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-mphenylenediamine 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

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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.

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