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: Cyanide **CAS REGISTRY NUMBER:** Not Applicable

AMBIENT WATER QUALITY VALUE: 200 ug/L

BASIS: Non-oncogenic, Chronic

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. Potential water quality values are derived below, and the value of 200 ug/L selected for cyanide as described under "Selection of Value."

II PRINCIPAL ORGANIC CONTAMINANT CLASSES AND SPECIFIC MCL (702.3)

A. Discussion

Cyanide does not have a Specific MCL for New York State as defined in 700.1.

Cyanide is not in a principal organic contaminant class as defined in 700.1.

The U.S. Environmental Protection Agency has established a maximum contaminant level goal (MCLG) and a MCL for cyanide of 200 ug/L.

B. Derivation of Water Quality Value

Because cyanide 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.

III ONCOGENIC EFFECTS (702.4)

U.S. EPA (1995) conducted a comprehensive evaluation of the oncogenic effects of cyanide 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's documentation for their oncogenic criteria has been reviewed. The Department concludes that cyanide 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.

IV NON-ONCOGENIC EFFECTS (702.5)

U.S. EPA (1995) also conducted a comprehensive review of toxicological data on non-oncogenic effects for cyanide 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 Howard and Hanzal (1955) 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 0.0216 mg/(kg · day), equivalent to an acceptable daily intake (ADI) developed under NYS procedures (702.5).

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:

$$\text{Water Quality Value} = \frac{[0.0216 \text{ mg/(kg} \cdot \text{day)}]\ [1000 \text{ ug/mg}]\ [70 \text{ kg}]\ [0.2]}{[2 \text{ L/day}]}$$

$$= 151 \text{ ug/L, rounded to } 200 \text{ ug/L}$$

V CHEMICAL CORRELATION (702.7)

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

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 non-oncogenic, chronic value of 200 ug/L (6 NYCRR 702.5) is the most stringent value derived by these procedures and is the ambient water quality value for cyanide.

VII REFERENCES

ATSDR (Agency for Toxic Substances and Disease Registry). 1995. A toxicological profile for cyanide (draft update for public comment).

Howard, J. and R. Hanzal. 1955. Chronic toxicity to rats of food treated with hydrogen cyanide. J. Agric. Food Chem. 13:325-329. [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
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Exhibit I

GREAT LAKES WATER QUALITY INITIATIVE
TIER 1 HUMAN HEALTH CRITERIA FOR
CYANIDES
CAS NO. 57-12-5

Tier 1 Human Noncancer Criterion

A review of the available literature indicates inadequate human data for quantitative risk assessment of cyanides based on human health effects. Qualitative data suggest that chronic dietary exposure to naturally occurring cyanogens in cassava results in thyroid abnormalities in African countries where cassava is a staple crop. Effects seen, including endemic goiter, cretinism and congenital hypothyroidism, were potentiated by low iodine intake and other dietary deficiencies. Tropical ataxic neuropathy has also been linked to chronic cyanide ingestion from cassava derivatives (Njoh, 1990). However, these data do not provide a dose-response relationship (EPA, 1985a; 1985b; ATSDR, 1988; Njoh, 1990).

From animal studies on the chronic oral toxicity of inorganic salts of cyanide, the most appropriate basis for HNV derivation for cyanides is the NOAEL from the chronic rat feeding study of Howard and Hanzal (1955). Weanling rats (10/sex/group) were offered food fumigated with hydrogen cyanide at dietary concentrations of 100 and 300 ppm HCN, averaging 73 and 183 mg CN^-/kg diet) for two years. Dose levels were approximately 4.6 or 10.8 mg CN^-/kg bw/day to females, and 3.6 or 7.5 mg CN^-/kg bw/day to males (EPA, 1985b, 1990). At termination, hematological values were within normal limits and neither gross nor microscopic examination of tissues (including thyroid) revealed evidence of pathology due to exposure in any of the exposure groups. Therefore, the NOAEL from this study is 10.8 mg CN^-/kg bw/day.

The database is judged to be sufficient for Tier 1 HNC derivation. The key study (Howard and Hanzal, 1955) provides a chronic NOAEL which is supported and supplemented by other data.

In a chronic study (Philbrick et al., 1979), ten male weanling rats were given 1500 ppm potassium cyanide in the diet for 11.5 months. The administered dose was approximately 75 mg KCN/kg bw/day, or 30 mg CN^-/kg bw/day (ATSDR, 1988; EPA, 1985a; 1985b). The cyanide exposure in rats receiving either normal or restricted diet resulted in reduced body weight gain, decreased thyroid gland activity and increased thyroid weights.

