p,p'-Dichlorodiphenyl dichloroethane (DDD); CASRN 72-54-8

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 DDD

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'-Dichlorodiphenyl dichloroethane (DDD)
CASRN — 72-54-8

Not available at this time.

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

Substance Name — p,p'-Dichlorodiphenyl dichloroethane (DDD)
CASRN — 72-54-8

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — p,p'-Dichlorodiphenyl dichloroethane (DDD)
CASRN — 72-54-8
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 — based on an increased incidence of lung tumors in male and female mice, liver tumors in male mice and thyroid tumors in male rats. DDD is structurally similar to, and is a known metabolite of DDT, a probable human carcinogen.

II.A.2. Human Carcinogenicity Data

None. Human epidemiological data are not available for DDD. 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 occupationally exposed workers and volunteers have been of insufficient duration to determine the carcinogenicity of DDT to humans.

II.A.3. Animal Carcinogenicity Data

Sufficient. Tomatis et al. (1974) fed DDD for 130 weeks at 250 ppm (TWA) to 60 CF-1 mice/sex. A statistically significant increase in incidence of lung tumors was seen in both sexes compared with controls. In males, a statistically significant increase in incidence of liver tumors was also seen.

NCI (1978) fed DDD at 411 and 822 ppm (TWA) to 50 B6C3F1 mice/sex/dose for 78 weeks. Actual doses were 350 or 630 ppm for 5 weeks, 375 or 750 ppm for 11 weeks, and 425 or 850 ppm for the next 62 weeks. After an additional 15 weeks, an increased incidence of hepatocellular carcinomas was seen in both sexes by comparison to controls, but the increase was not statistically significant.

NCI (1978) also fed DDD at 1647 and 3294 ppm TWA for males and 850 and 1700 ppm TWA for females for 78 weeks to 50 Osborne-Mendel rats/sex/dose. Males were fed 1400 or 2800 ppm for 23 weeks followed by 1750 or 3500 ppm for 55 weeks. Females were fed 850 or 1700 ppm for the entire 78 weeks. After an additional 35 weeks, an increased incidence of thyroid tumors (follicular cell adenomas and carcinomas) was observed in males. Due to a wide variation in incidence of these tumors in the control groups for DDD, DDE and DDT, the increased incidence was not statistically significant by comparison to concurrent controls. Although tumor incidence did not appear to be dose-related, the increase was significant at the low dose by comparison to historical controls. Thus, the pathologists' judgment and statistical results suggest a possible carcinogenic effect of DDD in male rats. NCI concluded that a definitive interpretation of the data was not possible.

II.A.4. Supporting Data for Carcinogenicity

DDD is structurally similar to, and is a metabolite of, DDT, a probable human carcinogen, in rats (Peterson and Robinson, 1964), mice (Gingell and Wallcave, 1976), and humans (Morgan and Roan, 1977).

Positive effects were found with DDD in mammalian cytogenetic assays and a host-mediated assay (ICPEMC, 1984).

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

II.B.1. Summary of Risk Estimates

Oral Slope Factor — 2.4E-1/mg/kg/day

Drinking Water Unit Risk — 6.9E-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 — liver
Test animals — mouse/CF-1, males
Route — diet
Reference — Tomatis et al., 1974

Administered Dose (ppm)	Human Equivalent Dose (mg/kg)/day	Tumor Incidence
0	0	33/98
250	2.45	31/59

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

DDD used in the Tomatis study was 99% pure p,p'-isomer. In the NCI bioassay, technical grade DDD was used, in which 60% of the material consisted of the p,p'-isomer. The composition of the remaining 40% was unspecified, but it was stated that analysis by gas chromatography revealed at least 19 impurities.

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 tested. The slope factor was calculated using tumor incidence data from only one dose. The slope factor was similar to, and within a factor of 2, of the slope factors for this same site of three other structurally similar compounds: DDT, 3.4E-1/mg/kg/day; DDE, 3.4E-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 — 06/03/1987, 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'-Dichlorodiphenyl dichloroethane conducted in November 2001 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'-Dichlorodiphenyl dichloroethane (DDD)
CASRN — 72-54-8

VI.A. Oral RfD References

None

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

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VII. Revision History

Substance Name — p,p'-Dichlorodiphenyl dichloroethane (DDD)
CASRN — 72-54-8

Date	Section	Description
08/22/1988	II.	Carcinogen summary on-line
12/03/2002	II.D.2.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — p,p'-Dichlorodiphenyl dichloroethane (DDD)
CASRN — 72-54-8
Last Revised — 08/22/1988

- 72-54-8
- 1,1-bis(4-chlorophenyl)-2,2-dichloroethane
- 1,1-bis(p-chlorophenyl)-2,2-dichloroethane
- 2,2-bis(p-chlorophenyl)-1,1-dichloroethane
- DDD
- 4,4'-DDD
- p,p'-DDD
- 1,1-dichloro-2,2-bis(p-chlorophenyl)ethane
- dichlorodiphenyl dichloroethane
- Dichlorodiphenyl dichloroethane, p,p'-
- dilene
- rothane
- TDE
- p,p'-TDE