

4-Chloro-*m*-phenylenediamine

4-Chloro-*m*-phenylenediamine [4-chloro-1,3-phenylenediamine] is used as a dye intermediate and a rubber-processing agent. Occupational exposure is likely for workers in the dye manufacturing and rubber industries.

4-Chloro-*m*-phenylenediamine 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

- Long-term feeding studies in mice
 - 78-week exposure and additional 17-week observation in male and female B6C3F₁ mice: NCI (1978)
 - *Increase in hepatocellular adenoma and carcinoma (combined) in females (by pairwise comparison and trend)*
 - *No treatment-related tumor findings in males*
- Long-term feeding studies in rats
 - 78-week exposure and additional 27-week observation in male and female F344 rats: NCI (1978)
 - *Increase in adrenal gland pheochromocytoma in males (by pairwise comparison and trend)*
 - *No treatment-related tumor findings in females*
- Intraperitoneal injection studies in mice
 - Male and female Strain A/St mice (i.p. injections 3 times per week for 8 weeks and additional 16-week observation): Maronpot *et al.* (1986, pp. 1101-1102)
 - *No treatment-related tumor findings*

Other relevant data

- Genotoxicity
 - Compilation and individual test evaluation: CCRIS (2006)
 - Mutagenicity in *Salmonella typhimurium* (positive and negative) and *E. coli* WP2 UVRA (negative) reverse mutation assays

- Chromosomal aberration assays in Chinese hamster lung cells (*positive and negative*) and Chinese hamster ovary cells (*positive and negative*)
- Structure activity considerations
 - Structurally similar to 4-chloro-*o*-phenylenediamine, which is an IARC Group 2B carcinogen: IARC (1987)
 - Ring-substituted 1,3-phenylenediamines, of which 4-chloro-*m*-phenylenediamine is one, and related compounds are generally carcinogenic: Milman and Peterson (1984, pp. 261, 263, 268, 271, 272)
 - The level of carcinogenicity concern for 4-chloro-*m*-phenylenediamine is rated 'high-to-moderate,' the highest rating by the U.S. EPA OncoLogic software, available at: <http://www.epa.gov/oppt/newchems/tools/oncologic.htm>

Review

- IARC (1982)

References¹

Chemical Carcinogenesis Research Information System (CCRIS, 2006) <http://toxnet.nlm.nih.gov> (accessed on July 2, 2009).

International Agency for Research on Cancer (IARC, 1982). *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Some Aromatic Amines, Anthraquinones and Nitroso Compounds, and Inorganic Fluorides Used in Drinking-water and Dental Preparations. Volume 27*, pp. 81-89. IARC, World Health Organization, Lyon, France.

International Agency for Research on Cancer (IARC, 1987). *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs Volume 1 to 42. Supplement 7*, p. 60. IARC, World Health Organization, Lyon, France.

Maronpot RR, Shimkin MB, Witschi HP, Smith LH, Cline JM (1986). Strain A mouse pulmonary tumor test results for chemicals previously tested in the National Cancer Institute carcinogenicity tests. *J Natl Cancer Inst.* **76**:1101-12.

Milman HA and Peterson C (1984). Apparent correlation between structure and carcinogenicity of phenylenediamines and related compounds. *Environ Health Perspect* **56**: 261-273.

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.

National Cancer Institute (NCI, 1978). Bioassay of 4-chloro-*m*-phenylenediamine for possible carcinogenicity. DHEW Publication No. (NIH) 78-1335. NCI-GC-TR-85. NIH, Bethesda, Maryland.