



WORLD HEALTH ORGANIZATION  
INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

IARC Monographs on the Evaluation of Carcinogenic Risks to Humans

## Volume 29 Some Industrial Chemicals and Dyestuffs

### Summary of Data Reported and Evaluation

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Benzyl chloride  
Benzal chloride  
Benzotrichloride  
Benzoyl chloride  
Benzene  
Benzidine and its sulphate, hydrochloride and dihydrochloride  
*para*-Benzoquinone dioxime  
Butyl benzyl phthalate  
4,4'-Diaminodiphenyl ether  
*ortho*- and *para*-Dichlorobenzenes  
3,3'-Dichlorobenzidine and its dihydrochloride  
Di(2-ethylhexyl) adipate  
Di(2-ethylhexyl) phthalate  
Direct Black 38  
Direct Blue 6  
Direct Brown 95  
2-Nitropropane

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Last updated: 13 April 1999

# BENZYL CHLORIDE

VOL.: 29 (1982) (p. 49)

## 5. Summary of Data Reported and Evaluation

### 5.1 Experimental data

Benzyl chloride was tested in mice by skin application and in rats by subcutaneous injection. Sarcomas at the injection site were observed in rats. A few skin carcinomas were observed in a limited number of mice, but their incidence was not statistically significant.

Benzyl chloride is a direct-acting mutagen to bacteria. It induces mitotic recombination in yeast and transforms hamster embryo cells.

The available data are inadequate to assess the teratogenicity of this compound to experimental animals.

### 5.2 Human data

Occupational exposure to benzyl chloride may occur during its manufacture and during its use in the production of benzyl phthalates, benzyl alcohol, quaternary ammonium salts, pharmaceuticals and benzyl esters; but no data were available on levels of exposure.

No data were available to assess the mutagenicity or teratogenicity of this compound to man.

No case report or epidemiological study involving exposure to benzyl chloride alone was available to the Working Group. Six cases of respiratory cancer have been reported among benzoyl chloride manufacturing workers in two small plants, who were also potentially exposed to benzyl chloride. The cases occurred in relatively young workers, three of whom were nonsmokers.

### 5.3 Evaluation

There is *limited evidence* that benzyl chloride is carcinogenic in experimental animals.

Although the epidemiological data were inadequate to evaluate the carcinogenicity of benzyl chloride alone, they provide *limited evidence* that employment in the production of benzoyl chloride and its chlorinated toluene precursors, which involves exposure to benzyl chloride, represents a carcinogenic risk to man.

No evaluation could be made of the carcinogenicity to man of benzyl chloride itself.

For definition of the italicized terms, see [Preamble Evaluation](#).

**Previous evaluation:** [Vol. 11 \(1976\)](#)

**Subsequent evaluation:** [Vol. 71 \(1999\)](#)

# BENZAL CHLORIDE

VOL.: 29 (1982) (p. 65)

## 5. Summary of Data Reported and Evaluation

### 5.1 Experimental data

In one experiment in which benzal chloride was tested by skin application in female mice, it produced squamous-cell carcinomas of the skin. In a concurrent experiment in which it was tested for a shorter duration, a low incidence of skin papillomas was observed.

In one study, benzal chloride was mutagenic to bacteria with metabolic activation and was positive in a *rec-assay* with *Bacillus subtilis*.

No data were available to assess the teratogenicity of this compound to experimental animals.

### 5.2 Human data

Occupational exposure to benzal chloride has and probably still does occur during its manufacture and conversion to benzaldehyde.

No data were available to assess the mutagenicity or teratogenicity of this compound to man.

No case report or epidemiological study involving exposure to benzal chloride alone was available to the Working Group. Six cases of respiratory cancer have been reported among benzoyl chloride manufacturing workers in two small plants, who were also potentially exposed to benzal chloride. The cases occurred in young workers, three of whom were nonsmokers.

### 5.3 Evaluation

There is *limited evidence* that benzal chloride is carcinogenic in experimental animals.

Although the epidemiological data were inadequate to evaluate the carcinogenicity of benzal chloride alone, they provide *limited evidence* that employment in the production of benzoyl chloride and its chlorinated toluene precursors, which involves exposure to benzal chloride, represents a carcinogenic risk to man.

No evaluation could be made of the carcinogenic risk to man of benzal chloride itself.

For definition of the italicized terms, see [Preamble Evaluation](#).

**Subsequent evaluation:** [Vol. 71 \(1999\)](#)

# BENZOTRICHLORIDE

VOL.: 29 (1982) (p. 73)

## 5. Summary of Data Reported and Evaluation

### 5.1 Experimental data

Benzotrichloride was tested in a series of three studies by skin application to female mice. It produced squamous-cell carcinomas of the skin in all three experiments; upper-digestive-tract tumours were also observed in two of the three experiments. An increase in the incidence of tumours at other sites was reported. In a study reported as an abstract, oral administration of benzotrichloride produced malignant tumours of the forestomach and lung in female mice.

Benzotrichloride was mutagenic to bacteria with metabolic activation, and was positive in a *rec*-assay with *Bacillus subtilis*.

No data were available to assess the teratogenicity of this compound to experimental animals.

### 5.2 Human data

Occupational exposure to benzotrichloride has and probably still does occur during its manufacture and use as an intermediate in the manufacture of benzoyl chloride, dyes, ultra-violet stabilizers and other derivatives.

No data were available to assess the mutagenicity or teratogenicity of this compound to man.

No case report or epidemiological study involving exposure to benzotrichloride alone was available to the Working Group. Six cases of respiratory cancer have been reported among benzoyl chloride production workers in two small plants, who were also potentially exposed to benzotrichloride. The cases occurred in young workers, three of whom were nonsmokers.

### 5.3 Evaluation

There is *sufficient evidence* that benzotrichloride is carcinogenic in mice.

