

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

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8 hour TWA	:	500 ppm (2085 mg/m ³)
STEL (15 mins)	:	-
Additional classification	:	-

<u>Substance:</u>

Heptane		CH ₃ -CH ₂ -CH ₂ -CH ₂ -CH ₂ -CH ₂ -CH ₃					
Synonyms EINECS N°	:	n-Hepta 205-563-		propylr	nethane		
EEC N°:	601-00	8-00-2	Class	sificatio	n:	F; R11	
CAS N°	:	142-82-5					
MWt	:	100.20					
						2	
Conversion fa	ctor (20	°C, 101kF	:	4.17 mg	g/m ³ = 1 ppm		

1 Occurrence/use

Pure heptane is a colourless volatile liquid with a faint hydrocarbon odour. It has a MPt of -90.7°C, a BPt of 98.4°C and a vapour pressure of 5.33 kPa at 22.3°C. The vapour density is 3.5 times that of air and it is explosive in the range 1.1 - 6.7% in air. The odour threshold is about 400 ppm (1668 mg/m³).

Heptane occurs in natural gas and crude oil (0.1 - 1.9%) and in the volatile oils of many kinds of conifer. A content of 2.5% has been reported in petroleum, and this results in the major proportion of heptane found in the atmosphere. Technical heptane is a mixture of isomers and some forms contain n-hexane, but highly purified heptane may be produced. It is used as an industrial solvent (for adhesives, lacquers and inks in gravure printing), as an extraction solvent and in manufacture of plastic foams and synthesis of toluene and alkylbenzenes. This summary refers to pure n-heptane and not to commercial forms that may contain n-hexane.

2 Health Significance

Heptane is absorbed from the lungs, and is excreted as metabolites in the urine. The major metabolite is 2-heptanol, but 2,5-heptanedione, which may cause peripheral polyneuropathy, has also been found in small amounts in urine of exposed humans and rats (Perbellini *et al.*, 1986).

No data concerning irritating effects on skin and eyes are available but, like other hydrocarbons, heptane could be expected to act as a weak irritant.

Heptane depresses the central nervous system, and is narcotic in rats and mice at concentrations greater than 8000 ppm ($33,360 \text{ mg/m}^3$). Takeuchi *et al.* (1980, 1981) exposed male rats to 2960 ppm ($12,343 \text{ mg/m}^3$) heptane for 12h/d, 7d/week for 16 weeks. No electrophysiological changes were observed at any time during the experiment, and the authors concluded that heptane failed to produce polyneuropathy. Decreased auditory sensitivity was seen in rats exposed to n-heptane for 6 h/day for 28 days at 4000 ppm ($16,680 \text{ mg/m}^3$), but not at 800 ppm (3336 mg/m^3) (Simonsen and Lund, 1995).

Heptane did not show mutagenic activity in a number of *in vitro* assays with bacteria, yeast and cultured mammalian cells (Brooks *et al.*, 1988).

No long term animal studies are available.

Few good human data are available. Patty and Yant (1929) reported a subjective effect

(slight vertigo) at 1000 ppm (4170 mg/m³) in volunteers exposed for 6 minutes, but that the exposure level was calculated not measured. The peripheral neurotoxic potencies of hexane and heptane in man have been compared by measuring the rates of 2,5-dexaniedione and 2,5-deptanedione formation in human volunteers (Störmer *et al*, 1994). These data indicate that the peripheral neurotoxic potency of heptane is more than 40 times lower than than of hexane.

3 Recommendation

The 16 week rat study of Takeuchi *et al.* (1980, 1981), indicating a NOAEL of about 3000 ppm (about 12,500 mg/m³) was considered to be the best available basis for setting exposure limits. In view of the lack of human data and of long term animal data, an uncertainty factor of 5 was considered to be appropriate. Taking into account the preferred value approach, the recommended 8-hour TWA is 500 ppm (2085 mg/m³).

No STEL or "skin" notation was considered to be necessary.

At the levels recommended, no measurement difficulties are foreseen.

4 Key Bibliography

Brooks, T.M., Meyer, A.L. and Hutson, D.H. (1988). The genetic toxicology of some hydrocarbon and oxygenated solvents. Mutagenesis <u>3</u>, 227-232.

Hansen, L. E. (1991). Occupational exposure limits: Criteria document for n-heptane.

Patty F.A., and Yant, W.P. (1929). Odor intensity and symptoms produced by commercial propane, butane, pentane, hexane and heptane vapor. U.S. Bureau of Mines Report of Investigation No. 2979.

Perbellini, L., Brugnone, F., Cocheo, V., De Rosa, E. and Bartolucci, G.B. (1986). Identification of the n-heptane metabolites in rat and human urine. Arch. Toxicol. <u>58</u>, 229-234.

Simonsen, L. and Lund, S. P. (1995). Four weeks inhalation exposure to n-heptane causes loss of auditory sensitivity in rats. Pharmacol. and Toxicol. <u>76</u>, 41-46.

Störmer, A., Kessler, W. and Filser, J. G. (1994). 2,5-Heptandion im Urin des Menschen nach Exposition gegen n-Heptan und n-Hexan. In: (Kessel R. ed.) Arbeitsmediziminische und umweltmedizinische Aspekte zu Altlasten - Bewertung und Bewältigung. Verhandlungen der Deutschen Gesellschaft für Arbeitsmedizin und Umweltmedizin e.V. 34. Jahrestagung, Gentner Verlag Stuttgart, pp 363-365.

Takeuchi, Y., Ono, Y., Hisanaga, N., Kitoh, J. and Sugiura, Y. (1980). A comparative study on the neurotoxicity of n-pentane, n-hexane and n-heptane in the rat. Br. J. Ind. Med. <u>37</u>, 241-247

Takeuchi, Y., Ono, Y., Hisanaga, N., Kitoh, J. and Sugiura, Y. (1981). A comparative study on the toxicity of n-pentane, n-hexane and n-heptane to the peripheral nerve of the rat. Clin. Toxicol. <u>18</u>, 1395-1402.