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NEW YORK STATE
HUMAN HEALTH FACT SHEET

Ambient Water Quality Value for
Protection of Sources of Potable Water

SUBSTANCE: Oxamyl **CAS REGISTRY NUMBER:** 23135-22-0

AMBIENT WATER QUALITY VALUE: 50 micrograms/liter (50 µg/L)

BASIS: Surface Water: General Organic Guidance Value (6 NYCRR 702.15(a)(1)(ii))

Groundwater: Former Reference to 10 NYCRR Subpart 5-1 Unspecified Organic Contaminant (UOC) General Maximum Contaminant Level (MCL).

INTRODUCTION

The physical, chemical and toxicological properties of oxamyl have been reviewed (Kennedy, 1986a,b; US EPA, 1987a,b, 1990, 1992). 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 and 6 NYCRR 702.15(a)(1).

SPECIFIC MCL AND PRINCIPAL ORGANIC CONTAMINANT CLASS (702.3)

Oxamyl does not have a Specific MCL (maximum contaminant level) as defined in 6 NYCRR 700.1(a)(41) and is not in a principal organic contaminant class as defined in 6 NYCRR 700.1(a)(34). Therefore, a water quality value cannot be derived under 6 NYCRR 702.3.

ONCOGENIC EFFECTS (702.4)

No oncogenic effects were observed in rats and mice under the conditions of long-term dietary studies (US EPA, 1990, 1992). However, the rat study did not meet the testing requirements for a two-year oncogenicity rat study used to support the federal registration of a pesticide because of missing histopathology data and insufficient clinical chemistry (US EPA, 1987a). Thus, the U.S. EPA has required a new study.

NON-ONCOGENIC EFFECTS (702.5)

Oxamyl is a carbamate insecticide that acts primarily through acetylcholinesterase inhibition. It causes neurological effects, serum biochemistry changes, including changes in acetylcholinesterase levels, and decreased body weight gain in laboratory animals (Kennedy, 1986b; US EPA, 1987b, 1990). In 1986, the U.S. EPA established an oral reference dose (equivalent to an acceptable daily intake) of 25 micrograms per kilogram per day (25 µg/kg/day) for oxamyl (see Exhibit 1, taken from US EPA, 1995), using procedures consistent with those outlined in paragraphs (a) and (b) of 6 NYCRR 702.5. The reference dose was derived by application of a 100-fold uncertainty factor to a U.S. EPA-identified

no-observed-effect level (NOEL) of 2.5 milligrams per kilogram per day (mg/kg/day) for decreased body weight gain and reduced food consumption in rats exposed, via food, for two years (Kennedy, 1986b). Given the NOEL of 2.5 mg/kg/day, a value of 175 µg/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)).

A daily dose of 2.5 mg/kg/day is not a clear-cut NOEL for reduced body weight gain in rats. In the two-year study (Kennedy, 1986b), male rats fed either 5 or 7.5 mg/kg/day grew slower than controls and consistently had mean body weights that were less than the controls, significantly so ($p < 0.05$) in 78% of the comparisons; the mean body weight of female rats at those doses were consistently and significantly ($p < 0.05$) lower than those of the controls. At 2.5 mg/kg/day, male rats grew slower than controls and had mean body weights that were slightly lower, but not significantly, when compared to controls at 1, 2, 3, 6, 12, and 24 months; the mean weight of the dosed males at 18 months was slightly higher than that of the controls. At 2.5 mg/kg/day, the mean body weights of female rats were slightly lower than controls at 1, 2, 3, 6, 12, 18, and 24 months, and the difference at 24 months was statistically significant ($p < 0.05$). Overall, the mean body weight of rats exposed to 2.5 mg/kg/day was lower than the mean body weight of the controls in 26 of 28 comparisons (body weights of dosed males and females were compared to the body weight of two groups of controls at seven different times). Thus, 2.5 mg/kg/day is not a clear-cut NOEL for reduced body weight gain, especially when the same effect was also observed at the same or a similar dose in four other studies (discussed below) and increased with dose in each study.

In a 90-day study in rats (Kennedy, 1986b), the mean body weight of female and male rats dosed with 2.5 mg/kg/day was lower (but not significantly) than the mean body weight of the control rats on days 28, 56 and 91. In addition, the mean body weight of weanlings born to rats dosed with 2.5 mg/kg/day was significantly ($p < 0.05$) lower than that of controls in both litters from a one-generation reproduction study (part of the 90-day study) (Kennedy, 1986b) and weanlings born to rats dosed with 2.5 mg/kg/day had lower mean body weights (but not significantly) in all six litters from a three-generation study (part of the two-year study) (Kennedy, 1986b). Lastly, pregnant rabbits exposed to 2 mg/kg/day during gestation days 6-19 had 61% lower mean maternal body weight gain than that of the controls (Kennedy, 1986b).

