Fact Sheet Date: June 1998

NEW YORK STATE
- HUMAN HEALTH FACT SHEET -

Ambient Water Quality Value for Protection of Sources of Potable Water

SUBSTANCE: 2,4-Dinitrophenol **CAS REGISTRY NUMBER:** 51-28-5

AMBIENT WATER QUALITY VALUE: 10 ug/L

BASIS: Non-oncogenic

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. Potential water quality values are derived below, and the value of 10 ug/L selected for 2,4-dinitrophenol as described under "Selection of Value."

PRINCIPAL ORGANIC CONTAMINANT CLASSES AND SPECIFIC MCL (702.3)

A. Discussion

2,4-Dinitrophenol does not have a Specific MCL for New York State as defined in 700.1 and is not in a principal organic contaminant class as defined in 700.1.

B. Derivation of Water Quality Value

Because 2,4-dinitrophenol does not have a Specific MCL and is not in a principal organic contaminant class, no water quality value can be derived based on 702.3.

ONCOGENIC EFFECTS (702.4)

U.S. EPA (1995) conducted a comprehensive evaluation of the oncogenic effects of 2,4-dinitrophenol as part of its criteria development for the Great Lakes Water Quality Initiative (GLI). The GLI was a joint undertaking by U.S. EPA and the Great Lakes States and included representatives of interest groups. Its final regulations and the criteria document for this substance received extensive public review in a formal rule making process. U.S. EPA does not consider 2,4-dinitrophenol to be carcinogenic. The Department concludes that 2,4-dinitrophenol does not meet New York's definition of an oncogen in 6 NYCRR 700.1. Therefore, a value based on oncogenic effects is not derived.

NON-ONCOGENIC EFFECTS (702.5)

U.S. EPA (1995) also conducted a comprehensive review of toxicological data on non-oncogenic effects for 2,4-dinitrophenol as part of criteria development under GLI. The Department reviewed the toxicological basis for EPA's non-oncogenic criteria and concludes it is appropriate for the derivation of a statewide value. Exhibit I, excerpted from U.S. EPA (1995), provides the scientific basis for their non-oncogenic criteria. These data will be used to develop a water quality value for protection from non-oncogenic effects using New York State procedures as described below.

U.S. EPA (1995) selected the results of the study by Horner (1942) as the most appropriate for deriving a water quality value based on non-oncogenic effects. From these, they calculated an acceptable daily exposure (ADE) of 0.0020 mg/(kg · day), equivalent to an acceptable daily intake (ADI) developed under NYS procedures (702.5). The ADE used by U.S. EPA is consistent with information in a recent toxicological profile (ATSDR, 1995).

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 drinking water, as follows:

$$\text{Water Quality Value} = \frac{[0.0020\ \text{mg/(kg} \cdot \text{day)}]\ [1000\ \text{ug/mg}]\ [70\ \text{kg}]\ [0.2]}{[2\ \text{L/day}]}$$

$$= 14\ \text{ug/L, rounded to } 10\ \text{ug/L}$$

CHEMICAL CORRELATION (702.7)

A value based on chemical correlation is not applicable because data are sufficient to evaluate 2,4-dinitrophenol based on section 702.5 and insufficient information was found upon which to derive a value based on chemical correlation to section 702.4.

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, chronic value of 10 ug/L (6 NYCRR 702.5) is the most stringent value derived by these procedures and is the ambient water quality value for 2,4-dinitrophenol.

REFERENCES

ATSDR (Agency for Toxic Substances and Disease Registry. 1995. Toxicological Profile for Dinitrophenols. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service.

Horner, W.D. 1942. Dinitrophenol and its relation to formation of cataracts. Arch. Opthal. 27:1097-1129. [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.

U.S. EPA (Environmental Protection Agency). 1995. Great Lakes Water Quality Initiative Criteria Documents for the Protection of Human Health. Washington, D.C.: Office of Water. EPA-820-B-95-006.

New York State Department of Environmental Conservation
Division of Water
SJS
December 23, 1997

EXHIBIT I

GREAT LAKES WATER QUALITY INITIATIVE
TIER 1 HUMAN HEALTH CRITERIA FOR
2,4-DINITROPHENOL
CAS NO. 51-28-5

Tier 1 Human Noncancer Criterion

A review of the available literature on the toxic effects and therapeutic use of 2,4-dinitrophenol (2,4-DNP) indicates that the HNC derivation is most appropriately based upon the human dose-response following exposure to 2,4-DNP as reviewed by Horner (1942).

Numerous studies on 2,4-DNP and its toxic effects on humans are available (Horner, 1942; SRC, 1981). Commonly-reported toxic effects included gastrointestinal disturbances (nausea, vomiting, loss of appetite), cutaneous rashes, neuritis, agranulocytosis of the bone marrow, and jaundice. Liver and kidney and cardiovascular damage was rarely reported. Evidence of cardiovascular effects was limited to abnormal electrocardiograms indicating functional abnormalities of the heart, although fragmentation of the heart muscle was reported in cases of fatal poisoning. Nine cases of mortality resulting from 2,4-DNP poisoning were cited. Death usually occurred within 24 hours after the onset of such toxic manifestations as dizziness, fatigue, dyspnea, high temperature, intense thirst, and excessive perspiration.

