1,8-DINITROPYRENE

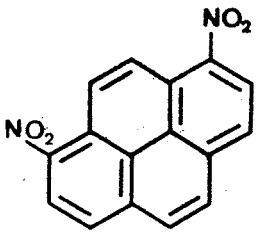
This substance was considered by a previous Working Group, in June 1983 (IARC, 1984). Since that time, new data have become available and these have been incorporated into the monograph and taken into consideration in the present evaluation.

1. Chemical and Physical Data

1.1 Synonyms

Chem. Abstr. Services Reg. No.: 42397-65-9
Chem. Abstr. Name: Pyrene, 1,8-dinitro-
IUPAC Systematic Name: 1,8-Dinitropyrene

1.2 Structural and molecular formulae and molecular weight



$C_{16}H_8N_2O_4$ Mol. wt: 292.3

1.3 Chemical and physical properties of the pure substance

(*a*) *Description*: Light-brown needles, recrystallized from benzene and methanol (Buckingham, 1985); yellow, fluffy, crystalline solid (Chemsyn Science Laboratories, 1988)

(*b*) *Melting-point*: >300°C (Buckingham, 1985); 300°C (Chemsyn Science Laboratories, 1988)

(*c*) *Spectroscopy data*: Ultra-violet, infra-red, nuclear magnetic resonance (Kaplan, 1981; Paputa-Peck *et al.*, 1983; Hashimoto & Shudo, 1984) and mass (Schuetzle & Jensen, 1985) spectral data have been reported.

1.4 Technical products and impurities

1,8-Dinitropyrene is available for research purposes at 98% (Aldrich Chemical Co., 1988) and ≥99% purity (Chemsyn Science Laboratories, 1988). It is also available in ^{14}C- or ^{3}H-labelled form in ≥98% radiochemical purity (Chemsyn Science Laboratories, 1988).

2. Production, Use, Occurrence and Analysis

2.1 Production and use

(*a*) *Production*

Mixtures of 1,3-, 1,6- and 1,8-dinitropyrenes are produced by the nitration of pyrene, and 1,8-dinitropyrene has been isolated and purified from such preparations (Yoshikura *et al.*, 1985).

(*b*) *Use*

1,8-Dinitropyrene has been reported to be a photosensitizer, increasing the spectral activity of bis-azide compounds with light (Tsunoda *et al.*, 1973). However, no evidence was found that 1,8-dinitropyrene is currently used commercially for this or other applications.

2.2 Occurrence

(*a*) *Engine exhaust*

1,8-Dinitropyrene has been found at a level of 3.4 mg/kg extract of particles from the exhaust of a heavy-duty diesel engine (Nakagawa *et al.*, 1983), and at $0.5 \pm 0.3 - 0.7 \pm 0.2$ mg/kg extract (Salmeen *et al.*, 1984), 0.4 mg/kg extract (Nishioka *et al.*, 1982) and 0.013-0.025 mg/kg particles (Gibson, 1983) from the exhausts of light-duty diesel engines.

(*b*) *Other occurrence*

Toners for use in photocopy machines have been produced in quantity since the late 1950s and have seen widespread use. 'Long-flow' furnace black was first used in photocopy toners in 1967; its manufacture involved an oxidation whereby some nitration also occurred. Subsequent changes in the production technique reduced the total extractable nitropyrene content from an uncontrolled level of 5–100 mg/kg to below 0.3 mg/kg (Rosenkranz *et al.*, 1980; Sanders, 1981; Butler *et al.*, 1983), and toners produced from this carbon black since 1980 have not been found to contain detectable levels of mutagenicity or, hence, nitropyrenes (Rosenkranz *et al.*, 1980; Butler *et al.*, 1983).

