

required by FFDCA section 408(d)(3). The summary of the petition was prepared by the petitioner and represents the view of the petitioner. The petition summary announces the availability of a description of the analytical methods available to EPA for the detection and measurement of the pesticide chemical residues or an explanation of why no such method is needed.

Interregional Research Project Number (IR-4) and Crompton Manufacturing Company, Inc.

PP 3E6517

EPA has received a pesticide petition (3E6517) from the Interregional Research Project Number (IR-4), 681 U.S. Hwy. #1 South, North Brunswick, NJ 08902 proposing, pursuant to section 408(d) of the FFDCA, 21 U.S.C. 346a(d), to amend 40 CFR 180.572 by establishing tolerances for residues of bifenazate, (diazinecarboxylic acid, 2-(4-methoxy-[1,1'-biphenyl]-3-yl), 1-methylethylester) in or on the following raw agricultural commodities (RACs): Vegetable, cucurbit, group at 0.6 part per million (ppm); vegetable, fruiting, group at 2.0 ppm; peppermint, tops at 25 ppm; spearmint, tops at 25 ppm; nut, tree, group at 0.2 ppm; almond, hulls at 10 ppm; okra at 2.0 ppm; and pistachio at 0.2 ppm. EPA has determined that the petition contains data or information regarding the elements set forth in section 408(d)(2) of the FFDCA; however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data support granting of the petition. Additional data may be needed before EPA rules on the petition. This notice includes a summary of the petition prepared by Crompton Manufacturing Company, Inc. (formerly Uniroyal Chemical Company), Middlebury, CT 06749.

A. Residue Chemistry

1. *Plant metabolism.* The nature of the residues of bifenazate in plants is adequately understood. The major residue in all plant metabolism studies is bifenazate. A minor, but significant metabolite is the diazene D3598, which was found to interconvert readily to/from bifenazate in the plant matrix during the analytical procedure.

2. *Analytical method.* Crompton has developed practical analytical methodology for detecting and measuring residues of bifenazate in or on RACs. As D3598, a significant metabolite, was found to interconvert readily to/from bifenazate, the analytical method was designed to convert all residues of D3598 to the parent

compound (bifenazate) for analysis. The method utilizes reversed phase high performance liquid chromatography (HPLC) to separate the bifenazate from matrix derived interferences, and oxidative coulometric electrochemical detection for the identification and quantification of this analyte.

B. Toxicological Profile

1. *Acute toxicity.* Bifenazate technical, acramite-50WS, and floramite SC have low acute oral, dermal, and inhalation toxicity in laboratory animals. The oral lethal dose LD₅₀ in rats and mice is greater than 5 grams/kilogram (g/kg) for acramite-50WS and the technical material. The oral LD₅₀ of floramite SC is greater than 5 g/kg in males and greater than 2 g/kg in females. The dermal LD₅₀ in rats of bifenazate technical and both formulations is greater than 5 g/kg. The inhalation lethal concentration LC₅₀ in the rats of bifenazate technical, acramite-50WS and floramite SC was found to be greater than 4.4, 5.2, and 1.8 milligrams/liter (mg/L), respectively. In eye irritation studies, acramite-50WS was a slight irritant, and bifenazate technical was non-irritating. Floramite SC was found to be irritating to the eyes. All 3 products were found to be non-irritating to the skin of rabbits and non-sensitizing on the skin of guinea pigs.

2. *Genotoxicity.* Bifenazate was evaluated and found to be negative in the Ames Reverse Mutation, Mouse Lymphoma, chinese hamster ovary (CHO) chromosome aberration and mouse micronucleus assays.

3. *Reproductive and developmental toxicity—i. Rabbit developmental study.* A range-finding study conducted in pregnant New Zealand white rabbits at dosage levels of 125, 250, 500, 750, and 1,000 milligrams/kilogram/day (mg/kg/day) demonstrated maternal toxicity at dosage levels of 500 mg/kg/day and greater and abortions at dosage levels of 250 mg/kg/day and greater. Bifenazate was then administered by oral gavage to pregnant New Zealand white rabbits at dosage levels of 10, 50, and 200 mg/kg/day. No test article related effects were seen at any dose level. The no observable adverse effect level (NOAEL) for maternal and developmental toxicity was greater than 200 mg/kg/day.

ii. *Rat developmental study.* Bifenazate did not produce developmental toxicity when administered by oral gavage to pregnant Sprague-Dawley CD rats at dosage levels of 10, 100, and 500 mg/kg/day. A reduction in maternal body weight gain was seen at dosage levels of 100 and 500 mg/kg/day. Clinical observations at 500 mg/kg/day included red material/

staining on body surfaces, pale extremities, and brown discharge. No developmental or teratogenic effects were observed at any dosage level. The NOAEL for maternal toxicity was 10 mg/kg/day and the NOAEL for developmental toxicity was greater than 500 mg/kg/day.

iii. *Rat reproduction study.* Bifenazate showed no effects on reproduction when fed to 2-generations of male and female Sprague-Dawley CD rats at dietary concentrations of 20, 80, and 200 ppm. At a dosage level of 200 ppm there was a reduction in body weight gain in F0 males and females. Food consumption was unaffected. There was a reduction in body weight gain in F1 females at all dosage levels and in F1 males at 80 and 200 ppm in the absence of effects on food consumption. Since the 20 ppm F1 males did not have a significant reduction in body weight gain, this dosage level can be considered a NOAEL for systemic adult toxicity. The reduction in body weight gain in the F1 females at 20 ppm would not be considered biologically significant because no effects were observed on reproductive parameters or in the F2 litter. The reproductive and developmental NOAEL was greater than 200 ppm (10 mg/kg/day).

4. *Subchronic toxicity—i. Thirteen-week rat feeding study.* Bifenazate was fed to male and female Sprague Dawley CD rats for 13 weeks at dietary concentrations of 40, 200, and 400 ppm. At dosage levels of 200 and 400 ppm there was a reduction in red blood cell (RBC) count and hemoglobin (Hgb). Food intake was reduced for 200 ppm females and 200 and 400 ppm males. Histopathological effects were seen in the liver, spleen, and adrenal cortex in males and females at 200 and/or 400 ppm. The maximum tolerated dose (MTD) was exceeded in females at 200 ppm and in males and females at 400 ppm. The NOAEL for subchronic toxicity in rats was 40 ppm (2 mg/kg/day).

ii. *Neurotoxicity assessment.* No treatment related effects were seen on neuro-behavior in a Standard Functional Observation Battery conducted at weeks 8 and 13 of the rat feeding study. No overt signs of anticholinergic activity, and no statistically significant effects on cholinesterase (ChE) activity were seen in rats in a 2-week feeding study at dose levels up to 400 ppm. Plasma, erythrocyte and brain ChE activity were evaluated in male and female rats fed bifenazate-treated diet at 0, 20, 200, or 400 ppm for 2 weeks. All animals survived until study termination and effects were only seen on body weight gain and food