UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: 04-MAR-2003

SUBJECT: PP#: 2E06409, 1E06254, 2E06506, 2E06406, 2E06435, 0E06203, 2E06414, 1E06237, 2E06458, 1E06074, 1E06225, 1E06268, 2E06421, 2E06417, and 2E06403. **Imidacloprid in/on Cranberry; Okra; Pop corn; Watercress; Guava, Papaya, Lychee, Avocado and Related Commodities; Root and Tuber Vegetables (Except Sugar Beets); Leaves of Root and Tuber Vegetables; Artichoke; Bushberry; Lingonberry; Juneberry; Salal; Legume Vegetables (Except Soybeans); Strawberry and Stonefruit. Health Effects Division (HED) Risk Assessment.** PC Code: 129099. DP Barcodes: D286101, D284746, D282414, D280766, D278760, D286722, D280447, and D285741. Case Nos: 294780, 294878, 295092, 294718, 293672, 295556, 294698, and 295477. Submissions: S610446, S619730, S614175, S609878, S605370, S624899, S609033, and S622162.

FROM: Jennifer R. Tyler, Chemist
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THRU: G. Jeffrey Herndon, Branch Senior Scientist
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TO: Robert Forrest/Shaja Brothers, PM Team 05
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Insecticide/Rodenticide Branch (IRB)/RD (7505C)

The HED of the Office of Pesticide Programs (OPP) is charged with estimating the risk to human health from exposure to pesticides. The RD of OPP has requested that HED evaluate hazard and exposure data and conduct dietary, occupational, residential and aggregate exposure assessments, as needed, to estimate the risk to human health that will result from proposed uses of imidacloprid [1-[(6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine] on cranberries; okra; pop corn; watercress; guava, papaya, lychee, avocado and related commodities; root and tuber vegetables (except sugar beets); leaves of root and tuber vegetables; artichokes;

bushberries; lingonberries; juneberries; salal; legume vegetables (except soybeans); strawberries and stonefruit.

A summary of the findings and an assessment of human risk resulting from the registered and proposed tolerances for imidacloprid is provided in this document. The risk assessment, the residue chemistry data review, and the dietary risk assessment were provided by Jennifer Tyler (RAB1), the hazard characterization by David Nixon (RAB1), the occupational/residential exposure assessment by Mark Dow (RAB1), and the drinking water assessment by Mike Barrett of the Environmental Fate and Effects Division (EFED).

Recommendation for Tolerances

The HED Hazard Identification Assessment Review Committee (HIARC) requested a 28-day inhalation toxicity study as a condition of registration. However, based on the low volatility and low inhalation toxicity (Category IV) of imidacloprid and inhalation margins of exposure (MOEs) >1000 for the proposed uses in this risk assessment, imidacloprid qualifies for a waiver of the 28-day inhalation toxicity study for the proposed uses [HED Standard Operating Procedure (SOP) 2002.01: *Guidance: Waiver Criteria for Multiple-Exposure Inhalation Toxicity Studies*, 08/15/02]. **The requirement for the 28-day inhalation toxicity study is waived for this action only.** If in the future, requests for new uses or formulations are submitted that may result in a significant change in either the toxicity profile or exposure scenarios, HED will reconsider this data requirement.

Provided revised Sections B and F with the modifications specified in Section 9.1 of this risk assessment are submitted, the residue chemistry and toxicological databases support the following (see Attachment 3 for a detailed listing of the HED-recommended tolerances):

1) the establishment of *unconditional registrations* and permanent tolerances for residues of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as the parent, in/on artichoke at 2.5 ppm; bushberry subgroup 13B, juneberry, lingonberry, salal at 3.5 ppm; fruit, stone, group 12 at 3.0 ppm; vegetable, legume, except soybean, group 6 at 4.0 ppm; strawberry at 0.50 ppm; corn, pop, grain at 0.05 ppm; corn, pop, stover at 0.20 ppm; cranberry at 0.05 ppm; mustard, seed at 0.05 ppm; okra at 1.0 ppm; watercress at 3.5 ppm; papaya, star apple, black sapote, mango, sapodilla, canistel, and mamey sapote at 1.0 ppm; guava, feijoa, jaboticaba, wax jambu, starfruit, passionfruit, and acerola at 1.0 ppm; vegetable, root and tuber, except sugar beet, group 1 at 0.4 ppm; and vegetable, leaves of root and tuber, group 2 at 4.0 ppm.

2) the establishment of *conditional registrations* and permanent tolerances for residues of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as the parent, in/on lychee, longan, Spanish lime, rambutan, pulasan, persimmon at 3.0 ppm and avocado at 1.0 ppm. The registration on lychee and related commodities should be made unconditional upon submission of residue data on lychee. The registration on avocado should be made unconditional upon official submission of residue data on avocado.

3) the establishment of an *unconditional registration* and a permanent tolerance for residues of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as the parent, in/on *imported* banana at 0.02 ppm.

Notes to RD:

- The tolerances for the following commodities under Section (a) of 40 CFR §180.472 should be deleted, as they will be covered under tolerances being recommended for in this risk assessment: bean, edible, podded; bean, succulent, shelled; dasheen, leaves; mango; potato chips; potato; turnip, greens; vegetable, tuberous and corm, subgroup; and watercress, upland.
- The tolerance for "apple" under Section (a) of 40 CFR §180.472 should be deleted, as it is included in "fruit, pome, crop group."
- The tolerance for "lettuce, head and leaf" under Section (a) of 40 CFR §180.472 should be deleted, as it is included in "leafy green subgroup."
- The time-limited tolerances for the following commodities under Section (b) of 40 CFR §180.472 should be deleted: blueberry; fruit, stone; plum, prune; strawberry; and vegetable, legume. The Section 18 Emergency Exemption use patterns for these commodities are the same as those being proposed in this risk assessment. In addition, these commodities will be covered under tolerances being recommended for in this risk assessment.
- The time-limited tolerances for "vegetable, legume" under Section (b) of 40 CFR §180.472 should be deleted, as they will be covered under the recommended tolerance for "vegetable, legume, except soybean, group 6." If a Section 18 Emergency Exemption use is requested for soybeans, then a time-limited tolerance on "soybean" should be established at 1.0 ppm.
- Language should be added to Section (a) of 40 CFR 180.472 specifying that "There are no U.S. registrations for banana as of *[date of Federal Register publication]*."

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1.0 EXECUTIVE SUMMARY

Imidacloprid is a systemic insecticide registered to control soil insects, sucking insects, chewing insects, and termites. It is effective against the larval, nymphal and adult stages. The primary mode of action is the disruption of the nervous system by acting as an inhibitor at nicotinic acetylcholine receptors. Imidacloprid blocks the signals that are induced by acetylcholine at the post-synaptic membrane, resulting in nerve function impairment.

The Interregional Research Project No. 4 (IR-4), on behalf of Agricultural Experiment Stations of several states, has submitted petitions for the registration of imidacloprid for use on cranberries; okra; pop corn; watercress; guava, papaya, lychee, avocado and related commodities; root and tuber vegetables (except sugar beets); leaves of root and tuber vegetables; artichokes; bushberries; lingonberries; juneberries; salal; legume vegetables (except soybeans); strawberries and stonefruit. The proposed registrations are amendments to the following currently registered products: Provado® 1.6 Flowable (F) (EPA Reg. No. 3125-457), a 1.6 lb active ingredient (a.i.)/gal liquid product intended for foliar applications; Admire® 2F (EPA Reg. No. 3125-422), a 2.0 lb. ai/gal liquid product intended for soil applications; Gaucho® 480 FS (EPA Reg. No. 7501-155), a 4.0 lb. ai/gal liquid product intended for use as a seed treatment; and Gaucho® 600 F (EPA Reg. No. 7501-173), a 5.0 lb. ai/gal liquid product intended for use as a seed treatment. In conjunction with these petitions, IR-4 has requested the establishment of permanent tolerances of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as the parent, in/on the aforementioned raw agricultural commodities (RACs).

In addition, Bayer Corporation has submitted a petition for permanent tolerances for residues of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as the parent, in/on imported bananas. The following products are used on bananas in Columbia, Costa Rica, Ecuador, Guatemala, and Honduras: Confidor® 70 Wettable Granular (WG; No EPA Reg. No.; 70% a.i.) and Confidor® 350 Suspension Concentration (SC; No EPA Reg. No.; 35% a.i.).

According to the OPP Reference Files System (REFS, M. Dow, 5/7/02), there are currently 82 registered products (excluding Section 18 registrations) containing imidacloprid as the a.i.. Imidacloprid is the a.i. in several agricultural products, ornamental turf/plant products, seed treatments, pet care products, as well as structural pest products.

The most recent Section 3 HED human health risk assessments were conducted in conjunction with petitions for the use of imidacloprid as a wood treatment (Memo, Y. Donovan, 3/12/01; D251355), and on edible podded/succulent shelled beans; turnip greens; cilantro; and sweet/field corn (Memo, Y. Donovan, 1/22/01; D267168). Since the completion of these risk assessments, the following has occurred: 1) submission of a developmental neurotoxicity (DNT) study; 2) a revisit to HED HIARC on 10/8/02, where incidental oral and dermal endpoints were selected; and 3) in accordance with the February 2002 OPP 10X guidance document, a revisit of the FQPA Safety Factor (SF) to evaluate the potential for increased susceptibility of infants and children to exposure to imidacloprid.

Hazard Assessment

Imidacloprid has low acute toxicity via the dermal and inhalation routes and moderate acute toxicity via the oral route. It is not an eye or dermal irritant and is not a dermal sensitizer. The nervous system is the primary target organ of imidacloprid. Nervous system effects evidenced as changes in clinical signs and Functional Observation Battery (FOB) assessments were seen in rat acute and subchronic neurotoxicity studies. These effects included decreased motor and locomotor activities, tremors, gait abnormalities, increased righting reflex impairments and body temperature, decreased number of rears and response to stimuli and decreases in forelimb and hindlimb grip strength. Also, in the rat developmental neurotoxicity study, a decrease in the caudate/putamen width was noted in female pups. Retinal atrophy was seen in high-dose females in the rat combined chronic toxicity/carcinogenicity study. No nervous system effects were noted in the mouse carcinogenicity or the reproduction and developmental studies or in the rabbit dermal or rat inhalation studies. The dog was less sensitive to the effects of imidacloprid. No effects were noted up to the highest dose tested in the chronic toxicity study. The rabbit appeared to be very sensitive as there was increased mortality in the oral developmental study at the highest dose tested. Increased incidence of mineralized particles in the thyroid colloid was noted in the rat combined chronic toxicity/carcinogenicity study. Body weight decrements were noted in the rat and/or mouse chronic and carcinogenicity studies, the rat subchronic neurotoxicity study, and the developmental, developmental neurotoxicity and reproduction studies. No effects were observed in the rabbit dermal or rat inhalation studies. There was no evidence of carcinogenic potential in either the rat chronic toxicity/carcinogenicity or mouse carcinogenicity studies and no concern for mutagenicity. There was no evidence of increased qualitative or quantitative susceptibility of rats or rabbits to *in utero* exposure to imidacloprid and no evidence of qualitative or quantitative increased susceptibility of rat offspring in the reproduction study. There was evidence of an increased qualitative susceptibility in the rat developmental neurotoxicity study. At the highest dose tested, maternal effects consisted largely of slight decreases in food consumption and body weight gain during early lactation, while pup effects included decreased body weight; decreased motor activity; decreased caudate/putamen width, females only [postnatal days (PNDs) 11 and adult]; and slight changes in performance in the water maze, males only, at the same dose.

On 11/10/93, the Reference Dose (RfD)/Peer Review Committee classified imidacloprid as a "Group E" chemical, no evidence of carcinogenicity for humans, by all routes of exposure based upon lack of evidence of carcinogenicity in rats and mice.

Dose Response Assessment and Food Quality Protection Act (FQPA) Decision

As mentioned previously, the HED HIARC met on 10/8/02 to select endpoints for risk assessment and to evaluate the potential for increased susceptibility of infants and children from exposure to imidacloprid according to the February 2002 OPP 10X guidance document. This was a re-evaluation of the toxicology database subsequent to the initial evaluation by the HIARC on 9/11/97. The special FQPA SF was reduced to 1x based on toxicological considerations by the HIARC (10/31/02; TXR # 0051292), the conservative residue assumptions used in the dietary and residential exposure risk assessments, and the completeness of the residue chemistry and environmental fate databases (evaluated by the risk assessment team).

Risk assessments were conducted for the following specific exposure scenarios listed below. The acute RfD (aRfD) was calculated by dividing the Lowest-Observed-Adverse-Effect-Level (LOAEL) by 300 [10X for interspecies extrapolation, 10X for intraspecies variation; and 3X uncertainty factor (UF) for the use of a LOAEL due to the lack of a No-Observed-Adverse-Effect-Level (NOAEL) in the acute neurotoxicity study]. The cRfD was calculated by dividing the NOAEL by 100 (10X for interspecies extrapolation, 10X for intraspecies variation). Since the special FQPA SF has been reduced to 1X, the acute and chronic population adjusted doses (aPAD and cPAD) are equal to the aRfD and cRfD, respectively. Since oral studies were selected for all durations of dermal and inhalation exposure, a 7% dermal absorption factor and a 100 % inhalation absorption factor are used in the route-to-route extrapolation. The level of concern for occupational dermal and inhalation exposures are for MOEs <100. For the occupational exposure assessment, dermal and inhalation exposure estimates can be combined because oral equivalent doses were used for these routes of exposure. The level of concern for residential oral, dermal and inhalation exposures are for MOEs <100. Short-term oral, dermal and inhalation exposure estimates can be aggregated because of the use of the same toxicity endpoint (decreased body weight gain) from the same study (oral rat developmental toxicity study).

Exposure Scenario	Dose	Endpoint	Study/Effect
Acute dietary	LOAEL = 42 mg/kg/day	aRfD and aPAD = 0.14 mg/kg/day	Decreased motor and locomotor activities/Acute neurotoxicity study in rats
Chronic dietary	NOAEL = 5.7 mg/kg/day	cRfD and cPAD = 0.057 mg/kg/day	Increased incidence of mineralized particles in the thyroid colloid/Chronic toxicity study in rats
Short-term oral	Oral NOAEL = 10 mg/kg/day	Target MOE = 100 (residential)	Decreased body weight gain and decreased corrected body weight gain in maternal animals/ Developmental toxicity study in rats
Short-term dermal	Oral NOAEL = 10 mg/kg/day	Target MOE = 100 (occupational and residential)	
Short-term inhalation	Oral NOAEL = 10 mg/kg/day	Target MOE = 100 (occupational and residential)	

Residential Exposure Estimates

HED has determined that residential handlers are likely to be exposed to imidacloprid residues via dermal and inhalation routes during handling, mixing, loading, and applying activities. In addition, there is potential for post-application exposure to adults (dermal route) and children/toddlers (dermal and incidental oral routes) from the many residential uses of imidacloprid. Due to the low vapor pressure of imidacloprid, post-application inhalation exposure is expected to be negligible. Based on the current use patterns, HED expects the duration of exposure to be short-term (1-30 days).

All residential handler and post-application exposures and risks resulted in MOEs of > 100; and, therefore, do not exceed HED's level of concern. The residential handler assessment is based upon the residential SOPs in conjunction with chemical-specific study data, and PHED unit exposures. The majority of the residential post-application assessment is based upon chemical-specific turf transferable residue (TTR) data or other chemical-specific post-application exposure study data. The chemical-specific study data as well as the surrogate study data used are reliable and also are not expected to underestimate risk to adults as well as to children. In a few instances where chemical-specific data were not available, the residential SOPs were used alone. As the

residential SOPs are based upon reasonable "worst-case" assumptions, they are not expected to underestimate risk.

Dietary Exposure Estimates
Acute and chronic dietary exposure analyses were conducted using the Dietary Exposure Evaluation Model-Food Commodity Intake Database (DEEM-FCID™; ver. 1.30) program which incorporates consumption data from the United States Department of Agriculture's (USDA's) Continuing Surveys of Food Intakes by Individuals (CSFII), 1994-1996/1998. For acute and chronic dietary risk estimates, HED's level of concern is for estimates that exceed 100% aPAD or cPAD, respectively.

A Tier 1 [conservative, deterministic assessment using tolerance-level residues, 100% crop treated (CT) information for registered and proposed commodities; and modified DEEM™ (version 7.76) processing factors for some commodities based on guideline processing studies] acute dietary exposure assessment was conducted for the general U.S. population and various population subgroups. The acute dietary exposure estimates are below HED's level of concern (<100% aPAD) at the 95th exposure percentile for the general U.S. population (25% of the aPAD) and all other population subgroups. The most highly exposed population subgroup is children 1-2 years old, at 64% of the aPAD. The acute assessment was highly conservative, using several upper-end assumptions. Inclusion of anticipated residues (ARs) and % CT data could be made in order to refine the acute dietary assessment.

A Tier 2 [partially refined, deterministic assessment using tolerance-level residues, and average weighted % CT information from Biological and Economical Analysis Division (BEAD) and modified DEEM™ (version 7.76) processing factors for some commodities based on guideline processing studies] chronic dietary exposure assessment was conducted for the general U.S. population and various population subgroups. The chronic dietary exposure estimates are below HED's level of concern (<100% cPAD) for the general U.S. population (11% of the cPAD) and all population subgroups. The most highly exposed population subgroup is children 1-2 years old, at 35% of the cPAD. The chronic assessment was conservative, using several upper-end assumptions. Additional refinements, such as inclusion of ARs and additional % CT information could be made in order to refine the chronic dietary assessment.

