

Dated: April 15, 2003.

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Pesticide Programs.

### Summary of Petition

The petitioner summary of the pesticide petition is printed below as 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.

### Bayer CropScience

PP 3F6556

EPA has received a pesticide petition (3F6556) from Bayer CropScience, 2 T.W. Alexander Drive, Research Triangle Park, NC 27709 proposing, pursuant to section 408(d) of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a(d), to amend 40 CFR part 180 by establishing a tolerance for residues of fluoxastrobin; 2-[[6-(2-chlorophenoxy)-5-fluoro-4-pyrimidinyl]oxy]phenyl (5,6-dihydro-1,4,2-dioxazin-3-yl)methanone-O-methylloxime in or on the raw agricultural commodities (RACs) alfalfa, forage at 0.05 parts per million (ppm), alfalfa, hay at 1.0 ppm, cotton, gin byproducts at 0.02 ppm, grain, cereal, forage at 0.10 ppm, grain, cereal, hay at 0.10 ppm, grain, cereal, straw at 0.10 ppm, grain, cereal, stover at 0.10 ppm, grass, forage at 0.10 ppm, grass, hay at 0.50 ppm, legume, seed at 0.01 ppm, legume, forage at 0.05 ppm, legume, hay at 0.05 ppm, peanut at 0.01 ppm, peanut, hay at 20 ppm, peanut, refined oil at 0.10 ppm, tomato, paste at 2.0 ppm, vegetable, fruiting, group at 1.0 ppm, vegetable, leafy, petioles, except brassica, subgroup at 5.0 ppm, and vegetable, tuberous and corm, subgroup at 0.01 ppm. Fluoxastrobin; 2-[[6-(2-chlorophenoxy)-5-fluoro-4-pyrimidinyl]oxy]phenyl (5,6-dihydro-1,4,2-dioxazin-3-yl)methanone-O-methylloxime, and its phenoxy-hydroxypyrimidine metabolite; 6-(2-chlorophenoxy)-5-fluoro-4-pyrimidinol in or on the RACs cattle, fat at 0.10 ppm, cattle, meat at 0.05 ppm, cattle, meat byproducts at 0.20 ppm, milk at 0.01 ppm, and milk, fat at 0.10 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.

### A. Residue Chemistry

1. *Plant metabolism.* The metabolism of fluoxastrobin in plants is adequately understood. Studies have been conducted to delineate the metabolism of radiolabeled fluoxastrobin in peanut, tomato, spring wheat, and various representative rotational crops, all showing similar results. The residue of concern is parent fluoxastrobin (sum of E and Z isomers).

2. *Analytical method.* Adequate analytical methodology using liquid chromatography/mass spectrometer/mass spectrometer (LC/MS/MS) detection is available for enforcement purposes.

3. *Magnitude of residues.* Complete residue data exists for fluoxastrobin on these crops and crop groupings. Magnitude of residue trials were conducted on peanut, potato, celery, tomato, pepper, and the rotational crops of alfalfa, cotton, cereal grains (corn, rice, sorghum and wheat), soybeans, other legume vegetables, and grasses. A cattle feeding study was performed in order to determine residues in meat and milk commodities. The data support the proposed tolerances.

### B. Toxicological Profile

1. *Acute toxicity.* Oral and dermal lethal dose (LD)<sub>50</sub> values were >2,000 milligrams/kilogram bodyweight (mg/kg) (bwt). Inhalation lethal concentrations (LC)<sub>50</sub> values were >4,998 milligrams/meters (mg/m<sup>3</sup>) air. Fluoxastrobin technical was not irritating to rabbit skin, was moderately irritating to eyes in rabbits, and was non-sensitizing dermally in the Magnusson/Kligman maximization test in guinea pigs. Acute toxicity studies for fluoxastrobin support an overall Toxicity Category III.

2. *Genotoxicity.* Several genotoxicity tests were conducted to test for point-mutagenic activity, chromosome aberration *in vitro* and *in vivo*, and for DNA repair. All tests conducted were negative, indicating no evidence of mutagenic or genotoxic potential.

3. *Reproductive and developmental toxicity.* An oral developmental toxicity study in rat did not reveal any evidence of teratogenic potential. The maternal no observed adverse effect level (NOAEL) was 300 mg/kg and the developmental NOAEL was 1,000 mg/kg bwt/day. An oral developmental toxicity study in rabbits demonstrated a maternal NOAEL of 25 mg/kg bwt/day, a developmental NOAEL of 100 mg/kg bwt/day and did not reveal any

teratogenic potential. A 2-generation study in rats, with a parental toxicity NOAEL of 73.7 mg/kg bwt/day for males and 86.7 mg/kg bwt/day for females, did not reveal evidence of a primary reproductive toxicity potential. The reproductive NOAEL was 763.6 mg/kg bwt/day for males and 806.5 mg/kg bwt/day in females.

4. *Subchronic toxicity.* A subchronic toxicity feeding study with rats over 90 days demonstrated a NOAEL of 7.3 and 18.3 mg/kg bwt/day for males and females, respectively, based on reduced body weights and alterations in several urinary tract-related clinical chemistry parameters, at the higher dose levels. In a subchronic feeding study in mice over 14 weeks, a NOAEL was not established based on decreased alanine aminotransferase (ALAT) and increased absolute and relative liver weights at the low dose level (21.7 and 35.3 mg/kg bwt/day for males and females respectively). A 14-week feeding study in dogs demonstrated a NOAEL of 3.0 mg/kg bwt/day based on decreased body weights and food consumption, and liver effects (enzyme induction, increased liver weights, cytoplasmic change), and thyroid effects (decreased T3).

5. *Chronic toxicity.* A 24-month chronic/oncogenicity feeding study in rats demonstrated a NOAEL of 53.0 and 35.2 mg/kg bwt/day for males and females, respectively. An oncogenicity study in the mouse revealed a NOAEL of 18.5 and 29.5 mg/kg bwt/day for males and females, respectively based on liver effects. There was no indication in the rat or mouse for an oncogenic effect of fluoxastrobin. A 1-year feeding study with dogs demonstrated a NOAEL of 1.7 and 1.5 mg/kg bwt/day for males and females, respectively based on decreased body weights and slight liver effects (increased alkaline phosphatase (Aph) and liver weights).

6. *Animal metabolism.* Metabolism and pharmacokinetic studies in the rats, lactating goats, and laying hens demonstrate that fluoxastrobin residues are rapidly absorbed, metabolized, and eliminated. There was no evidence of accumulation of residues in any tissues or organs. The metabolic pattern was always complex and numerous metabolites were identified. The main metabolic reactions, however, are very comparable for all tested animal species and most metabolites were present at low levels. Based on the available metabolism data, fluoxastrobin and phenoxy-hydroxypyrimidine are the proposed residues of concern in animals.

7. *Metabolite toxicology.* The residues of concern are fluoxastrobin its