

## Benz[a]anthracene; CASRN 56-55-3

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 Benz[a]anthracene

**File First On-Line 12/01/1990**

| Category (section)               | Assessment Available? | Last Revised |
|----------------------------------|-----------------------|--------------|
| Oral RfD (I.A.)                  | not evaluated         |              |
| Inhalation RfC (I.B.)            | not evaluated         |              |
| Carcinogenicity Assessment (II.) | yes                   | 12/01/1990   |

## I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Benz[a]anthracene  
CASRN — 56-55-3

Not available at this time.

## **I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)**

Substance Name — Benz[a]anthracene  
CASRN — 56-55-3

Not available at this time.

---

## **II. Carcinogenicity Assessment for Lifetime Exposure**

Substance Name — Benz[a]anthracene  
CASRN — 56-55-3  
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 — B2; probable human carcinogen

Basis — Based on no human data and sufficient data from animal bioassays. Benz[a]anthracene produced tumors in mice exposed by gavage; intraperitoneal, subcutaneous or intramuscular injection; and topical application. Benz[a]anthracene produced mutations in bacteria and in mammalian cells, and transformed mammalian cells in culture.

## II.A.2. Human Carcinogenicity Data

None. Although there are no human data that specifically link exposure to benz[a]anthracene to human cancers, benz[a]anthracene 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; Lee et al., 1976; Brockhaus and Tomingas, 1976).

## II.A.3. Animal Carcinogenicity Data

Sufficient. Benz[a]anthracene administration caused an increase in the incidence of tumors by gavage (Klein, 1963); dermal application (IARC, 1973); and both subcutaneous injection (Steiner and Faulk, 1951; Steiner and Edgecomb, 1952) and intraperitoneal injection (Wislocki et al., 1986) assays. A group of male B6AF1/J mice was exposed to gavage solutions containing 3% benz[a]anthracene in Methocel-Aerosol O.T. (dioctyl ester of sodium sulfo- succinic acid), 3 doses/week for 5 weeks (total dose of approximately 225 mg/mouse, 500 mg/kg/day) or the vehicle (Klein, 1963). Mice were evaluated for tumors on days 437-444 and 547 after treatment was initiated. A statistical analysis was not reported. Increased incidences of pulmonary adenoma and hepatoma in treated vs. control mice were reported by the authors at both observation times. The incidence of pulmonary adenoma at 437-444 days was 37/39 (95%) in treated animals vs. 10/38 (26%) in controls; whereas at 547 days, 19/20 (95%) treated animals and 7/20 (35%) controls had pulmonary adenomas. The incidence of hepatomas at 437 to 440 days was 18/39 (46%) in treated animals compared with 0/38 among the vehicle controls. After 547 days, the hepatoma incidences increased to 20/20 for the treated animals versus 2/20 (10%) for vehicle controls.

Mice (strain and sex not specified) were exposed to a single gavage dose of 0.5 mg benz[a]anthracene in mineral oil (approximately 17 mg/kg). No tumors were reported in 13 mice examined 16 months after exposure. In another part of the study, multiple gavage treatments, 8 or 16 treatments at 3-7 day intervals over a 16-month period, resulted in forestomach papillomas in 2/27 treated mice compared with 0/16 in vehicle controls (Bock and King, 1959).

Groups of male and female CD-1 mice (n=90-100) received intraperitoneal injections of benz[a]anthracene in DMSO on days 1, 8, and 15 of age (total dose = 638 ug/mouse) (Wislocki et al., 1986). Tumors were evaluated in animals that died spontaneously after weaning and in all remaining animals at 1 year after exposure. In treated male mice, a statistically significant increase in the incidence of liver adenomas or carcinomas (31/39 treated vs. 2/28 controls) occurred; 25/39 had carcinomas. Female mice did not develop liver tumors. The incidence of pulmonary adenomas or carcinomas in benz[a]anthracene-treated males (6/39, with a majority of adenomas) was increased but not statistically significantly relative to the vehicle controls (1/28).

