VALUE(S) ADDED 7-24-85

FACT SHEET REVISED _____

VALUE(S) REMOVED _____

AMBIENT SURFACE WATER QUALITY STANDARDS DOCUMENTATION

CHEMICAL: o-Toluidine

CAS NO.(s): 95-53-4

BASIS (Human/Aquatic): Human

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

STANDARD: 0.6 ug/l Note A

REMARKS:

SUMMARY INFORMATION:

The toxicologic data base for this compound has been reviewed.[1,2] 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 at a wide variety of sites in male and female rats and mice, including the liver, spleen, scrotum, abdominal cavity, subcutaneous tissue, urinary bladder and mammary gland.[3,4]

STANDARD DERIVATION:

Dose-response data from the National Cancer Institute[3] bioassay were used for extrapolation. Using the protocol in Part 701.4 and a linearized multistage extrapolation procedure (GLOBAL82)[5], an o-toluidine concentration of 0.6 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 o-toluidine is 0.6 ug/l.

Calculations:

1. National Cancer Institute Bioassay Data

The incidence of tumors of the subcutaneous tissue in male rats fed o-toluidine hydrochloride in the diet at levels of 0, 3,000 and 6,000 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
3,000 ppm	112 mg/kg/day
6,000 ppm	225 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. In addition, rats were exposed to o-toluidine hydrochloride and since o-toluidine comprises 75% of the molecular weight of that compound, doses were multiplied by 0.75 to calculate average daily doses of o-toluidine during lifetime.

3. Data Input for GLOBAL82 Computer Program

Dose (mg/kg/day)	Number of animals with tumors	Number of experimental animals
0	0	20
112	28	50
225*	27*	49*

*Since the dose-response data indicate that the number of responders reached a plateau at an average daily dose of 112 mg/kg, the data from the highest dose level were omitted from input into the GLOBAL82 program.

4. GLOBAL82 Result (for animals)

The lower 95% confidence limit value of the o-toluidine dose corresponding to an increased lifetime cancer risk of 1×10^{-6} for the experimental animals was 0.10 ug/kg/day.

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

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

$$0.10 \text{ ug/kg/day} \times \left(\frac{0.37 \text{ kg}}{70 \text{ kg}}\right)^{0.33} \approx 0.018 \text{ ug/kg/day}$$

6. Calculation of the o-toluidine 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.

$$\frac{0.018 \text{ ug/kg/day} \times 70 \text{ kg}}{2 \text{ l/day}} = 0.62 \text{ ug/l}$$

REFERENCES:

(1) International Agency for Research on Cancer. 1978. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 16: 349-366.

(2) International Agency for Research on Cancer. 1982. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. 27: 155-175.

(3) National Cancer Institute. 1979. Bioassay of o-toluidine hydrochloride for possible carcinogenicity. Carcinogenesis Tech. Rep. Ser. No. 153..

(4) Weisburger, E.K. et al. 1978. Testing of twenty-one environmental aromatic amines or derivatives for long-term toxicity or carcinogenicity. J. Environ. Path. Toxicol. 2: 325-356.

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

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