

p,p'-Dichlorodiphenyldichloroethylene (DDE); CASRN 72-55-9

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 DDE

File First On-Line 08/22/1988

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	not evaluated	
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	yes	08/22/1988

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — p,p'-Dichlorodiphenyldichloroethylene (DDE)
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Not available at this time.

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

Substance Name — p,p'-Dichlorodiphenyldichloroethylene (DDE)
CASRN — 72-55-9

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — p,p'-Dichlorodiphenyldichloroethylene (DDE)
CASRN — 72-55-9
Last Revised — 08/22/1988

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 — increased incidence of liver tumors including carcinomas in two strains of mice and in hamsters and of thyroid tumors in female rats by diet.

II.A.2. Human Carcinogenicity Data

Human epidemiological data are not available for DDE. Evidence for the carcinogenicity in humans of DDT, a structural analog, is based on autopsy studies relating tissue levels of DDT to cancer incidence. These studies have yielded conflicting results. Three studies reported that tissue levels of DDT and DDE were higher in cancer victims than in those dying of other diseases (Casarett et al., 1968; Dacre and Jennings, 1970; Wasserman et al., 1976). In other studies no such relationship was seen (Maier-Bode, 1960; Robinson et al., 1965; Hoffman et al., 1967). Studies of volunteers and workers occupationally exposed to DDT have been of insufficient duration to determine the carcinogenicity of DDT to humans.

II.A.3. Animal Carcinogenicity Data

Sufficient. NCI (1978) administered DDE in feed at TWA doses of 148 and 261 ppm to 50 B6C3F1 mice/sex/dose for 78 weeks. After an additional 15 weeks, a dose-dependent and statistically significant increase in incidence of hepatocellular carcinomas was observed in males and females in comparison with controls. Increased weight loss and mortality was observed in females.

Tomatis et al. (1974) administered 250 ppm DDE in feed for lifetime (130 weeks) to 60 CF-1 mice/sex. A statistically significant increase in incidence of hepatomas was observed in both males and females in comparison with controls. In females, 98% of the 55 surviving exposed animals developed hepatomas, compared to 1% of the surviving controls.

Rossi et al. (1983) administered DDE in feed for 128 weeks to 40-46 Syrian Golden hamsters/sex/dose at doses of 500 and 1000 ppm. After 76 weeks, a statistically significant increase in incidence of neoplastic nodules of the liver were observed in both sexes in comparison with vehicle-treated controls.

NCI (1978) also fed DDE at TWA doses of 437 and 839 ppm for males and 242 and 462 ppm for females for 78 weeks to 50 Osborne-Mendel rats/sex/ dose, with an additional 35 week observation period. A dose-dependent trend in incidence of thyroid tumors was observed in females which was statistically significant by the Cochran Armitage trend test after adjustment for survival. The Fischer Exact test, however, was not statistically significant. Overall, the results of the bioassay were not considered by NCI to provide convincing evidence for carcinogenicity.

II.A.4. Supporting Data for Carcinogenicity

DDE was mutagenic in mouse lymphoma (L5178Y) cells and Chinese hamster (V79) cells, but not in Salmonella (ICPEMC, 1984). DDE is structurally similar to and a metabolite of DDT

(Peterson and Robinson, 1964; Gingell and Wallcave, 1976; Morgan and Roan, 1977) which is a probable human carcinogen.

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

II.B.1. Summary of Risk Estimates

Oral Slope Factor — 3.4E-1/mg/kg/day

Drinking Water Unit Risk — 9.7E-6/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)	1E+1 ug/L
E-5 (1 in 100,000)	1 ug/L
E-6 (1 in 1,000,000)	1E-1 ug/L

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

Tumor Type — hepatocellular carcinomas, hepatomas

Test animals — mouse/B6C3F1; mouse/CF-1; hamsters/Syrian Golden

Route — diet

Reference — NCI, 1978; Tomatis et al., 1974; Rossi et al., 1983

Administered Dose (ppm)	Human Equivalent Dose (mg/kg)/day	Tumor Incidence		Reference
		female	male	
Mouse/B6C3F1; hepatocellular carcinomas				
0	0.0	0/19	0/19	NCI, 1978
148	0.90	19/47	7/41	
261	1.584	34/48	17/47	
Mouse/CF-1; hepatomas				
0	0	1/90	33/98	Tomatis et al., 1974
250	2.45	54/55	39/53	
Hamsters/Syrian Golden; neoplastic nodules (hepatomas)				
0	0	0/31	0/42	Rossi et al., 1983
500	4.79	7/30	4/39	
1000	9.57	8/39	6/39	

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

NCI (1978) used DDE of about 95% purity, while that used by Tomatis et al. (1974) and Rossi et al. (1983) was 99% pure. In the hamster study, Rossi et al. described the observed lesions as neoplastic liver nodules or hepatocellular tumors, using these terms interchangeably. The oral quantitative estimate is a geometric mean of six slope factors computed from incidence data by sex from the studies cited in Section II.A.3.

The unit risk should not be used if the water concentration exceeds 1E+3 ug/L, since above this concentration the slope factor may differ from that stated.

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

An adequate number of animals was observed. The geometric mean obtained using the slope factors from the mouse studies alone is 7.8E-1/mg/kg/day. This is within a factor of 2 of that derived from the mouse and hamster studies combined. In addition, the slope factor for DDE was within a factor of 2 of the slope factors for liver tumors for three structurally similar compounds: DDT, 3.4E-1/mg/kg/day; DDD, 2.4E-1/mg/kg/day; and Dicofol, 4.4E-1/mg/kg/day.

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

Not available

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

II.D.1. EPA Documentation

Source Document — U.S. EPA, 1980, 1985

The 1985 Carcinogen Assessment Group's report has received Agency Review. The 1980 Hazard Assessment Report has received peer review.

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

Agency Work Group Review — 06/24/1987

Verification Date — 06/24/1987

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 p,p'-Dichlorodiphenyldichloroethylene (DDE) 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.

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

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).

III. [reserved]

IV. [reserved]

V. [reserved]

VI. Bibliography

Substance Name — p,p'-Dichlorodiphenyldichloroethylene (DDE)
CASRN — 72-55-9

VI.A. Oral RfD References

None

VI.B. Inhalation RfD References

None

VI.C. Carcinogenicity Assessment References

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VII. Revision History

Substance Name — p,p'-Dichlorodiphenyldichloroethylene (DDE)
CASRN — 72-55-9

Date	Section	Description
08/22/1988	II.	Carcinogen summary on-line
10/28/2003	II.D.2.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — p,p'-Dichlorodiphenyldichloroethylene (DDE)
CASRN — 72-55-9
Last Revised — 08/22/1988

- 72-55-9
- 2,2-BIS(4-CHLOROPHENYL)-1,1-DICHLOROETHENE
- 2,2-BIS(p-CHLOROPHENYL)-1,1-DICHLOROETHYLENE
- DDE
- p,p'-DDE
- DDT DEHYDROCHLORIDE
- 1,1-DICHLORO-2,2-BIS(p-CHLOROPHENYL)ETHYLENE
- DICHLORODIPHENYLDICHLOROETHYLENE
- Dichlorodiphenyldichloroethylene, p,p'-
- 1,1'-DICHLOROETHENYLIDENE)BIS(4-CHLOROBENZENE)
- ETHYLENE, 1,1-DICHLORO-2,2-BIS(p-CHLOROPHENYL)-
- NCI-C00555