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Reference Dose for Chronic Oral Exposure (RfD)

0452

Benzo[k]fluoranthene; CASRN 207-08-9

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 Benzo[k]fluoranthene

File First On-Line 11/01/1990

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	no data	
Inhalation RfC Assessment (I.B.)	no data	
Carcinogenicity Assessment (II.)	on-line	03/01/1994

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name -- Benzo[k]fluoranthene
CASRN -- 207-08-9

Not available at this time.

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Carcinogenicity Assessment for Lifetime Exposure

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Quantitative Estimate of



9939

__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 -- Benzo[k]fluoranthene
 CASRN -- 207-08-9
 Last Revised -- 03/01/1994

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. Benzo[k]fluoranthene produced tumors after lung implantation in mice and when administered with a promoting agent in skin-painting studies. Equivocal results have been found in a lung adenoma assay in mice. Benzo[k]fluoranthene is mutagenic in bacteria.

___II.A.2. Human Carcinogenicity Data

None. Although there are no human data that specifically link exposure to benzo[k]fluoranthene to human cancers, benzo[k]fluoranthene 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 a lifetime implant study, female Osborne-Mendel rats (27-35/group) received lung implants of 0.16 mg (0.65 mg/kg), 0.83 mg (3.4 mg/kg) or 4.15 mg (17 mg/kg) benzo[k]fluoranthene in 0.05 mL of a 1:1 (v:v) mixture of beeswax and trioctanoin (Deutsch-Wenzel et al., 1983). Controls consisted of an untreated group and a group receiving an implant of the vehicle. Median survival times (weeks) were: 118 (untreated controls), 104 (vehicle controls); 114 (0.16 mg dose); 95 (0.83 mg dose); 98 (4.15 mg dose). The incidences of epidermoid carcinomas in the lung and thorax (combined) showed a statistically significant

dose-related increase. The observed incidences were: untreated controls, 0/35; vehicle controls, 0/35; low-dose, 0/35; mid-dose, 3/31; high-dose, 12/27.

Groups of 16-17 male and 18 female newborn CD-1 mice received intraperitoneal injections of benzo[k]fluoranthene in DMSO on days 1, 8 and 15 after birth (total dose approximately 126 ug/mouse) and were sacrificed at 52 weeks of age (LaVoie et al., 1987). The incidence of hepatic adenomas and hepatomas was increased in treated male mice (3/16) relative to vehicle controls (1/17), although this increase was not statistically significant. No liver tumors were found in females. Lung adenomas were found in treated male (1/16) and female (3/18) mice, whereas none were reported for the controls. This assay is considered to be a short-term, in vivo, lung tumor assay.

Benzo[k]fluoranthene has yielded positive results for initiating activity in several mouse skin-painting assays. A single dermal application of 11 mg benzo[k]fluoranthene to 20 Swiss mice in a 63-week study did not induce tumors (Van Duuren et al., 1966). However, when the same dose was followed by promoting treatments with croton resin, 18/20 animals developed papillomas and 5/20 developed carcinomas. LaVoie et al. (1982) applied doses of 0, 30, 100 or 1000 ug benzo[k]fluoranthene (10 doses each, every other day, in 0.1 mL acetone) to the skin of groups of 20 Crl:CD-1 mice. This regimen was followed by treatment with 2.5 ug 12-O-tetradecanoyl phorbol-13-acetate (TPA) (a tumor promoter), 3 times/week for 20 weeks. Increases in the percentage of tumor-bearing animals (0, 5, 25, 75), as well as the number of tumors per animal (0, 0.1, 0.4, 2.8), appeared to be dose-related. These results were corroborated by reports of Amin et al. (1985a,b).

II.A.4. Supporting Data for Carcinogenicity

Tests for mutagenicity in prokaryotic cells have produced positive results. Tests for reverse mutation in Salmonella typhimurium strain TA100 and TA98 yielded positive results for benzo[k]fluoranthene in the presence of a metabolic activation system (rat liver S9) (LaVoie et al., 1980; Hermann et al., 1980).

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

Not available.

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

Not available.

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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 (301)345-2870 (phone), (301)345-2876 (FAX) or Hotline.IRIS@epamail.epa.gov (internet address).

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__VI. Bibliography

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__VI.A. Oral RfD References

None

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__VI.B. Inhalation RfC References

None

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__VI.C. Carcinogenicity Assessment References

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Amin, S., N. Hussain, G. Balanikas, K. Huie and S.S. Hecht. 1985b. Mutagenicity and tumor initiating activity of methylated benzo[k]fluoranthenes. *Cancer Lett*. 26: 343-347.

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occurring environmental polycyclic aromatic hydrocarbons. *J. Natl. Cancer Inst.* 71(3): 539-543.

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LaVoie, E.J., S.S. Hecht, S. Amin, V. Bedenko and D. Hoffmann. 1980. Identification of mutagenic dihydrodiols as metabolites of benzo(j)fluoranthene and benzo(k)fluoranthene. *Cancer Res.* 40: 4528-4532.

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U.S. EPA. 1984. *Carcinogen Assessment of Coke Oven Emissions.* Office of Health and Environmental Assessment, Washington, DC. EPA 600/6-82-003F. NTIS PB84-170181.

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.

Van Duuren, B.L., A. Sivak, A. Segal, L. Orris and L. Langseth. 1966. The tumor-promoting agents of tobacco leaf and tobacco smoke condensate. *J. Natl. Cancer Inst.* 37(4): 519-526.

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_VII. Revision History

Substance Name -- Benzo[k]fluoranthene
CASRN -- 207-08-9

Date	Section	Description
11/01/1990	II.	Carcinogen assessment on-line
11/01/1990	VI.	Bibliography on-line
01/01/1992	IV.	Regulatory action section on-line
09/01/1993	II.	Carcinogenicity assessment noted as pending change
09/01/1993	II.D.2.	Work group review date added
11/01/1993	II.D.2.	Work group review date added
02/01/1994	II.D.3.	Secondary contact's phone number changed
03/01/1994	II.	Pending change note removed; no change
03/01/1994	II.D.2.	Work group review date added
08/01/1995	II.D.2.	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

Substance Name -- Benzo[k]fluoranthene

CASRN -- 207-08-9

Last Revised -- 11/01/1990

207-08-9

Benzo(k)fluoranthene

Dibenzo(b,jk)fluorene

HSDB 6012

11,12-BENZO(k)FLUORANTHENE

11,12-Benzofluoranthene

2,3,1',8'-Binaphthylene

8,9-BENZOFLUORANTHENE

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