# Recommendation from Scientific Expert Group

# on Occupational Exposure Limits

# for Ethylbenzene

8 hour TWA : 100 ppm (442 mg/m<sub>3</sub>) STEL (15 mins) : 200 ppm (884 mg/m)

Additional classification : "skin"

### Substance:

## Ethylbenzene

EEC N° : 601-023-00-4 Classification : F; R11 Xn; R20

CAS  $N^{\circ}$  : 100-41-4

MWt : 106.17

Conversion factor (20°C, 101 kPa)  $: 4.42 \text{ mg/m}^3 = 1 \text{ ppm}$ 

## Occurrence/use:

Ethylbenzene is a flammable, colourless liquid with an aromatic odour. It has MPt of -94.9°C, a BPt of 136.2°C and a vapour pressure of 2 kPa at 20°C. It has a vapour density of 3.7 times that of air and is explosive in the range 1.2 - 6.8 % in air. The odour threshold is about 2 ppm (9 mg/m<sup>3</sup>).

Ethylbenzene is used in the production of styrene and it is an important solvent in the rubber and plastics industries. It is a constituent of technical grade xylene and occurs in gasoline and, in small amounts, in tobacco smoke. The production rate in the EEC is in excess of 1000 tonnes per annum. Occupational exposure to pure ethylbenzene is uncommon as it usually occurs together with other solvents such as xylene.

#### Health Significance:

Ethylbenzene is well-absorbed through the lungs and skin. The majority is rapidly eliminated in the urine, but small amounts may be retained in fatty tissues.

Ethylbenzene has anaesthetic properties at high exposure levels (Yant *et al.*, 1930), suggesting that CNS effects may also be important at lower exposures. Changes in noradrenaline and dopamine levels in the hypothalamus have been observed in rats exposed to 2000 ppm (8840 mg/m³) ethylbenzene for 6 hours/day for 3 days (Anderson *et al.*, 1981), although no behavioural changes were reported.

In a 28 day inhalation study, the NOAELs were 382 ppm (1688 mg/m³) in rats and mice and 782 ppm (3456 mg/m³) in rabbits. Minor effects, such as increased liver weight and leukocyte counts, were seen at the LOAELs of 782 ppm (3456 mg/m³) in rats and mice and 1610 ppm (7116 mg/m³) in rabbits (Cragg *et al.*, 1989). A subchronic inhalation study of ethylbenzene (6 h/d, 5 d/week for 13 weeks) has also been reported by NTP (1992). Increased liver weights were seen in male rats exposed to 250 ppm (1105 mg/m³) and female rats exposed to 500 (2210 mg/m³). Increased kidney weights were seen at higher exposure levels. No microscopic lesions associated with either liver or kidney weights were observed. Increased lung weights and signs of lung inflammation were seen in almost all rats exposed at and above 250 ppm (1105 mg/m³) ethylbenzene, but the incidence and severity of the lesions were not dose-related (NTP, 1992).

Decreased numbers of pregnancies were noted in female rats exposed to 100 or 1000 ppm (442 or 4420 mg/m<sup>3</sup>) for 6-7 h/d during the pregestation period (Hardin *et al.*, 1981). This effect was not dose-related and the study was not considered to be an adequate basis for proposing exposure limits.

There are no adequate data on carcinogenic effects. Ethylbenzene was not mutagenic in the Drosophila recessive lethal test (Donner *et al.*, 1980) or in *Salmonella* (NTP, 1992) and did not induce chromosomal aberrations or sister chromatid exchanges in Chinese Hamster Ovary cells or micronuclei in peripheral blood of mice (NTP, 1992). However a positive result was obtained in the L5178Y tk /tk mouse lymphoma assay (McGregor *et al.*, 1988).

The critical effect of ethylbenzene is irritation of the eye, nose and throat. There is practically no information on toxic effects of ethylbenzene alone in humans because exposure generally occurs in combination with other solvents. An exposure level of 200 ppm (884 mg/m³) has been reported to be irritative (Ruth, 1986), although limited details were given.

