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: Benzene **CAS REGISTRY NUMBER:** 71-43-2

AMBIENT WATER QUALITY VALUE: 1 ug/L

BASIS: Oncogenic

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 1 ug/L is selected for benzene as described under "Selection of Value."

II PRINCIPAL ORGANIC CONTAMINANT CLASSES AND SPECIFIC MCL (702.3)

A. Discussion

Benzene does not have a Specific MCL as defined in 700.1. However, benzene is in principal organic contaminant class iv as defined in 700.1.

The U.S. Environmental Protection Agency has established a maximum contaminant level goal (MCLG) of zero ug/L and a MCL of 5 ug/L for drinking water for benzene.

Under the State Sanitary Code (10 NYCRR Part 5, Public Water Supplies),

the New York State Department of Health has established a general maximum contaminant level of 5 ug/L for principal organic contaminants such as benzene in drinking water.

B. Derivation of Water Quality Value

Because benzene is in a principal organic contaminant class and has no Specific MCL, regulations require that the water quality value not exceed 5 ug/L.

III ONCOGENIC EFFECTS (702.4)

U.S. EPA conducted a comprehensive evaluation of the oncogenic effects of benzene as part of its criteria development for the Great Lakes Water Quality Initiative (GLI) (U.S. EPA, 1995). 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 benzene is an oncogen under New York's definition in 6 NYCRR 700.1 and that U.S. EPA's toxicological basis is appropriate for derivation of a statewide value.

Exhibit I, excerpted from U.S. EPA (1995), provides U.S. EPA's scientific basis for their criteria. These data will be used to calculate a water quality value for protection from oncogenic effects using New York State procedures as described below.

U.S. EPA (1995) selected the results of the Rinsky et al. (1981) and Ott et al. (1978) epidemiologic studies as the most appropriate dose-response data for deriving a water quality value. A summary of the data sets showing statistically and biologically significant increases in response is presented in Exhibit I. U.S. EPA derived an oral cancer slope factor of 2.9×10^{-2} $[mg/(kg \cdot day)]^{-1}$ from the geometric mean of four maximum likelihood point estimates from the above studies, which was adjusted for the results in Wong et al. (1983).

The slope factor is converted to a human dose, at a lifetime risk level of one-in-one million as shown below.

$$\text{Human dose} = \frac{\text{risk}}{\text{slope}} = \frac{10^{-6}}{2.9 \times 10^{-2}\ [mg/(kg \cdot day)]^{-1}}$$

$$= 3.4 \times 10^{-5}\ mg/(kg \cdot day) \equiv 0.034\ ug/(kg \cdot day)$$

The human dose above is converted to a potential water quality value based on a 70 kg adult consuming 2 liters of water per day as follows:

$$\text{Water Quality Value} = \frac{[0.034 \text{ ug/(kg} \cdot \text{day)}]\ [70 \text{ kg}]}{[2 \text{ L/day}]} = 1.2 \text{ ug/L, rounded to 1 ug/L}$$

IV NON-ONCOGENIC EFFECTS (702.5)

U.S. EPA (1995) also conducted a comprehensive review of toxicological data on non-oncogenic effects for benzene 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 II, 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 Wolf et al. (1956) 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 7.1×10^{-4} 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:

$$\text{Water Quality Value} = \frac{[7.1 \times 10^{-4} \text{ mg/(kg} \cdot \text{day)}]\ [1000 \text{ ug/mg}]\ [70 \text{ kg}]\ [0.2]}{[2 \text{ L/day}]} = 5 \text{ ug/L}$$

V CHEMICAL CORRELATION (702.7)

A value based on chemical correlation for oncogenic or non-oncogenic effects is not applicable because data are sufficient to evaluate these effects.

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 oncogenic value of 1 ug/L (6 NYCRR 702.4) is the most stringent value derived by these procedures and is the ambient water quality value for benzene.

VII 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: 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
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EXHIBIT I
(From U.S. EPA, 1995)

GREAT LAKES WATER QUALITY INITIATIVE
TIER I HUMAN HEALTH CRITERIA FOR BENZENE
CAS NO. 71-43-2

Tier 1 Human Cancer Criterion

According to the weight-of-evidence method for the classification of carcinogens, benzene is a Class A carcinogen (known human carcinogen) (IARC, 1982; EPA, 1987; 1989). This is based on sufficient evidence from epidemiologic studies on the incidence of non-lymphocytic leukemia from occupational exposure, and increased incidence of neoplasms in rats and mice exposed to benzene by inhalation and gavage (EPA, 1987). In addition, numerous studies have found a significant increase in chromosomal aberrations of bone marrow cells and peripheral lymphocytes from workers exposed to benzene (IARC, 1982). The data are sufficient to derive a Tier 1 HCC for benzene.