1,8-Dinitropyrene was found in an extract of a pre-1979 sample of furnace black that had been after-treated by an oxidation-nitration process, at a level of 23.4 mg/kg (Sanders, 1981). One lot of this grade made in 1980 was found to contain 0.16 mg/kg (Giammarise

et al., 1982). An undetermined level of 1,8-dinitropyrene was detected in an extract of a formerly available commercial furnace black produced before 1980 (Ramdahl & Urdal, 1982).

Small amounts of dinitropyrenes are generated by kerosene heaters, which are used extensively in Japan for heating residences and offices (Tokiwa *et al.*, 1985). Such open, oil-burning space heaters were found to emit dinitropyrenes at a rate of 0.2 ng/h after only 1 h of operation; a mixture of 1,8- and 1,6-dinitropyrenes was found at 3.25 ± 0.63 mg/kg particulate extract, accounting for 27% of the mutagenic activity of the sample. Gas and liquified petroleum gas (LPG) burners, widely used for home heating and cooking, also produced detectable amounts of dinitropyrenes: 0.68 mg/kg extract (28% of mutagenicity) and 0.96 mg/kg extract (58% of mutagenicity), respectively. The authors suggested that dinitropyrenes result from the incomplete combustion of fuel in the presence of at least a few micrograms per cubic metre of nitrogen dioxide.

According to Takayama *et al.* (1985) and Pitts (1987), several dinitropyrenes have been detected in respirable particulates from ambient atmospheric samples. Gibson (1986) reported higher amounts in heavy industrialized areas than in nonindustrialized urban and suburban sites. Levels of 1,8-dinitropyrene in samples of airborne particulates are given in Table 1.

2.3 Analysis

See the monograph on 1-nitropyrene.

3. Biological Data Relevant to the Evaluation of Carcinogenic Risk to Humans

3.1 Carcinogenicity studies in animals[1]

(*a*) *Oral administration*

Rat: A group of 36 female weanling CD rats received oral intubations of 10 μmol-[3 mg]/kg bw 1,8-dinitropyrene (purity, >99%) dissolved in dimethyl sulfoxide (DMSO; 1.7 μmol[0.5 mg]/ml DMSO) three times per week for four weeks (average total dose, 16 μmol[4.7 mg]/rat) and were observed for 76–78 weeks (King, 1988). A vehicle control group of 36 animals received DMSO only. The number of animals with mammary tumours was significantly increased in treated animals (22/36) as compared to controls (12/35; $p < 0.05$).

(*b*) *Subcutaneous administration*

Mouse: A group of 20 male BALB/c mice, six weeks old, received subcutaneous injections of 0.05 mg 1,8-dinitropyrene (purity, >99.9%) dissolved in 0.2 ml DMSO once a

[1]The Working Group was aware of a study in progress by single subcutaneous injection in mice (IARC, 1988).

Table 1. 1,8-Dinitropyrene levels in atmospheric particulates

Sample	1,8-Dinitropyrene concentration		Reference
	Particulate extract (mg/kg)	Atmosphere (pg/m³)	
Tokyo, Japan		0.658	Tanabe *et al.* (1986)
Bermuda (remote)			Gibson (1986)
Summer	0.0035	0.07[a]	
Winter	0.0044	0.06[a]	
Delaware, USA (rural)			Gibson (1986)
Summer	0.0024	0.06[a]	
Warren, MI, USA (suburban)			Gibson (1986)
Winter	<0.004	<0.10[a]	
Summer	0.0021	0.13[a]	
Detroit, MI, USA (urban)			Gibson (1986)
Summer	0.0025	0.34[a]	
River Rouge, MI, USA (industrial)			Gibson (1986)
Summer	0.0131	1.26[a]	
Dearborn, MI, USA (industrial)			Gibson (1986)
Summer	0.02	3.80[a]	
Southeast, MI, USA			Siak *et al.* (1985)
Summer	0.46	0.04	
Santiago, Chile			Tokiwa *et al.* (1983)
(urban)	0.2	–	

