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: Nitrobenzene **CAS REGISTRY NUMBER:** 98-95-3

AMBIENT WATER QUALITY VALUE: 0.4 micrograms/liter (0.4 ug/L)

BASIS: Oncogenic Effects

INTRODUCTION

The physical, chemical and toxicological properties of nitrobenzene have been reviewed (ATSDR, 1990; US EPA, 1980, 1987). The following ambient water quality values were derived using these and other references and the procedures outlined in 6 NYCRR 702.2 through 702.7.

SPECIFIC MCL AND PRINCIPAL ORGANIC CONTAMINANT CLASS (702.3)

Nitrobenzene does not have a Specific MCL (maximum contaminant level) as defined in 6 NYCRR 700.1 and is in principal organic contaminant class iv as defined in 6 NYCRR 700.1. Therefore, a water quality value of 5 ug/L can be derived based on 6 NYCRR 702.3(b).

ONCOGENIC EFFECTS (702.4)

Studies on the oncogenicity of oral doses of nitrobenzene were not found. However, inhaled nitrobenzene induces lung, thyroid and mammary gland tumors in mice, liver and kidney tumors in Fischer 344 rats and liver tumors in Sprague-Dawley rats (CIIT, 1993). Tumors were not restricted to the site of contact (i.e., respiratory tract), which suggests that ingested nitrobenzene would also be oncogenic. Available data on non-oncogenic effects indicate that short-term inhalation and oral exposure damages the same organs (blood, spleen, central nervous system, liver, testes) (ATSDR, 1990; CIIT, 1993).

A study conducted by the Chemical Industry Institute of Toxicology (CIIT, 1993) can be used to derive a water quality value based on oncogenic effects. The dose-response data for nitrobenzene were evaluated and a cancer potency factor of 0.0845 per milligram per kilogram per day (0.0845 $(mg/kg/day)^{-1}$) was derived using procedures consistent with those outlined in paragraphs (a) through (e) of 6 NYCRR 702.4. In the absence of sufficient scientific evidence to support the use of alternative procedures, the linearized multistage model (extra risk) and a cross-species scaling factor based on the assumption that lifetime cancer risks are equal when daily administered doses are in proportion to body weights raised to the 3/4 power were used. The cancer potency factor was based on the most sensitive response in the most sensitive sex and species: the incidence of hepatocellular adenoma or carcinoma (1/69, 4/69, 5/70, and 16/70) in male Fischer 344 rats exposed to 0, 5, 25 or 125 milligrams per cubic meter of air (mg/m^3), respectively, for 6 hours/day, 5 days/week, for two years (CIIT, 1993). These concentrations become 0, 0.89, 4.5 or 22 mg/m^3, respectively, when adjusted for continuous exposure. The inhaled doses were converted to absorbed doses (0, 0.66, 3.3 or 16 mg/kg/day, respectively) by using a daily inhalation rate of 0.35 cubic meters of air per day (m^3/day) for a 0.38-kg rat (US EPA, 1988) and an 80% absorption factor for inhaled nitrobenzene (Salmowa et al., 1963).

In summary, the cited cancer potency factor of 0.0845 $(mg/kg/day)^{-1}$ is based on the incidence of hepatocellular adenoma or carcinoma (1/69, 4/69, 5/70, and 16/70) in male Fischer 344 rats absorbing nitrobenzene doses of 0, 0.66, 3.3 or 16 mg/kg/day, respectively. The water concentration corresponding to the lower bound estimate on the ingested dose associated with an excess lifetime human cancer risk of one-in-one million is 0.4 ug/L, assuming that all ingested nitrobenzene is absorbed, and the procedure in paragraph (f) of 6 NYCRR 702.4.

NON-ONCOGENIC EFFECTS (702.5)

Nitrobenzene damages the blood, liver, kidneys, spleen, adrenal cortex and testes of laboratory animals, and has similar effects after inhalation and oral exposures (ATSDR, 1990; CIIT, 1993). Because data on the non-oncogenic effects of oral nitrobenzene exposure are limited, the U.S. EPA used the results of a 90-day inhalation study conducted by the Chemical Industry Institute of Toxicology as the basis for their oral reference dose. In 1985, the U.S. EPA established an oral reference dose (equivalent to an acceptable daily intake) of 0.5 micrograms per kilogram per day (0.5 ug/kg/day) for nitrobenzene (Exhibit 1, taken from US EPA, 1995), using procedures consistent with those outlined in paragraphs (a) and (b) of 6 NYCRR 702.5. This reference dose was derived by application of a 10,000-fold uncertainty factor to a lowest-observed-effect level (an absorbed dose of 4.6 mg/kg/day, which is 80% of the inhaled dose) for hematologic, adrenal, renal and hepatic lesions in mice intermittently exposed to 25 mg/m^3 for 6 hours/day, 5 days/week, for 90 days. A value of 3.5 ug/L is derived using the procedure outlined in paragraph (e) of 6 NYCRR 702.5, assuming a 100% absorption factor for ingested nitrobenzene, and allowing 20% of the acceptable daily intake to come from drinking water (6 NYCRR 702.5(c)).

