

passion fruit, and acerola). IR-4 received a request from Florida for the use of imidacloprid on guava. Magnitude of the residue data were collected from Florida on guava to support a tolerance on guava and related crops.

- *Corn, pop.* No crop-specific data were submitted with the petition proposing imidacloprid tolerances on popcorn. IR-4 proposes that EPA translates residue data from field corn to popcorn in order to establish the requested tolerances.

- *Mustard seed.* No crop-specific data are being submitted with this petition proposing an imidacloprid tolerance on mustard seed. IR-4 proposes that EPA translates residue data from canola to mustard seed in order to establish the tolerance based upon the botanical and cultural similarities of the crops. Additionally, Canada has a crop group for oil seeds (crop group 20) which contains mustard seed and has canola as one of the representative commodities.

#### B. Toxicological Profile

EPA has evaluated the available imidacloprid toxicity data and considered its validity, completeness, and reliability as well as the relationship of the results of the studies to human risk. EPA has also considered available information concerning the reliability of the sensitivities of major identifiable subgroups of consumers, including infants and children. The nature of the toxic effects caused by imidacloprid is discussed in Unit II.A. of the final rule on imidacloprid pesticide tolerances published in the **Federal Register** of September 18, 1998 (63 FR 49837) (FRL-6027-1). Please refer to this document should you desire detailed toxicological information on imidacloprid.

1. *Animal metabolism.* The metabolism of NTN 33893 (imidacloprid) in rats was reported in seven studies. The data show that imidacloprid was rapidly absorbed and eliminated in the excreta (90% of the dose within 24 hours), demonstrating no biologically significant differences between sexes, dose levels, or route of administration. Elimination was mainly renal (70–80% of the dose) and fecal (17–25%). The major part of the fecal activity originated in the bile. Total body accumulation after 48 hours consisted of 0.5% of the radioactivity with the liver, kidney, lung, skin, and plasma being the major sites of accumulation. Therefore, bioaccumulation of imidacloprid is low in rats. Maximum plasma concentration was reached between 1.1 and 2.5 hours.

Two major routes of biotransformation were proposed for imidacloprid. The first route included an oxidative cleavage of the parent compound rendering 6-chloronicotinic acid and its glycine conjugate. Dechlorination of this metabolite formed the 6-hydroxynicotinic acid and its mercapturic acid derivative. The second route included the hydroxylation followed by elimination of water of the parent compound rendering NTN 35884. A comparison between [methylene-<sup>14</sup>C]-imidacloprid and [imidazolidine-4,5-<sup>14</sup>C]imidacloprid showed that while the rate of excretion was similar, the renal portion was higher with the imidazolidine-labeled compound. In addition, accumulation in tissues was generally higher with the imidazolidine-labeled compound.

A comparison between imidacloprid and one of its metabolites, WAK 3839, showed that the total elimination was the same for both compounds. The proposed metabolic pathways for these two compounds were different. WAK 3839 was formed following pretreatment (repeated dosing) of imidacloprid.

2. *Endocrine disruption.* The toxicology data base for imidacloprid is current and complete. Studies in this data base 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. These studies revealed no primary endocrine effects due to imidacloprid.

#### C. Aggregate Exposure

1. *Dietary exposure.* Assessments were conducted to evaluate potential risks due to chronic and acute dietary exposure of the U.S. population and selected population subgroups to residues of imidacloprid. These analyses cover all registered crops including rotational crops; uses pending with EPA Registration Division's 2002 work plan including dry beans, peas, bushberries, lingonberry, junberries, salal, carrots, turnips, okra, cranberries, artichoke (globe), watercress, beet roots, leaves of root and tuber vegetables, stone fruit, mamey sapote, guava, feijoa, jaboticaba, wax jambu, starfruit, passion fruit, acerola, strawberry, cucumber (greenhouse), and tomato (greenhouse), and an import tolerance petition on bananas, active and proposed section 18 uses on blueberries, cranberries, table beets, strawberries and turnips.

Novigen sciences, Inc.'s Dietary Exposure Evaluation Model (DEEM™), which is licensed to Bayer Corporation, was used to estimate the chronic and acute dietary exposure. This software uses the food consumption data from

the 1994–1998 United States Department of Agriculture (USDA) Continuing Surveys of Food Intake by Individuals (CSFII).

The endpoint for acute dietary risk assessments is based on neurotoxicity characterized by decreases in motor or locomotor activity in female rats at 42 milligrams/kilogram body weight/day (mg/kg bwt/day) (the lowest observed adverse effect level (LOAEL) from an acute neurotoxicity study). Based on an uncertainty factor (UF) of 10x for interspecies and 10x for intraspecies, the acute reference dose (RfD) = 0.42 mg/kg bwt/day. EPA has determined that an additional UF for FQPA (reduced to 3x) applies to all population subgroups for acute risk. Application of the additional 3x safety factor results in an acute population adjusted dose (aPAD) 0.14 mg/kg bwt/day or a margin of exposure (MOE) of 300.

For chronic dietary analyses, EPA has established the RfD for imidacloprid at 0.057 mg/kg/day based on a no-observed adverse effect level (NOAEL) of 5.7 mg/kg bwt/day from a rat chronic toxicity carcinogenicity study and UF of 10x for interspecies and 10x for intraspecies. EPA has determined that an additional UF for FQPA (reduced to 3x) applies to all population subgroups for chronic risk. Application of the additional 3x safety factor results in a chronic population adjusted dose (cPAD) of 0.019 mg/kg bwt/day.

The registrant believes that results from the acute and chronic dietary exposure analyses described below demonstrate a reasonable certainty that no harm to the overall U.S. population or any population subgroup will result from the use of imidacloprid on currently registered and pending uses.

- i. *Food.* Acute and chronic (Tier 3) risk assessments were made using the results of field trials conducted at maximum label application rates and the shortest pre-harvest intervals. For some of the vegetable crops, the residue data were collected at 1.5x or greater than the maximum label rate of 0.5 lb active ingredient/acre per season. In addition, no adjustments were made to account for dissipation of residues during storage, transportation from the field to the consumer, washing or peeling. Therefore, the actual dietary exposure will be less than that presented here.

For the chronic analysis, mean field trial residues were calculated. For the acute Monte Carlo analysis, the entire distribution of residue field trial data were used for the “non-blended” and “partially blended” foods as determined by EPA's standard operating procedure (SOP) 99.6. For the foods considered as