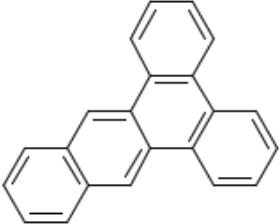
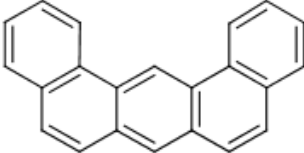
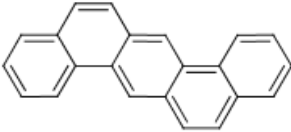


Dibenzanthracenes and Dibenz[a,c]anthracene

Dibenzanthracenes are polycyclic aromatic hydrocarbons (PAHs) that are ubiquitous products of incomplete combustion. Sources include cigarette smoke, gasoline engine exhaust and industrial emissions including fuel combustion, coke oven and coal-tar distillation. Human exposure may occur in occupational settings, and to the general public from contaminated air, food or water.

There are three dibenzanthracenes isomers: dibenz[a,c]anthracene, dibenz[a,j]anthracene and dibenz[a,h]anthracene. Their chemical structures are shown below. Dibenz[a,h]anthracene is listed as a carcinogen under Proposition 65. The data for this chemical are also compiled since they inform consideration of dibenzanthracenes as a group.

| Chemical name | Dibenz[a,c]anthracene | Dibenz[a,j]anthracene | Dibenz[a,h]anthracene Proposition 65 carcinogen |
|---------------|--|--|---|
| Structure |  |  |  |

Dibenzanthracenes (as a chemical group) and one individual chemical within the group (*i.e.*, dibenz[a,c]anthracene) each passed the animal data screen, underwent a preliminary toxicological evaluation, and are being brought to the Carcinogen Identification Committee (CIC) for consultation. This is a compilation of the relevant studies identified during the preliminary toxicological evaluation. The CIC is being asked to advise OEHHA on whether dibenzanthracenes as a group, or dibenz[a,c]anthracene alone, or both should be considered for listing at a future CIC meeting.

Epidemiological data

No cancer epidemiology studies on dibenzanthracenes were identified.

Animal carcinogenicity data

Dibenz[a,c]anthracene

- Skin application (2x/week for 65 weeks and observed for lifetime) in female Swiss mice: Lijinsky *et al.* (1970) as reviewed in IARC (2010, p. 253)
 - *Increase in skin carcinoma (by pairwise comparison)*
- Single subcutaneous (s.c.) injection in male and female C57BL/6J, DBA/2J and B6D2F₁ mice and observed for 12 months: Kouri *et al.* (1983) as reviewed in IARC (2010, pp. 427-428)
 - *No treatment-related tumor findings*
- Three intraperitoneal (i.p.) injections of 400 nmol in newborn male B6C3F₁ mice and observed for 12 months: von Tungeln *et al.* (1999) as reviewed in IARC (2010, pp. 353 & 428)
 - *Increase in liver adenoma (by pairwise comparison)*

Initiation-promotion studies, as reviewed in IARC (2010)

- Single s.c. injection of dibenz[a,c]anthracene, followed 2 weeks later by croton oil in acetone (3x/week for up to 66 weeks) in female Swiss mice: Van Duuren *et al.* (1968) as cited by IARC (2010, p. 280)
 - *No treatment-related tumor findings*
- Single s.c. injection of dibenz[a,c]anthracene, followed 2 weeks later by TPA in acetone (3x/week for up to 60 weeks) in female Swiss mice: Van Duuren *et al.* (1970) as cited by IARC (2010, p. 281)
 - *Increase in skin papilloma (by pairwise comparison) and carcinoma (marginal by pairwise comparison, p=0.053)*
- Single dermal application of dibenz[a,c]anthracene, followed 1 week later by TPA (2x/week for 34 weeks) in female CD-1 mice: Scribner (1973) as cited by IARC (2010, p. 281)
 - *Increase in skin papilloma (by pairwise comparison)*
- Single dermal application of dibenz[a,c]anthracene, followed 1 week later by TPA (2x/week for 67 weeks) in female CD-1 mice: Chouroulinkov *et al.* (1983) as reviewed by IARC (2010, pp. 281 & 427)
 - *No treatment-related tumor findings*

Dibenz[a,j]anthracene

- Skin application (2x/week for 60 or 81 weeks and observed for lifetime) in female Swiss mice: Lijinsky *et al.* (1970) as reviewed in IARC (2010, p. 256)
 - *Increase in skin carcinoma (by pairwise comparison)*
- Single s.c. injection and observed for life in female Swiss mice: Lijinsky *et al.* (1970) as reviewed in IARC (2010, p. 309)
 - *No treatment-related tumor findings*

Initiation-promotion studies, as reviewed in IARC (2010)

- Single dermal application of dibenz[a,j]anthracene, followed by TPA (2x/week for 20 weeks) in female SENCAR mice: Sawyer *et al.* (1987) as reviewed by IARC (2010, pp. 282 & 432)
 - *Increase in skin papilloma (by pairwise comparison)*
- Single dermal application of dibenz[a,j]anthracene, followed by TPA (2x/week for 14 weeks) in female SENCAR mice: Harvey *et al.* (1988) as reviewed by IARC (2010, pp. 283 & 433)
 - *Increase in skin papilloma (by pairwise comparison)*

