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: Heptachlor **CAS REGISTRY NUMBER: 76-44-8**

AMBIENT WATER QUALITY VALUE: 0.04 ug/L

BASIS: Oncogenic

I INTRODUCTION

This value applies to the water column and is designed to protect humans from the effects of contaminants in souces of drinking water; it is referred to as a Health (Water Source) or H(WS) value.

Regulations (6 NYCRR 702.2) require that the water quality value be based on the procedures in sections 702.3 through 702.7. A previous fact sheet supported a value of 0.009 ug/L for the sum of heptachlor and heptachlor epoxide (NYS, 1984). Available information on heptachlor was examined as described in "Scope of Review," below. Potential water quality values are derived below, and the value of 0.04 ug/L selected as described under "Selection of Value."

II PRINCIPAL ORGANIC CONTAMINANT CLASSES AND SPECIFIC MCL (702.3)

A. Discussion

Heptachlor has a Specific MCL of 0.4 ug/L as defined in 700.1. This is a maximum contaminant level for drinking water adopted by the New York State Department of Health under the State Sanitary Code (10 NYCRR Part 5, Public Water Supplies). Heptachlor is also in principal organic contaminant class vi as defined in 700.1.

The U.S. Environmental Protection Agency has established a maximum contaminant level goal (MCLG) of 0 and a MCL of 0.4 ug/L for drinking water for heptachlor.

B. Derivation of Water Quality Value

Because heptachlor has a Specific MCL, the fact that it is also in a principal organic class does not bear upon the water quality value. Regulations require that the water quality value not exceed the Specific MCL of 0.4 ug/L.

III ONCOGENIC EFFECTS (702.4)

A. Data

U.S. EPA (1995) classifies heptachlor as B2, a probable human carcinogen. This is based on sufficient evidence in animals: benign and malignant liver tumors were induced in both sexes of three strains of mice. Also, U.S. EPA noted that several structurally related substances are liver carcinogens.

IARC (1991) states that there exists sufficient evidence in experimental animals for the carcinogenicity of heptachlor. They state that this substance "is possibly carcinogenic to humans" and categorize it in Group 2B.

Heptachlor is an oncogen is defined in 6 NYCRR 700.1.

U.S. EPA (1995) presents four data sets for hepatocellular carcinomas in mice (Table 1).

B. Discussion and Selection of Data

U.S. EPA (1995) presents an oral slope factor for heptachlor of 4.5 $(mg/kg/day)^{-1}$. This slope factor is the geometric mean of four slope factors: 12.4, 14.9, 2.79 and 0.83 $(mg/kg/day)^{-1}$ per for C3H male and female and B6C3F1 male and female mice, respectively. U.S. EPA (1995) notes that despite some difference in the magnitude of the responses, "a combined risk estimate was chosen because the two strains are related and so that relevant data will not be discarded."

The Department does not agree with U.S. EPA's approach of including the Davis study in their calculation of the geometric mean. It is a poorly documented, single-dose study of questionable quality, using heptachlor of unspecified purity. It was completed in 1965, prior to the existence of Good Laboratory Practice (GLP) guidelines, and was never published as a formal

report. Both control and dosed groups showed excessive early mortality, and data on tumor onset and cause of death were not provided. Although it does give qualitative evidence that heptachlor causes liver tumors in mice, it is of limited value for quantitative risk assessment. It will not be used as the basis for a value in this fact sheet.

Table 1

Oral Dose-Response Data for Heptachlor
(from U.S. EPA, 1995)

Administered Dose (ppm)	Human Equivalent Dose (mg/kg)/day	Tumor Incidence	Reference
Mouse/C3H, male			
0	0.000	22/73	Davis, 1965 as evaluated by Reuber, cited in Epstein, 1976
10	0.108	64/87	
Mouse/C3H, female			
0	0.000	2/53	
10	0.108	57/78	
Mouse/B6C3F1, male (matched controls)			
0	0.000	5/19	NCI, 1977
6.1	0.063	11/46	
13.8	0.140	34/47	
Mouse/B6C3F1, female (matched controls)			
0.0	0.000	2/10	
9.0	0.094	3/47	
18*	0.188	30/42	

*Data on this line not included in U.S. EPA (1995) but added for completeness (Bogdan, 1995).

