Phosmet

Phosmet (Imidian) is a broad-spectrum organophosphate insecticide used on nut and fruit trees, grapes, and on cattle and swine for tick and flea control. Exposure may occur to pesticide applicators and agricultural and horticultural workers, and to the general public through ingestion of residues present in food.

Phosmet 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

- Two-year feeding studies in mice
  - Male and female $B6C3F_1$ mice: as reviewed in U.S. EPA (1994)
    - *Increase in hepatocellular adenoma and carcinoma (combined) in males (by pairwise comparison and trend) with apparent early onset*
    - *Increases in hepatocellular carcinoma, hepatocellular adenoma and carcinoma (combined), and mammary gland adenocarcinoma (uncommon tumor) in females (by trend)*

- Two-year feeding studies in rats
  - Male and female Sprague-Dawley rats: as reviewed in U.S. EPA (1994)
    - *No treatment-related tumor findings*

Other relevant data

- Genotoxicity
  - A potent direct-acting mutagen, expected to be a methylating agent: (U.S. EPA, 1994)
  - Mutations in *Salmonella typhimurium* and *Saccharomyces cerevisiae* assays (*positive*): Vlčková *et al.* (1993)
  - *HGPRT* mutations in Chinese hamster V 79 cells (*positive*): Slameňová *et al.* (1992)
  - DNA single-strand breaks in human fibroblastoid cells *(positive)*: Slameňová *et al.* (1992)
  - Guanine N^7-alkylation *in vivo* in male AB Jena/Halle mouse liver and kidneys (*negative*): Dedek *et al.* (1984)

    - Chromatid-type aberrations in exposed workers in Hungary (*statistically significant increase*): Kiraly *et al.* (1979)
    - Morphological transformation in Syrian hamster embryo cells (*positive*): Slameňová *et al.* (1992)
    - Other genotoxic tests as reviewed in U.S. EPA (1994)
        - *E. coli* reverse mutation assay (*negative*)
        - *B. subtillis* assay (*negative*)
        - Dominant lethal test in rabbit *(inconclusive)*
        - Mouse lymphoma forward mutation *(positive)*
        - Mouse lymphoma structural chromosomal aberrations *(positive)*
        - Mouse lymphoma sister chromatid exchange *(positive)*
        - DNA damage assay in human fibroblastoid cells (*negative*)
        - Morphological transformation of BALB/3T3 cells *(positive)*
        - Micronucleus test in mouse bone marrow (*negative*)

- Liver alterations
    - Single intraperitoneal (i.p.) injection of diethylnitrosamine (on day 1), four i.p. injections of N-methyl-N-nitrosourea (on days 2,5,8 and 11), N-bis-(2-hydroxypropyl)-nitrosamine in drinking water for two weeks, followed by phosmet in diet for 16 weeks in male F344 rats (*increase in glutathione-positive liver foci*): Hasegawa *et al.* (1993)

- Structure activity considerations: U.S. EPA (1994)
    - Structurally similar to dimethoate, a U.S. EPA Group C carcinogen (based on increases in hemolymphoreticular tumors in male $B6C3F_1$ mice and hemangioma/hemangiosarcoma of the spleen and skin and angioma/angiosarcoma of the lymph in male Wistar rats
    - The carcinogen formaldehyde is a probable metabolite of phosmet

Reviews

- U.S. EPA (1994, 2001)

References[1]

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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.

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Kiraly J, Szentesi I, Ruzicska M, Czeize A (1979). Chromosome studies in workers producing organophosphate insecticides. *Arch Environ Contam Toxicol* **8**:309-319.

Slameňová D, Dusinská M, Gabelová A, Bohusová T, Ruppová K (1992). Decemtione (Imidan)-induced single-strand breaks to human DNA, mutations at the HGPRT locus of V79 cells, and morphological transformations of embryo cells. *Environ Mole Muta* **20**:73-78.

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