

Dibenz[a,h]anthracene; CASRN 53-70-3

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 Dibenz[a,h]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 — Dibenz[a,h]anthracene
CASRN — 53-70-3

Not available at this time.

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

Substance Name — Dibenz[a,h]anthracene
CASRN — 53-70-3

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Dibenz[a,h]anthracene

CASRN — 53-70-3

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.

Dibenz[a,h]anthracene produced carcinomas in mice following oral or dermal exposure and injection site tumors in several species following subcutaneous or intramuscular administration. Dibenz[a,h]anthracene has induced DNA damage and gene mutations in bacteria as well as gene mutations and transformation in several types of mammalian cell cultures.

II.A.2. Human Carcinogenicity Data

None. Although there are no human data that specifically link exposure to dibenz[a,h]anthracene with human cancers, dibenz[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).

II.A.3. Animal Carcinogenicity Data

Sufficient. Dibenz[a,h]anthracene has been shown to be carcinogenic when administered to mice by the oral route (Snell and Stewart, 1962, 1963). Instead of drinking water DBA/2 mice (21/sex) were given a water-olive oil emulsion containing 0.2 mg/mL dibenz[a,h]anthracene ad libitum. Average exposure was estimated to be 0.85 mg/day for males and 0.76 mg/day for females. The control groups (25 male and 10 female) received the water-olive oil emulsion in place of water. The mice did not tolerate the olive oil vehicle well and all 4 groups lost weight after a few weeks exposure and eventually became emaciated and dehydrated. Animals that died spontaneously or that became moribund were examined for tumors. The duration of the experiment was 279 and 237 days for males and females, respectively, in the dosed groups and 351 and 226 days for male and female controls. Mice developed pulmonary adenomas (treated males, 14/14; control males 1/23; treated females, 13/13; control females, 0/6), pulmonary carcinomas (treated males, 14/14; control males, 0/23; treated females, 10/13; control females, 0/6), mammary carcinoma (treated females, 12/13; control females, 0/6) and hemangioendothelioma (treated males, 10/14; control males, 0/23; treated females, 6/13; control females, 0/6). No statistical analyses appear to have been performed.

Mammary carcinomas were observed in two strains of female mice following gavage with dibenz[a,h]anthracene (Biancifiiori and Caschera, 1962; Berenblum and Haran, 1955). Biancifiiori and Caschera (1962) observed mammary carcinomas when female Balb/c (1/20) and pseudo-pregnant female (obtained by mating virgin females with vasectomized males) Balb/c (13/24) mice were treated for 15 weeks with a twice-weekly gavage containing 0.5% dibenz[a,h]anthracene (total dose was 15 mg/animal). Mammary carcinomas occurred in 2/30 pseudo-pregnant females not dosed with dibenz[a,h]anthracene. Previous studies indicated that mammary carcinomas did not occur in virgin Balb/c females (Biancifiiori et al., 1959). A single 1.5-mg dose of dibenz[a,h]anthracene in polyethylene glycol [average molecular weight (a.m.u.) 400] (PEG-400) produced forestomach papillomas in 2/42 male Swiss mice after 30 weeks. In this short-term study no mice developed tumors when treated with PEG alone (1 time/week) for 30 weeks (0/20) (Berenblum and Haran, 1955).

Dibenz[a,h]anthracene has produced positive results in mouse skin painting assays for complete carcinogenicity. Swiss mice developed carcinomas following dermal exposure to dibenz[a,h]anthracene at concentrations of 0.001% or greater (Wynder and Hoffman, 1959; Van

Duuren et al., 1967). Numerous studies that demonstrate complete carcinogenic activity and initiating activity are summarized in IARC (1973) and U.S. EPA (1990).

