Fact Sheet Date: March 12, 1998

NEW YORK STATE
- HUMAN HEALTH FACT SHEET -

Ambient Water Quality Value
Based on Human Consumption of Fish

SUBSTANCE: Toluene **CAS REGISTRY NUMBER:** 108-88-3

AMBIENT WATER QUALITY VALUE: 6000 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 toluene 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 toluene has been reviewed. U.S. EPA does not consider toluene to be carcinogenic, and the Department concludes that toluene is not an oncogen under New York's definition in 6 NYCRR 700.1.

The Department reviewed the toxicological basis for U.S. 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 toluene using New York State procedures as described below.

U.S. EPA (1995a) selected the results of the study by NTP (1990) 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 0.223 mg/(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, 1995c). 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 toluene 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:

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

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

Table 1 Baseline BAFs for Toluene (U.S. EPA, 1995c)	
Trophic Level	Baseline BAF (L/kg)
3	527
4	516

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 2.713 (U.S. EPA, 1995c); K_{ow} = 516

The FCMs, from U.S. EPA (1995b) are 1.018 and 1.004 for trophic levels 3 and 4, respectively.

$$\text{Predicted Baseline } BAF_{TL3} = (FCM_{TL3})\ (K_{ow})$$

$$= (1.018)\ (516) = 525 \text{ L/kg}$$

$$\text{Predicted Baseline } BAF_{TL4} = (FCM_{TL4})\ (K_{ow})$$

$$1$$

$$= (1.004)\ (516) = 518 \text{ L/kg}$$

These values are slightly different than the values presented in Table 1; the difference is considered negligible and due to rounding. For consistency with U.S. EPA, this fact sheet will use the values in Table 1 as the baseline BAFs for toluene.

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 0.223 mg [≡ 223 ug] toluene/(kg · day) as described above. The acceptable daily intake from fish consumption is:

0.2 x 223 ug toluene/(kg · day) = 44.6 ug toluene/(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 (1995a) 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 (1995a) 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 U.S. 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 516, the fraction freely dissolved is calculated to be 1.000

As described above, the baseline BAFs for toluene for trophic levels 3 and 4 are 527 and 516 L/kg respectively.

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} = [(527 L/kg)(0.0182) + 1](1.000) = 10.6 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} = [(516 L/kg)(0.0310) + 1](1.000) = 17.0 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.

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

$$WQV = \frac{44.6\ ug\ toluene/(kg \cdot day) \times 70\ kg}{[(10.6\ L/kg)(0.24) + (17.0\ L/kg)(0.76)] \times 0.033\ kg/day}$$

= 6120 ug/L, rounded to 6000 ug/L

REFERENCES

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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

February 6, 1997

EXHIBIT I

GREAT LAKES WATER QUALITY INITIATIVE
TIER 1 HUMAN HEALTH CRITERIA FOR
TOLUENE
CAS NO. 108-88-3

Tier 1 Human Noncancer Criterion

A review of the available literature indicates inadequate human data for quantitative risk assessment of toluene based on human health effects. Occupational exposure, cigarette smoking and deliberate inhalation of solvents found in various preparations ("glue sniffing") are common means of human exposure to toluene (NTP, 1990). Chronic exposure to toluene vapors at levels of approximately 200-800 ppm have been associated primarily with CNS effects, possibly peripheral nervous system effects, hepatomegaly and hepatic function changes, and renal function effects (EPA, 1987). Although these findings provide qualitative evidence of the human toxicity of toluene, specific exposure levels were not provided and these data do not provide a dose-response relationship (EPA, 1987; EPA, 1990; NTP, 1990).

The majority of the subchronic-chronic studies on toluene are inhalation studies determining behavioral or histopathologic effects of toluene exposure. The most appropriate basis for HNV derivation for toluene is the NOAEL from a 13-week rat gavage study (NTP, 1990). In this study, toluene in corn oil was administered by gavage to groups of weanling F344/N rats and B6C3F1 mice (10/sex/group) at dose levels of 0, 312, 625, 1250, 2500 or 5000 mg/kg, 5 days per week for 13 weeks. All rats at 5000 mg/kg died during the first week, and 8/10 rats at 2500 mg/kg died, two of which were due to gavage errors. Histopathologic changes were observed in the liver, kidney, brain and urinary bladder at $\geq$ 1250 mg/kg. The NOAEL for the rats is 312 mg/kg/day with a LOAEL based on liver and kidney weight changes in male rats at 625 mg/kg. Because the exposure was for 5 days/week, these doses are converted to time-weighted-average doses of 223 and 446 mg/kg/day, respectively (EPA, 1990).

As described above, NTP (1990) also conducted a 13-week gavage study in B6C3F1 mice. All mice that received 5000 mg/kg died during the first week, and 40% of those that received 2500 mg/kg died before the end of the 13-week gavage study. Clinical signs observed in mice at $\geq$ 2500 mg/kg included sub-convulsive jerking, prostration, impaired grasping reflex, bradypnea, hypothermia, hypoactivity and ataxia. The final mean body weight of males at 2500 mg/kg was lower than that of vehicle controls. At $\geq$ 1250 mg/kg, relative liver weights were increased for mice, but this increase was not statistically significant. The NOAEL for this study was 1250 mg/kg and the LOAEL was 2500 mg/kg. Adjusting the doses for 5 days/week exposure provides time-weighted-average NOAEL and LOAEL doses of 893 and 1786 mg/kg/day, respectively.

