technical Hexachlorocyclohexane (t-HCH); CASRN 608-73-1

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 t-HCH

File First On-Line 03/31/1987

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	not evaluated	
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	yes	03/31/1987

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — technical Hexachlorocyclohexane (t-HCH)
CASRN — 608-73-1

Not available at this time.

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

Substance Name — technical Hexachlorocyclohexane (t-HCH)
CASRN — 608-73-1

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — technical Hexachlorocyclohexane (t-HCH)
CASRN — 608-73-1
Last Revised — 03/31/1987

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 — Assays in four strains of mice have yielded positive carcinogenicity results for t-HCH administered in the diet.

II.A.2. Human Carcinogenicity Data

Inadequate. One case report of a Japanese sanitation employee with acute leukemia was associated with occupational exposure to HCH and DDT (Hoshizaki et al., 1969).

II.A.3. Animal Carcinogenicity Data

t-HCH has been reported to increase the incidences of liver neoplasms in four strains of mice (Hanada et al., 1973; Goto et al., 1972; Kashyap et al., 1979; Nigam et al., 1984; Bhatt et al., 1981; Munir et al., 1983; Nagasaki et al., 1972a,b; Munir and Bhide, 1984).

Munir et al. (1983) gave dietary t-HCH at 0, 125, 250 or 500 ppm to male Swiss mice from age 8-10 weeks. Animals were killed at 8-11, 12-14, 15-17 or 18-22 months of age. Both treatment dose- and duration-related increases in incidence of benign hepatic nodules and hepatocellular carcinomas were observed. Hanada et al. (1973) fed groups of 10-11 each male and female dd mice diets containing 0, 100, 300 or 600 ppm t-HCH for a period of 32 weeks. Mice were maintained on basal diet an additional 6 weeks. At the end of this time incidence of liver nodules and hepatomas was increased in both males and females of the two upper dose groups. Nagasaki also administered dd mice dietary t-HCH. Males only received basal diet (14 mice) or 6.6 ppm (20), 66.0 ppm (20) or 660.0 ppm (20) t-HCH. Treatment was for 24 weeks, at which time the animals were killed. Cellular hyperplasia of the liver was treatment-related. Nodules and hepatomas were seen in 100% of the highest dose animals, but not in the two lower dose groups. Goto et al. (1972) observed increases in liver weight of ICR-JCL mice fed 600 ppm t-HCH in the diet. All t-HCH-treated mice developed hepatomas. Dietary t-HCH at levels up to 500 ppm has not been shown to produce tumors in Wistar rats or Syrian golden hamsters after 30 months of treatment (Munir et al., 1983).

II.A.4. Supporting Data for Carcinogenicity

No data on genetic toxicology of t-HCH are available. Alpha-HCH, which comprises approximately 65% of t-HCH, has been observed to produce similar results to t-HCH in carcinogen bioassays.

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

II.B.1. Summary of Risk Estimates

Oral Slope Factor - 1.8E+0 per (mg/kg)/day

Drinking Water Unit Risk — 5.1E-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)	2E+0 ug/L
E-5 (1 in 100,000)	2E-1 ug/L
E-6 (1 in 1,000,000)	2E-2 ug/L

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

Tumor Type: liver nodules and hepatocellular carcinomas
Test animals: mouse/Swiss, male
Route: diet
Reference: Munir et al., 1983

Administered Dose		Human Equivalent Dose (mg/kg)/day	Tumor Incidence
ppm	**(mg/kg)/day**		
0	0	0	2/22
125	16.25	0.299	8/20
250	32.50	0.598	12/12

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

Animal doses were converted from ppm to mg/kg/day by multiplying by a food factor of 0.13. Control data are from a similar experiment in male Swiss mice reported in the same paper. Unlike the treated animals, which were killed at 15-17 months, the controls were killed at 15-20 months. The data set chosen was for those mice treated over the greatest proportion of their lifespan. The slope factor calculation included an adjustment for the short duration of the experiment. The human equivalent dose was calculated by multiplying the transformed dose by

(0.03/70)**1/3 for body weight adjustment and (15/24)**3 to adjust the length of the experiment to the lifespan of the animal.

The unit risk should not be used if the water concentration exceeds 200 ug/L, since above this concentration the unit risk may not be appropriate.

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

The number of animals treated was relatively small, and the dose range was limited. Slope factors using data of Nagasaki et al. (1972a,b) and data from Munir et al. (1983) for mice killed at 12-14 months were 7.4 and 1.2 per (mg/kg)/day, respectively. These values are generally supportive of the risk estimate.

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

II.C.1. Summary of Risk Estimates

Inhalation Unit Risk — 5.1E-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)	2E-1 ug/cu.m
E-5 (1 in 100,000)	2E-2 ug/cu.m
E-6 (1 in 1,000,000)	2E-3 ug/cu.m

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

The inhalation risk estimates were calculated from the oral exposure 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 20 ug/cu.m, since above this concentration the unit risk may not be appropriate.

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

See II.B.4.

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

II.D.1. EPA Documentation

Source Document — U.S. EPA, 1986

The 1986 Health and Environmental Effects Profile has received an Agency review.

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

Agency Work Group Review — 12/17/1986

Verification Date — 12/17/1986

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 technical Hexachlorocyclohexane (t-HCH) 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 — technical Hexachlorocyclohexane (t-HCH)
CASRN — 608-73-1

VI.A. Oral RfD References

None

VI.B. Inhalation RfD References

None

VI.C. Carcinogenicity Assessment References

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Nigam, S.K., B.C. Lakkad, A.B. Karnik and K.M. Thakore. 1984. Ultrastructural changes in liver of mice exposed to hexachlorocyclohexane. Ind. J. Exp. Biol. 22(4): 199-204.

U.S. EPA. 1986. Health and Environmental Effects Profile for Hexachlorocyclohexanes. 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.

VII. Revision History

Substance Name — technical Hexachlorocyclohexane (t-HCH)
CASRN — 608-73-1

Date	Section	Description
10/28/2003	II.D.2.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — technical Hexachlorocyclohexane (t-HCH)
CASRN — 608-73-1
Last Revised — 03/31/1987

- 319-84-6 (alpha-HCH)

- 319-85-7 (beta-HCH)
- 319-86-8 (delta-HCH)
- 58-89-9 [gamma-HCH (lindane)]
- 608-73-1
- 6108-10-7 (epsilon-HCH)
- 6108-11-8 (zeta-HCH or iota-HCH)
- 6108-12-9 (eta-HCH)
- 6108-13-0 (theta-HCH)
- t-HCH
- Hexachlorocyclohexane, technical
- mixture of HCH isomers
- mixture of 1,2,3,4,5,6-hexachlorocyclohexane isomers