Collectively, the results of the two-year study and the four other studies (90-day, one-generation and three-generation studies in rats and a teratology study in rabbits) show that the mean body weight of animals exposed to 2 or 2.5 mg/kg/day (or the mean body weight of their offspring) was lower than the mean body weight of the control animals in 40 of 42 pair-wise comparisons. Qualitative statements by the investigator and the U.S. EPA suggest that the dosed animals did not consume less food than the controls. Kennedy (1986b) stated that male and female rats at the highest dose (7.5 mg/kg/day) in the two-year study (and the three-generation study) consumed slightly less food than the controls or other dosed groups; this suggests that the food consumption of rats in the other three groups (control, 2.5 mg/kg/day and 5 mg/kg/day) were similar. Kennedy (1986b) also reported that the consumption rates of the animals exposed to 2.5 mg/kg/day (rats in the 90-day and one-generation study) or 2 mg/kg/day (rabbits in the teratology study) were "slightly more" or "compared favorably" to those of controls. Based on their evaluation of the two-year rat study, the U.S. EPA identified 2.5 mg/kg/day as a NOEL for reduced food consumption (see Exhibit 1). These data suggest that 2.5 mg/kg/day is a lowest-observed-effect level (LOEL) for reduced body weight in rats, and that the reduction was not caused by reduced food intake.

If an uncertainty factor of 300 is applied to the the LOEL of 2.5 mg/kg/day, an oral reference dose (equivalent to an acceptable daily intake) of 8.3 µg/kg/day can be derived using procedures consistent with those outlined in paragraphs (a) and (b) of 6 NYCRR 702.5. A factor of 300 was used to account for variability among humans, differences between animals and humans and the use of a lowest-observed-effect level. Use of a 1,000-fold uncertainty factor was not necessary since the effects at the lowest-observed-effect level were not severe. A value of 58 µg/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)).

AESTHETIC CONSIDERATIONS (702.6)

Data on the levels of oxamyl that would impair the aesthetic quality of water were not found.

CHEMICAL CORRELATION (702.7)

Although available data were not sufficient to evaluate oxamyl based on oncogenic effects (6 NYCRR 702.4) or aesthetic considerations (6 NYCRR 702.6), a value based on chemical correlation was not derived because of insufficient data.

OTHER STANDARDS AND GUIDELINES

Under the New York State Department of Health regulations for drinking-water standards (10 NYCRR Part 5), oxamyl is an unspecified organic contaminant (UOC) and has a maximum contaminant level (MCL) of 50 µg/L. Under the Safe Drinking Water Act, the federal maximum contaminant goal (MCLG) and the MCL for oxamyl are both 200 µg/L (rounded from the calculated value of 175 µg/L), assuming a 70-kg adult drinks 2 L/day and allocating 20% of the U.S. EPA reference dose (25 µg/kg/day) to drinking water (US EPA, 1992).

SELECTION OF VALUE

Surface Water:

According to 6 NYCRR 702.15(a)(1), a guidance value may be derived for substances that do not have a standard in 6 NYCRR 703.5 and shall be the more stringent of the values derived using the procedures found in 6 NYCRR 702.3 through 702.7, or, in some cases, a general organic guidance value of 50 µg/L. Although applying the procedures of 6 NYCRR 702.5 to the available non-oncogenic data on oxamyl yields values greater than 50 µg/L (i.e., 58 or 175 µg/L), data gaps exist in the toxicological data base for oxamyl. The U.S. EPA (1987a) guidance document for the re-registration of pesticide products containing oxamyl noted inadequacies in the available toxicological studies and significant data gaps for acute, subchronic, chronic and reproductive/developmental toxicity. The U.S. EPA reference dose for oxamyl is based on a study that didn't meet the testing requirements for studies used to support pesticide registrations (US EPA, 1987a, 1995). Consequently, the U.S. EPA confidence level in the oxamyl reference dose is medium to low, based on low confidence in the critical study because it was of "inadequate quality" and medium to low confidence in the data base. Other areas of uncertainty include the oncogenicity of oxamyl and the relationships between acetycholinesterase inhibition and observed effects (i.e., neurological effects or reduced body weight gain). Accordingly, the data are not adequate and sufficient

to justify a value greater than 50 µg/L, based on both oncogenic and non-oncogenic effects, as described in 6 NYCRR 702.15(a)(1)(ii). Thus, a guidance value of 50 µg/L (based on the organic guidance value) is selected as the water quality value for oxamyl.

