beta-Hexachlorocyclohexane (beta-HCH); CASRN 319-85-7

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 beta-HCH

File First On-Line 09/30/1987

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	not evaluated	
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	yes	09/30/1987

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — beta-Hexachlorocyclohexane (beta-HCH)
CASRN — 319-85-7

Not available at this time.

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

Substance Name — beta-Hexachlorocyclohexane (beta-HCH)
CASRN — 319-85-7

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — beta-Hexachlorocyclohexane (beta-HCH)
CASRN — 319-85-7
Last Revised — 09/30/1987

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 — C; possible human carcinogen

Basis — Increases in benign liver tumors in CF1 mice fed beta-HCH

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

Positive or marginally positive tumorigenic responses, characterized as benign hepatomas or hepatocellular carcinomas, have been observed in two strains of mice. The studies are limited in that small numbers of animals were used, no dose-response data are available, not all of the animals were examined histologically, or the duration of exposure was less than lifetime.

Thorpe and Walker (1973) fed 30 each male and female CF1 mice dietary beta-HCH at 200 ppm for 110 weeks. This resulted in 12% mortality of males and 25% of females during the first 3 months. A significantly increased incidence of liver tumors was observed in treated males and females.

No statistically significant evidence of increased tumor incidence as a consequence of beta-HCH feeding was seen in several small (5-20/group) studies with male and female dd mice fed 0-600 ppm for 24-32 weeks (Nagasaki et al., 1972; Hanada et al. 1973; Ito et al., 1973) or in male Wistar rats (Ito et al., 1975; Fitzhugh et al., 1950) fed 0-1000 ppm for >72 weeks.

Goto et al. (1972) maintained male ICR-JCL mice on a diet containing 600 ppm beta-HCH for 26 weeks. Relative liver weight was increased in the treated animals, and there was histologic evidence of benign neoplasms at an unspecified incidence.

II.A.4. Supporting Data for Carcinogenicity

No data on genetic toxicology of beta-HCH are available.

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 — 5.3E-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 — hepatic nodules and hepatocellular carcinomas
Test Animals — Mouse/CF1, male
Route — diet
Reference — Thorpe and Walker, 1973

Administered Dose (ppm)	Human Equivalent Dose (mg/kg)/day	Tumor Incidence
0	0	11/45
200	1.96	22/24

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

Animal TWA dose (26 mg/kg/day) was calculated based on exposure and lifetime of 110 weeks (reported). This unit risk should not be used if water concentration exceeds 200 ug/L, since above this concentration the slope factor may differ from that stated.

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

The risk estimate was calculated on data from only one non-zero dose group. Relatively few animals and limited number of doses were used. A slope factor based on the data of Nagasaki et al. (1972) was calculated to be 4.7 per (mg/kg)/day and one based on Ito et al. (1973) to be 6.3 per (mg/kg)/day. These are generally supportive of the slope factor derived from Thorpe and Walker, which is the only available chronic study.

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

II.C.1. Summary of Risk Estimates

Inhalation Unit Risk — 5.3E-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 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 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 HEEP has received Agency Review.

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

Agency Work Group Review — 10/29/1986, 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 beta-Hexachlorocyclohexane (beta-HCH) 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 — beta-Hexachlorocyclohexane (beta-HCH)
CASRN — 319-85-7

VI.A. Oral RfD References

None

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

Goto, M., M. Hattori and T. Miyagawa. 1972. Contribution on ecological chemistry. II. Formation of hepatoma in mice after ingestion of HCH isomers in high doses. Chemosphere. No. 6. p. 279-282.

Fitzhugh, O.G., A.A. Nelson, and J.P. Frawley. 1950. The chronic toxicities of technical benzene hexachloride and its alpha, beta, and gamma isomers. J. Pharmacol. Exp. Therap. 100: 59-66.

Hanada, M., C. Yutani and T. Miyaji. 1973. Induction of hepatoma in mice by benzene hexachloride. Gann. 64: 511-513.

Hoshizaki, H., Y. Niki, H. Tajima, Y. Terada and A. Kasahara. 1969. A case of leukemia following exposure of insecticide. Nippon Ketsueki Gakkai Zasshi. 32(4): 672-677.

Ito, N., H. Nagasaki, M. Arai, S. Makiura, S. Sugihara and K. Hirao. 1973. Histopathologic studies on liver tumorigenesis induced in mice by technical polychlorinated biphenyls and its promoting effect on liver tumors induced by benzene hexachloride. J. Natl. Cancer Inst. 51(5): 1637-1646.

Ito, N., H. Nagasaki, H. Aoe, et al. 1975. Brief communication: Development of hepatocellular carcinomas in rats treated with benzene hexachloride. J. Natl. Cancer Inst. 54(3): 801-805.

Nagasaki, H., S. Tomii, T. Mega, M. Marugami and N. Ito. 1972. Carcinogenicity of benzene hexachloride. In: Proc. 2nd International Symposium of the Princess Takamatsu Cancer Research Fund. Topics in Chemical Carcinogenesis, W. Nakahara, S. Takayama, T. Sugimura and S. Odashima, Ed. University Park Press, Baltimore, MD. p. 343-353.

Thorpe, E. and A.I.T. Walker. 1973. Toxicology of dieldrin (HEOD). II. Comparative long-term oral toxicity studies in mice with dieldrin, DDT, phenobarbitone, beta-HCH and gamma-HCH. Food Cosmet. Toxicol. 11: 433-442.

U.S. EPA. 1986. Health and Environmental Effects Profile for Hexachloro- cyclohexanes. 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 — beta-Hexachlorocyclohexane (beta-HCH)
CASRN — 319-85-7

Date	Section	Description
12/03/2002	II.D.2.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — beta-Hexachlorocyclohexane (beta-HCH)
CASRN — 319-85-7
Last Revised — 09/30/1987

- 319-85-7
- BENZENEHEXACHLORIDE, trans-alpha-
- BETA-ISOMER
- beta-BHC
- CYCLOHEXANE, 1,2,3,4,5,6-HEXACHLORO-, beta-
- CYCLOHEXANE, 1,2,3,4,5,6-HEXACHLORO-, trans-
- CYCLOHEXANE, beta-1,2,3,4,5,6-HEXACHLORO-
- CYCLOHEXANE, 1,2,3,4,5,6-HEXACHLORO-, beta-isomer
- ENT 9,233
- beta-HCH
- beta-HEXACHLOROBENZENE
- 1-alpha,2-beta,3-alpha,4-beta,5-alpha,6-beta-HEXACHLOROCYCLOHEXANE
- Hexachlorocyclohexane, beta-
- beta-1,2,3,4,5,6-HEXACHLOROCYCLOHEXANE
- beta-LINDANE
- trans-alpha-BENZENEHEXACHLORIDE