Although the epidemiological data were inadequate to evaluate the carcinogenicity of benzotrichloride alone, they provide *limited evidence* that employment in the production of benzoyl chloride and its chlorinated toluene precursors, which involves exposure to benzotrichloride, represents a carcinogenic risk to man.

For definition of the italicized terms, see [Preamble Evaluation](#).

**Subsequent evaluation:** [Vol. 71 \(1999\)](#)

# BENZOYL CHLORIDE

VOL.: 29 (1982) (p. 83)

## 5. Summary of Data Reported and Evaluation

### 5.1 Experimental data

Benzoyl chloride was tested in two sets of experiments by skin application to female mice. A few skin carcinomas were observed in treated mice, but their incidence was not statistically significant.

There is no clear evidence that benzoyl chloride is mutagenic in bacterial systems; it was negative in a *rec-assay* with *Bacillus subtilis*.

No data were available to assess the teratogenicity of this compound to experimental animals.

### 5.2 Human data

Occupational exposure to benzoyl chloride has and probably still does occur during its manufacture and use in the production of benzoyl peroxide, herbicides and other derivatives.

No data were available to assess the mutagenicity or teratogenicity of this compound to man.

No case report or epidemiological study involving exposure to benzoyl chloride alone was available to the Working Group. Six cases of respiratory cancer have been reported among benzoyl chloride production workers in two small plants. The cases occurred in young workers, three of whom were nonsmokers.

### 5.3 Evaluation

There was *inadequate evidence* for the carcinogenicity of benzoyl chloride in experimental animals.

Although the epidemiological data were inadequate to evaluate the carcinogenicity of benzoyl chloride alone, they provide *limited evidence* that employment in the production of benzoyl chloride and its chlorinated toluene derivatives represents a carcinogenic risk to man.

No evaluation could be made on the carcinogenicity to man of benzoyl chloride itself.

For definition of the italicized terms, see [Preamble Evaluation](#).

**Subsequent evaluation:** [Suppl. 7 \(1987\)](#); [Vol. 71 \(1999\)](#)

# BENZENE

VOL.: 29 (1982) (p. 93)

## 5. Summary of Data Reported and Evaluation

### 5.1 Experimental data

Benzene has been tested in rats by intragastric administration and inhalation exposure, and in mice by skin application, inhalation exposure and subcutaneous injection. Oral administration to rats resulted in an increase in the incidence of Zymbal-gland carcinomas. Anaemia, lymphocytopenia and bone-marrow hyperplasia and an increased incidence of lymphoid tumours occurred in male mice exposed by inhalation to benzene; in similar inhalation studies with another strain of mice and with rats there was no evidence of a leukaemic response. Experiments involving skin application or subcutaneous injection of benzene did not produce evidence of carcinogenicity, but most of these experiments were inadequate.

Benzene does not induce specific gene mutations in bacterial systems or in *Drosophila melanogaster*. A single report showed no evidence for the induction of point mutation in mammalian cells; however, benzene induced cytogenic abnormalities (chromosomal aberrations and sister chromatid exchanges) in mammalian cells *in vitro*.

The micronucleus test in mice and rats has been consistently positive. Numerous studies have shown that benzene exposure of experimental animals *in vivo* leads to the induction of chromosomal aberrations in the bone-marrow cells.

Exposure to benzene may damage the testis. Evidence from most studies in mice, rats, guinea-pigs and rabbits suggests that benzene is not teratogenic at doses that are fetotoxic and embryolethal.

### 5.2 Human data

Workers and the general public are exposed to benzene as a result of a variety of activities in which it is processed, generated or used. Major contributors to benzene emissions into air include: (1) gasoline production, storage, transport, vending and combustion; (2) production of other chemicals from benzene; and (3) indirect production of benzene (e.g., in coke ovens). The last is the major source of benzene emissions into water.

Chronic human exposure to benzene results in leucopenia, thrombocytopenia, anaemia or combinations of these. At early stages of such blood dyscrasias, these effects appear to be reversible. Exposure to high doses for longer periods of time may lead to pancytopenia, which results from aplasia of the bone marrow and is considered to be an irreversible stage of the disease.

Benzene crosses the human placenta. There is a clear correlation between exposure to benzene and the appearance of chromosomal aberrations in the bone marrow and peripheral lymphocytes of individuals exposed to high levels of benzene (> 100 ppm). Such levels of exposure usually lead to clinical symptoms of benzene-induced blood dyscrasias. These aberrations may persist for many years after exposure and after manifestations of haematotoxicity. The results are not so clear with lower levels (< 100 ppm). Although aberrations have been reported following chronic exposures to as little as 10 ppm, this has not been a consistent finding. Environmental factors and exposure to other agents may have interacted with benzene in these studies of low exposure.

Many case reports and case series have described the association of leukaemia with exposure to benzene, either alone or in combination with other chemicals. Most cases were acute myelogenous leukaemia, although some were monocytic, erythroblastic or lymphocytic; and some lymphomas have been noted.

Two follow-up studies showed high incidences of leukaemia among individuals ascertained as cases of benzene haemopathy.

A series of epidemiological studies, both cohort and case-control, showed statistically significant associations between leukaemia (predominantly myelogenous) and occupational exposure to benzene and benzene-containing solvents. These results were replicated in a number of countries and different industries. In the epidemiological studies of people exposed primarily to benzene, statistically significant excesses of leukaemia were observed.

### **5.3 Evaluation**

There is *limited evidence* that benzene is carcinogenic in experimental animals.

It is established that human exposure to commercial benzene or benzene-containing mixtures can cause damage to the haematopoietic system, including pancytopenia. The relationship between benzene exposure and the development of acute myelogenous leukaemia has been established in epidemiological studies.