What remains are the slope factors of 2.79 and 0.83 $(mg/kg/day)^{-1}$ for male and female B6C3F1 mice respectively. As it is unknown whether males or females best predict overall human response and even whether these similar slopes indicate differences other than random experimental variability, we will use their geometric mean as the basis of the water quality value for heptachlor.

C. Derivation of Water Quality Value

The geometric mean of the two slopes, 2.79 and 0.83 $(mg/kg/day)^{-1}$ is 1.52 $(mg/kg/day)^{-1}$. This slope factor was calculated by U.S. EPA using an interspecies scaling of doses based on the 2/3 power of relative body weights. Proposed New York State regulations call for such scaling to be done on the basis of the 3/4 power of relative body weights. An adjustment to U.S. EPA's slope is needed to account for the different scaling methods.

The adjustment factor for mouse data (body weight of 0.030 kg) is a multiplication factor of 0.52, which results in a slope of 0.790 $(mg/kg/day)^{-1}$.

At a one-in-one million lifetime cancer risk level, a human dose is calculated:

$$\text{human dose} = \frac{1 \times 10^{-6} \times 10^{3}\ ug/mg}{0.790\ (mg/kg/day)^{-1}} = 1.27 \times 10^{-3}\ ug/kg/day$$

A potential water quality value is then calculated, assuming a human body weight of 70 kg and a water consumption rate of 2 L/day:

$$\text{Water Quality Value} = \frac{1.27 \times 10^{-3}\ ug/kg/day \times 70\ kg}{2\ L/day}$$

$$= 0.0444\ ug/L, \text{ rounded to } 0.04\ ug/L$$

IV NON-ONCOGENIC EFFECTS (702.5)

A. Data

U.S. EPA's (1995) oral reference dose for heptachlor was calculated from a no-observed-effect level (NOEL) of 0.15 mg/kg/day for liver weight increases in male rats in a 2-year feeding study (Velsicol, 1955a). The lowest-effect level (LEL) in this study was 0.25 mg/kg/day. In its Reregistration Eligibility Document (RED), U.S. EPA (1992) based its RfD for heptachlor on what is apparently the same study.

U.S. EPA (1992) also reported liver lesions (but no increase in tumors) in CF rats given heptachlor in the diet at 0.35 mg/kg/day for 110 weeks.

ATSDR (1993) reported lowest-observed-adverse-effect-levels (LOAELs) of 0.25 mg/kg/day in the rat for both developmental (decreased embryo survival) and reproductive (decreased fertility in females) effects (Green, 1970). NOAELs were not established for either effect. In the reproductive study, increased numbers of resorptions were noted, apparently where male and female Sprague-Dawley rats received the test diet of this level for 60 days, with females continuing on it through gestation. In a second phase of the study, rats receiving this dose for 2 generations exhibited a marked decrease in pregnancy rates.

U.S. EPA (1992) reported increased pup mortality in a 7-week study in male and female rats at 0.35 mg/kg/day heptachlor, with no reproductive effects in rodents at or below 0.25 mg/kg/day.

B. Derivation of Water Quality Value

1. Selection of Data

The study by Velsicol (1955a) was judged the most appropriate for deriving a water quality value based on non-oncogenic effects, because it is of sufficient duration and yields both a NOEL and LEL. ATSDR (1993) did not list any more stringent NOAEL or LOAEL from chronic exposure.

2. Calculation of Acceptable Daily Intake (ADI)

An ADI is calculated from the study of Velsicol (1955a) by dividing the NOEL of 0.15 mg/kg/day by a total uncertainty factor (UF) of 100 as follows:

$$\text{ADI} = \frac{0.15 \text{ mg/kg/day}}{100} = 0.0015 \text{ mg/kg/day}$$

This UF was selected to account for both interspecies differences (10) and potential sensitive individuals (10). U.S. EPA (1995) used a different UF, 300, that included a factor of 3 to account for the lack of a study in a second species. This extra UF was not required under 6 NYCRR 702.5, and judged not necessary in this case.

