Fact Sheet Date: March 12, 1998

NEW YORK STATE
- HUMAN HEALTH FACT SHEET -

Ambient Water Quality Value for Protection of Sources of Potable Water

SUBSTANCE: 3-Methylstyrene and 4-Methylstyrene

CAS REGISTRY NUMBER: 100-80-1 622-97-9

AMBIENT WATER QUALITY VALUE: 5 ug/L*

* Value applies to each isomer (3- and 4-) individually.

BASIS:

Surface Water: Principal Organic Contaminant Classes

Groundwater: Former Reference to 10 NYCRR Subpart 5-1 Principal Organic Contaminant (POC) General Maximum Contaminant Level (MCL)

SUMMARY OF INFORMATION

Vinyl toluene (3- and 4-methylstyrene mixture, CAS No. 25013-15-4)[1] (CH_3-C_6H_4-C_2H_3) is used as a monomer in the plastics and surface-coating industries. 3- and 4-methylstyrene are in a principal organic contaminant class (class iv).

A search of relevant databases revealed little information on 3- or 4-methyl-styrene as pure isomers. Some information on acute oral toxicity in mammals was found. No information on the results of human exposure to 3- or 4-methylstyrene was found. Several studies exist using exposure of animals by various routes, predominantly inhalation, to vinyl toluene.

Acute Toxicity

For 4-methylstyrene, oral LD_{50} values for rats and mice are 2,255 mg/kg and 1,072 mg/kg, respectively (RTECS, 1994).
In a short-term experiment, Heinonen and Vainio (1980) exposed rats (500 mg/kg), mice (100 or 500 mg/kg), and hamsters (100 or 500 mg/kg) to vinyl toluene, intraperitoneally.

[1] In this paper, "vinyl toluene" will be used only for the mixture of isomers.

Compared to controls, all species showed time- and dose-dependent decreases in glutathione content in the liver and kidneys. Drug oxidation reactions and UDP-glucuronosyl transferase activity in liver were enhanced. The highest dose caused acute decreases of cytochrome P450 content and 7-ethoxycoumarin O-deethylase activity in mouse liver microsomes. The mice were more vulnerable than the rats. Adult rabbits exposed to a high concentration of 3-methylstyrene (4100 mg/kg, 12 h/d for 7 days) showed a marked depletion of brain dopamine (Romanelli et al., 1986).

Chronic Toxicity

In a 2-year inhalation bioassay where rats were exposed to 0, 456 or 1368 mg/kg vinyl toluene (65-71% 3-methylstyrene and 32-35% 4-methylstyrene) 6 h/d, 5 d/wk, bodyweights of exposed rats were lower than controls and exposed rats had hyperplasia of the respiratory epithelium and erosion and cysts of the olfactory epithelium. In the same study, male and female mice were exposed to 82, or 206 mg/kg vinyl toluene 6 h/d, 5 d/wk. Exposed groups had lower bodyweights than controls, hyperplasia of the respiratory epithelium and chronic active inflammation of nasal passage and bronchioles. The lowest-observed-effect-level (LOEL) for this study is 82 mg/kg vinyl toluene (48.5 mg/m^3) in mice (NTP, 1990).

In a 13 week study, rats were exposed to 0, 25, 60, 160, 400, or 1,000 ppm (115, 272, 730, 1828, 4570 mg/kg) vinyl toluene by inhalation for 6 h/d, 5 d/wk (NTP, 1990). The final mean bodyweights of rats exposed to 1828-4570 mg/kg were 8-19% lower than that of controls for males and 6-12% lower for females. Relative liver weights for rats at 4570 mg/kg were significantly greater than those for controls. Nephropathy increased with dose in male rats exposed to 730 - 4570 mg/kg. Compound induced lesions were not observed in females. The no-observed-effect-level (NOEL) for nephropathy in males is 60 ppm (272 mg/kg).

In the same 13 week study, mice were exposed to 0, 10, 25, 60 or 160 ppm (82, 205, 495, 1319 mg/kg) vinyl toluene by inhalation. The final mean bodyweights of male and female mice exposed to 205 - 1319 mg/kg were 12-20% and 13-16% lower than those of controls. Inflammation of the lung was observed in 5/10 male and 3/9 female mice exposed to 160 ppm. Metaplasia of the nasal turbinates was seen in all exposed groups. These results agree with the findings of the two year inhalation study in male and female mice. The LOEL is 10 ppm (82 mg/kg) in mice (NTP, 1990).

