

2,4,6-Trichlorophenol; CASRN 88-06-2

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 2,4,6-Trichlorophenol

File First On-Line 01/31/1987

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	not evaluated	
Inhalation RfC (I.B.)	message	07/01/1991
Carcinogenicity Assessment (II.)	yes	06/01/1990

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — 2,4,6-Trichlorophenol

CASRN — 88-06-2

Not available at this time.

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

Substance Name — 2,4,6-Trichlorophenol
CASRN — 88-06-2

The health effects data for 2,4,6-trichlorophenol were reviewed by the U.S. EPA RfD/RfC Work Group and determined to be inadequate for derivation of an inhalation RfC. For additional information on health effects of this chemical, interested parties are referred to the EPA documentation listed below.

U.S. EPA. 1980. Ambient Water Quality Criteria for Chlorinated Phenols. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Water Regulations and Standards, Washington, DC.

U.S. EPA. 1983. Reportable Quantity for 2,4,6-Trichlorophenol. 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.

U.S. EPA. 1984. Health Effects Assessment for 2,4,6-Trichlorophenol. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Emergency and Remedial Response, Washington, DC. PB 86-134582.

U.S. EPA. 1989. Drinking Water Criteria Document for Chlorophenols. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Drinking Water, Washington, DC.

Agency Work Group Review — 04/24/1991

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfC for 2,4,6-Trichlorophenol conducted in September 2002 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.

EPA Contacts:

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).

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — 2,4,6-Trichlorophenol

CASRN — 88-06-2

Last Revised — 06/01/1990

Section II provides information on three aspects of the carcinogenic assessment for the substance in question; the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral exposure and from inhalation exposure. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. The rationale and methods used to develop the carcinogenicity information in IRIS are described in The Risk Assessment Guidelines of 1986 (EPA/600/8-87/045) and in the IRIS Background Document. IRIS summaries developed since the publication of EPA's more recent Proposed Guidelines for Carcinogen Risk Assessment also utilize those Guidelines where indicated (Federal Register 61(79):17960-18011, April 23, 1996). Users are referred to Section I of this IRIS file for information on long-term toxic effects other than carcinogenicity.

II.A. Evidence for Human Carcinogenicity

II.A.1. Weight-of-Evidence Characterization

Classification — B2; probable human carcinogen

Basis — Based on no human data and sufficient evidence in animals; namely, increased incidence of lymphomas or leukemias in male rats and hepatocellular adenomas or carcinomas in male and female mice.

II.A.2. Human Carcinogenicity Data

None.

II.A.3. Animal Carcinogenicity Data

Sufficient. 2,4,6-Trichlorophenol (96-97% pure) was added to the diet of 50 each male and female F344 rats and B6C3F1 mice (NCI, 1979). In rats 2,4,6- trichlorophenol was administered at 5000 or 10,000 ppm in feed for 106 or 107 weeks. Male mice also received 5000 or 10,000

ppm of 2,4,6-trichlorophenol for 105 weeks. Female mice were initially administered 10,000 or 20,000 ppm of 2,4,6-trichlorophenol in feed. As the animals were observed to have decreased body weights, these concentrations were lowered to 2500 and 5000 ppm at week 38 (TWA dose = 5214 or 10,428 ppm). While both rodent species showed dose-related decreases in mean body weight, no increased mortality nor other toxic signs were observed.

In male but not female rats, there were dose-related increases in lymphomas or leukemias which were significantly elevated over controls. The incidence of lymphomas or leukemias in males was 4/20, 25/50, and 29/50 for control, low- and high-dose groups, respectively, the majority of which were leukemias. In some treated male rats in which no leukemia was observed, leukocytosis and monocytosis of peripheral blood and hyperplasia of the bone marrow were noted.

