VALUE(S) ADDED 7-24-85

FACT SHEET REVISED _____

VALUE(S) REMOVED _____

AMBIENT SURFACE WATER QUALITY STANDARDS DOCUMENTATION

CHEMICAL: Azobenzene

CAS NO.(s): 103-33-3

BASIS (Human/Aquatic): Human

WATER CLASSIFICATION: AA; AA-s; A; A-s

STANDARD: 0.5 ug/l Note A

REMARKS:

SUMMARY INFORMATION:

The toxicologic data base for this compound has been reviewed.[1] It is an animal oncogen as defined in Part 701.1(p). Chronic exposure of laboratory animals to this compound via the diet has resulted in a significant increase in the incidence of tumors of the spleen and other abdominal organs in male and female rats.[2] It has also shown genotoxic activity in short-term tests.[3-5]

STANDARD DERIVATION:

Dose-response data from a National Cancer Institute[3] carcinogenesis bioassay were used for extrapolation. Using the protocol in Part 701.4 and a linearized multistage extrapolation procedure (GLOBAL82)[6], an azobenzene concentration of 0.5 ug/l in water was calculated to correspond to an increased human cancer risk of 1×10^{-6} over a lifetime (see calculations below). The recommended ambient water quality standard for azobenzene is 0.5 ug/l.

Calculations:

1. National Cancer Institute Bioassay Data

The incidence of mesenchymal tumors of the abdominal viscera in male rats fed azobenzene in the diet at levels of 0, 200 and 400 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)*

Concentration in diet	Average Daily Intake During Lifetime
0	0 mg/kg/day
200 ppm	10 mg/kg/day
400 ppm	20 mg/kg/day

*Since specific information on food consumption was not provided, the general formula ppm in diet x 0.05 = daily dose in mg/kg/day was used to calculate the average daily intake for rats at each dose level during exposure.

3. Data Input for GLOBAL82 Computer Program

Dose (mg/kg/day)	Number of animals with tumors	Number of experimental animals
0	0	20
10	6	49
20	31	49

4. GLOBAL82 Result (for animals)

The lower 95% confidence limit value of the azobenzene dose corresponding to an increased lifetime cancer risk of 1×10^{-6} for the experimental animals was 8×10^{-2} ug/kg/day.

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

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

$$8 \times 10^{-2} \text{ ug/kg/day} \times \left(\frac{0.40 \text{ kg}}{70 \text{ kg}}\right)^{0.33} = 1.5 \times 10^{-2} \text{ ug/kg/day}$$

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

$$\frac{0.015 \text{ ug/kg/day} \times 70 \text{ kg}}{.2 \text{ l/day}} = 0.52 \text{ ug/l}$$

REFERENCES:

(1) International Agency for Research on Cancer. 1975. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 8: 75-81.

(2) National Cancer Institute. 1979. Bioassay of azobenzene for possible carcinogenicity. Carcinogenesis Tech. Rep. Ser. No. 154.

(3) Sina, J.F. et al. 1983. Evaluation of the alkaline elution/rat hepatocyte assay as a predictor of carcinogenic/mutagenic potential. Mut. Res. 113: 357-391.

(4) McCann, J. et al. 1975. Detection of carcinogens as mutagens in the Salmonella/microsome test: assay of 300 chemicals. Proc. Nat. Acad. Sci. USA. 72: 5135-5139.

(5) Gaudin, D. et al. 1971. DNA repair inhibition: a possible mechanism of action of cocarcinogens. Biochem. Biophy. Res. Comm. 45: 630-636.

(6) Howe, R.B. and K.S. Crump. 1982. GLOBAL82 Computer Program. Science Research Systems, Inc., Ruston, LA.

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