Other studies reported effects on nerve function due to vinyl toluene exposure. In rats exposed by inhalation to vinyl toluene at concentrations of 456 and 1370 mg/kg for 12 wks, decreased motor conduction velocity in the tail and also decreased amplitude of the evoked motor action were observed (Snyder, 1989). Similar results were reported in another experiment with Wistar rats exposed to 273, 547 or 1640 mg/kg vinyl toluene vapor 6 h/d, 5 d/wk up to 15 weeks (Seppalainen and Savolainem, 1982). Acid proteinase activity in the cerebral homogenate increased at 8 weeks in 1640 mg/kg rats and at 15 weeks in 547 mg/kg rats. Electrophysiological changes typical of axonal degeneration occurred

in rats exposed to 547 or 1640 mg/kg but not at 273 mg/kg. These studies demonstrate that vinyl toluene can cause systemic effects.

Genetic Toxicity

It appears the mutagenic metabolite methylstyrene 7,8-oxide is capable of being formed by metabolism of both isomers (NTP, 1990). Methylstyrene 7,8-oxide is an alkylating agent (Norppa and Vainio, 1983b).

Vinyl toluene did not induce gene mutations in Salmonella typhimurium strains TA98, TA100, TA1535, or TA1537 with or without exogenous metabolic activation (S9). Vinyl toluene was positive in the mouse lymphoma assay for induction of trifluorothymidine resistance in L5178Y/TK cells in the absence of S9; it was not tested with S9. Vinyl toluene did not induce sister chromatid exchanges or chromosomal aberrations in Chinese hamster ovary cells with or without S9 (NTP, 1990). Norppa and Vainio (1983a) and Norppa (1981b), however, found distinct dose-dependent increases in sister chromatid exchanges using 2-, 3- or 4-methylstyrene and 3- and 4-methyl mixed isomers (vinyl toluene).

A single intraperitoneal dose of vinyl toluene (100, 200, 300 or 500 mg/kg) in mice caused a significant increase in micronucleated polychromatic erythrocytes at 200, 300, 500 mg/kg (Norppa, 1981a). At 100, 200, 300 mg/kg, a slight decrease in the ratio of polychromatic to normochromatic erythrocytes was seen. There was no increase in normachromatic cells with micronuclei.

Oncogenicity

No evidence of oncogenicity was found in a 2-year inhalation bioassay of vinyl toluene in male or female rats exposed to 100 or 300 ppm or in male or female B6C3F_1 mice exposed to 82 or 205 mg/kg vinyl toluene (NTP, 1990).

DERIVATION OF VALUE

Based on the structural similarity of the isomers 3- and 4-methylstyrene, the likelihood of similar metabolism to the vinyl toluene 7,8-oxide (NTP, 1990) and the similar genetic toxicity of these two compounds (Norppa and Vainio, 1983a,b), a value could be derived on the basis of effects from vinyl toluene.

The effects seen after inhalation exposure to vinyl toluene demonstrate that the chemical is absorbed and produces systemic effects. Inhalation data from a well- designed study, in the absence of oral data, could be used to derive a drinking water value.

In mice exposed to vinyl toluene by inhalation, a LOEL of 10 ppm (82 mg/kg) was found for both males and females for the occurrence of hyperplasia of the respiratory epithelium and metaplasia of the nasal turbinates (NTP, 1990). The animal dose in mg/kg/day is:

Animal dose = 82 mg/kg x 5/7 x 6/24 = 15 mg/kg/day

where 5/7 x 6/24 = corrections for less than continuous exposure

Absorption is assumed at 100%.

If an uncertainty factor of 1,000 is applied to the NOEL of 15 mg/kg/d (10 for intra-, 10 for inter-species variation and 10 for use of a LOEL), an Acceptable Daily Intake of 15 ug/kg/d is calculated. Basing a water value on a 70 kg human consuming 2 liters of water per day and 20% consumption of vinyl toluene from water, yields a water quality value of 105 ug/L.

Surface Water

Regulations [6 NYCRR 702.2(b)] require that the value be the most stringent of the values derived using the procedures found in sections 702.3 through 702.7. The principal organic contaminant class value of 5 ug/L (702.3(b)) represents the most stringent value that can be derived for 3- and 4-methylstyrene. Therefore, the ambient surface water quality value for 3- and 4-methylstyrene is 5 ug/L for each isomer individually.

Groundwater

The principal organic contaminant (POC) groundwater standard of 5 ug/L (6 NYCRR 703.5) applies to 3- and 4-methylstyrene isomers, individually. This standard became effective on January 9, 1989 by inclusion by reference to 10 NYCRR Subpart 5-1 standards. The basis and derivation of the POC standard are described in a separate fact sheet.

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SEARCH STRATEGY

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