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: delta-Hexachlorocyclohexane **CAS REGISTRY NUMBER:** 319-86-8

AMBIENT WATER QUALITY VALUE: 0.04 ug/L

BASIS: Chemical Correlation to Oncogenic

I INTRODUCTION

The Ambient Water Quality Value applies to the water column and is designed to protect humans from the effects of contaminants in sources 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 0.02 ug/L for hexachlorocyclohexane (HCH) and the sum of the isomers alpha-HCH, beta-HCH, gamma-HCH, delta-HCH and epsilon-HCH (NYS, 1985). Available information published after 1985 on delta-HCH 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

delta-Hexachlorocyclohexane does not have a Specific MCL as defined in 700.1. However, delta-hexachlorocyclohexane is in a principal organic contaminant class (vi) as defined in 700.1.

The U.S. Environmental Protection Agency has not established a maximum contaminant level goal (MCLG) or a MCL for drinking water for delta-hexachlorocyclohexane.

Under the State Sanitary Code (10 NYCRR Part 5, Public Water Supplies), the New York State Department of Health has established a general maximum contaminant level of 5 ug/L for principal organic contaminants such as delta-hexachlorocyclohexane in drinking water.

B. Derivation of Water Quality Value

Because delta-hexachlorocyclohexane is in a principal organic contaminant class and has no Specific MCL, a water quality value of 5 ug/L can be derived based on 702.3(b).

III ONCOGENIC EFFECTS (702.4)

U.S. EPA (1997) classifies delta-hexachlorocyclohexane in class D, not classifiable as to human carcinogenicity. IARC (1987) classifies hexachlorocyclohexanes in Group 2B (possibly carcinogenic to humans) but lists no separate entry for delta-hexachlorocyclohexane.

There are no oncogenic data on which to base a quantitative risk assessment. Goto et al. (1972) reported benign and malignant liver tumors in ICR-JCl mice after 26 weeks of exposure to a diet containing 600 ppm of a mixture of delta-hexachlorocyclohexane and epsilon-hexachlorocyclohexane. However, the study was inadequately reported and the exact number of animals with tumors was unclear.

delta-Hexachlorocyclohexane has not been found to be carcinogenic in male Wistar rats exposed to 25 or 50 mg/kg/day in the diet for 24 or 48 weeks (Ito et al., 1975) or in male dd mice exposed to 13-65 mg/kg/day in the diet for 24 weeks (Ito et al., 1973b). However, these studies are inadequate to assess the oncogenic potential of delta-hexachlorocyclohexane because of small sample sizes (20 animals or less per dose level) and short exposure durations.

IV NON-ONCOGENIC EFFECTS (702.5)

A. Data

Ito et al. (1973b) exposed 20 male dd mice to 13, 32.5, or 65 mg/kg/day of delta-hexachlorocyclohexane for 24 weeks. No oval cells, bile duct proliferation or hyperplasia were noted. An inconclusive finding of liver cell hypertrophy was noted at 65 mg/kg/day. Male rats exposed to 50 mg/kg/day for 48 weeks showed a similar finding, with no effect at 24 weeks or at a

lower dose (25 mg/kg/day) for 24 or 48 weeks (Ito et al., 1975). The authors identified a NOAEL (no-observed-effect-level) of 25 mg/kg/day.

B. Derivation of Water Quality Value

1. Selection of Data

The study by Ito et al. (1975) was judged the most appropriate for deriving a water quality value based on non-oncogenic effects. It was selected because it utilizes a larger portion of lifespan of the test animal.

2. Calculation of Acceptable Daily Intake (ADI)

An ADI is calculated from the study of Ito et al. (1975) by dividing the NOAEL of 25 mg/kg/day by a total uncertainty factor of 1000 as follows:

$$ADI = \left(\frac{25}{1000} \right) \text{ mg/kg/day} = 0.025 \text{ mg/kg/day}$$

This uncertainty factor was selected to account for intra- and interspecies differences (10 x 10) and for the use of a less-than-lifetime study (10).

3. Calculation of Water Quality Value

A 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:

$$\text{Water Quality Value} = \frac{(0.025 \text{ mg/kg/day})\ (1000 \text{ ug/mg})\ (70 \text{ kg})\ (0.2)}{(2 \text{ L/day})} = 175 \text{ ug/L, rounded to } 200 \text{ ug/L}$$

V CHEMICAL CORRELATION (702.7)

A. Data

The toxicologic database for delta-hexachlorocyclohexane has been reviewed (ATSDR, 1997; Goto et al., 1972; Ito et al., 1973b, 1975; USEPA, 1997). Although there are limited data on its non-oncogenic and oncogenic effects, the data are not sufficient for establishing a specific water quality value on the basis of sections 702.4 or 702.5.

The chemical structure, metabolic pathways, and target organs of five hexachlorocyclohexane isomers (alpha, beta, gamma, delta and epsilon) are similar (ATSDR, 1997); moreover, all have oncogenic potential in mice (see reviews in ATSDR, 1997; IARC, 1979). The collective evidence from studies on the oncogenic potential of individual isomers (alpha, beta, gamma, and delta) and mixtures of isomers (including mixtures of delta and epsilon) indicate that the potency of alpha-hexachlorocyclohexane to induce oncogenic effects in the liver of mice is greater than that of the other isomers (Hanada et al., 1973; Ito et al., 1973a,b). However, the evidence is not sufficient to rank the relative potencies of beta-, gamma-, delta-, and epsilon-hexachlorocyclohexane (Hanada et al., 1973; Ito et al., 1973a,b).