Drinking Water Exposure Estimates
Per the recommendations of the HED Metabolism Assessment Review Committee (MARC), EFED provided drinking water estimated environmental concentration (EECs) for imidacloprid and its degradates (imidacloprid urea, imidacloprid guanidine, and imidacloprid olefin). The Tier 1, FQPA Index Reservoir Screening Tool (FIRST) and Screening Concentration in Ground Water (SCI-GROW) models were used to derive the surface and ground water EECs, respectively. In the absence of definitive data on the persistence and mobility of the degradates (imidacloprid urea, imidacloprid guanidine, and imidacloprid olefin), the total residues were modeled using tentatively identified total residue data from aerobic soil metabolism studies, and then assuming that the partitioning of all residues was at the same degree as imidacloprid parent. Degradate persistence and mobility data (especially from aerobic soil metabolism and batch equilibrium adsorption/desorption studies) are needed to more accurately model the total residues. However, EFED does not expect these to be exceeded under real-world usage

conditions. Application to citrus fruits provided the highest exposure scenario; and, therefore, the drinking water EECs were derived for this use.

For surface water, the acute (peak) and chronic (annual average) EECs are 36.04 ppb and 17.24 ppb, respectively. The acute and chronic ground water EEC is 2.09 ppb. All EEC values are less than the lowest drinking water level of comparison (DWLOC) values of 510 ppb, 410 ppb, and 370 ppb (specifically for the "children 1-2 years old" population subgroup) determined for the acute, short-term, and chronic scenarios, respectively. Therefore, the EECs do not exceed HED's level of concern.

Aggregate Exposure Scenarios and Risk Conclusions
For the proposed uses, human health aggregate risk assessments have been conducted for the following exposure scenarios: acute aggregate exposure (food + drinking water), short-term aggregate exposure (food + drinking water + residential), and chronic aggregate exposure (food + drinking water). Intermediate- and long-term aggregate risk assessments were not performed because, based on the current use patterns, HED does not expect exposure durations that would result in intermediate- or long-term exposures. A cancer aggregate risk assessment was not performed because imidacloprid is not carcinogenic. All potential exposure pathways were assessed in the aggregate risk assessment. Dietary (food and drinking water), handler and post-application residential exposures were considered, as necessary, because there is a potential for individuals to be exposed concurrently through these routes. **All aggregate exposure and risk estimates do not exceed HED's level of concern for the scenarios listed above.**

Occupational Exposure Estimates
Based on the proposed use patterns, short-term (1-30 days) dermal and inhalation exposures are expected for commercial and private (i.e., grower operators) applicators. The application techniques that are assessed include aerial, ground-boom open-cab, air-blast open cab, and high-pressure hand-wand. No chemical-specific data are available with which to assess potential exposure to pesticide handlers (i.e., mixer/loaders and applicators). Therefore, estimates of exposure are based on study data available in the Pesticide Handler Exposure Database Version 1.1 (PHED, Surrogate Exposure Guide, 8/98). In addition, as there are no chemical-specific data with which to assess exposure to persons involved in the commercial treatment of seeds using imidacloprid, HED used the results of a proprietary study.

Short-term (1-30 days) dermal exposures are expected for post-application agricultural activities. Post-application inhalation exposure is expected to be negligible. There are no chemical-specific data with which to estimate post-application exposure of agricultural workers to dislodgeable residues of pesticide. Therefore, post-application worker exposure is estimated using HED procedure that assumes 20% of the application rate is available as dislodgeable foliar residue (DFR) on the day of treatment. The HED Science Advisory Council for Exposure (ExpoSAC; Policy 003.1, Rev. 7 Aug. 2000, Regarding Agricultural Transfer Coefficients; Amended ExpoSAC Meeting notes - 13 Sept 01) lists a number of possible post-application agricultural activities relative to some of the subject crops that result in potential pesticide exposure to agricultural workers. The activities related to high-bush blueberries (hand harvesting fruit, and pruning and training vines) are reported as having the highest (i.e., most conservative) possibility of transferring foliar dislodgeable pesticide residues to humans.

Since the HED ExpoSAC asserts that there is a possibility that commercial agricultural workers might be exposed to intermediate-term handler and post-application exposures, HED calculated exposures and risks which represent both short/intermediate-term (1 day-6 months) durations. Provided commercial pesticide handlers use label-prescribed personal protective equipment (PPE) (i.e., long pants, long-sleeved shirt, shoes + socks and the respective protective gloves), all MOEs are >100. In addition, all occupational post-application MOEs are >100. Therefore, handler inhalation and dermal, and post-application dermal exposure is not of concern for agricultural workers.

The interim Worker Protection Standard (WPS) restricted entry interval (REI) is 12 hours, based on Toxicity Category IV for acute dermal, acute inhalation, primary eye irritation and primary skin irritation. This REI is sufficient to protect workers.

Recommendations for Tolerances

The HED HIARC requested a 28-day inhalation toxicity study as a condition of registration. However, based on the low volatility and low inhalation toxicity (Category IV) of imidacloprid and inhalation MOEs >1000 for the proposed uses in this risk assessment, imidacloprid qualifies for a waiver of the 28-day inhalation toxicity study for the proposed uses [SOP 2002.01: *Guidance: Waiver Criteria for Multiple-Exposure Inhalation Toxicity Studies*, 08/15/02]. **The requirement for the 28-day inhalation toxicity study is waived for this action only.** If in the future, requests for new uses or formulations are submitted that may result in a significant change in either the toxicity profile or exposure scenarios, HED will reconsider this data requirement.

Provided revised Sections B and F with the modifications specified in Section 9.1 of this risk assessment are submitted, the residue chemistry and toxicological databases support the following (see Attachment 3 for a detailed listing of the HED-recommended tolerances):

1) the establishment of *unconditional registrations* and permanent tolerances for residues of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as the parent, in/on artichoke at 2.5 ppm; bushberry subgroup 13B, juneberry, lingonberry, salal at 3.5 ppm; fruit, stone, group 12 at 3.0 ppm; vegetable, legume, except soybean, group 6 at 4.0 ppm; strawberry at 0.50 ppm; corn, pop, grain at 0.05 ppm; corn, pop, stover at 0.20 ppm; cranberry at 0.05 ppm; mustard, seed at 0.05 ppm; okra at 1.0 ppm; watercress at 3.5 ppm; papaya, star apple, black sapote, mango, sapodilla, canistel, and mamey sapote at 1.0 ppm; guava, feijoa, jaboticaba, wax jambu, starfruit, passionfruit, and acerola at 1.0 ppm; vegetable, root and tuber, except sugar beet, group 1 at 0.4 ppm; and vegetable, leaves of root and tuber, group 2 at 4.0 ppm.

2) the establishment of *conditional registrations* and permanent tolerances for residues of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as the parent, in/on lychee, longan, Spanish lime, rambutan, pulasan, persimmon at 3.0 ppm and avocado at 1.0 ppm. The registration on lychee and related commodities should be made unconditional upon submission of residue data on lychee. The registration on avocado should be made unconditional upon official submission of residue data on avocado.

3) the establishment of an *unconditional registration* and a permanent tolerance for residues of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as the parent, in/on *imported* banana at 0.02 ppm.

Notes to RD:

- The tolerances for the following commodities under Section (a) of 40 CFR §180.472 should be deleted, as they will be covered under tolerances being recommended for in this risk assessment: bean, edible, podded; bean, succulent, shelled; dasheen, leaves; mango; potato chips; potato; turnip, greens; vegetable, tuberous and corm, subgroup; and watercress, upland.
- The tolerance for "apple" under Section (a) of 40 CFR §180.472 should be deleted, as it is included in "fruit, pome, crop group."
- The tolerance for "lettuce, head and leaf" under Section (a) of 40 CFR §180.472 should be deleted, as it is included in "leafy green subgroup."
- The time-limited tolerances for the following commodities under Section (b) of 40 CFR §180.472 should be deleted: blueberry; fruit, stone; plum, prune; strawberry; and vegetable, legume. The Section 18 Emergency Exemption use patterns for these commodities are the same as those being proposed in this risk assessment. In addition, these commodities will be covered under tolerances being recommended for in this risk assessment.
- The time-limited tolerances for "vegetable, legume" under Section (b) of 40 CFR §180.472 should be deleted, as they will be covered under the recommended tolerance for "vegetable, legume, except soybean, group 6." If a Section 18 Emergency Exemption use is requested for soybeans, then a time-limited tolerance on "soybean" should be established at 1.0 ppm.
- Language should be added to Section (a) of 40 CFR 180.472 specifying that "There are no U.S. registrations for banana as of *[date of Federal Register publication]*."

2.0 PHYSICAL/CHEMICAL PROPERTIES CHARACTERIZATION

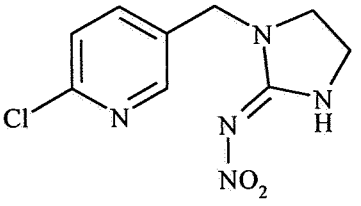
2.1 Identification of Active Ingredient

Registrant:	IR-4, Bayer
Common name:	Imidacloprid
Pesticide Type:	Insecticide
Chemical Class:	Pyridylmethylamine (acetamiprid, imidacloprid, nitenpyram, thiacloprid)
Target Pests:	Aphids, cucumber beetles and whiteflies (including Sweet potato or Silverleaf whitefly)
Mode of Action:	Disrupts the nervous system as an inhibitor at nicotinic acetylcholine receptors. It blocks the signals that are induced by acetylcholine at the post-synaptic membrane, resulting in nerve function impairment.
Formulations:	2 lb ai/gal; 1.6 lb ai/gal; 4 lbs ai/gal; 5 lb ai/gal
% a.i.:	21.4%; 17.4%; 40.7%; 48.7%
Trade Names:	Admire™ 2 Flowable; Provado® 1.6 Flowable; Gaucho 480® Flowable; Gaucho® 600 Flowable
EPA Reg Nos.:	3125-422; 3125-457; 7501-155; 7501-173
CAS Number:	13826-41-3
PC Code:	129099
Chemical name:	1-[(6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine
Empirical Formula:	$C_9H_{10}ClN_5O_2$
Molecular Weight:	255.7

Provado® 1.6 Flowable (F) (EPA Reg. No. 3125-457), a 1.6 lb active ingredient (a.i.)/gal liquid product intended for foliar applications; Admire® 2F (EPA Reg. No. 3125-422), a 2.0 lb. ai/gal liquid product intended for soil applications; Gaucho® 480 FS (EPA Reg. No. 7501-155), a 4.0

lb. ai/gal liquid product intended for use as a seed treatment; and Gaucho® 600 F (EPA Reg. No. 7501-173), a 5.0 lb. ai/gal liquid product intended for use as a seed treatment.

2.2 Structural Formula



Imidacloprid

See Attachment 1 for structures of all pertinent metabolites mentioned in this risk assessment.

2.3 Physical and Chemical Properties

Product chemistry data were previously submitted and reviewed in conjunction with PP#3F4169/3H5655 (Memo, F. Griffith, 9/20/93, D185148). Supplementary product chemistry data were reviewed in connection with PP#3F4169/3H5655 (Memo, F. Griffith, 6/8/94, D200233), and as a result of a change in the manufacturing process (Memo, F. Griffith, 11/28/94, D208038). Note that all property values are given at 25°C unless noted otherwise.

Appearance:	Colorless crystals with a weak characteristic color
Vapor Pressure:	1.5×10^{-9} mmHg
Water Solubility:	0.51 g/l (20 degrees C)
Partition Coefficient (Octanol/Water):	0.57 (at 22 °C)
Melting Point:	143.8 °C

Imidacloprid is a solid at room temperature with a low vapor pressure; thus, any losses due to volatilization/sublimation are expected to be minimal.

3.0 HAZARD CHARACTERIZATION

The existing toxicological database for imidacloprid supports the establishment of permanent tolerances for residues of imidacloprid in/on the RACs resulting from the proposed uses.

3.1 Hazard Profile

Imidacloprid is a systemic chloro-nicotinyl insecticide that disrupts the nervous system at nicotinic acetylcholine receptors. The toxicology database for imidacloprid is basically complete. The HIARC did request a 28-day inhalation study to characterize the direct effects of

imidacloprid on the pulmonary system and any systemic effects via the inhalation route. Imidacloprid has low acute toxicity via the dermal and inhalation routes and moderate acute toxicity via the oral route. It is not an eye or dermal irritant and is not a dermal sensitizer.

The nervous system is the primary target organ of imidacloprid. Nervous system effects on clinical signs and FOB assessments were seen in rat acute and subchronic neurotoxicity studies. These effects included decreased motor and locomotor activities, tremors, gait abnormalities, increased righting reflex impairments and body temperature, decreased number of rears and response to stimuli and decreases in forelimb and hindlimb grip strength. Also, in the rat developmental neurotoxicity study, a decrease in the caudate/putamen width was noted in female pups. Retinal atrophy was seen in high-dose females in the rat combined chronic toxicity/carcinogenicity study. No nervous system effects were noted in the mouse carcinogenicity or the reproduction and developmental studies or in the rabbit dermal or rat inhalation studies.

The dog was less sensitive to the effects of imidacloprid. No effects were noted up to the highest dose tested (72 mg/kg/day) in the chronic toxicity study. The rabbit appeared to be very sensitive as there was increased mortality in the oral developmental study at the highest dose tested (72 mg/kg/day). Increased incidence of mineralized particles in the thyroid colloid was noted in the rat combined chronic toxicity/carcinogenicity study. Body weight decrements were noted in the rat and/or mouse chronic and carcinogenicity studies, the rat subchronic neurotoxicity study, and the developmental, developmental neurotoxicity and reproduction studies. No effects were observed in the rabbit dermal or rat inhalation studies.

Long-term dietary administration of imidacloprid did not result in an overall treatment-related increase in incidence of tumor formation in rats or mice. On 11/10/93, the RfD/Peer Review Committee classified imidacloprid as a "Group E" chemical, no evidence of carcinogenicity for humans, by all routes of exposure based upon lack of evidence of carcinogenicity in rats and mice.

Imidacloprid was clastogenic in two *in vitro* cytogenetic studies [chromosome aberrations and sister chromatical exchange (SCE)] with human lymphocytes at cytotoxic doses and was negative in *in vivo* cytogenetic assays. Imidacloprid was also negative for unscheduled DNA synthesis, bacterial DNA repair tests and mitotic gene conversion in yeast and other mutagenicity studies. Overall, the data suggest that imidacloprid is negative for mutagenicity.

Oral rat developmental studies showed no increased qualitative or quantitative susceptibility of the fetus to imidacloprid *in utero*. Maternal toxicity resulted in decreased body weight gain and decreased corrected body weight gain. An increase in the incidence of wavy ribs in fetuses was noted at the same dose where maternal toxicity was observed. No increased qualitative or quantitative susceptibility of the fetus was noted *in utero* in the oral rabbit developmental study. Developmental effects included abortion, total litter resorptions, increased postimplantation loss due to increased late resorptions, decreased fetal weights, and very low incidences of skeletal alterations, including fused, asymmetric, missing, and/or abnormally ossified sternebrae, and/or shortened tail. Maternal toxic effects in the rabbit included maternal deaths, decreased maternal absolute body weights, body weight gain, and food consumption. Maternal and developmental

effects were equally severe; therefore, the is no qualitative susceptabiblity. Parental and offspring toxicity included body weight decrements at similar dosages in the rat multi-generation reproduction study. There was no increased qualitative or quantitative susceptibility following pre/post natal exposure to rats in this study. There was evidence of an increased qualitative susceptibility in the rat developmental neurotoxicity study. At the highest dose tested, maternal effects consisted largely of slight decreases in food consumption and body weight gain during early lactation, while pup effects included decreased body weight, decreased motor activity, decreased caudate/putamen width, females only (PNDs 11 and adult), and slight changes in performance in the water maze, males only, at the same dose.

Methylene-labeled imidacloprid was rapidly absorbed with approximately 90% of the administered dose being eliminated within 24 hours and 96% within 48 hours. There were no biologically significant differences between sexes, dose levels, or route of administration. Urinary excretion was the major route of elimination (70-80% of recovered radioactivity), with a lesser amount eliminated in feces (17-25% of recovered radioactivity). Biliary excretion was a major contributor to fecal radioactivity (36.6% vs. 4.8% of recovered radioactivity in bile-fistulated animals). Total tissue burden after 48 hours accounted for only approximately 0.5% of the recovered radioactivity, with major sites of accumulation being the liver, kidney, lung, skin, and plasma and minor sites being the brain and testes. Maximum plasma concentration occurred between 1.1 and 2.5 hours, and elimination half-lives (calculated from two exponential terms) were 3 and 26-118 hours. There were two major evident routes of biotransformation. The first included an oxidative cleavage of the parent compound to give 6-chloronicotinic acid (6-CNA) and its glycine conjugate. Dechlorination of this metabolite formed the 6-hydroxynicotinic acid and its mercapturic acid derivative. The second included the hydroxylation of imidazolidine followed by elimination of water of the parent compound to give NTN 35884.

