, slight irritation of the nose and throat was reported at 100 ppm (300 mg/m³) for 3–5 mins and slight eye irritation at 200 ppm (600 mg/m³). Exposure to 200 ppm (600 mg/m³) for eight working hours was considered tolerable by the 10 individuals (Nelson, *et al.*, 1943). A test of the appropriateness of this estimate under real exposure conditions has not been described.

A number of studies conducted by Dick, *et al.* (1984, 1988, 1989, 1992) with groups of 16 to 25 volunteers showed no significant neurobehavioural changes with exposure to MEK at 200 ppm for four hours. Symptoms of irritation were reported in only one of the four studies. Most data in workers relate to combined exposure with other solvents and are therefore inconclusive with respect to MEK exposure alone. Analysis of such data supports the conclusion from animal data, that MEK interacts synergistically with other solvents, particularly n-hexane. Chia, *et al.* (1993) conducted psychological tests on 19 workers exposed to mixtures of solvents comprised mainly of MEK at concentrations of 11 to 127 ppm (33 to 381 mg/m³). The other solvents were cyclohexanone (1–9 ppm), tetrahydrofuran (7–22 ppm) and toluene (2–13 ppm). No dose-response relationships were observed, but the performance of the exposed workers was significantly poorer than that of controls in three of the tests. Headaches, irritation of the eyes and nose, coughing and irritability were reported more frequently by exposed individuals than by controls. The authors noted that exposure levels were underestimated because of extensive skin contact.

Recommendation

The subchronic inhalation study on rats by Cavender, *et al.* (1983) was considered to be the starting point for deriving the 8-hour TWA. An uncertainty factor of 10, applied to the NOAEL of 2 500 ppm (7 500 mg/m³) to allow for the absence of long-term studies, would result in an exposure level of 250 ppm. Human volunteer studies have indicated no significant adverse effects with single four-hour exposures to 200 ppm. Combining these two strands of evidence and using preferred numbers, the recommended 8-hour TWA is 200 ppm (300 mg/m³). Limited data (Elkins, 1951) indicate that a STEL (15 mins) of 300 ppm (900 mg/m³) is required to limit peaks in exposure that could result in irritative effects.

A 'skin' notation is required as dermal absorption could contribute substantially to the total body burden.

It should be noted that the recommended limit value does not reflect the possible potentiating effect of MEK in combined exposure with other solvents.

At the level recommended no measurement difficulties are foreseen.

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