B. Derivation of Water Quality Value

Three hexachlorocyclohexane isomers (alpha-hexachlorocyclohexane, beta-hexachlorocyclohexane, and gamma-hexachlorocyclohexane) are classified as animal oncogens under 6 NYCRR 700.1; their ambient water quality values based on oncogenic effects are 0.01 ug/L, 0.04 ug/L, and 0.05 ug/L, respectively (NYS, 1997a,b,c). Given the similarities of the hexachlorocyclohexane isomers and the available data that indicates that the potency of alpha-hexachlorocyclohexane to induce oncogenic effects in mice is greater than that of the other isomers, an ambient water quality value of 0.04 ug/L is derived for delta-hexachlorocyclohexane based on its chemical correlation to other hexachlorocylohexanes, specifically beta-hexachlorocyclohexane and gamma-hexachlorocyclohexane. The value was based on the geometric mean of the values for beta- and gamma-hexachlorocyclohexane (as shown below) because of the uncertainties regarding the relative oncogenic potency of delta-hexachlorocyclohexane compared to beta- and gamma-hexachlorocyclohexane.

Water Quality Value = $[(0.04 \text{ ug/L})(0.05 \text{ ug/L})]^{0.5}$ = 0.045, rounded to 0.04 ug/L

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 from 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 chemical correlation value of 0.04 ug/L (6NYCRR 702.7) is the most stringent value derived by these procedures and is the ambient water quality value for delta-hexachlorocyclohexane.

VII REFERENCES

ATSDR (Agency for Toxic Substances and Disease Registry). 1997. Toxicological Profile on Alpha-, Beta-, Gamma- and Delta-Hexachlorocyclohexane. Draft update. Washington, DC: Public Health Service.

Goto, M., M. Hattori, T. Miyagawa, and M. Enomoto. 1972. Contribution to ecological chemistry. II. Hepatoma formation in mice after administration of hexachlorocyclohexane isomers in high doses. Chemosphere 6:279-282.

Hanada, M., C. Yutani, and T. Miyaji. 1973. Induction of hepatoma in mice by benzene hexachloride. Gann. 64:511-513. (As cited in IARC, 1979).

IARC (International Agency for Research on Cancer). 1979. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Hexachlorocyclohexane. 20:195-239.

IARC (International Agency for Research on Cancer). 1987. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Supplement 7. Lyon, France. pp.45, 220-222.

Ito, N., H. Nagasaki, M. Arai, et al. 1973a. Histopathologic studies on liver tumorigenesis induced in mice by technical polychlorinated biphenyls and its promoting effect on liver tumors induced by benzene hexachloride. J. Natl. Cancer Inst. 51:1637-1646.

Ito, N., H. Nagasaki, M. Arai et al. 1973b. Histologic and ultrastructural studies on the hepatocarcinogenicity of benzene hexachloride in mice. J. Natl. Cancer Inst. 51:817-826.

Ito, N., H. Nagasaki, H. Aoe et al. 1975. Development of hepatocellular carcinomas in rats treated with benzene hexachloride. J. Natl. Cancer Inst. 54:801-805.

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). 1985. Ambient Surface Water Quality Standards Documentation. Hexachlorocyclohexanes (HCH) and the isomers alpha-, beta-, gamma-, delta- and epsilon-HCH. Albany, NY: Department of Health.

NYS (New York State). 1997a. Human Health Fact Sheet. Ambient Water Quality Value for Protection of Sources of Potable Waters. alpha-Hexachlorocyclohexane. Albany, NY: Department of Environmental Conservation.

NYS (New York State). 1997b. Human Health Fact Sheet. Ambient Water Quality Value for Protection of Sources of Potable Water. beta-Hexachlorocyclohexane. Albany, NY: Department of Environmental Conservation.

NYS (New York State). 1997c. Human Health Fact Sheet. Ambient Water Quality Value for Protection of Sources of Potable Water. gamma-Hexachlorocyclohexane. Albany, NY: Department of Environmental Conservation.

U.S. EPA (Environmental Protection Agency). 1997. delta-Hexachlorocyclohexane. On-line. Integrated Risk Information System (IRIS). Cincinnati, OH: Office of Research and Development, Environmental Criteria and Assessment Office.

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 delta-hexachlorocyclohexane; 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 ambient water quality criteria document (document not found).

- U.S. EPA health advisory (document not found).

- U.S. EPA drinking water criteria document (document not found).

The sources below were reviewed by NYS (1985).

- Howe, R.B. and K.S. Crump. 1982. GLOBAL82 Computer Program. Science Research Systems, Inc., Ruston, LA.

- International Agency for Research on Cancer. 1974. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 5:47-74.

- International Agency for Research on Cancer. 1979. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 20:195-223.

- National Academy of Sciences. 1977. Drinking Water and Health, Vol. 1. National Academy of Sciences. Washington, D.C.

- National Academy of Sciences. 1980. Drinking Water and Health, Vol. 3. National Academy Press. Washington, D.C.

- Thorpe, E. and A.I.T. Walker. 1973. The toxicology of dieldrin (HEOD). II. Comparative long-term oral toxicity studies in mice with dieldrin, DDT, phenobarbitone, beta-BHC and gamma-BHC. Fd. Cosmet. Toxicol. 11:433-442.

- U.S. Environmental Protection Agency. 1980. Ambient water quality criteria for hexachlorocyclohexane. NTIS No. PB81-117659.

The sources above are deemed adequate to assess the literature through 1994.

AS
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