U.S. Environmental Protection Agency

Integrated Risk Information System

Fluoranthene (CASRN 206-44-0)

MAIN CONTENTS

0444

Fluoranthene; CASRN 206-44-0

Health assessment information on a chemical substance is included in IRIS only after a comprehensive review of chronic toxicity data by U.S. EPA health scientists from several Program Offices and the Office of Research and Development. The summaries presented in Sections I and II represent a consensus reached in the review process. Background information and explanations of the methods used to derive the values given in IRIS are provided in the Background Documents.

STATUS OF DATA FOR Fluoranthene

File First On-Line 09/01/1990

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	on-line	07/01/1993
Inhalation RfC Assessment (I.B.)	no data	09/01/1994
Carcinogenicity Assessment (II.)	on-line	12/01/1990

_I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name -- Fluoranthene
CASRN -- 206-44-0
Last Revised -- 07/01/1993

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
Nephropathy, increased liver weights, hematological alterations, and clinical effects	NOAEL: 125 mg/kg/day LOAEL: 250 mg/kg/day	3000	1	4E-2 mg/kg/day

Mouse Subchronic Study

U.S. EPA, 1988

*Conversion Factors: None

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

U.S. EPA. 1988. 13-Week mouse oral subchronic toxicity study. Prepared by Toxicity Research Laboratories, Ltd., Muskegon, MI for the Office of Solid Waste, Washington, DC.

Male and female CD-1 mice (20/sex/group) were gavaged for 13 weeks with 0, 125, 250, or 500 mg/kg/day fluoranthene. A fifth group of mice (30/sex) was established in the study for baseline blood evaluations. Body weight, food consumption, and hematological and serum parameter values were recorded at regular intervals during the experiment. At the end of 13 weeks, the animals were sacrificed and autopsied, which included organ weight measurement and histological evaluation. All treated mice exhibited nephropathy, increased salivation, and increased liver enzyme levels in a dose-dependent manner. However, these effects were either not significant, not dose-related, or not considered adverse at 125 mg/kg/day. Mice exposed to 500 mg/kg/day had increased food consumption and increased body weight. Mice exposed to 250 and 500 mg/kg/day had statistically increased SGPT values and increased absolute and relative liver weights. Compound-related microscopic liver lesions (indicated by pigmentation) were observed in 65 and 87.5% of the mid- and high-dose mice, respectively. Based on increased SGPT levels, kidney and liver pathology, and clinical and hematological changes, the LOAEL is considered to be 250 mg/kg/day, and the NOAEL is 125 mg/kg/day.

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

UF -- An uncertainty factor of 3000 reflects 10 for interspecies conversion, 10 for intraspecies variability, and 30 for use of a subchronic study for chronic RfD derivation, and for lack of supporting reproductive/developmental toxicity data and toxicity data in a second species.

MF -- None

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

A developmental study was performed in which fluoranthene was administered once via intraperitoneal injection to pregnant C57/B6 mice on gestational day 6, 7, 8 or 9 (Irvin and Martin, 1987). An increased rate of embryo resorption was observed. The data were reported in an abstract, but a complete report was not located. No

Quantitative Estimate of Carcinogenic Risk from Oral Exposure
- Summary of Risk Estimates
- Dose-Response Data
- Additional Comments
- Discussion of Confidence

Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure
- Summary of Risk Estimates
- Dose-Response Data
- Additional Comments
- Discussion of Confidence

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inhalation studies were located.

IARC (1983) cites several acute studies in which fluoranthene was administered to mice or rats intraperitoneally. No adverse effects were observed; however, only survival or body weight was monitored. Gerarde (1960, cited by IARC, 1983) administered 500 mg/kg/day for 7 days to mice, and Haddow et al. (1937) administered a single 30 mg dose of fluoranthene to rats.

__I.A.5. Confidence in the Oral RfD

Study -- Medium
Database -- Low
RfD -- Low

Confidence in the principal study is medium, as it is a well-designed study that identified both a LOAEL and a NOAEL for several sensitive endpoints using an adequate number of animals. Confidence in the database is low; developmental, reproductive, or toxicity data in a second species following oral exposure to fluoranthene has not been adequately tested. Reflecting medium confidence in the principal study and low confidence in the database, 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, 1988

Agency Work Group Review -- 01/22/1986, 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).

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

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Not available at this time.

