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NEW YORK STATE
- HUMAN HEALTH FACT SHEET -

Ambient Water Quality Value for
Protection of Sources of Potable Water

SUBSTANCE: p,p'-DDE **CAS REGISTRY NUMBER:** 72-55-9

AMBIENT WATER QUALITY VALUE: 0.2 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 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 0.01 ug/L for the sum of p,p'-DDD, p,p'-DDE and p,p'-DDT (NYS, 1984). Available information on p,p'-DDE was examined as described in "Scope of Review," below. Potential water quality values are derived below, and the value of 0.2 ug/L selected as described under "Selection of Value."

II PRINCIPAL ORGANIC CONTAMINANT CLASSES AND SPECIFIC MCL (702.3)

A. Discussion

p,p'-DDE does not have a Specific MCL as defined in 700.1. However, it is in principal organic contaminant class iii as defined in 700.1.

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

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 p,p'-DDE in drinking water.

B. Derivation of Water Quality Value

Because p,p'-DDE is in a principal organic contaminant class and has no Specific MCL, regulations require that the water quality value not exceed 5 ug/L.

III ONCOGENIC EFFECTS (702.4)

A. Data

Wolff et al. (1993) studied sera from blood specimens of 14,290 persons in the New York University Women's Health Study, and concluded that there was a strong association between breast cancer and serum p,p'-DDE.

U.S. EPA (1994) classifies p,p'-DDE as B2, a probable human carcinogen, based on "increased incidence of liver tumors including carcinomas in two strains of mice and in hamsters and of thyroid tumors in female rats by diet." p,p'-DDE is an oncogen as defined in 6 NYCRR 700.1.

U.S. EPA (1994) notes that animal carcinogenicity data are "sufficient" and presents the following summary:

> "NCI (1978) administered DDE in feed at TWA [time-weighted average] doses of 148 and 261 ppm to 50 B6C3F1 mice/sex/dose for 78 weeks. After an additional 15 weeks, a dose-dependent and statistically significant increase in incidence of hepatocellular carcinomas was observed in males and females in comparison with controls. Increased weight loss and mortality was observed in females.
>
> "Tomatis et al. (1974) administered 250 ppm DDE in feed for lifetime (130 weeks) to 60 CF-1 mice/sex. A statistically significant increase in incidence of hepatomas was observed in both males and females in comparison with controls. In females, 98% of the 55 surviving exposed animals developed hepatomas, compared to 1% of the surviving controls.
>
> "Rossi et al. (1983) administered DDE in feed for 128 weeks to 40-46 Syrian Golden hamsters/sex/dose at doses of 500 and 1000 ppm. After 76 weeks, a statistically significant increase in incidence of neoplastic nodules of the liver were observed in both sexes in comparison with vehicle-treated controls.
>
> "NCI (1978) also fed DDE at TWA doses of 437 and 839 ppm for males and 242 and 462 ppm for females for 78 weeks to 50 Osborne-Mendel rats/sex/dose, with an additional 35 week observation period. A dose-dependent trend in incidence of thyroid tumors was observed in females which was statistically significant by the Cochran Armitage trend test after adjustment for survival. The Fischer Exact test, however, was not statistically significant.

Overall, the results of the bioassay were not considered by NCI to provide convincing evidence for carcinogenicity.

"Supporting Data:

"DDE was mutagenic in mouse lymphoma (L5178Y) cells and chinese hamster (V79) cells, but not in Salmonella (ICPEMC, 1984). DDE is structurally similar to and a metabolite of DDT (Peterson and Robinson, 1964; Gingell and Wallcave, 1976; Morgan and Roan, 1977) which is a probable human carcinogen."

U.S. EPA (1994) presents on IRIS an oral slope factor for p,p'-DDE of 0.34 $(mg/kg/day)^{-1}$. Dose extrapolation was via the linearized multistage procedure, for extra risk, and the slope factor is the geometric mean of six slope factors calculated from incidence data by sex from NCI (1978), Tomatis et al. (1974) and Rossi et al. (1983). U.S. EPA (1994) provides oral dose-response data, shown here as Table 1.

Table 1

Oral Dose-Response Data
(from U.S. EPA, 1994)

Species/Strain Tumor Type	Dose: Administered (ppm)	Dose: Human Equivalent (mg/kg/day)	Tumor Incidence (female)	Tumor Incidence (male)	Reference
Mouse/B6C3F1; hepatocellular carcinomas	0 148 261	0.0 0.90 1.584	0/19 19/47 34/48	0/19 7/41 17/47	NCI, 1978
Mouse/CF-1; hepatomas	0 250	0 2.45	1/90 54/55	33/98 39/53	Tomatis et al., 1974
Hamsters/Syrian Golden; neoplastic nodules (hepatomas)	0 500 1000	0 4.79 9.57	0/31 7/30 8/39	0/42 4/39 6/39	Rossi et al., 1983

U. S. EPA also (1988) derived a potency factor for p,p'-DDE of 3.82 $(mg/kg/day)^{-1}$ based on a single study (see Discussion, below).

