Toxaphene; CASRN 8001-35-2

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 Toxaphene

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 — Toxaphene
CASRN — 8001-35-2

Not available at this time.

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

Substance Name — Toxaphene
CASRN — 8001-35-2

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Toxaphene
CASRN — 8001-35-2
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 — The classification is based on increased incidence of hepatocellular tumors in mice and thyroid tumors in rats and is supported by mutagenicity in Salmonella.

II.A.2. Human Carcinogenicity Data

None.

II.A.3. Animal Carcinogenicity Data

Sufficient. Two long-term carcinogenicity bioassays with toxaphene have been performed in rats and mice with both species showing a carcinogenic response. Dietary toxaphene was administered for 18 months at doses of 0, 7, 20 and 50 ppm to 54 B6C3F1 mice/sex/group. Animals were observed 6 months post-treatment. An increased incidence of hepatocellular carcinomas and neoplastic nodules (adenomas) was seen in both sexes and was statistically significant in males administered 50 ppm (Litton Bionetics, 1978).

In a second study (NCI, 1979), dietary toxaphene was administered to 50 Osborne-Mendel rats/sex/group and 50 B6C3F1 mice/sex/group for 80 weeks. Rats received TWA doses of 556 and 1112 ppm for males and 540 and 1080 ppm for females. The animals were observed for 28-30 weeks post-treatment. Controls consisted of 10 matched controls/sex and 45 additional pooled controls/sex. A statistically significant dose-related increased incidence of thyroid tumors (adenomas and carcinomas) was seen in both male and female rats.

Mice received TWA doses of 99 and 198 ppm for both sexes. Controls consisted of 10 matched controls/sex and 40 additional pooled controls/sex. A statistically significantly increased incidence of liver cancer in treated animals was observed and was dose-related (NCI, 1979).

II.A.4. Supporting Data for Carcinogenicity

Toxaphene is mutagenic to Salmonella (Hill, 1977). It was negative in a modified dominant lethal assay of male ICR/Ha Swiss mice (Epstein, 1972). No significant differences were found between rates of chromosomal aberrations in leukocytes of workers occupationally exposed to toxaphene and of unexposed workers (U.S. EPA, 1978).

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

II.B.1. Summary of Risk Estimates

Oral Slope Factor — 1.1E+0 per (mg/kg)/day

Drinking Water Unit Risk — 3.2E-5 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+0 ug/L
E-5 (1 in 100,000)	3E-1 ug/L
E-6 (1 in 1,000,000)	3E-2 ug/L

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

Tumor Type — hepatocellular carcinomas and neoplastic nodules
Test animals — mouse/B6C3F1, males
Route — diet
Reference — Litton Bionetics, 1978

Administered Dose		Human Equivalent Dose (mg/kg)/day	Tumor Incidence
(ppm)	**(mg/kg)/day)**		
0	0.0	0	10/53
7	0.91	0.051	10/54
20	2.6	0.144	12/53
50	6.5	0.361	18/51

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

The Litton Bionetics (1978) study was used for derivation of a slope factor because more dose levels were used, and a positive carcinogenic response was found at a lower dose than in the NCI study (1979). Weight of the animals was assumed to be 0.03 kg, and animal lifetime was taken as 735 days, the duration of the experiment.

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

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

An adequate number of animals was observed. A dose-response effect was seen in a study with 3 non-zero dose levels.

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

II.C.1. Summary of Risk Estimates

Inhalation Unit Risk — 3.2E-4 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-2 ug/cu.m
E-6 (1 in 1,000,000)	3E-3 ug/cu.m

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

The unit risk was calculated from the oral data presented in II.B.2.

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

The unit risk should not be used if the air concentration exceeds 3.1E+1 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, 1978, 1980

The values in the 1980 Ambient Water Quality Criteria document have received both Agency and outside review.

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

Agency Work Group Review — 03/05/1987

Verification Date — 03/05/1987

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 Toxaphene conducted in September 2002 identified one or more significant new studies. IRIS users may request the references for those studies from 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 — Toxaphene
CASRN — 8001-35-2

VI.A. Oral RfD References

None

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

Epstein, S.S. E. Arnold, J. Andrea, W. Bass and Y. Bishop. 1972. Detection of chemical mutagens by the dominant lethal assay in the mouse. Toxicol. Appl. Pharmacol. 23(2): 288-325.

Hill, R.N. 1977. Memorandum to Fred Hageman. Off. Spec. Pestic. Rev., U.S. EPA. December 15.

Litton Bionetics. 1978. Carcinogenic evaluation in mice: Toxaphene. Final report. Prepared by Litton Bionetics, Inc., Kensington, MD for Hercules, Inc., Wilmington, DE. LBI Project No. 20602.

NCI (National Cancer Institute). 1979. Bioassay of Toxaphene for Possible Carcinogenicity. Carcinogenesis Testing Program. Division of Cancer Cause and Prevention. NCI, National Institute of Health, Bethesda, Maryland, 20014. U.S. Department of Health, Education and Welfare. DHEW Publication No. (NIH) 79-837.

U.S. EPA. 1978. Occupational Exposure to Toxaphene. A Final Report by the Epidemiologic Studies Program, Human Effects Monitoring Branch, Benefits and Field Studies Division, OPP, OTS, EPA.

U.S. EPA. 1980. Ambient Water Quality Criteria for Toxaphene. 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 440/5-80-076. NTIS PB 81-117863.

VII. Revision History

Substance Name — Toxaphene
CASRN — 8001-35-2

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 — Toxaphene
CASRN — 8001-35-2
Last Revised — 08/22/1988

- 8001-35-2
- alltox
- chlorinated-camphene
- geniphene
- penphene
- phenacide

- toxadust
- toxakil
- Toxaphene