Anthracene; CASRN 120-12-7

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 Anthracene

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	01/01/1991

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Anthracene
CASRN — 120-12-7
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
No observed effects **Subchronic Toxicity Study in Mice** **U.S. EPA, 1989**	NOEL: 1000 mg/kg/day LOAEL: none	3000	1	3E-1 mg/kg/day

* Conversion Factors: none

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

U.S. EPA. 1989. Subchronic toxicity in mice with anthracene. Final Report. Hazelton Laboratories America, Inc. Prepared for the Office of Solid Waste, Washington, DC.

Anthracene was administered to groups of 20 male and female CD-1 (ICR)BR mice by oral gavage at doses of 0, 250, 500, and 1000 mg/kg/day for at least 90 days. Mortality, clinical signs, body weights, food consumption, opthalmology findings, hematology and clinical chemistry results, organ weights, organ-to-body weight ratios, gross pathology, and histopathology findings were evaluated. No treatment-related effects were noted. The no- observed-effect level (NOEL) is the highest dose tested (1000 mg/kg/day).

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

UF — An uncertainty factor of 3000 was used: 10 to account for interspecies extrapolation, 10 for intraspecies variability and 30 for both the use of a subchronic study for chronic RfD derivation and for lack of reproductive/developmental data and adequate toxicity data in a second species.

MF — None

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

In a chronic bioassay (Schmahl, 1955), a group of 28 BD I and BD III rats received anthracene in the diet, starting when the rats were approximately 100 days old. The daily dosage was 5 to 15 mg/rat, and the experiment was terminated when a total dose of 4.5 g/rat was achieved, on the 550th experimental day. The rats were observed until they died, with some living more than 1000 days. No treatment-related effects on lifespan or gross and histological appearance of tissues were observed. Body weights were not mentioned, and hematological parameters were not measured. No chronic LOAEL could be determined from this study.

I.A.5. Confidence in the Oral RfD

Study — Low
Database — Low
RfD — Low

Confidence in the study is low. It was a well-designed experiment examining a variety of toxicological endpoints; however, failure to identify a LOAEL precludes a higher level of confidence. Confidence in the database is low, because of the lack of adequate toxicity data in a second species and developmental/reproductive studies. Low confidence in the RfD follows.

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

Source Document — U.S. EPA, 1987

ECAO-CIN Internal Review and Limited Agency Review.

Other EPA Documentation — U.S. EPA,1989

Agency Work Group Review — 10/19/1989, 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 — Anthracene
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Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Anthracene
CASRN — 120-12-7
Last Revised — 01/01/1991

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. A group of 28 BDI or BDIII rats (sex not specified) were fed a diet containing anthracene in oil, 6 days/week for 78 weeks, and observed until natural death, approximately 700 days (Schmahl, 1955). The total dose was 4.5 g anthracene/rat (approximately 28 mg/kg/day). No concurrent controls were used. No tumors were observed.

Groups of 60 female 3-to 6-month-old Osborne-Mendel rats were observed for 55-81 weeks after receiving a single lung implant of anthracene (0.5 mg/rat, approximately 2 mg/kg) dissolved in a 1:1 (v:v) mixture of beeswax and trioctanoin (0.1 mL) (Stanton et al., 1972). Controls received an implant of the vehicle. No tumors were observed.

Tests for complete carcinogenicity and initiating activity in mouse skin- painting assays have not shown positive results. No tumors were observed in an assay of initiating activity in which Crl:CD/1 (ICR)BR female albino mice were exposed to 1 mg anthracene in acetone, and then treated with 12-o- tetradecanoyl-phorbol-13 acetate as the promoting agent 3 times/week for 20 weeks (LaVoie et al., 1985).

A single dermal application of 10 um anthracene (purity not stated) in benzene was administered to 30 female CD-1 mice; this initial application was followed 7 days later by twice-weekly applications of 5 um 12-0-tetradecanoyl phorbol-13-acetate (TPA) for 35 weeks. Survival in the group was 93% after 35 weeks. By week 20 of the test, 2/28 mice had developed skin tumors; this increased to 4/28 by week 35. In the control group, in which 30 mice received only the TPA applications, a mouse developed a skin tumor at week 25 (Scribner, 1973).

