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: Simazine **CAS REGISTRY NUMBER:** 122-34-9

AMBIENT WATER QUALITY VALUE: 0.5 micrograms/liter (0.5 ug/L)

BASIS: Oncogenic Effects

INTRODUCTION

The physical, chemical, and toxicological properties of simazine have been reviewed (IARC, 1991; US EPA, 1988a, 1990, 1992, 1994). 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)

Simazine does not have a Specific MCL (maximum contaminant level) as defined in 6 NYCRR 700.1 and it is not in a principal organic contaminant class as defined in 6 NYCRR 700.1. Therefore, a water quality value cannot be derived under 6 NYCRR 702.3.

ONCOGENIC EFFECTS (702.4)

There are two studies in rats that indicate simazine induces mammary gland tumors (U.S. EPA, 1990). The authors of the first study reported an excess of thyroid and mammary gland tumors in high-dosed Charles River female rats, but the U.S. EPA (1990) noted that complete histopathological detail were not provided nor was statistical significance evaluated. The U.S. EPA (1990) considered the study unsuitable for evaluating the oncogenicity of simazine because the animals in all groups showed high incidences of respiratory and ear infections.

However, a second, scientifically valid study showed that simazine caused statistically significant increases in mammary gland tumors in female Sprague-Dawley rats (U.S. EPA, 1990, 1992).

Simazine, atrazine, propazine, and cyanazine have similar chemical structures and are all classified as chlorotriazine herbicides (Stevens and Sumner, 1991). All have a six-membered ring composed of three nitrogens and three carbons arranged symmetrically (i.e., alternating) about the ring. Substitutions occur in the 2-, 4-, and 6-positions; all four compounds have a chlorine substitution at the 2-position and similar substitutions (amino groups) at the other two positions. For example, simazine has an ethylamino group at the 4- and 6-position whereas atrazine has an ethylamino group at the 4-position but an isopropylamino group at the 6-position. All four compounds induced mammary gland tumors in rats (US EPA, 1992, 1994), and one of them (atrazine) is an oncogen under 6 NYCRR 700.1. Thus, the mammary gland is a target organ for chlorotriazine herbicides.

Given the above, simazine is an oncogen under 6 NYCRR 700.1. The U.S. EPA (1988b, 1991) evaluated the dose-response data for simazine and calculated a cancer potency factor of 0.12 per milligram per kilogram per day (0.12 $(mg/kg/day)^{-1}$) using procedures consistent with those outlined in paragraphs (a) through (e) of 6 NYCRR 702.4. This cancer potency factor was calculated by the U.S. EPA using a cross-species scaling factor for carcinogen risk assessment based on the assumption that lifetime cancer risks are equal when daily administered doses are in proportion to body weights raised to the 2/3 power (the surface area scaling factor). Proposed New York State regulations state that the scaling factor should be 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. This change requires application of an adjustment factor to cancer potency factors calculated using a cross-species scaling factor based on surface area.

The cancer potency factor was based on the most sensitive response in the most sensitive sex and species; the incidence of malignant mammary gland tumors (16/89, 13/80, 20/75, and 40/78) in female Sprague-Dawley rats exposed to dietary doses of 0, 0.5, 5.3, or 63 mg/kg/day for two years. A modified linearized multistage model (extra risk) that included consideration of variable partial lifetime exposure (i.e., a time-to-tumor model) was used because there was significant early mortality among the rats dosed with simazine. An adjusted cancer potency factor (0.0768 $(mg/kg/day)^{-1}$) was calculated by multiplying the U.S. EPA cancer potency factor of 0.12 $(mg/kg/day)^{-1}$ by 0.64 (the adjustment factor for a rat body weight of 0.35 kg). The water concentration corresponding to the lower bound estimate (i.e., lower 95% confidence limit) of the dose associated with an excess lifetime human cancer risk of one-in-one million is 0.5 ug/L, based on the adjusted cancer potency factor and the procedure in paragraph (f) of 6 NYCRR 702.4.

NON-ONCOGENIC EFFECTS (702.5)

Simazine causes decreased food consumption, body weight gain, and damages blood cells in laboratory animals (US EPA, 1990, 1992, 1995). In 1991, the U.S. EPA derived an oral reference dose (equivalent to an acceptable daily intake) of 5 micrograms per kilogram per day (5 ug/kg/day) for simazine (Table 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 100-fold uncertainty factor to a no-observed-effect level of 0.5 mg/kg/day for decreased body weight gain and significant changes in hematological parameters in female rats exposed, via food, for two years. A value of 35 ug/L is derived using the procedure outlined in paragraph (e) of 6 NYCRR 702.5 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 was not derived because there were sufficient data to derive values based on oncogenic effects (6 NYCRR 702.4) and non-oncogenic effects (6 NYCRR 702.5).

OTHER STANDARDS AND GUIDELINES

Under New York State Department of Health regulations for drinking-water standards (10 NYCRR Part 5), simazine is an unspecified organic contaminant (UOC) and has a maximum contaminant level (MCL) of 50 ug/L. Under the Safe Drinking Water Act, the federal maximum contaminant level goal (MCLG) and the MCL for simazine are both 4 ug/L (rounded from the calculated value of 3.5 ug/L), assuming a 70-kg adult drinks 2 L/day, allocating 20% of the U.S. EPA reference dose (5 ug/kg/day) to drinking water and applying an additional uncertainty factor of 10 for possible oncogenic effects (U.S. EPA, 1992). The World Health Organization's recommended guideline for simazine in drinking water is 2 ug/L (rounded from the calculated value of 1.6 ug/L), assuming a 60-kg adult drinking 2 L/day and allocating 10% of the WHO reference dose (0.52 ug/kg/day) to drinking water (WHO, 1993).

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 0.5 ug/L (based on oncogenic effects) and is the value selected as the water quality value for simazine.

REFERENCES

IARC (International Agency for Research on Cancer). 1991. Simazine. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. 53:495-513. Lyon: World Health Organization.

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.

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1. Integrated Risk Information System (IRIS). Cincinnati, OH: Office of Research and Development, Environmental Criteria and Assessment Office.

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SEARCH STRATEGY: ON-LINE TOXICOLOGIC DATABASE

Toxline (1981 to January 1995) was searched linking the CAS Registry Number of simazine with the keyword "toxicity."

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