In a comparison between [methylene-^{14}C] imidacloprid and [imidazolidine-4,5-^{14}C] imidacloprid, the rates of excretion were similar; however, the renal portion was higher with the imidazolidine-labeled test material (90% vs. 75% of recovered radioactivity for methylene-labeled test material. The imidazolidine-labeled test material also demonstrated higher accumulation in the tissues (approximately 1% of recovered radioactivity), with the major sites of accumulation being the liver, kidney, lung, and skin, and the minor sites being brain and muscle.

In a comparison between [methylene-^{14}C] imidacloprid and WAK 3839 (a metabolite of imidacloprid), there were no significant differences in the absorption, distribution, and excretion of the total radioactivity. More radioactivity was found in the tissues of the animals receiving imidacloprid at the 1.0 and 150.0 dose levels (respectively 0.9% and 3.4% vs. 0.2% of administered radioactivity for the WAK 3839 group). The major sites of accumulation of WAK 3839 included lung, renal fat, liver, and kidney, with minor sites being the testis and brain. WAK 3839 was formed during pretreatment (chronic oral dosing) of imidacloprid; however, the proposed metabolic pathways of the two compounds were different.

Table 1. Acute Toxicity of Imidacloprid Technical Grade Active Ingredient (TGAI).

Guideline No./Study Type		MRIDs	Results	Tox Category
870.1100	Acute Oral	42055331	LD_{50} = 424 mg/kg (M) LD_{50} > 450 mg/kg (F)	II
870.1200	Acute Dermal	42055332	LD_{50} > 5000 mg/kg	IV
870.1300	Acute Inhalation	42256317	LC_{50} > 5.33 mg/L	IV
870.2400	Primary Eye Irritation	42055334	Not an eye irritant	IV
870.2500	Primary Skin Irritation	42055335	Not a dermal irritant	IV
870.2600	Dermal Sensitization	42055336	Not a dermal sensitizer	N/A

Table 2. Toxicity Profile of Imidacloprid Technical.

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.3100 90-Day oral toxicity rodents (rats)	NA	NA
870.3150 90-Day oral toxicity (nonrodents)	NA	NA
870.3200 21/28-Day dermal toxicity (rabbits)	42256329 (1990) Acceptable/guideline 0 or 1000 mg/kg/day 6 hr/day, 5 d/week	NOAEL = 1000 mg/kg/day (HDT) LOAEL = not identified
870.3250 90-Day dermal toxicity	NA	NA
870.3465 4-Week inhalation toxicity (rat)	42273001 (1989) Acceptable/guideline 0, 0.0055, 0.035, or 0.191 mg/L/day, 6 hr/day, 5 d/week for 4 weeks	NOAEL = 0.191 mg/L/day (HDT) LOAEL = not identified
870.3700a Prenatal developmental toxicity (rats)	42256338 (1992) Acceptable/guideline F: 0, 10, 30, or 100 mg/kg/day	**Maternal** NOAEL = 10 mg/kg/day LOAEL = 30 mg/kg/day based on decreased body weight gain and decreased corrected body weight gain. **Developmental** NOAEL = 30 mg/kg/day LOAEL = 100 mg/kg/day based on a slight increase in the incidence of wavy ribs.

Table 2. Toxicity Profile of Imidacloprid Technical.

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.3700b Prenatal developmental toxicity (rabbits)	42256339 (1992) Acceptable/guideline F: 0, 8, 24, or 72 mg/kg/day	**Maternal** NOAEL = 24 mg/kg/day LOAEL = 72 mg/kg/day based on maternal deaths and decreased maternal absolute body weights, body weight gains, and food consumption. **Developmental** NOAEL = 24 mg/kg/day LOAEL = 72 mg/kg/day based on abortion, total litter resorptions, increased postimplantation loss due to increased late resorptions, decreased fetal weights, and very low incidences of skeletal alterations.
870.3800 Reproduction and fertility effects (rats)	42256340 (1990) Acceptable/guideline 0, 100, 250, or 700 ppm F_0 (M/F): 0, 8.1/8.8, 20.1/22.1, or 56.7/62.8 mg/kg/day F_1 (M/F): 0, 6.4/7.2, 16.5/18.9, or 47.3/52.3 mg/kg/day	**Parental/Systemic** NOAEL = 16.5 mg/kg/day LOAEL = 47.3 mg/kg/day based on decreased premating weight gain by F_0 males and females and F_1 females and decreased gestational weight gain by F_1 females. **Reproductive** NOAEL = 47.3 mg/kg/day (HDT) LOAEL = not identified **Offspring** NOAEL = 16.5 mg/kg/day LOAEL = 47.3 mg/kg/day based on decreased pup body weights in both litters of both generations.
870.4100a Chronic toxicity (rodents)	NA; see 870.4300	NA
870.4100b Chronic toxicity (dogs)	42273002 (1989) Acceptable/guideline 0, 200, 500, or 1250/2500 ppm M/F: 0, 6.1, 15, or 41(first 16 wks.), then 72 mg/kg/day	NOAEL = 72 mg/kg/day (HDT) LOAEL = not identified
870.4200a Carcinogenicity (rats)	NA; see 870.4300	NA
870.4200b Carcinogenicity (mice)	42256335 (1991) Acceptable/guideline with 42256336 0, 100, 330, or 1000 ppm M: 0, 20, 66, or 208 mg/kg/day F: 0, 30, 104, or 274 mg/kg/day 42256336 (1991) 0 or 2000 ppm M: 0 or 414; F: 0 or 424 mg/kg/day	NOAEL = Males: 208 mg/kg/day; Females: 274 mg/kg/day LOAEL = Males: 414 mg/kg/day; Females: 424 mg/kg/day based on decreased body weights, food consumption and water intake. **No evidence of carcinogenicity.**

Table 2. Toxicity Profile of Imidacloprid Technical.

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.4300 Combined Chronic/carcinogenicity (rats)	42256331 (1989) Acceptable/guideline with 42256332 0, 100, 300, or 900 ppm M: 0, 5.7, 16.9, or 51.3 mg/kg/day F: 0, 7.6, 24.9, or 73.0 mg/kg/day 42256332 (1991) 0 or 1800 ppm M: 0 or 102.6; F: 0 or 143.7 mg/kg/day	NOAEL = Males: 5.7 mg/kg/day; Females: 7.6 mg/kg/day LOAEL = Males: 16.9 mg/kg/day; Females: 24.9 mg/kg/day based on thyroid toxicity (increased incidence of mineralized particles in thyroid colloid) in males. **No evidence of carcinogenicity.**
870.5100 Bacterial reverse mutation	42256341 Acceptable/guideline	Negative for inducing reverse mutation in bacteria exposed to doses up to 5000 ug/plate.
870.5100 Bacterial reverse mutation	42256343 Acceptable/guideline	Negative up to 12,500 ug/plate.
870.5100 Bacterial reverse mutation	42256363 Acceptable/guideline	Negative up to 5500 ug/plate.
870.5300 *In vitro* mammalian cell gene mutation	42256342 Acceptable/guideline	Negative for inducing forward mutation in Chinese Hamster Ovary (CHO) (mammalian) cells treated up to 1222 ug/mL.
870.5300 *In vitro* mammalian cell gene mutation	42256364 Acceptable/guideline	Negative up to 2000 ug/mL.
870.5300 *In vitro* mammalian cell gene mutation	42256365 Acceptable/guideline	Negative up to 2000 ug/mL.
870.5375 *In vitro* mammalian chromosome abberation (HL)	42256345 Acceptable/guideline	Positive at 500 ug/mL - S9 and 1300 ug/mL +S9, both cytotoxic doses
870.5375 *In vitro* mammalian chromosome abberation (CHV79)	42256370 Acceptable/guideline	Negative up to 1000 ug/mL.
870.5375 *In vitro* mammalian chromosome abberation (CHO)	42256371 Acceptable/guideline	Negative up to 1000 ug/mL.
870.5380 Mammalian germ cell chromosome abberation (mouse)	42256348 Unacceptable/guideline	Negative, but only tested up to 80 mg/ml.

Table 2. Toxicity Profile of Imidacloprid Technical.

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.5385 Mammalian bone marrow chromosome aberration (chinese hamster)	42256344 Acceptable/guideline	Negative for chromosome breakage up to 2000 ug/mL.
870.5395 Mammalian micronucleus (mouse)	42256347 Unacceptable/guideline	Negative, but only tested up to 80 mg/kg.
870.5395 Mammalian micronucleus (mouse)	42256366 Acceptable/guideline	Negative up to 50 mg/kg IP, toxic dose.
870.5395 Mammalian micronucleus (mouse)	42256367 Unacceptable/guideline	Negative up to 80 mg/kg IP, a non-toxic dose.
870.5395 Mammalian micronucleus (mouse)	42256368 Unacceptable/guideline	Negative up to 100 mg/kg PO, a non-toxic dose.
870.5395 Mammalian micronucleus (mouse)	42256369 Acceptable/guideline	Negative up to 160 mg/kg PO, toxic dose.
870.5500 DNA damage/repair *REC* assay	41156351 Acceptable/guideline	Negative up to 5000 ug/disc, the limit of solubility, with or without activation.
870.5550 Unscheduled DNA synthesis (RPH)	42256352 Acceptable/guideline	Negative up to 750 ug/mL, a cytotoxic dose.
870.5575 Mitotic gene conversion	42256353 Acceptable/guideline	Negative for crossing-over in yeast cells exposed with/without activation to precipitating levels of test article (5,000-10,000 ug/mL).
870.5550 Unscheduled DNA synthesis (RPH)	42256372 Acceptable/guideline	Negative up to cytotoxic doses (1333 ug/mL).
870.5900 *In vitro* sister chromatid exchange (CHO)	42256349 Acceptable/guideline	Positive at 500 ug/mL -S9 and 2000 ug/mL +S9, both cytotoxic doses.
870.5900 *In vitro* sister chromatid exchange (CHO)	47256350 Acceptable/guideline	Negative at cytotoxic doses of 400 ug/mL -S9 and 1250 ug/mL +S9.
870.59.15 *In vivo* sister chromatid exchange (chinese hamster bone marrow)	42256346 Acceptable/guideline	Negative up to 2000 mg/kg.

Table 2. Toxicity Profile of Imidacloprid Technical.

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.6200a Acute neurotoxicity screening battery rat	43170301 (1994) 43285801 (1994) Acceptable/guideline 0, 42, 151, or 307 mg/kg	NOAEL = not identified. LOAEL = 42 mg/kg based on decreased motor and locomotor activities observed in females.
870.6200b Subchronic neurotoxicity screening battery rat	43286401 (1994) Minimum 0, 150, 1000, or 3000 ppm M: 0, 9.3, 63.3, or 196 mg/kg/day F: 0, 10.5, 69.3, or 213 mg/kg/day	NOAEL = 9.3 mg/kg/day. LOAEL = 63.3 mg/kg/day based on decreased body weight gain.
870.6300 Developmental neurotoxicity (rat)	45537501 (2001) Acceptable/non-guideline 0, 100, 250, or 750 ppm Gest.: 0, 8.0-8.3, 19.4-19.7, or 54.7-58.4 mg/kg/day Lact.: 0, 12.8-19.5, 30.0-45.4, or 80.4-155.0 mg/kg/day	**Maternal** NOAEL = 20 mg/kg/day. LOAEL = 55 mg/kg/day based on decreased food consumption and body weight gain during lactation. **Offspring** NOAEL = 20 mg/kg/day. LOAEL = 55 mg/kg/day based on decreased body weight and body weight gain, decreased motor activity and decreased caudate/putamen width in females.

Table 2. Toxicity Profile of Imidacloprid Technical.

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.7485 Metabolism and pharmacokinetics rat	42256354 (1990) 42256356 (1987) M&F: 1.0 or 20.0 mg/kg (labeled) as single oral dose or 1.0 mg/kg unlabeled orally followed by 1.0 mg/kg single oral dose (labeled) or 1.0 mg/kg (labeled) single dose IV M: 20.0 mg/kg single oral dose or 1.0 mg/kg single duodenal dose 42256357 (1991) M&F: 1.0 mg/kg single oral dose M: 1.0 or 150 mg/kg single oral dose 42256373 (1990) M: 1.0 or 150 mg/kg single oral dose or 80.0 mg/kg single oral dose after 1 year 1800 ppm 42256355 (1987) M: 1.0 mg/kg single oral or IV dose 42256358 (1990) 42256359 (1990) Acceptable/guideline	Methylene-labeled imidacloprid was rapidly absorbed with approximately 90% of the administered dose being eliminated within 24 hours and 96% within 48 hours. There were no biologically significant differences between sexes, dose levels, or route of administration. Urinary excretion was the major route of elimination (70-80% of recovered radioactivity), with a lesser amount eliminated in feces (17-25% of recovered radioactivity). Biliary excretion was a major contributor to fecal radioactivity (36.6% vs. 4.8% of recovered radioactivity in bile-fistulated animals). Total tissue burden after 48 hours accounted for only approximately 0.5% of the recovered radioactivity, with major sites of accumulation being the liver, kidney, lung, skin, and plasma and minor sites being the brain and testes. Maximum plasma concentration occurred between 1.1 and 2.5 hours, and elimination half-lives (calculated from two exponential terms) were 3 and 26-118 hours. There were two major evident routes of biotransformation. The first included an oxidative cleavage of the parent compound to give 6-CNA and its glycine conjugate. Dechlorination of this metabolite formed the 6-hydroxynicotinic acid and its mercapturic acid derivative. The second included the hydroxylation of imidazolidine followed by elimination of water of the parent compound to give NTN 35884. In a comparison between [Methylene-14C] Imidacloprid and [Imidazolidine-4,5-14C] Imidacloprid, the rates of excretion were similar; however, the renal portion was higher with the imidazolidine-labeled test material. The imidazolidine-labeled test material also demonstrated higher accumulation in the tissues, with the major sites of accumulation being the liver, kidney, lung, and skin, and the minor sites being brain and muscle. In a comparison between [Methylene-14C] Imidacloprid and WAK 3839, there were no significant differences in the absorption, distribution, and excretion of the total radioactivity. More radioactivity was found in the tissues of the animals receiving imidacloprid at the 1.0 and 150.0 dose levels. The major sites of accumulation of WAK 3839 included lung, renal fat, liver, and kidney, with minor sites being the testis and brain. WAK 3839 was formed during pretreatment (chronic oral dosing) of imidacloprid; however, the proposed metabolic pathways of the two compounds were different.
870.7600 Dermal penetration	NA	NA

3.2 FQPA Considerations

On 10/08/2002, the HED HIARC evaluated the potential for increased susceptibility of infants and children from exposure to imidacloprid according to the February 2002 OPP 10X guidance document. The HIARC concluded that the toxicology database was complete for FQPA

purposes and that there are no residual uncertainties for pre-/post-natal toxicity (Memo, D. Nixon, 10/31/02; TXR NO. 0051292). Based on the on the hazard data, the HIARC recommended the special FQPA SF be reduced to 1x. The imidacloprid risk assessment team evaluated the quality of the exposure data; and, based these data, recommended that the special FQPA SF be reduced to 1x. The recommendation is based on the following:

- There is no quantitative or qualitative evidence of increased susceptibility of rat and rabbit fetuses to in utero exposure in developmental studies. There is no quantitative or qualitative evidence of increased susceptibility of rat offspring in the multi-generation reproduction study.
- There is evidence of increased qualitative susceptibility in the rat developmental neurotoxicity study, but the concern is low since: 1) the effects in pups are well-characterized with a clear NOAEL; 2) the pup effects occur in the presence of maternal toxicity with the same NOAEL for effects in pups and dams; and, 3) the doses and endpoints selected for regulatory purposes are protective of the pup effects noted at higher doses in the developmental neurotoxicity study. Therefore, there are no residual uncertainties for pre-/post-natal toxicity in this study.
- The toxicological database is complete for FQPA assessment.
- The *acute* dietary food exposure assessment utilizes existing and proposed tolerance level residues and 100% CT information for all commodities. By using these screening-level assessments, actual exposures/risks will not be underestimated.
- The *chronic* dietary food exposure assessment utilizes existing and proposed tolerance level residues and % CT data verified by BEAD for several existing uses. For all proposed uses, 100% CT is assumed. The chronic assessment is somewhat refined and based on reliable data and will not underestimate exposure/risk.
- The dietary drinking water assessment utilizes water concentration values generated by model and associated modeling parameters which are designed to provide conservative, health protective, high-end estimates of water concentrations which will not likely be exceeded.
- The residential handler assessment is based upon the residential SOPs in conjunction with chemical-specific study data in some cases and PHED unit exposures in other cases. The majority of the residential post-application assessment is based upon chemical-specific TTR data or other chemical-specific post-application exposure study data. The chemical-specific study data as well as the surrogate study data used are reliable and also are not expected to underestimate risk to adults as well as to children. In a few cases where chemical-specific data were not available, the SOPs were used alone. The residential SOPs are based upon reasonable "worst-case" assumptions and are not expected to underestimate risk. These assessments of exposure are not likely to underestimate the resulting estimates of risk from exposure to imidacloprid.

Table 3. Summary of FQPA SFs for Imidacloprid.