In a study by Tewe and Maner (1981b), pregnant Yorkshire pigs (6/dose group) were fed fresh cassava diets containing 0, 276 or 521 mg cyanide (added as KCN) per kg of fresh cassava offered during gestation and parturition. On the 110th day of gestation, two gilts per dose group were sacrificed and the fetuses were evaluated. The remaining gilts in each dose group were allowed to naturally deliver and were then maintained on a diet with no cyanide throughout the 56-day lactation period. No serious interference was observed

with the production of the first litter of offspring by gilts receiving cassava diets containing up to 521 ppm added cyanide during gestation. Gilts in the high dose group, exhibited possible adverse effects on the thyroid (increased weight) and kidney (proliferation of glomerular cells). The high exposure level also suggests a LOAEL for developmental effects, as the 110-day-old fetuses had decreased relative spleen, thyroid and heart weights. The evidence that the thyroid may be a sensitive target organ in pigs lends support to the thyroid effects reported by Jackson (1988; see later discussion). However, data interpretation is difficult due to the small number of gilts evaluated (2/dose group). The administered levels of 276 and 521 ppm CN^- in the diet convert to 7.7 and 17 mg CN^-/kg bw/day for the gilts, using the reported animal body weights and food intake from the study. The NOAEL for this study was 276 ppm CN^- in the diet, or approximately 7.7 mg CN^-/kg bw/day.

Another developmental study (Tewe and Maner, 1981a) reports that 500 ppm KCN administered in the diet to rats resulted in a decreased protein efficiency ratio among offspring during the postweaning growth phase. The dose level has been converted to approximately 50 mg CN^-/kg/day assuming a 10% food conversion factor (ATSDR, 1988), or approximately 10.6 mg CN^-/kg/day per EPA (1985b).

Other available oral studies are more limited in design, including the only relevant study with drinking water exposure. Palmer and Olson (1979) gave 7 male Sprague-Dawley rats 200 mg/l KCN in water (or 80 mg/l CN^-; 10 mg CN^-/kg/day per EPA, 1985a) or 200 ppm KCN in diet (80 mg CN^-/kg food; 8 mg CN^-/kg/day per EPA, 1985a) for 21 days. At the end of the study, the only parameters evaluated were body weight and liver weight. Liver weights were increased over controls following drinking water exposure only. Although inadequate for criteria derivation, this study suggests that cyanide via drinking water is more potent for inducing effects than feeding studies, but is less potent than gavage exposures.

In another noteworthy but limited study, the effects of oral cyanide on glucose metabolism, thyroid function and an array of behavioral indices were evaluated in miniature pigs (Jackson, 1988). Three swine/dose group (mixed sexes) received 0, 0.4, 0.7 or 1.2 mg CN^-/kg/day by intraoral bolus as KCN in aqueous solution, daily for 24 weeks. The author reports that treatment resulted in a dose-related increase in the fasting blood glucose level, dose-related decreases in T_3 and T_4 thyroid hormones, and numerous altered behaviors. By Chi-square analyses these changes were determined to be significant, even in the low exposure group with regard to some parameters. The alterations noted were more pronounced in the high-dose group, particularly for thyroid hormone levels, the parameter most clearly indicative of adverse effects. Suppression of T_3 and T_4 was dose-related with a much stronger response in the high-dose group (roughly double the effect seen in the mid-dose group at 24 weeks). However, the limitations of the study design and reporting are substantial (Papa, 1990, personal communication). Some of the most critical deficiencies in design or reporting include: small animal numbers per group; lack of body weight and organ weight data; exposure pattern as a single daily bolus dose; unclear biological significance of the reported biochemical effects; no report of the variance about the mean for T_3, T_4, and blood glucose values; and the distribution of sexes among the four

groups was not reported. The latter point appears critical because from the 12 animals distributed evenly among the four groups, five were females, and seven were castrated males. The castrated males were, therefore, unevenly represented among the groups and the castration effect on thyroid levels and behavior is likely to be significant (Papa, 1990, personal communication).

The 2-year dietary exposure study by Howard and Hanzal (1955) has been selected as the key study for the derivation of the risk assessment of cyanide in drinking water by EPA (1985a, 1985b, 1990). Those assessments have applied an additional uncertainty factor of 5 due to the dietary method of exposure. This is intended to account for the relative tolerance to cyanide when it is ingested with food rather than when it is ingested in drinking water. The value of 5 was based on an evaluation of cyanide-binding affinity of food and the GI absorption of cyanide in food versus drinking water by Dr. Ernest Foulkes of the University of Cincinnati who served as an external reviewer for EPA (1985a) (Papa, 1990, personal communication). This 5-fold (or 20%) adjustment factor for differential bioavailability between cyanide in feed and in drinking water is concluded to be appropriate and scientifically supportable in a more recent analysis (Pearsall and Chrostowski, 1990).

The HNC is therefore derived from the HNOAEL dose of 10.8 mg CN^-/kg/day in rats via feed (Howard and Hanzal, 1955), and an uncertainty factor of 500.

$$\text{ADE} = \frac{\text{NOAEL}}{\text{UF}} = \frac{\text{10.8 mg } CN^-\text{/kg/d}}{500} = 2.16 \times 10^{-2} \text{ mg/kg/d}$$

Where: Uncertainty Factor = 500, composed of:

10x for interspecies variability
10x for intraspecies differences
5x adjustment for bioavailability,
feed vs. drinking water

References:

Agency for Toxic Substances and Disease Registry (ATSDR). 1988. Toxicological Profile for Cyanide. U.S. Public Health Service. ATSDR/TP-88/12.

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Tewe, O. and J. Maner. 1981a. Long-term and carry-over effect of dietary inorganic cyanide (KCN) in the life cycle performance and metabolism of rats. Toxicol. Applied Pharmacol. 58:1-7.

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