Fact Sheet Date: April 2000

NEW YORK STATE
- HUMAN HEALTH FACT SHEET -

Ambient Water Quality Value for Protection of Sources of Potable Water

SUBSTANCE: Carbon disulfide **CAS REGISTRY NUMBER:** 75-15-0

AMBIENT WATER QUALITY VALUE: 60 ug/L

BASIS: Non-oncogenic effects

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 a water quality guidance value be based on the procedures in sections 702.3 through 702.7. Potential water quality values for carbon disulfide are derived below, and the value of 60 ug/L was selected as described under "Selection of Value."

PRINCIPAL ORGANIC CONTAMINANT CLASSES AND SPECIFIC MCL (702.3)

A. Discussion

Carbon disulfide does not have a Specific MCL for New York State as defined in 700.1. It is not considered to be an organic substance, so a determination as to whether it is in a principal organic contaminant class as defined in 700.1 is not relevant. US EPA does not regulate it under the Safe Drinking Water Act, nor have they issued a drinking water health

advisory for it.

Under the State Sanitary Code, (10 NYCRR Part 5, Public Water Supplies), the New York State Department of Health (DOH) does not regulate carbon disulfide as either a principal organic contaminant (POC) or an unspecified organic contaminant (UOC) and has not established a specific maximum contaminant level (MCL) for carbon disulfide in drinking water.

B. Derivation of Water Quality Value

Because carbon disulfide does not have a Specific MCL and is not in a principal organic contaminant class, a water quality value cannot be derived based on 702.3.

ONCOGENIC EFFECTS (702.4)

Insufficient information was found to adequately assess the oncogenic potential for carbon disulfide. US EPA (1998) has not completely evaluated the evidence for human carcinogenic potential of carbon disulfide under its IRIS program. ATSDR (1996) found no studies in animals by any route of exposure and “no definitive evidence” in humans.

Genotoxicity studies of carbon disulfide in a number of tests including Salmonella typhimurium and Escherichia coli, both with and without metabolic activation, were negative (ATSDR, 1996). In human lymphocytes, Garry et al. (1990) did find a dose-related increase in sister chromatid exchanges ($p < 0.05$) but only with microsomal activation with S-9.

This substance does not meet the definition for an oncogen under New York State regulations (700.1); thus, a value based on oncogenic effects cannot be derived.

NON-ONCOGENIC EFFECTS (702.5)

A. Data

Adequate human data or data from long-term oral studies on animals that could serve as the basis for an ambient water quality value were not found. The results of some less-than lifetime animal studies are available; these and some human occupational results are described below.

Jones-Price et al. (1984a,b) studied the toxicity and teratogenicity of oral exposure to carbon disulfide in rats and rabbits. In the rat study (1984a) carbon disulfide was given in corn oil at 0, 100, 200, 400 and 600 mg/kg/day to CD rats on gestational days (gd) 6 through 15. Animals were terminated on gd 20. Dams (confirmed pregnant females) at all dose levels

exhibited a significant reduction in gestational body weight gain. At dose levels of 200 mg/kg/day and above, mean fetal weight was significantly reduced. However, no significant differences were found in either fetal resorptions or malformations at any dose level. Thus, maternal toxicity was exhibited at all dose levels tested, and fetal toxicity at and above 200 mg/kg/day.

In the rabbit study, carbon disulfide was given orally in corn oil at 0, 25, 75 and 150 mg/kg/day on gd 6 through 19. Animals were terminated on gd 30 and 23 - 28 dams per group evaluated. Data collected included gravid uterus weight, number of implantation sites, and live, dead or resorbed fetuses. Weight and malformations in live fetuses were assessed. In the two highest dosed groups, maternal weight gain was significantly below controls, and there were significant increases in both relative and absolute liver weights. Jones-Price et al. (1984b) concluded these changes were treatment-related. Thus, maternal toxicity was observed at both 75 mg/kg/day and 150 mg/kg/day.

