

**AMBIENT SURFACE WATER QUALITY  
STANDARDS DOCUMENTATION****CHEMICAL:** 5-Chloro-o-toluidine**CAS NO. (s):** 95-79-4**BASIS (Human/Aquatic):** Human**WATER CLASSIFICATION:** AA; AA-S; A; A-S**STANDARD:** 0.7 ug/l **Note A****REMARKS:****SUMMARY INFORMATION:**

The toxicologic data base for this compound is limited. However, 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 hemangiosarcomas (numerous sites) and liver tumors in male and female mice.<sup>1</sup> Although corroboration of the oncogenicity of 5-chloro-o-toluidine is lacking, it is structurally similar to 4-chloro-o-toluidine which was also oncogenic in mice exposed via the diet and which also caused hemangiosarcomas at numerous sites.<sup>2</sup> In addition, both compounds may have induced a dose-related increase in the occurrence of adrenal gland tumors in rats.

**STANDARD DERIVATION:**

Dose-response data from a National Cancer Institute<sup>1</sup> carcinogenesis bioassay were used for extrapolation. Using the protocol in Part 701.4 and a linearized multistage extrapolation procedure (GLOBAL82)<sup>3</sup>, a 5-chloro-o-toluidine concentration of 0.7 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 5-chloro-o-toluidine is 0.7 ug/l.

**Calculations:****1. National Cancer Institute Bioassay Data**

The incidence of liver tumors in female mice fed 5-chloro-o-toluidine in the diet at levels of 0, 2,000 and 4,000 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)\*

<u>Concentration in diet</u>	<u>Average Daily Intake During Lifetime</u>
0	0 mg/kg/day
2,000 ppm	172 mg/kg/day
4,000 ppm	344 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 lived an additional 13 weeks without exposure after being exposed for 78 weeks; therefore, average daily doses during exposure were multiplied by 0.86 to calculate average daily doses during lifetime.

3. Data Input for GLOBAL82 Computer Program

<u>Dose (mg/kg/day)</u>	<u>Number of animals with tumors</u>	<u>Number of experimental animals</u>
0	0	20
172	21	50
344	31	43

4. GLOBAL82 Result (for animals)

The lower 95% confidence limit value of the 5-chloro-o-toluidine dose corresponding to an increased lifetime cancer risk of  $1 \times 10^{-6}$  for the experimental animals was 0.23 ug/kg/day.

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

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

$$0.23 \text{ ug/kg/day} \times \left( \frac{0.035 \text{ kg}}{70 \text{ kg}} \right)^{0.33} = 0.019 \text{ ug/kg/day}$$

6. Calculation of the 5-chloro-o-toluidine 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.

$$\frac{0.019 \text{ ug/kg/day} \times 70 \text{ kg}}{2 \text{ l/day}} = 0.66 \text{ ug/l}$$

**REFERENCES:**

- (1) National Cancer Institute. 1979. Bioassay of 5-chloro-o-toluidine for possible carcinogenicity. Carcinogenesis Tech. Rep. Ser. No. 187.
- (2) National Cancer Institute. 1979. Bioassay of 4-chloro-o-toluidine hydrochloride for possible carcinogenicity. Carcinogenesis Tech. Rep. Ser. No. 165.
- (3) Howe, R.B. and K.S. Crump. 1982. GLOBAL82 Computer Program. Science Research Systems, Inc., Ruston, LA.

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