Malathion

Malathion is a broad-spectrum organophosphorous insecticide. Uses include controlling pests on food and feed crops, ornamental nursery stock, pastures and rangeland, and building perimeters. It has been used in pest eradication programs against mosquitoes and Mediterranean fruit flies. It is also used to treat head lice. Exposures may occur in the occupational setting, through its use as a treatment for lice, through contact with treated areas, and through consumption of treated food and water.

Malathion passed the human and animal data screens, 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

- Case-control studies
  - Population- based multicenter study of men in Canada with non-Hodgkins lymphoma: McDuffie *et al*. (2001)
    - *Increased odds ratio associated with exposure to malathion*
- Cohort studies
  - Prospective study of 19,717 U.S. licensed malathion pesticide applicators in the Agricultural Health Study (1993-1997): Bonner *et al*. (2007)
    - *No association of malathion exposure with any cancer*
- Review of earlier epidemiological studies *(positive and negative)*: ATSDR (2003, pp. 37-39)

Animal carcinogenicity data

- Long-term feeding studies of malathion in mice
  - 18-month studies in male and female B6C3F_1 mice: Slauter (1994), as reviewed by U.S. EPA (2000, pp. 3-10)
    - *Increases in liver adenoma and adenoma and carcinoma (combined) in male and female mice (by pairwise comparison and trend)*
  - 80-week exposure and additional 14-15 week observation in male and female B6C3F_1 mice: NCI (1978), as reviewed by U.S. EPA 1990, pp. 12-14)
    - *No treatment-related tumor findings*
    - *U.S. EPA (2000, p. 2) notes an increase in liver carcinoma in males*

- Long-term feeding studies of malathion in rats
    - Two-year studies in male and female F344 rats: Daly (1996), as reviewed by U.S. EPA (2000, pp. 11-23)
        - *Increase in liver adenoma and carcinoma (combined) in females (by pairwise comparison and trend) and in rare nasal adenomas in males and females*
    - 103-week studies in male and female Fischer 344 rats: NCI (1979), as reviewed by U.S. EPA (1990, pp. 7-10)
        - *No treatment-related tumor findings*
        - *U.S. EPA (2000, p. 2) notes increases in pheochromocytoma of the adrenal gland and leukemia in males*
    - 80-week exposure and additional 29-33 week observation in male and female Osborne-Mendal rats: NCI (1978), as reviewed by U.S. EPA (1990, pp. 4-7)
        - *No treatment-related tumor findings*
        - *U.S. EPA (2000, p. 2) notes increases in pheochromocytoma of the adrenal gland, c-cell neoplasms of the thyroid gland, and follicular cell neoplasms of the thyroid gland in males and follicular cell neoplasms of the thyroid gland in females*
    - Two-year studies in male and female Sprague-Dawley rats: Rucci *et al*. (1980), as reviewed by U.S. EPA (1990, pp. 10-12)
        - *U.S. EPA considered the studies invalid*

- Subcutaneous injection study of malathion in rats
    - Female Sprague-Dawley rats (39-day old rats received s.c. injections twice per day for five days with observation for 28 months): Cabello *et al*. (2001, Table 3)
        - *Increase in mammary tumors (by pairwise comparison)*

- Long-term feeding studies of the metabolite malaoxon
    - 103-week studies in male and female B6C3F_1 mice: NCI (1979), as reviewed by U.S. EPA (1990, pp. 18-19)
        - *No treatment-related tumor findings*
    - Two-year studies in male and female F344 rats: Daly (1996), as reviewed by U.S. EPA (2000, pp. 24-25)
        - *Increase in mononuclear cell leukemia in males (by pairwise comparison and trend)*
        - *U.S. EPA (2000) concluded there were no treatment-related tumor findings*

- 103-week studies in male and female Fischer 344 rats: NCI (1979), as reviewed by U.S. EPA (1990, pp. 14-18)
    - *Increases in thyroid c-cell adenoma and carcinoma (combined) in males and females (by pairwise comparison and trend)*
    - *In addition to the increases in c-cell neoplasms of the thyroid gland in males and females, U.S. EPA (2000, p. 2) notes increases in pheochromocytoma of the adrenal gland and lymphoma in males and mammary gland adenomas in females*

Other relevant data

- Genotoxicity of malathion
    - Reviews: ATSDR (2003, pp. 99-104); U.S. EPA (2000, pp. 25-27); U.S. EPA (1990, pp. 20-22)
        - Bacterial gene mutation assays (*positive and negative*)
        - *Drosophila* mutation assays (*positive and negative*)
        - Mammalian cell mutation assays (*positive*)
        - *In vitro* assays for chromosomal aberrations (*positive and negative*), micronuclei (*positive and negative*), and sister chromatid exchange (*positive*)
        - *In vivo* assays in rodents for chromosomal aberrations (*positive and negative*), micronuclei (*positive and negative*), sister chromatid exchange (*positive*), and mutations (*negative*)
        - *In vivo* assays in humans for chromosomal aberrations (*positive*), micronuclei (*negative*), and mutations (*negative*)
        - DNA damage/methylation (*positive and negative*)

- Genotoxicity of the metabolite malaoxon
    - Reviews: ATSDR (2003, p. 99, 104); U.S. EPA (2000, p. 26); U.S. EPA (1990, p. 23)
        - Bacterial gene mutation assays (*negative*)
        - Mouse lymphoma cell forward mutation assay (*positive*)
        - Chromosomal aberrations in Chinese hamster ovary (CHO) cells (*negative*)
        - Sister chromatid exchange in CHO cells (*positive*)
        - DNA damage (*positive*)

- Cell proliferation studies
    - 16-day old female Sprague-Dawley rats (s.c. injections twice per day for five days, assessed 16 hours after last injection): Cabello *et al*. (2001, Table 1)
        - *No increase in density of mammary gland terminal end buds*
    - 39-day old female Sprague-Dawley rats (s.c. injections twice per day for five days, assessed 16 hours after last injection): Cabello *et al*. (2001, Table 2)
        - *Increase in density of mammary gland terminal end buds*

Review

- U.S. EPA (2000)
    - 2000 cancer classification reported in U.S. EPA (2009)

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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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