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#### A. Residue Chemistry

1. *Plant metabolism.* The metabolism of cyprodinil is adequately understood for the purpose of the proposed tolerances.

2. *Analytical method.* Syngenta has developed and validated analytical methodology for enforcement purposes. This method (Syngenta Crop Protection Method AG-631B) has passed an Agency petition method validation for several commodities and is currently the enforcement method for cyprodinil. An extensive data base of method validation data using this method on various crop commodities is available.

3. *Magnitude of residues.* Complete residue data to support the requested tolerances for almond, hulls, Brassica, head and stem (Subgroup 5A), Brassica, leafy greens (Subgroup 5B), turnip, greens, herbs (Subgroup 19A), and lychee, longan, rambutan, pulasan, and Spanish lime have been submitted. The requested tolerances are adequately supported.

#### B. Toxicological Profile

An assessment of toxic effects caused by cyprodinil is discussed in Unit III.A. and Unit III.B. of the **Federal Register** dated June 22, 2001 (66 FR 33478) (FRL-6778-7).

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

2. *Metabolite toxicology.* The residues of concern for tolerance setting purposes is the parent compound. Based on structural similarities to genotoxic nucleotide analogs, there was concern that the pyrimidine metabolites (CGA-249287, NOA-422054) may be more toxic than the parent compound. However, EPA's review indicates similar results in acute oral and mutagenicity studies with both the parent compound and the CGA-249287 metabolite. EPA concluded that the toxicity of the CGA-249287 and NOA-422054 metabolites is no greater than that of the parent, conditional on submission and review of confirmatory data of an acute oral toxicity study and bacterial reverse mutation assay for the NOA-422054 metabolite. Although, the metabolites CGA-232449 and CGA-263208 were determined to be of potential toxicological concern, there are not expected to be more toxic than cyprodinil per se.

3. *Endocrine disruption.* Cyprodinil does not belong to a class of chemicals known or suspected of having adverse effects on the endocrine system. Developmental toxicity studies in rats

and rabbits and a reproduction study in rats gave no indication that cyprodinil might have any effects on endocrine function related to development and reproduction. The chronic studies also showed no evidence of a long-term effect related to the endocrine system.

#### 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. All consumption data for these assessments were taken from the USDA's 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 pending uses on watercress, bushberries, caneberries, juneberries, ligonberries, pistachios, and salal.

i. *Food—a. Acute exposure.* Acute dietary risk assessments are performed for a food-use pesticide if a toxicological study has indicated the possibility of an effect of concern occurring as a result of a 1 day or single exposure. EPA has not conducted an acute dietary risk assessment since no toxicological endpoint of concern was identified during the review of the available data.

b. *Chronic exposure.* Percent of crop treated values were estimated based upon economic, pest and competitive pressures. The values used in these assessments were: (Almonds, pome fruits, stone fruits and grapes), 100%; onions 9%; strawberries 42%; watercress, 95%; berries, 13%; pistachios, herbs, 80%; crop group 5A and 5B, carrots, turnip, greens, lychee, longan and Spanish lime, 10%.

ii. *Drinking water.* Estimated Environmental Concentrations (EECs) of cyprodinil in drinking water were determined by EPA. EPA groundwater model Screening Concentration in Groundwater (SCI-GROW) was used to determine acute and chronic estimated environmental concentrations in ground water and the Agency's surface water model, EPA's pesticide root zone model/exposure analysis modeling system (PRZM/EXAMS) was used to determine acute and chronic EECs estimated environmental concentrations in surface water. Based on the model outputs, the EEC cyprodinil are 0.04 parts per billion (ppb) for acute and chronic exposure to ground water and 32 ppb and 6 ppb for acute and chronic exposure, respectively, to surface water.

2. *Non-dietary exposure.* There is a potential residential post-application exposure to adults and children entering

residential areas treated with cyprodinil. Since the Agency did not select a short-term endpoint for dermal exposure, only intermediate dermal exposures were considered. Based on the residential use pattern, no long-term post-application residential exposure is expected.

#### D. Cumulative Effects

Section 408(b)(2)(D)(v) requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." EPA does not have, at this time, available data to determine whether cyprodinil has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment. For the purposes of this tolerance action, EPA has not assumed that cyprodinil has a common mechanism of toxicity with other substances.

#### E. Safety Determination

The chronic dietary exposure analysis (food only) showed that exposure from all established and proposed cyprodinil uses would be 7.48% of the chronic reference dose (cRfD) for the most sensitive subpopulation, children 1-2 years old. EPA has determined that reliable data support using the standard margin of exposure (MOE) and uncertainty factor (100 for combined interspecies and intraspecies variability) for cyprodinil and that an additional safety factor of 10 is not necessary to be protective of infants and children.

Acute Drinking Water Levels of Comparison (DWLOC) were calculated based on an acute populated adjusted dose (aPAD) of 1.5 milligrams/kilogram/day. For the acute assessment, the females (13-50 years) subpopulation generated an acute DWLOC of approximately 44,600 ppb. The acute EEC of 32 ppb is considerably less than 44,600 ppb. For the chronic assessment, the children 1-2 years old subpopulation generated the lowest chronic DWLOC of approximately 280 ppb. Thus, the chronic DWLOC of 280 ppb is considerably higher than the chronic EEC of 6 ppb.

Syngenta has considered the potential aggregate exposure from food, water and non-occupational exposure routes and concluded that aggregate exposure is not expected to exceed 100% of the chronic reference dose and that there is a reasonable certainty that no harm will result to infants and children from the aggregate exposure to cyprodinil.