Dibenz[a,h]anthracene

Dibenz[a,h]anthracene is a Proposition 65 carcinogen (1988) and an IARC 2A carcinogen (2010). Positive evidence from animal carcinogenicity studies is seen with multiple routes of exposure in multiple species at multiple tumor sites:

- Dermal application in mice (skin papilloma and carcinoma, lung adenoma)
- S.c. injection in mice (sarcoma, fibrosarcoma, lung tumor) and rats (sarcoma)
- I.p. injection in mice (lung adenoma)
- Oral administration in mice (forestomach tumor including carcinoma, mammary carcinoma, lung carcinoma, hemangioendothelioma)
- Intrapulmonary implantation in mice (lung adenoma) and rats (lung carcinoma)
- Intratracheal injection in rats (lung carcinoma, liver adenoma and carcinoma) and hamsters (lung tumor including carcinoma)
- Intravenous administration in mice (lung tumor)

Multiple initiation-promotion studies have demonstrated the initiating activity of this Proposition 65 carcinogen in mice (IARC, 2010, pp. 282 & 429).

Other relevant data

- Genotoxicity studies, as reviewed by IARC (1983, 2010) and GENETOX (1995)

Dibenz[a,c]anthracene

- Mutagenicity assays in *Salmonella typhimurium* (with S9) and mammalian cells in culture (*positive*)
- Forward mutation assays in Chinese hamster V79 cells (*positive*)
- DNA damage in *Bacillus subtilis* (*positive*)
- Unscheduled DNA synthesis *in vitro* (*inconclusive*)
- Sister chromatid exchange in Chinese hamster ovary cells (*negative*)
- Cell transformation assays in Syrian hamster embryo cells (*positive and inconclusive*)
- Cell transformation assays in mouse embryo cells (*negative*)

Dibenz[a,j]anthracene

- Mutagenicity assays in *Salmonella typhimurium* (with S9) (*positive*)
- Formation of DNA adducts in mouse epidermis after topical application (*positive*)
- Induced mutation in proto-oncogene (Ha-ras codon 61) in mouse skin papilloma (*positive*)

Dibenz[a,h]anthracene

- Mutagenicity assays in *Salmonella typhimurium* (with S9) (*positive*)
 - Forward mutation assays in Chinese hamster cells (*positive*)
 - DNA damage in *E. Coli* and *Bacillus subtilis* (*positive*)
 - Sex-linked recessive lethal gene mutation in *Drosophila melanogaster* (*positive*)
 - Sister chromatid exchange in Chinese hamster ovary cells *in vitro* (*positive*)
 - Unscheduled DNA synthesis *in vitro* (*positive*)
 - Sister chromatid exchange *in vivo* (*positive*)
 - Formation of DNA adducts (*positive*)
 - Cell transformation assays in Fischer rat embryo cells, Syrian hamster embryo cells and mouse embryo cells (*all positive*)
- Structure activity considerations
 - Each of the three dibenzanthracenes has one or more “bay regions,” areas bounded by three aromatic rings, where diol epoxides are commonly formed.

- Many dibenzanthracene metabolites are mutagenic or tumor initiators. Examples are given below:
 - Dibenz[*a,c*]anthracene-10,11-dihydrodiol
 - mutagenic
 - tumor initiator
 - Dibenz[*a,j*]anthracene-3,4-diol
 - mutagenic
 - tumor initiator
 - Dibenz[*a,j*]anthracene-3,4-diol-1,2-oxide
 - mutagenic
 - tumor initiator
 - Dibenz[*a,h*]anthracene-3,4-diol
 - Mutagenic
 - Tumor initiator
 - Dibenz[*a,h*]anthracene-3,4-diol-1,2-oxide
 - Mutagenic

Reviews

- IARC (1983, 2010)

References¹

GENE-TOX database (1995). Dibenz[*a,c*]anthracene. Toxnet, National Library of Medicine. Available at: [http://toxnet.nlm.nih.gov/cgi-bin/sis/search/r?dbs+genetox:@term+@rn+@rel+"215-58-7"](http://toxnet.nlm.nih.gov/cgi-bin/sis/search/r?dbs+genetox:@term+@rn+@rel+)

International Agency for Research on Cancer (IARC, 1983). *IARC Monographs on the Evaluation of Carcinogenic Risk to Humans. Polynuclear Aromatic Compounds. Part I Chemical, Environmental and Experimental Data.* Volume 32. IARC, Lyon, pp. 289-297, 299-308.

International Agency for Research on Cancer (IARC, 2010). *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Some Non-heterocyclic Polycyclic Aromatic Compounds and Some Related Exposures.* Volume 92. IARC, Lyon, pp. 36, 253-256, 280-283, 304-309, 318-319, 322, 333-334, 353, 368-369, 386-387, 408, 427-433, 468-471, 594-596, 762, 770-773.

¹ Excerpts or the complete publication have been provided to members of the Carcinogen Identification Committee, in the order in which they are discussed in this document.