Indeno[1,2,3-cd]pyrene; CASRN 193-39-5

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 Indeno[1,2,3-cd]pyrene

File First On-Line 12/01/1990

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	not evaluated	
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	yes	12/01/1990

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Indeno[1,2,3-cd]pyrene
CASRN — 193-39-5

Not available at this time.

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

Substance Name — Indeno[1,2,3-cd]pyrene
CASRN — 193-39-5

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Indeno[1,2,3-cd]pyrene
CASRN — 193-39-5
Last Revised — 12/01/1990

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 no human data and sufficient data from animal bioassays. Indeno[1,2,3-cd]pyrene produced tumors in mice following lung implants, subcutaneous injection and dermal exposure. Indeno[1,2,3-cd]pyrene tested positive in bacterial gene mutation assays.

II.A.2. Human Carcinogenicity Data

None. Although there are no human data that specifically link exposure to indeno[1,2,3-cd]pyrene to human cancers, indeno[1,2,3-cd]pyrene is a component of mixtures that have been associated with human cancer. These include coal tar, soots, coke oven emissions and cigarette smoke (U.S. EPA, 1984, 1990; IARC, 1984).

II.A.3. Animal Carcinogenicity Data

Sufficient. In carcinogen bioassays indeno[1,2,3-cd]pyrene exposure resulted in increased incidences of epidermoid carcinomas in a lung implantation study (Deutsch-Wenzel et al., 1983), injection site sarcomas in a subcutaneous injection assay (Lacassagne et al., 1963) and skin tumors in dermal application studies (Hoffman and Wynder, 1966; Rice et al., 1985a, 1986).

In a lifetime implant study, 3-month-old female Osborne-Mendel rats (35/group) received lung implants of indeno[1,2,3-cd]pyrene in 0.05 mL of a 1:1 (v:v) mixture of beeswax and trioctanoin (Deutsch-Wenzel et al., 1983). Rats received either 0.16 mg (0.65 mg/kg), 0.83 mg (3.4 mg/kg) or 4.15 mg (17 mg/kg) indeno[1,2,3-cd]pyrene. Controls consisted of an untreated group and a group receiving an implant of the vehicle. Median survival times in weeks were as follows: untreated controls, 118; vehicle controls, 104; low-dose, 116; mid-dose, 109; and high-dose, 92. Incidence of epidermoid carcinomas in the lung and thorax (combined) showed a statistically significant dose-related increase. The incidences were: untreated controls, 0/35; vehicle controls, 0/35; low-dose, 4/35 (11%); mid-dose, 8/35 (23%); and high-dose, 21/35 (60%).

Groups of male and female CD-1 mice (n=32) received intraperitoneal injections of indeno[1,2,3-cd]pyrene in dimethyl sulfoxide (DMSO) on days 1, 8 and 15 after birth (total dose = 580 ug/mouse) and were evaluated for tumors upon sacrifice at 52 weeks of age (LaVoie et al., 1987). One male mouse (1/11) developed a lung adenoma, no tumors occurred in female mice. Tumor incidence was not significantly different from vehicle controls. This test is considered to be a short-term lung tumor assay.

In mouse skin painting assays, indeno[1,2,3-cd]pyrene tested positive for cancer-initiating activity in several mouse strains (Hoffmann and Wynder, 1966; Rice et al., 1985a, 1986). In the Hoffmann and Wynder (1966) study female Swiss albino Ha/ICR/Mil mice (20/group) were given topical applications of indeno[1,2,3-cd]pyrene prepared as dioxane (at 0.05 and 0.1%) or in acetone solutions (at 0.01, 0.05 and 0.1%). Dioxane preparations did not induce skin tumors. By contrast, acetone solutions of indeno[1,2,3-cd]pyrene produced skin tumors in a dose-related fashion. No tumors were observed in animals painted with 0.01 or 0.05% indeno[1,2,3-cd]pyrene in acetone; 0.1% induced six papillomas and three carcinomas beginning at 9 months; and 0.5% resulted in seven papillomas and five carcinomas with the first tumor appearing at 3 months. The authors also reported that a total dose of 250 mg indeno[1,2,3- cd]pyrene delivered in 10 applications in 2 days was a sufficient initiating dose when followed by promotion with croton oil.

