

Joan E. Denton, Ph.D., Director

Headquarters • 301 Capitol Mall, Rm. 205 • Sacramento, California 95814-4308

Oakland Office • Mailing Address: 1515 Clay Street, 16th Floor • Oakland, California 94612



Winston H. Hickox
Agency Secretary



Gray Davis
Governor

MEMORANDUM

David P. Spath, Ph.D., Chief
Division of Drinking Water and Environmental Management Branch
Department of Health Services
601 North 7th Street, Mail Stop 92
P.O. Box 942732
Sacramento, California 94234-7320

VIA: George V. Alexeeff, Ph.D., DABT *GA*
Deputy Director for Scientific Affairs

Anna M. Fan, Ph.D., Chief *AMF*
Pesticide and Environmental Toxicology Section

FROM: Robert A. Howd, Ph.D., Chief *RA. Howd*
Water Toxicology Unit

DATE: June 7, 2000

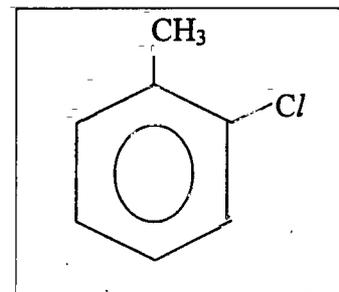
SUBJECT: PROPOSED ACTION LEVEL FOR 2-CHLOROTOLUENE

As you requested in your memorandum of January 5, 2000, we reviewed your department's proposed action level for 2-chlorotoluene in drinking water. We concur with your proposed level of 140 µg/L, based on a subchronic rat study by Gibson *et al.* (1974).

2-Chlorotoluene is also known as ortho-chlorotoluene and 2-chloro-1-methyl benzene. At 20°C, this chemical is a liquid with a vapor pressure of 2.7 Torr and a water solubility of 0.377 g/L.

This compound is used as a solvent and a chemical intermediate in the manufacture of pesticides, dyes, and pharmaceuticals (U.S. EPA, 1985). Because of its vapor pressure, the chemical will typically exist in the vapor phase in the atmosphere. If released to

water, a river model volatilization half-life is 3.4 hours with adsorption to suspended solids and sediments another favored fate. The compound is not likely to undergo hydrolysis or significantly bioaccumulate in aquatic organisms (HSDB, 2000).



Quistad *et al.* (1983) examined metabolism of 2-chlorotoluene in rats. 2-Chlorotoluene is quickly absorbed into blood. Following a single, 1 mg/kg-day oral dose of [¹⁴C] 2-chlorotoluene, 85-92 percent and five to eight percent of the administered ¹⁴C were respectively recovered in the urine and feces. The major urinary metabolites, along with the ranges of relative percentages reported, were: (1) a glycine conjugate of 2-chlorobenzoic acid, 20-23 percent; (2) a β-glucuronide of 2-chlorobenzyl alcohol, 35-42 percent; and (3) a mercapturic acid, 13-21percent (ACGIH, 1980).

The health and toxicity data available for 2-chlorotoluene are limited. 2-Chlorotoluene has a relatively low animal acute oral toxicity in (newborn) rats of >1600 mg/kg-day and in mice of 2500 mg/kg-day (IRIS, 2000). Sublethal acute effects in rats include moderate to marked weakness and vasodilation (ACGIH, 1980). There are several subchronic studies and no chronic studies available.

Gibson and associates (1974a) studied the toxicity of daily doses of 2-chlorotoluene in the dog. Sixteen beagles of each sex were divided into four groups, consisting of 5, 20, and 80 mg/kg_{bw}-day 2-chlorotoluene and a fourth group given 5 percent aqueous acacia (0.5 mg/kg_{bw}-day) as a vehicle control. Daily doses were administered by capsule. Treatment for male and female dogs was for 96 and 95 days, respectively. No treatment-related changes in body weight or effects on hematology, clinical biochemistry, or urinalysis occurred. Examinations included hematocrit, hemoglobin, red blood cells, white blood cells, prothrombin time, platelets, mean corpuscular volume, calcium, serum glucose, blood urea nitrogen, total bilirubin, alkaline phosphatase, and serum glutamic oxaloacetic transaminase. There were no treatment-related effects on organ weights. For dogs receiving 5, 20, and 80 mg/kg_{bw}-day 2-chlorotoluene there were no differences observed compared to controls, and the no-observed-adverse-effect-level (NOAEL) in the study was 80 mg/kg_{bw}-day.

Gibson *et al.* (1974b) examined the subchronic effects of daily oral doses of 2-chlorotoluene in the rat. For this study, weanling Harlan rats (about 125 grams each) were divided into four groups of 20 rodents/sex. Daily, for 103 or 104 days, animals were given 0, 20, 80, or 320 mg/kg-day 2-chlorotoluene via gavage. Hematological data such as hemoglobin, red blood cell count, white blood cell count, prothrombin times, blood urea nitrogen, and blood glucose were determined. At autopsy, weights of liver, kidney, spleen, heart, thyroid, adrenal, and prostate and testes or uterus and ovaries were determined. Histopathologic examinations were performed on colon, duodenum, ileum, jejunum, lungs, lymph nodes, mammary, pancreas, parathyroid, salivary glands, skin, stomach, striated muscle, thymus, and urinary bladder. The authors noticed the following differences from the controls. In males, while the mean body weight did not differ from the controls at 20 mg/kg-day (the study no-observed-adverse-effect-level [NOAEL]), the mean body weights for males were significantly lower at the 80 and 320 mg/kg-day levels. Further, and also in males, statistically significant increases in the adrenal weights of the 80 and 320 mg/kg-day dose groups were observed (the study LOAEL). No

significant differences were observed for females. On the basis of this study's findings of statistically significant differences in body weight and adrenal weight for male rats at the 80 mg/kg-day level (LOAEL), the 20 mg/kg-day dose level is used as the NOAEL to calculate the action level.

The 20 mg/kg-day NOAEL is identical to that proposed in your memorandum. We would add only a mention of significant adrenal weight gains at the LOAEL of 80 mg/kg-day to the justification for derivation of the NOAEL. The public health protective level "C" is then calculated as follows:

$$C = \frac{\text{NOAEL} \times \text{BW} \times \text{RSC}}{\text{UF} \times \text{DWC}} = \text{health protective value in mg/L}$$

where,

- NOAEL = no-observed-adverse-effect-level, 20 mg/kg-day as the absence of body weight decrease and adrenal weight increase in male rats,
BW = adult human body weight, 70 kg (default value),
RSC = relative source contribution, 0.2 (default value)
UF = uncertainty factor of 1000 (10-fold for inter-species variation, 10-fold for human variability, 10-fold to account for the use of a subchronic study for determining a lifetime value), and
DWC = adult drinking water consumption, 2 L/day (default).

Accordingly,

$$C = \frac{20 \text{ mg/kg-day} \times 70 \text{ kg} \times 0.2}{1000 \times 2 \text{ L/day}} = 0.14 \text{ mg/L} = 140 \text{ } \mu\text{g/L}$$

Based on the health protective concentration calculated, the Office of Environmental Health Hazard Assessment recommends and supports an action level of 140 ppb ($\mu\text{g/L}$) for o-chlorotoluene in drinking water. Should you have any questions about this review, please contact me at (510) 622-3168.

References

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