	LOAEL to NOAEL (UF_L)	**Subchronic to Chronic (UF_S)**	**Incomplete Database (UF_{DB})**	**Special FQPA SF (Hazard and Exposure)**
Magnitude of Factor	3x	1x	1x	1x
Rationale for the Factor	Use of LOAEL, no NOAEL	Not required	Not required	Not required
Endpoints to which the Factor is Applied	Acute Dietary	Not Applicable	Not Applicable	Not Applicable

3.3 Dose-Response Assessment

Acute Dietary Endpoint: The rat acute neurotoxicity study was used to select the dose and endpoint for establishing the aRfD of 0.14 mg/kg/day for the general U.S. population. The LOAEL of 42 mg/kg was based upon the decrease in motor and locomotor activities observed in

females. This RfD is applicable to the general population, including infants and children, and is also protective of developmental effects which may occur in females of reproductive age. The maternal and developmental effects in the rabbit study, though severe, occurred at higher doses, and this endpoint is adequately protective of those effects. A 300-fold uncertainty factor (3x UF_L; and 10x for interspecies extrapolation and 10x for intraspecies variation) was incorporated in the aRfD. A 3X uncertainty factor for the use of a LOAEL was judged to be adequate (as opposed to a 10X) because: 1) the LOAEL (42 mg/kg) is comparable to the LOAELs seen in adults in the developmental rat study (30 mg/kg/d) and the two-generation reproduction study [47/52 mg/kg/d (male/female)] and in the offspring in the DNT study (55 mg/kg/d); 2) the extrapolated NOAEL of 14 mg/kg (42/3 = 14) is comparable to the NOAEL of 20 mg/kg/d established in the offspring in the DNT; and, 3) the neurotoxic effects in this study showed a good dose response which resulted in minimal effects on motor activity and locomotor activity at the LOAEL. The special FQPA SF of 1x is applicable for the acute dietary risk assessment. Thus, the aPAD is 0.14 mg/kg.

Chronic Dietary Endpoint: The rat combined chronic toxicity/carcinogenicity study was used to select the dose and endpoint for establishing the cRfD of 0.057 mg/kg/day for the general U.S. population. The NOAEL of 5.7 mg/kg/day was based upon an increased incidence of mineralized particles in the thyroid colloid in males at the LOAEL of 16.9 mg/kg/day. The mineralized particles are interpreted to be the result of imidacloprid selectively localizing in the thyroid colloid, resulting in increased clumping and basophilia of the colloid. The clumping may result in a decrease in the uptake of organic iodine which can cause a decrease in the production of thyroid hormones (T_3 and T_4). In addition, this may result in a decrease in the ability of the follicular cells to phagocytize the colloid and release active thyroid hormones. These observations are the best available indicator of thyroid organ toxicity since T_3, T_4 and TSH were not measured in the rat combined chronic toxicity/carcinogenicity study. A 100-fold uncertainty factor (10x for interspecies extrapolation and 10x for intraspecies variation) was incorporated into the cRfD. The special FQPA SF of 1x is applicable for the chronic dietary risk assessment. Thus, the cPAD is 0.057 mg/kg/day.

Carcinogenicity: The RfD/Peer Review Committee classified imidacloprid as a "Group E" (no evidence of carcinogenicity for humans) chemical based on adequate studies in two animal species; therefore, a cancer risk assessment is not required.

Short-Term Incidental Oral Endpoint: A short-term incidental oral endpoint was selected from the rat developmental toxicity study. The maternal NOAEL of 10 mg/kg/day was chosen based upon decreased body weight gain and decreased corrected body weight gain at the LOAEL of 30 mg/kg/day. This study and endpoint are appropriate for the population of concern (infants and children) and the route and duration of exposure.

Intermediate-Term Incidental Oral Endpoint: An intermediate-term incidental oral endpoint was selected from the rat subchronic neurotoxicity study. The NOAEL of 9.3 mg/kg/day was chosen based upon decreased body weight gain at the LOAEL of 63.3 mg/kg/day. This study and endpoint are appropriate for the population of concern (infants and children) and for the route and duration of exposure.

Dermal Penetration:
Dermal Absorption Factor: 7.2% (this value was rounded to 7% for risk assessment purposes) No dermal absorption study was submitted. The rabbit dermal NOAEL is 1000 mg/kg/day with no systemic effects noted in the 28-day dermal toxicity study. In the developmental toxicity study, the rabbit maternal NOAEL/LOAEL (based on maternal deaths and decreased maternal absolute body weights, body weight gains, and food consumption) is 24/72 mg/kg/day. An upper-bound estimate of dermal absorption (7.2%) was calculated by comparing the maternal LOAEL from the rabbit developmental study (870.3700b) with the NOAEL from the rabbit dermal study (870.3250).

Short-Term Dermal Endpoint: A short-term dermal endpoint was selected from the rat developmental toxicity study. The maternal NOAEL of 10 mg/kg/day was chosen based upon decreased body weight gain and decreased corrected body weight gain at the LOAEL of 30 mg/kg/day. A 21-day dermal study in rabbits was submitted with no systemic effects noted up to 1000 mg/kg/day; however, the dermal study did not evaluate FOB and other neurological parameters. Since there are neurotoxic effects noted in both adult and offspring rats via the oral route that were not evaluated in the dermal study, the HIARC chose an oral endpoint for this risk assessment to adequately protect against neurotoxicity via dermal exposure. The chosen endpoint is from a study of the appropriate duration of exposure and is at a comparable dose where neurotoxic signs were noted in the rat acute neurotoxicity study. A dermal absorption factor of 7% was applied for route-to-route extrapolation. This dose/endpoint is appropriate for short-term exposure risk assessment.

Intermediate-term Dermal Endpoint: An intermediate-term dermal endpoint was selected from the rat subchronic neurotoxicity study. The NOAEL of 9.3 mg/kg/day was chosen based upon decreased body weight gain at the LOAEL of 63.3 mg/kg/day. A 21-day dermal study in rabbits was submitted with no systemic effects noted up to 1000 mg/kg/day; however, the dermal study did not evaluate FOB and other neurological parameters. Since there are neurotoxic effects noted in both adult and offspring rats via the oral route that were not evaluated in the dermal study, the HIARC chose an oral endpoint for this risk assessment to adequately protect against neurotoxicity via dermal exposure. The chosen endpoint is from a study of the appropriate duration of exposure and is at a comparable dose where neurotoxic signs were noted in the rat acute neurotoxicity study. A dermal absorption factor of 7% was applied for route-to-route extrapolation. This dose/endpoint is appropriate for intermediate-term exposure risk assessment.

Long-term Dermal Endpoint: A long-term dermal endpoint was selected from the rat combined chronic toxicity/carcinogenicity study. The NOAEL of 5.7 mg/kg/day was based upon an increased incidence of mineralized particles in the thyroid colloid in males at the LOAEL of 16.9 mg/kg/day. No long-term dermal study was submitted. A dermal absorption factor of 7% was applied for route-to-route extrapolation. This dose/endpoint is appropriate for long-term exposure risk assessment.

Short-term Inhalation Endpoint: A short-term inhalation endpoint was chosen from the rat developmental study. The maternal NOAEL of 10 mg/kg/day was chosen based upon decreased body weight gain and decreased corrected body weight gain at the LOAEL of 30 mg/kg/day. The submitted 28-day inhalation study (MRID 42273001) did not test up to the limit dose and no

systemic toxicity was observed up to the highest dose tested 0.191 mg/L. Also FOB and other neurological parameters were not evaluated. An inhalation absorption factor of 100% should be applied. This dose/endpoint is appropriate for short-term exposure risk assessment.

Intermediate-term Inhalation Endpoint: An intermediate-term inhalation endpoint was chosen from the rat subchronic neurotoxicity study. The NOAEL of 9.3 mg/kg/day was chosen based upon decreased body weight gain at the LOAEL of 63.3 mg/kg/day. This dose and endpoint are appropriate for the duration of exposure. The submitted 4-week inhalation study (MRID 42273001) did not test up to the limit dose and no systemic toxicity was observed up to the highest dose tested 0.191 mg/L. Also, FOB and other neurological parameters were not evaluated. An inhalation absorption factor of 100% should be applied. This dose/endpoint is appropriate for intermediate-term exposure risk assessment.

Long-term Inhalation Endpoint: A long-term inhalation endpoint was selected from the rat combined chronic toxicity/carcinogenicity study. The NOAEL of 5.7 mg/kg/day was based upon an increased incidence of mineralized particles in the thyroid colloid in males at the LOAEL of 16.9 mg/kg/day. No long-term inhalation study was submitted. An inhalation absorption factor of 100% should be applied. This dose/endpoint is appropriate for long-term exposure risk assessment.

MOE for Occupational/Residential Risk Assessments: A MOE of 100 is required for short-, intermediate-, and long-term occupational risk assessments for both dermal and inhalation routes of exposure. A MOE of 100 is required for residential risk assessments for all routes of exposure for any duration. For short-/intermediate-/long-term oral, dermal and inhalation exposures, the following route-to-route extrapolation was followed: the inhalation (using 100% absorption) and dermal (using 7% absorption) exposures were converted to equivalent oral doses, combined, and then compared to their respective oral NOAELs since all of the dermal and inhalation endpoints are based on oral equivalents.

As per FQPA, 1996, when there are potential residential exposures to the pesticide, aggregate risk assessment must consider exposures from three major sources: oral, dermal and inhalation exposures. The toxicity endpoints selected for these routes of exposure may be aggregated as follows: For short-term exposure, oral and dermal and inhalation endpoints can be aggregated because of the use of oral equivalents and a common endpoint (decreased body weight gain).

The doses and toxicological endpoints selected for various exposure scenarios are summarized in Table 4.

Table 4. Summary of Toxicological Dose and Endpoints for Imidacloprid for Use in Human Health Risk Assessment[1].

Exposure Scenario	Dose Used in Risk Assessment, UF	* Special FQPA SF and Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary all populations	LOAEL = 42 mg/kg/day UF = 300 **Acute RfD** = 0.14 mg/kg	FQPA SF = 1X **aPAD** = aRfD / FQPA SF = 0.14 mg/kg	Acute neurotoxicity - rat LOAEL = 42 mg/kg, based upon the decrease in motor and locomotor activities observed in females.
Chronic Dietary all populations	NOAEL= 5.7 mg/kg/day UF = 100 **Chronic RfD** = 0.057 mg/kg/day	FQPA SF = 1X **cPAD** = cRfD / FQPA SF = 0.057 mg/kg/day	Combined chronic tox/carcinogenicity - rat LOAEL = 16.9 mg/kg/day, based upon increased incidence of mineralized particles in thyroid colloid in males.
Short-Term Oral (1-30 days)	oral study NOAEL= 10 mg/kg/day	**LOC for MOE** = 100 (Residential, includes the FQPA SF)	Developmental toxicity - rat Maternal LOAEL = 30 mg/kg/day, based upon decreased body weight gain and corrected body weight gain.
Intermediate-Term Oral (1- 6 months)	oral study NOAEL= 9.3 mg/kg/day	**LOC for MOE** = 100 (Residential, includes the FQPA SF)	Subchronic neurotoxicity - rat LOAEL = 63.3 mg/kg/day, based upon decreased body weight gain.
Short-Term Dermal (1-30 days)	oral study NOAEL= 10 mg/kg/day (dermal absorption rate = 7.2%)[2]	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes the FQPA SF)	Developmental toxicity - rat Maternal LOAEL = 30 mg/kg/day, based upon decreased body weight gain and corrected body weight gain.
Intermediate-Term Dermal (1-6 months)	oral study NOAEL= 9.3 mg/kg/day (dermal absorption rate = 7.2%)[2]	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes the FQPA SF)	Subchronic neurotoxicity - rat LOAEL = 63.3 mg/kg/day, based upon decreased body weight gain.
Long-Term Dermal (> 6 months)	oral study NOAEL= 5.7 mg/kg/day (dermal absorption rate = 7.2%)[2]	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes the FQPA SF)	Combined chronic tox/carcinogenicity - rat LOAEL = 16.9 mg/kg/day, based upon increased incidence of mineralized particles in thyroid colloid in males.
Short-Term Inhalation (1-30 days)	oral study NOAEL= 10 mg/kg/day (inhalation absorption rate = 100%)	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes the FQPA SF)	Developmental toxicity - rat Maternal LOAEL = 30 mg/kg/day, based upon decreased body weight gain and corrected body weight gain.

Table 4. Summary of Toxicological Dose and Endpoints for Imidacloprid for Use in Human Health Risk Assessment[1].

Exposure Scenario	Dose Used in Risk Assessment, UF	* Special FQPA SF and Level of Concern for Risk Assessment	Study and Toxicological Effects
Intermediate-Term Inhalation (1- 6 months)	oral study NOAEL= 9.3 mg/kg/day (inhalation absorption rate = 100%)	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes the FQPA SF)	Subchronic neurotoxicity - rat LOAEL = 63.3 mg/kg/day, based upon decreased body weight gain.
Long-Term Inhalation (> 6 months)	oral study NOAEL= 5.7 mg/kg/day (inhalation absorption rate = 100%)	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes the FQPA SF)	Combined chronic tox/carcinogenicity - rat LOAEL = 16.9 mg/kg/day, based upon increased incidence of mineralized particles in thyroid colloid in males.
Cancer (oral, dermal, inhalation)	no evidence of carcinogenicity for humans	Not applicable	No evidence of carcinogenicity in rats and mice.

[1] UF = uncertainty factor, FQPA SF = Special FQPA SF, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, MOE = margin of exposure, LOC = level of concern.
[2] A dermal apsorption of 7% was used for risk assessment purposes.

3.4 Endocrine Disruption

EPA is required under the Federal Food Drug and Cosmetic Act (FFDCA), as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was scientific bases for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA has authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

When the appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, imidacloprid may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

4.0 EXPOSURE ASSESSMENT

4.1 Summary of Proposed Uses

Imidacloprid is a systemic insecticide registered for use in controlling aphids, leafhoppers, thrips, "adult beetles," whiteflies, cranberry weevil, black-vine weevil, strawberry root weevil, Cuban May beetle, Colorado potato beetle, Japanese beetle, rose chafer, fruit flies, apple maggot and flea beetles. Its mode of action is the disruption of the nervous system by acting as an inhibitor at nicotinic acetylcholine receptors. Imidacloprid blocks the signals that are induced by acetylcholine at the post-synaptic membrane, resulting in nerve function impairment.

According to the OPP REFS (M. Dow, 5/7/02), there are 82 registered products (excluding Section 18 registrations) that contain imidacloprid as the a.i.. Imidacloprid is registered for use on a variety of agricultural commodities as well as on indoor residential and commercial/institutional sites including eating establishments, hospitals, food marketing, storage and distribution centers. Imidacloprid can be used on pets as well several outdoor residential sites. It is registered for use as a pre- and post-construction termiticide, and as a preservative to plastic, textile and rubber products. Imidacloprid products are registered for use in irrigation systems, human drinking water systems, sewage systems, streams and rivers, rights of way, aircraft, ships, boats, trailers, railway cars, automobiles[1].

The proposed new uses are amendments to the following currently registered products: Provado® 1.6 F (Reg. No. 3125-457), a 1.6 lb ai/gal liquid product intended for foliar applications; Admire® 2 F (Reg. No. 3125-422), a 2.0 lb. ai/gal liquid product intended for soil applications; Gaucho® 480 FS (Reg. No. 7501-155), a 4.0 lb. ai/g liquid product intended for use as a seed treatment; and Gaucho® 600 Flowable (Reg. No. 7501-173), a 5.0 lb. ai/gal liquid product intended for use as a seed treatment. In addition, the following products are used on bananas in Columbia, Costa Rica, Ecuador, Guatemala, and Honduras: Confidor® 70 Wettable Granular (WG; No EPA Reg. No.; 70% a.i.) and Confidor® 350 Suspension Concentration (SC; No EPA Reg. No.; 35% a.i.).

Imidacloprid is being proposed for use on the following RACs: imported banana; cranberry; okra; pop corn; watercress; guava, papaya, lychee, avocado and related commodities; root and tuber vegetables (except sugar beets); leaves of root and tuber vegetables; artichoke; bushberry; lingonberry; juneberry; salal; legume vegetables (except soybeans); strawberry and stonefruit. The proposed application rates vary by crop and application method. The range of application rates are 0.376-0.5 lb a.i./A, 0.0469-0.1 lb a.i./A, and 0.25-1.0 lb a.i./hundredweight (cwt) of seed for foliar, soil and seed treatment applications, respectively. The maximum seasonal application rate is 0.5 lb ai/A regardless of formulation or method of application. Typically, one soil application can be made per season. For foliar applications, the number of applications, application interval, and PHI vary by crop. A summary of the proposed use patterns can be found in Table 5.

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[1] The preceding list of uses represents a summary, but is not all inclusive. Note that REFS lists a site code 65015, which relates to human drinking water systems. This entry in REFS is an error (personal communication between G. Herndon and D. Kenny, 2/11/03). This label is for termiticide use, and specifies **not** to use around wells and cisterns.

The petitioners provided end-use product labels and a summary of the proposed imidacloprid use directions [i.e., maximum use rates (single), dilution information, and preharvest intervals (PHIs)] for all the commodities associated with this risk assessment. The proposed use patterns are acceptable and are supported by the available residue data, with the exception of the following:

PP#2E6406 and 2E6435: On 12/18/02, the HED Chemistry Scientific Advisory Council (ChemSAC) recommended that a 7-day PHI is adequate based on the available residue data on papaya, guava, mamey sapote and mango. **Revised Section Bs should be submitted by the petitioner.**

In addition, the petitioner should specify a minimum spray volume on the labels. The rates should reflect those used in the crop field trial studies.