In the female mice, however, the incidence of pulmonary adenomas was significantly elevated in the treated group (6/32) when compared with vehicle controls (0/31).

Benz[a]anthracene yielded positive results in tests for complete carcinogenicity and initiating activity in skin painting assays in C3H/He, CAF1 and ICR/Ha mouse strains. These studies are reviewed in IARC (1973).

Subcutaneous injection of benz[a]anthracene in tricapylin into C57Bl mice (40-50/group) produced injection site sarcomas 9 months after treatment (Steiner and Falk, 1951; Steiner and Edgecomb, 1952). The sarcoma incidences were: uninjected controls, 0/76; tricapylin controls, 3/28 (11%); 0.05 mg, 5/43 (12%); 0.2 mg, 11/43 (26%); 1.0 mg, 15/31 (48%); 5.0 mg, 49/145 (34%); and 10 mg, 5/16 (31%). The results of similar experiments in this series were combined (Steiner and Edgecomb, 1952). A statistical analysis of the results was not reported. Survival was roughly equivalent in all groups (70%).

Klein (1952) showed that an intramuscular injection of benz[a]anthracene in combination with 1 or 3% croton oil produced injection site fibrosarcomas and hemangioendotheliomas in Strain A-derived albino mice; 3/24 mice injected with benz[a]anthracene and 1% croton oil and 1/26 mice injected with benz[a]anthracene and 3% croton oil developed tumors. None of the 30 mice injected with benz[a]anthracene and 0.1% croton oil and none of the 30 mice injected with benz[a]anthracene and 5% croton oil developed tumors. In the control groups none of the 35 mice injected only with 1% croton oil and none of the 32 mice injected only with benz[a]anthracene developed tumors. The survival rate for all groups was roughly equivalent (74%).

#### **II.A.4. Supporting Data for Carcinogenicity**

The results of tests for DNA damage in *Escherichia coli* have not been positive at concentrations of benz[a]anthracene up to 250 ug/mL and 1000 ug/well (Rosenkrantz and Poirier, 1979; DeFlora et al., 1984). Positive results were obtained in tests for reverse mutation in five different strains of *Salmonella typhimurium* and for forward mutation in one strain (McCann et al., 1975; Coombs et al., 1976; Simmon, 1979; Salamone et al., 1979; Bartsch et al., 1980; DeFlora et al., 1984; Norpoth et al., 1984; Utesch et al., 1987; Bos et al., 1988; Kaden et al. 1979).

Benz[a]anthracene produced positive results in an assay for mutations in *Drosophila melongaster* (Fahmy and Fahmy, 1973).

Tests for DNA damage, mutation, chromosomal effects and cell transformation in a variety of eukaryotic cell preparations have yielded mostly positive results. Benz[a]anthracene tested positive for DNA damage in primary rat hepatocytes and HeLa cells (Probst et al., 1981; Martin

et al., 1978). It also tested positive for forward mutation in Chinese hamster cells, V79 cells, mouse lymphoma L5178Y cells and rat liver epithelial cells (Slaga et al., 1978; Krahn and Heidelberger, 1977; Amacher et al., 1980; Amacher and Turner, 1980; Tong et al., 1981). Benz[a]anthracene tested positive for chromosomal affects in Chinese hamster ovary cells (Pal, 1981). Tests for cell transformation (cell morphology) have yielded positive results in Syrian hamster embryo cells and mouse prostate C3HG23 cells (Pienta et al., 1977; DiPaolo et al., 1969, 1971; Marquardt and Heidelberger, 1972).

Current theories on mechanisms of metabolic activation of polycyclic aromatic hydrocarbons are consistent with a carcinogenic potential for benz[a]anthracene. Benz[a]anthracene has a "bay-region" structure (Jerina et al., 1978). It is metabolized by mixed function oxidases to reactive "bay-region" diol epoxides that are mutagenic in bacteria and tumorigenic in mouse skin painting assays (Booth and Sims, 1974; Wood et al., 1977a,b).

---

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

Not available.

---

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

Not available.

