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: Mirex **CAS REGISTRY NUMBER:** 2385-85-5

AMBIENT WATER QUALITY VALUE: 0.03 micrograms/liter (0.03 ug/L)

BASIS: Oncogenic Effects

INTRODUCTION

The physical, chemical, and toxicological properties of mirex have been reviewed (ATSDR, 1993; IARC, 1979; US EPA, 1987, 1995). 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)

Mirex does not have a Specific MCL (maximum contaminant level) as defined in 6 NYCRR 700.1 and is in principal organic contaminant class v 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)

Mirex induces liver tumors in mice, liver, adrenal and kidney tumors in male rats and mononuclear cell leukemia in female rats (Innes et al., 1969; NTP 1990; Ulland et al., 1977) and is an oncogen under 6 NYCRR 700.1.

The NTP (1990) study can be used to derive a water quality value based on oncogenic effects. It was selected over the studies by Innes and Ulland for several factors, including the length of

the exposure period, the number of dose levels, the number of animals at risk and the comprehensiveness of the histopathology. The dose-response data were evaluated and a cancer potency factor of 1.2 per milligram per kilogram per day (1.2 $(mg/kg/day)^{-1}$) 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 percentage of male rats, the more sensitive sex, that had one or more of the three tumor types (liver, adrenal, or kidney) causally related to mirex exposure. These data were obtained by reviewing the tumor pathology report for each animal in the study and identifying those animals that had at least one of the tumor types. This approach is consistent with the existing and proposed US EPA guidelines for carcinogen risk assessment (US EPA, 1986, 1996, 1997).

Among F344/N male rats (0.35 kg mean body weight) receiving 0, 0.007, 0.07, 0.7, 1.8, or 3.8 mg/kg/day via food for two years, the incidences of rats with liver tumors (neoplastic nodules or hepatocellular carcinomas), adrenal tumors (pheochromocytomas or malignant pheochromocytomas), or kidney tumors (transitional-cell papillomas) were 16/51, 10/51, 17/52, 23/52, 26/50, and 35/50, respectively (NTP, 1990). The water concentration corresponding to the lower bound estimate on the dose associated with an excess lifetime human cancer risk of one-in-one million is 0.03 ug/L, based on the above cancer potency factor and the procedure in paragraph (f) of 6 NYCRR 702.4.

NON-ONCOGENIC EFFECTS (702.5)

Mirex damages the parathyroid gland, kidney, liver, spleen, thyroid, testes, and adversely affects reproduction and fetal development (US EPA, 1987; 1995). In 1992, the U.S. EPA established an oral reference dose (equivalent to an acceptable daily intake) of 0.2 micrograms per kilogram body weight per day (0.2 ug/kg/day) for mirex (Exhibit 1, taken from US EPA, 1995), using procedures consistent with those outlined in paragraphs (a) and (b) of 6 NYCRR 702.5. This replaced the previous reference dose of 0.002 ug/kg/day (US EPA, 1995). This new reference dose was derived by application of a 300-fold uncertainty factor to (to account for variability among humans, differences between animals and humans, and the lack of multi-generational data on reproductive and cardiovascular toxicity data) a no-observed-effect-level (NOEL) of 70 ug/kg/day for liver and thyroid effects in rats exposed for two years (NTP, 1990). A value of 1.6 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)).

Alternatively, the application of a 100-fold uncertainty factor (to account for variability among humans and differences between animals and humans) to the NOEL of 70 ug/kg/day yields value of 4.9 ug/L, 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)). Both values are above the value based on oncogenic effects (0.03 ug/L).

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), mirex is a principal organic contaminant (POC) and has a maximum contaminant level (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 0.03 ug/L (based on oncogenic effects) and is the value selected as the water quality value for mirex.

REFERENCES

ATSDR (Agency for Toxic Substance and Disease Registry). 1993. Toxicological Profile for Mirex and Chlorecone. Atlanta, GA: U.S. Department of Health and Human Services, U.S. Public Health Service.

Innes J.R.M, B.M. Ulland, M.G. Vallerio and others. 1969. Bioassay of pesticides and industrial chemicals for tumorigenicity in mice: A Preliminary Note. J. Nat. Cancer Inst. 42:1104-1114.

IARC (International Agency for Research on Cancer). 1979. Monographs on the Evaluation of Carcinogenic Risks to Humans. Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs. Volumes 1 to 42. Supplement 7. Lyon: IARC.

NTP (National Toxicology Program). 1990. Toxicology and Carcinogenesis Studies of Mirex (CAS No. 2385-85-5) in F344/N Rats (Feed Studies) Technical Report Series No. 313. Bethesda, MD: U.S. Department of Health and Human Services, U.S. Public Health Service.

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.

U.S. EPA (U.S. Environmental Protection Agency). 1986. Guidelines for Carcinogen Risk Assessment. Fed. Register. 51:33992-34003.

U.S. EPA (U.S. Environmental Protection Agency). 1987. Health Effects Assessment for Mirex. EPA-600-8-88-046. Cincinnati, OH: Environmental Criteria and Assessment Office.

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

U.S. EPA (U.S. Environmental Protection Agency). 1996. Proposed Guidelines for Carcinogen Risk Assessment; Notice. Fed. Register. 61:17960-18011.

U.S. EPA (U.S. Environmental Protection Agency). 1997. Science Advisory Board Review of the Office of Research and Development; Proposed Guidelines for Cancer risk Assessment. Review Draft Report. EPA-SAB-EHC-LTR-97-0XX. US EPA, Washington, DC.

Ulland, B.M., N.P. Page, R.A. Squire and others. A carcinogenicity assay of mirex in Charles River CD rats. J. Nat. Cancer Inst. 58:133-140.

SEARCH STRATEGY: ON-LINE TOXICOLOGIC DATABASE

Toxline (1981 to July 1994) and Medline (1980 to July 1994) were searched using the software Grateful Med and linking mirex with the keyword "toxicity."

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