In both male and female mice there was a statistically significant trend in the incidence of combined hepatocellular adenomas and carcinomas. Pairwise comparisons of the incidence in high- and low-dose male mice and high-dose female mice with concurrent controls were also statistically significant. The incidence of carcinomas alone was not significantly elevated in males, but these data were not given for females. The combined incidence in the control, low- and high-dose groups for males was 4/20 (20%), 32/49 (65%), and 39/47 (83%) and for females it was 1/20 (5%), 12/50 (24%), and 24/48 (50%), respectively.

A 20% solution of 2,4,6-trichlorophenol in benzene, applied dermally 2 times/week for 15 weeks, did not promote skin tumors in four strains of mice (albino Suher, Holtzman, C3H and CAF) initiated with 9,10-dimethyl-1,2-benzanthracene (Boutwell and Bosch, 1959). In a study of 120 pesticides, both male and female mice of two strains were gavaged from day 7 to 28 of age with 100 mg 2,4,6-trichlorophenol/kg bw. This was followed by 18 months of dietary exposure to 260 ppm (approximately 20 to 25 mg/kg total). Four tumor groups (hepatomas, lymphomas, pulmonary tumors, and total mice with tumors) were statistically analyzed. The results, pertaining to carcinogenicity, were reported to be inconclusive and to require further evaluation (No data were given) (Innes et al., 1969).

Stoner et al. (1986) dosed either intraperitoneally or by gavage, 16 male and 16 female A/J mice per group with various concentrations of 2,4,6-trichlorophenol in tricaprillin 3 times/week for 8 weeks. Animals were killed 24 weeks after initiation of dosing. In this short-term assay, the lungs were histologically examined; other tissues were histologically examined only if there was evidence of a gross lesion. 2,4,6-trichlorophenol did not induce lung tumors at cumulative doses of 240, 600, or 1200 mg/kg when administered intraperitoneally or 1200 mg/kg when administered by gavage.

II.A.4. Supporting Data for Carcinogenicity

2,4,6-Trichlorophenol in the absence and presence of hepatic homogenates (S9) was not mutagenic for *Salmonella typhimurium* (Rasanen et al., 1977; Kinae et al., 1981). It was mutagenic for *Saccharomyces cerevesiae*, but had no effect on mitotic recombination (Fahrig et al., 1978). It has been reported as mutagenic in the mouse spot test, but is ranked among the weakest mutagens tested in that assay (Fahrig et al., 1978).

2,4,6-TCP (greater than 99.5% pure) at concentrations up to 100 ug/mL did not induce mutations to 6-thioguanine resistance in V79 Chinese hamster cells when tested without exogenous metabolic activation (Jansson and Jansson, 1986). 2,4,6-TCP induced DNA-damage in the *Bacillus subtilis* rec assay (Kinae et al., 1981).

II.B. Quantitative Estimate of Carcinogenic Risk from Oral Exposure

II.B.1. Summary of Risk Estimates

Slope Factor for Dietary Use — $1.1E-2$ per (mg/kg)/day

Drinking Water Unit Risk — $3.1E-7$ per (ug/L)

Extrapolation Method — Linearized multistage procedure, extra risk

Drinking Water Concentrations at Specified Risk Levels:

Risk Level	Concentration
E-4 (1 in 10,000)	$3E+2$ ug/L
E-5 (1 in 100,000)	$3E+1$ ug/L
E-6 (1 in 1,000,000)	$3E+0$ ug/L

II.B.2. Dose-Response Data (Carcinogenicity, Oral Exposure)

Tumor Type: leukemia
Test animals: rat/F344, male
Route: diet
Reference: NCI, 1979

-----Dose-----			
Administered (ppm)	Transformed Animal Dose (mg/kg/day)	Human Equivalent (mg/kg/day)	Tumor Incidence
0	0	0	3/20
5,000	258	44.6	23/50
10,000	544	94.4	29/50

II.B.3. Additional Comments (Carcinogenicity, Oral Exposure)

Dose conversion used a feeding rate of 0.0187 kg/day and body weights for rats of 0.362 kg and 0.344 for the low and high doses, respectively. The human equivalent doses were calculated by multiplying the animal transformed doses by the cube root of the ratio of the rat body weight to the reference human body weight (70kg). The slope factor for the hepatocellular carcinoma response in male mice is 2.0E-2 per (mg/kg)/day (U.S. EPA, 1984), which is about twice the value estimated here for the rat data.

