

pyrazol-3-yl]oxy]methyl]phenyl carbamate] in or on the following raw agricultural commodities: [lettuce, leaf and lettuce, head at 22 parts per million (ppm)], [vegetable, leaves of root and tuber, group 2 at 16 ppm], and [brassica, head and stem, subgroup 5A at 5 ppm]. EPA has determined that the petitions contain 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 petitions. Additional data may be needed before EPA rules on the petitions. This summary has been prepared by Bayer Corporation, Research Triangle Park, NC 27709.

A. Residue Chemistry

1. *Plant metabolism.* Nature of the residue studies (OPPTS 860.1300) were conducted in grape, potato and wheat as representative crops in order to characterize the fate of pyraclostrobin in all crop matrices. Pyraclostrobin demonstrated a similar pathway and fate in all three crops. In all three crops the pyraclostrobin residues of concern (ROC) of were characterized as parent (pyraclostrobin) and BAS 500-3), methyl-N[[[1-(4-chlorophenyl) pyrazol-3-yl]oxy]o-tolyl] carbamate.

2. *Analytical method.* In plants the method of analysis is aqueous organic solvent extraction, column clean up and quantitation by LC/MS/MS. In animals the method of analysis involves base hydrolysis, organic extraction, column clean up and quantitation by LC/MS/MS or derivatization (methylation) followed by quantitation by gas chromatography/mass spectrometry (GC/MS).

3. *Magnitude of residues.* Field trials were carried out in order to determine the magnitude of the residue in the following crops: Brassica, head and stem; lettuce, head and leaf; and turnip greens to satisfy the requirements for a crop group tolerance for pyraclostrobin in leaves of root and tuber vegetables. Field trials were carried out using the maximum label rate, the maximum number of applications, and the minimum preharvest interval for each crop or crop group.

B. Toxicological Profile

1. *Acute toxicity.* Based on available acute toxicity data pyraclostrobin and its formulated products do not pose acute toxicity risks. The acute toxicity studies place technical pyraclostrobin in toxicity category IV for acute oral; category III for acute dermal and category II for acute inhalation. Pyraclostrobin is category III for both eye and skin irritation, and it is not a

dermal sensitizer. Two formulated end use products are proposed, an emulsifiable concentrate (EC) and an extruded granule (EG). The EC has an acute oral toxicity category of II, acute dermal of III, acute inhalation of IV, eye and skin irritation categories of III, and is not a dermal sensitizer. The WG has acute oral and dermal toxicity categories of III, acute inhalation of IV, eye irritation of III, skin irritation of IV and is not a dermal sensitizer.

2. *Genotoxicity.* Ames test (1 study; point mutation): Negative; *in vitro*. CHO/HGPRT Locus Mammalian Cell Mutation Assay (1 study; point mutation): Negative; *in vitro* V79 Cells CHO Cytogenetic Assay (1 study; chromosome damage): Negative; *in vivo*. Mouse micronucleus (1 study; chromosome damage): Negative; *in vitro* rat hepatocyte (1 study; DNA damage and repair): Negative; pyraclostrobin has been tested in a total of 5 genetic toxicology assays consisting of *in vitro* and *in vivo* studies. It can be stated that pyraclostrobin did not show any mutagenic, clastogenic or other genotoxic activity when tested under the conditions of the studies mentioned above. Therefore, pyraclostrobin does not pose a genotoxic hazard to humans.

3. *Reproductive and developmental toxicity.* The reproductive and developmental toxicity of pyraclostrobin was investigated in a 2-generation rat reproduction study as well as in rat and rabbit teratology studies. There were no adverse effects on reproduction in the two-generation study so the no observed adverse effect level (NOAEL) is the highest dose tested (HDT) of 300 ppm (32.6 milligrams/kilogram body weight/day (mg/kg bwt/day)). Parental and pup toxicity in the form of reduced body weight gain were observed at the HDT only. Therefore, the parental systemic and developmental toxicity NOAEL's are the same at 75 ppm (8.2 mg/kg bwt).

No teratogenic effects were noted in either the rat or rabbit developmental studies. In the rat study, maternal toxicity observed at the mid and high dose consisted of decreased food consumption and body weight gain. Developmental changes noted at the high dose were increased incidences of dilated renal pelvis and cervical ribs with no cartilage. The maternal NOAEL was 10 mg/kg bwt and the developmental NOAEL was 25 mg/kg bwt.

In the rabbit teratology study, maternal toxicity observed at the mid and high doses consisted of decreased food consumption and body weight gain (severe at the high dose). An increased post-implantation loss was also

observed at the mid and high doses due to an increase in early resorptions. In rabbits, these types of effects are often observed with significant stress on the mothers (as seen by the body weight gain decrease in this study) and not indicative of frank developmental toxicity. The NOAEL for both maternal and developmental toxicity was 5 mg/kg bwt.

4. *Subchronic toxicity.* The subchronic toxicity of pyraclostrobin was investigated in 90-day feeding studies with rats, mice, and dogs, and in a 28-day dermal administration study in rats. A 90-day neurotoxicity study in rats was also performed. Generally, mild toxicity was observed. At high dose levels in feeding studies, general findings in all three species were decreased food consumption and body weight gain and a thickening of the duodenum. Anemia occurred at high dose levels in both rats and mice with accompanying extramedullary hematopoiesis of the spleen in rats. In rats only, a finding of liver cell hypertrophy was indicative of a physiological response to the handling of the chemical. Overall, only mild toxicity was observed in oral subchronic testing.

In the 28-day repeat dose dermal study, no systemic effects were noted up to the HDT of 250 mg/kg bwt/day.

In a 90-day rat neurotoxicity study, a direct neurotoxic effect was not observed.

5. *Chronic toxicity.* Pyraclostrobin was administered to groups of 5 male and 5 female purebred Beagle dogs in the diet at concentrations of 0, 100, 200 and 400 ppm over a period of 12 months. Signs of toxicity were observed at the high dose. Diarrhea was observed throughout the study period for both sexes. High dose males and females initially lost weight and body weight gain was decreased for the entire study period for females. Hematological changes observed were an increase in white blood cells in males, and an increase in platelets in both sexes at the high dose. Clinical chemistry demonstrated a decrease in serum total protein, albumin, globulins and cholesterol in high dose animals of both sexes possibly due to the diarrhea and reduced nutritional status of the animals. The NOAEL was 200 ppm (ca. 5.5 mg/kg bwt/day males; 5.4 mg/kg bwt/day females).

In a carcinogenicity study, pyraclostrobin was administered to groups of 50 male and 50 female Wistar rats at dietary concentrations of 0; 25; 75, and 200 ppm for 24 months. In a companion chronic toxicity study, 20 rats/sex were used at the same dose