Numerous epidemiologic and case studies have shown a relationship between leukemia and exposure to benzene (IARC, 1982). The oral slope factor for benzene based on human data is estimated to be 2.9E-2 $(mg/kg/day)^{-1}$ (EPA, 1987). The unit risk estimate is based on the geometric mean of four maximum likelihood point estimates using pooled data from the studies of Rinsky et al. (1981) and Ott et al. (1978), which was then adjusted for the results from the Wong et al. (1983) study as described by EPA (1987).

The slope factor (q_1^*) of the dose-response curve for the carcinogenic effects of benzene by the oral route, 2.9E-2 $(mg/kg/day)^{-1}$ is used in the calculation of the HCC for benzene.

References:

International Agency for Research on Cancer (IARC). 1982. IARC Monograph: Evaluation of the Carcinogenic Risk of Chemicals to Humans, Volume 29, WHO Publications Center, USA, Albany, NY, pp 1-416.

Ott, M.G., J.C. Townsend, W.A. Fishbeck and R.A. Langner. 1978. Mortality among individuals occupationally exposed to benzene. Arch. Environ. Health., 33: 3-10.

Rinsky. R.A., R.J. Young and A.B. Smith. 1981. Leukemia in benzene workers. Am. J. Ind. Med. 2: 217-245.

U.S. Environmental Protection Agency (EPA). 1987. Health Effects Assessment for Benzene. EPA/600/8-89/086. Cincinnati, OH.

U.S. Environmental Protection Agency (EPA). 1987. Integrated Risk Information System (IRIS database). Chemical file for benzene (CAS No. 71-43-2). Verification Date 10/9/87. Last Reviewed 10/9/87.

U.S. Environmental Protection Agency (EPA). 1980. Ambient Water Quality Criteria Document for Benzene. Washington, DC. EPA 440/5-80-018.

Wong, O., R.W. Morgan and M.D. Wharton. 1983. Comments on the NIOSH study of leukemia in benzene workers. Technical report submitted to Gulf Canada, Ltd., by Environmental Health Associates.

EXHIBIT II
(From U.S. 1995)

GREAT LAKES WATER QUALITY INITIATIVE
TIER I HUMAN HEALTH CRITERIA FOR BENZENE
CAS NO. 71-43-2

Tier 1 Human Noncancer Criterion

Acute exposure to benzene vapors by humans is often associated with neurotoxicity characterized by loss of sensation, vertigo, headache and depression of the central nervous system. Hematopoietic toxicity involving changes in the bone marrow, spleen, and thymus has been associated with benzene exposure. Benzene has also been found to cause embryo/fetotoxicity in experimental animals (EPA, 1980).

There are few chronic or oral studies available which examine the noncarcinogenic effects of benzene. The subchronic oral study by Wolf et al. (1956) was considered appropriate for Tier 1 HNC derivation. In this study, female Wistar rats in groups of 10 were administered benzene in olive oil by gavage for 5 days/week for six months. A group of 20 rats served as controls. Dose levels were 0, 1, 10, 50, and 100 mg/kg/bw/day. During this period hematologic examinations were performed on selected animals. Growth, body weight, organ weights, behavior, urea nitrogen in blood, histopathological changes and bone marrow counts were also evaluated. Rats exposed to 50 and 100 mg/kg/day exhibited leukopenia and erythrocytopenia, whereas these effects were marginal in the 10 mg/kg/day group. The 1 mg/kg/day dose level was considered the NOAEL for this study. This dose is equivalent to 0.71 mg/kg/day after being adjusted for exposure for only 5 days/week.

The findings of the Wolf et al. (1956) study are supported by the results of a chronic study by NTP (1986). In this study, C57BL16N mice and F344 rats (50 animals/sex/group) were administered benzene orally at doses of 0, 50, 100 or 200 mg/kg, 5 days/week, for 103 weeks. An additional group consisting of female rats and mice of both sexes were administered 25 mg/kg. Blood was taken for analysis from 10 animals/sex/group at various times during the study. The results of the study showed dose-related leukopenia in rats and mice of each sex for the first 18 months of the study. However, at 24 months, the numbers of white blood cells in high dose male rats, high dose female rats, and mid-dose male mice were higher than controls. Numbers of white blood cells in dosed female mice were not significantly different from controls.

Hematopoietic toxicity of benzene following exposure via inhalation was reported by Deichmann et al. (1963). In this study, groups of male and female Sprague-Dawley rats were exposed 5 hours/day, 4 days/week, for periods ranging from 5 weeks to 7 months, to benzene concentrations of 0, 15, 29, 31, 44, 47, 61, 65, or 831 ppm. Several hematologic parameters, and other parameters including body weight, food intake and

blood benzene levels were determined periodically during the study. Following 2-4 weeks of exposure, groups exposed to benzene concentrations of 61 to 831 ppm demonstrated a significantly increased level of leukopenia. Hematopoietic effects were moderate in groups exposed to 44 to 47 ppm for 5-8 weeks. Exposure to 31 ppm benzene for over 4 months did not induce changes in the hematopoietic system and was considered a NOAEL for this study. Based on the conditions of exposure and an assumed absorption factor of 50% (EPA, 1987), a NOAEL of 2.35 mg/kg/day was calculated. This value is comparable to the value calculated in the Wolf et al. (1956) study.