Table 5. Summary of Proposed Use Patterns for Imidacloprid.

PP/ID#[a]	Use/ Commodity	Proposed Formulation(s)[1]	PHI [2] (days)	Max. #App. /yr.	Maximum Application Rate (lb.ai/A)		RTI [3] (days)	Restrictions	
					per app.	per yr			
TROPICAL FRUITS									
2E06435	Guava, Feijoa, Jaboticaba, Wax Jambu, Starfruit, Passionfruit, Acerola	Provado 1.6F	15	5	0.1	0.5	7	Foliar applications.	
2E06406	Papaya, Star Apple, Black Sapote, Mango, Sapodilla, Canistel, Mamey Sapote	Provado 1.6F	6	5	0.1	0.5	10	Foliar applications.	
	Lychee, Longan, Spanish Lime, Rambutan, Pulasan, Persimmon								
	Avocado	Admire 2F	6	5	0.1	0.5	NA	Soil applications.	
LEGUME VEGETABLES									
2E06403	Vegetable, legume, except soybean, group 6	Admire 2F	21	1	0.375	0.375	21	Soil applications	Regardless of the type of application (soil or foliar), do not apply more than 0.5 lb ai/A/year.
		Provado 1.6F	7	3	0.044	0.132	7	Foliar applications	
		Gaucho 480F	NA	1	0.25 lb ai/cwt seed	0.25 lb ai/cwt seed	NA	Commercial seed treatment	

Table 5. Summary of Proposed Use Patterns for Imidacloprid.

PP/ID#[a]	Use/ Commodity	Proposed Formulation(s)[1]	PHI [2] (days)	Max. #App. /yr.	Maximum Application Rate (lb.ai/A)		RTI [3] (days)	Restrictions	
					per app.	per yr			
ROOT AND TUBER VEGETABLES (EXCEPT SUGAR BEETS) LEAVES OF ROOT AND TUBER VEGETABLES									
2E6506	Root and Tuber Vegetables, except Sugar Beet	Admire 2F	21	NS	0.375	0.375	NS	Applied either as an in-furrow treatment over the planting material before covering w soil or as a side-dress no later than 45 days after planting Do not apply more than 0.375 lb ai/A/year as a single soil application.	Regardless of the type of application (soil or foliar), do not apply more than 0.5 lb ai/A/year.
		Provado1.6F	7	1 - radish 3 - other	0.047	0.047 - radish 0.141 - other	5	Foliar applications.	
2E06409	Leaves of Root and Tuber Veg.	Admire 2F	21	NS	0.375	0.375	NS	Soil applications	Regardless of the type of application (soil or foliar), do not apply more than 0.5 lb ai/A/year.
		Provado® 1.6F	7	3	0.047	0.141	5	Foliar applications.	
STONEFRUIT									
2E06421	Cherry, plums, prunes, plumcots	Provado® 1.6F	7	5	0.1	0.5	10	Foliar applications.	
	Peach, apricots, nectarines		0	3	0.1	0.3	7		

Table 5. Summary of Proposed Use Patterns for Imidacloprid.

PP/ID#[a]	Use/ Commodity	Proposed Formulation(s)[1]	PHI [2] (days)	Max. #App. /yr.	Maximum Application Rate (lb.ai/A)		RTI [3] (days)	Restrictions	
					per app.	per yr			
BUSHBERRY									
1E06268	Lowbush blueberry	Provado 1.6F	21	2	0.1	0.2	21	Foliar applications.	
	Highbush blueberry, salal, Juneberry	Admire 2F	7	1	0.5	0.5	7	Soil applications. Irrigate 1 hour before and immediately after application.	Regardless of the type of application (soil or foliar), do not apply more than 0.5 lb ai/A/year.
		Provado 1.6F	3	2	0.1	0.2	7	Foliar applications.	
OTHER CROPS									
1E06268	Banana (Imported)	Confidor 70 WG	0	1	0.31	0.31	NA	Basal drench application.	
		Confidor 350 SC	0	1	0.31	0.31	NA		
0E06203	Cranberry	Admire 2F	30	1	0.5	0.5	NA	Can be applied 1) through crop irrigation systems in sufficient water to move the material into the root zone or 2) as a foliar spray at max. rate of 0.5 lb ai/A. As a foliar spray, it must be followed immediately with sufficient overhead irrigation water to wash material into the root zone.	
2E06458	Mustard Seed	Gaucho 480 F	NA	1	1.0	1.0	NA	Treated seeds are not to be used for or mixed with food or livestock feed, or processed for oil.	
		Gaucho 600 F	NA	1	1.0	1.0	NA		
1E06254	Okra	Admire 2F	21	1	0.5	0.5	NA	Applied 1) in narrow band centered on the plant row from 14 days before planting to the day of planting; 2) at planting as an in-furrow spray at or below the seed level; 3) as a post-seeding or transplant soil drench; 4) as a side dress after the plants are established; or 5) in drip, trickle irrigation water.	
		Provado 1.6F	0	5	0.047	0.234	5	Foliar application.	

Table 5. Summary of Proposed Use Patterns for Imidacloprid.

PP/ID#[a]	Use/ Commodity	Proposed Formulation(s)[1]	PHI [2] (days)	Max. #App. /yr.	Maximum Application Rate (lb.ai/A)		RTI [3] (days)	Restrictions	
					per app.	per yr			
2E06414	Corn, pop Corn, pop, stover	Gaucho 600F	NA	1	0.25 lb ai/cwt seed	0.25 lb ai/cwt seed	NA	Commercial seed treatment.	
		Gaucho 480F	NA	1	0.25 lb ai/cwt seed	0.25 lb ai/cwt seed	NA		
2E06417	Strawberry	Admire 2F	30	1	0.375	0.375	NA	Soil applications.	Regardless of the type of application (soil or foliar), do not apply more than 0.5 lb ai/A/year.
		Provado 1.6F	7	3	0.047	0.14	5	Foliar applications.	
1E06237	Watercress	Admire 2F	21	NS	0.38	0.38	NS	Applications may be made by 1) in a narrow band (≤2" and 1-2" below the seed depth) centered on the plant row in the bedding operation, ≤ 14 days prior to planting; 2) as an in-furrow spray at or below seed level or a narrow (≤2") surface band above the seed line (with incorporation to a depth of 1½" and irrigation within 24 hours) during planting; and 3) as a post-seeding drench, transplant drench, or hill drench in sufficient water to insure incorporation into the root zone. Use on upland watercress not permitted in CA.	Regardless of the type of application (soil or foliar), do not apply more than 0.5 lb ai/A/year.
		Provado 1.6F	7	NS	0.047	0.23	5-7	Foliar applications.	
1E6225	Artichoke	Provado 1.6F	7	2	0.25	0.50	21	Foliar applications.	

4.2 Dietary Exposure/Risk Pathway

The residue chemistry data submitted in support of proposed petitions were in the following HED-memoranda: Imported Banana (PP#1E06074, J. Tyler, 12/11/02, D263990); Cranberry (PP#0E6203, J. Tyler, 8/22/02, D271814); Okra (PP#1E6254, J. Tyler, 11/4/02, D285962); Pop corn (PP#1E06074, J. Tyler, 10/17/02, D287731); Watercress (PP#0E6237, J. Tyler, 9/30/02, D271824); Guava, Papaya, Lychee, Avocado and Related Commodities (PP#s 2E06406 and 2E06435, J. Tyler, 1/17/03, D286907); Root and Tuber Vegetables (except sugar beets), and Leaves of Root and Tuber Vegetables (PP#s2E6506 and 2E06409, J. Tyler, 1/30/03, D286233); Artichoke, Bushberry, Lingonberry, Juneberry, and Salal (PP#s1E6225 and 1E6268, G. Herndon, 1/27/03, D287694); Legume Vegetables (Except Soybeans), Strawberry and Stonefruit (PP#s2E6403, 2E6417, and 2E6421, G. Herndon, 1/27/03, D287693). The drinking water assessment was completed by EFED on 2/10/03 (Memo, M. Barrett, D278110). The acute and chronic dietary exposure assessment was completed in a HED-memorandum dated 2/20/03 (J. Tyler, D287027). A residential exposure assessment for imidacloprid was prepared in an HED memorandum dated 2/26/03 (Memo, M. Dow; D281610).

4.2.1 Residue Profile

Background

IR-4, on behalf of Agricultural Experiment Stations in several states, has submitted petitions to register the use of imidacloprid on numerous RACs. The petitioners are proposing the establishment of permanent tolerances for the combined residues of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as the parent, in/on the following RACs: artichoke (2.5 ppm); cranberry (0.05 ppm); mustard, seed (0.05 ppm); okra (1.0 ppm); corn, pop (0.05 ppm); corn, pop, stover (0.2 ppm); strawberry (0.5 ppm); watercress (3.5 ppm); guava, feijoa, jaboticaba, wax jambu, starfruit, passionfruit and acerola (1.0 ppm); avocado, papaya, star apple, black sapote, mango, sapodilla, canistel, and mamey sapote (1 ppm); lychee, longan, Spanish lime, rambutan, pulasan, and persimmon (4.0 ppm); bushberry, lingonberry, juneberry, and salal (3.5 ppm); vegetable, leaves of root and tuber, group (4.0 ppm); vegetable, root and tuber, except sugar beet, group 1 (0.4 ppm); fruit, stone, group 12 (3.0 ppm); and vegetable, legume, except soybean, group 6 (4.0 ppm).

Bayer Corporation has submitted a petition to register the use of imidacloprid on imported bananas. The petitioner is proposing the establishment of permanent tolerances for the combined residues of the insecticide imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as the parent, in/on banana (0.01 ppm).

Tolerances are currently established for the combined residues of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as the parent, under 40 CFR §180.472(a) in/on various plant and livestock commodities. Section 18 Emergency Exemption tolerances with expiration/revocation dates are established in/on plant commodities under 40 CFR §180.472(b), and indirect or inadvertent tolerances are established as a result of application of the pesticide to growing crops and other non-food crops under 40 CFR §180.472(d).

There are no established Codex, or Mexican maximum residue limits (MRLs) for imidacloprid in/on any of the proposed uses. There are currently Canadian MRLs for residues of imidacloprid and metabolites containing the 6-chloropicolyl moiety on mustard seed (0.05 ppm), mango (0.2 ppm) and potato (0.3 ppm). For mustard seed, the Canadian tolerance expression and MRL are equivalent to the US tolerance expression and recommended tolerance. However, the Canadian MRLs for mango and potato are lower than the US-recommended tolerance levels, harmonization is not possible at this time.

Nature of the Residue in Plants and Livestock

Data concerning the metabolism of imidacloprid in apples, potatoes, tomatoes, eggplant, cottonseed, field corn, tobacco, ruminants, and poultry have been submitted and reviewed in conjunction with PP#3F4169/3H5655 (Memos, F. Griffith, 9/20/93, D185148; 6/8/94, D200233; and 2/29/96, D217632). The results of the aforementioned plant and livestock metabolism studies were presented to the HED Metabolism Committee (Memo, F. Griffith, 6/18/93; No Barcode). The nature of imidacloprid residues in plants and livestock is adequately understood. The residue of concern in plants and livestock is imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as the parent, as specified in 40 CFR §180.472.

Plants: Imidacloprid is metabolized by three pathways as follows: 1) hydroxylation of the dihydroimidazole ring of imidacloprid to form the 4-hydroxy, 5-hydroxy, and dihydroxy imidacloprid followed by the loss of water to form the olefin; 2) reduction and loss of the nitro group on the dihydroimidazole ring to form the nitrosimino imidacloprid, then the guanidine imidacloprid, and finally the urea imidacloprid; and 3) bridge cleavage of the C-N bond to form the 6-chloropicolyl alcohol (6-CPA) which rapidly forms the glucoside and 6-CNA, and dihydroimidazole.

Ruminants: Imidacloprid is metabolized by 3 pathways as follows: 1) hydroxylation of the dihydroimidazole ring of imidacloprid to form 4-hydroxy, 5-hydroxy, plus the glucuronide conjugates of each monohydroxy metabolite, and the dihydroxy imidacloprid followed by the loss of water to form the olefin imidacloprid; 2) reduction and loss of the nitro group on the dihydroimidazole ring to form aminoguanidine imidacloprid, then the guanidine imidacloprid and finally the urea imidacloprid; and 3) opening of the dihydroimidazole ring with loss of the ethyl group and subsequent oxidation. The first step is forming the nitroguanidine imidacloprid, next the ring open guanidine which can also form both the guanidine imidacloprid and the dihydroxy guanidine imidacloprid. This metabolite can form picolylic urea, and picolylic amine which is oxidized to 6-CNA which then can conjugate with glycine.

Poultry: Imidacloprid is metabolized by 3 pathways as follows: 1) hydroxylation of the dihydroimidazole ring of imidacloprid to form 4-hydroxy, 5-hydroxy and the dihydroxy imidacloprid followed by loss of water to form the olefin; 2) reduction and loss of the nitro group on the dihydroimida-zole ring to form the dihydroxyguanidine imidacloprid, and 3) opening of the dihydroimidazole ring with the loss of the ethyl group and subsequent oxidation. The first step is formation of nitroguanidine imidacloprid, followed by the open ring guanidine imidacloprid which can also form from both the dihydroxy guanidine imidacloprid and the guanidine imidacloprid. This metabolite can form picolylic amine which is oxidized to 6-CNA.

The identified residues in plants, livestock and poultry are imidacloprid and its metabolites which contain the 6-chloropyridinyl moiety. All residues are determined as 6-CNA, then converted to imidacloprid equivalents. See Attachment 1 for structures of all metabolites pertinent to this risk assessment.

Residue Analytical Methods

Adequate enforcement methods are available for determination of imidacloprid residues of concern in plants (Bayer Gas Chromatography/Mass Spectrometry (GC/MS) Method 00200) and livestock commodities (Bayer GC/MS Method 00191). These methods have undergone successful EPA petition method validations (PMVs), and the registrant has fulfilled the remaining requirements for additional raw data, method validation, independent laboratory validation (ILV), and an acceptable confirmatory method (Memos, F. Griffith, 6/18/93, D187911; 6/1/94, D202113; 6/8/94, D200233; 6/8/95, D213252; and 12/18/95; D221591).

Plants: Bayer GC/MS Method 00200 is a common moiety method that uses a 3:1 methanol/1% sulfuric acid extraction, filtering through Celite/filter paper, XAD-4 resin column clean-up, oxidation of parent and metabolites to 6-CNA by refluxing in a 32% sodium hydroxide (NaOH) solution combined with a 5% potassium permanganate ($KMnO_4$) solution, extracted 3 times with methyl t-butyl ether, then N-methyl-N-(trimethylsilyl) trifluroacetamide (MSFTA) derivatization for 1 hour, and determination by capillary GC/MS selective ion monitoring at m/z 214, 216, 170, and 140. The limit of detection (LOD) and limit of quatitation (LOQ) for the GC/MS Method 00200 are 0.01 and 0.05 ppm, respectively, in plant commodities.

Adequate concurrent method recovery data are available for all subject petitions. Samples were analyzed for imidacloprid and the metabolites imidacloprid guanidine (WAK 4140), imidacloprid olefin (WAK 3745), hydroxy imidacloprid (WAK 4103), and 6-CNA using various modifications of Bayer GC/MS Method 00200. These data indicate that the GC/MS method is adequate for determining residues of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as the parent, in/on the proposed uses.

Livestock: Bayer GC/MS Method 00191 is also a common moiety method for total imidacloprid and its metabolite residue containing the 6-chloro-pyridinyl moiety in milk, eggs, and livestock tissues using a methanol/ water extraction, hexane partitioning when necessary, resin column cleanup, permanganate oxidation, silyl derivatization, and determination in a capillary GC-MS selective ion monitoring at m/z 214.

Multiresidue Method (MRM)

Bayer Corporation previously submitted adequate MRM recovery data for imidacloprid and the metabolites WAK 4140, WAK 3745, WAK 4103, and 6-CNA through Food and Drug Administration (FDA) Protocols A through E (Memos, F. Griffith, 6/18/93, D187911; 7/15/93, D193027; 6/8/94, D200233; and 6/22/94, D194206). Imidacloprid and its metabolites were not recoverable by these methods. The results of the MRM testing for imidacloprid were forwarded to FDA for inclusion in the Pesticide Analytical Method Volume I (PAM I) (Memo, F. Griffith 7/15/93, D193005).

Magnitude of Residues in Plants

Crop field trial data were submitted on artichoke, banana, cranberry, strawberry, guava, avocado (preliminary data), papaya, mamey sapote, blueberry, carrot, garden beet, radish, peach, cherry, plum, shelled dry bean, shelled dry pea, shelled succulent pea, and edible podded pea in support of the subject petitions. No residue data were submitted for mustard seed, okra, pop corn, watercress and lychee. In all crop field trial studies, data were acquired on the combined residues of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as the parent. The proposed tolerances for all commodities will be expressed as "the combined residues of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as parent....."

In general, detectable residues of imidacloprid and its metabolites containing 6-chloropyridinyl moiety, all expressed as the parent are likely to be found in samples of raw and processed commodities following foliar applications only, or a combination of soil and foliar applications. Typically, residues were low (<LOQ) in commodities following soil applications only or preplant applications (i.e. seed treatments).

