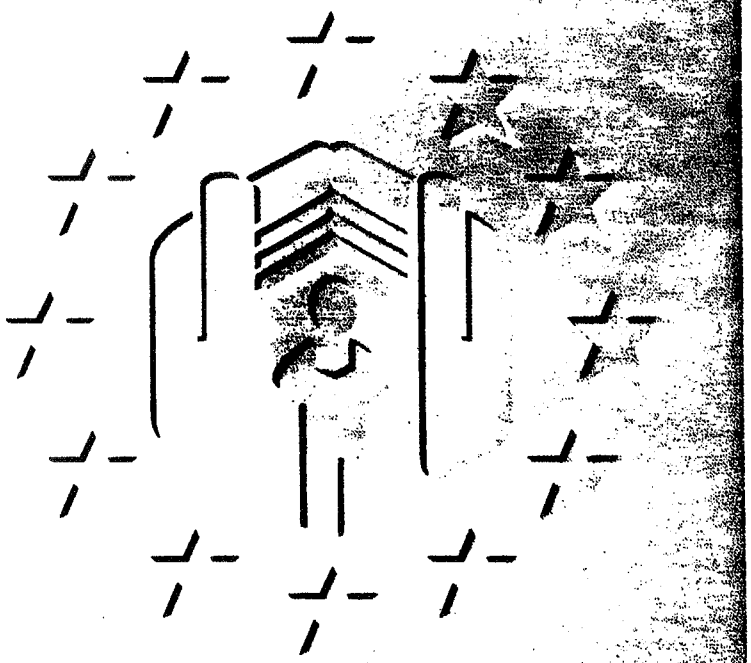
EUROPEAN COMMISSION

Occupational exposure limits

Recommendations of the Scientific Expert Group 1991-92



Health and safety

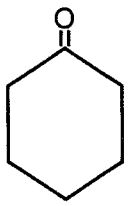
Report
EUR 15091 EN

Cyclohexanone

8-hour TWA: 10 ppm (40.8 mg/m^3)
STEL (15 minutes): 20 ppm (81.6 mg/m^3)
Additional classification: 'Skin'

Substance

Cyclohexanone



Synonyms: Cyclohexyl ketone
Einecs No: 203-631-1
EEC No: 606-010-00-7; Classification: R10 Xn; R20
CAS No: 108-94-1
MWt: 98.15
Conversion factor (20°C, 101 kPa): 4.08 mg/m^3 = 1 ppm

Occurrence/use

Cyclohexanone is a colourless to pale yellow liquid with an odour suggestive of peppermint and acetone. It has a melting-point of – 45°C, a boiling-point of 155°C and a vapour pressure of 0.69 kPa at 25°C. It has a vapour density of 3.4 times that of air and is explosive over the range 1.1 to 9.4%. The odour threshold is approximately 0.12 ppm (0.5 mg/m^3).

The production rate of cyclohexanone in the European Community is in excess of 10 000 tonnes per annum. It is predominantly used in nylon manufacturing and as a solvent for lacquers, resins, polymers, glues, dyes and other applications. Technical grade cyclohexanone may contain other chemicals, such as cyclohexanol and phenol. Cyclohexanone may occur together with other solvents, especially in glues and lacquers.

Health significance

Cyclohexanone is readily absorbed by inhalation, skin contact and ingestion and has a low acute toxicity by all routes of exposure (Gupta et al., 1979; Smyth et al., 1969; Deichmann et al., 1943; Savolainen, 1982).

The critical effect of cyclohexanone is irritation to the eyes and upper respiratory tract. There is evidence that a three to five-minute exposure to cyclohexanone is irritating to throat and eyes in concentrations as low as 75 ppm (306 mg/m^3), but 25 ppm (102 mg/m^3) was considered to be tolerable by most individuals over this short exposure period (Nelson et al., 1943). Systemic

toxicity has been demonstrated at higher exposure levels. Treon et al. (1943) reported that rabbits exposed to 190 ppm (775 mg/m^3) cyclohexanone (six hours a day, five days a week for 10 weeks) developed barely demonstrable degenerative changes in the liver and kidney. Greener et al. (1982) established a NOAEL of 100 mg/kg/day for intravenous injection of cyclohexanone in rats.