[a]Calculated by the Working Group

week for 20 weeks (Otofuji *et al.*, 1987). A positive control group of 20 males received of 0.05 mg benzo[*a*]pyrene, and a further 20 mice were untreated. Animals were observed for 60 weeks or until moribund. The first subcutaneous tumour in the benzo[*a*]pyrene-treated group was seen in week 21; all 16 mice surviving beyond this time developed sarcomas at the injection site. After 60 weeks, 6/15 mice injected with 1,8-dinitropyrene had developed subcutaneous tumours; no such tumour was found in untreated controls ($p < 0.05$). All of the subcutaneous tumours were diagnosed histologically as malignant fibrous histiocytomas [a term used as a specific diagnosis for some subcutaneous and intraperitoneal sarcomas]. Some animals in the 1,8-dinitropyrene-treated group developed tumours in the lung and liver.

Rat: Ten male Fischer 344/DuCrj rats, six weeks old, received subcutaneous injections of 0.2 mg 1,8-dinitropyrene ([purity unspecified] impurities: 0.4% 1,3-dinitropyrene, <0.05% other nitropyrenes) dissolved in 0.2 ml DMSO twice a week for ten weeks (total dose, 4 mg; Ohgaki *et al.*, 1984). A control group of 20 rats received injections of 0.2 ml

DMSO only. The animals were killed between days 140 and 169. Sarcomas developed at the site of injection in all treated rats between days 113 and 127. No 'tumorous' change was observed in other organs of the treated rats, and no local tumour developed among control animals.

Two groups of ten male Fischer 344/DuCrj rats, six weeks old, received subcutaneous injections of 0.002 or 0.02 mg 1,8-dinitropyrene ([purity unspecified] impurities: 0.4% 1,3-dinitropyrene) dissolved in 0.2 ml DMSO twice a week for ten weeks (total doses, 0.04 or 0.4 mg; Ohgaki *et al.*, 1985). A control group of 20 rats received injections of 0.2 ml DMSO only. All treated animals were killed on day 320 and control rats on day 650. Sarcomas developed at the site of injection between days 123 and 156 in all rats treated with 0.4 mg 1,8-dinitropyrene and between days 213 and 320 in 9/10 rats treated with 0.04 mg 1,8-dinitropyrene. No tumour was observed in other organs of the treated rats or at the injection site in control animals.

A group of 37 female newborn CD rats received subcutaneous injections of 1,8-dinitropyrene (purity, >99%; total dose, 6.3 μmol [1.8 mg]) dissolved in DMSO (1.7 μmol[0.5 mg]/ml DMSO) into the suprascapular region once a week for eight weeks (King, 1988). A group of 40 or more animals injected with DMSO alone served as controls. Average survival was 163 days for treated animals and 495 days for controls. Malignant fibrous histiocytomas developed rapidly at the injection site in treated rats; the first tumour was seen 122 days after the initial injection, and by 20 weeks all treated rats had developed this tumour. In addition, eight rats (22%) in this group had leukaemia. Controls developed neither malignancy ($p < 0.0001$ and $p < 0.005$).

(*d*) *Intraperitoneal administration*

Mouse: Groups of 90 or 100 male and female newborn CD-1 mice received three intraperitoneal injections of 1,8-dinitropyrene (total dose, 200 nmol [58.7 μg]; purity, >99%) in 10, 20 and 40 μl DMSO on days 1, 8 and 15 after birth; a total dose of 560 nmol [140 μg] benzo[*a*]pyrene (purity, >99%) as three injections; or three injections of DMSO only (Wislocki *et al.*, 1986). Treatment of a second vehicle control group was begun ten weeks after that of the other groups. At 25–27 days, when the mice were weaned, 31 males and 33 females in the treated group, 37 males and 27 females in the positive control group and 28 and 31 males and 45 and 34 females in the two vehicle control groups were still alive. All remaining mice were killed after one year. In the group injected with 1,8-dinitropyrene, 5/31 male mice developed liver tumours (four with adenomas, one with a carcinoma). No increase in the incidences of lung tumours or malignant lymphomas was observed in males or females as compared to DMSO-treated animals. Benzo[*a*]pyrene induced liver tumours in 18/37 males and in 0/27 females and lung adenomas in 13/37 males and 13/27 females; the latter incidences were significantly higher than those in DMSO controls ($p < 0.005$). In the two DMSO control groups, 2/28 and 5/45 males had liver adenomas and 1/28 and 4/45 lung tumours, and 0/31 and 0/34 females had liver tumours and 0/31 and 2/34 lung tumours. [The Working Group noted the small number of animals per group and the short observation period.]

