Pyrene; CASRN 129-00-0

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 Pyrene

File First On-Line 09/01/1990

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	09/01/1990
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	yes	09/01/1990

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Pyrene
CASRN — 129-00-0
Last Revised — 09/01/1990

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
Kidney effects (renal tubular pathology, decreased kidney weights) **Mouse Subchronic Oral Bioassay** **U.S. EPA, 1989**	NOAEL: 75 mg/kg/day LOAEL: 125 mg/kg/day	3000	1	3E-2 mg/kg/day

*Conversion Factors: None

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

U.S. EPA. 1989. Mouse Oral Subchronic Toxicity of Pyrene. Study conducted by Toxicity Research Laboratories, Muskegon, MI for the Office of Solid Waste, Washington, DC.

Male and female CD-1 mice (20/sex/group) were gavaged with 0, 75, 125, or 250 mg/kg/day pyrene in corn oil for 13 weeks. The toxicological parameters examined in this study included body weight changes, food consumption, mortality, clinical pathological evaluations of major organs and tissues, and hematology and serum chemistry. Nephropathy, characterized by the presence of multiple foci of renal tubular regeneration, often accompanied by interstitial lymphocytic infiltrates and/or foci of interstitial fibrosis, was present in 4, 1, 1, and 9 male mice in the control, low-, medium-, and high-dose groups, respectively. Similar lesions were seen in 2, 3, 7, and 10 female mice in the 0, 75, 125, and 250 mg/kg treatment groups. The kidney lesions were described as minimal or mild in all dose groups. Relative and absolute kidney weights were reduced in the two higher dosage groups. Based on the results of this study, the low dose (75 mg/kg/day) was considered the NOAEL and 125 mg/kg/day the LOAEL for nephropathy and decreased kidney weights.

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

UF — An uncertainty factor of 3000 reflects 10 each for intra- and interspecies variability, 10 for the use of a subchronic study for chronic RfD derivation, and an additional 3 to account for the lack of both toxicity studies in a second species and developmental/reproductive studies.

MF — None

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

White and White (1939) fed six male rats (unspecified strain) a diet containing 2000 mg pyrene/kg for 40 days. The average reported food intake for two animals was 6.1 g/day, and the average body weight for these two animals was 94.3 g. A decrease in body weight gain was observed in two animals. The authors stated that this body weight gain was representative of the whole group; although there was no change in food intake. White and White (1939) also observed enlarged livers and increased hepatic lipid content in animals treated with pyrene, benzpyrene or methylcholanthrene in the diet; however, incidence data were not reported and it is unclear whether this effect occurred in the pyrene treated rats. Interpretation of this study is further complicated by the lack of experimental controls and statistical analysis, small sample size, and incomplete reporting of histopathology results.

I.A.5. Confidence in the Oral RfD

Study — Medium
Database — Low
RfD — Low

Confidence in the principal study is medium, as it was a well-designed experiment that examined a variety of toxicological endpoints and identified both a NOAEL and LOAEL for the critical effect. Confidence in the database is low, due to the lack of supporting subchronic, chronic, and developmental/reproductive studies. Accordingly, confidence in the RfD is low.

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

Source Document — This assessment is not presented in any existing U.S. EPA document.

Other EPA Documentation — U.S. EPA, 1989

Agency Work Group Review — 11/15/1989

Verification Date — 11/15/1989

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 — Pyrene
CASRN — 129-00-0

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Pyrene
CASRN — 129-00-0
Last Revised — 09/01/1990

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 — D, not classifiable as to human carcinogenicity

Basis — Based on no human data and inadequate data from animal bioassays.

II.A.2. Human Carcinogenicity Data

None.