Subcutaneous injection of dibenz[a,h]anthracene induced sarcomas at the site of injection in several animal species. Groups (>19) of C3H mice received single subcutaneous injections of dibenz[a,h]anthracene in tricapylin at doses ranging from 0.0019-8 mg (approximately 0.09-360 mg/kg). No controls appear to have been used in this experiment (Bryan and Shimkin, 1943). Tumor latency appeared to decrease and the incidence of injection site sarcomas appeared to increase with dose (>76% at doses >0.06 mg or 2.8 mg/kg). A single subcutaneous injection of 2.4, 4.7, 9.3, 18.7, 37.5, or 75 ug dibenz[a,h]anthracene into groups of 100 NMRI mice was reported to produce a dose-related increase in tumor incidence (37/100, 39/100, 44/100, 56/100, 65/100, and 69/100, respectively) by the 114th week after injection (Pfeiffer, 1977). No concurrent controls were reported; however, a spontaneous tumor rate for NMRI mice was previously reported to be 0-2% (Pfeiffer, 1973). The development of fibrosarcomas from a single subcutaneous injection of 150 ug dibenz[a,h]anthracene was shown to be higher in AHH+ strains of mice than in AHH- strains.

Lubet et al. (1983) found that subcutaneous injections of dibenz[a,h]anthracene were associated with fibrosarcoma development in mice, but only for some strains. Four strains of mice used included two, C3H/HeJ and C57B1/6J, that respond to 3-methylcholanthrene treatment with increased levels and types of hepatic enzymes, including AHH. Two strains, AKR/J and DBA/2J were nonresponders. Groups of 30 animals were injected with a single dose of 150 mg dibenz[a,h]anthracene in 0.05 mL trioctanoin and observed for 9 months. A control group for each strain, consisting of 10 animals each, received a subcutaneous injection of 0.05 mL trioctanoin alone. The tumor incidence in the treated animals varied between 0 and 80%, depending on the strain. Tumor incidences were higher in the C3H and C57B1 mice but not in AKR or DBA mice. Likewise, the average latency period (in days) for fibrosarcoma development varied with the strain and tended to be inversely correlated with the tumor incidence rate. Numerous earlier studies that demonstrate the carcinogenicity of parenterally injected dibenz[a,h]anthracene in a variety of species are summarized in IARC (1973) and U.S. EPA (1990).

II.A.4. Supporting Data for Carcinogenicity

Dibenz[a,h]anthracene has produced positive results in bacterial DNA damage and mutagenicity assays and in mammalian cell DNA damage, mutagenicity and cell transformation assays. In bacterial DNA damage assays, positive results were obtained in *Escherichia coli* and *Bacillus subtilis* at exposure levels of 12-50 ug/well. Dibenz[a,h]anthracene tested positive for reverse mutation in *Salmonella typhimurium* strains TA100 and TA98 (3-5 ug/plate) and positive for forward mutation in strain TM677 (21 ug/mL) (McCann et al., 1975; Andrews et al., 1978;

Baker et al., 1980; Hermann, 1981; Kaden et al., 1979). In mammalian cell DNA damage assays, positive results were obtained in human foreskin epithelial cells not activated with mixed-function oxidase (MFO) inducers (1-100 ug/mL) and in HeLa cells (28 ng/mL) activated with 3-methylcholanthrene (Lake et al., 1978; Martin et al., 1978). When Syrian hamster embryo cells and rat hepatocytes not activated with MFO inducers were exposed to 20-30 ug/mL the results were not positive (Casto, 1979; Probst et al., 1981). Dibenz[a,h]anthracene induced forward mutations in Chinese hamster embryo cells exposed to concentrations of 1 ug/mL or greater (Huberman and Sachs, 1976; Krahn and Heidelberger, 1977; Huberman, 1978). It transformed several types of mammalian cells exposed to concentrations of 10 ug/mL or greater; these cell types included: Syrian hamster embryo cells, mouse C3H10T 1/2 cells and mouse prostate C3H cells (DiPaolo et al., 1969; Chen and Heidelberger, 1969; Pienta et al., 1977; Casto et al., 1977; Casto, 1979; Reznikoff et al., 1973; Lubet et al., 1983).

