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CASWELL FILE

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Avermectin (Also Called Abamectin) - 89-CA-10 - Section 18 Request to Use Avermectin on Strawberries in California

Caswell No.: 63AB
Project No.: 9-0736A
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FROM: William Dykstra, Reviewer
Review Section I
Toxicology Branch I - Insecticide, Rodenticide Support
Health Effects Division (TS-769C)

TO: Donald Stubbs, Section Head
Emergency Response and Minor Use Section
Registration Support Branch
Registration Division (TS-767C)

THRU: Edwin Budd, Section Head
Review Section I
Toxicology Branch - Insecticide, Rodenticide Support
Health Effects Division (TS-769C)

The California Department of Food and Agriculture (CDFA) requests a FIFRA section 18 specific exemption for the use of avermectin to control two-spotted spider mites on strawberries.

The formulation to be used is Avid 0.15 EC. Inerts are cleared under 180.1001.

Avid 0.15 EC will be applied by ground equipment at an application rate of 0.02 lb ai/A. A total of up to 4 applications will be made on 11,000 acres of strawberries. The minimum interval between applications is 7 days. The preharvest interval is 3 days.

The proposed action level is 0.02 ppm on strawberries.

No permanent tolerances have been established for avermectin. Temporary tolerances and experimental use permit (EUP) programs are currently in effect for citrus and cotton.

The proposed label for the section 18 for strawberries does not include the signal word, precautionary labeling, and Statement of Practical Treatment. A copy of the proposed label for strawberries is attached.

A copy of a label for a section 18 on celery is also included, since this label details the signal word, precautionary labeling and Statement of Practical Treatment.

CDFA should include on their proposed label for the section 18 for strawberries, the correct label signal word, precautionary labeling and Statement Practical Treatment to protect farmworkers.

In the Dykstra memorandum of April 23, 1987, the margins of safety (MOSs) for mixer/loader and sprayers (both with and without gloves) range from 350 to 1163 when maternolethality is the toxic endpoint and from 1399 to 4651 when cleft-palate (a developmental effect) is the toxic endpoint. Based on oral communication on February 6, 1989 with C. Lunchick of the Non-Dietary Exposure Branch regarding expected exposure to workers in the section 18 use for strawberries, it was concluded that the exposure to workers including pickers, in the section 18 use for strawberries would be less than the exposure to workers in the citrus EUP program. Therefore, the MOSs for workers in the section 18 use for strawberries are acceptable (greater than 100).

Pivotal toxicity data which were available in support of the temporary tolerances and EUP programs are listed below:

- Rat Acute Oral LD_{50}: 10.6 mg/kg (males); 11.3 mg/kg (females);
- Dermal Sensitization in Guinea Pig (Abamectin): negative for skin sensitization;
- 14-Week Oral Rat Study: NOEL $\geq$ 0.4 mg/kg/day (HDT);
- 18-Week Oral Dog Study: NOEL = 0.25 mg/kg/day;
- 1-Year Dog Study: NOEL = 0.25 mg/kg/day;
- Rat Teratology Study (Abamectin): negative for terata up to 1.6 mg/kg/day (HDT);

- Rabbit Teratology Study (Abamectin): negative for terata up to 2.0 mg/kg/day (HDT);

- Mouse Teratology Study (Abamectin): teratogenic LEL = 0.4 mg/kg/day (cleft-palate); teratogenic NOEL = 0.2 mg/kg/day;

- Mouse Teratology Study (delta-8,9-isomer): teratogenic LEL = 0.10 mg/kg/day (cleft-palate); teratogenic NOEL = 0.06 mg/kg/day;

- Mouse Maternotoxicity Study (Abamectin): LEL = 0.075 mg/kg/day (lethality); NOEL = 0.05 mg/kg/day;

- Mouse Maternotoxicity Study (delta-8,9-isomer): LEL = 0.50 mg/kg/day (lethality); NOEL = 0.10 mg/kg/day;

- Two-Generation Rat Reproduction Study: NOEL = 0.12 mg/kg/day;

- Rat Metabolism Study;

- Ames Mutagenicity Assay (Abamectin): negative;

- Mutagenicity Assay for Chromosomal Aberration *In Vitro* in Chinese Hamster Ovary Cells: negative;

- Mammalian Cell Mutagenic Assay (Abamectin): negative for V-79 cells;

- Rat Hepatocyte Mutagenicity Study (Abamectin): under conditions of the study, abamectin (0.3 and 0.6 mM) caused an induction of single strand DNA breaks in rat hepatocytes *in vitro*; no effect was observed when the assay was carried out on hepatocytes from rats dosed *in vivo* at the LD_{50} dose level (10.6 mg/kg); and

- *In Vivo* Bone Marrow Mutagenicity Cytogenetic Study: negative in male mice at doses of 1.2 and 12.0 mg/kg.

Additionally, preliminary evaluation of a 94-week chronic toxicity/oncogenicity mouse study and a 2-year chronic toxicity/oncogenicity rat study did not reveal any potential oncogenic effects.

Toxicological studies with the delta-8,9-isomer and polar degradates of avermectin are required before permanent tolerances can be established.

The provisional acceptable daily intake (PADI) is based on the NOEL of 0.12 mg/kg/day in the two-generation rat reproduction study. A thousandfold safety factor was used to calculate the PADI. At the LEL of 0.40 mg/kg/day in the study, effects included increased retinal folds in the weanlings, increase of dead pups, decreased viability indices, decreased lactation indices, and decreased pup body weight.

$$PADI = \frac{NOEL}{SF}$$

$$PADI = \frac{0.12 \text{ mg/kg/day}}{1000}$$

$$PADI = 0.00012 \text{ mg/kg/day}$$

A new TAS analysis and menu screen analysis are required from the Special Analysis and Outreach Section of the Science Analysis and Coordination Branch. These analyses are needed to determine the percent PADI utilized and MOS for developmental toxicity and maternolethality.

Conclusion and Recommendation

If the Science Analysis and Coordination Branch can conclude that the percent PADI utilized is less than 100 percent and the MOS for developmental toxicity and maternolethality are greater than 100, the section 18 for strawberries can be toxicologically supported.

Attachments