

7. *Metabolite toxicology.* Two specific metabolites, KKO 2254 and WAK 6999, were examined toxicologically. In addition to negative Ames tests, the acute toxicological potential for both sexes, as measured by LD₅₀, was determined to be >2,000 mg/kg for both metabolites. In light of these findings no special toxicological concerns, exceeding that of thiacloprid, would be expected from the metabolites of the parent compound.

8. *Endocrine disruption.* The toxicology database for thiacloprid is current and complete. Studies in this database include evaluation of the potential effects on reproduction and development and an evaluation of the pathology of the endocrine organs following short- or long-term exposure.

C. Aggregate Exposure

1. *Dietary exposure.* Acute and chronic dietary analyses were conducted to estimate exposure to potential thiacloprid residues in/on the following crops: Fruit, pome, group; fruit, stone, group; and cotton using the DEEM^T software (Version 7.76) from Exponent, Inc. The 94–94.98 CSFII consumption database was used along with anticipated residues and processing factors where available. Projected percent crop treated values were incorporated into both the acute and chronic dietary exposure analyses at 20%, 10%, and 5% for pome fruit, stone fruit, and cotton, respectively. Exposure estimates to water were made based upon modeling. The acute reference dose (aRfD) (aRfD = 0.031 mg/kg/bwt/day) was based upon an acute NOEL of 3.1 mg/kg/bwt/day from the acute oral neurotoxicity study in rats and an uncertainty factor of 100. The chronic reference dose (cRfD) (cRfD = 0.012 mg/kg/bwt/day) was based upon a chronic NOEL of 1.2 mg/kg/bwt/day and an uncertainty factor of 100.

i. *Food.* The acute dietary exposure estimates at the 99.9th percentile for the U.S. population was calculated to be approximately 7% of the aRfD. The population subgroup with the highest exposure was non-nursing infants (<1 year old) at approximately 15% of the aRfD. Chronic dietary exposure estimates from residues of thiacloprid for the U.S. population was 0.2% of the cRfD. The population subgroup with the highest exposure was non-nursing infants with 1% of the cRfD utilized.

ii. *Drinking water.* EPA's Standard Operating Procedure (SOP) for Drinking Water Exposure and Risk Assessments was used to perform the drinking water analysis for thiacloprid. This SOP utilizes a variety of tools to conduct drinking water assessment. These tools

include water models such as SCI-GROW, FIRST, GENECC, PRZM/EXAMS, and monitoring data. If monitoring data are not available then the models are used to predict potential residues in surface water and ground water. In the case of thiacloprid, monitoring data do not exist, therefore, FIRST and SCIGROW models were used to estimate a water residue. The calculated drinking water levels of comparison (DWLOC) for acute and chronic exposures for all adults and children greatly exceed the modeled thiacloprid drinking water estimated concentrations (DWECC). The acute DWLOC values are 1013 parts per billion (ppb) for adults (U. S. population) and 267 ppb for children. The worst case DWECC for acute scenarios is calculated to be 10.95 ppb using the FIRST surface water model. The chronic DWLOC values are 430 ppb for adults and 122 ppb for children. The DWECC for the worst case chronic scenario is 0.62 ppb (FIRST).

2. *Non-dietary exposure.* There are no current plans to support thiacloprid uses on turf or ornamental plants, including homeowner uses.

D. Cumulative Effects

Thiacloprid is thought to be part of a class of chemistry called the chloro-nicotinyls. For this class of chemistry and its registered compounds EPA has not yet conducted a detailed review of common mechanisms to determine whether it is appropriate, or how to include these chemicals in a cumulative risk assessment. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, thiacloprid does not appear to produce a toxic metabolite produced by other substances. For the purposes of these tolerance actions; therefore, EPA has not assumed that thiacloprid has a common mechanism of toxicity with other substances.

E. Safety Determination

1. *U.S. population.* Using the conservative exposure assumptions described in Unit C. of this petition and based on the completeness of the toxicity data, it can be concluded that acute dietary exposure to residues of thiacloprid from all proposed uses will utilize less than 7% of the aRfD for the U.S. population and 15% of the aRfD for the most highly exposed subpopulation (non-nursing infants). EPA generally has no concerns for exposures below 100% of the reference dose (RfD), because the RfD represents the level at or below which exposure will not pose any appreciable risk to human health.

Additionally, the acute DWLOC was calculated to be nearly 100 times greater than thiacloprid residues in water predicted by conservative models. The chronic dietary exposure occupies 0.2% of the cRfD for the U.S. population and 1% of the cRfD for the most highly exposed subpopulation (non-nursing infants). EPA generally has no concerns for exposures below 100% of the RfD, because the RfD represents the level at or below which daily aggregate exposure over a lifetime will not pose appreciable risks to human health. The chronic DWLOC was calculated to be nearly 700 and 200 times greater than the thiacloprid residues in water predicted by conservative models. Therefore, there is a reasonable certainty that no harm will result to the general U.S. population from aggregate acute or chronic exposure to thiacloprid residues from proposed uses.

2. *Infants and children.* In assessing the potential for additional sensitivity of infants and children to residues of thiacloprid, the data from developmental studies in both rat and rabbit and a 2-generation reproduction study in rats have been considered. The developmental toxicity studies evaluate potential adverse effects on the developing animal resulting from pesticide exposure of the mother during prenatal development. The reproduction study evaluates effects from exposure to the pesticide on the reproductive capability of mating animals through 2 generations, as well as any observed systemic toxicity.

FFDCA section 408 provides that EPA may apply an additional safety factor for infants and children in the case of threshold effects to account for pre- and post-natal effects and the completeness of the toxicity database. Based on current toxicological data requirements, the toxicology database for thiacloprid relative to pre- and post-natal effects is complete. Further for thiacloprid, the NOEL of 1.2 mg/kg/bwt/day from the 2-year chronic toxicity/carcinogenicity study, which was used to calculate the cRfD (discussed in Unit C.1. of this petition), is already lower than the NOELs from the developmental studies in rats (10 mg/kg/bwt/day) and rabbits (2 mg/kg/bwt/day) and lower than the NOEL from the 2-year reproductive toxicity study in rats (50 mg/kg/bwt/day). Since a 100-fold uncertainty factor is already used to calculate the RfD, an additional safety factor for infants and children is not warranted.

Using the conservative exposure assumptions described in Unit C. of this petition, Bayer CropScience has concluded that the total aggregate exposure to thiacloprid from all