The results of the CIIT a two-year inhalation study of nitrobenzene were not available when the U.S. EPA derived their reference dose, but provide alternative data for use in deriving a reference dose. A lowest-observed-effect level (LOEL) of 0.6 mg/kg/day for bile duct inflammation and spleen congestion was observed in male Sprague-Dawley rats exposed to 5 mg/m^3 for 6 hours/day, 5 days/week (CIIT, 1993). This LOEL represents the absorbed dose (80% of inhaled dose) for 0.65 kg rats with a daily inhalation rate of 0.51 m^3/day (US EPA, 1988). If an uncertainty factor of 1,000 is applied to this dose, an oral reference dose (equivalent to an acceptable daily intake) of 0.6 ug/kg/day for nitrobenzene can be derived using procedures consistent with those outlined in paragraphs (a) and (b) of 6 NYCRR 702.5. An uncertainty factor of 1,000 was used to account for variability among humans, differences between animal and humans, and the use of a lowest-observed-effect level. A value of 4 ug/L is derived using the procedure outlined in paragraph (e) of 6 NYCRR 702.5, assuming a 100% absorption factor for ingested nitrobenzene, and allowing 20% of the acceptable daily intake to come from drinking water (6 NYCRR 702.5(c)).

CHEMICAL CORRELATION (702.7)

A value based on chemical correlation is not applicable because data are sufficient to evaluate nitrobenzene based on both of the sections 6 NYCRR 702.4 and 702.5.

OTHER STANDARDS AND GUIDELINES

Under the New York State Department of Health regulations for drinking-water standards (10 NYCRR Part 5), nitrobenzene is a principal organic contaminant (POC) and has a MCL of 5 ug/L.

SELECTION OF VALUE

According to 6 NYCRR 702.2(b), the selected ambient water quality value shall be the most stringent of the values derived using the procedures found in 6 NYCRR 702.3 through 702.7. This value is 0.4 ug/L (based on oncogenic effects) and is the value selected as the water quality value for nitrobenzene.

REFERENCES

Amoore, J.E. and E. Hautala. 1983. Odor as an aid to chemical safety: Odor thresholds compared with Threshold Limit Values and volatilities for 214 industrial chemicals in air and water dilution. J. Appl. Tox. 3:272-290.

ATSDR (Agency for Toxic Substances and Disease Registry). 1990. Toxicological Profile for Nitrobenzene. TP-90-19. Atlanta, GA: U.S. Department of Health and Human Services, U.S. Public Health Service.

Austern, B.M. et al. 1975. Gas chromatographic determination of selected organic compounds added to waste water. Environ. Sci. Tech. 9:588 (cited in US EPA, 1980).

CIIT (Chemical Industry Institute of Toxicology). 1993. A Chronic Inhalation Toxicity Study of Nitrobenzene in B6C3F1 Mice, Fischer F344 Rats and Sprague-Dawley (CD) Rats. Research Triangle Park, NC: CIIT.

6 NYCRR (New York State Codes, Rules and Regulations). Water Quality Regulations, Surface Water and Groundwater Classifications and Standards: Title 6 NYCRR, Chapter X, Parts 700 - 705. Albany, NY: New York State Department of Environmental Conservation.

10 NYCRR (New York State Codes, Rules and Regulations). Public Water Systems: Title 10 NYCRR, Chapter 1, State Sanitary Code, Subpart 5-1. Albany, NY: New York State Department of Health, Bureau of Public Water Supply Protection.

Salmowa, J, J. Piotrowski and U. Neuhorn. 1963. Evaluation of exposure to nitrobenzene. Brit. J. Indus. Med. 20:41-46.

U.S. EPA (U.S. Environmental Protection Agency). 1980. Ambient Water Quality Criteria for Nitrobenzene. EPA/440/5-80/061. Washington, DC: Office of Water Regulations and Standards.

U.S. EPA (U.S. Environmental Protection Agency). 1987. Health Effects Assessment for Nitrobenzene. EPA/600/8-88/049. Cincinnati, OH: Environmental Criteria and Assessment Office.

U.S. EPA (U.S. Environmental Protection Agency). 1988. Reference Physiological Parameters in Pharmacokinetic Modeling.

EPA/600/6-88/004. Washington, DC: Office of Health and Environmental Assessment.

U.S. EPA (U.S. Environmental Protection Agency). 1995. Nitrobenzene. On-Line as of May 1. Integrated Risk Information System (IRIS). Cincinnati, OH: Office of Research and Development, Environmental Criteria and Assessment Office.

Verschueren, K. 1983. Handbook of Environmental Data on Organic Chemicals, 2nd Edit. New York, NY: Van Nostrand Reinhold.

SEARCH STRATEGY: ON-LINE TOXICOLOGIC DATABASE

Toxline (1981 to April, 1995) was searched linking the CAS Registry Number for nitrobenzene with the keyword "toxicity."

Bureau of Toxic Substance Assessment/gmr05&kgb02
New York State Department of Health
August, 1995

93196PRO0448