Rat: A group of 36 female weanling CD rats received intraperitoneal injections of 10 μmol[3 mg]/kg bw 1,8-dinitropyrene (purity, >99%) dissolved in DMSO (1.7 μmol [0.5 mg]/ml DMSO) three times per week for four weeks (total dose, 16 μmol[4.7 mg]/rat); 36 control animals were treated with DMSO only (King, 1988). Treatment with 1,8-dinitropyrene resulted in early deaths 12–15 weeks after the initial treatment. The first intraperitoneal tumour was detected at week 17; after 44 weeks, 29/33 of the treated rats had developed malignant fibrous histiocytomas in the peritoneal cavity ($p < 0.0001$), and a significantly increased incidence of myelocytic leukaemia (7/33) was observed in this group ($p < 0.01$). Neither malignancy developed among 31 vehicle controls after an observation period of 76–78 weeks.

3.2 Other relevant data

(a) *Experimental systems*

(i) *Absorption, distribution, excretion and metabolism*

N,N'-Diacetyl-1,8-diaminopyrene, 1,8-diaminopyrene, 1-acetylamino-8-nitro-pyrene, 1-amino-8-nitropyrene and unidentified polar metabolites were detected in the faeces of conventional male CD rats treated orally with 1.0 μmol [0.3 mg] 1,8-dinitropyrene. In germ-free rats treated similarly, only 1-amino-8-nitropyrene and the polar metabolites were found. In both groups of animals, *N*-(deoxyguanosin-8-yl)-1-amino-8-nitropyrene was detected as the major DNA adduct in both liver and mammary gland; however, the extent of binding was considerably lower in the germ-free rats (Heflich *et al.*, 1986a).

Under an argon atmosphere, rat and dog liver cytosol catalysed the reduction of 1,8-dinitropyrene to 1-amino-8-nitropyrene, 1-nitro-8-nitrosopyrene and 1,8-diamino-pyrene. During this reduction, metabolites were formed that bound to exogenous DNA. When acetyl coenzyme A was added to the rat liver cytosolic incubations, 1-acetylamino-8-nitropyrene was also detected as a metabolite, and the extent of binding was increased 39-fold (Djurić *et al.*, 1985). Subsequent studies showed that *Salmonella typhimurium* TA98, rat liver microsomes obtained from a 105 000 *g* supernatant, human liver cytosol and Chinese hamster ovary cell cytosol also reduced 1,8-dinitropyrene to 1-nitro-8-nitroso-pyrene and 1-amino-8-nitropyrene (Djurić *et al.*, 1986; Heflich *et al.*, 1986b).

1-Nitro-8-nitrosopyrene, 1-amino-8-nitropyrene and 1,8-diaminopyrene were detected as metabolites in rat mammary gland cytosol incubated with 1,8-dinitropyrene under anaerobic conditions. When incubations were conducted in the presence of acetyl coenzyme A, binding to exogenous tRNA occurred. Incubation with intact rat mammary gland cells resulted in the formation of 1-amino-8-nitropyrene and 1-acetylamino-8-nitropyrene (King *et al.*, 1986; Imaida *et al.*, 1988).