Reports linking exposure to benzene with other malignancies were considered to be inadequate for evaluation.

There is *sufficient evidence* that benzene is carcinogenic to man.

For definition of the italicized terms, see [Preamble Evaluation](#).

**Previous evaluation:** [Vol. 7 \(1974\)](#)

**Subsequent evaluation:** [Suppl. 7 \(1987\)](#)

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# BENZIDINE AND ITS SULPHATE, HYDROCHLORIDE AND DIHYDROCHLORIDE

VOL.: 29 (1982) (p. 149)

## 5. Summary of Data Reported and Evaluation

### 5.1 Experimental data

Benzidine and its dihydrochloride were tested in mice, rats and hamsters by oral administration, in mice and rats by subcutaneous administration and in rats by inhalation and intraperitoneally. Following its oral administration to mice of different strains, both sexes, newborn and adult, and following its subcutaneous administration, it significantly increased the incidence of liver-cell tumours (benign and malignant). In female rats, it markedly increased the incidence of mammary tumours; and in male and female hamsters, it increased the incidence of liver tumours following its oral administration. The subcutaneous administration of benzidine or its sulphate to rats produced a high incidence of Zymbal-gland tumours; colonic tumours were also reported. The results of the inhalation study in rats could not be interpreted. The intraperitoneal administration of benzidine to rats resulted in a marked increase in the incidence of mammary and Zymbal-gland tumours. It was also tested in dogs by oral administration, producing bladder carcinomas. Studies in fish, rabbits and frogs could not be evaluated.

The metabolites of benzidine, *N,N'*-diacetylbenzidine and *N*-hydroxy-*N,N'*-diacetylbenzidine, produced mammary and Zymbal-gland tumours in rats following their intraperitoneal injection.

Benzidine and urine from rats fed benzidine are mutagenic to *Salmonella typhimurium* with metabolic activation. Benzidine is mutagenic to *Drosophila melanogaster*. It inhibits DNA synthesis in HeLa cells and in renal and hepatic cells in mice *in vivo*. It induces unscheduled DNA synthesis in HeLa cells and in rat hepatocytes. Benzidine transformed Syrian hamster embryo cells and was positive in the BHK21 clone-13 cell system.

The data were inadequate to assess the teratogenicity of this compound to experimental animals.

### 5.2 Human data

Occupational exposure to benzidine or its dihydrochloride has and probably still does occur during their manufacture and conversion to derived dyes and during the use of those dyes. When benzidine is used for blood testing or to enhance fingerprints, laboratory or field workers may be exposed. Environmental exposure can occur under certain conditions, when benzidine-based dyes are converted to benzidine in streams into which dye-containing wastes have been discharged.

No data were available to assess the mutagenicity or teratogenicity of benzidine to man.

Occupational exposure to benzidine has been strongly associated with bladder cancer in numerous case reports from many countries. The association has also been observed in several epidemiological studies. In one extreme instance, all five of a group of workers continuously employed in benzidine manufacture for 15 years or more developed bladder cancer.

### 5.3 Evaluation

There is *sufficient evidence* that benzidine is carcinogenic to mice, rats, hamsters and dogs.

There is *sufficient evidence* that benzidine is carcinogenic to man.

For definition of the italicized terms, see [Preamble Evaluation](#).

**Previous evaluation:** [Vol. 1 \(1972\)](#)

**Subsequent evaluation:** [Suppl. 7 \(1987\)](#)

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# ***para*-BENZOQUINONE DIOXIME**

**VOL.:** 29 (1982) (p. 185)

**CAS No.:** 105-11-3

**Chem. Abstr. Name:** 2,5-Cyclohexadiene-1,4-dione, dioxime

## **5. Summary of Data Reported and Evaluation**

### **5.1 Experimental data**

*para*-Benzoquinone dioxime was tested for carcinogenicity at two dose levels in mice and rats by oral administration. No significant increase in the number of neoplasms was observed in male rats; but in females given the high dose, a significant increase in the number of transitional-cell papillomas and carcinomas of the urinary bladder occurred. In mice, no carcinogenic effect was observed.

No data were available to assess the mutagenicity or teratogenicity of this compound.

### **5.2 Human data**

Occupational exposure to *para*-benzoquinone dioxime probably occurs during its manufacture, its use as a rubber vulcanizing agent and its conversion to chemical derivatives.

No data were available to assess the mutagenicity or teratogenicity of this compound to man.

No case report or epidemiological study was available to the Working Group.

### **5.3 Evaluation**

There is *limited evidence* that *para*-benzoquinone dioxime is carcinogenic to rats.

No case report or epidemiological study was available.

No evaluation could be made of the carcinogenicity of *para*-benzoquinone dioxime to man.

For definition of the italicized terms, see [Preamble Evaluation](#).

**Subsequent evaluation:** [Vol. 71 \(1999\)](#)

### **Synonyms *para*-Benzoquinone Dioxime**

- Actor Q
- 1,4-Benzoquinone dioxime
- Dibenzo PQD
- G-M-F
- PQD
- QDO
- *para*-Quinone dioxime
- *para*-Quinone oxime

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# BUTYL BENZYL PHTHALATE

**VOL.:** 29 (1982) (p. 193)

**CAS No.:** 85-68-7

**Chem. Abstr. Name:** 1,2-Benzenedicarboxylic acid, butyl

## 5. Summary of Data Reported and Evaluation

### 5.1 Experimental data

Butyl benzyl phthalate was tested in mice and female rats by oral administration and in male mice by intraperitoneal injection. A somewhat higher incidence of monocytic leukaemias was observed in female rats. In mice, no increased incidence of tumours was observed.

Butyl benzyl phthalate was not mutagenic for *Escherichia coli*, *Bacillus subtilis*, *Salmonella typhimurium* or *Saccharomyces cerevisiae* or in the mouse lymphoma assay.

