Pentachlorobenzene; CASRN 608-93-5

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 Pentachlorobenzene

File First On-Line 01/31/1987

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	01/31/1987
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	yes	11/01/1992

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Pentachlorobenzene
CASRN — 608-93-5
Last Revised — 01/31/1987

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of substances that are also carcinogens. Therefore, it is essential to refer to other sources of

information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

I.A.1. Oral RfD Summary

Critical Effect	Experimental Doses*	UF	MF	RfD
Liver and kidney toxicity **Subchronic Rat Oral Bioassay (including weanlings)** **Linder et al., 1980**	NOAEL: none LOAEL: 8.3 mg/kg/day	10,000	1	8E-4 mg/kg/day

*Conversion Factors: none

I.A.2. Principal and Supporting Studies (Oral RfD)

Linder, R., T. Scotti, J. Goldstein, K. McElroy and D. Walsh. 1980. Acute and subchronic toxicity of pentachlorobenzene. J. Environ. Pathol. Toxicol. 4: 183-196.

This study utilized 8 experimental groups (3 male, 5 female) of 10 rats each. A statistically significant increase in kidney weights, a decreased heart weight, and an increase in hyaline droplets in proximal kidney tubules was noted in rats receiving 8.3 mg/kg/day. Female rats receiving the next highest dose, 18 mg/kg/day, and their offspring showed increased liver/body weight ratios. At higher doses (up to 72 mg/kg/day) animals of both sexes showed hepatocellular enlargement, increase in adrenal and kidney weights, increased WBC counts, and lowered RBC indices. Suckling pups of dams receiving 18 mg/kg/day and higher doses of pentachlorobenzene developed tremors. The lowest dose of 8.3 mg/kg/day is considered a LOAEL.

Linder et al. (1980) published a chart on estimated dietary dosage of pentachlorobenzene from which a figure of 8.3 mg/kg/day was estimated for male rats receiving 125 ppm in the diet. The 1985 Health Assessment Document for Chlorinated Benzenes reports an estimated dosage of approximately 11 mg/kg/day calculated from the same data.

I.A.3. Uncertainty and Modifying Factors (Oral RfD)

UF — The composite uncertainty factor of 10,000 represents 10 each for the expected interspecies and interhuman variability to the toxicity of this compound in lieu of specific data, 10 to extrapolate a subchronic effect level to its chronic counterpart, and 10 to drop the LOAEL into the expected range of a NOAEL.

MF — None

I.A.4. Additional Studies/Comments (Oral RfD)

An ADI of 0.0167 mg/kg was reported in the 1980 Ambient Water Quality Criteria for Chlorinated Benzenes. This was based on a paper by Khera and Villaneuve (1975) dealing with reproductive effects of short-term (10 days) feeding in rats.

I.A.5. Confidence in the Oral RfD

Study — Medium
Database — Low
RfD — Low

The study rates a medium confidence because several effects were monitored, and both adult animals and neonates were tested. The study does not rate higher than medium because a NOAEL was not established and only a moderate number of animals was used. The database rates a low confidence because few data exist to support this analysis. Confidence in the RfD can be considered low to medium.

I.A.6. EPA Documentation and Review of the Oral RfD

Source Document — U.S. EPA, 1983

The ADI in the 1983 Health and Environmental Effects Profile document has received an Agency Review with the help of two external scientists.

Other EPA Documentation — U.S. EPA, 1985

Agency Work Group Review — 10/09/1985

Verification Date — 10/09/1985

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfD for pentachlorobenzene conducted in August 2003 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.

I.A.7. EPA Contacts (Oral RfD)

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).

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

Substance Name — Pentachlorobenzene
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Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Pentachlorobenzene
CASRN — 608-93-5
Last Revised — 11/01/1992

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 — D; not classifiable as to human carcinogenicity

Basis — No human data and no animal data available.

II.A.2. Human Carcinogenicity Data

None.

II.A.3. Animal Carcinogenicity Data

None.

II.A.4. Supporting Data for Carcinogenicity

Haworth et al. (1983) reported that pentachlorobenzene at concentrations of 0, 33.3, 333.3, 1000 and 3333.3 ppm did not produce reverse mutations in four strains of Salmonella typhimurium (TA98, TA100, TA1535 and TA1537) in the presence or absence of rat liver microsomes (S9). Similar results wee reported at unpecified concentrations (presumably the same) by the same group in an abstract (Lawlor et al., 1979). Pentachlorobenzene was also negative in Chinese hamster ovary cell assays for induction of sister chromatid exchanges and chromosomal aberrations (NTP, 1991). In 13-week rat and mouse micronucleus assays, pentachlorobenzene tested negative in all exposed groups (NTP, 1991). The metabolites of pentachlorobenzene (chlorobenzene, tetrachlorophenols, tetrachlorobenzenes, trichlorophenols, trichlorobenzenes, pentachlorophenol, tetrachlorohydroquinone) were all negative for gene mutation assays in Salmonella (Haworth et al., 1983; Zeiger et al., 1988; NTP, 1991). Some of the metabolites (e.g., pentachlorophenol), have shown evidence of clastogenic activity in vitro (Galloway et al., 1987; NTP, 1991).