A low level of DNA adduct formation (fewer than five adducts per 10^6 nucleotides) was detected by ^{32}P-postlabelling in C3H 10T1/2 mouse embryo fibroblasts incubated with 1,8-dinitropyrene (Hsieh *et al.*, 1986). Several DNA adducts were detected when similar incubations were conducted with [^{3}H]1,8-dinitropyrene. Incubation of Chinese hamster

ovary cells with 1,8-dinitropyrene resulted in the formation of 1-amino-8-nitropyrene and a DNA adduct identified as *N*-(deoxyguanosin-8-yl)-1-amino-8-nitropyrene (Heflich *et al.*, 1986b).

As reported in an abstract, the major DNA adduct in rabbit tracheal epithelial cells incubated with 1,8-dinitropyrene and its partially reduced derivative, 1-nitroso-8-nitropyrene, was *N*-(deoxyguanosin-8-yl)-1-amino-8-nitropyrene (Norman *et al.*, 1988). Anaerobic bacterial suspensions from human faeces and intestinal contents of rhesus monkeys and rats were reported to reduce 1,8-dinitropyrene to 1-amino-8-nitropyrene and 1,8-diaminopyrene (Cerniglia *et al.*, 1986).

1,8-Dinitropyrene is metabolized to 1-amino-8-nitropyrene, 1,8-diaminopyrene, 1-*N*-acetylamino-8-nitropyrene and *N*,*N*′-diacetyl-1,8-diaminopyrene by several strains of *S. typhimurium* (Bryant *et al.*, 1984; Heflich *et al.*, 1985; Orr *et al.*, 1985). *N*-(Deoxyguanosin-8-yl)-1-amino-8-nitropyrene has been detected in DNA of *S. typhimurium* cells (Helflich *et al.*, 1985; Andrews *et al.*, 1986). In *S. typhimurium* TA1538, the concentration of this adduct was correlated with the induction of frameshift mutations (Heflich *et al.*, 1985).

(ii) *Toxic effects*

Intraperitoneal administration of 1,8-dinitropyrene to young male Sprague-Dawley rats (three times at 2.5 mg/kg bw) resulted in increases in the activities of aryl hydrocarbon hydroxylase, 7-ethoxycoumarin-*O*-deethylase, aminopyrine-*N*-demethylase and 1-nitropyrene reductase in liver microsomes over that in controls (Chou *et al.*, 1987).

(iii) *Genetic and related effects*

The genetic and related effects of nitroarenes and of their metabolites have been reviewed (Rosenkranz & Mermelstein, 1983; Beland *et al.*, 1985; Rosenkranz & Mermelstein, 1985; Tokiwa & Ohnishi, 1986).

1,8-Dinitropyrene (0.0003 μg/ml) induced DNA damage in *S. typhimurium* TA1535 (Nakamura *et al.*, 1987) and preferentially inhibited the growth of DNA repair-deficient *Bacillus subtilis* (Horikawa *et al.*, 1986 (0.01–0.04 μg/disc); Tokiwa *et al.*, 1986 (0.02 μg/disc)). It was mutagenic to *Escherichia coli* WP2 *uvrA* pKM101 (McCoy *et al.*, 1985a) and to *S. typhimurium* TA96, TA97, TA98, TA100, TA102, TA104, TA1537 and TA1538 (Rosenkranz *et al.*, 1980; Löfroth, 1981; Mermelstein *et al.*, 1981; Pederson & Siak, 1981; Tokiwa *et al.*, 1981; Nakayasu *et al.*, 1982; Morotomi & Watanabe, 1984; Pitts *et al.*, 1984; Heflich *et al.*, 1985; McCoy *et al.*, 1985b; Rosenkranz *et al.*, 1985; Tokiwa *et al.*, 1985; Fifer *et al.*, 1986; Holloway *et al.*, 1987; Zielinska *et al.*, 1987).