Groundwater:

A groundwater standard of 50 µg/L exists for oxamyl. This standard became effective on January 9, 1989 by reference to the 10 NYCRR Subpart 5-1 general MCL for unspecified organic contaminants (UOCs). The basis and derivation of the UOC value is described in a separate fact sheet.

REFERENCES

Kennedy, G.L. Jr. 1986a. Acute toxicity studies with oxamyl. Fund. Appl. Toxicol. **6**:423-429.

Kennedy, G.L., Jr. 1986b. Chronic toxicity, reproductive, and teratogenic studies with oxamyl. Fund. Appl. Toxicol. **7**:106-118. (Same as du Pont, 1972a, as cited in IRIS).

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.

US EPA (U.S. Environmental Protection Agency). 1987a. Guidance for the Reregistration of Pesticide Products Containing Oxamyl as the Active Ingredient. Washington, DC: Office of Pesticides and Toxic Substances.

US EPA (U.S. Environmental Protection Agency). 1987b. Oxamyl: Health Advisory. Washington, DC: Office of Drinking Water.

US EPA (U.S. Environmental Protection Agency). 1990. National Primary Drinking Water Regulations; Synthetic Organic Chemicals and Inorganic Chemicals; Proposed Rule. Fed. Register. **55**:30370-30448.

US EPA (U.S. Environmental Protection Agency). 1992. National Primary Drinking Water Regulations; Synthetic Organic Chemicals and Inorganic Chemicals; Final Rule. Fed. Register. **57**:31776-31849.

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

SEARCH STRATEGY: ON-LINE TOXICOLOGIC DATABASE

Toxline (1981 to August, 1995) was searched linking the CAS Registry Number of oxamyl with the keyword "toxicity."

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

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Exhibit 1: Oral Reference Dose Summary for Oxamyl (CAS Registry Number 23135-22-0) Taken from the On-Line Integrated Risk Information System (IRIS) of the U.S. Environmental Protection Agency (as of August 1, 1995).

REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

Substance Name: Oxamyl
CASRN: 23135-22-0

RfD ASSESSMENT SUMMARY TABLE

Crit. Dose: 2.5 mg/kg-day [Study 1 NOAEL(adj)]
UF: 100 MF: 1 RfD: 2.5E-2 mg/kg-day Confidence: Medium

Crit Effect: (1) Decreased body weight gain and food consumption

	NOAEL (Study 1)	LOAEL (Study 1)
Reported	50 ppm	100 ppm
ADJ	2.5 mg/kg-day	5 mg/kg-day
Study Type	2-Year Rat Feeding/ Oncogenic Study	2-Year Rat Feeding/ Oncogenic Study
Reference	du Pont, 1972a	du Pont, 1972a

1) du Pont, 1972a
2-Year Rat Feeding/ Oncogenic Study

Critical Effect: Decreased body weight gain and food consumption

Defined Dose Levels:
NOAEL= 50 ppm
NOAEL(ADJ)= 2.5 mg/kg-day
LOAEL= 100 ppm
LOAEL(ADJ)= 5 mg/kg-day

Conversion Factors: 1 ppm = 0.05 mg/kg/day (assumed rat food consumption)

DISCUSSION OF PRINCIPAL AND SUPPORTING STUDIES

E.I. du Pont de Nemours and Company. 1972a. MRID No. 00083352, 00113400. Available from EPA. Write to FOI, EPA, Washington, DC 20460.

Four hundred twenty albino rats (55/sex/dose) were fed 0, 50, 100 and 150 ppm oxamyl in their diets for 2 years. At 100 and 150 ppm, there was a decreased rate of body weight gain. Cholinesterase depression was observed in the males at 150 ppm after 8 days, but returned to normal by 1 month. No clinical signs of toxicity were observed at 150 ppm.

UNCERTAINTY AND MODIFYING FACTORS

UNCERTAINTY FACTORS:

An uncertainty factor of 100 was used to account for the inter- and intraspecies differences. Although significant data gaps exist (studies must be repeated), an additional UF was not considered necessary since existing information on oxamyl indicates that the toxicological endpoint(s) will not be affected by repeating the studies.

CONFIDENCE IN THE RfD

Study: Low Data Base: Medium RfD: Medium

The critical study was of inadequate quality and is given a low confidence rating. Other studies in the data base are supportive; confidence in the data base can be considered medium to low. Confidence in the RfD can also be considered medium to low.