II.A.3. Animal Carcinogenicity Data

Inadequate. Groups of 14-29 newborn male and 18-49 newborn female CD-1 mice on 1, 8, and 15 days of age received intraperitoneal injections of pyrene (purity unknown) in dimethyl sulfoxide (DMSO) (total dose = 40, 141 or 466 ug/mouse), or DMSO alone (Wislocki et al., 1986). Tumors were evaluated in animals that died spontaneously after weaning and in all remaining animals at 1 year after exposure. The mid-dose group was initiated 10 weeks after the other groups and had a separate vehicle control. The survival rate in the high-dose groups (male and female) was 25 to 35%; most of the mice died between the last injection and weaning. This high mortality was not observed in the control, low- or mid-dose groups (the survival rates were not stated). A statistically significant increase in the incidence of liver carcinomas occurred in the mid-dose males (3/25) relative to their vehicle control group (0/45), but not in the high-dose males (1/14) or low-dose males (0/29) or in female mice, when compared with their respective controls. The incidences of total liver tumors (adenomas and carcinomas), lung tumors or malignant lymphomas were not statistically significantly elevated in treated animals. The results of this 1-year experiment were not considered to be positive because of the overall lack of tumorigenic response in the short-term.

Mouse skin-painting assays of pyrene as a complete skin carcinogen or as an initiator of carcinogenicity were either not positive or inconclusive (Badger et al., 1940; Horton and Christian, 1974; Van Duuren and Goldschmidt, 1976; Salaman and Roe, 1956; Scribner, 1973).

A subcutaneous pyrene injection did not produce tumors in Jackson A mice; the mice were observed for 18 months after injection (Shear and Leiter, 1941).

II.A.4. Supporting Data for Carcinogenicity

In DNA damage assays in Escherichia coli and Bacillus subtilis pyrene was not mutagenic (Ashby and Kilbey, 1981). In bacterial gene mutation tests both positive (Kinae et al., 1981; Bridges et al., 1981; Matijasevic and Zeiger, 1985; Sakai et al., 1985; Kaden et al., 1979; Bos et al., 1988) and negative (McCann et al., 1975; LaVoie et al., 1979; Ho et al., 1981; Bos et al., 1988) results have been reported. The consensus conclusion on the international collaborative study (which involved 20 bacterial test sets) was that protocol or evaluation criteria were critical factors in individual test verdicts. Pyrene induced increased incidence of mitotic gene conversion but not other genetic endpoints in yeast (de Serres and Hoffman, 1981). Pyrene did not induce an increase in sex-linked recessive lethals in Drosophila (Valencia and Houtchens, 1981).

Mixed results have also been observed in mammalian assays in vitro, again with protocol and evaluation criteria being a factor in at least some of the cases. In the collaborative study Evans and Mitchell (1981) concluded pyrene was positive for SCE induction in CHO cells when all concentrations were different from controls, but no apparent increase when the concentration was increased 10-fold. In the same volume, two other laboratories reported pyrene negative both for SCE and for chromosome aberrations in CHO cells (Brookes and Preston, 1981). Tong et al. (1981) also reported that pyrene did not induce SCE in a rat liver epithelial cell system. Jotz and Mitchell (1981) reported pyrene was positive in the L5178Y mouse lymphoma gene mutation assay.

Pyrene did not induce chromosome aberrations (as detected by micronuclei) or SCE in bone marrow of several mouse strains receiving i.p. injections of pyrene (Purchase and Ray, 1981). Results of mammalian cell transformation assays in a variety of cell types have not been positive (DiPaolo et al., 1969; Pienta et al., 1977; Casto, 1979; Chen and Heidelberger, 1969; DiPaolo et al., 1972; Kakunaga, 1973; Evans and DiPaolo, 1975).

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, 1990

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

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

Agency Work Group Review — 02/07/1990

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 — Pyrene
CASRN — 129-00-0

VI.A. Oral RfD References

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VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

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VII. Revision History

Substance Name — Pyrene
CASRN — 129-00-0

Date	Section	Description
09/01/1990	I.A, II.	Oral RfD summary and cancer assessment on-line

VIII. Synonyms

Substance Name — Pyrene
CASRN — 129-00-0
Last Revised — 09/01/1990

- 129-00-0
- BENZO(DEF)PHENANTHRENE
- HSDB 4023
- NSC 17534
- PYREN [GERMAN]
- PYRENE
- BETA-PYRENE