Based on residue decline data available on cranberry, papaya, cherry, plum, peach, strawberry, and shelled dry pea, shelled succulent pea, edible podded pea, the PHIs seem to have little bearing on residues of imidacloprid over the range of 0 to 21 days. No significant decline of the combined residues of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as the parent, was observed throughout the decline studies.

A summary table of the results of the crop field trial studies can be found in Attachment 2 of this risk assessment.

PP#1E6225 - Artichoke: Adequate crop field data on artichoke were submitted and indicate that the combined residues of imidacloprid and its metabolites will not exceed a tolerance of 2.5 ppm in/on artichoke.

PP#1E6268 - Bushberry, Lingonberry, Juneberry and Salal: Adequate crop field trial data on blueberry (highbush and lowbush) were submitted and indicate that the combined residues of imidacloprid and its metabolites will not exceed a tolerance of 3.5 ppm in/on bushberry subgroup 13B, lingonberry, juneberry and salal.

PP#2E6421 - Stonefuit: Adequate crop field trial data on cherry, plum and peach were submitted and indicate that the combined residues of imidacloprid and its metabolites will not exceed a tolerance of 3.0 ppm in/on fruit, stone, group 12.

PP#2E6417 - Strawberry: Adequate crop field trial data on strawberry were submitted and indicate that the combined residues of imidacloprid and its metabolites will not exceed a tolerance of 0.5 ppm in/on strawberry.

PP#2E6403 - Legume Vegetables, Except Soybean: Crop field trial data were submitted on shelled dry bean, shelled dry pea, shelled succulent pea, and edible podded pea. These residue data, as well as previously submitted residue data on succulent shelled beans (PP# 0E6104, Y.

Donovan, D263673) and edible podded beans (PP# 0E06101,Y. Donovan, 5/5/00, D263347) are adequate and indicate that residues of imidacloprid and its metabolites will not exceed the proposed tolerance of 4.0 ppm in/on vegetable, legume, except soybeans, group 6.

PP#1E06074 - Imported Banana: Adequate crop field trials data on banana were submitted and indicate that the combined residues of imidacloprid and its metabolites will not exceed a tolerance of 0.02 ppm in/on imported bananas. Although the company has proposed a 0-day PHI, the crop field trials were conducted using a 7-day PHI. Additional samples were collected at 0, 14, 21 and 35 days for residue decline determination. The data were determined to be adequate. No quantifiable residues were observed in the residue decline samples. As the product is applied as a soil drench and imidacloprid and its metabolites are systemic, the residues from the 7-day PHI would likely be higher than the residues from the 0-day PHI. Therefore, the submitted residue data support the proposed 0-day PHI. **A revised Section F should be submitted to include: 1) the correct tolerance expression of "imidacloprid (1-[(6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine) and its metabolites containing the 6-chloropyridinyl moiety, all expressed as 1-[(6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine,..." and 2) the HED-recommended tolerance of 0.02 ppm.**

PP#0E6203 - Cranberry: Adequate crop field trial data on cranberry were submitted and indicate that the combined residues of imidacloprid and its metabolites will not exceed the proposed tolerance of 0.05 ppm in/on cranberry. HED notes that in Section F of the subject petition the chemical name for the a.i. is presented incorrectly as "1-[(6-chloro-3-pyridinyl)methyl]-*N*-2-imidazolidinimine." **A revised Section F should be submitted with the chemical name corrected as follows: 1-[(6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine.**

PP#2E06414 - Corn, Pop: No pop corn field trial data were submitted in support of PP# 2E6414. HED can generally translate field corn grain/stover data to pop corn grain/stover provided adequate field corn data are available and the use patterns are the same. Adequate field corn residue data have been submitted by the petitioner and reviewed by HED in conjunction with PP#6F04682 (Memo, Y. Donovan, 7/12/00; D224074). Although the proposed application rate for pop corn (0.25 lb ai/cwt) is less than the current application rate for field corn (0.5 lb ai/cwt), the available field trial data for field corn will support the proposed tolerances for the combined residues of imidacloprid and its metabolites in/on corn, pop, grain (0.05 ppm) and corn, pop, stover (0.20 ppm). HED notes that in Section F of the subject petition, the chemical name for the a.i. is presented incorrectly as "1-[(6-chloro-3-pyridinyl)methyl]-*N*-2-imidazolidinimine." **A revised Section F should be submitted with the following: 1) the correct chemical name for imidacloprid: 1-[(6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine and 2) the correct commodity definition for pop corn: corn, pop, grain.**

PP#2E06458 - Mustard, seed: No mustard seed field trial data were submitted in support of this petition. On 3/28/01, the HED ChemSAC determined that canola seed treatment field trial data may be translated to mustard seed provided that residues in the harvested seed are nonquantifiable (ChemSAC Minutes; 5/17/01). In addition, since this decision, ChemSAC agreed to establish Oilseed Crop Group 20 ("Reviewer's Guide...", B. Schneider, 14-JUN-2002). Canola is the representative crop that covers several oilseeds, including mustard seed. Adequate

canola residue data have been submitted by the petitioner and reviewed by HED in conjunction with PP#5F4534 (Memos, F. Griffith, 9/25/95, D216234; and Y. Donovan, 7/12/00, D224074). The available field trial data for canola will support the proposed tolerances for the combined residues of imidacloprid and its metabolites in/on mustard, seed at 0.05 ppm. HED notes that in Section F of the subject petition, the chemical name for the a.i. is presented incorrectly as "1-[(6-chloro-3-pyridinyl)methyl]-*N*-2-imidazolidinimine." **A revised Section F should be submitted to include the correct chemical name for imidacloprid "1-[(6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine."**

PP#1E6254 - Okra: No okra field trial data were submitted in support of this petition. Okra is not currently a member of the fruiting vegetables crop group; however, IR-4 has submitted a Crop Group amendment to EPA to add okra to the Fruiting Vegetables Crop Group, and this proposal is currently undergoing analysis. HED has preliminarily determined that okra should be added to the Fruiting Vegetables Crop Group, and will present this analysis to the HED ChemSAC in the near future. HED has also determined that field residue data for fruiting vegetables are applicable to okra (Memo, G. Herndon, 4/30/01; D274312). Adequate residue data on fruiting vegetables (tomatoes and peppers) have been submitted by the petitioner and reviewed by HED in conjunction with PP#3F4231 (Memo, F. Griffith, 6/22/94, D194206). The proposed use pattern for okra matches the current use pattern for fruiting vegetables. Therefore, the previously submitted field trial data for fruiting vegetables (tomatoes and peppers) will support the proposed tolerance of 1.0 ppm for the combined residues of imidacloprid and its metabolites in/on okra. HED notes that in Section F of the subject petition, the chemical name for the a.i. is presented incorrectly as "1-[(6-chloro-3-pyridinyl)methyl]-*N*-2-imidazolidinimine." **A revised Section F should be submitted with the chemical name corrected as follows: 1-[(6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine.**

PP#0E6237- Watercress: No watercress field trial data were submitted in support of this petition. However, HED concludes that the available head and leaf lettuce data may be translated to watercress based on the following information: (i) the identical use pattern of imidacloprid on leafy vegetables and the proposed use pattern on watercress; (ii) the similarities in growth pattern of watercress and the growth patterns of upland cress and garden cress (members of leafy vegetable crop group), and (iii) the limited acreage of watercress production (~500 acres nationwide). The available data for head and leaf lettuce will support the proposed tolerance of 3.5 ppm for the combined residues of imidacloprid in/on watercress. HED notes that in Section F of the subject petition, the chemical name for the a.i. is presented incorrectly as "1-[(6-chloro-3-pyridinyl)methyl]-*N*-2-imidazolidinimine." **A revised Section F should be submitted with the chemical name corrected as follows: 1-[(6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine.**

PP#2E6406 - Avocado, Papaya, Star Apple, Black Sapote, Mango, Sapodilla, Canistel, Mamey Sapote, Lychee, Longan, Spanish Lime, Rambutan, Pulasan, and Persimmon: Crop field trial data were submitted on papaya, and mamey sapote in support of this petition. HED has determined that residue data on papaya can be translated to black sapote, canistel, mamey sapote, mango, sapodilla, and star apple ("Reviewer's Guide...", B. Schneider, 14-JUN-2002). The submitted residue data, as well as the previously submitted residue data on mango (PP# 4F4285, F. Griffith, 7/22/94, D197675) are adequate and indicate that residues of imidacloprid and its

metabolites will not exceed the proposed tolerance of 1.0 ppm in/on papaya, black sapote, canistel, mamey sapote, mango, sapodilla, and star apple.

No residue data on lychee were submitted in support of this petition. HED has determined that residue data on lychee can be translated to longan, Spanish lime, rambutan, and pulasan ("Reviewer's Guide...", B. Schneider, 14-JUN-2002). It was proposed that the previously submitted residue data on cherries, which was submitted in support of a tolerance for residues of imidacloprid in/on stone fruit (PP#2E6421), be used in lieu of lychee data. The cherry residue data represents worst-case surface area-to-weight ratio, and should represent a worst-case scenario for any tropical fruits. This proposal was presented to the HED ChemSAC on 12/18/02. The ChemSAC recommended that the cherry data can be used to establish **a *conditional* registration and permanent tolerance of 3.0 ppm in/on lychee, longan, Spanish lime, rambutan, and pulasan. For an unconditional registration, the petitioner should submit crop trial data on lychee.**

Preliminary crop field trial data on avocado were submitted and reviewed by HED and was determined to be **adequate to establish a *conditional* registration and a permanent tolerance of 3.0 ppm in/on avocado. For an unconditional registration, the petitioner should officially submit crop trial data on avocado.**

PP#2E6435 - Guava, Feijoa, Jaboticaba, Wax Jambu, Starfruit, Passionfruit, and Acerola: Crop field trial data on guava were submitted in support of this petition. HED has determined that residue data on guava can be translated to feijoa, jaboticaba, wax jambu, starfruit, passionfruit, and acerola ("Reviewer's Guide...", B. Schneider, 14-JUN-2002). The submitted residue data are adequate and indicate that residues of imidacloprid and its metabolites will not exceed the proposed tolerances of 1.0 ppm in/on papaya, black sapote, canistel, mamey sapote, mango, sapodilla, and star apple.

PP#s 2E06409 and 2E06506 - Root and Tuber Vegetables, Except Sugar Beets and Leaves of Root and Tuber Vegetables: Crop field trial data were submitted on radish (tops and roots), garden beet (tops and roots), and carrot. These residue data, as well as previously submitted residue data on potato (PP#3F04169, F. Griffith, D185148) and turnip greens (PP# 9E06041,Y. Donovan, 5/30/00, D263673) are adequate and indicate that residues of imidacloprid and its metabolites will not exceed the proposed tolerance of 0.4 ppm in/on vegetable, root and tuber, except sugar beet, group 1, and 4.0 ppm in/on vegetable, leaves of root and tuber, group 2.

Magnitude of Residues in Processed Commodities

According to the current guidance the processed commodities associated with the subject petitions are potatoes (granules/flakes and chips, peel wet) and plum (prunes). The result of a processing study on potatoes were submitted and reviewed by HED (PP#3F04169, F. Griffith, D185148). Based on the results of that study, tolerances for residues of imidacloprid in/on potato, chip and potato, waste were established at 0.4 ppm and 0.9 ppm, respectively. The recommended tolerance of 0.4 ppm for residues of imidacloprid in/on root and tuber vegetables, except sugar beets, will cover potato, chips. There is currently a Section 18 Emergency Exemption tolerance of 10 ppm on plum, prune. The results of a processing study on plums, prunes were submitted and reviewed by HED (Memo, G. Herndon, 1/27/03, D287694). The

concentration factor for dried plums was determined to be 3x. The recommended tolerance of 3.0 ppm for residues of imidacloprid in/on stone fruit is adequate to cover dried prunes. Therefore, tolerances on potato, chips and plum, prune are no longer needed.

Magnitude of Residues in Meat, Milk, Poultry and Eggs (MMPE)

Ruminants: No ruminant feeding study was submitted with the subject petitions. The ruminant feed items associated with the subject petitions are carrot (culls), potatoes (culls and processed potato waste), and pop corn grain and stover. Permanent tolerances have been previously established for the combined residues of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, expressed as the parent, in/on several livestock commodities (Memo, F.Griffith, 9/21/93; D185148). The results of a ruminant feeding study was submitted and reviewed by HED in the 9/21/98 memo. From the results of that study, HED estimated the maximum theoretical dietary burden (MTDB) using proposed and established imidacloprid tolerances. The total dietary burdens, calculated using worst case diets, were 20 ppm (consisting of 60% wheat forage, 20% potato waste, and 20% wet apple pomace) for dairy cattle, and 12 ppm (consisting of 25% wheat forage, 35% potato waste, and 40% wet apple pomace) for beef cattle. Based on these results, the appropriate tolerances were established. In conjunction with the petition for the use of imidacloprid on field corn (PP#6F04682), HED determined that field corn will not have a significant effect on the previously calculated MTDB, and an increase in livestock tolerances were not needed (Memo, Y. Donovan, 7/12/00, D224074). As pop corn livestock feed commodities are used interchangeably with field corn feed commodities in the diet of ruminants, pop corn feed items are not expected to significantly change the MTDB. In addition, HED does not expect carrot culls and potato culls to result in a higher MTDB. Therefore, the current tolerances for ruminants are adequate.

Poultry: There are no poultry feed items associated with the subject petitions. However, an acceptable poultry feeding study has been submitted and reviewed with PP# 3F4169/3H5655 (Memos, F. Griffith, 9/20/93, D185148; and 6/8/94, D200233).

Confined and Field Accumulation in Rotational Crops

According to the current guidance the following crops associated with this risk assessment are considered to be rotated: okra, mustard seed, strawberry, root and tuber vegetables, and legume vegetables. Adequate rotational crop data have been submitted and reviewed by HED (Memo, F. Griffith 8/9/94; PP#3F04169). The data were used to establish the current rotational crop tolerances under 40 CFR §180.472(d) for indirect and inadvertent residues of imidacloprid (Memo, G. Kramer, 9/23/96; D228500). The Provado® 1.6F, Admire® 2F, Gaucho® 480 F and Gaucho® 600 F labels specify a 0-day plantback interval (PBI) for all crops on the label, a 30-day PBI for crops listed under §180.472(d), and a 12-month PBI for all non-labeled crops. RD should ensure that the rotational crop specifications be updated to include all crops not covered under §180.472.

4.2.2 Dietary Exposure Analyses

Imidacloprid acute and chronic dietary exposure assessments were conducted using DEEM-FCID™, Version 1.30), which incorporates consumption data from USDA's CSFII, 1994-1996 and 1998. The 1994-96, 98 data are based on the reported consumption of more than 20,000

individuals over two non-consecutive survey days. Foods "as consumed" (e.g., apple pie) are linked to EPA-defined food commodities (e.g. apples, peeled fruit - cooked; fresh or N/S; baked; or wheat flour - cooked; fresh or N/S, baked) using publicly available recipe translation files developed jointly by USDA/ARS and EPA. Consumption data are averaged for the entire U.S. population and within population subgroups for chronic exposure assessment, but are retained as individual consumption events for acute exposure assessment.

For chronic exposure and risk assessment, an estimate of the residue level in each food or food-form (e.g., orange or orange juice) on the food commodity residue list is multiplied by the average daily consumption estimate for that food/food form. The resulting residue consumption estimate for each food/food-form is summed with the residue consumption estimates for all other food/food-forms on the commodity residue list to arrive at the total average estimated exposure. Exposure is expressed in mg/kg body weight/day and as a percent of the cPAD. This procedure is performed for each population subgroup.

For acute exposure assessments, individual one-day food consumption data are used on an individual-by-individual basis. The reported consumption amounts of each food item can be multiplied by a residue point estimate and summed to obtain a total daily pesticide exposure for a deterministic (Tier 1 or Tier 2) exposure assessment, or "matched" in multiple random pairings with residue values and then summed in a probabilistic (Tier 3/4) assessment. The resulting distribution of exposures is expressed as a percentage of the aPAD on both a user (i.e., those who reported eating relevant commodities/food forms) and a per-capita (i.e., those who reported eating the relevant commodities as well as those who did not) basis. In accordance with HED policy, per capita exposure and risk are reported for all tiers of analysis. However, for Tiers 1 and 2, significant differences in user vs. per capita exposure and risk are identified and noted in the risk assessment.

The results of the acute and chronic assessments are listed in Table 6. DEEM-FCID™ (Ver. 1.30) estimates the dietary exposure for the U.S. population and 28 population subgroups. Based on an analysis of 1994-96, 98 CSFII consumption data which took into account dietary patterns and number of survey respondents, HED determined that the following population groupings were appropriate for regulatory purposes (only the exposure estimates for these populations are reported in this document): U.S. Population, all infants (<1 year old), children 1-2 years old, children 3-5 years old, children 6-12 years old, youth 13-19 years old, females 13-49 years old, adults 20-49 years old, and/or adults 50+ years old.

