

Guideline 860.1300) were conducted in grapes, lettuce and beans as representative crops in order to characterize the fate of Boscalid (BAS 510 F) in all crop matrices. In all three crops the BAS 510 F Residues of Concern (ROC) were characterized as parent BAS 510 F. A confined rotational crop study also determined that parent was the residue of concern in the representative crops of radish, lettuce and wheat.

2. *Analytical method.* In plants the parent residue is extracted using an aqueous organic solvent mixture followed by liquid/liquid partitioning and a column clean up. Quantitation is by GC/MS. The extract is treated with enzymes in order to release the conjugated glucuronic acid metabolite. The residues are then isolated by liquid/liquid partition followed by column chromatography. The hydroxylated metabolite is acetylated followed by a column clean-up. The parent and acetylated metabolite are quantitated by GC/ECD.

3. *Magnitude of the residues.* Field trials were carried out in order to determine the magnitude of the residue in soybean and soybean aspirated grain fraction. Field trials were conducted in the United States and Canada in the required regions. Field trials were carried out using the maximum label rate, the maximum number of applications, and the minimum preharvest interval. In addition, a processing study was conducted on the soybean to determine concentration factors. Tier III field rotational crop studies were conducted to support rotational crop tolerances for soybean.

#### B. Toxicological Profile

1. *Acute toxicity.* Based on available acute toxicity data BAS 510 F and its formulated products do not pose acute toxicity risks. The acute toxicity studies place technical BAS 510 F in toxicity category IV for acute oral; category III for acute dermal and category IV for acute inhalation. BAS 510 F is category IV for both eye and skin irritation, and it is not a dermal sensitizer. Two formulated end use products are proposed, a Water Dispersible Granule (WG) termed BAS 510 02F containing 70% BAS 510 F and a Water Dispersible Granule (WG) termed BAS 516 02F containing a 2:1 mixture of BAS 510 F and BAS 500F. BAS 510 02F has an acute oral toxicity category of III, acute dermal of III, acute inhalation of IV, eye irritation of III, skin irritation of IV, and is not a dermal sensitizer. BAS 516 02F has an acute oral toxicity category of III, acute dermal 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 Cell 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. BAS 510 F has been tested in a total of 5 genetic toxicology assays consisting of *in vitro* and *in vivo* studies. It can be stated that BAS 510 F did not show any mutagenic, clastogenic or other genotoxic activity when tested under the conditions of the studies mentioned above. Therefore, BAS 510 F does not pose a genotoxic hazard to humans.

3. *Reproductive and developmental toxicity.* The reproductive and developmental toxicity of BAS 510 F was investigated in a two-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 at any dose tested. Pup effects were observed, with parental toxicity, at the highest dose tested only. In both parental generations, reduced food consumption and reduced bodyweight gain were observed at 10,000 ppm. Both absolute and relative liver weights were increased 21% in F<sub>1</sub> generation parental females at the high dose of 10,000 ppm only. Hepatocellular centrilobular hypertrophy (usually slight) was observed in many animals of both sexes in both the F<sub>0</sub> and F<sub>1</sub> generations at 1,000 ppm, and in all animals of both sexes at 10,000 ppm. Additionally, some of the parental male rats at 10,000 ppm, in both generations, displayed centrilobular liver cell degeneration. Developmental toxicity was seen at 1,000 ppm in the form of decreased pup weights in the F<sub>2</sub> males, and at 10,000 ppm in the form of decreased pup weight for both males and females of both the F<sub>1</sub> and F<sub>2</sub> generations. The parental systemic and developmental toxicity NOAEL's are both 100 ppm (12 mg/kg/day).

No teratogenic effects were noted in either the rat or rabbit developmental studies. In the rat study, evidence of maternal or developmental toxicity was not observed at any dose (highest dose tested of 1,000 mg/kg/day). Neither a maternal nor developmental LOAEL were found since the highest dose tested was the NOAEL in both studies.

In the rabbit teratology study, maternal toxicity observed at the mid dose of 300 mg/kg bw consisted of

discolored/reduced feces in one dam and an abortion in one dam. This finding is not necessarily indicative of a definitive test substance related adverse effect. The dam which displayed the fecal alterations and abortion also displayed decreased body weight and body weight gain - compared to the group mean - during gestation. These decreases occurred even prior to compound administration. Food consumption was also dramatically decreased in this dam compared to the other animals in the group. Every day from gestation day 1 to 12, this dam had food consumption values, which were less than half the mean for the group (compound administration began on day GD 7). From gestation day 13 to 26 (when the animal aborted and was sacrificed) this dam ate essentially nothing (food consumption during this time period was less than or equal to 1.5 grams/day). These decreases in body weight, body weight gain, and food consumption, prior to compound administration, all indicate an animal in poor health and this poor state of health, rather than compound exposure, was likely the reason for the fecal alterations and abortion.

At the high dose of 1,000 mg/kg bw a maternal body weight gain decrease compared to controls of 81% was observed during the treatment period. Reduced food consumption, reduced body weight and abortions in three dams, were also seen at 1,000 mg/kg/day. Evidence of developmental toxicity was not seen at any dose tested.

Developmental neurotoxicity was not observed at any dose in the developmental neurotoxicity study. No maternal toxic effects were noted at any dose in this study. No developmental toxicity was seen at the low dose of 12 mg/kg/day (100 ppm). Reduced body weights and body weight gains were seen at 118 mg/kg/day (1,000 ppm) during PND 1-4. Reduced body weights and body weight gains were seen at 1,183 mg/kg/day (10,000 ppm) as well as decreased absolute pup brain weight at day 11 p.p. (both sexes) and decreased brain length (males only) at day 11 p.p. The reduced pup brain weights and decreased brain length go hand-in-hand and both are due to the decreased pup weights seen at this dose. In this respect, it should be noted that pup brain weights relative to body weight at p.p. 11 were not significantly different from controls at this dose.

Though no maternal toxicity was seen in this study, other studies using similar doses of BAS 510 F resulted in maternal toxicity. A dose of 118 mg/kg/day in female rats of the same strain in the