B. Selection of Data and Derivation of Water Quality Value

The approach of U. S. EPA (1994) which derives a slope of 0.34 $(mg/kg/day)^{-1}$ is believed the appropriate basis for a potential water quality value for p,p'-DDE for oncogenic effects. 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 (body weight of 0.030 kg) and hamster (body weight of 0.12 kg) data is a multiplication factor of 0.543, based on a weighted average of the number of slopes from each species, which results in a slope of 0.185 $(mg/kg/day)^{-1}$.

At the one-in-one million risk level, the slope factor of 0.185 $(mg/kg/day)^{-1}$ corresponds to a human dose of 5.41×10^{-3} ug/kg/day as shown below:

$$\text{Human dose} = \frac{\text{risk level}}{\text{slope factor}}$$

$$= \frac{1 \times 10^{-6} \times 1000 \text{ ug/mg}}{0.185 \text{ (mg/kg/day)}^{-1}} = 5.41 \times 10^{-3} \text{ ug/kg/day}$$

Multiplying by an animal body weight of 70 kg and dividing by a drinking water consumption rate of 2 L/day, a potential water quality value is calculated as follows:

$$\frac{5.41 \times 10^{-3} \text{ ug/kg/day} \times 70 \text{ kg}}{2 \text{ L/day}} = 0.189 \text{ ug/L, rounded to } 0.2 \text{ ug/L}$$

C. Discussion

The water quality value of 0.2 ug/L differs from the one derived within the previous fact sheet (NYS, 1984). As stated above, the approach of U.S. EPA (1994), as adjusted, is believed appropriate.

The current fact sheet also supports a separate value for p,p'-DDE, rather than one for the sum of p,p'-DDE, p,p'-DDT and p,p'-DDD as previously derived. A separate value is consistent with U.S. EPA's approach on IRIS and in the National Toxics Rule (U.S. EPA, 1994; 1992).

The 1988 U.S. EPA slope of 3.82 $(mg/kg/day)^{-1}$ based on a single study was prepared in support of reportable quantity adjustments pursuant to CERCLA. A single study was used to maintain consistency in the ranking of

carcinogens. This is inconsistent with the approach on IRIS and EPA's National Toxics Rule (U.S. EPA, 1992) and is not used in this fact sheet.

IV NON-ONCOGENIC EFFECTS (702.5)

A. Data

U.S. EPA (1994) lists "no data" for its oral RfD assessment for p,p'-DDE.

ATSDR (1994) lists a NOAEL of 10 mg/kg/day for p,p'-DDE from a 9-week oral rat study by Kornburst et al. (1986). For rat chronic oral exposure to this substance, ATSDR lists a "serious" LOAEL of 12 mg/kg/day for an hepatic effect (centrilobular necrosis) from the work of NCI (1978). They also list a LOAEL of 41.5 mg/kg/day for p,p'-DDE in the hamster for hepatocellular necrosis from Rossi et al. (1983).

Lembowicz et al. (1991) fed mouse neonates a mixture of organic chlorine compounds (78% DDE) at a daily dose of 44.8 ng/g body weight for 6 weeks. The mixture was obtained from human milk samples. Significant hematological effects, specifically increased lymphocytes, granulocytes and leucoblasts were reported. Changes in hepatocytic endoplasmic reticulum were also reported.

B. Derivation of Water Quality Value

1. Selection of Data

   The study by NCI (1978) was judged the most appropriate for deriving a water quality value based on non-oncogenic effects. It was selected because of its long duration. The results of Lembowicz, which could yield a more stringent value, were not used because the study was on a mixture.

2. Calculation of Acceptable Daily Intake (ADI)

   An ADI is calculated from the study of NCI (1978) by dividing the LOAEL of 12 mg/kg/day by a total uncertainty factor of 1000 as follows:

$$ADI = \frac{12\ mg/kg/day}{1000} = 0.012\ mg/kg/day$$

This uncertainty factor was selected to account for intraspecies (10) and interspecies (10) differences and because of using a LOAEL instead of a NOAEL (10).

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:

$$\text{Water Quality Value} = \frac{(0.012\ mg/kg/day)(1000\ ug/mg)(70\ kg)(0.2)}{2\ L/day}$$

= 84 ug/L, rounded to 80 ug/L

V CHEMICAL CORRELATION (702.7)

No basis was found for deriving a water quality value for p,p'-DDE using chemical correlation.

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 0.2 ug/L (6 NYCRR 702.4) is the most stringent value derived from these procedures and is the ambient water quality value for p,p'-DDE.