The following should be noted:

- Several commodities associated with the proposed uses currently have tolerances (permanent and Section 18 Emergency Exemption) established under 40 CFR §180.472. For both acute and chronic assessments, HED-recommended tolerances associated with the proposed petitions were used instead of the established tolerances, with the exception of plum, prune and cranberry. For these commodities, current Section 18 Emergency Exemption tolerances were higher than the HED-recommended permanent tolerance. Therefore, the Section 18 tolerances were used as a conservative assumption.
- The following commodities associated with the current petitions were not reported in DEEM-FCID™: mustard seed, wax jambu, star apple, black sapote, sapodilla, Spanish lime, pulasan, juneberry, lingonberry, and salal. Adequate data are available for the determination of tolerance levels, as discussed in the applicable residue chemistry memos. In cases where data translation was used, the HED ChemSAC approved of translating from related crops. Most of the crops that used translated data are minor crops

having relatively low consumption. For certain crops, the consumption is so low that they are not included in the DEEM-FCID™ program. In these cases, the DEEM-FCID™ program underestimates the exposure to imidacloprid residues from these crops; however, because the consumption levels of these crops is so low (on a national basis), inclusion of these crops would likely make no difference in the overall predicted exposures to imidacloprid residues.

- There are currently tolerances for residues of imidacloprid in/on grape juice, raisins, tomato paste and tomato puree; therefore, the DEEM™ Version 7.76 processing factors for these processed commodities were reduced to 1. Default DEEM™ Version 7.76 processing factors were used for all other registered and proposed processed commodities.

4.2.2.1 Acute Dietary Exposure Analysis

An unrefined, Tier 1 acute dietary exposure assessment was conducted for the general U.S. population and various population subgroups, using tolerance-level residues and assuming 100% CT for all registered and proposed commodities.

The acute dietary exposure estimates are below HED's level of concern (<100% aPAD) at the 95th exposure percentile for the general U.S. population (25% of the aPAD) and all other population subgroups. The most highly exposed population subgroup is children 1-2 years old, at 64% of the aPAD. The acute assessment was highly conservative, using several upper-end assumptions. ARs and %CT data could be used in order to refine the acute assessment.

4.2.2.2 Chronic Dietary Exposure Analysis

A partially refined, Tier 2 chronic dietary exposure assessment was conducted for the general U.S. population and various population subgroups. Tolerance-level residues were used for all registered and proposed commodities. Average, weighted % CT information provided by BEAD was used for the following commodities: apples, Brussels sprouts, broccoli, cabbage, cantaloupe, cauliflower, collards, cotton, cucumber, eggplant, grapefruit, grapes, honeydew, kale, lemons, limes, mustard greens, oranges, pears, peppers, pumpkin, spinach, squash, sugarbeet, tangerines, tomatoes, watermelon, and wheat. 100% CT information was used for all other commodities.

The chronic dietary exposure estimates are below HED's level of concern (<100% cPAD) for the general U.S. population (11% of the cPAD) and all population subgroups. The most highly exposed population subgroup is children 1-2 years old, at 35% of the cPAD. The chronic assessment was conservative, using upper-end assumptions. Additional refinements, such as inclusion of ARs and additional % CT data, could be made in order to refine the chronic assessment.

Table 6. Summary of Dietary Exposure and Risk for Imidacloprid

Population Subgroup	Acute Dietary[1]		Chronic Dietary[2]		Cancer Dietary
	Dietary Exposure (mg/kg/day)	% aPAD	Dietary Exposure (mg/kg/day)	% cPAD	
U.S. Population (total)	0.035373	25	0.006514	11	NA[3]
All Infants (< 1 year old)	0.075240	54	0.015038	26	

Table 6. Summary of Dietary Exposure and Risk for Imidacloprid

Population Subgroup	Acute Dietary[1]		Chronic Dietary[2]		Cancer Dietary
	Dietary Exposure (mg/kg/day)	% aPAD	Dietary Exposure (mg/kg/day)	% cPAD	
U.S. Population (total)	0.035373	25	0.006514	11	NA[3]
Children 1-2 years old	0.089369	64	0.019898	35	
Children 3-5 years old	0.066219	47	0.014076	25	
Children 6-12 years old	0.041805	30	0.008560	15	
Youth 13-19 years old	0.026434	19	0.004793	8.4	
Adults 20-49 years old	0.023241	17	0.004858	8.5	
Females 13-49 years old	0.023679	17	0.004753	8.3	
Adults 50+ years old	0.024073	17	0.005737	10	

1. Acute dietary endpoint of 0.14 mg/kg/day applies to the general U.S. population and all population subgroups.
2. Chronic dietary endpoint of 0.057 mg/kg/day applies to the general U.S. population and all population subgroups.
3. NA = not applicable. The RfD/Peer Review Committee classified imidacloprid as a "Group E" (no evidence of carcinogenicity for humans) chemical based on adequate studies in two animal species; therefore, a cancer risk assessment is not required.

4.3 Water Exposure/Risk Pathway

In a meeting on 12/18/02, the HED MARC met to discuss the imidacloprid degradates of concern in drinking water only (see Attachment 1 for structures of all metabolites pertinent to this risk assessment). Environmental fate data suggest that imidacloprid is rapidly transformed under anaerobic conditions, and is particularly photolabile in water. In an aqueous photolysis study, three degradates (imidacloprid urea, imidacloprid guanidine, and imidacloprid olefin) were found at levels >10% of the applied dose in 2 hours. The combined residue level of these three degradates, which are likely to be found in surface water, is >40%. Judging from the structures, these degradates, which all have weaker electron withdrawing groups than the parent, are likely to be of lower toxicity than the parent, particularly from the neurotoxicity perspective. This is because a strong electron withdrawing group is thought to be related to the affinity of the chemical to the acetylcholine receptor (I. Yamamoto "Nicotine and Nicotinoids: 1962 to 1997" in *Nicotinoid Insecticides and the Nicotinic Acetylcholine Receptor*, I. Yamamoto and J.E. Casida eds, Springer-Verlag Tokyo Berlin Heidelberg New York, 1999, p. 23.). However, there is not enough toxicological information to exclude these three degradates from the drinking water assessment. Therefore, MARC recommended that for surface water risk assessment, the degradates of concern should be parent and the three degradates: imidacloprid urea, imidacloprid guanidine, and imidacloprid olefin (Memo, J. Tyler 1/13/03; D28740). Per the MARC's recommendation, EFED further investigated the ground water literature and imidacloprid database in order to determine whether the degradates (imidacloprid urea, imidacloprid guanidine, and imidacloprid olefin) are likely to reach ground water.

Available environmental fate data also suggest that imidacloprid is stable to hydrolysis, and

typically persists for many months in soil. Therefore, the parent will likely be the major residue in ground water. However, in an anaerobic aquatic study, the guanidine metabolite was found at 66% of the applied dose at day 300, indicating a potential for significant exposure to guanidine in anaerobic ground water. The results of an analysis of the monitoring data for degradates (ground-water only) show that imidacloprid parent is the dominant residue with imidacloprid urea the most likely degradate to occur. Modeling of total residues, using the limited available data on degradate persistence and mobility, resulted in only modest increases over the upper-bound surface water exposure estimates than that of parent alone.

Therefore, EFED provided revised, Tier 1 EECs for ground water (using SCI-GROW) and surface water (using FIRST) for imidacloprid and its degradates (imidacloprid urea, imidacloprid guanidine, and imidacloprid olefin) (see Table 7). In the absence of definitive data on the persistence and mobility of these degradates, the total residues were modeled using tentatively identified total residue data from aerobic soil metabolism studies, and then assuming that the partitioning of all residues was at the same degree as imidacloprid parent. Degradate persistence and mobility data (especially from aerobic soil metabolism and batch equilibrium adsorption / desorption studies) are needed to more accurately model the total residues. However, EFED does not expect these to be exceeded under real-world usage conditions.

Table 7. Estimated Tier 1 Concentrations of Imidacloprid in Drinking Water.

Chemical	Surface Water (ug/L)		Groundwater (ug/L)
	Acute	Chronic	Acute and Chronic
Imidacloprid total residues[1]	36.04	17.24	2.09

1. Imidacloprid and its degradates (imidacloprid urea, imidacloprid guanidine, and imidacloprid olefin).

4.4 Residential Exposure/Risk Pathway

HED previously conducted a non-occupational, residential exposure assessment for imidacloprid (for turf and pet uses) (Memo, Y. Donovan, 1/22/01, D268562). The endpoints have changed as a result of the 10/8/02 HIARC meeting; therefore, residential pesticide handler and post-application exposures are reassessed here.

4.4.1 Residential Use Pattern

As mentioned previously, REFS (5/7/02) indicates that there are currently 82 registered products (excluding Section 18 registrations) that contain imidacloprid as the a.i.. These products are registered for use on residential ornamental lawns, golf courses, ornamental plantings (i.e., flowering plants, foliage plants, herbaceous perennial plants, and woody plant, shrubs and trees). Imidacloprid is also registered for indoor as well as outdoor residential uses. It is registered as a pre- and post-construction termiticide.

4.4.1.1 Residential Handler Exposure

HED has determined that residential handlers are likely to be exposed to imidacloprid residues via dermal and inhalation routes during handling, mixing, loading, and applying activities. Based on the current use patterns, HED expects duration of exposure to be short-term (1-30 days). HED does not expect imidacloprid to result in exposure durations that would result in intermediate- or long-term exposure.

Using the Pesticide Product Label System (PPLS), HED determined the use patterns of each product in terms of pesticide handlers (See Table 8). The various types of products intended for residential use are used to control several different pests. Therefore, **HED believes that it is highly unlikely that a residential handler would be concurrently exposed to more than one formulation containing imidacloprid at any given time (i.e., apply a granular, then apply a topical flea control product, then apply a ready-to-use (RTU) product).**

In addition, there are numerous registered products intended for use by commercial applicators to residential sites only. These include gel baits for cockroach control; products intended for commercial ornamental, lawn and turf pest control; products for ant control; and products used as preservatives for wood products, building materials, textiles and plastics. As these products are intended for use by commercial applicators only, they will not be addressed in terms of residential pesticide handler.

Table 8. Summary of Residential "Handler" Use Patterns.

Site	Product	Formulation	Application Rate	Number of Applications	Comments
Lawns & Turf Ornamental Plantings	Merit® 0.62 G Insecticide (EPA Reg. No. 3125-416)	Granular 0.62 %	0.4 lb a.i./A	1/yr	Applied with broadcast by push-type "drop" or rotary spreader.
Flowers, Ground Covers, Shrubs, House Plants	Merit® RTU (EPA Reg. No. 3125-501)	RTU Pump Sprayer 0.012 % 24 fl.oz.	"Spray till point of run-off"	"As needed" 7 - 14 day intervals	
Indoor & Outdoor Residential Potted Plants	Merit® 2.5 PR (EPA Reg No. 3125-531)	Plant "spikes" 0.8 oz (20 g) 10 two gram spikes 2.5 %	The package will treat 4-5 eight inch pots	Efficacious for 8 weeks	Formulation contains fertilizer and Bitrex. Not for use on edible plants/herbs etc.
Potting Medium for Indoor or Outdoor Plant Containers	Merit® PM Plus Fertilizer (EPA Reg. No. 3125-532)	0.015 % RTU potting medium - largest container 19 lb 3 oz		Efficacious 4 months	Used as medium for new seedlings or as additional medium when transplanting to larger containers. Label directs use of rubber gloves. Medium contains sphagnum, bark, perlite, vermiculite, limestone and fertilizers

Table 8. Summary of Residential "Handler" Use Patterns.

Site	Product	Formulation	Application Rate	Number of Applications	Comments
Lawns, Trees, Shrubs, Flowers	Merit® + Tempo Concentrate (EPA Reg. No. 3125-505)	Liquid concentrate 0.70 % 32 fl oz	0.001098 lb a.i./5000 ft^2	"Repeat if needed" in 7 - 14 days	For use on out-door, non-food residential plants. Assumed applied via compressed air or garden hose-end sprayer.
Trees & Shrubs	Merit® 2.94 TLC (EPA Reg. No. 3125-554)	Liquid concentrate 2.95 % one gallon = largest container size	Depends on plant stem size. One gallon treats 20 "medium" trees or 42 "average" shrubs	1/yr	Applied to soil by pouring dilute from a bucket or a watering can around bases of plant "stems"/trunks.
Cats & Dogs	Advantage® 110 (EPA Reg. No. 11556-121)	RTU liquid 9.1 %	Max rate = 5.0 ml for dogs >55 lb	1/mo if needed	Packaged in "dropper" vials. The end cap is removed and one half the contents dropped between the scapulae and one half on the lumbrosacral region. No rubbing or other contact is directed.

The scenarios likely to result in adult dermal and/or inhalation residential handler exposures are as follows:

- Dermal and inhalation exposure from using a granular push-type spreader.
- Dermal exposure from using potted plant spikes.
- Dermal exposure from using a plant potting medium..
- Dermal and inhalation exposure from using a garden hose-end sprayer (dermal and inhalation exposure from using a RTU trigger pump spray is expected to be negligible).
- Dermal and inhalation exposure from using a water can/bucket for soil drench applications.
- Dermal exposure from using pet spot-on.

Table 9 lists the estimated residential handler exposures and risks for the scenarios listed above. All residential handler exposures and risks resulted in MOEs > 100 and, therefore, do not exceed HED's level of concern.

Table 9. Summary of Residential Handler Exposures and Risks [1].

Activity	Exposure/Dose (mg a.i./kg bw/day)	MOE
Granular/Push-type Spreader Application	Dermal + inhalation 0.0000162	72,000
RTU Trigger Pump Spray	Negligible (see hose end spray)	
Potted Plant Spikes	Dermal (inhalation negligible) 0.00392	2,600

Table 9. Summary of Residential Handler Exposures and Risks [1].

Activity	Exposure/Dose (mg a.i./kg bw/day)	MOE
Plant Potting Medium	Dermal (inhalation negligible) 0.01	1,000
Garden Hose-end Spray	Dermal + Inhalation 0.0000539	190,000
Soil Drench - Water Can/Bucket	Dermal + Inhalation 0.0007	14,000
Pet Spot-On	Dermal (inhalation negligible) 0.025	400

[1] A detailed explanation of how each value was calculated can be found following this table.

Resident-applicator Granular Push-type Spreader: The resident-applicator using push-type spreader to apply granules scenario was assessed using HED SOPs for Residential Exposure Assessments (12/18/97) in conjunction with unit exposures developed by the Outdoor Residential Exposure Task Force (ORETF) and cited as ExpoSAC policy (Memo, G. Bangs, MRID 449722-01, 30 4/01). The dermal unit exposure for an applicator wearing short pants and short sleeved shirt plus shoes and socks = 0.68 mg a.i./lb handled. The inhalation unit exposure is 0.00091 mg a.i./lb handled. Dermal absorption is 7%. The rate of application is taken from Merit® 0.62 G insecticide (Reg. No. 3125-416). Exposure is then estimated as:

0.68 mg a.i./lb handled * 0.4 lb handled/A * 0.5 A/day * 0.07 ÷ 70 kg bw = 0.000136 mg a.i./kg bw/day$_{dermal}$
0.00091 mg a.i./lb handled * 0.4 lb handled/A * 0.5 A/day ÷ 70 kg bw = 0.0000026 mg a.i./kg bw/day$_{inhalation}$
Dermal + Inhalation exposure = 0.000139 mg a.i./kg bw/day
MOE = NOAEL/Dose = 10 mg a.i./kg bw/day/0.000139 mg a.i./kg bw/day = **72,000**

Resident-applicator RTU: Merit® RTU is 0.012 % imidacloprid in a 24 fl. oz. trigger pump spray bottle. This exposure scenario was not formally assessed here. HED expects that exposure from use of the entire contents (i.e., 24 fl.oz.) will not exceed the exposure associated with the use of a garden hose-end sprayer, which is assessed later in this document.

