o-Chlorotoluene; CASRN 95-49-8

Human health assessment information on a chemical substance is included in the IRIS database only after a comprehensive review of toxicity data, as outlined in the IRIS assessment development process. Sections I (Health Hazard Assessments for Noncarcinogenic Effects) and II (Carcinogenicity Assessment for Lifetime Exposure) present the conclusions that were reached during the assessment development process. Supporting information and explanations of the methods used to derive the values given in IRIS are provided in the guidance documents located on the IRIS website.

STATUS OF DATA FOR o-Chlorotoluene

File First On-Line 02/01/1990

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	02/01/1990
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	not evaluated	

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

I.A. Reference Dose for Chronic Oral Exposure (RfD)

Substance Name — o-Chlorotoluene
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Last Revised — 02/01/1990

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of substances that are also carcinogens. Therefore, it is essential to refer to other sources of

information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

I.A.1. Oral RfD Summary

Critical Effect	Experimental Doses*	UF	MF	RfD
Decrease in body weight gain **15-Week Rat Study Oral Exposure (gavage)** **Gibson et al., 1974a**	NOAEL: 20 mg/kg/day LOAEL: 80 mg/kg/day	1000	1	2E-2 mg/kg/day

*Conversion Factors: none

I.A.2. Principal and Supporting Studies (Oral RfD)

Gibson, W.R., F.O. Gossett, G.R. Koenig and F. Marroquin. 1974a. The toxicity of daily oral doses of o-chlorotoluene in the rat. Toxicology Division, Lilly Research Laboratories. Submitted to Test Rules Development Branch, Office of Toxic Substances, U.S. EPA, Washington, D.C.

o-Chlorotoluene in an aqueous solution containing 5% acacia as the emulsifying agent was administered by gavage to weanling Harlan rats (20 males and 20 females/group) at doses of 0, 20, 80, or 320 mg/kg/day for 103 or 104 days. At doses of 80 and 320 mg/kg/day, male rats developed a statistically significant decrease in mean body weight gain (15% and 22%, respectively) and an increase in adrenal weight. Increased heart and testes weights, an increase in white blood cell (WBC) count, and a decrease in prothrombin time were observed in males at the 320 mg/kg/day dose level. At the 80 mg/kg/day dose, blood urea nitrogen (BUN) was increased in males. No histological changes related to intake of o-chlorotoluene were seen in this study. A NOAEL of 20 mg/kg/day is indicated and the LOAEL is 80 mg/kg/day.

Adult male and female beagle dogs (four/sex/level) were given gelatin capsules containing an aqueous emulsion of o-chlorotoluene in 5% acacia at doses of 0, 5, 20, or 80 mg/kg/day daily for 97 days (Gibson et al., 1974b). At 1, 2, and 4 weeks and at 2 and 3 months, the dogs were examined for hematological and biochemical changes, as well as for changes in urinalyses. No

changes were observed in body weight nor were any histological changes evident. Females treated at the 80 mg/kg/day dose level developed a transient increase in platelet count which returned to normal after 14 weeks of exposure. Since the effects were transient, the authors did not consider the increased platelet count to be treatment related. A NOAEL of 80 mg/kg/day is indicated for dogs in this study.

I.A.3. Uncertainty and Modifying Factors (Oral RfD)

UF — An uncertainty factor of 1000 was used: 10 to account for interspecies extrapolation, 10 for differences in individual human sensitivity, and 10 for use of a subchronic study.

MF — None

I.A.4. Additional Studies/Comments (Oral RfD)

No oral reproductive or developmental toxicity studies are available. Huntingdon Research Center (1983a,b) exposed rats (25 animals/dose) and rabbits (16 animals/dose) to o-chlorotoluene vapor for 6 hours/day during days 6 to 19 (rats) and 6 to 28 (rabbits) of gestation. In rats, there was an increase in malformed fetuses at doses of 9000 mg/cu.m (1710 mg/kg/day), but not at 1000 mg/cu.m (190 mg/kg/day) and 3000 mg/cu.m (570 mg/kg/day); the authors concluded that malformations in one fetus at the 1000 mg/cu.m dose were not related to treatment. In rabbits, no fetal effects were observed at doses of 1500 (150), 4000 (400) and 15,000 mg/cu.m (1500 mg/kg/day).

I.A.5. Confidence in the Oral RfD

Study — Medium
Database — Low
RfD — Low

The confidence in the study is medium because of the number of animals and doses used and because several parameters were studied. The confidence in the database is low since no specific pattern of toxicity was observed at the higher doses. Considering no chronic or pertinent oral reproductive or developmental data are available, the overall confidence in the RfD is rated low.

I.A.6. EPA Documentation and Review of the Oral RfD

Source Document — U.S. EPA, 1985

Other EPA Documentation — None

Agency Work Group Review — 07/20/1989, 09/21/1989

Verification Date — 09/21/1989

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfD for o-Chlorotoluene conducted in August 2003 did not identify any critical new studies. IRIS users who know of important new studies may provide that information to the IRIS Hotline at hotline.iris@epa.gov or 202-566-1676.

I.A.7. EPA Contacts (Oral RfD)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or hotline.iris@epa.gov (internet address).

I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)

Substance Name — o-Chlorotoluene
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Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — o-Chlorotoluene
CASRN — 95-49-8

This substance/agent has not undergone a complete evaluation and determination under US EPA's IRIS program for evidence of human carcinogenic potential.

III. [reserved]
IV. [reserved]
V. [reserved]

VI. Bibliography

Substance Name — o-Chlorotoluene
CASRN — 95-49-8

VI.A. Oral RfD References

Gibson, W.R., F.O. Gossett, G.R. Koenig and F. Marroquin. 1974a. The toxicity of daily oral doses of o-chlorotoluene in the rat. Toxicology Division, Lilly Research Laboratories. Submitted to Test Rules Development Branch, Office of Toxic Substances, U.S. EPA, Washington, DC.

Gibson, W.R., F.O. Gossett, G.R. Koenig and F. Marroquin. 1974b. The toxicity of daily oral doses of o-chlorotoluene in the dog. Toxicology Division, Lilly Research Laboratories. Submitted to Test Rules Development Branch, Office of Toxic Substances, U.S. EPA, Washington, DC.

Huntingdon Research Center. 1983a. Effect of 2-chlorotoluene vapour on pregnancy of the rat. Submitted to Test Rules Development Branch, Office of Toxic Substances, U.S. EPA, Washington, DC.

Huntingdon Research Center. 1983b. Effect of 2-chlorotoluene vapour on pregnancy of the New Zealand White rabbit. Submitted to Test Rules Development Branch, Office of Toxic Substances, U.S. EPA, Washington, DC.

U.S. EPA. 1985. Health and Environmental Effects Profile for Chlorotoluene (o-, m-, p-). Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC.

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — o-Chlorotoluene
CASRN — 95-49-8

Date	Section	Description
02/01/1990	I.A.	Oral RfD summary on-line
10/28/2003	I.A.6.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — o-Chlorotoluene
CASRN — 95-49-8
Last Revised — 02/01/1990

- 95-49-8
- AI3-15912 [USDA]
- BENZENE, 1-CHLORO-2-METHYL- (9CI)
- 1-CHLORO-2-METHYLBENZENE
- 2-CHLORO-1-METHYLBENZENE
- 2-CHLOROTOLUENE
- O-CHLOROTOLUENE
- ORTHO-CHLOROTOLUENE

- HSDB 5291
- 1-METHYL-2-CHLOROBENZENE
- 2-METHYLCHLOROBENZENE
- TOLUENE, O-CHLORO- (8CI)
- O-TOLYL CHLORIDE