---

## **II.D. EPA Documentation, Review, and Contacts (Carcinogenicity Assessment)**

### **II.D.1. EPA Documentation**

Source Document — U.S. EPA, 1984

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 (202)566-1676 (phone), (202)566-1749 (FAX) or [hotline.iris@epa.gov](mailto:hotline.iris@epa.gov) (internet address).

---

**III. [reserved]**

**IV. [reserved]**

**V. [reserved]**

---

## **VI. Bibliography**

Substance Name — Benz[a]anthracene  
CASRN — 56-55-3

### **VI.A. Oral RfD References**

None

---

### **VI.B. Inhalation RfC References**

None

---

### **VI.C. Carcinogenicity Assessment References**

Amacher, D.E. and G.N. Turner. 1980. Promutagen activation by rodent-liver post mitochondrial fractions in the L5178Y/TK cell mutation assay. *Mutat. Res.* 74: 485-501.

Amacher, D.E., S.C. Paillet, G.N. Turner and D.S. Salsburg. 1980. Point mutations at the thymidine kinase locus in L5178Y mouse lymphoma cells. II. Test validation and interpretation. *Mutat. Res.* 72: 447-474.

Bartsch, H., C. Malaveille, A.M. Camus, et. al. 1980. Validation and comparative studies on 180 chemicals with *S. typhimurium* strains and V79 Chinese hamster cells in the presence of various metabolizing systems. *Mutat. Res.* 76: 1-50.

Bock, F.G. and D.W. King. 1959. A study of the sensitivity of the mouse forestomach toward certain polycyclic hydrocarbons. *J. Natl. Cancer Inst.* 23(4): 833-839.

Booth, J. and P. Sims. 1974. 8,9-Dihydro-8,9-dihydroxybenz[a]anthracene 10,11-oxide: A new type of polycyclic aromatic hydrocarbon metabolite. *FEBS Lett.* 47(1): 30-33.

Bos, R.P., J.L.G. Theuws, F.J. Jongeneelen and P.Th. Henderson. 1988. Mutagenicity of bi-, tri and tetra-cyclic aromatic hydrocarbons in the "taped- plate assay" and in the conventional *Salmonella* mutagenicity assay. *Mutat. Res.* 204: 203-206.

Brockhaus, A. and R. Tomingas, 1976. Emission of polycyclic hydrocarbons from combustion processes in small heating units and their concentration in the atmosphere. *Staub-Reinhalt. Luft.* 36(3): 96-101.

Coombs, M.M., C. Dixon and A.M. Kissonerghis. 1976. Evaluation of the mutagenicity of compounds of known carcinogenicity, belonging to the benz[a]anthracene, chrysene, and cyclopenta[a]phenanthrene series, using Ames's test. *Cancer Res.* 36: 4525-4529.

DeFlora, S., P. Zanicchi, A. Camoirano, C. Bennicelli and G.S. Badolati. 1984. Genotoxic activity and potency of 35 compounds in the Ames reversion test and in a bacterial DNA-repair test. *Mutat. Res.* 133(3): 161-198.

DiPaolo, J.A., J.P. Donovan and R.L. Nelson. 1969. Quantitative studies of in vitro transformation by chemical carcinogens. *J. Natl. Cancer Inst.* 42(5): 867-874.

DiPaolo, J.A., P.J. Donovan and R.L. Nelson. 1971. Transformation of hamster cells in vitro by polycyclic hydrocarbons without cytotoxicity. *Proc. Natl. Acad. Sci. USA.* 68(12): 2958-2961.

Fahmy, O.G. and M.J. Fahmy. 1973. Oxidative activation of benz(a)anthracene and methylated derivatives in mutagenesis and carcinogenesis. *Cancer Res.* 33: 2354-2361.

IARC (International Agency for Research on Cancer). 1973. Certain Polycyclic Aromatic Hydrocarbons and Heterocyclic Compounds. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Polynuclear Aromatic Compounds. Vol. 3. Lyon, France.