Kennaway (1924) administered 40% anthracene (purity unknown) either in lanolin or as an ether-extract to two groups of 100 mice each (sex and strain not stated). In the lanolin-group, 44% of the mice survived 131 days and in the ether-extract group only 6% survived until day 160. In the lanolin-group 1/44 surviving mice had developed a papilloma by day 131; no mice had developed tumors in the ether-extract by day 160. No information pertaining to the use of a control group was given.

Druckrey and Schmahl (1955) administered a diet containing anthracene in oil 6 days/week to 28 BDI or BDIII rats (sex not stated) for 78 weeks. The total dose was 4.5 g anthracene/rat. No treatment-related tumors were found, and no control groups appear to have been utilized.

II.A.4. Supporting Data for Carcinogenicity

Tests for DNA damage and gene mutations in prokaryotes have generally shown negative results. Negative results were observed in tests for DNA damage in Escherichia coli at concentrations up to 250 ug/mL and Bacillus subtilis at 62 ug/mL (Rosenkrantz and Poirier, 1979; McCarroll et al., 1981; DeFlora et al., 1984). Negative results were obtained in tests for reverse mutation in six strains of Salmonella typhimurium, at concentrations up to 1000 ug/plate (McCann et al., 1975; Simmon, 1979a; LaVoie et al., 1979; Salamone et al., 1979; Ho et al., 1981; DeFlora et al., 1984; Bos et al., 1988). Tests for forward mutation at 40 ug/mL were negative (Kaden et al., 1979). Positive results for reverse mutation in Salmonella typhimurium (TA97) at 10 ug/plate were reported (Sakai et al., 1985). Anthracene was tested in bacterial assays in 20 laboratories as part of an international collaborative study. One lab reported a positive in TA100 without activation, one lab reported a positive in TA98 and TA100 but only with S9 and all other labs reported negative results (Bridges et al., 1981).

Anthracene has consistently been negative in yeast test systems measuring mitotic recombination (Simmon, 1979b; de Serres and Hoffman, 1981), gene conversion, mutation and chromosome loss (de Serres and Hoffman, 1981).

Tests for DNA damage, mutation, chromosome effects and cell transformation in a variety of eukaryotic cell preparations have shown negative results. Anthracene showed negative results in tests for DNA damage (DNA synthesis) in primary rat hepatocytes (1 ug/mL), Chinese hamster ovary cells (1000 ug/mL), or HeLa cells (100 ug/mL) (Williams, 1977; Probst et al., 1981; Garrett and Lewtas, 1983; Martin et al., 1978; Martin and McDermid, 1981). It yielded negative results in tests for forward mutation in Chinese hamster V79 cells (125 ug/mL), mouse lymphoma L5178Y cells (18 ug/mL) and human lymphoblastoid cells (36 ug/mL) (Knapp et al., 1981; Amacher and Turner, 1980; Amacher et al., 1980; Barfknecht et al., 1981). Results obtained in tests for sister- chromatid exchange and chromosome breaks in Chinese hamster D6 cells and rat liver epithelial ARL-18 cells at 178 ug/mL were negative (Abe and Sasaki, 1977; Tong et al., 1981). Results reported in tests for cell transformation (morphological changes) at concentrations up to 30 ug/mL in mouse BALB/3T3 cells, guinea pig fetal cells, Syrian hamster embryo cells and mouse embryo C3H10T1/2 cells (DiPaolo et al., 1972; Evans and DiPaolo, 1975; Pienta et al., 1977; Lubet et al., 1983) were negative. In the international collaborative study negative results were reported with in vitro assays measuring unscheduled DNA synthesis, sister chromatid exchange, chromosome aberrations, and gene mutations (Brookes and Preston, 1981).

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 received 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 — Anthracene
CASRN — 120-12-7

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 — Anthracene
CASRN — 120-12-7

Date	Section	Description
09/01/1990	I.A.	Oral RfD summary on-line
01/01/1991	II.	Carcinogen assessment on-line

VIII. Synonyms

Substance Name — Anthracene
CASRN — 120-12-7
Last Revised — 09/01/1990

- 120-12-7
- ANTHRACEN [GERMAN]
- ANTHRACENE
- ANTHRACIN
- GREEN OIL
- HSDB 702
- NSC 7958
- PARANAPHTHALENE
- TETRA OLIVE N2G