The concentration of inhaled ethyl benzene necessary to depress the respiratory rate in mice by 50% due to sensory irritation (RD50) was calculated to be about 1430 ppm (6321 mg/m<sup>3</sup>) over a period of about 5 mins (De Ceaurriz *et al.*, 1981). If the response was measured after a longer exposure period (30 mins), depression of the respiratory rate was found to occur at a concentration of 4060 ppm (17945 mg/m<sup>3</sup>) which probably can be explained by a fade in response due to adaptation (Nielsen and Alarie, 1982).

#### Recommendation:

The report by Ruth (1986), of irritation in humans at 200 ppm (884 mg/m³), was considered to be the best available basis for proposing occupational exposure limits. The recommended 8-hour TWA is 100 ppm (442 mg/m³). A STEL (15 mins) of 200 ppm (884 mg/m³) was proposed to limit peaks of exposure which could result in irritation. These limits are not contradicted by the study of De Ceaurriz *et al.*, (1981), reporting an RD50 of 1430 ppm (6321 mg/m³) for inhibition of respiratory irritation in mice. A "skin" notation was recommended as dermal absorption could contribute substantially to the total body burden.

At the levels recommended, no measurement difficulties are foreseen.

#### **Key Bibliography:**

Anderson, K., Fuxe, K., Nilsen, O.G., Toftgård, R., Eneroth, P. and Gustafsson, J-Å. (1981). Production of discrete changes in dopamine and noradrenaline levels and turnover in various parts of the rat brain following exposure to xylene, ortho-, meta-, and para-xylene, and ethylbenzene. Toxicol. Appl. Pharmacol. 60 535-548.

Cragg, S. T., Clarke, E. A., Daly, I. W., Miller, R. R., Terrill, J. B. and Oullette, R. E. (1989). Subchronic inhalation toxicity of ethylbenzene in mice, rats and rabbits. Fund. Appl. Toxicol. <u>13</u>, 399-408.

De Ceaurriz, J.C., Micillino, J.A., Bonnet, P. and Guenier, J.P. (1981). Sensory irritation caused by various industrial airborne chemicals. Toxicol. Letts. 9, 137-143.

Donner, M. Mäki-Paakkanen, J., Norppa, H., Sorsa, M. and Vainio, H. (1980). Genetic toxicology of xylenes. Mutat. Res. <u>74</u> 171-172.

Engström, K. and Elovaara, E (1986). Nordiska expertgruppen för gränsvärdesdolumentation. 67. Etylbensen. Arbete och Hälsa <u>19</u>, 1-43 (in Swedish).

Hardin, B.D., Bond, G.P., Sikov, M.R., Andrew, F.D., Beliles, R.P. and Niemeier, R.W. (1981). Testing of selected workplace chemicals for teratogenic potential. Scand. J. Work Environ. Health Suppl. 4 66-75.

Lundberg, P. (1987). Scientific basis for Swedish occupational standards VIII. Consensus report for ethylbenzene. Arbete och Hälsa 39, 74-81.

McGregor, D.B., Brown, A., Cattanach, P., Edwards, I., McBride, D., Riach, C. and Caspary, W.J. (1988). Responses of the L5178Y tk+/tk- mouse lymphoma cell forward mutation assay: III Coded chemicals. Environ. Mol. Mutagen. 12 85-154.

Nielsen, G.D. and Alarie, Y. (1982). Sensory irritation, pulmonary irritation and respiratory stimulation by airborne benzene and alkylbenzenes: Prediction of safe industrial exposure levels and correlation with their thermodynamic properties. Toxicol. Appl. Pharmacol. <u>65</u> 459-477.

NTP (1992). Toxicity studies nof ethylbenzene (CAS No. 100-41-4) in F344/N rats and B6C3F1 mice (inhalation studies). National Toxicology Program. NIH Publication No. 92-3129, NIH.

Ruth, J.H. (1986). Odour thresholds and irritation levels of several chemical substances: A review. Am. Ind. Hyg. Assoc. J. <u>47</u> A142-A151.

Yant, W.P., Schrenk, H.H., Waite, C.P. and Patty, F.A. (1930). Acute response of guinea pigs to vapours of some new commercial organic compounds. II. Ethylbenzene. Publ. Health Rep. <u>45</u> 1241-1250.