3. Calculation of Water Quality Value

A potential water quality value is calculated from the ADI, above, based on a 70 kg adult consuming 2 liters of water per day and allocating 20% of the ADI to come from drinking water, as follows:

$$\text{Water Quality Value} = \frac{(0.0015 \text{ mg/kg/day})(1000 \text{ ug/mg})(70 \text{ kg})(0.2)}{2 \text{ L/day}}$$

$$= 10.5 \text{ ug/L, rounded to } 10 \text{ ug/L}$$

V CHEMICAL CORRELATION (702.7)

A value based on chemical correlation was not derived because it was judged not necessary given the extensive database on the health effects of this substance.

VI SELECTION OF VALUE

The H(WS) value is designed to protect humans from oncogenic and non-oncogenic effects from contaminants in sources of drinking water. To protect for these effects, 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 oncogenic value of 0.04 ug/L (6 NYCRR 702.4) is the most stringent value derived by these procedures and is the ambient water quality value for heptachlor.

Not only does this value differ numerically from the one presented previously (NYS, 1984) but it applies to heptachlor alone, instead of the sum of heptachlor and heptachlor epoxide. This approach is judged appropriate and is consistent with that of U.S. EPA.

VII REFERENCES

ATSDR (Agency for Toxic Substances and Disease Registry). 1993. Toxicological Profile for Heptachlor/Heptachlor Epoxide Update. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.

Bogdan, K. 1995. New York State Department of Health. Personal Communication.

Davis, K.J. 1965. Pathology Report on Mice Fed Aldrin, Dieldrin, Heptachlor and Heptachlor Epoxide for Two Years. Internal FDA memorandum to Dr. A.J. Lehman, July 19. [As cited by U.S. EPA, 1995].

Epstein, S.S. 1976. Carcinogenicity of heptachlor and chlordane. Sci. Total Environ.

6: 103-154 [as cited by U.S. EPA, 1995].

Green, V.A. 1970. Effects of pesticides on rat and chick embryo. In: Hemphill, D, ed. Trace substance environmental health 3, Proc 3rd Ann Conf, University of Missouri, 183-209. [As cited by ATSDR, 1993].

IARC (International Agency for Research on Cancer). 1991. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. 53: 115-175. Lyon, France.

NCI (National Cancer Institute). 1977. Bioassay of Heptachlor for Possible Carcinogenicity. NCI Carcinogenesis Tech. Rep. Ser. No. 9. [As cited by U.S. EPA, 1995].

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.

NYS (New York State). 1984. Ambient Surface Water Quality Standards Documentation. Heptachlor and Heptachlor epoxide. Albany, N.Y.: Department of Health.

U.S. EPA (Environmental Protection Agency). 1992. Reregistration Eligibility Document (RED): Heptachlor. PB92-191105. Washington, D.C.

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

Velsicol Chemical Corporation. 1955a. MRID No. 00062599. Available from EPA. Write to FOI, EPA, Washington, D.C. 20460. [As cited by U.S. EPA, 1995].

VIII SCOPE OF REVIEW

Several of the widely-recognized sources listed below can provide a comprehensive review and often a quantitative assessment of the toxicity of a substance. These sources were searched for information on heptachlor; where none was found it is so noted.

- IRIS (U.S. EPA's Integrated Risk Information System). On-line database.
- RTECS (Registry of Toxic Effects of Chemical Substances). On-line database.
- CCRIS (Chemical Carcinogenesis Research Information System). On-line database.
- ATSDR (Agency for Toxic Substances and Disease Registry) toxicological profile.
- IARC (International Agency for Research on Cancer) Monographs Supplement 7.
- U.S. EPA health advisory.
- U.S. EPA drinking water criteria document.

The sources below were reviewed by NYS (1984).

- NAS (National Academy of Sciences). 1977. Drinking Water and Health, Vol. 1. National Academy of Sciences. Washington, D.C.
- NAS (National Academy of Sciences). 1982. An Assessment of the Health Risks of Seven Pesticides used for Termite Control. National Academy Press. Washington, D.C.
- IARC (International Agency for Research on Cancer). 1974. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 5:173-191.
- IARC (International Agency for Research on Cancer). 1979. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 20: 129-155.

! USEPA (U.S. Environmental Protection Agency). 1980. Ambient water quality criteria for heptachlor. NTIS No. PB81-117632.

The sources above are deemed adequate to assess the literature through 1989. Coverage of more recent literature was provided by a New York State Library on-line search of the databases listed below.

! NTIS (National Technical Information Service)

! TOXLINE

! BIOSIS

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