To examine the initiating capability of the compound's major metabolites in mouse skin, indeno[1,2,3-cd]pyrene was applied to the shaved backs of 20 Crl:CD-1(ICR)BR female mice (Rice et al., 1986). Acetone solutions were applied every other day for 10 days for a total

initiating dose of 1 mg indeno[1,2,3-cd]pyrene. This was followed 10 days later by applications of the promotor tetradecanoylphorbol (TPA) (0.0025% in 100 mL acetone) 3 times/week for 20 weeks. Tumor incidence was essentially 100%. Indeno[1,2,3- cd]pyrene-1,2-diol and -1,2-oxide treatment both resulted in 80% tumor incidence in contrast to 8-hydroxy- and acetone-treated controls (approximately 25 and 5%, respectively).

An earlier initiation-promotion bioassay performed by Rice et al. (1985a) showed a pronounced dose-response relationship for tumors. Following the same protocol described above, an 80% tumor incidence was observed in mice receiving a total initiating dose of 1 mg indeno[1,2,3-cd]pyrene with an average of about four tumors/mouse after 22 weeks of promotion. However, when the total initiating dose was decreased to 100 or 300 mg/mouse, the number of tumor-bearing mice was not significantly increased.

Injection site sarcomas were reported in 10/14 male and 1/14 female XVIIc/Z mice administered 3 injections at 1-month intervals of 0.6 mg indeno[1,2,3-cd]pyrene. No concurrent controls appear to have been run in this experiment; the authors report, however, that in this mouse strain no spontaneous subcutaneous tumors have been reported (Lacassagne et al., 1963).

II.A.4. Supporting Data for Carcinogenicity

Indeno[1,2,3-cd]pyrene produced positive results in reverse mutation assays in Salmonella typhimurium strains TA100 and TA98 (2-3 ug/plate) (LaVoie et al., 1979; Hermann et al., 1980; Rice et al., 1985b).

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

Not available.

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, 1984, 1990

The 1990 Drinking Water Criteria Document for Polycyclic Aromatic Hydrocarbons has received Agency and external review.

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

Agency Work Group Review — 02/07/1990, 08/05/1993, 09/21/1993, 02/02/1994

Verification Date — 02/07/1990

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 — Indeno[1,2,3-cd]pyrene
CASRN — 193-39-5

VI.A. Oral RfD References

None

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

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Rice, J.E., T.J. Hosted, Jr., M.C. DeFloria, E.J. LaVoie, D.L. Fischer and J.C. Wiley, Jr. 1986. Tumor-initiating activity of major in vivo metabolites of indeno[1,2,3-cd]pyrene on mouse skin. Carcinogenesis. 7(10): 1761-1764.

U.S. EPA. 1984. Carcinogen Assessment of Coke Oven Emissions. Office of Health and Environmental Assessment, Washington, DC. EPA 600/6-82-003F. NTIS PB 84-170181.

U.S. EPA. 1990. Drinking Water Criteria Document for Polycyclic Aromatic Hydrocarbons (PAHs). Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Drinking Water, Washington, DC. Final Draft. ECAO-CIN-D010, September, 1990.

VII. Revision History

Substance Name — Indeno[1,2,3-cd]pyrene
CASRN — 193-39-5

Date	Section	Description
12/01/1990	II.	Carcinogen assessment on-line

VIII. Synonyms

Substance Name — Indeno[1,2,3-cd]pyrene
CASRN — 193-39-5
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- 193-39-5
- Indeno(1,2,3-cd)pyrene
- HSDB 5101
- indeno(1,2,3-cd)pyrene
- o-PHENYLENEPYRENE
- RCRA WASTE NUMBER U137
- 1,10-(O-PHENYLENE)PYRENE
- 1,10-(1,2-Phenylene)pyrene

- 2,3-o-PHENYLENEPYRENE
- 2,3-PHENYLENEPYRENE