

substituents. Further metabolic reactions occur including cleavage of the phenyl ring to produce substituted pyrimidines. The major metabolite was AE C614276 (46% of the kidney residues, 63% of the milk residues) resulting from hydroxylation of the phenyl ring. Hydroxylation of the pyrimidinyl ring of pyrimethanil resulted in formation of minor amounts of AE C614277. Hydroxylation of the methyl groups of pyrimethanil resulted in formation of minor amounts of AE C614278. Hydroxylation of the methyl groups of AE C614276 resulted in formation of minor amounts of AE C614800.

7. *Metabolite toxicology.* The primary residue of concern in both crop and animal commodities is pyrimethanil. In the animal metabolism, since major metabolites are produced following the oral administration of pyrimethanil, toxicology data for metabolites are completely supported by data obtained for pyrimethanil.

8. *Endocrine disruption.* Chronic, life span, and multi-generational bioassays in mammals and acute and subchronic studies on aquatic organisms and wildlife did not reveal endocrine effects. Any endocrine related effects would have been detected in this definitive array of required tests. The probability of any such effect due to agricultural uses of pyrimethanil is negligible.

#### C. Aggregate Exposure

1. *Dietary exposure.* Tolerances are proposed under 40 CFR part 180 for pyrimethanil in or on citrus fruits and pome fruits following postharvest application. An import tolerance for wine grapes has been approved by the EPA. A petition for registration of pyrimethanil on bananas is pending at EPA. In March 2002, registration applications and tolerance petitions were filed for tree nuts, bulb vegetables, grapes, stone fruits (except cherries), pome fruit (preharvest application), tuberous and corm vegetables, strawberries, and tomatoes. There are no residential uses proposed for pyrimethanil. Therefore, potential human risk scenarios cover aggregate exposure from food residues and drinking water.

i. *Food.* Refined estimates of acute dietary exposure from potential pyrimethanil residues with the addition of postharvest uses on citrus and pome fruits are all well under 100% of the acute reference dose (RfD) at the 99.9th percentile. The most highly exposed sub population of non-nursing infants utilizes 13.35% of the RfD, while the U.S. population utilizes 6.1%. These potential dietary exposures were

estimated in a Tier 3 Monte Carlo risk assessment using the Dietary Exposure Evaluation Model (DEEM) software (Novigen 2001). The 1994–96, 1998 Continuing Surveys of Food Intake by Individuals (CSFII) consumption data from USDA was used which includes the Supplemental Children's Survey (1998). Residue values included in the assessment were distributions of the field trial values incorporating percent crop treated (PCT) as zeroes for all non-blended and partially blended items. Blended items were included as the average residue and adjusted for PCT. These PCT values are the anticipated market share of pyrimethanil for the crops at market maturity (5 years). Concentration factors derived from processing studies were included where appropriate. Secondary residues for meat and milk were included in the assessment. These were calculated using theoretical dietary burdens from sensible diets for beef and dairy cattle and tissue to feed ratios from the ruminant feeding study.

Refined chronic dietary exposure estimates resulting from the proposed uses of pyrimethanil are well within acceptable limits for all population subgroups examined. The most highly exposed group of non-nursing infants utilized 0.9% of the reference dose with the U.S. population utilizing 0.2% of the reference dose. A Tier 3 chronic analysis was done using the DEEM software, (Novigen 2001). The 1994–96, 1998 CSFII consumption data from USDA were used. Average anticipated residue values were calculated from the appropriate field trial studies conducted for pyrimethanil. The average residue values were adjusted by the projected PCT at product maturity. Concentration factors derived from processing studies were included where appropriate. Secondary residues were calculated using theoretical dietary burdens derived from sensible diets for beef and dairy cattle and tissue to feed ratios from the ruminant feeding study.

ii. *Drinking water.* EPA's Standard Operating Procedure (SOP) for Drinking Water Exposure and Risk Assessments was followed to perform the Tier One drinking water assessment. This SOP uses a variety of tools to conduct drinking water assessments, including water models such as Screening Concentrations in Ground Water (SCI-GROW), First Index Reservoir Screening Tool (FIRST), Pesticide Root Zone Model/Exposure Analysis Modeling System (PRZMS/EXAMS), and monitoring data. If monitoring data are not available then the models are used to predict potential residues in surface and ground water and the highest levels

(whether ground or surface) are assumed to be the drinking water residue. In the case of pyrimethanil, monitoring data are not available. SCI-GROW and FIRST were used to estimate a drinking water residue. Calculation of the Drinking Water Estimated Concentration (DWECC) for surface water for the worst case pyrimethanil use scenario results in a acute DWECC of 122 ppb and a chronic DWECC of 37 ppb. Drinking Water Levels of Comparison (DWLOCs) calculated based on the acute and chronic risk assessments described above are many fold higher than these conservative DWECCs. The adult acute and chronic DWLOCs are 9,860 ppb and 5,936 ppb respectively. Children's acute and chronic DWLOCs are 2,641 ppb and 1,686 ppb respectively.

2. *Non-dietary exposure.* Pyrimethanil products are not labeled for residential uses (food or non-food), thereby eliminating the potential for residential exposure or non-occupational exposure.

#### 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." There are no available data to determine whether pyrimethanil has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, pyrimethanil does not appear to form a toxic metabolite produced by other substances. For the purposes of the tolerance petition, it has been assumed that pyrimethanil does not have a common mechanism of toxicity with other substances.

#### E. Safety Determination

1. *U.S. population.* Using the assumptions and data described above, based on the completeness and reliability of the toxicity data, it is concluded that dietary risk from the proposed uses of pyrimethanil are acceptable for all populations examined. Chronic exposure for the U.S. population utilizes 0.2% (0.000392 mg/kg bw/day) of the chronic reference dose. Acute exposure for the U.S. population utilizes 6.1% (0.018287 mg/kg bw/day) of the acute reference dose. The most highly exposed population of non-nursing infants utilizes only 0.9% of the chronic reference dose and