All dosed groups showed significant ($p < 0.05$) increases in the percentage per litter of resorbed, nonlive (dead plus resorbed) or affected (nonlive plus malformed) fetuses. The incidences of resorptions were 12.30%, 32.47%, 41.60% and 61.16% in vehicle through 150 mg/kg/day groups. However, only the incidence of malformed fetuses per litter in the high-dosed group (19.51%) was significantly higher than the incidence in controls (5.72%). The low dose of 25 mg/kg/day carbon disulfide produced fetotoxicity but "no distinctive evidence" of toxicity to the dams. Thus, the lowest dose level of 25 mg/kg/day represents an effect level for this study.

Hardin et al. (1981) investigated the potential for teratogenic effects from inhalation exposure of rats and rabbits to carbon disulfide. Both species were exposed to 62.3 mg/m^3 (20 ppm) for 6 hours/day and 124.6 mg/m^3 (40 ppm) (exposure period not given) for 34 weeks before breeding and during the entire pregnancy period; no effects on fetal development were found. US EPA (1998) identified the highest exposure level of 124.6 mg/m^3, equivalent to 11.0 mg/kg/day, as a no-observed-effect level (NOEL) for this study; a lowest-observed-effect level (LOEL) was not found.

Many studies have been done on workers exposed to carbon disulfide (ATSDR, 1996; US EPA, 1998). The critical effect identified in these studies is an extrarespiratory effect - peripheral nervous system dysfunction. The US EPA (1998) derived a benchmark concentration based on this critical effect and the data reported in Johnson et al. (1983). ATSDR (1996) utilized the same study as the basis for their Minimal Risk Level based on neurological effects via inhalation. Additional occupational studies have identified visionand the heart as other targets of carbon disulfide toxicity (Lee et al.,1996; Vanhoorne et al., 1996; Bortkiewicz et al., 1997; Drexler et al., 1996; Price et al., 1996;1997).

B. Derivation of Value

The oral study of Jones et al. (1984b) on rabbits is the most appropriate basis for an ambient water quality value for non-oncogenic effects. It showed fetal toxicity at levels below that of the oral rat study (Jones-Price et al., 1984a). Thus, it is the more sensitive oral study and is preferred over the rat study because there are insufficient data to determine confidently which species (rats or rabbits) is a better surrogate for humans. It is preferred over the Hardin et al. (1981) inhalation study, which formed the basis for US EPA's (1998) oral reference dose (RfD), because it eliminates the need, and thus the uncertainties, associated with a route-to-route extrapolation. In addition, the oral LOEL identified in the Jones et al. (1984b) study on rabbits was lower than the estimated NOEL derived from the Hardin et al. (1981) inhalation study. Thus, the effect level of 25 mg/kg/day for fetal resorption in rabbits identified in Jones-Price et al. (1984b) is selected as the appropriate basis for the derivation of an ambient water quality value for the protection of sources of drinking water.

An acceptable daily intake (ADI) of 0.0083 mg/kg/day is calculated from the effect level (25 mg/kg/day):

$$\text{ADI} = \frac{\text{Effect Level}}{\text{UF}} = \frac{25 \text{ mg/kg/day}}{3{,}000} = 0.0083 \text{ mg/kg/day}$$

The total uncertainty factor (UF) of 3,000 consists of factors of 10 for intraspecies (human) variability, 10 for extrapolating between experimental animals and humans, 10 for the use of an effect level instead of a no-observed-effect level, and 3 to account for the lack of a complete database (particularly the lack of a chronic oral study). The regulations, 702.5(b), state that the magnitude of the total UF "... shall reflect the quantity and quality of the toxicologic data, the degree of confidence in the data and the nature of the effects of concern." The additional UF of 3 for the incomplete database is appropriate under this provision.

A potential ambient water quality value is calculated from the ADI (0.0083 mg/kg/day) using a human body weight of 70 kg, a daily water consumption rate of 2 L/day, and apportioning 20% of the ADI to drinking water:

$$\text{Water Quality Value} = \frac{(0.0083 \text{ mg/kg/day})\ (1000 \text{ ug/mg})\ (70 \text{ kg})\ (0.2)}{(2 \text{ L/day})} =$$

$$= 58.1 \text{ ug/L, rounded to } 60 \text{ ug/L}$$

CHEMICAL CORRELATION (702.7)

A potential water quality value for carbon disulfide using chemical correlation was not derived because values have not been derived for similar substances under 702.4 or 702.5.

