

AMBIENT SURFACE WATER QUALITY  
STANDARDS DOCUMENTATIONCHEMICAL: BenzidineCAS NO.(s): 92-87-5BASIS (Human/Aquatic): HumanWATER CLASSIFICATION: AA; AA-s; A; A-sSTANDARD: 0.02 ug/l Note AREMARKS:SUMMARY INFORMATION:

The toxicologic data base for this compound has been reviewed.<sup>1-3</sup> It is an animal oncogen as defined in Part 701.1(p). Chronic exposure of laboratory animals to this compound via the diet or after gavage or subcutaneous doses has resulted in a significant increase in the incidence of liver tumors (mice and hamsters), mammary and zymbal gland tumors (rats) and bladder tumors (dogs).<sup>2,4</sup> It is also a human carcinogen.<sup>2</sup> A carcinogenesis bioassay sponsored by the National Toxicology Program is in progress and the standard may be modified once the results are available for review.

STANDARD DERIVATION:

Dose-response data from the Vesselinovitch et al.<sup>4</sup> bioassay were used for extrapolation. Using the protocol in Part 701.4 and a linearized multistage extrapolation procedure (GLOBAL82)<sup>5</sup>, a benzidine concentration of 0.02 ug/l in water was calculated to correspond to an increased human cancer risk of  $1 \times 10^{-6}$  over a lifetime (see calculations below). The recommended ambient water quality standard for benzidine is 0.02 ug/l.

Calculations:1. Vesselinovitch et al. Bioassay Data

The incidence of liver tumors in female mice fed benzidine dihydrochloride in the diet at time-weighted average levels of 0, 50 and 100 ppm during the exposure period is the dose-response data for the most sensitive tumor type in the most sensitive species and sex, occurring at a statistically significant level.

2. Average Daily Intake (for animals)\*

<u>Concentration in diet</u>	<u>Average Daily Intake During Lifetime</u>
0	0 mg/kg/day
50 ppm	3.6 mg/kg/day
100 ppm	7.2 mg/kg/day

\*Since specific information on food consumption was not provided, the general formula ppm in diet x 0.10 = daily dose in mg/kg/day was used to calculate the average daily intake for mice at each dose level during exposure. In addition, mice were exposed to benzidine dihydrochloride and since benzidine comprises 72% of the molecular weight of that compound, doses were multiplied by 0.72 to calculate average daily doses of benzidine during lifetime.

3. Data Input for GLOBAL82 Computer Program

<u>Dose (mg/kg/day)</u>	<u># of animals with tumors</u>	<u># of experimental animals</u>
0	0	100
3.6	13	50
7.2	32	50

4. GLOBAL82 Result (for animals)

The lower 95% confidence limit value of the benzidine dose corresponding to an increased lifetime cancer risk of  $1 \times 10^{-6}$  for the experimental animals was  $7.9 \times 10^{-3}$  ug/kg/day.

5. Conversion of the animal dose (ug/kg/day) to a human dose using surface area conversion rule

$$\text{rodent dose (ug/kg/day)} \times \left( \frac{\text{animal body wt. (kg)}}{\text{human body wt. (kg)}} \right)^{0.33} = \text{human dose (ug/kg/day)}$$

$$7.9 \times 10^{-3} \text{ ug/kg/day} \times \left( \frac{0.03 \text{ kg}}{70 \text{ kg}} \right)^{0.33} = 6.1 \times 10^{-4} \text{ ug/kg/day}$$

6. Calculation of the benzidine level in water corresponding to an increased cancer risk of  $1 \times 10^{-6}$  for a 70 kg human ingesting 2 liters of contaminated water per day over a lifetime.

$$\frac{0.00061 \text{ ug/kg/day} \times 70 \text{ kg}}{2 \text{ l/day}} = 2.1 \times 10^{-2} \text{ ug/l}$$

REFERENCES:

- (1) International Agency for Research on Cancer. 1972. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 1: 80-86.
- (2) International Agency for Research on Cancer. 1982. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 29: 149-183.
- (3) U.S. Environmental Protection Agency. 1980. Ambient water quality criteria for benzidine. NTIS No. PB81-117343.
- (4) Vesselinovitch, S.D. et al. 1975. Factors modulating benzidine carcinogenicity bioassay. Cancer Res. 35: 2814-2819.
- (5) Howe, R.B. and K.S. Crump. 1982. GLOBAL82 Computer Program. Science Research Systems, Inc. Ruston, LA.

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