# 3-Nitrofluoranthene

- 3-Nitrofluoranthene is an environmental contaminant produced by the nitration of fluoranthene. It has been measured in ambient air particulates and in diesel engine exhaust. 3-Nitrofluoranthene is not produced or used in commercial quantities. It is a nitrated polycyclic aromatic hydrocarbon.
- 3-Nitrofluoranthene 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 in rats
  - o F344/DuCrj male rats (injected "twice a week for 15 times" and observed up to day 377: Ohgaki *et al.* (1982)
- Intraperitoneal injection studies in mice
  - Newborn male and female Swiss-Webster BLU:Ha (ICR) mice (injected on day one, eight, and 15, and observed until age 26 weeks): Busby et al. (1989)
  - Newborn male B6C3F<sub>1</sub> mice (injected on day one, eight, and 15 and observed until one year of age): Von Tungeln *et al.* (1999)
- Intrapulmonary implantation studies in rats
  - o Male F344/DuCrj rats (observed for 100 weeks): Horikawa et al. (1991)

### Other relevant data

- Genotoxicity
  - o DNA repair tests in
    - Human hepatocytes: Yoshimi et al. (1987)
    - Rat hepatocytes: Mori *et al.* (1987)
    - Mouse hepatocytes: Mori *et al.* (1987)
  - o Salmonella typhimurium mutagenicity assays: Ball et al. (1988); Consolo et al. (1989); Shane et al. (1991)
  - o Chinese hamster V79 cell HGPRT mutagenicity assay: Berry et al. (1985)
  - O Syrian hamster embryo cell transformation assay: DiPaolo et al. (1983)
  - o K- and H-ras mutations in B6C3F<sub>1</sub> mouse liver: Von Tungeln et al. (1999)
  - o DNA adduct formation: Dietrich et al. (1988)
  - o Reviews: Tokiwa et al. (1993)

- Structural activity considerations
  - O Structurally similar to 3,7-dinitrofluoranthene and 3,9-dinitrofluoranthene, which are listed under Proposition 65 as carcinogens.

#### Reviews

- IARC (1984)
- Tokiwa *et al.* (1993)

# References<sup>1</sup>

Ball LM, Kohan MJ, Williams K, Nishioka MG, Gold A, Lewtas J (1988). Metabolism and activation pathways of the environmental mutagen 3-nitrofluoranthene. In: Cooke M, Dennis J., eds, *Polynuclear Aromatic Hydrocarbons: A Decade of Progress*. Columbus, OH: Batelle Press, pp. 59-70.

Berry DL, Schoofs GM, Vance WA (1985). Mutagenicity of nitrofluoranthenes, 3-aminofluoranthene and 1-nitropyrene in Chinese hamster V79 cells. *Carcinogenesis* **6**:1403-7.

Busby WF, Stevens EK, Martin CN, Chow FL, Garner RC (1989). Comparative lung tumorigenicity of parent and mononitro-polynuclear aromatic hydrocarbons in the BLU:Ha newborn mouse assay. *Toxicol Appl Pharmacol* **99**:555-63.

Consolo MC, Anders M, Howard PC (1989). Mutagenicity of the phenolic microsomal metabolites of 3-nitrofluoranthene and 1-nitropyrene in strains of *Salmonella typhimurium*. *Mutat Res* **210**:263-9.

Dietrich AM, Guenat CR, Tomer KB, Ball LM (1988). Identification and characterization of the major DNA adduct formed chemically and *in vitro* from the environmental genotoxin 3-nitrofluoranthene. *Carcinogenesis* **9**:2113-9.

DiPaolo JA, DeMarinis AJ, Chow FL, Garner RC, Martin CN, Doniger J (1983). Nitration of carcinogenic and non-carcinogenic polycyclic aromatic hydrocarbons results in products able to induce transformation of Syrian hamster cells. *Carcinogenesis* **4**:357-359.

Horikawa K, Sera N, Otofuji T, Murakami K, Tokiwa H, Iwagawa M, Izumi K, Otsuka H (1991). Pulmonary carcinogenicity of 3,9- and 3,7-dinitrofluoranthene, 3-nitrofluoranthene and benzo[a]pyrene in F344 rats. *Carcinogenesis* **12**:1003-7.

Chemical for CIC Consultation: 3-Nitrofluoranthene

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<sup>&</sup>lt;sup>1</sup> 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.

International Agency for Research on Cancer (IARC, 1984). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Polynuclear Aromatic Hydrocarbons, Part 2, Carbon Blacks, Mineral Oils (Lubricant Base Oils and Derived Products) and Some Nitroarenes. Volume 33. IARC, Lyon, France.

Mori H, Sugie S, Yoshimi N, Kinouchi T, Ohnishi Y (1987). Genotoxicity of a variety of nitroarenes and other nitro compounds in DNA-repair tests with rat and mouse hepatocytes. *Mutat Res* **190**:159-67.

Ohgaki H, Matsukura N, Morino K, Kawachi T, Sugimura T, Morita K, Tokiwa H, Hirota T (1982). Carcinogenicity in rats of the mutagenic compounds 1-nitropyrene and 3-nitrofluoranthene. *Cancer Letters* **15**:1-7.

Shane BS, Squadrito GL, Church DF, Pryor WA (1991). Comparative mutagenicity of nitrofluoranthenes in *Salmonella typhimurium* TA98, TA98NR, and TQ98/1,8DNP<sub>6</sub>. *Environ Mole Muta* **17**:130-8.

Tokiwa H, Horikawa K, Ohnishi Y (1993). Genetic toxicology and carcinogenicity of mono- and dinitrofluoranthenes. *Mutat Res* **297**:181-95.

Von Tungeln LS, Xia Q, Herreno-Saenz D, Bucci TJ, Heflich RH, Fu PP (1999). Tumorigenicity of nitropolycyclic aromatic hydrocarbons in the neonatal B6C3F<sub>1</sub> mouse bioassay and characterization of *ras* mutations in liver tumors from treated mice. *Cancer Lett* **146**:1-7.

Yoshimi N, Mori H, Sugie S, Owata H, Kinouchi T, Ohnishi Y (1987). Genotoxicity of a variety of nitroarenes in DNA repair tests with human hepatocytes. *Jpn J Cancer Res* (*Gann*) **78**:807-13.