While the contaminants in the 2,4,6-TCP used in NCI (1979) were not determined, Firestone et al. (1972) found 49 ppm of 1,3,6,8-TCDD and 93 ppm of 2,3,7-trichlorodibenzo-p-dioxin, as well as unquantified amounts of tetra-, penta- and hexa-chlorinated dibenzofurans in commercial grade 2,4,6- trichlorophenol. If the 2,4,6-trichlorophenol used in NCI (1979) was contaminated with 1,3,6,8-TCDD (less than or equal to 4%), the liver tumor incidence observed in the NCI (1979) study could be obscured since this chemical may induce liver tumors. When the Toxic Equivalency Factor approach (U.S. EPA, 1987) is used, and the same amount of contamination as shown by Firestone et al. (1972) is assumed, the risk determined for the development of hepatocellular carcinomas and adenomas in male mice that is due to this contaminant could

theoretically account for the observed tumors. Confidence in use of this data set for quantitation is decreased. Since chlorinated dibenzodioxins do not induce leukemia, the rat data are more appropriate for derivation of the slope factor.

The unit risk should not be used if the water concentration exceeds 3E+4 ug/L, since above this concentration the unit risk may not be appropriate.

II.B.4. Discussion of Confidence (Carcinogenicity, Oral Exposure)

Adequate numbers of animals were observed for their lifetime.

II.C. Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure

II.C.1. Summary of Risk Estimates

Inhalation Unit Risk — 3.1E-6 per (ug/cu.m)

Extrapolation Method — Linearized multistage procedure, extra risk

Air Concentrations at Specified Risk Levels:

Risk Level	Concentration
E-4 (1 in 10,000)	3E+1 ug/cu.m
E-5 (1 in 100,000)	3E+0 ug/cu.m
E-6 (1 in 1,000,000)	3E-1 ug/cu.m

II.C.2. Dose-Response Data for Carcinogenicity, Inhalation Exposure

Calculated from oral data in Section II.B.2.

II.C.3. Additional Comments (Carcinogenicity, Inhalation Exposure)

The unit risk should not be used if the air concentration exceeds 3E+2 ug/cu.m, since above this concentration the unit risk may not be appropriate.

II.C.4. Discussion of Confidence (Carcinogenicity, Inhalation Exposure)

This inhalation risk estimate was based on oral data.

II.D. EPA Documentation, Review, and Contacts (Carcinogenicity Assessment)

II.D.1. EPA Documentation

Source Document — U.S. EPA, 1980, 1984, 1987, 1989

The values in the Ambient Water Quality Criteria Document for Chlorinated Phenols (1980) received extensive peer and public review. The Drinking Water Criteria Document on Chlorinated Phenols has received OHEA review.

II.D.2. EPA Review (Carcinogenicity Assessment)

Agency Work Group Review — 06/26/1986, 10/29/1986, 05/30/1989, 09/07/1989

Verification Date — 09/07/1989

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the cancer assessment for 2,4,6-Trichlorophenol conducted in September 2002 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.

II.D.3. EPA Contacts (Carcinogenicity Assessment)

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III. [reserved]

IV. [reserved]

V. [reserved]

VI. Bibliography

Substance Name — 2,4,6-Trichlorophenol

CASRN — 88-06-2

VI.A. Oral RfD References

None

VI.B. Inhalation RfC References

U.S. EPA. 1980. Ambient Water Quality Criteria for Chlorinated Phenols. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Water Regulations and Standards, Washington, DC.

U.S. EPA. 1983. Reportable Quantity for 2,4,6-Trichlorophenol. 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.

U.S. EPA. 1984. Health Effects Assessment for 2,4,6-Trichlorophenol. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Emergency and Remedial Response, Washington, DC. PB 86-134582.