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_II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name -- Fluoranthene
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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 -- 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. Data from fluoranthene skin-painting bioassays was judged inadequate because no increases in tumor incidences were observed and the group sizes tested were small.

Fluoranthene has been tested as a complete carcinogen in mouse skin- painting assays at doses ranging approximately from 1.5 mg/mouse/week for 52 weeks to 100 mg/mouse/week for 82 weeks; the results of these studies have been consistently non-positive (Suntzeff et al., 1957; Wynder and Hoffmann, 1959; Hoffmann et al., 1972; Horton and Christian, 1974).

Suntzeff et al. (1957) administered a 10% solution of fluoranthene in acetone by topical application 3 times/week to unspecified numbers of CAF, Jackson, Swiss and Millerton mice. No tumors were found by 13 months. Wynder and Hoffmann (1959) administered a 0.1% solution of fluoranthene in acetone onto the backs of 20 female Swiss (Millerton) mice 3 times/week for life. No tumors were found. Hoffmann et al. (1972) administered 50 uL of a 1% fluoranthene solution to the backs of 20 female Swiss-albino Ha/ICR/Mill mice 3 times/week for 12 months. All treated mice survived and no tumors were observed. As part of the same study, 30 mice received 0.1 mg fluoranthene in 50 uL acetone every second day for a total of 10 doses. Promotion by dermal application of 2.5% croton oil in acetone was initiated 10 days later and continued for 20 weeks. A single papilloma was noted in 29 surviving mice. Horton and Christian (1974) administered 50 mg fluoranthene in decalin or in decalin:n-dodecane (50:50) to the backs of 15 male C3H mice. The mice were treated 2

times/week for 82 weeks. No skin tumors were observed.

__II.A.4. Supporting Data for Carcinogenicity

In a short-term in vivo lung tumor assay by Busby et al. (1984), CD-1 mice (20-30/sex/dose) received intraperitoneal injections of dimethyl sulfoxide (DMSO) or fluoranthene in DMSO on days 1, 8, and 15 after birth; total doses were 0, 700 ug (163 mg/kg) or 3500 ug (815 mg/kg) fluoranthene. Animals were necropsied at 24 weeks of age. Visible lung tumors were tabulated at necropsy and examined histologically; all tissue masses and organs exhibiting abnormal growth were examined histologically. A statistically significant increase in the incidence of combined lung adenomas and adenocarcinomas occurred in the male-female combined high-dose group (28/48) when compared with vehicle controls (5/55). In the combined high-dose groups 80% of the lung tumors were adenomas and 20% adenocarcinomas; no adenocarcinomas occurred in the control groups. Lung tumor response in the combined low-dose groups (10/51) was not statistically different from controls. Lung tumor incidence was significantly elevated in high-dose males (20/27 vs. 1/27 controls) but not in low-dose males (7/31) or in high- or low-dose females (8/21 and 3/20, respectively, vs. 4/28 in the controls).

Fluoranthene produced positive results in mouse co-carcinogen skin- painting assays with benzo[a]pyrene. This combination of chemicals increased the formation of benzo [a]pyrene-DNA adducts (Van Duuren and Goldschmidt, 1976; Rice et al., 1988).

Barry et al. (1935) administered 300 mg fluoranthene in benzene by dermal application (number of applications not stated) to 20 mice (type unspecified). The survival rate was 35% after 6 months and 20% at 1 year. No tumors were found by 501 days. Shear (1938) administered four doses of 10 mg fluoranthene in glycerol by subcutaneous injection to strain A mice. Six out of 14 mice survived for 18 months; no tumors were found by 19 months. In a skin-painting assay fluoranthene (100 ug) was administered to 20 Swiss albino Ha/ICR mice, 3 times/week for 1 year; 3.3% of the mice in both this group and in a similar acetone-control group tumors were observed in 3.3% of the mice in both the treated and acetone-control groups (LaVoie et al., 1979).

Evidence for mutagenicity of fluoranthene is equivocal. The results of mutagenicity assays of fluoranthene in several strains of Salmonella typhimurium have been positive (Kaden et al., 1979; Kinae et al., 1981; LaVoie et al., 1982; Babson et al., 1986; Bos et al., 1988) and not positive (Tokiwa et al., 1977; Kinae et al., 1981; Bos et al., 1987). Evidence for mutagenicity in mammalian cells is also equivocal: results of tests for chromosomal effects in Chinese hamster cells have been both positive (Palitti et al., 1986) and not positive (DeSaliva et al., 1988). A test for gene mutations in human lymphoblast cells was not positive (Crespi and Thilly, 1984), whereas results of tests in different mutant Chinese hamster ovary cell lines have been both positive (Hoy et al., 1984; Li, 1984) and not positive (Hoy et al., 1984).