IARC (International Agency for Research on Cancer). 1984. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Polynuclear Aromatic Compounds. Part 3. Industrial Exposures in Aluminum Production, Coal Gasification, Coke Production, and Iron and Steel Founding. Vol. 34. World Health Organization.

Jerina, D.M., H. Yagi, R.E. Lehr, et al. 1978. The bay-region theory of carcinogenesis by polycyclic aromatic hydrocarbons. In: Polycyclic Hydrocarbons and Cancer: Vol. 1, Environment, Chemistry, and Metabolism, H.V. Gelboin and P.O.P. Ts'O, Ed. Academic Press, NY. p. 173-188.

Kaden, D.A., R.A. Hites and W.G. Thilly. 1979. Mutagenicity of soot and associated polycyclic aromatic hydrocarbons to *Salmonella typhimurium*. *Cancer Res.* 39: 4152-4159.

Klein, M. 1952. Effect of croton oil on induction of tumors by 1,2- benzanthracene, desoxycholic acid, or low doses of 20-methylcholanthrene in mice. *J. Natl. Cancer Inst.* 13: 333-341.

Klein, M. 1963. Susceptibility of strain B6AF/J hybrid infant mice to tumorigenesis with 1,2-benzanthracene, deoxycholic acid, and 3- methylcholanthrene. *Cancer. Res.* 23: 1701-1707.

Krahn, D.F. and C. Heidelberger. 1977. Liver homogenate-mediated mutagenesis in Chinese hamster V79 cells by polycyclic aromatic hydrocarbons and aflatoxins. *Mutat. Res.* 46: 27-44.

Lee, M.L., M. Novotny and K.D. Bartle. 1976. Gas chromatography/mass spectrometric and nuclear magnetic resonance studies of carcinogenic polynuclear aromatic hydrocarbons in tobacco and marijuana smoke condensates. *Anal. Chem.* 48(2): 405-416.

Marquardt, H. and C. Heidelberger. 1972. Influence of "feeder cells" and inducers and inhibitors of microsomal mixed-function oxidases on hydrocarbon- induced malignant transformation of cells derived from C3H mouse prostate. *Cancer Res.* 32: 721-725.

Martin, C.N., A.C. McDermid and R.C. Garner. 1978. Testing of known carcinogens and noncarcinogens for their ability to induce unscheduled DNA synthesis in HeLa cells. *Cancer Res.* 38: 2621-2627.

McCann, J.E., E. Choi, E. Yamasaki and B.N. Ames. 1975. Detection of carcinogens as mutagens in the *Salmonella*/microsome test: Assay of 300 chemicals. *Proc. Natl. Acad. Sci. USA.* 72(12): 5135-5139.

Norpoth, K., A. Kemena, J. Jacob and C. Schumann. 1984. The influence of 18 environmentally relevant polycyclic aromatic hydrocarbons and Clophen A50, as liver monooxygenase inducers, on the mutagenic activity of benz[a]anthracene in the Ames test. *Carcinogenesis*. 5(6): 747-752.

Pal, K. 1981. The induction of sister-chromatid exchanges in Chinese hamster ovary cells by K-region epoxides and some dihydrodiols derived from benz[a]anthracene, dibenz[a,c]anthracene and dibenz[a,h]anthracene. *Mutat. Res.* 84: 389-398.

Pienta, R.J., J.A. Poiley and W.B. Leberherz, III. 1977. Morphological transformation of early passage golden Syrian hamster embryo cells derived from cryopreserved primary cultures as a reliable in vitro bioassay for identifying diverse carcinogens. *Int. J. Cancer*. 19: 642-655.

Probst, G.S., R.E. McMahon, L.E. Hill, C.Z. Thompson, J.K. Epp and S.B. Neal. 1981. Chemically-induced unscheduled DNA synthesis in primary rat hepatocyte cultures: A comparison with bacterial mutagenicity using 218 compounds. *Environ. Mutagen.* 3: 11-32.