Current theories on mechanisms of metabolic activation of polycyclic aromatic hydrocarbons are consistent with a carcinogenic potential for dibenz[a,h]anthracene. Dibenz[a,h]anthracene has a "bay-region" structure (Jerina et al., 1978). It is metabolized by mixed-function oxidases to dihydrodiols that are mutagenic in bacteria and tumorigenic in mouse skin painting assays and when injected into newborn mice (Wood et al., 1978; Nordqvist et al., 1979; Slaga et al., 1980; Buening et al., 1979).

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, 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 (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 — Dibenz[a,h]anthracene

CASRN — 53-70-3

VI.A. Oral RfD References

None

VI.B. Inhalation RfC References

None

VI.C. Carcinogenicity Assessment References

Andrews, A.W., L.H. Thibault and W. Lijinsky. 1978. The relationship between carcinogenicity and mutagenicity of some polynuclear hydrocarbons. *Mutat. Res.* 51: 311-318.

Baker, R.S.U., A.M. Bonin, I. Stupans and G.M. Holder. 1980. Comparison of rat and guinea pig as sources of the S9 fraction in the Salmonella/mammalian microsome mutagenicity test. *Mutat. Res.* 71: 43-52.

Berenblum, I. and N. Haran. 1955. The influence of croton oil and of polyethylene glycol-400 on carcinogenesis in the forestomach of the mouse. *Cancer Res.* 15: 510-516.

Biancifiori, C. and F. Caschera. 1962. The relation between pseudo- pregnancy and the chemical induction by four carcinogens of mammary and ovarian tumours in BALB/c mice. *Br. J. Cancer.* 16: 722-730.

Biancifiori, C., G.M. Bonser and F. Caschera. 1959. The influence of pseudo- pregnancy on the induction of mammary tumors by methylcholanthrene in mice of Balb/c strain. *Br. J. Cancer.* 13: 662-668.

Bryan, W.R. and M.B. Shimkin. 1943. Quantitative analysis of dose-response data obtained with three carcinogenic hydrocarbons in strain C3H male mice. *J. Natl. Cancer Inst.* 3: 503-531.

Buening, M.K., W. Levin, A.W. Wood, et al. 1979. Tumorigenicity of the dihydrodiols of dibenzo[a,h]anthracene on mouse skin and in newborn mice. *Cancer Res.* 39: 1310-1314.

Casto, B.C. 1979. Polycyclic hydrocarbons and Syrian hamster embryo cells: Cell transformation, enhancement of viral transformation and analysis of DNA damage. In: *Polynuclear Aromatic Hydrocarbons*, P.W. Jones and P. Leber, Ed. Ann Arbor Science Publ., Ann Arbor, MI. p. 51-66.

Casto, B.C., N. Janosko and J.A. DiPaolo. 1977. Development of a focus assay model for transformation of hamster cells in vitro by chemical carcinogens. *Cancer Res.* 37: 3508-3515.

Chen, T.T. and C. Heidelberger. 1969. Quantitative studies on the malignant transformation of mouse prostate cells by carcinogenic hydrocarbons in vitro. *Int. J. Cancer.* 4: 166-178.

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

Hermann, M. 1981. Synergistic effects of individual polycyclic aromatic hydrocarbons on the mutagenicity of their mixtures. *Mutat. Res.* 90(4): 399-409.

Huberman, E. 1978. Cell transformation and mutability of different genetic loci in mammalian cells by metabolically activated carcinogenic polycyclic hydrocarbons. In: *Polycyclic*

Hydrocarbons and Cancer, Vol. 2. Molecular and Cell Biology, H.V. Gelboin and P.O.P. Tso, Ed. Academic Press, NY. p. 161-174.

Huberman, E. and L. Sachs. 1976. Mutability of different genetic loci in mammalian cells by metabolically activated carcinogenic polycyclic hydrocarbons. Proc. Natl. Acad. Sci. USA. 73(1): 188-192.

