

1,3-Dinitropyrene

1,3-Dinitropyrene is an environmental contaminant produced by the nitration of pyrene. It has been measured in engine exhaust (e.g., diesel exhaust particulate) and emissions from kerosene heaters and gas burners. It is a nitrated polycyclic aromatic hydrocarbon.

1,3-Dinitropyrene passed the animal data screen, underwent a preliminary toxicological evaluation, and is being brought to the Carcinogen Identification Committee for consultation. This is a compilation of the relevant studies identified during the preliminary toxicological evaluation.

Epidemiological data

No cancer epidemiology studies were identified.

Animal carcinogenicity data

- Subcutaneous injection studies
 - Six-week-old male F344/DuCrj rats (two injections per week for ten weeks, observed up to day 347): Ohgaki *et al.* (1984)
 - Newborn female CD rats (eight weekly injections, observed for up to 67 weeks): Imaida *et al.* (1995)
 - Six-week-old male BALB/c mice (20 weekly injections, observed for 60 weeks): Otofujii *et al.* (1987)
- Intraperitoneal injection studies
 - Newborn CD-1 mice (injected on day 1, 8, and 15, observed for up to one year: Wislocki *et al.* (1986)
 - Weanling female CD rats (injected three times a week for four weeks, observed for 78 weeks): Imaida *et al.* (1991)
- Gavage studies in rats
 - Weanling female CD rats (gavaged three times a week for four weeks, observed for 78 weeks): Imaida *et al.* (1991)
 - Female weanling CD rats (gavaged three times a week for four weeks and observed for 76-78 weeks): King *et al.* (1988), as reviewed in IARC (1989, pp. 203-204)

Other relevant data

- Genotoxicity
 - Chromosomal aberrations in Chinese hamster lung cells: Sawada *et al.* (1991)
 - Micronuclei assays in rat, mouse, hamster, and human cell lines: Roscher and Wiebel (1992)

- *Salmonella typhimurium* TM677 forward mutation assays: Busby *et al.* (1994a)
 - Human B-lymphoblastoid (MCL-5) cell forward mutation assay: Busby *et al.* (1994b)
 - DNA adducts in human mammary epithelial cells: Carmichael *et al.* (1996)
 - Reviews: IARC (1989, pp. 206-207); CCRIS (2006)
- Structural activity considerations
 - Structurally similar to 1,6-dinitropyrene and 1,8-dinitropyrene, which are listed under Proposition 65 as carcinogens.

Reviews

- IARC (1989)

References¹

Busby WF, Penman BW, Crespi CL (1994a). Human cell mutagenicity of mono- and dinitropyrenes in metabolically competent MCL-5 cells. *Mutation Research* **322**:233-242.

Busby WF, Smith H, Bishop WW, Thilly WG (1994b). Mutagenicity of mono- and dinitropyrenes in the *Salmonella typhimurium* TM 677 forward mutation assay. *Mutation Research* **322**:221-232.

Carmichael PL, Stone EM, Grover PL, Gusterson BA, Phillips DH (1996). Metabolic activation and DNA binding of food mutagens and other environmental carcinogens in human mammary epithelial cells. *Carcinogenesis* **17**:1769-1772.

Chemical Carcinogenesis Research Information System (CCRIS, 2006)
<http://toxnet.nlm.nih.gov> (accessed on February 13, 2009).

Imaida K, Lee M-S, Land SJ, Wang CY, King CM (1991). Carcinogenicity of dinitropyrenes in the weanling female CD rat. *Carcinogenesis* **12**:1187-1191.

Imaida K, Lee M-S, Land SJ, Wang CY, King CM (1995). Carcinogenicity of nitropyrenes in the newborn female rat. *Carcinogenesis* **16**:3027-3030.

International Agency for Research on Cancer (IARC, 1989). *International Agency for Research on Cancer Monographs on the Evaluation of Carcinogenic Risks to Humans*.

¹ Copies of these listed references, as either the abstract, the relevant sections of the publication, or the complete publication, have been provided to members of the Carcinogen Identification Committee. These references have been provided in the order in which they are discussed in this document.

Diesel and Gasoline Engine Exhausts and Some Nitroarenes. Volume 46. IARC, Lyon, France.

Ohgaki H, Negishi C, Wakabayashi K, Kusama K, Sato S, Sugimura T (1984). Induction of sarcomas in rats by subcutaneous injection of dinitropyrenes. *Carcinogenesis* **5**:583-585.

Otofuji T, Horikawa K, Maeda T, Sano N, Izumi K, Otsuka H, Tokiwa H (1987). Tumorigenicity test of 1,3- and 1,8-dinitropyrene in BALB/c mice. *J Natl Cancer Inst* **79**:185-188.

Roscher E, Wiebel FJ (1992). Genotoxicity of 1,3- and 1,6-dinitropyrene: induction of micronuclei in a panel of mammalian test cell lines. *Mutation Research* **278**:11-17.

Sawada M, Sofuni T, Ishidate M (1991). Decreased clastogenicity of dinitropyrenes in Chinese hamster lung (CHL) subclone cells with low NADPH-cytochrome P-450 reductase activity. *Mutation Research* **264**:37-41.

Wislocki PG, Bagan ES, Lu AYH, Dooley KL, Fu PP, Han-Hsu H, Beland FA, Kadlubar FF (1986). Tumorigenicity of nitrated derivatives of pyrene, benz[*a*]anthracene, chrysene and benzo[*a*]pyrene in the newborn mouse assay. *Carcinogenesis* **7**:1317-1322.