U.S. EPA. 1989. Drinking Water Criteria Document for Chlorophenols. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Drinking Water, Washington, DC.

VI.C. Carcinogenicity Assessment References

Boutwell, R.K. and D.K. Bosch. 1959. The tumor-promoting action of phenol and related compounds for mouse skin. *Cancer Res.* 19: 413-424.

Fahrig, R., C.A. Nilsson and C. Rappe. 1978. Genetic activity of chlorophenols and chlorophenol impurities. In: *Pentachlorophenol: Chemistry, Pharmacology and Environmental Toxicology*, K.R. Rao, Ed. Plenum Press, New York. p. 325-338.

Firestone, D., J. Ress, N.L. Brown, R.P. Barron and J.N. Damico. 1972. Determination of polychlorodibenzo-p-dioxins and related compounds in commercial chlorophenols. *J. Assoc. Off. Anal. Chem.* 55(1): 85-92.

Innes, J.R.M., B.M. Ulland, M.G. Valerio, et al. 1969. Bioassay of pesticides and industrial chemicals for tumorigenicity in mice: A preliminary note. *J. Natl. Cancer Inst.* 42(6): 1101-1114.

Jansson, K. and V. Jansson. 1986. Inability of chlorophenols to induce 6-thioguanine-resistant mutants in V79 Chinese hamster cells. *Mutat. Res.* 171: 165-168.

Kinae, N., T. Hashizume, T. Makita, I. Tomita, I. Kimura and H. Kanamori. 1981. Studies on the toxicity of pulp and paper mill effluents. I. Mutagenicity of the sediment samples derived from Kraft Paper Mills. *Water Research.* 15: 17-24.

NCI (National Cancer Institute). 1979. Bioassay of 2,4,6-Trichlorophenol for Possible Carcinogenicity. U.S. DHEW Publ. No. NCI-CG-TR-155.

Rasanen, L., M.L. Hattula and A.U. Arstila. 1977. The mutagenicity of MCPA and its soil metabolites, chlorinated phenols, catechols and some widely used slimicides in Finland. *Bull. Environ. Contam. Toxicol.* 18(5): 565-571.

Stoner, G.D., P.B. Conran, E.A. Greisiger, J. Stober, M. Morgan and M.A. Pereira. 1986. Comparison of two routes of chemical administration on the lung adenoma response in strain A/J mice. *Toxicol. Appl. Pharmacol.* 82: 19-31.

U.S. EPA. 1980. Ambient Water Quality Criteria Document for Chlorinated Phenols. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Water Regulations and Standards, Washington, DC. EPA-440/5-80-032. NTIS PB- 81-117434.

U.S. EPA. 1984. Health Effects Assessment for 2,4,6-Trichlorophenol. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Emergency and Remedial Response, Washington, DC. EPA/540/1-86-047. NTIS PB-86-134582/AS.

U.S. EPA. 1987. Interim Procedures for Estimating Risks Associated with Exposures to Mixtures of Chlorinated Dibenzo-p-dioxins and Dibenzofurans (CDDs and CDFs). Risk Assessment Forum, Washington, DC. EPA/625/3-87/012.

U.S. EPA. 1989. Drinking Water Criteria Document for Chlorophenols. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Drinking Water, Washington, DC. (External Review Draft).

VII. Revision History

Substance Name — 2,4,6-Trichlorophenol
CASRN — 88-06-2

Date	Section	Description
10/01/1989	II.	Withdrawn; new assessment verified (in preparation)
06/01/1990	II.	Carcinogen assessment replaced; quant. estimates changed
07/01/1991	I.B.	Inhalation RfC message on-line
12/03/2002	I.B., II.D.2.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — 2,4,6-Trichlorophenol

CASRN — 88-06-2

Last Revised — 01/31/1987

- 88-06-2
- Dowicide 2S
- NCI-C02904
- Omal
- phenachlor
- Phenol, 2,4,6-trichloro-
- RCRA waste number U231
- 2,4,6-Trichlorophenol
- Trichlorophenol, 2,4,6-