

Method AG-597B) has passed an Agency petition method validation for several commodities and is currently the enforcement method for fludioxonil. This method has also been forwarded to the Food and Drug Administration for inclusion into PAM II. An extensive data base of method validation data using this method on various crop commodities is available.

3. *Magnitude of residues.* Complete residue data for Brassica, head and stem (subgroup 5e.c.), Brassica leafy greens (subgroup 5e.c.), turnip, greens, herb (subgroup 19e.c.), and lychee, longan, rambutan, pulasan, and Spanish lime have been submitted. The requested tolerances are adequately supported by field research data.

#### B. Toxicological Profile

An assessment of toxic effects caused by fludioxonil is discussed in Unit III.A. and Unit III.B. of the **Federal Register** of August 2, 2002 (67 FR 50354) (FRL-7188-7).

1. *Animal metabolism.* The metabolism of fludioxonil in rats is adequately understood.

2. *Metabolite toxicology.* The residues of concern for tolerance setting purposes is fludioxonil, the parent compound. Consequently, there is no additional concern for toxicity of metabolites.

3. *Endocrine disruption.* Fludioxonil does not belong to a class of chemicals known for having adverse effects on the endocrine system. No estrogenic effects have been observed in the various short-term and long-term studies conducted with various mammalian species.

#### C. Aggregate Exposure

1. *Dietary exposure.* A Tier III acute and chronic dietary exposure evaluation was made using the Dietary Exposure Evaluation Model (DEEM™), version 7.76 from exponent. Empirically derived processing studies for apple juice (0.09X), apple pomace (6.77X), and grape juice (0.36X) were used in these assessments. The apple juice processing factor was used as a surrogate for pear juice and all other processing factors used DEEM™ defaults. All consumption data for these assessments were taken from the U.S. Department Agriculture (USDA) Continuing Survey of Food Intake by Individuals (CSFII) with the 1994–96 consumption data base and the Supplemental CSFII children's survey (1998) consumption data base. These exposure assessments included all registered uses and uses proposed in this submission: Brassica, head and stem (subgroup 5e.c.), Brassica, leafy greens (subgroup 5e.c.), turnip, greens, carrot, herbs (subgroup 19e.c.), lychee, longan, and Spanish

lime. Secondary residues in animal commodities were estimated based on the theoretical worst-case, yet nutritionally adequate animal diets and transfer information from feeding studies.

i. *Food.* For the purposes of assessing the potential dietary exposure under the proposed tolerances, Syngenta Crop Protection has estimated aggregate exposure from all crops for which tolerances are established or proposed. These assessments utilized residue data from field trials where fludioxonil was applied at the maximum intended use rate and samples were harvested at the minimum pre-harvest interval (PHI) to obtain maximum residues. Percent of crop treated (PCT) values were estimated based upon economic, pest and competitive pressures. The values used in these assessments were: All seed treatment uses, 100%; apricots and pistachios, 10%; cherries, 16%; nectarines, 49%; onions, 9%; peaches, 22%; plums, 25%; other stone fruit, 20%; strawberries, 42%; watercress, 95%; berries, 13%; salal, 13%; herbs, 80%; crop group 5e.c. and 5e.c., carrots, and lychee, turnips and longan 10%.

ii. *Acute exposure.* An acute reference dose (aRfD) of 1.0 milligram/kilogram body weight (mg/kg/bwt) day for the females 13–50 years subpopulation only was based on a no observed adverse effect level (NOAEL) of 100 mg/kg/bwt day from a rat teratology study and an uncertainty factor of 100X. No additional FQPA safety factor was applied. For the purpose of aggregate risk assessment, the exposure value was expressed in terms of margin of exposure (MOE) which was calculated by dividing the NOAEL by the exposure for each population subgroup. In addition, exposure was expressed as a percent of the aRfD. Acute exposure to the females 13–50 years subpopulation resulted in a MOE of 9,933 (1.01%) of the aRfD of the 1.0 mg/kg bwt/day. Since the benchmark MOE for the assessment was 100 and since EPA generally has no concern for exposures below 100% of the RfD, Syngenta believes that there is a reasonable certainty that no harm will result from dietary (food) exposure to residues arising from the current and proposed uses for fludioxonil.

iii. *Chronic exposure.* The chronic reference dose (cRfD) for fludioxonil is 0.033 mg/kg bwt/day and is based on a 1-year study in dogs with a NOAEL of 3.3 mg/kg bwt/day and an Uncertainty Factor (UF) of 100X. No additional Food Quality Protection Act (FQPA) safety factor was applied. The fludioxonil Tier III chronic dietary exposure assessment was based upon residue field trial results. For the purpose of aggregate risk

assessment, the exposure values were expressed in terms of MOE which was calculated by dividing the NOAEL by the exposure for each population subgroup. In addition, exposure was expressed as a percent of the RfD. Chronic exposure to the most exposed subpopulation (children 1 and 2 years old) resulted in a MOE of 2,668 (3.75%) of the cRfD of 0.033 mg/kg bwt/day. Since the benchmark MOE for this assessment was 100 and since EPA generally has no concern for exposures below 100% of the RfD, Syngenta believes that there is a reasonable certainty that no harm will result from dietary (food) exposure to residues arising from the current and proposed uses for fludioxonil.

iv. *Drinking water.* Another potential source of exposure of the general population to residues of fludioxonil are residues in drinking water. Fludioxonil rapidly degrades via photolysis on the soil surface and in water. The half-lives are 1 day and 10 days, respectively. This potential for rapid degradation reduces the potential for ground water or surface water exposure. Fludioxonil soil/solution partition coefficients vary from 991 to 2,440 indicating a relatively high affinity for binding to soil. Estimated Environmental Concentrations (EECs) of fludioxonil in drinking water were determined for the highest use rate of fludioxonil (turfgrass use). Scenning Concentration in Ground Water (SCI-GROW) (Version 2.2) was used to determine acute and chronic ECCs in ground water and FQPA Index Reservoir Screening Tool (FIRST) (Version 1.0) was used to determine acute and chronic estimated environmental concentrations in surface water. Based on the model outputs, the ECCs of fludioxonil are 0.174 parts per billion (ppb) for acute and chronic exposure to ground water and 70 ppb and 33 ppb for acute and chronic exposure, respectively, to surface water. Acute Drinking Water Levels of Comparison (DWLOC) were calculated based on an acute Populated Adjusted Dose (aPAD) of 1 mg/kg/day. For the acute assessment, the females (13–50 years) subpopulation generated an acute DWLOC of approximately 30,000 ppb. Thus, the acute DWLOC of 30,000 ppb is considerably higher than the acute EEC of 70 ppb. Chronic DWLOC were calculated based on a cRfD of 0.033 mg/kg/day. For the chronic assessment, the children 1 and 2 years old subpopulation generated the lowest chronic DWLOC of approximately 320 ppb. Thus, the chronic DWLOC of 320 ppb is considerably higher than the chronic EEC of 33 ppb.