No data were available to assess the teratogenicity of this compound to experimental animals.

### 5.2 Human data

Occupational exposure to butyl benzyl phthalate has and probably still does occur during its manufacture, its use as a plasticizer and in the further processing or use of plasticized products containing it.

No data were available to assess the mutagenicity or teratogenicity of this compound to man.

No case report or epidemiological study was available to the Working Group.

### 5.3 Evaluation

The available studies were inadequate to evaluate the carcinogenicity of butyl benzyl phthalate to mice and rats.

No case report or epidemiological study was available.

No evaluation could be made of the carcinogenic risk to man of butyl benzyl phthalate.

**Subsequent evaluations:** Suppl. 7 (1987) (p. 59: **Group 3**); [Vol. 73 \(1999\)](#)

### Synonyms

- BBP
- Benzyl *n*-butyl phthalate
- Butylbenzyl phthalate
- *n*-Butyl benzyl phthalate
- Butyl phenylmethyl 1,2-benzenedicarboxylate
- Palatinol BB
- Phthalic acid, benzyl butyl ester
- Santicizer 160
- Sicol 160

- Unimoll BB

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# 4,4'-DIAMINODIPHENYL ETHER

**VOL.:** 29 (1982) (p. 203)

**CAS No.:** 101-80-4

**Chem. Abstr. Name:** Benzenamine, 4,4'-oxybis-

## 5. Summary of Data Reported and Evaluation

### 5.1 Experimental data

4,4'-Diaminodiphenyl ether was tested in mice and rats by oral administration and by subcutaneous injection. In two studies in rats, it produced benign and malignant liver-cell tumours following oral or subcutaneous administration; and following its oral administration in one study, benign and malignant follicular-cell tumours of the thyroid were produced. Other studies in rats by oral and subcutaneous administration were not adequate for evaluation. In a study in mice by oral administration it produced benign and malignant liver-cell tumours in females given the high dose and in males given the low dose and adenomas of the Harderian gland in animals of both sexes.

4,4'-Diaminodiphenyl ether is mutagenic to *Salmonella typhimurium* with metabolic activation.

No data were available to assess its teratogenicity to experimental animals.

### 5.2 Human data

Occupational exposure to 4,4'-diaminodiphenyl ether probably occurs during its manufacture and its conversion to polyimide-type resins.

No data were available to assess the mutagenicity or teratogenicity of this compound to man.

No case report or epidemiological study was available to the Working Group.

### 5.3 Evaluation

There is *sufficient evidence* for the carcinogenicity of 4,4'-diaminodiphenyl ether in mice and rats.

No case report or epidemiological study was available.

For definition of the italicized terms, see [Preamble Evaluation](#).

**Previous evaluation:** [Vol. 16 \(1978\)](#)

**Subsequent evaluation:** Suppl. 7 (1987) (p. 61: **Group 2B**)

### Synonyms

- 4-Aminophenyl ether
- *para*-Aminophenyl ether
- Bis(4-aminophenyl) ether
- Bis(*para*-aminophenyl)ether

- 4,4'-Diaminobiphenyl ether
- Diaminodiphenyl ether
- *para,para'*-Diaminodiphenyl ether
- 4,4'-Diaminodiphenyl oxide
- 4,4'-Diaminophenyl ether
- 4,4'-Diaminophenyl oxide
- Oxybis(4-aminobenzene)
- 4,4'-Oxybis(aniline)
- *para,para'*-Oxybis(aniline)
- 4,4'-Oxybis(benzenamine)
- *para,para'*-Oxydianiline
- Oxydianiline
- 4,4'-Oxydiphenylamine
- Oxydi-*para*-phenylenediamine

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# *ortho*- AND *para*-DICHLOROBENZENES

VOL.: 29 (1982) (p. 213)

## 5. Summary of Data Reported and Evaluation

### 5.1 Experimental data

No adequate study on *ortho*-dichlorobenzene was available to the Working Group, and no data were available on *para*-dichlorobenzene.

No data were available to evaluate the teratogenicity of these compounds to experimental animals.

Neither *ortho*- nor *para*-dichlorobenzene was mutagenic to *Salmonella typhimurium*. Mutagenic or clastogenic activity in other cell systems has not been substantiated.

### 5.2 Human data

Occupational exposure to *ortho*-dichlorobenzene occurs during its manufacture, its conversion to 3,4-dichloroaniline and other derivatives and its use as a solvent in toluene diisocyanate production and for other purposes. Its use in manufacturing and solvents may also be significant sources of discharges into water.

Occupational exposure to *para*-dichlorobenzene occurs during its manufacture, its conversion to polyphenylene sulphide resins and its use as an air deodorant and moth control agent. These two uses are also potential sources of exposure for the general population.

One case report has suggested an association between leukaemia and exposure to dichlorobenzenes.

No data were available to assess the mutagenicity or teratogenicity of this compound to man.

### 5.3 Evaluation

No adequate data were available to evaluate the carcinogenicity of *ortho*- or *para*-dichlorobenzene to experimental animals.

The epidemiological data were *inadequate* to evaluate the carcinogenicity of dichlorobenzenes.

No evaluation could be made of the carcinogenicity of *para*- or *ortho*-dichlorobenzene to man.

For definition of the italicized terms, see [Preamble Evaluation](#).

