

## Amitraz

Amitraz (BAAM) is a formamidine insecticide and miticide registered under the U.S. Environmental Protection Agency (U.S. EPA) for use on cattle, swine, and dogs to control various insects such as ticks, lice and mange mites. Tolerances for amitraz have been established by the U.S. EPA for several commodities, including cattle and pig meat, milk, and imported cottonseed. Registration for use on pear and cotton has been voluntarily cancelled since 2006. Exposures to the general public may occur through consumption of food products containing residues, and through contact with pets treated with tick control products containing amitraz.

Amitraz 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
  - 80-week studies in male and female CFLP mice: as reviewed in U.S. EPA (1991)
    - *Increase in lymphoreticular tumors in females (by pairwise comparison and trend)*
    - *No treatment-related tumor findings in males*
  - 104-week studies in male and female B6C3F<sub>1</sub> mice: as reviewed in U.S. EPA (1991)
    - *Increases in hepatocellular carcinoma and hepatocellular adenoma and carcinoma combined in females (by pairwise comparison and trend)*
    - *Increase in lung adenoma in males (by pairwise comparison and trend)*
- 104-week feeding studies in rats
  - Male and female Wistar rats: as reviewed in U.S. EPA (1991)
    - *No treatment-related tumor findings*

## Other relevant data

- Genotoxicity
  - as reviewed in U.S. EPA (1991, pp. 19-23)
    - *Salmonella typhimurium* mutation assays of parent compound (*negative*) and its metabolites (*positive for 2,4-dimethylaniline; negative for others*)
    - Mouse lymphoma cell mutation assay of parent compound (*negative*) and its metabolites (*positive for 2,4-dimethylaniline only*)
    - *In vitro* chromosomal aberrations (*negative*)
    - Mouse dominant lethal assays (*positive and negative*)
    - Unscheduled DNA synthesis (UDS) in human embryonic cells with parent compound and its metabolites (*negative*)
    - Morphological transformation of mouse embryo fibroblasts with parent compound and the metabolite 2,4-dimethylaniline (*negative*)
- P450 induction (*positive*): Ueng *et al.* (2004)
- Anti-estrogenic activity *in vitro* and *in vivo* (*positive*): Ueng *et al.* (2004)
- Structure activity considerations: U.S. EPA (1991)
  - Structurally similar to chlordimeform, another formamidine pesticide, that is a carcinogen listed under Proposition 65
  - Amitraz and chlordimeform are metabolized to structurally similar metabolites
  - Structurally similar metabolites of amitraz (2,4-dimethylaniline) and chlordimeform (4-chloro-2-methylaniline) are mutagenic and induce tumors in rodents

## Reviews

- U.S. EPA (1991, 2006)

## References<sup>1</sup>

Ueng TH, Hung CC, Wang HW, Chan PK (2004). Effects of amitraz on cytochrome P450-dependent monooxygenase and estrogenic activity in MCF-7 human breast cancer cells and immature female rats. *Food Chem Toxicol* **42**:1785-94.

U.S. EPA (1991). *Peer Review of Amitraz (BAAM®)*. Memorandum from Health Effects Division to Registration Division. January 3, 1991.

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<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.

U.S. EPA (2006). *Amitraz: Second Report of the Cancer Assessment Review Committee*, PC Code: 106201, Memorandum from the Cancer Assessment Review Committee. July 18, 2006.