

establishing these proposed tolerances. Unchanged parent thiacloprid accounted for 70% or greater of the residues in all plant metabolism studies (cotton, tomato, and apple), with the exception of the material identified in cotton seed. In cotton seed, the main component was the 6-chloronicotinic acid metabolite, accounting for 45.8%. All residues contained the 6-chloro-pyridinyl moiety. In animals, parent thiacloprid was the major component in all edible tissues, milk, and eggs. All residues and metabolites in the animal tissues contained the 6-chloro-pyridinyl moiety, same as in the plant tissues. Therefore, the residues of concern are the combined residues of thiacloprid and its metabolites containing the 6-chloro-pyridinyl moiety, all calculated as thiacloprid.

2. *Analytical method.* The analytical method for determining residues in pome fruit and cotton samples is a common moiety method for thiacloprid and its metabolites containing the 6-chloro-pyridinyl moiety. This method utilizes oxidation, derivatization, and analysis by capillary gas chromatography with a mass-selective (MS) detector. There is a confirmatory method specific for thiacloprid and several metabolites utilizing high performance liquid chromatography (HPLC) with Electrospray MS/MS-detection. This HPLC/MS-MS method was used for analysis of the stone fruit samples. Thiacloprid and its metabolites are stable in cotton and pome fruit commodities for at least 24 months and in stone fruit commodities for at least 10 months when the commodities are frozen.

3. *Magnitude of residues—Cotton—*Field trials were conducted with cotton in 12 different locations, representing 6 different EPA regions. Three foliar applications were made to mature cotton plants at a rate of 0.1 lb active ingredient/acre (a.i./A) with 3 to 11 days between applications. The pre-harvest interval (PHI) ranged from 12 to 20 days. The highest average field trial was 0.73 ppm in undelinted cotton seed. For gin trash, the HAFI residue was 10.10 ppm. The processing study, conducted with cottonseed, indicated no concentration in any cottonseed processed commodities.

*Pome fruit (apple/pear)—*A total of 18 field trials (12 apple and 6 pear) were conducted in 6 different EPA regions. Applications were made as ground-based foliar sprays at 0.25 lb ai/A with 6- to 8-day intervals. The highest residue at 30-day PHI was 0.277 ppm, in apples. The highest residue at a 45-day PHI was 0.258 ppm, occurring in pears. Although residues in pome fruit

did not consistently decline in relation to sampling intervals, residues were generally lower at the longer PHI (45 days) in harvest experiments. In the apple processing study, residues concentrated in the wet pomace (1.8X) but did not concentrate in the apple juice. A home processing study indicated significant reduction in residues.

*Stone fruits (sweet cherry/peach/plum)—*A total of 24 field trials (7 sweet cherry, 11 peach, and 6 plum) were conducted in different EPA regions (3 for sweet cherry, 7 for peach, and 3 for plum). Applications were made as ground-based foliar sprays at 0.25 lb ai/A with 6- to 8-day intervals. The highest residue at the 14-day PHI was 0.423 ppm, in peaches. The highest residue at a 28-day PHI was 0.359 ppm, occurring in peaches. Residues in stone fruit raw agricultural commodities (RACs) consistently declined in relation to sampling intervals, with lower residues at the longer PHI (28 days).

B. Toxicological Profile

1. *Acute toxicity.* The acute oral LD₅₀ values for thiacloprid technical ranged from 444 (female) to 836 (male) milligram/kilogram (mg/kg) in the rat. The acute dermal LD₅₀ was greater than 2,000 mg/kg in rats. The 4-hour rat inhalation LD₅₀ ranged from 1,223 (female) to >2,535 (male) mg/meter cubed (m³) air (aerosol). Thiacloprid was not irritating to rabbit skin or eyes. Thiacloprid did not cause skin sensitization in guinea pigs.

2. *Genotoxicity.* Extensive mutagenicity studies conducted to investigate point and gene mutations, DNA damage and chromosomal aberration show thiacloprid to be non-genotoxic.

3. *Reproductive and developmental toxicity.* In a 2-generation reproduction study, Sprague-Dawley rats were administered dietary levels of thiacloprid at levels of 0, 50, 300, and 600 ppm. The no-observed-adverse-effect-levels (NOAELs) for reproductive parameters was established at 50 ppm, based on increased liver and thyroid weight gains in the parental and F1 generations. A developmental toxicity study was conducted with Wistar rats gavaged at 0, 2, 10, and 50 mg/kg. The following NOAELs were determined: Maternal toxicity, 10 mg/kg/day and developmental toxicity, 10 mg/kg/day. A developmental toxicity study was conducted with rabbits treated orally by gavage at 0, 2, 10, and 45 mg/kg. The following NOAELs were determined: Maternal toxicity, 2 mg/kg/body weight (bwt)/day and developmental toxicity, 2 mg/kg/day. From the developmental

toxicity studies in rats and rabbits, no primary developmental toxic potential could be derived. Additionally, a developmental neurotoxicity study was conducted at dietary doses of 0, 50, 300, or 500 ppm in the female Sprague-Dawley rat. The targeted concentration of 50 ppm was considered a NOAEL for maternal toxicity and the F1 offspring. No specific neurobehavioral effects in the offspring were identified up to and including the highest dose tested of 500 ppm.

4. *Subchronic toxicity.* 90-day feeding studies were conducted in rats, mice, and dogs. In the subchronic rat and dog studies, the demonstrated NOAELs were 25 ppm and 1,000 ppm, respectively. The subchronic mouse study did not demonstrate a NOAEL at the lowest level (50 ppm) tested.

5. *Chronic toxicity.* A 2-year rat chronic toxicity/oncogenicity study demonstrated a NOAEL of 25 ppm. Liver enzyme induction occurred at doses of > 50 ppm. A 2-year mice oncogenicity demonstrated a NOAEL at the lowest dose of 30 ppm. A 1-year chronic toxicity study in dogs demonstrated a NOAEL of 250 ppm, with slight prostatic weight increases in some of the 1,000 ppm animals (possibly due to different maturation in the animals) being the only treatment-related findings. There is significant evidence that thiacloprid is not acting through a genetic mechanism (all genotoxicity studies are negative). Thiacloprid should be managed using a margin-of-exposure extrapolation. The dose response to thiacloprid shows the following pattern: First, at lower dose levels, thiacloprid induces liver enzymes. At moderate dose levels in animals, it increases liver enzymes and aromatase is induced. At the highest dose levels, repeated administration of thiacloprid induces liver enzymes, including aromatase, which leads to hormonal effects such as elevated estrogen levels, which indirectly cause uterine tumors in rats and ovarian luteomas in mice. High-dose thyroid tumors seen in the chronic rat study were determined to be related to thyroid hormone imbalance and not a direct effect of thiacloprid.

6. *Animal metabolism.* In animals, parent thiacloprid was the major component in all edible tissues, milk, and eggs. All residues and metabolites in the animal tissues contained the 6-chloro-pyridinyl moiety, same as in the plant tissues. Therefore, the residues of concern are the combined residues of thiacloprid and its metabolites containing the 6-chloro-pyridinyl moiety, all calculated as thiacloprid.