Rosenkrantz, H.S. and L.A. Poirier. 1979. Evaluation of the mutagenicity and DNA-modifying activity of carcinogens and noncarcinogens in microbial systems. *J. Natl. Cancer Inst.* 62(4): 873-892.

Salamone, M.F., J.A. Heddle and M. Katz. 1979. The mutagenic activity of thirty polycyclic aromatic hydrocarbons (PAH) and oxides in urban airborne particulates. *Environ. Int.* 2: 37-43.

Simmon, V.F. 1979. In vitro mutagenicity assays of chemical carcinogens and related compounds with *Salmonella typhimurium*. *J. Natl. Cancer Inst.* 62(4): 893-899.

Slaga, T.J., E. Huberman, J.K. Selkirk, R.G. Harvey and W.M. Braken. 1978. Carcinogenicity and mutagenicity of benz[a]anthracene diols and diol-epoxides. *Cancer Res.* 38: 1699-1704.

Steiner, P.E. and J.H. Edgecomb. 1952. Carcinogenicity of 1,2- benzanthracene. *Cancer Res.* 12: 657-659.

Steiner, P.E. and H.L. Falk. 1951. Summation and inhibition effects of weak and strong carcinogenic hydrocarbons: 1,2-Benzanthracene, chrysene, 1:2:5:6- dibenzanthracene and 20-methylcholanthrene. *Cancer Res.* 11: 56-63.

Tong, C., M.F. Laspia, S. Telang and G.M. Williams. 1981. The use of adult rat liver cultures in the detection of the genotoxicity of various polycyclic aromatic hydrocarbons. *Environ. Mutagen.* 3: 477-487.

U.S. EPA. 1984. Carcinogen Assessment of Coke Oven Emissions. Office of Health and Environmental Assessment, Washington, DC. EPA 600/6-82-003F. NTIS PB 84-170181.

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.

Utesch, D., H. Glatt and F. Oesch. 1987. Rat hepatocyte-mediated bacterial mutagenicity in relation to the carcinogenic potency of benz(a)anthracene, benzo(a)pyrene and twenty-five methylated derivatives. *Cancer Res.* 47: 1509- 1515.

Wislocki, P.G., E.S. Bagan, A.Y.H. Lu, et al. 1986. Tumorigenicity of nitrated derivatives of pyrene, benz[a]anthracene, chrysene and benzo[a]pyrene in the newborn mouse assay. *Carcinogenesis.* 7(8): 1317-1322.

Wood, A.W., R.L. Chang, W. Levin, et al. 1977a. Mutagenicity and cytotoxicity of benz[a]anthracene diol epoxides and tetrahydro-epoxides: Exceptional activity of the bay region 1,2-epoxides. *Proc. Natl. Acad. Sci. USA.* 74(7): 2746-2750.

Wood, A.W., W. Leven. R.L. Chang, et al. 1977b. Tumorigenicity of five dihydrodiols of benz[a]anthracene on mouse skin: Exceptional activity of benz[a]anthracene 3,4-dihydrodiol. *Proc. Natl. Acad. Sci. USA.* 74(8): 3137-3179.

---

## VII. Revision History

Substance Name — Benz[a]anthracene  
CASRN — 56-55-3

| Date       | Section | Description                   |
|------------|---------|-------------------------------|
| 12/01/1990 | II.     | Carcinogen assessment on-line |

## VIII. Synonyms

Substance Name — Benz[a]anthracene

CASRN — 56-55-3

Last Revised — 12/01/1990

- 56-55-3
- Benz(a)anthracene
- benz(a)anthracene
- Benzanthracene
- Benzanthrene
- BENZO(a)ANTHRACENE
- BENZO(b)PHENANTHRENE
- Benzoanthracene
- HSDB 4003
- NSC 30970
- RCRA WASTE NUMBER U018
- Tetraphene
- 1,2-BENZ(a)ANTHRACENE
- 1,2-Benzanthracene
- 1,2-BENZANTHRAZEN [German]
- 1,2-BENZANTHRENE
- 1,2-BENZOANTHRACENE
- 2,3-Benzophenanthrene