EPA (1985) suggested that the Wolf et al. (1956) and Chang (1972) studies could be used to establish a range of acceptable daily intake (ADI) values. In the Chang (1972) study 119 workers occupationally exposed to benzene were examined. Hematological abnormalities were reported in 28 of the workers. These abnormalities included 21 workers with anemia, 2 with leukopenia, and 5 with anemia and leukopenia. Based on an estimate of exposure duration and benzene concentration, the researcher derived an exponential function which suggested a threshold level of 10 ppm for hematologic effects. This study was not used for criterion development due to the absence of reliable data on the actual exposure concentrations for the individual employees.

Rozen et al. (1984) examined the effect of inhalation exposure to 0, 10, 31, 100 and 301 ppm benzene on B- and T-lymphocyte mitogen-induced blastogenesis in C57B1 mice. Exposure to benzene at all doses for 6 hours/day for 6 days resulted in a significant depression in femoral lipopolysaccharide (LPS)-induced B-colony forming ability while total numbers of B-lymphocytes were significantly depressed at 100 and 300 ppm. Splenic phytohemagglutinin (PHA)-induced blastogenesis was significantly depressed at 31, 100 and 300 ppm while total numbers of T-lymphocytes were significantly depressed at 100 and 300 ppm. This study was not used for risk assessment because it used the inhalation route of exposure and it is questionable whether the effects produced in this study are biologically significant and adverse.

Few studies using the oral route of exposure have examined the reproductive/developmental effects of benzene. Nawrot and Staples (1979) administered 0.3, 0.5 or 1.0 ml/kg/day (790, 1320 and 2640 mg/kg/day, respectively) benzene to pregnant CD-1 mice during days 6-15 or 12-15 of gestation. Despite some maternal lethality and embryonic resorptions at the two higher doses, no evidence of teratology was seen.

$$\text{ADE} = \frac{\text{NOAEL}}{\text{UF}} = \frac{0.71 \text{ mg/kg/d}}{1000} = 7.1 \times 10^{-4} \text{ mg/kg/d}$$

Where: Uncertainty Factor = 1000, composed of:
- 10x for interspecies variability
- 10x for intraspecies differences
- 10x for subchronic exposure duration

References:

Chang, I.W. 1972. Study on the threshold limit value of benzene and early diagnosis of benzene poisoning. J. Cath. Med. Coll. 23:429.

Deichmann, W.B., W.E. MacDonald. and E. Bernal. 1963. The hematopoietic tissue toxicity of benzene vapors. Toxicol. Appl. Pharmacol. 5:201-224.

International Agency for Research on Cancer (IARC). 1982. IARC Monograph: Evaluation of the Carcinogenic Risk of Chemicals to Humans, Volume 29, WHO Publications Center, USA, Albany, NY, pp 1-416.

National Toxicology Program (NTP). 1986. Toxicology and Carcinogenesis Studies of Benzene in F344/N Rats and B6C3F1 Mice (Gavage Studies). NTP Technical Report Series. 289., National Toxicology Program, Research Triangle Park, NC.

Nawrot, P.S. and R.F. Staples. 1979. Embryo-fetal toxicity and teratogenicity of benzene and toluene in the mouse. Teratology. 19:41a.

Rozen, M.G., C.A. Snyder, and R.E. Albert. 1984. Depressions in B- and T-lymphocyte mitogen-induced blastogenesis in mice exposed to low concentrations of benzene. Toxicol. Letters. 20:343-349.

U.S. Environmental Protection Agency (EPA). 1987. Integrated Risk Information System (IRIS database). Chemical file for benzene (CAS No. 71-43-2). Verification Date 10/9/87. Last Reviewed 10/9/87.

U.S. Environmental Protection Agency (EPA). 1985. Drinking Water Criteria Document for Benzene (Final Draft). U.S. Environmental Protection Agency, PB86-118122. Washington, D.C.

U.S. Environmental Protection Agency (EPA). 1980. Ambient Water Quality Criteria Document for Benzene. Washington, DC. EPA 440/5-80-018.

Wolf, M.A., V.K. Rowe, D.D. McCollister, R.L. Hollingsworth and F. Oyen. 1956. Toxicological studies of certain alkylated benzenes and benzene. A.M.A. Arch. Indust. Health. 14:357-398.