**Previous evaluation:** [Vol. 7 \(1974\)](#)

**Subsequent evaluations:** [Suppl. 7 \(1987\)](#); [Vol. 73 \(1999\)](#)

# 3,3'-DICHLOROBENZIDINE AND ITS DIHYDROCHLORIDE

VOL.: 29 (1982) (p. 239)

## 5. Summary of Data Reported and Evaluation

### 5.1 Experimental data

3,3'-Dichlorobenzidine was tested in mice, rats, hamsters and dogs by oral administration, in rats by subcutaneous administration and in mice by transplacental exposure. Following its oral administration, it produced liver-cell tumours in mice, hepatocellular carcinomas in dogs, mammary and Zymbal-gland tumours in rats and carcinomas of the urinary bladder in hamsters and dogs. Increased incidences of leukaemias were observed in rats following oral administration and in mice following transplacental exposure.

3,3'-Dichlorobenzidine is mutagenic to *Salmonella typhimurium* with or without metabolic activation and induces unscheduled DNA synthesis in HeLa cells.

No data were available on the teratogenicity of this compound to experimental animals.

### 5.2 Human data

Occupational exposure to 3,3'-dichlorobenzidine dihydrochloride has and probably still does occur during its manufacture and conversion to derived pigments. Rubber workers were formerly and may still be exposed to 3,3'-dichlorobenzidine used for curing polyurethane elastomers.

No data were available to assess the mutagenicity or teratogenicity of this compound to man.

No case report on exposure to 3,3'-dichlorobenzidine was available to the Working Group. Although three retrospective epidemiological studies of workers exposed to 3,3'-dichlorobenzidine gave no evidence for carcinogenicity, the studies were of insufficient quality or statistical power to permit confident exclusion of that possibility. Because 3,3'-dichlorobenzidine and benzidine may be made in the same plant, the possibility cannot be excluded that dichlorobenzidine has contributed to the incidence of human bladder cancer attributed to benzidine.

### 5.3 Evaluation

There is *sufficient evidence* that 3,3'-dichlorobenzidine is carcinogenic in mice, rats, hamsters and dogs.

The epidemiological data are inadequate to evaluate the carcinogenicity of 3,3'-dichlorobenzidine to man.

For definition of the italicized terms, see [Preamble Evaluation](#).

**Previous evaluation:** [Vol. 4 \(1974\)](#)

**Subsequent evaluation:** [Suppl. 7 \(1987\)](#)

# DI(2-ETHYLHEXYL) ADIPATE

**VOL.:** 29 (1982) (p. 257)

**CAS No.:** 103-23-1

**Chem. Abstr. Name:** Hexanedioic acid, bis(2-ethylhexyl) ester

## 5. Summary of Data Reported and Evaluation

### 5.1 Experimental data

Di(2-ethylhexyl) adipate was tested in mice and rats by oral administration. It induced significant increases in the incidence of liver-cell tumours in male and female mice. No increase in tumour incidence was observed in rats.

The data were inadequate to assess the teratogenicity of this compound to experimental animals.

Di(2-ethylhexyl) adipate induces dominant lethal mutations and reduces fertility in mice. Mutagenicity tests in *Salmonella typhimurium* were negative.

### 5.2 Human data

Occupational exposure to di(2-ethylhexyl) adipate occurs during its production, its use as a plasticizer and its use as a lubricant and functional fluid. Its presence as a plasticizer in polyvinyl chloride film used for wrapping food may result in exposure of the general public.

No data were available to assess the mutagenicity or teratogenicity of this compound to man.

No case report or epidemiological study was available to the Working Group.

### 5.3 Evaluation

There is *limited evidence* that di(2-ethylhexyl) adipate is carcinogenic in mice.

No case report or epidemiological study on this compound was available.

No evaluation could be made of the carcinogenicity of 2-ethylhexyl) adipate to man.

For definition of the italicized terms, see [Preamble Evaluation](#).

**Subsequent evaluation:** [Vol. 77 \(2000\)](#)

### Synonyms

- Adipol 2EH
- BEHA
- Bis(2-ethylhexyl) adipate
- Bisoflex DOA
- DEHA
- Di-2-ethyl hexyl adipate

- Dioctyl adipate
- DOA
- Effomoll DOA
- Ergoplast AdDO
- Flexol A26
- Hexanedioic acid, dioctyl ester
- Kodaflex DOA
- Mollan S
- Monoplex DOA
- Octyl adipate
- Plastomoll DDA
- PX-238
- Reomol DOA
- Rucoflex Plasticizer DOA
- Sicol 250
- Staflex DOA
- Truflex DOA
- Uniflex DOA
- Vestinol OA
- Wickenol 158
- Witamol 320

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# DI(2-ETHYLHEXYL) PHTHALATE

**VOL.:** 29 (1982) (p. 269)

**CAS No.:** 117-81-7

**Chem. Abstr. Name:** 1,2-Benzenedicarboxylic acid, bis(2-ethylhexyl)

## 5. Summary of Data Reported and Evaluation

### 5.1 Experimental data

Di(2-ethylhexyl) phthalate was tested in mice and rats by oral administration: It significantly increased the incidence of benign and malignant liver-cell tumours in animals of both species, and a dose-response relationship was observed.

Di(2-ethylhexyl) phthalate can cause testicular damage in rats. There is evidence that this compound and its metabolite, mono(2-ethylhexyl) phthalate, are teratogenic and embryolethal to rodents.

Di(2-ethylhexyl) phthalate was not mutagenic to *Salmonella typhimurium*. However, it caused dominant lethal mutations in mice after systemic but not oral administration.

### 5.2 Human data

Occupational exposure to di(2-ethylhexyl) phthalate probably occurs during its manufacture, its use as a plasticizer, its use in dielectric fluids for electrical capacitors and in the further processing or use of plasticized products containing it. Its reported widespread occurrence in ambient air, in drinking, river and ocean waters, in industrial effluents, in foods and in blood stored in plasticized bags indicates environmental exposure and exposure of the general human population.

No data were available to assess the mutagenicity or teratogenicity of this compound to man.

No adequate epidemiological study was available to the Working Group.