VII REFERENCES

ATSDR (Agency for Toxic Substances and Disease Registry). 1994. Toxicological Profile for 4,4'-DDT, 4,4'-DDE, 4,4'-DDD (update). Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.

Gingell, R. and L. Wallcave. 1976. Species differences in the acute toxicity and tissue distribution of DDT in mice and hamsters. Toxicol. Appl. Pharmacol. 28:385. [As cited by U.S. EPA, 1994]

ICPEMC (International Commission for Protection Against Environmental Mutagens and Carcinogens). 1984. Report of ICPEMC task group 5 on the differentiation

between genotoxic and nongenotoxic carcinogens. ICPEMC Publication No. 9. Mutat. Res. 133:1-49. [As cited by U.S. EPA, 1994]

Kornburst, D., B. Gillis, B. Collins et al. 1986. Effects of 1-dichloro-2,2-bis[p-chlorophenyl]ethane (DDE) on lactation in rats. J. Toxicol Environ Health 17:23-36. [As cited by ATSDR, 1994]

Morgan, D.P. and C.C. Roan. 1977. The metabolism of DDT in man. Essays Toxicol. 5:39. [As cited by U.S. EPA, 1994]

NCI (National Cancer Institute). 1978. Bioassays of DDT, TDE and p,p'-DDE for possible carcinogenicity. CAS No. 50-29-3, 72-54-8 and 72-55-9. NCI-CG-TR-131. [As cited by ATSDR, 1994]

NCI (National Cancer Institute). 1978. Bioassays of DDT, TDE and p,p'-DDE for possible carcinogenicity (CAS No. 50-29-3, 72-54-8, 72-55-9). NCI Report No. 131. DHEW Publ. No. (NIH) 78-1386. [As cited by U.S. EPA, 1994]

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 Water Supply Protection.

NYS (New York State). 1984. Ambient Surface Water Quality Standards Documentation. DDT; DDD and DDE. Albany, N.Y.: Department of Health.

Peterson, J.R. and W.H. Robinson. 1964. Metabolic products of p,p'-DDT in the rat. Toxicol. Appl. Pharmacol. 6:321. [As cited by U.S. EPA, 1994]

Rossi, L., O. Barbieri, M. Sanguineti, J.R.P. Cabral, P. Bruzzi and L. Santi. 1983. Carcinogenicity study with technical-grade DDT and DDE in hamsters. Cancer Res. 43:776-781. [As cited by ATSDR, 1994 and U.S. EPA, 1994]

Tomatis, L., V. Turusov, R.T. Charles and M. Boicchi. 1974. Effect of long-term exposure to 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene, ` to 1,1-dichloro-2,2-bis (p-chlorophenyl)ethane, and to the two chemicals combined on CF-1 mice. J. Natl. Cancer Inst. 52(3):883-891. [As cited by U.S. EPA, 1994]

U.S. EPA (Environmental Protection Agency). 1988. Evaluation of the Potential Carcinogenicity of DDE (72-55-9). Washington, DC: Office of Health and

Environmental Assessment, Carcinogen Assessment Group. EPA/600/8-91/100. PB93-185247.

U.S. EPA (Environmental Protection Agency). 1992. Water Quality Standards; Establishment of Numeric Criteria for Priority Toxic Pollutants; States Compliance. Fed. Register 57(246):60848-60923. December 22, 1992.

U.S. EPA (Environmental Protection Agency). 1994. p,p'-Dichlorodiphenyl-dichloroethylene (DDE). On-line. Integrated Risk Information System (IRIS). Cincinnati, OH: Office of Research and Development, Environmental Criteria and Assessment Office.

Wolff, M.S., P.G. Toniolo, E.W. Lee, M. Rivera and N. Dubin. 1993. Blood levels of organochlorine residues and breast cancer. J. Natl Cancer Inst. 85:648-652.

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 DDE; where none was found it is so noted.

- IRIS (U.S. EPA's Integrated Risk Information System) (on-line).
- RTECS (Registry of Toxic Effects of Chemical Substances) (on-line).
- CCRIS (Chemical Carcinogenesis Research Information System). On-line database.
- ATSDR (Agency for Toxic Substances and Disease Registry) toxicological profile.
- U.S. EPA ambient water quality criteria document.
- U.S. EPA health advisory (document not found).
- U.S. EPA drinking water criteria document (document not found).
- IARC (International Agency for Research on Cancer) Monographs Supplement 7 (substance not listed).

The sources below were reviewed by NYS (1984).

- IARC (International Agency for Research on Cancer). 1974. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 5: 83-124.

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

- U.S. Environmental Protection Agency. 1980. Ambient water quality criteria for DDT. NTIS No. PB81-117491.

The sources above were deemed adequate to assess the literature through 1990. Coverage of 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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