TOXICITY SUMMARY FOR BENZO[*k*]FLUORANTHENE

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EXECUTIVE SUMMARY

Benzo[*k*]fluoranthene, a crystalline solid with a chemical formula of $C_{20}H_{12}$ and a molecular weight of 252.32 (Lide, 1991), is a polycyclic aromatic hydrocarbon (PAH) with one five-membered and four six-membered rings. There is no commercial production or known use of this compound (IARC, 1983). Benzo[*k*]fluoranthene is found in fossil fuels and occurs ubiquitously in products of incomplete combustion (IARC, 1983) and in soils, groundwater, and surface waters at hazardous waste sites (ATSDR, 1990).

No absorption or excretion data were available for benzo[*k*]fluoranthene; however, by analogy to structurally-related PAHs, primarily benzo[*a*]pyrene, it would be expected to be absorbed from the gastrointestinal tract, lungs, and skin (U.S. EPA, 1991). Rat liver microsomes have been shown to metabolize benzo[*k*]fluoranthene to the dihydrodiol, 8,9-dihydro-8,9-dihydroxy benzo[*k*]fluoranthene (LaVoie et al., 1980).

No data were found concerning the acute, subchronic, chronic, developmental, or reproductive toxicity of benzo[*k*]fluoranthene. Because of a lack of toxicity data, an oral reference dose (RfD) or inhalation reference concentration (RfC) have not been derived (U.S. EPA, 1994).

No long-term oral or inhalation bioassays were available to assess the carcinogenicity of benzo[*k*]fluoranthene. Benzo[*k*]fluoranthene was tested for carcinogenicity in dermal application, subcutaneous (s.c.) injection, lung implantation, and intraperitoneal (i.p.) injection studies. Dermal applications of 0.5% solutions of benzo[*k*]fluoranthene for life produced only a few skin papillomas in mice (Wynder and Hoffmann, 1959), but in initiation-promotion assays, benzo[*k*]fluoranthene was active as an initiator of skin carcinogenesis (LaVoie et al., 1982; Amin et al., 1985). Injection site sarcomas developed in mice given three s.c. injections of 0.6 mg benzo[*k*]fluoranthene (Lacassagne et al., 1963) and dose-related increases of epidermoid carcinomas of the lungs were reported in rats receiving single lung implants of 0.16-4.15 mg benzo[*k*]fluoranthene (Deutsch-Wenzel et al., 1983). In a short-term assay, hepatic and lung tumors occurred in newborn mice receiving 2.1 µmol benzo[*k*]fluoranthene via i.p. injection (LaVoie et al., 1987).

Based on no human data and sufficient evidence for carcinogenicity in animals, EPA has assigned a weight-of-evidence classification of B2, probable human carcinogen, to benzo[*k*]fluoranthene (U.S. EPA, 1994).

1. INTRODUCTION

Benzo[*k*]fluoranthene (CAS Reg. No. 207-08-9), also known as 8,9-benzofluoranthene; 11,12-benzofluoranthene; 2,3,1',8'-binaphthylene; and dibenzo(b,j,k)fluorene (IARC, 1983) is a polycyclic aromatic hydrocarbon (PAH) with one five-membered and four six-membered rings. It is a crystalline solid with a chemical formula of $C_{20}H_{12}$, a molecular weight of 252.32, a melting point of 217°C (Lide, 1991), and a boiling point of 480°C (IARC, 1983). Benzo[*k*]fluoranthene is insoluble in water, but is soluble in acetic acid, benzene, and ethanol (IARC, 1983). It has a vapor pressure of 9.59×10^{-11} mm Hg at 25°C, an estimated octanol/water partition coefficient of 6.04-6.44 (U.S. EPA, 1987), and a Henry's Law constant of 3.87×10^{-5} (ATSDR, 1990).

There is no commercial production or commercial use of benzo[*k*]fluoranthene; small amounts of this compound are used for research (IARC, 1983). Benzo[*k*]fluoranthene is found in fossil fuels and occurs ubiquitously in products of incomplete combustion. It has been detected in mainstream cigarette smoke; gasoline engine exhaust; emissions from burning of coal and from oil-fired heating; lubricating oils; used motor oils; crude oils (IARC, 1983); and in soils, surface waters, and groundwater at hazardous waste sites (ATSDR, 1990). Benzo[*k*]fluoranthene is one of a number of PAHs on EPA's priority pollutant list (ATSDR, 1990).

2. METABOLISM AND DISPOSITION

2.1. ABSORPTION

Data regarding the gastrointestinal or pulmonary absorption of benzo[*k*]fluoranthene in humans or animals were not available. However, data from structurally-related PAHs, primarily benzo[*a*]pyrene, suggest that benzo[*k*]fluoranthene would be absorbed from the gastrointestinal tract, lungs, and skin (U.S. EPA, 1991).

2.2. DISTRIBUTION

No human or animal data were available concerning the tissue distribution of benzo[*k*]fluoranthene.

2.3. METABOLISM

No data were available concerning the *in vivo* metabolism of benzo[*k*]fluoranthene. In *in vitro* metabolism studies using rat liver microsomes, LaVoie et al. (1980) identified 8,9-dihydro-8,9-dihydroxy benzo[*k*]fluoranthene as the major metabolite of benzo[*k*]fluoranthene.

2.4. EXCRETION

No human or animal data were available concerning the excretion of benzo[*k*]fluoranthene.

3. NONCARCINOGENIC HEALTH EFFECTS

3.1. ORAL EXPOSURES

Information on the acute, subchronic, chronic, developmental, or reproductive oral toxicity of benzo[*k*]fluoranthene in humans or animals was not available. Because of a lack of toxicity data, an oral reference dose (RfD) for benzo[*k*]fluoranthene has not been derived (U.S. EPA, 1994).