### 5.3 Evaluation

There is *sufficient evidence* for the carcinogenicity of di(2-ethylhexyl) phthalate in mice and rats.

No adequate epidemiological study was available.

For definition of the italicized terms, see [Preamble Evaluation](#).

**Subsequent evaluation:** [Vol. 77 \(2000\)](#)

### Synonyms

- BEHP
- 1,2-Benzenedicarboxylic acid, bis(ethylhexyl) ester
- Bis(2-ethylhexyl) 1,2-benzenedicarboxylate
- Bis(2-ethylhexyl) ester of phthalic acid
- Bis(2-ethylhexyl) phthalate

- Bisoflex 81
- Bisoflex DOP
- Compound 889
- DAF 68
- DEHP
- Di(ethylhexyl) phthalate
- Dioctyl phthalate
- DOP
- Ergoplast FDO
- Ethylhexyl phthalate
- 2-Ethylhexyl phthalate
- Eviplast 80
- Eviplast 81
- Fleximel
- Flexol DOP
- Good-Rite GP 264
- Hatcol DOP
- Kodaflex DOP
- Mollan O
- Nuoplaz DOP
- Octoil
- Octyl phthalate
- Phthalic acid dioctyl ester
- Platinol AH
- Platinol DOP
- Pittsburgh
- PX-138
- Reomol DOP
- Reomol D 79P
- Sicol 150
- Staflex DOP
- Truflex DOP
- Vestinol AH
- Vinicizer 80
- Witcizer 312

# DIRECT BLACK 38

**VOL.:** 29 (1982) (p. 295)

**CAS No.:** 1937-37-7

**Chem. Abstr. Name:** 2,7-Naphthalenedisulfonic acid, 4-amino-3- {[4'-((2,4-diaminophenyl)azo)(1,1'-biphenyl)-4-yl]azo}-5-hydroxy-6-(phenylazo)-, disodium salt

## 5. Summary of Data Reported and Evaluation

### 5.1 Experimental data

Direct Black 38 was tested by oral administration in mice and rats and by bladder implantation in mice. In one study in mice, the compound produced hepatocellular carcinomas and mammary carcinomas following its administration in drinking-water. The other study in mice was inadequate for evaluation. Oral administration to rats of one commercial sample of Direct Black 38 resulted in hepatocellular carcinomas in males and neoplastic nodules in males and females sacrificed 13 weeks after start of exposure to the highest dose at which animals survived. Lower doses produced only liver-cell changes such as foci of cellular alteration. In another study in rats, sacrificed after 60 weeks' exposure to the dye in drinking-water, mucosal hyperplasia and carcinoma of the bladder and carcinomas of the liver and colon were seen.

One study has shown that Direct Black 38 and the urine of hamsters given this compound are mutagenic to *Salmonella typhimurium* with metabolic activation.

One limited study in rats has shown it to be embryolethal but not teratogenic.

### 5.2 Human data

Occupational exposure to Direct Black 38 has and probably still does occur during its production and its use for the dyeing of textiles, leather and paper. Benzidine and its metabolic derivatives have been detected in the urine of workers exposed to direct azo dyes.

No data were available to assess the mutagenicity or chromosomal effects of this compound to man.

No study of exposure to Direct Black 38 alone was available to the Working Group. An epidemiological study of silk dyers and painters who had multiple exposure to benzidine-based and other dyes indicated that those exposures were strongly associated with the occurrence of bladder cancer. Case reports and other epidemiological studies support the existence of such a relationship.

### 5.3 Evaluation

There is *sufficient evidence* that commercial Direct Black 38 is carcinogenic to rats.

Although the epidemiological data were *inadequate* to evaluate the carcinogenicity in man of Direct Black 38 alone, they, together with the presence of benzidine in the urine of exposed workers, provide *sufficient evidence* that occupational exposure to benzidine-based dyes represents a carcinogenic risk to man.

For definition of the italicized terms, see [Preamble Evaluation](#).

**Subsequent evaluation:** [Suppl. 7 \(1987\)](#)

## Synonyms

- Ahco Direct Black GX
- Airedale Black ED
- Aizen Direct Deep Black EH
- Aizen Direct Deep Black GH
- Aizen Direct Deep Black RH
- Amanil Black GL
- Amanil Black WD
- Apomine Black GX
- Atlantic Black BD
- Atlantic Black C
- Atlantic Black E
- Atlantic Black EA
- Atlantic Black GAC
- Atlantic Black GG
- Atlantic Black GXCW
- Atlantic Black GXOO
- Atlantic Black SD
- Atul Direct Black E
- Azine Deep Black EW
- Azocard Black EW
- Azomine Black EWO
- Belamine Black GX
- Bencidal Black E
- Benzanil Black E
- Benzo Deep Black E
- Benzoform Black BCN-CF
- Benzo Leather Black E
- Black 2EMBL
- Black 4EMBL
- Brasilamina Black GN
- Brilliant Chrome Leather Black H
- C.I. 30235
- C.I. Direct Black 38
- C.I. Direct Black 38, disodium salt
- Calcomine Black
- Calcomine Black EXL
- Carbide Black E
- Chloramine Black C
- Chloramine Black EC
- Chloramine Black ERT
- Chloramine Black EX
- Chloramine Black EXR
- Chloramine Black XO
- Chloramine Carbon Black S
- Chloramine Carbon Black SJ
- Chloramine Carbon Black SN
- Chlorazol Black E
- Chlorazol Black EA
- Chlorazol Black E (Biological Stain)
- Chlorazol Black EN
- Chlorazol Burl Black E
- Chlorazol Leather Black ENP
- Chlorazol Silk Black G
- Chrome Leather Black E
- Chrome Leather Black EC
- Chrome Leather Black EM
- Chrome Leather Black G