Conflicting results have been reported concerning the induction by 1,8-dinitropyrene of gene conversion in the yeast, *Saccharomyces cerevisiae*: positive results were reported in strain JDI (1.6–25 μg/ml) (Wilcox & Parry, 1981; Wilcox *et al.*, 1982) and negative results in strain D4 at up to 500 μg/ml (McCoy *et al.*, 1983). It has been suggested that these differences reflect intracellular oxygen levels (Rosenkranz & Mermelstein, 1983).

As determined by alkaline elution, 1,8-dinitropyrene induced a marginal effect on the formation of single-strand DNA breaks in primary mouse hepatocytes at 5–20 μM (Møller

& Thorgeirsson, 1985) and in cultured Chinese hamster V79 cells at the only dose tested, 15 μM (Saito *et al.*, 1984); it also caused single-strand DNA breaks in cultured rat hepatoma cells (3–10 μM), but it did not induce DNA-protein cross-links at 15 μM (Møller & Thorgeirsson, 1985). It activated the synthesis of viral DNA in polyoma virus-transformed rat fibroblasts at 0.5–2.0 μg/ml (Lambert & Weinstein, 1987).

1,8-Dinitropyrene induced unscheduled DNA synthesis in mouse and rat hepatocytes (Mori *et al.*, 1987 (1.0×10^{-5}–1.0×10^{-2} mg/ml)), in rabbit lung Clara and alveolar type II cells (Haugen *et al.*, 1986 (0.63–10.0 ng/ml)) and, as reported in an abstract, in human hepatocytes (Yoshimi *et al.*, 1987); however, the combined results from Eddy *et al.* (1985, 1986) suggest that unscheduled DNA synthesis was not induced in human hepatoma-derived HepG2 cells at up to 2 μg/ml. 1,8-Dinitropyrene (2.5 μg/ml) did not exhibit preferential toxicity for DNA repair-deficient human xeroderma pigmentosum fibroblasts (Arlett, 1984).

1,8-Dinitropyrene (0.025–2.5 μg/ml) induced mutations to thioguanine, methotrexate, ouabain and arabinofuranosyl cytosine resistance in cultured mouse lymphoma L5178Y cells (Cole *et al.*, 1982; Arlett, 1984) and at the thymidine kinase locus (0.1–5 μg/ml; Edgar, 1985). It induced mutations at the *hprt* locus of cultured Chinese hamster CHO cells (Li & Dutcher, 1983 (0.2–2 μg/ml); Edgar & Brooker, 1985 (0.05–5 μg/ml); Heflich *et al.*, 1986b (2–20 μM)). It also induced mutation to diphtheria toxin resistance (Nakayasu *et al.*, 1982 (0.03–8 μg/ml)) in cultured Chinese hamster lung fibroblasts and to ouabain resistance in V79 cells (Takayama *et al.*, 1983 (0.01–0.1 μg/ml); Katoh *et al.*, 1984 (0.1 μg/ml)). It was reported in an abstract that 1,8-dinitropyrene (100–500 ng/ml) induced mutation to ouabain resistance in human diploid lymphoblasts (Sanders *et al.*, 1983). At up to 2 μg/ml, it did not induce mutation at the *hprt* locus of human hepatoma-derived HepG2 cells (Eddy *et al.*, 1985, 1986) or of normal and xeroderma pigmentosum human fibroblasts [probably at 2.5 μg/ml] (Arlett, 1984).

1,8-Dinitropyrene induced sister chromatid exchange in cultured Chinese hamster CHO cells (Nachtman & Wolff, 1982 (1.6 μM); Edgar & Brooker, 1985 (0.05–5 μg/ml), but did not induce micronuclei in cultured normal and xeroderma pigmentosum human fibroblasts (Arlett, 1984; 2.5 μg/ml). It induced chromosomal aberrations in cultured Chinese hamster CHO cells (Edgar & Brooker, 1985 (0.05–5 μg/ml)) and, to some extent, in human fibroblasts (Wilcox *et al.*, 1982 (0.02–5.0 μg/ml)). It induced chromosomal aberrations, primarily of the chromatid type, in rat epithelial cells (Danford *et al.*, 1982 (0.01–2.5 μg/ml); Wilcox *et al.*, 1982). As reported in an abstract, 1,8-dinitropyrene at 0.025 μg/ml induced chromosomal aberrations in cultured Chinese hamster lung fibroblasts (Matsuoka *et al.*, 1987).