3.2. INHALATION EXPOSURES

Information on the acute, subchronic, chronic, developmental, or reproductive oral toxicity of benzo[*k*]fluoranthene in humans or animals following inhalation exposure was not available. Because of a lack of toxicity data, an inhalation reference concentration (RfC) for benzo[*k*]fluoranthene has not been derived (U.S. EPA, 1994).

3.3. OTHER ROUTES OF EXPOSURE

Information on the acute, subchronic, chronic, developmental, or reproductive oral toxicity of benzo[*k*]fluoranthene in humans or animals by other routes of exposure was not available.

3.4. TARGET ORGANS/CRITICAL EFFECTS

No data were available to identify target organs/critical effects for oral, inhalation, or other routes of exposure to benzo[*k*]fluoranthene.

4. CARCINOGENICITY
4.1. ORAL EXPOSURES

Information on the carcinogenicity of benzo[*k*]fluoranthene in humans or animals following oral exposure was not available.

4.2. INHALATION EXPOSURES
4.2.1. Human

Although there are no human data that specifically link exposure to benzo[*k*]fluoranthene to human cancers, benzo[*b*]fluoranthene is a component of mixtures that have been associated with human cancer. These mixtures include coal tar, soots, coke oven emissions, and cigarette smoke (U.S. EPA, 1994).

4.2.2. Animal

Information on the carcinogenicity of benzo[*k*]fluoranthene in animals following inhalation exposure was not available.

4.3. OTHER ROUTES OF EXPOSURE
4.3.1. Human

Information on the carcinogenicity of benzo[*k*]fluoranthene in humans by other routes of exposure was not available.

4.3.2. Animal

Benzo[*k*]fluoranthene was tested for carcinogenicity in skin application, initiation-promotion, lung implant, subcutaneous (s.c.) injection, and intraperitoneal (i.p.) injection bioassays.

Wynder and Hoffmann (1959) applied 0.1 or 0.5% solutions of benzo[*k*]fluoranthene in acetone three times weekly to the skin of three groups of 20 female Swiss mice. No untreated or vehicle controls were used. At the end of the 13th month, all surviving mice (8/20 and 3/20 treated with the low and high dose, respectively) were killed. Skin papillomas developed in two mice receiving the high dose; no skin tumors were seen in the low dose group. Habs et al. (1980) found no significant increase in tumor incidence when groups of 40 female NMRI mice were given dermal applications of 3.4, 5.6, or 9.2 µg benzo[*k*]fluoranthene two times weekly for life. Only one tumor was found in a mouse receiving the highest dose.

LaVoie et al. (1982) evaluated the tumor-initiating activity of benzo[*k*]fluoranthene by applying initiation doses of 0, 3, 10, or 100 µg benzo[*k*]fluoranthene in acetone (10 doses, every other day) to the skin of groups of 20 Crl:CD-1 mice. This procedure was followed by treatment with 12-0-tetradecanoyl-phorbol-13-acetate (TPA), 3 times weekly for 20 weeks. There was a dose-related increased incidence of skin tumors, predominantly squamous cell papillomas. Skin tumors were seen in 0, 5, 25, and 75% of mice treated with 0, 10, 30, or 100 µg benzo[*k*]fluoranthene, respectively. Using a similar initiation/promotion protocol, Amin et al. (1985) applied 101 µg benzo[*k*]fluoranthene in acetone every 2 days for 20 days to the skin of 20 female Crl:CD-1 mice, followed 10 days later by TPA treatment 3 times weekly for 20 weeks. Skin tumors were reported in 0 and 37% of vehicle control and treated mice, respectively.

Female Osborne-Mendel rats (27-35/group) received single lung implants of 0.16, 0.83, or 4.15 mg benzo[*k*]fluoranthene in a mixture of beeswax and trioctanoin (Deutsch-Wenzel et al., 1983). An untreated group and a group receiving the vehicle served as controls. Granulomatous inflammatory lesions developed at the injection sites. After a lifetime of observation, there was a dose-related increase of epidermoid carcinomas of the lung. The observed incidences were: untreated controls, 1/35; vehicle controls, 0/35; low dose group, 0/35; mid dose group, 3/31; and high dose group, 12/27.

Sixteen male and 14 female XVII nc/Z mice were given s.c. injections of 0.6 mg benzo[*k*]fluoranthene in olive oil once a month for 3 months (Lacassagne et al., 1963). Injection site sarcomas developed in both male and female mice, respectively. The average latency period for sarcomas was 203 days (males) and 210 days (females).

LaVoie et al. (1987) administered i.p. injections of benzo[*k*]fluoranthene in dimethyl sulfoxide to 16 male and 18 female CD-1 mice on days 1, 8, and 15 of life at a total dose of 2.1 µmol/mouse. The animals were sacrificed at 52 weeks of age. Hepatic tumors (adenomas and hepatomas combined) were seen in 3/16 of treated male mice; one hepatoma was seen in 1/17 of male controls. No hepatic tumors developed in female treated mice or in female controls. Lung adenomas were found in 1/16 and 3/18 treated male and female mice, respectively; no lung tumors occurred in controls.

4.4. EPA WEIGHT-OF-EVIDENCE

Classification -- B2; probable human carcinogen (U.S. EPA, 1994)
Basis -- Based on no human data and sufficient data from animal bioassays.
Benzo[*k*]fluoranthene produced tumors in mice after lung implantation and when administered by dermal application with a promoting agent. Equivocal results were obtained in a lung adenoma assay with mice. Benzo[*k*]fluoranthene was mutagenic in bacteria.

4.5. CARCINOGENICITY SLOPE FACTORS

None were calculated.

5. REFERENCES

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