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

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

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.

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.

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.

Lake, R.S., M.L. Kropko, M.R. Pezzutti, R.H. Shoemaker and H.J. Igel. 1978. Chemical induction of unscheduled DNA synthesis in human skin epithelial cell cultures. Cancer Res. 38: 2091-2098.

Lubet, R.A., E. Kiss, M.M. Gallagher, C. Dively, R.E. Kouri and L.M. Schectman. 1983. Induction of neoplastic transformation and DNA single-strand breaks in C3H/10T1/2 clone 8 cells by polycyclic hydrocarbons and alkylating agents. J. Natl. Cancer Inst. 71(5): 991-997.

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.

Nordqvist, M., D.R. Thakker, W. Levin, et al. 1979. The highly tumorigenic 3,4-dihydrodiol is a principal metabolite formed from dibenzo[a,h]anthracene by liver enzymes. *Mol. Pharmacol.* 16: 643-655.

Pfeiffer, E.H. 1973. Investigations on the carcinogenic burden by air pollution in man. VII. Studies on the oncogenetic interaction of polycyclic aromatic hydrocarbons. *Zbl. Bakt. Hyg., I. Abt. Orig. B.* 158: 69-83.

Pfeiffer, E.H. 1977. Oncogenic interaction of carcinogenic and non- carcinogenic polycyclic aromatic hydrocarbons in mice. In: *Air Pollutants and Cancer in Man*, U. Mohr, D. Schmaehl and L. Tomatis, Ed. IARC, Lyon, France. p. 69-77.

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.

Reznikoff, C.A., J.S. Bertram, D.W. Brankow and C. Heidelberger. 1973. Quantitative and qualitative studies of chemical transformation of cloned C3H mouse embryo cells sensitive to postconfluence inhibition of cell division. *Cancer Res.* 33: 3239-3249.

Slaga, T.J., G.L. Gleason, G. Mills, et al. 1980. Comparison of the skin tumor-initiating activities of dihydrodiols and diol-epoxides of various polycyclic aromatic hydrocarbons. *Cancer Res.* 40: 1981-1984.

Snell, K.C. and H.L. Stewart. 1962. Pulmonary adenomatosis induced in DBA/2 mice by oral administration of dibenz[a,h]anthracene. *J. Natl. Cancer Inst.* 28(5): 1043-1049.

Snell, K.C. and H.L. Stewart. 1963. Induction of pulmonary adenomatose in DBA/2 mice by the oral administration of dibenz[a,h]anthracene. *Acta. Un. Int. Cancer.* 19: 692-694.

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.

Van Duuren, B.L., L. Langseth, B.M. Goldschmidt, et al., 1967. Carcinogenicity of epoxides, lactones and peroxy compounds. VI. Structure and carcinogenic activity. J. Natl. Cancer Inst. 21: 623.

Wood, A.W., W. Levin, P.E. Thomas, et al. 1978. Metabolic activation of dibenzo[a,h]anthracene and its dihydrodiols to bacterial mutagens. Cancer Res. 38(7): 1967-1973.

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

VII. Revision History

Substance Name — Dibenz[a,h]anthracene
CASRN — 53-70-3

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

VIII. Synonyms

Substance Name — Dibenz[a,h]anthracene
CASRN — 53-70-3
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- 53-70-3

- Dibenz(a,h)anthracene
- DB(a,h)A
- DBA
- dibenz(a,h)anthracene
- DIBENZO(a,h)ANTHRACENE
- HSDB 5097
- NSC 22433
- RCRA WASTE NUMBER U063
- 1,2,5,6-DIBENZANTHRACEEN [Dutch]
- 1,2,5,6-dibenzanthracene
- 1,2:5,6-BENZANTHRACENE
- 1,2:5,6-DIBENZ(a)ANTHRACENE
- 1,2:5,6-Dibenzanthracene
- 1,2:5,6-DIBENZOANTHRACENE