Fact Sheet Date: March 12, 1998

NEW YORK STATE
- HUMAN HEALTH FACT SHEET -

Ambient Water Quality Value
Based on Human Consumption of Fish

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

AMBIENT WATER QUALITY VALUE: 400 ug/L

BASIS: Bioaccumulation

INTRODUCTION

This value applies to the water column and is designed to protect humans from the effects of waterborne contaminants that may bioaccumulate in fish; it is referred to as a Health (Fish Consumption) or H(FC) value. The H(FC) value is based on three components, the toxicity of the substance to humans, the extent to which it bioaccumulates in fish, and the rate of fish consumption.

SUMMARY OF INFORMATION

A. Toxicity

U.S. EPA (1995a) conducted a comprehensive evaluation of the oncogenic and non-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's documentation for their criteria for 2,4-dinitrophenol has been reviewed. U.S. EPA does not consider 2,4-dinitrophenol to be carcinogenic, and the Department concludes that 2,4-dinitrophenol is not an oncogen under New York's definition in 6 NYCRR 700.1.

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 (1995a), provides the scientific basis for their non-oncogenic criteria. These data will be used to derive an acceptable daily intake for 2,4-dinitrophenol using New York State procedures as described below.

U.S. EPA (1995a) 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, or 2.0 ug 2,4-dinitrophenol/(kg · day), equivalent to an acceptable daily intake (ADI) developed under NYS procedures (702.5).

B. Bioaccumulation

A measurement of bioaccumulation is necessary to derive a value to protect human consumers of fish. Bioaccumulation is the process by which a substance becomes concentrated in an organism through the organism's exposure to the contaminant in food and water. Bioaccumulation is represented numerically by a bioaccumulation factor, or BAF, which is the ratio of the concentration of a substance in the organism to that in the water column.

The term bioconcentration also describes the concentration of a substance in an organism relative to the concentration in the water column. A bioconcentration factor (BCF), however, is measured with exposure to the contaminant by water only. A BCF may be equal to the BAF for many substances, but can substantially underestimate it for others.

U.S. EPA (1995b) has promulgated, as final Federal regulations, procedures for deriving bioaccumulation factors. The procedures are believed appropriate for deriving statewide values and are being used in this fact sheet.

A key aspect of this procedure is that bioaccumulation is believed to be related to the concentration of freely dissolved substance. Hydrophobic organic substances are considered to exist in water in three phases: freely dissolved, sorbed to dissolved organic matter and sorbed to suspended solids (U.S. EPA, 1995b). Because BAF determinations are often based on measurements of total or dissolved substance, a measured BAF must be adjusted based on the estimated fraction of freely dissolved material. In addition, because measured BAFs are determined based on the percent lipid in the species studied, they are adjusted, or normalized, to 100% lipid to allow comparison of BAFs derived from species with different tissue lipid fractions. A BAF adjusted for both fraction freely dissolved and normalized to 100% lipid is referred to as a "baseline BAF."

Although bioaccumulation is related to the freely dissolved substance, water quality criteria are based on total substance. A baseline BAF, therefore, is readjusted to

a final BAF by the expected fraction freely dissolved and fish lipid content for the waters for which criteria are established. The relationship of field-measured or final BAF to the baseline BAF is shown in equation 1:

(Eq. 1) $$\text{Baseline BAF} = \left[\frac{\text{Field or Final BAF}}{f_{fd}} {}^{-1} \right] \left[\frac{1}{f_l} \right]$$

where f_l = fraction of tissue that is lipid and f_{fd} = fraction of substance that is freely dissolved.

U.S. EPA (1995c) presented the following equation for estimating f_{fd}:

(Eq. 2) $$f_{fd} = \frac{1}{1 + \frac{(DOC)(K_{ow})}{10} + (POC)(K_{ow})}$$

where K_{ow} is the n-octanol-water partition coefficient of the substance in question, and DOC and POC are concentrations of dissolved and particulate organic carbon, respectively, in kg/L. The basis for this equation is described by U.S. EPA (1995c).

When deriving a baseline BAF from a field-measured BAF, DOC and POC levels under which the field BAF was determined are used to calculate a f_{fd}. When the baseline BAF is readjusted to yield a final BAF, the DOC and POC levels appropriate for the applicability of the criterion are used.

Derivation of Baseline BAFs

U.S. EPA (1995c), as part of the documentation for the Great Lakes Water Quality Initiative, presents baseline BAFs for a number of substances. The procedures (U.S. EPA, 1995b,c) provide a hierarchy of methods to calculate a baseline BAF. The only baseline BAF presented by U.S. EPA (1995c) for 2,4-dinitrophenol is a predicted baseline BAF that is based on a predicted BCF and food chain multiplier (FCM). For this, a predicted baseline BCF equals K_{ow} and the FCM is derived from log K_{ow}. A predicted baseline BAF is calculated from a predicted BCF by using the equation:

$$\text{Predicted Baseline BAF} = (FCM)\ (K_{ow})$$

The predicted baseline BAFs for trophic levels 3 and 4 for 2,4-dinitrophenol from U.S. EPA (1995c) are shown in Table 1.

Table 1

Baseline BAFs for 2,4-Dinitrophenol (U.S. EPA, 1995c)

Trophic Level	Baseline BAF (L/kg)
3	37
4	37

These values have been reviewed and are believed appropriate for both the Great Lakes and the rest of the State. The data U.S. EPA used and calculations needed to derive these values are shown below. (Note: The readjustment of these baseline BAFs to final BAFs is described under Derivation of Water Quality Values).