There is no evidence of neurotoxic, allergic or immunotoxic effects of cyclohexanone within the concentration range significant for occupational exposure.

Induction of chromosomal aberrations by cyclohexanone has been observed *in vitro* in human lymphocytes (Collin, 1971) and *in vivo* in bone marrow of rats injected subcutaneously with 100 mg/kg cyclohexanone (de Hondt et al., 1983), suggesting that it may be a potential carcinogen. However, a two-year study in which cyclohexanone was administered in the drinking water at doses of up to 25 000 ppm to mice, and 6 500 ppm to rats, did not provide sufficient evidence for carcinogenicity (Lijinsky and Kovatch, 1986).

Recommendation

The studies of Treon et al. (1943), indicating a LOAEL of 190 ppm (775 mg/m^3) for systemic effects in rabbits, and of Nelson et al. (1943), indicating a NOAEL of 25 ppm (102 mg/m^3) for irritation to the throat and eyes of human volunteers, were considered to be the best available bases for proposing a limit. An uncertainty factor of 2 was applied to allow for the limitations of the Nelson study. The recommended 8-hour TWA is 10 ppm (40.8 mg/m^3). This is not contradicted by the Greener et al. (1982) study, establishing a NOAEL for systemic effects of 100 mg/kg/day by intravenous injection. A STEL (15 minutes) of 20 ppm (81.6 mg/m^3) is proposed to limit peaks in exposure which could result in irritation. A 'skin' notation is also recommended as dermal absorption could contribute substantially to the total body burden.

At the level recommended no measurement difficulties are foreseen.

Studies are required to determine whether the potential conversion of cyclohexanone to cyclohexanol is sufficient to result in testicular toxicity.

Key bibliography

'Occupational exposure limits. Criteria document for cyclohexanone', EUR 14219, Danish National Institute of Occupational Health, Department of Toxicology and Biology.

Collin, J. P. (1971) 'Effet cytogenetique du cyclamate de soude, de la cyclohexanone et du cyclohexanol' *Diabetes*, 19, pp. 215-221.

Deichmann, W. B. and Le Blanch, T. J. (1943) 'Determination of the approximate lethal dose with about six animals', *Journal of Industrial Hygiene and Toxicology*, 25, pp. 415-417.

Greener, Y., Martis, L. and Indacochea-Redmond, N. (1982) 'Assessment of the toxicity of cyclohexanone administered intravenously to Wistar and Gunn rats', *J. Toxicol. Environ. Health*, 10, pp. 385-396.

Gupta, P. K., Lawrence, W. H., Turner, J. E. and Autian, J. (1979) 'Toxicological aspects of cyclohexanone', *Toxicol. Appl. Pharmacol.*, 49, pp. 525-533.

de Hondt, H. A., Temtamy, S. A. and Abd-Aziz, K. B. (1983) 'Chromosomal studies on laboratory rats *(Rattus norvegicus)* exposed to an organic solvent (cyclohexanone)', *Egypt. J. Genet. Cytol.*, 12, pp. 31-41.

Lijinsky, W. and Kovatch, R. M. (1986) 'Chronic toxicity study of cyclohexanone in rats and mice', *Journal of the National Cancer Institute*, 77, pp. 941-949.

Nelson, K. W., Ege, J. F., Ross, jr., M., Woodman, L. E. and Silverman, L. (1943) 'Sensory response to certain industrial solvent vapours', *Journal of Industrial Hygiene and Toxicology*, 25, p. 282.

Savolainen, H. (1982) 'Neurotoxicity of industrial chemicals and contaminants: Aspects of biochemical mechanisms and effects', *Arch. Toxicol. Supplement*, 5, pp. 71-83.

Smyth, H. F., Carpenter, C. P., Weil, C. S., Pozzani, U. C., Stiegel, J. A. and Nycum, J. S. (1969) 'Range-finding toxicity data: list VII', *Amer. Ind. Hygiene. Ass. J.*, 30, pp. 470-476.

Treon, J. F., Crutchfield, W. E. jr and Kitzmiller, K. V. (1943) 'The physiological response of animals to cyclohexane, methylcyclohexane and derivatives of these compounds', *Journal of Industrial Hygiene and Toxicology*, 25, pp. 323-347.