In the study by Horner (1942), bilateral cataract formation was frequently observed in patients receiving 2,4-DNP as a weight-loss agent. The study reported that cataracts developed in more than 164 persons after the use of dinitrophenol, an estimated incidence of 0.86 percent. The study did not include a control group, however the researcher noted that this type of cataract is not expected to occur in some of the age groups which exhibited cataracts in the study. Formation of cataracts occurred either during dosing or within several months to a year after the final dose was taken. Cataracts were observed in patients receiving as little as 2 mg/kg bw/day which was the lower range of the recommended therapeutic dose for obesity. This LOAEL determined from the Horner (1942) study was deemed sufficient for the derivation of a Tier 1 HNC.

In a 6-month feeding study, male rats (from the Breeding and Laboratory Institute, Brooklyn, NY) were administered 2,4-DNP at dietary levels of 0, 100, 200, 500 and 1000 ppm for 178-179 days (Spencer et al., 1948). There were 14, 12, 12, 9 and 14 rats per dietary level, respectively. An additional 10 rats were fed 2000 ppm but after 24 days this group experienced 40% mortality and the remaining animals at 2000 ppm were sacrificed and examined at this time. These animals were emaciated and had empty

gastrointestinal tracts, enlarged spleens with hemosiderosis, testicular atrophy, and increased levels of blood urea nitrogen. Rats fed 1000 ppm 2,4-DNP suffered a reduction in body weight gain of 10-15%, a slight depletion of body fat, a very slight increase in the average weight of the kidneys, and a very slight decrease in the weight of the heart. Blood urea nitrogen levels were elevated in 2/14 animals at 1000 ppm. Reduced growth occurred at 500 ppm and a significant increase (between 91% and 92% above controls) in kidney weights occurred at all dietary concentrations. The authors concluded that the male rats maintained for six months on diets containing 200 ppm (and presumably 100 ppm) showed no appreciable ill effects. However, because there was a statistically significant increase in kidney weights at all dietary concentrations, the dose of 100 ppm may be considered the LOAEL for this study. Using a food consumption value of 0.08 kg/kg bw (EPA, 1988), the LOAEL for the Spencer et al. (1948) study was 8 mg/kg bw/day. This is very close to the LOAEL of 2.0 mg/kg bw/day which was calculated using the human data from Horner (1942). EPA (1980) derived an Acceptable Daily Intake (ADI) from an estimated NOAEL of 5.4 mg/kg/day (100 ppm group) from the study by Spencer et al. (1948).

In a teratology study with 2,4-DNP, Gibson (1973) reported that neither intraperitoneal (7.7 and 13.6 mg/kg/day) nor oral (25.5 and 38.2 mg/kg/day) doses of 2,4-DNP administered to pregnant Swiss-Webster mice during early organogenesis (days 10-12 of gestation) produced morphological defects. However, the higher intraperitoneal dose was embryotoxic and the higher intraperitoneal and oral doses produced overt signs of toxicity (hyperexcitability and hyperthermia) in the dams.

The HNV is derived from the LOAEL (2.0 mg/kg bw/day) determined from the human data summarized by Horner (1942) using an uncertainty factor of 1000. This approach is consistent with the derivation of the oral RfD for 2,4-DNP by EPA (1986).

$$\text{ADE} = \frac{\text{NOAEL}}{\text{UF}} = \frac{2\ \text{mg/kg/d}}{1000} = 2.0 \times 10^{-3}\ \text{mg/kg/d}$$

Where: Uncertainty Factor = 1000, composed of:

10x for interspecies variability
10x for intraspecies differences
10x for subchronic exposure duration

References:

Gibson, J.E. 1973. Teratology studies in mice with 2-secbutyl-4, 6-dinitrophenol (dinoseb). Food Cosmet. Toxicol.11:31-43.

Horner, W.D. 1942. Dinitrophenol and its relation to formation of cataracts. Arch. Ophthal. 27:1097-1121.

Spencer, H.C., V.K. Rowe, E.M. Adams and D.D. Irish. 1948. Toxicological studies on laboratory animals of certain alkyl dinitrophenols used in agriculture. J. Indus. Hyg. Toxicol. 30:10-25.

Syracuse Research Corporation (SRC), Center for Chemical Hazard Assessment. 1981. Information Profiles on Potential Occupational Hazards: Nitrophenols. Prepared for National Institute for Occupational Safety and Health (NIOSH), Rockville, MD. PB89-215842/XAD. PHS-NIOSH-210-79-0030.

U.S. Environmental Protection Agency (EPA). 1988. Recommendations For And Documentation Of Biological Values For Use In Risk Assessment. PB88-179874.

U.S. Environmental Protection Agency (EPA). 1986. Integrated Risk Information System (IRIS database). Chemical file for 2,4-dinitrophenol (51-28-5). Verification Date 2/5/86. Last Reviewed 2/5/86.

U.S. Environmental Protection Agency (EPA). 1980. Ambient Water Quality Criteria Document for Nitrophenols. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Water Regulations and Standards, Criteria and Standards Division, Washington, DC. EPA 440/5-80-063.