- Chrome Leather Brilliant Black ER
- Coir Deep Black C
- Columbia Black EP
- Diacotton Deep Black
- Diacotton Deep Black RX
- Diamine Deep Black EC
- Diamine Direct Black E
- Diaphtamine Black V
- Diazine Black E
- Diazine Direct Black E
- Diazine Direct Black G
- Diazol Black 2V Diphenyl Deep Black G
- Direct Black 3
- Direct Black A
- Direct Black BRN
- Direct Black CX
- Direct Black CXR
- Direct Black E
- Direct Black EW
- Direct Black EX
- Direct Black FR
- Direct Black GAC
- Direct Black GW
- Direct Black GX
- Direct Black GXR
- Direct Black JET
- Direct Black Meta
- Direct Black Methyl
- Direct Black N
- Direct Black RX
- Direct Black SD
- Direct Black WS
- Direct Black Z
- Direct Deep Black E
- Direct Deep Black EAC
- Direct Deep Black EA-CF
- Direct Deep Black E Extra
- Direct Deep Black EW
- Direct Deep Black EX
- Enianil Black CN
- Erie Black B
- Erie Black BF
- Erie Black GAC
- Erie Black GXOO
- Erie Black JET
- Erie Black NUG
- Erie Black RXOO
- Erie Brilliant Black S
- Erie Direct Black G Extra
- Erie Fibre Black VP
- Fenamin Black E
- Fibre Black VF
- Fixanol Black E
- Formaline Black C
- Formic Black C
- Formic Black CW
- Formic Black EA
- Formic Black MTG
- Formic Black TG

- Hispamin Black EF
- Interchem Direct Black Z
- Kayaku Direct Deep Black EX
- Kayaku Direct Deep Black GX
- Kayaku Direct Deep Black S
- Kayaku Direct Leather Black EX
- Kayaku Direct Special Black AAX
- Lurazol Black BA
- Meta Black
- Mitsui Direct Black EX
- Mitsui Direct Black GX
- Nippon Deep Black
- Nippon Deep Black GX
- Paper Black BA
- Paper Black T
- Paper Deep Black C
- Paramine Black B
- Paramine Black E
- Peeramine Black E
- Peeramine Black GXOO
- Phenamine Black BCN-CF
- Phenamine Black CL
- Phenamine Black E
- Phenamine Black E 200
- Pheno Black EP
- Pheno Black SGN
- Pontamine Black E
- Pontamine Black EBN
- Sandopel Black EX
- Seristan Black B
- Telon Fast Black E
- Tertrodirect Black E
- Tertrodirect Black EFG
- Tetrazo Deep Black G
- Union Black EM
- Vondacel Black N

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Last updated: 9 April 1998

# DIRECT BLUE 6

**VOL.:** 29 (1982) (p. 311)

**CAS No.:** 2602-46-2

**Chem. Abstr. Name:** 2,7-Naphthalenedisulfonic acid, 3,3'-[(1,1'-biphenyl)-4,4'-diylbis(azo)]bis(5-amino-4-hydroxy)-, tetrasodium salt

## 5. Summary of Data Reported and Evaluation

### 5.1 Experimental data

Oral administration to rats of one commercial sample of Direct Blue 6 resulted in hepatocellular carcinomas and neoplastic nodules in males and females sacrificed 13 weeks after start of exposure to the highest dose at which animals survived. Lower doses produced only liver-cell changes such as foci of cellular alteration.

Direct Blue 6 is teratogenic in rats only when injected during the first half of pregnancy.

No data were available to assess the mutagenicity of this compound.

### 5.2 Human data

Occupational exposure to Direct Blue 6 has and probably still does occur during its production and its use for the dyeing of textiles, leather and paper. Benzidine and its metabolic derivatives have been detected in the urine of workers exposed to direct azo dyes.

No data were available to assess the mutagenicity or chromosomal effects of this compound to man.

No study of exposure to Direct Blue 6 was available to the Working Group. An epidemiological study of silk dyers and painters who had multiple exposure to benzidine-based and other dyes indicated that those exposures were strongly associated with the occurrence of bladder cancer. Case reports and other epidemiological studies support the existence of such a relationship.

### 5.3 Evaluation

There is *sufficient evidence* that commercial Direct Blue 6 is carcinogenic to rats.

Although the epidemiological data were *inadequate* to evaluate the carcinogenicity to man of Direct Blue 6 alone, they, together with the presence of benzidine in the urine of exposed workers, provide *sufficient evidence* that occupational exposure to benzidine-based dyes represents a carcinogenic risk to man.

For definition of the italicized terms, see [Preamble Evaluation](#).

**Subsequent evaluation:** [Suppl. 7 \(1987\)](#)

### Synonyms

- Airedale Blue 2BD
- Aizen Direct Blue 2BH
- Amanil Blue 2BX

- Atlantic Blue 2B
- Atul Direct Blue 2B
- Azocard Blue 2B
- Azomine Blue 2B
- Belamine Blue 2B
- Bencidal Blue 2B
- Benzanil Blue 2B
- Benzo Blue BBA-CF
- Benzo Blue BBN-CF
- Benzo Blue GS
- Blue 2B
- Blue 2B Salt
- Brasilamina Blue 2B
- Calcomine Blue 2B
- Chloramine Blue 2B
- Chlorazol Blue B
- Chlorazol Blue BP
- Chrome Leather Blue 2B
- CI 22610
- C.I. 22610
- C.I. Direct Blue 6
- C.I. Direct Blue 6, Tetrasodium Salt
- Cresotine Blue 2B
- Diacotton Blue BB
- Diamine Blue 2B
- Diamine Blue BB
- Diaphtamine Blue BB
- Diazine Blue 2B
- Diazol Blue 2B
- Diphenyl-4,4'-bis-azo-2"-8"-amino-1"-naphthol-3",6"-disulphonatesodium
- Diphenyl Blue 2B
- Diphenyl Blue KF
- Diphenyl Blue M2B
- Direct Blue A
- Direct Blue 2B
- Direct Blue BB
- Direct Blue GS
- Direct Blue K
- Direct Blue M2B
- Direct Blue WBB
- Enianil Blue 2BN
- Fenamin Blue 2B
- Fixanol Blue 2B
- Hispamin Blue 2B
- Indigo Blue 2B
- Kayaku Direct
- Kayaku Direct Blue BB
- Mitsui Direct Blue 2BN
- Naphtamine Blue 2B
- Niagara Blue B
- Niagara Blue 2B
- Nippon Blue BB
- Paramine Blue 2B
- Phenamine Blue BB
- Pheno Blue 2B
- Pontamine Blue BB
- Tertrodirect Blue 2B
- Vondacel Blue 2B

