

## 2,6-Dichloro-*p*-Phenylenediamine

2,6-Dichloro-*p*-phenylenediamine is an intermediate used in dye and resin manufacture. It is a metabolite of the fungicide Dicloran (2,6-dichloro-4-nitroaniline), and has been detected in soil. Studies do not indicate any appreciable uptake of dicloran or its metabolites from soil by plants, including vegetables. Exposure may occur in the dye and resin industries, and at sites treated with Dicloran.

2,6-Dichloro-*p*-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
  - 103-week exposure and additional 8-week observation in male and female B6C3F<sub>1</sub> mice: NTP (1982)
    - *Increased hepatocellular adenoma and carcinoma (combined) in males and females (by pairwise comparison and trend)*
- Long-term feeding studies in rats
  - 103-week exposure in male and female F344 rats: NTP (1982)
    - *No treatment-related tumor findings in males or females*

### Other relevant data

- Genotoxicity
  - *Salmonella typhimurium* mutation assays (*positive*): Mortelmans *et al.* (1986), as reviewed in IARC (1986)
  - Syrian hamster embryo cell transformation assays: Hatch *et al.* (1986) (*some activity*); Tu *et al.* (1986) (*equivocal*)
  - Mouse lymphoma forward mutation assays (*positive*): McGregor *et al.* (1988)
  - *In vitro* chromosomal aberrations in Chinese hamster ovary cells (*positive*): Gulati *et al.* (1989), as reviewed in CCRIS (2006)

- Structure activity considerations
  - The level of carcinogenicity concern for 2,6-dichloro-*p*-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>
  - Structurally similar to other phenylenediamine compounds that are listed under Proposition 65 as carcinogens, including 4-chloro-*o*-phenylenediamine, *o*-phenylenediamine and its salts, 2,4-dinitrotoluene, 2,6-dinitrotoluene and 2,4-diaminotoluene.

## Review

- IARC (1986)

## References<sup>1</sup>

Chemical Carcinogenesis Research Information System (CCRIS, 2006) <http://toxnet.nlm.nih.gov> (accessed on June 11, 2009).

Hatch GG, Anderson TM, Lubet RA, Kouri RE, Putman DL, Cameron JW, Nims RW, Most B, Spalding JW, Tennant RW, *et al.* (1986). Chemical enhancement of SA7 virus transformation of hamster embryo cells: Evaluation by interlaboratory testing of diverse chemicals. *Environ Mutagen* **8**:515-31.

International Agency for Research on Cancer (IARC, 1986). *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Some Chemicals Used in Plastics and Elastomers*. Vol. 39. IARC, World Health Organization, Lyon, France.

McGregor DB, Brown A, Cattnach P, Edwards I, McBride D, Riach C, Caspary WJ (1988). Responses of the L5178Y tk+/tk- mouse lymphoma cell forward mutation assay: III. 72 coded chemicals. *Environ Mol Mutagen* **12**:85-154.

National Toxicology Program (NTP, 1982). *NTP Technical Report on the Carcinogenesis Bioassay of 2,6-Dichloro-*p*-phenylenediamine (CAS No. 609-20-1) in F344 rats and B6C3F<sub>1</sub> mice (Feed Study)*. NTP-80-36. NIH publication No. 82-1775. TR-219. U.S. Department of Health and Human Services, NIH, Bethesda, MD.

Tu A, Hallowell W, Pallotta S, Sivak A, Lubet RA, Curren RD, Avery MD, Jones C, Sedita BA, Huberman E, *et al.* (1986). An interlaboratory comparison of transformation in Syrian hamster embryo cells with model and coded chemicals. *Environ Mutagen* **8**: 77-98.

<sup>1</sup> 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.