VALUE(S) ADDED 7-24-85

FACT SHEET REVISED _____

VALUE(S) REMOVED _____

AMBIENT SURFACE WATER QUALITY STANDARDS DOCUMENTATION

CHEMICAL: 2,6-Dinitrotoluene (DNT)

CAS NO.(s): 606-20-2

BASIS (Human/Aquatic): Human

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

STANDARD: 0.07 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 liver tumors in male and female rats.[2,3]

STANDARD DERIVATION:

Dose-response data from a Chemical Industry Institute of Toxicology (CIIT)[2] carcinogenesis bioassay in which long-term dietary exposure to technical grade DNT, composed of 76% 2,4-DNT, 19% 2,6-DNT and 5% other isomers, caused liver tumors in male and female rats were used for extrapolation. This study was used to derive the guideline for 2,6-DNT because it provided good data for extrapolation procedures and several other studies (see below) indicated that the carcinogenic action of technical DNT is primarily due to 2,6-DNT. (1) An earlier bioassay sponsored by the National Cancer Institute showed that dietary doses of 2,4-DNT did not induce liver tumors in rats or mice.[4] (2) Over 85% of the rats given dietary doses of 14 or 7 mg/kg/day of 2,6-DNT for one year developed liver carcinomas but none of the rats given a dietary dose of 35 mg/kg/day of 2,4-DNT for one year developed liver carcinomas.[3] (3) 2,6-DNT was much more active in short-term tests of genotoxic activity than was 2,4-DNT (approximately 20 times more active in one case).[5] Using the protocol in Part 701.4 and a linearized multistage extrapolation procedure (GLOBAL82)[6], a 2,6-DNT concentration of 0.07 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 2,6-DNT is 0.07 ug/l.

Calculations:

1. Chemical Industry Institute of Toxicology

The incidence of liver tumors in male rats fed technical DNT in the diet at levels to provide doses of 0, 3.5 and 14.0 mg/kg/day 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)*

Average Daily Intake During Lifetime
0 mg/kg/day
0.66 mg/kg/day
2.66 mg/kg/day

*Specific information on food consumption was provided by CIIT.[2] However, rats were exposed to technical DNT and since 2,6-DNT comprised 19% of the mixture, doses were multiplied by 0.19 to calculate average daily doses of 2,6-DNT during lifetime.

3. Data Input for GLOBAL82 Computer Program

Dose (mg/kg/day)	Number of animals with tumors	Number of experimental animals
0	1	120
0.66	10	130
2.66	98	128

4. GLOBAL82 Result (for animals)

The lower 95% confidence limit value of the 2,4-DNT dose corresponding to an increased lifetime cancer risk of 1×10^{-6} for the experimental animals was 0.013 ug/kg/day.

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

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

$$0.013 \text{ ug/kg/day} \times \left(\frac{0.30 \text{ kg}}{70 \text{ kg}}\right)^{0.33} = 0.002 \text{ ug/kg/day}$$

6. Calculation of the 2,6-DNT 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.

$$\frac{0.002 \text{ ug/kg/day} \times 70 \text{ kg}}{2 \text{ l/day}} = 0.07 \text{ ug/l}$$

REFERENCES:

(1) U.S. EPA. 1980. Ambient water quality criteria for dinitrotoluene. NTIS No. PB81-117566.

(2) Chemical Industry Institute of Toxicology (CIIT). 1982. 104-week chronic toxicity study in rats. Dinitrotoluene, Final Report. CIIT Docket #12362. Research Triangle Park, N.C.

(3) Popp, J.A. and T.B. Leonard. 1983. Hepatocarcinogenicity of 2,6-dinitrotoluene (DNT). Proc. Am. Assoc. Cancer Res. 24: 91. (Abstract)

(4) National Cancer Institute. 1978. Bioassay of 2,4-dinitrotoluene for possible carcinogenicity. Carcinogenesis Tech. Rep. Ser. No. 54.

(5) Mirsalis, J.C. and B.E. Butterworth. 1982. Induction of unscheduled DNA synthesis in rat hepatocytes following *in vivo* treatment with dinitrotoluene. Carcinogenesis. 3: 241-245.

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

KB/pb

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