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 non-oncogenic value of 60 ug/L (702.5) is the most stringent value derived from these procedures and is the ambient water quality value for carbon disulfide.

REFERENCES

ATSDR (Agency for Toxic Substances and Disease Registry). 1996. Toxicological Profile for Carbon Disulfide (Update). Atlanta, GA.

Bortkiewicz, A., E. Gadzicka and W. Szymczak. 1997. Heart rate variability in workers exposed to carbon disulfide. Journal of the Autonomic Nervous System. 66:62-68.

Drexler, H., K. Ulm, R. Hardt, M. Hubmann, T. Goen, E. Lang, J. Angerer and G. Lehnert. 1996. Carbon disulphide. IV. Cardiovascular function in workers in the viscose industry. International Archives of Occupational and Environmental Health 69:27-32.

Garry, V.F., R.L. Nelson, J. Griffith and M. Harkins. 1990. Preparation for human study of pesticide applicators: Sister chromatid exchanges and chromosome alterations in cultured human lymphocytes exposed to selected fumigants. Teratogenesis, Carcinogenesis and Mutagenesis 10:21-29.

Hardin, B.D., G.P. Bond, M.R. Sikov, F.D. Andrew, R.P. Beliles and R.W. Niemeier. 1981. Testing of selected workplace chemicals for teratogenic potential. Scandanavian Journal of Work, Environment and Health 7(Suppl. 4): 66-75 [As cited in U.S. EPA, 1998].

Johnson, B.L., J. Boyd, J.R. Burg, S.T. Lee, C. Xintaras and B.E. Albright. 1983. Effects on the peripheral nervous system of worker's exposure to carbon disulfide. Neurotoxicology 4:53-65 [As cited in ATSDR, 1996 and U.S. EPA, 1998].

Jones-Price, C., R.W. Tyl, M.C. Marr and C.A. Kimmel. 1984a. Teratologic Evaluation of

Carbon Disulfide (CAS No. 75-15-0) Administered to CD Rats on Gestational Days 6 through 15. National Center for Toxicological Research, Jefferson AR. Govt. Reports Announcements and Index, Issue 15. NTIS PB 84-192343.

Jones-Price, C., R.W. Tyl, M.C. Marr and C.A. Kimmel. 1984b. Teratologic Evaluation of Carbon Disulfide (CAS No. 75-15-0) Administered to New Zealand White Rabbits on Gestational Days 6 through 15. National Center for Toxicological Research, Jefferson AR. Govt. Reports Announcements and Index, Issue 15. NTIS PB 84-192350.

Lee, E., S. Kim, H. Kim, K. Kim and Y. Yum. 1996. Carbon disulfide poisoning in Korea with social and historical background. Journal of Occupational Health 38: 155-161

6 NYCRR (New York State Codes, Rules and Regulations). Water Quality Regulations, Surface Water and Groundwater Classifications and Standards: Title 6, Chapter X, Parts 700 - 706. 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.

Price, B., T. Berner, R.T. Henrich, J.M. Stewart and E.J. Moran. 1996. A benchmark concentration for carbon disulfide: Analysis of the NIOSH carbon disulfide database. Regulatory Toxicology and Pharmacology 24: 171-176 [As cited in Price et al., 1997].

Price, B., T.S. Bergman, M. Rodriguez, R.T. Henrich and E.J. Moran. 1997. A review of carbon disulfide exposure data and the association between carbon disulfide exposure and ischemic heart disease mortality. Regulatory Toxicology and Pharmacology 26: 119-128.

US EPA (U.S. Environmental Protection Agency). 1998. Carbon disulfide. On-Line as of September 28. Integrated Risk Information System (IRIS).

Vanhoorne, M., A. De Rouck and D. Bacquer. 1996. Epidemiological study of the systemic ophthalmological effects of carbon disulfide. Archives of Environmental Health 51(3):181-188.

New York State Department of Environmental Conservation
Division of Water
SJS
September 1,1999