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# DIRECT BROWN 95

**VOL.:** 29 (1982) (p. 321)

**CAS No.:** 16071-86-6

**Chem. Abstr. Name:** Cuprate (2-), (5-[4'-((2,6-dihydroxy-3-((2-hydroxy-5-sulfophenyl)-azo)phenyl)azo)(1,1'-biphenyl)-4-yl)azo]-2-hydroxy benzoato(4-)-, disodium salt

## 5. Summary of Data Reported and Evaluation

### 5.1 Experimental data

Oral administration to rats of one commercial sample of Direct Brown 95 resulted in one hepatocellular carcinoma and several neoplastic nodules in females sacrificed 13 weeks after start of exposure to the highest dose at which animals survived. The study in mice was inadequate for evaluation.

No data were available to assess the mutagenicity or teratogenicity of Direct Brown 95.

### 5.2 Human data

Occupational exposure to Direct Brown 95 has and probably still does occur during its production and its use for the dyeing of textiles, leather and paper. Benzidine and its metabolic derivatives have been detected in the urine of workers exposed to direct azo dyes.

No data were available to assess the mutagenicity or teratogenicity of Direct Brown 95 to man.

No study of exposure to Direct Brown 95 alone was available to the Working Group. An epidemiological study of silk dyers and painters who had multiple exposure to benzidine-based and other dyes indicated that those exposures were strongly associated with the occurrence of bladder cancer. Case reports and other epidemiological studies support the existence of such a relationship.

### 5.3 Evaluation

The number of preneoplastic lesions in rats and the precocity of their onset indicate a carcinogenic effect similar to that of Direct Black 38. The present data, however, provide only *limited evidence* that commercial Direct Brown 95 is carcinogenic to rats.

Although the epidemiological data were *inadequate* to evaluate the carcinogenicity to man of Direct Brown 95 alone, they, together with the presence of benzidine in the urine of exposed workers, provide *sufficient evidence* that occupational exposure to benzidine-based dyes represents a carcinogenic risk to man.

For definition of the italicized terms, see [Preamble Evaluation](#).

**Subsequent evaluation:** [Suppl. 7 \(1987\)](#)

### Synonyms

- Aizen Primula Brown BRLH
- Aizen Primula Brown PLH
- Amanil Fast Brown BRL
- Amanil Supra Brown LBL

- Atlantic Fast Brown BRL
- Atlantic Resin Fast Brown BRL
- Belamine Fast Brown BRLL
- Benzanil Supra Brown BRLL
- Benzanil Supra Brown BRLN
- Brown 4EMBL
- C.I. 30145
- C.I. Direct Brown
- Calcodur Brown BRL
- Chloramine Fast Brown BRL
- Chloramine Fast Cutch Brown PL
- Chlorantine Fast Brown BRLL
- Chrome Leather Brown BRLL
- Chrome Leather Brown BRSL
- Copper, dihydrogen(5-[(4'-((2,6-dihydroxy-3-((2-hydroxy-5-sulphophenyl)azo)phenyl)azo)-4-biphenylazo]salicylato(2-))-, disodium salt
- Cuprofix Brown GL
- Derma Fast Brown W-GL
- Dermafix Brown PL
- Dialuminous Brown BRS
- Diaphtamine Light Brown BRLL
- Diazine Fast Brown RSL
- Diazol Light Brown BRN
- Dicorel Brown LMR
- Diphenyl Fast Brown BRL
- Direct Brown BRL
- Direct Fast Brown BRL
- Direct Fast Brown LMR
- Direct Light Brown BRS
- Direct Supra Light Brown ML
- Durazol Brown BR
- Durofast Brown BRL
- Eliamina Light Brown BRL
- Enianil Light Brown BRL
- Fastolite Brown BRL
- Fastusol Brown LBRSA
- Fastusol Brown LBRSN
- Fenaluz Brown BRL
- Helion Brown BRSL
- Hispaluz Brown BRL
- KCA Light Fast Brown BR
- Kayarus Supra Brown BRS
- Paranol Fast Brown BRL
- Peeramine Fast Brown BRL
- Pontamine Fast Brown BRL
- Pontamine Fast Brown NP
- Pyrazol Fast Brown BRL
- Pyrazoline Brown BRL
- Saturn Brown LBR
- Sirius Supra Brown BRL
- Sirius Supra Brown BRS
- Solantine Brown BRL
- Solar Brown PL
- Solex Brown R
- Solius Light Brown BRLL
- Solius Light Brown BRS
- Sumilight Supra Brown BRS
- Suprazo Brown BRL
- Suprexcel Brown BRL

- Tertrodirect Fast Brown BR
- Tetramine Fast Brown BRDN Extra
- Tetramine Fast Brown BRP
- Tetramine Fast Brown BRS
- Triantine Brown BRS
- Triantine Fast Brown OG
- Triantine Fast Brown OR
- Triantine Light Brown BRS
- Triantine Light Brown OG

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