In rat and monkey metabolism studies, Engst et al. (1976) and Rozman et al. (1979) identified pentachlorophenol (classified as B2, probable human carcinogen) and 2,3,4,5-tetrachlorophenol as major metabolites of pentachlorobenzene. Other chlorinated phenols were also identified as

metabolites. Pentachlorophenol has also been identified in the urine of rabbits administered pentachlorobenzene (Kohli et al., 1976).

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

None.

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

None.

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

II.D.1. EPA Documentation

Source Document — U.S. EPA, 1989

The Health and Environmental Effects Document for Pentachlorobenzene has received Agency and external review.

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

Agency Work Group Review — 09/05/1991, 04/01/1992

Verification Date — 04/01/1992

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 pentachlorobenzene 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 — Pentachlorobenzene
CASRN — 608-93-5

VI.A. Oral RfD References

Khera, K.S. and D.C. Villeneuve. 1975. Teratogenicity studies on halogenated benzenes (pentachloro-, pentachloronitro-, and hexabromo-) in rats. Toxicology. 5(1): 117-122.

Linder, R., T. Scotti, J. Goldstein, K. McElroy and D. Walsh. 1980. Acute and subchronic toxicity of pentachlorobenzene. J. Environ. Pathol. Toxicol. 4: 183-196.

U.S. EPA. 1983. Health and Environmental Effects Profile for Pentachlorobenzene. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste, Washington, DC.

U.S. EPA. 1985. Health Assessment Document for Chlorinated Benzenes. Office of Health and Environmental Assessment, Washington, DC. EPA 600/8-84-O15F.

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

Engst, R., R.M. Macholz, M. Kujawa, H.J. Lewerenz and R. Plass. 1976. The metabolism of lindane and its metabolites gamma-2,3,4,5,6- pentachlorocyclohexene, pentachlorobenzene and pentachlorophenol in rats and the pathways of lindane metabolism. J. Environ. Sci. Health, Part B. 11(2): 95-117.

Galloway, S.M., M.J. Armstrong, C. Reuben et al. 1987. Chromosome aberrations and sister chromatid exchanges in Chinese hamster ovary cells: Evaluations of 108 chemicals. Environ. Molec. Mutagen. 10(Suppl. 10): 1-175.

Haworth, S., T. Lawlor, K. Mortelmans, W. Speck and E. Zeiger. 1983. Salmonella mutagenicity test results for 250 chemicals. Environ. Mutagen. Suppl. 1: 3-142.

Kohli, J., D. Jones and S. Safe. 1976. The metabolism of higher chlorinated benzene isomers. Can. J. Biochem. 54(3): 203-208.

Lawlor, T., S.R. Haworth and P. Voytek. 1979. Evaluation of the genetic activity of nine chlorinated phenols, seven chlorinated benzenes and three chlorinated hexanes. Environ. Mutagen. 1(2): 143. (Abstract)

NTP (National Toxicology Program). 1991. Toxicity Studies of Pentachlorobenzene in F344/N Rats and B6C3F1 Mice (Feed Studies). National Toxicology Program, Research Triangle Park, NC. NIH Publ. No. 91-3125.

Rozman, K., J. Williams, W.F. Mueller, F. Coulston and F. Korte. 1979. Metabolism and pharmacokinetics of pentachlorobenzene in the rhesus monkey. Bull. Environ. Contam. Toxicol. 22: 190-195.

U.S. EPA. 1980. Ambient Water Quality Criteria for Chlorinated Benzenes. 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/440/5-80/028. NTIS PB81-117392.

U.S. EPA. 1984. Health Assessment Document for Chlorinated Benzenes. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH. EPA/600/8-84-015F. NTIS PB85-150332.

U.S. EPA. 1989. Health and Environmental Effects Document for Pentachlorobenzene. 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.

Zeiger, E., B. Anderson, S. Haworth, T. Lawlor and K. Mortelmans. 1988. Salmonella mutagenicity tests: IV. Results from the testing of 300 chemicals. Environ. Molec. Mutagen. 11(Suppl. 12): 1-158.

VII. Revision History

Substance Name — Pentachlorobenzene
CASRN — 608-93-5

Date	Section	Description
11/01/1992	II.	Carcinogenicity assessment on-line
10/28/2003	I.A.6, II.D.2	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — Pentachlorobenzene
CASRN — 608-93-5
Last Revised — 01/31/1987

- 608-93-5
- BENZENE, PENTACHLORO-
- Pentachlorobenzene
- QCB
- RCRA WASTE NUMBER U183