4-Chloro-\textit{m}-phenylenediamine

4-Chloro-\textit{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-\textit{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 \textit{et al.} (1986, pp. 1101-1102)
    - *No treatment-related tumor findings*

**Other relevant data**

- **Genotoxicity**
    - 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)

**References**


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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.