1,8-Dinitropyrene at 1.7–17 μM induced morphological transformation in Syrian hamster embryo cells (DiPaolo *et al.*, 1983). It was reported in an abstract that no transformation activity was observed when 1,8-dinitropyrene was tested at concentrations of up to 250 μg/ml in BALB/c 3T3 cells (Tu *et al.*, 1982).

Rat sarcomas induced by this chemical contained activated c-Ki-*ras* oncogenes (Ochiai *et al.*, 1985; Tahira *et al.*, 1986).

(*b*) *Humans*

No data were available to the Working Group.

3.3 Epidemiological studies and case reports of carcinogenicity in humans

No data were available to the Working Group.

4. Summary of Data Reported and Evaluation

4.1 Exposure data

1,8-Dinitropyrene has been detected in some carbon blacks and in particulate emissions from diesel engines, kerosene heaters and gas burners. It has also been found at low concentrations in ambient air.

4.2 Experimental data

1,8-Dinitropyrene was tested for carcinogenicity by oral administration in rats, by subcutaneous injection in mice and in young and newborn rats and by intraperitoneal injection in newborn mice and rats. After oral administration, it increased the incidence of mammary tumours. After subcutaneous injection, it produced sarcomas at the site of injection in mice and rats and an increased incidence of leukaemia in newborn rats. After intraperitoneal injection, it induced injection-site sarcomas and leukaemia in rats and liver tumours in male mice.

4.3 Human data

No data were available to the Working Group.

4.4 Other relevant data

Metabolism of 1,8-dinitropyrene led to DNA adduct formation *in vivo* and *in vitro*. It induced chromosomal aberrations but not DNA damage, mutation or micronuclei in cultured human cells. It induced DNA damage, sister chromatid exchange, chromosomal aberrations, mutation and morphological transformation in cultured rodent cells and DNA damage and mutation in bacteria.

4.5 Evaluation[1]

There is *sufficient evidence* for the carcinogenicity in experimental animals of 1,8-dinitropyrene.

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[1]For definitions of the italicized terms, see Preamble, pp. 25–28.

Summary table of genetic and related effects of 1,8-dinitropyrene

Nonmammalian systems													Mammalian systems																									
Prokaryotes		Lower eukaryotes				Plants			Insects				*In vitro*																*In vivo*									
													Animal cells								Human cells								Animals							Humans				
D	G	D	R	G	A	D	G	C	R	G	C	A	D	G	S	M	C	A	T	I	D	G	S	M	C	A	T	I	D	G	S	M	C	DL	A	D	S	M	C	A
+	+		?										+	+	+		+		+[1]		–	–		–[1]	+[1]				+[1]										

A, aneuploidy; C, chromosomal aberrations; D, DNA damage; DL, dominant lethal mutation; G, gene mutation; I, inhibition of intercellular communication; M, micronuclei; R, mitotic recombination and gene conversion; S, sister chromatid exchange; T, cell transformation

In completing the table, the following symbols indicate the consensus of the Working Group with regard to the results for each endpoint:

+ considered to be positive for the specific endpoint and level of biological complexity
+[1] considered to be positive, but only one valid study was available to the Working Group
– considered to be negative
–[1] considered to be negative, but only one valid study was available to the Working Group
? considered to be equivocal or inconclusive (e.g., there were contradictory results from different laboratories; there were confounding exposures; the results were equivocal)

No data were available from studies in humans on the carcinogenicity of 1,8-dinitropyrene.

Overall evaluation

1,8-Dinitropyrene *is possibly carcinogenic to humans (Group 2B).*

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