Social Europe

Recommendation from the Scientific Expert Group on Occupational Exposure Limits for cyclohexanone

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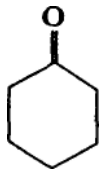
8 hour TWA:	10 ppm (40,8 mg/m^3)
STEL (15 mins):	20 ppm (81,6 mg/m^3)
Notation:	skin

Substance:

Cyclohexanone



Synonyms : cyclohexyl ketone
EINECSN^0 : 203-631-1
EECN° : 606-010-00-7
Classification: RIO Xn; R20
CAS N° : 108-94-1
MWt : 98.15

Conversion factor (20°C, lOlkPa) : 4.08 mg/m^3 = l ppm

1 Occurrence/use

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

The production rate of Cyclohexanone in the EEC 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.

2 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 3-5 minute exposure to cyclohexanone is irritating to throat and eyes in concentrations as low as 75 ppm (306 mg/rrr), but 25 ppm (102 mg/nr[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) cyclohexanone (6h/day, 5 days/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 2 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 clear evidence for carcinogenicity (Lijinsky and Kovatch, 1986).

3 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 study of Greene* *et al* (1982), establishing a NOAEL for systemic effects of

100 mg/kg/day by intravenous injection. A S ILL (15 minš) 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.

4 Bibliography

Principal reference

SEG/CDO/12A (1991). Criteria document for occupational exposure limit values. Cyclohexanone. Prepared by Dept of Toxicology and Biology, Danish National Institute of Occupational Health.

Key Studies

Collin, J.P. (1971). Effect cytogenetique du cyclamate de soude, de la cyclohexanone et du cyclohexanol. Diabètes 19, 215-221.

Deichmann, W.B. and Le Blanch, T.J. (1943). Determination of the approximate lethal dose with about six animals. J. Ind. Hyg. Toxicol. 25,415-417.

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, 385-396.

Gupta, P.K., Lawrence, W.H., Turner, J.E. and Autian, J. (1979). Toxicological aspects of cyclohexanone. Toxicol. Appl. Pharmacol. 49, 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, 31-41.

Lijinsky, W. and Kovatch, R.M. (1986). Chronic toxicity study of cyclohexanone in rats and mice. J. Nati. Cancer Inst. 77, 941-949.

Nelson, K.W., Ege, J.F., Ross, M.Jr., Woodman, L.E. and Silverman, L. (1943). Sensory response to certain industrial solvent vapours. J. Ind. Hyg. Toxicol. 25, 282.

Savolainen, H. (1982). Neurotoxicity of industrial chemicals and contaminants: Aspects of biochemical mechanisms and effects. Arch. Toxicol. Suppl. 5, 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. Arner. Ind. Hyg. Ass. J. 30, 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. J. Ind. Hyg. Toxicol. 25. 323-347.