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

None.

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

None.

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_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 -- 05/03/1990

Verification Date -- 05/03/1990

__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).

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_VI. Bibliography

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_VI.A. Oral RfD References

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IARC (International Agency for Research on Cancer). 1983. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Polynuclear Aromatic Compounds, Part 1. Chemical, Environmental and Experimental Data.

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_VI.B. Inhalation RfC References

None

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_VI.C. Carcinogenicity Assessment References

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Hoffmann, D., F. Rathkamp, S. Nesnow and E.L. Wynder. 1972. Fluoranthenes: Quantitative determination in cigarette smoke, formation by pyrolysis and tumor-initiating activity. J. Natl. Cancer. Inst. 49(4): 1165-1175.

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carcinogenic activity among aromatic hydrocarbons: Contrast between chrysene and benzo[b]triphenylene. J. Natl. Cancer Inst. 53(4): 1017-1020.

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LaVoie, E.J., E.V. Bedenko, N. Hirota, S.S. Hecht and D. Hoffmann. 1979. A comparison of the mutagenicity, tumor-initiating activity and complete coarcinogenicity of polynuclear aromatic hydrocarbons. In: Polynuclear Aromatic Hydrocarbons, P.W. Jones and P. Leber, Ed. Ann Arbor Science Publishers, Ann Arbor, MI. p. 705-721.

LaVoie, E.J., S.S. Hecht, V. Bedenko and D. Hoffmann. 1982. Identification of the mutagenic metabolites of fluoranthene, 2-methylfluoranthene and 3-methylfluoranthene. Carcinogenesis. 3(8): 841-846.

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Palitti, F., R. Cozzi, M. Fiore, et al. 1986. An in vitro and in vivo study on mutagenic activity of fluoranthene: comparison between cytogenic studies and HPLC analysis. Mutat. Res. 174(2): 125-130.

Rice, J.E., M.C. Defloria, C. Sensenhauser and E.J. Lavoie. 1988. The influence of fluoranthene on the metabolism and DNA binding of benzo[a]pyrene in vivo in mouse skin. Chem.-Biol. Interact. 68(1-2): 127-136.

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Suntzeff, V., A.B. Croninger, E.L. Wynder, E.V. Cowdry and E.A. Graham. 1957. Use of sebaceous-gland test of primary cigarette-tar fractions and of certain noncarcinogenic polycyclic hydrocarbons. Cancer. 10(2): 250-254.

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Wynder, E.L. and D. Hoffmann. 1959. A study of tobacco carcinogenesis. VII. The role of higher polycyclic hydrocarbons. Cancer. 12: 1079-1086.

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_VII. Revision History

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CASRN -- 206-44-0

Date	Section	Description
09/01/1990	I.A.	Oral RfD summary on-line
09/01/1990	VI.	Bibliography on-line
12/01/1990	II.	Carcinogen assessment on-line
12/01/1990	VI.C.	Carcinogen assessment references added
07/01/1991	I.A.7.	Primary and secondary contacts changed
01/01/1992	IV.	Regulatory Action section on-line
07/01/1993	I.A.6.	Other EPA Documentation added
09/01/1994	I.B.	Inhalation RfC now under review
08/01/1995	I.B.	EPA's RfD/RfC and CRAVE workgroups were discontinued in May, 1995. Chemical substance reviews that were not completed by September 1995 were taken out of IRIS review. The IRIS Pilot Program replaced the workgroup functions beginning in September, 1995.
04/01/1997	III., IV., V.	Drinking Water Health Advisories, EPA Regulatory Actions, and Supplementary Data were removed from IRIS on or before April 1997. IRIS users were directed to the appropriate EPA Program Offices for this information.

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_VIII. Synonyms

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206-44-0
1,2-BENZACENAPHTHENE
BENZENE, 1,2-(1,8-NAPHTHALENEDIYL)-
BENZENE, 1,2-(1,8-NAPHTHYLENE)-
BENZO(JK)FLUORENE
FLUORANTHENE
HSDB 5486
IDRYL
1,2-(1,8-NAPHTHYLENE)BENZENE
NSC 6803
RCRA WASTE NUMBER U120

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