Log K_{ow} is 1.570 (U.S. EPA, 1995c); K_{ow} = 37.2; values for FCM are 1.00 for both trophic levels 3 and 4. For both trophic levels:

Predicted Baseline BAF = (FCM) (K_{ow})
= (1.00) (37.2) = 37.2, or 37 L/kg

DERIVATION OF WATER QUALITY VALUE

As required by 6 NYCRR 702.8(a) the water quality value must equal the acceptable daily intake from fish consumption divided by a bioaccumulation factor and by a fish consumption rate of 0.033 kg/day.

A. Acceptable Daily Intake From Fish Consumption

As required by 6 NYCRR 702.8(b), the most stringent acceptable daily intake from fish consumption is 20% of the ADI for non-oncogenic effects, as determined from 6 NYCRR 702.5. This value is 2.0 ug 2,4-dinitrophenol/(kg · day) as described above. The acceptable daily intake from fish consumption is:

0.2 x 2.0 ug 2,4-dinitrophenol/(kg · day) = 0.40 ug 2,4-dinitrophenol/(kg · day)

B. Final BAF

As described above, a baseline BAF is adjusted by the fish lipid fraction and the fraction freely dissolved to yield a final BAF for the substance. Equation 1 (above) is rearranged to solve for final BAF:

Final BAF = [(baseline BAF)(f_l) + 1](f_{fd})

where values for f_l and f_{fd} are appropriate to criteria for New York State. Because, as described below, humans are exposed to fish from two trophic levels, this calculation is performed to generate final BAFs for trophic levels 3 and 4.

A fish lipid content of 3% had previously been used when calculating BAFs for deriving criteria for New York State. U.S. EPA (1995b) apportions daily fish consumption between fish of trophic levels 3 and 4. Specifically, 24% is assigned to trophic level 3 fish, with a standardized lipid fraction of 0.0182 (1.82%), and 76% to trophic level 4 fish, with a standardized lipid fraction of 0.0310 (3.1%). The weighted average lipid fraction of trophic level 3 and 4 fish is thus 0.028 (2.8%), which is very close to the value of 3% that had been used in New York State. U.S. EPA's apportionment approach is believed to be protective of human consumers of fish statewide, and will be used in the derivation of the water quality value in this fact sheet to achieve consistency with requirements for the Great Lakes System.

For deriving f_{fd} values for the Great Lakes, U.S. EPA (1995b) procedures use DOC and POC values of 2 and 0.04 mg/L respectively. The POC level of 0.04 mg/L is on the low end for the Great Lakes but U.S. EPA selected it to ensure protection throughout the System.

Data on levels of DOC and POC were examined for fresh and marine waters in New York State. Levels of DOC vary somewhat through the State but are fairly close to 2 mg/L. The f_{fd} is not very sensitive to changes in concentration of DOC. Levels of POC in New York State range from zero to several mg/L, but a sufficient number of near-zero values were found such that the level that EPA uses for the Great Lakes System seems appropriate for statewide standards and at the same time provides consistency with the Federal requirements for the Great Lakes System.

Using these values for DOC and POC, equation 2 (above) becomes:

$$f_{fd} = \frac{1}{1 + (0.00000024\ kg/L)(K_{ow})}$$

With a K_{ow} of 37.2, the fraction freely dissolved is calculated to be 1.000.

As described above, the baseline BAFs for 2,4-dinitrophenol for trophic levels 3 and 4 are each 37 L/kg.

The final BAF for trophic level 3 is calculated as:

Final BAF_{TL3} = [(baseline BAF_{TL3})($f_{l\ TL3}$) + 1](f_{fd}) =

Final BAF_{TL3} = [(37 L/kg)(0.0182) + 1](1.000) = 1.67 L/kg

The final BAF for trophic level 4 is calculated as:

Final BAF_{TL4} = [(baseline BAF_{TL4})($f_{l\ TL4}$) + 1](f_{fd}) =

Final BAF_{TL4} = [(37 L/kg)(0.0310) + 1](1.000) = 2.15 L/kg

C. Human Exposure (Fish Consumption)

6 NYCRR 702.8 requires that H(FC) values be based on a fish consumption rate of 0.033 kg/day.

D. Calculation of Water Quality Value

The water quality value (WQV) is derived using a human body weight of 70 kg and a daily fish consumption rate of 0.033 kg as shown below. The fish consumption is apportioned as 24% trophic level 3 and 76% trophic level 4.

$$WQV = \frac{\text{Acceptable Daily Intake from Fish Consumption x 70 kg}}{[(BAF_{TL3})(0.24) + (BAF_{TL4})(0.76)] \text{ x } 0.033 \text{ kg/day}}$$

$$WQV = \frac{0.40 \text{ ug 2,4-dinitrophenol/(kg} \cdot \text{day) x 70 kg}}{[(1.67 \text{ L/kg})(0.24) + (2.15 \text{ L/kg})(0.76)] \text{ x } 0.033 \text{ kg/day}}$$

= 417 ug/L, rounded to 400 ug/L

REFERENCES

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: Department of Environmental Conservation.

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

U.S. EPA (Environmental Protection Agency). 1995b. Final Water Quality Guidance for the Great Lakes System. 60 Federal Register: 15366-15425. March 23, 1995.

U.S. EPA (Environmental Protection Agency). 1995c. Great Lakes Water Quality Initiative Technical Support Document for the Procedure to Determine Bioaccumulation Factors. Office of Water. EPA-820-B95-005.

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
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.