Another subchronic oral toxicity study was conducted by Wolf et al. (1956), in which female Wistar rats were administered toluene by stomach tube at doses of 0, 118, 354 and 590 mg/kg/day, 5 days/week for a total of 138 doses (converted to time-weighted-average doses of approximately 0, 18, 253, and 422 mg/kg/day per EPA, 1990). No adverse effects were observed at any dose level in any of the parameters monitored: growth, appearance and behavior, mortality, organ/body weight, blood urea nitrogen levels, bone marrow counts, peripheral blood counts or morphology of major organs. The NOAEL for this study was 422 mg/kg/day as the time-weighted-average dose.

NYLAR mice were exposed pre- and post-natally to toluene provided in the drinking water at concentrations of 0, 16, 80 and 400 ppm (Kostas and Hotchin, 1981). Rotorod performance was measured at 45 and 55 days of age. An inverse dose-response relationship in the effects was noted in which rotorod performance was improved with increasing dose. No effects were observed for the following reproductive measurements: maternal fluid consumption, offspring mortality rate, development of eye or ear openings, or surface-righting response, resulting in a NOAEL of 400 ppm. Assuming mice consume water at appoximately 0.24 l/kg bw/day (EPA, 1988), the NOAEL was approximately 96 mg/kg/day.

Nawrot and Staples (1979) administered 0.3, 0.5 or 1.0 ml/kg bw toluene, 3 times/day (equivalent to approximately 780, 1300 and 2600 mg/kg/day, per EPA, 1990) to pregnant CD-1 mice from days 6-15 of gestation. No method of exposure was mentioned in this limited information abstract. Teratogenic effects were reported at 2600 mg/kg/day and increased embryolethality was reported at $\geq$ 780 mg/kg/day, therefore the LOAEL for this study was 780 mg/kg/day.

No other subchronic-chronic oral toxicity studies were identified in the available literature for toluene. Chronic inhalation studies include NTP (1990), in which F344/N rats and B6C3F1 mice (60/sex/dose) were exposed to vapors of toluene, 6.5 hours/day, 5 days/week for 2 years. Dose levels were 0, 120 (mice only), 600 or 1200 ppm. Ten animals/group (except male mice) were removed at 15 months for toxicologic evaluation. At 15 months, there was an increased incidence and severity in the erosion of olfactory epithelium, and degeneration of respiratory epithelium was increased in the exposed rats. At the end of the study inflammation of nasal mucosa and metaplasia of olfactory epithelium were increased in exposed females rats. Nephropathy was seen in almost all rats with a severity somewhat increased in exposed rats. For mice, no biologically relevant increase in any nonneoplastic lesion was observed.

Chronic inhalation of toluene was studied in F344 rats exposed to 30, 100 or 300 ppm (113, 377 or 1130 mg/m^3) toluene 6 hours/day, 5 days/week for 24 months (Gibson and Hardisty, 1983; CIIT, 1980, as cited in NTP, 1990; EPA, 1990; and EPA, 1987). A dose-related reduction in hematocrit values was reported in female rats exposed to 100 and 300 ppm. Increased corpuscular hemoglobin concentration was reported in females at 300 ppm.

In a perinatal study with CD-1 mice (Courtney et al., 1986), toluene was administered by

inhalation at 200 and 400 ppm (750 and 1500 mg/m^3, respectively) to pregnant female CD-1 mice 7 hours/day from days 6-16 of gestation. Fetotoxicity was observed at 400 ppm with a significant shift in the fetal rib profile. An increased body weight in the neonates on day 1 postpartum was observed at 400 ppm. At 200 ppm, there was an increase in dilated renal pelves which the authors concluded might reflect desynchronization of maturation with respect to development and growth. Assuming that mice breathe appoximately 1.7 m^3/kg/day (EPA, 1988), the 7 hours/day 200 ppm LOAEL and 400 ppm FEL convert to approximately 370 and 740 mg/kg/day, respectively, as daily administered doses.

The Tier 1 HNC is derived from the NOAEL dose of 312 mg/kg (converted to 223 mg/kg/day for 5 days/week administration) from the 13-week oral rat study by NTP (1990) with an uncertainty factor of 1000. The uncertainty factor accounts for interspecies variation, intraspecies differences, and subchronic exposure duration. This approach should be protective of developmental effects, as suggested by the limited developmental toxicity data. This approach is consistent with the risk assessment of toluene for the oral RfD and the drinking water health advisory developed by EPA (1990; 1987).

$$\text{ADE} = \frac{223 \text{ mg/kg/d}}{1{,}000} = 2.23 \times 10^{-1} \text{ mg/kg/day}$$

Where: Uncertainty Factor = 1,000, composed of:

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

References:

Chemical Industry Institute of Technology (CIIT). 1980. A 24-Month Inhalation Toxicology Study in Fischer-344 Rats Exposed to Atmospheric Toluene. CIIT, Research Triangle Park, NC. As cited in EPA, 1987; EPA, 1990; NTP, 1990.

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