Resident-applicator/Potted Plant Spikes: Merit® 2.5 PR consists of 10 two gram "spikes" of which 2.5 % is imidacloprid. Plant "spikes" are semi-solid cylindrically shaped objects with the diameter of a lead pencil and about an inch long. They are composed of a mixture of imidacloprid, fertilizers/plant nutrients and decomposable bonding materials. There are no specific unit exposure data relative to this use; therefore, HED used the PHED **"hand"** unit exposure for an applicator applying granular bait by hand. HED believes that use of the hand applied granular unit exposure *overestimates* the exposure actually experienced from the use of plant "spikes." Essentially, only the tips of one or two fingers and one thumb are necessary to push "spikes" into potting soil. HED assumes that the entire package is used at one time. One package of 10 "spikes" will treat 4 - 5 eight inch plant pots. The label directs a user to "push spikes down into the soil..." Since the vapor pressure of imidacloprid is 1.5×10^{-9} mm Hg at 20°C, HED believes inhalation exposure in this case is negligible. So, 10 two gram "spikes"

equal 20 g product of which 2.5% is imidacloprid = 0.5 g a.i. (0.5 g a.i. ÷ 453.6 g/lb = 0.0011 lb a.i.). The unit exposure for the hand is 356 mg a.i./lb handled and is for a "gloved" i.e., "protected" hand. The unit exposure is back-calculated to account for 90% protection of a gloved hand and the ungloved unit exposure is 3,560 mg a.i./lb handled. Exposure is then estimated as:

3,560 mg a.i./lb handled * 0.0011 lb a.i. handled/day * 7 % Derm. Abs. ÷ 70 kg bw = 0.00392 mg a.i./kg bw/day.
MOE = NOAEL/DOSE ∴ 10 mg a.i./kg bw/day ÷ 0.00392 mg a.i./kg bw/day = **2,600**

Resident-applicator/Plant Potting Medium: Merit® PM plus fertilizer (Reg. No. 3125-532) is a plant potting medium for use in indoor or outdoor containers. It contains 0.015 % imidacloprid. The largest container net weight is 19.19 lb of which 0.015 % is imidacloprid = 0.00288 lb a.i. HED assumes that one large container is used per day. As with the assessment of plant "spikes" above, HED utilizes the SOP unit exposure value for hands for residential applicator applying granular bait by hand. The hand unit exposure is corrected to equate to an "ungloved" (i.e., unprotected hand). Exposure is then estimated as:

3,560 mg a.i./lb handled * 0.00288 lb handled/day * 7 % D.A. ÷ 70 kg bw = 0.01 mg a.i./kg bw/day
MOE = NOAEL/DOSE ∴ 10 mg a.i./kg bw/day ÷ 0.1 mg a.i./kg bw/day = **1,000**

Resident-applicator using Garden Hose-end Sprayer: Merit® Concentrate Insecticide (Reg. No. 3125-500) contains 2.94 % imidacloprid and is a liquid concentrate for dilution and use in pump up sprayers or garden hose-end sprayers. HED policy indicates a larger area per day may be treated with a hose-end sprayer which results in possible contact with more a.i. per day. Therefore, exposure from a hose-end sprayer is assessed versus that of a compressed air sprayer. The unit density of this product is 1.6 g/ml (pers. comm. D. Kenny, Registration Division, 25 OCT 02). Using a conversion factor (Oil & Colour Chemists Assoc. www.occa.org.uk) g/ml are converted to lb/gal by multiplying by 0.09978. Thus 1.6 g/ml * 0.09978 = 0.1596 lb/gal of which 2.94 % is imidacloprid or 0.00469 lb/gal imidacloprid. 0.00469 lb/gal ÷ 128 fl oz/gal = 0.0000366 lb a.i./fl oz. The maximum rate of application is 6 fl oz/1000 ft^2. Therefore, 0.0000366 lb a.i./fl oz * 6 fl oz/1000 ft^2 = 0.0002196 lb a.i./1000 ft^2. HED SOPs assume 0.5 acre treated per day (rounded to 22,000 square feet treated per day); therefore, 0.0048312 lb a.i. will be applied per day. The unit exposure value for a residential handler using open pour mixing/loading for a garden hose-end sprayer is 11 mg/lb handled (dermal) and 0.016 mg/lb handled (inhalation) (Memo, G. Bangs, MRID 449722-01; 30 APR 01; Summary of HEDs Reviews of ORETF Chemical Handler Exposure Studies). Thus, exposure is estimated as:

11.0 mg a.i./lb handled * 0.0002196 lb a.i./1000 ft^2 * 22,000 ft^2/day * 7 % dermal absorption ÷70 kg bw = 0.000053 mg a.i./kg bw/day for dermal.
0.016 mg a.i./lb handled * 0.0002196 lb a.i./1000 ft^2 * 22,000 ft^2/day ÷ 70 kg bw = 0.0000011 mg a.i./kg bw/day.
Dermal + inhalation = 0.0000541 mg a.i./kg bw/day. **MOE = NOAEL/Dose** ∴
10mg a.i./kg bw/day ÷ 0.0000541 mg a.i./kg bw/day = **190,000**

Resident-applicator/Soil Drench Using Bucket or Watering Can: Merit® 2.94 TLC is a liquid concentrate intended for use as a systemic soil drench application using a pail or watering can. The largest product container is 3.78 liters and HED assumes that equates to 3780 grams of

which 2.94 % is imidacloprid, or 111 g a.i. HED assumes the contents of one container is used per day which will treat 20 medium trees or 42 average sized shrubs. The total 111 g a.i. = 0.245 lb a.i. The unit exposures are taken from the Residential SOPs with dermal = 2.9 mg/lb handled and inhalation = 0.0012 mg/lb handled. The unit exposures are for a residential handler using liquid, open pour mixing. Exposure is then estimated as:

2.9 mg a.i./lb handled * 0.245 lb handled/day * 7 % dermal absorption ÷ 70 kg bw = 0.0007 mg a.i./kg bw/day (dermal)
0.0012 mg a.i./lb handled * 0.245 lb handled/day ÷ 70 kg bw = 0.0000042 mg a.i./kg bw/day.
Dermal + inhalation = 0.0007 and with **MOE = NOAEL/DOSE**, 10 mg a.i./kg bw/day ÷ 0.0007 = **14,000**

Resident-applicator Pet Spot-On: HED believes that imidacloprid applied as label directed will result in negligible handler exposure. However, there is a possibility that the residential handler may pet the dog immediately following application. Therefore, HED has provided an assessment that will estimate the combined residential handler and post-application exposure and risk from this worst-case scenario. A handler uses a dropper to deliver 2.5 ml to two spots on a dog's back (total = 455 mg a.i.). There should be no contact with any material and if there is contact, HED believes it would be minimal. There are no chemical-specific data nor any applicable surrogate data with which to assess this method of application. There is an unpublished study (Fichtel, M. and R. Krebber. 27 MAR 1996, Imidacloprid (Bay t 7391) - Stroke Test in Dogs after Topical Application of Imidacloprid Spot-on 10%; Bayer Animal Health Development AH-D ID: 16051) which was designed to determine residues that persons with close physical contact to a treated animal might experience. ***UNTIL FORMALLY NOTIFIED OTHERWISE THE STUDY SHOULD BE CONSIDERED PROPRIETARY AND SUBJECT TO DATA COMPENSATION.*** The study used cotton gloves as dosimeters. Sixteen dogs received a 500 mg dose as would a dog receiving a maximum treatment dose from Advantage 110 Flea Adulticide (Reg. No. 11556-121), one half of which was administered between the scapulae (shoulders) and one half on the rump (lumbosacral region) according to label directions. Samples were taken from each treatment site separately (i.e., shoulders separately from rump area) and consisted of 30 strokes, one per second at about 20 cm per stroke such as not to overlap the treated areas. A new dosimeter glove was used for each "site" change and for each dog. Residues were analyzed after extraction with acetonitrile using HPLC with UV detector (recovery rates of 83-94%). Summary data are:

(mg imidacloprid/glove +/- SEM)	
10 min	24.9 +/- 6.4
1 hr	17.3 +/- 3.3
12 hr	3.9 +/- 1.1
24 hr	2.7 +/- 0.7

The **total dose** from the four sampling times over 24 hours is 48.8 mg imidacloprid. This is derived from purposeful stroking of a treated animal, on the treatment loci. HED herein uses the data from sampling at ten minutes post-application and assumes that a pesticide handler would not receive a greater dose if applied according to label directions than what was measured via cotton glove dosimetry from purposeful stroking of treatment loci. Cotton glove dosimeters are highly sorbent and in this case, dermal absorption is 7%. Therefore, an estimate of exposure is:

24.9 mg a.i./day * 7 % dermal absorption ÷ 70 kg bw = 0.025 mg a.i./kg bw/day
MOE = NOAEL/DOSE where 10 mg a.i./kg bw/day ÷ 0.025 mg a.i./kg bw/day = **400**

4.4.1.2 Residential Post-Application Exposure

HED has determined that there is potential for short-term (1 to 30 days), post-application exposure to adults and children/toddlers from the many residential uses of imidacloprid. Due to residential application practices and the half-lives observed in the turf transferable residue study, intermediate- and long-term post-application exposures are not expected. The scenarios likely to result in dermal (adult and child/toddler), and incidental non-dietary (child/toddler) short-term post-application exposures are as follows:

- Toddler oral hand-to-mouth exposure from contacting treated turf.
- Toddler incidental oral ingestion of granules.
- Toddler incidental oral ingestion of pesticide-treated soil.
- Toddler incidental oral exposure from contacting treated pet.
- Toddler dermal exposure from contacting treated turf.
- Toddler dermal exposure from "hugging" treated pet/contacting treated pet.
- Adult dermal exposure from contacting treated turf.
- Adult golfer dermal exposure from contacting treated turf.
- Adolescent golfer dermal exposure from contacting treated turf.
- Adult dermal exposure from contacting treated pet

Based on the low vapor pressure of imidacloprid, post-application inhalation exposure is expected to be negligible. Table 10 lists the estimated residential post-application exposures and risks for the scenarios listed above. All residential post-application exposures and risks resulted in MOEs > 100; and, therefore, do not exceed HED's level of concern.

Table 10. Summary of Residential Post-Application Exposures and Risks for Imidacloprid. [1]

Activity	Exposure (Dose) mg a.i./kg bw/day	MOE
Toddler oral hand to mouth exposure from contacting treated turf	0.0059	1,700
Toddler incidental oral exposure from ingestion of granules	0.12	350
Toddler incidental oral exposure from ingestion of treated soil	0.00002	500,000
Toddler dermal exposure from contacting treated turf	0.001	10,000

Table 10. Summary of Residential Post-Application Exposures and Risks for Imidacloprid. [1]

Activity	Exposure (Dose) mg a.i./kg bw/day	MOE
Toddler incidental oral exposure from contacting treated pet	10 min hand wipe data = 0.00276 1 hr hand wipe data = 0.0019 12 hr hand wipe data = 0.0004332 24 hr hand wipe data = 0.0003	3,600 5,200 23,000 33,000
Toddler dermal exposure from pet "hug"/contacting treated pet	0.036	280
Adult dermal exposure from contacting treated turf	0.00053	19,000
Adult golfer exposure from contacting treated turf	0.00016	63,000
Child golfer exposure from contacting treated turf	0.000272	37,000
Adult post-application exposure from contacting treated pet	See Section 4.4.1.1 Residential Handler	

[1] A detailed explanation of how each value was calculated can be found following this table.

As noted earlier, HED conducted a "Non-Occupational/Residential Exposure Assessment for Imidacloprid - Turf and Pet Uses" (Memo, Y. Donovan, 1/22/01, D268562). The 1/22/01 memo cites an HED review (Memo L. Lasota, 11/14/96, D223275, MRID# 43923901) of a study of imidacloprid DFRs from turf as well as passive monitoring of dermal and inhalation exposure measured during the course of prescribed "jazzercise" activities. The accepted study provides compound-specific turf transferable residue data as well as dermal transfer factors relative for use in assessing non-occupational, post-application, dermal exposures. The HED memo of 1/22/01 did not utilize the study data as no dermal or inhalation toxicological endpoints had been identified at that time. In the current assessment, where applicable, data and information from the 1996 LaSota memo are utilized to estimate dermal, and post-application exposures. The half-lives of imidacloprid at the three study locations were 2.0 days in Florida, 0.9 day in New Jersey, and 1.1 days in Kansas.

Relative to post-application exposure, spray drift is often a potential source of exposure to residents nearby to agricultural spraying operations. This is particularly the case with aerial operations, but to a lesser extent, could also be a potential source of exposure from ground application methods. As indicated in this assessment, imidacloprid can be directly applied to residential turf. The rates of application to residential turf are generally equal to or greater than the agricultural rates of application. The resulting Margins of Exposure are not of concern to HED. Therefore, based on this assessment, HED believes that it is unlikely that there is higher potential for risk of exposure to spray drift from agricultural uses of this chemical than have been assessed for direct residential applications.

In addition, as mentioned previously, imidacloprid is registered as a termiticide. Due to the low volatility of imidacloprid, coupled with the fact that it is used pre- and post-construction only, HED does not expect there to be potential for post-application residential exposure to imidacloprid from this use. Therefore, a post-application exposure assessment was not conducted for this use scenario.

Toddler Oral Hand-to-Mouth Exposure from Contacting Treated Turf: Children's short-term oral hand-to-mouth exposure was assessed in the HED memo of 1/22/01 using HED SOPs for Residential Exposure Assessments (12/18/97). The estimated Average Daily Oral Dose was 0.0059 mg a.i./kg bw/day. Using the short-term incidental oral NOAEL identified by the HIARC (8/10/02) of 10 mg a.i./kg bw/day, the MOE for short-term oral hand-to-mouth (i.e., incidental oral exposure from contacting treated turf grass) is as follows:

NOAEL ÷ Average Daily Dose = MOE
10 mg a.i./kg bw/day ÷ 0.0059 mg a.i./kg bw/day = **1700**

Toddler Incidental Oral Ingestion of Granules: Children's incidental oral exposure from ingestion of granules was assessed in the HED memo dated 1/22/01 using HED SOPs for Residential Exposure Assessments (12/18/97). The estimated Average Daily Oral Dose was 0.12 mg a.i./kg bw/day. Using the LOAEL of 42 mg a.i./kg bw/day acute dietary endpoint identified by HIARC, the MOE for incidental ingestion of granules is as follows:

LOAEL ÷ Average Daily Dose = MOE
42 mg a.i./kg bw/day ÷ 0.12 mg a.i./kg bw/day = **350**

Toddler Incidental Oral Ingestion of Pesticide Treated Soil: Children's incidental oral ingestion of pesticide-treated soil was estimated using HED SOPs for Residential Exposure Assessments (12/18/97) as follows:

PDRt for incidental ingestion of soil = SRt * IgR * CF1

where:	PDRt	=	potential dose rate on day "t" (mg/day)
	Srt	=	soil residue on day "t" (ug/g)
	IgR	=	ingestion rate of soil (mg/day) (100 mg/day)
	CF1	=	weight unit conversion factor to convert the ug of residues on the soil to grams to provide units of mg/day (1E-6 g/ug)
and:	SRt	=	AR * F * (1-D)t * CF2 * CF3 * CF4
where:	AR	=	application rate (lb ai/acre) (0.4 lb a.i./A)
	F	=	fraction of a.i. available in uppermost cm of soil (fraction/cm) (1.0/cm)
	D	=	fraction of residue that dissipates daily
	t	=	post-application day on which exposure is being assessed (day zero)
	CF2	=	weight unit conversion factor to convert the lbs a.i. in the application rate to ug for the soil residue value (4.54E+8 ug/lb)
	CF3	=	area unit conversion to convert the surface area units (acre) in the application rate to cm^2 for the SR value (2.47E-8 acre/cm^2)
	CF4	=	volume to weight unit conversion factor to convert the volume units (cm^3) to weight units for the SR value (0.67 cm^3/g soil)

0.4 lb a.i./A * 1.0/cm * $(1-0)^0$ * 4.54 x 10^8 µg/lb * 2.47 x 10^{-8} A/cm^2 * 0.67 cm^3/g soil = 3.0 µg/g soil and 3.0 µg/g soil * 100 mg/day * 1 x 10^{-6} g/µg = 0.0003 mg/day ÷ 15 kg body wt = 0.00002 mg a.i./kg bw/day average daily oral dose from incidental oral ingestion of pesticide-treated soil.
MOE = 10 mg a.i./kg bw/day ÷ 0.00002 mg a.i./kg bw/day = **500,000**

Toddler Incidental Oral Ingestion from Contacting a Treated Pet: Toddler incidental oral ingestion from touching a treated pet was assessed using HED SOPs for Residential Exposure Assessments (12/18/97) 9.2.2 "Post-application Potential Dose Among Toddlers from Incidental Nondietary Ingestion of Pesticide Residues on Pets from Hand-to-Mouth Transfer." The SOPs utilize certain assumptions in lieu of chemical-specific data. The unpublished study [Fichtel, M. and R. Krebber. 27 MAR 1996, Imidacloprid (Bay t 7391) - Stroke Test in Dogs after Topical Application of Imidacloprid Spot-on 10%; Bayer Animal Health Development AH-D ID: 16051] designed to measure possible post-application exposure was used. See residential-applicator pet spot-on section on page 49 for a detailed explanation. In summary, data were collected from 16 beagle dogs who were each treated with 500 mg of imidacloprid 10% Spot-on. The study used hand-wipes of the treated areas over 24 hours.

Summary results:

(mg imidacloprid/glove +/- SEM)	
10 min	24.9 +/- 6.4
1 hr	17.3 +/- 3.3
12 hr	3.9 +/- 1.1
24 hr	2.7 +/- 0.7

The dosimetry data are used in conjunction with the SOPs (i.e., using the SOPs but substituting measured DFRs for the otherwise assumed 20% of administered dose). Further, ExpoSAC believes that it is likely there would be one event per day. Therefore, the resulting MOEs are calculated as follows:

10 min post-application: 24.9 mg a.i./6000 cm^2 * .5 (=50 % saliva extraction factor) * 20 cm^2/event * 1 event/day ÷ 15 kg bw = 0.00276. MOE = NOAEL ÷ DOSE or 10 mg a.i./kg bw/day ÷ 0.00276mg a.i./kg bw/day = **3,600**

1 hr post-application: 17.3 mg a.i./6000 cm^2 * .5 (= 50 % saliva extraction factor) * 20 cm^2/event * 1 event/day ÷ 15 kg bw = 0.0019 mg a.i./kg bw/day. MOE = NOAEL ÷ DOSE or 10 mg a.i./kg bw/day ÷ 0.0019mg a.i./kg bw/day = **5,200**

12 hr post-application: 3.9 mg a.i./6000 cm^2 * .5 (= 50 % saliva extraction factor)* 20 cm^2/event * 1 event/day ÷ 15 kg bw = 0.000433 mg a.i./kg bw/day. MOE = NOAEL ÷ DOSE or 10 mg a.i./kg bw/day ÷ 0.0004332mg a.i./kg bw/day = **23,000**

24 hr post-application: 2.7 mg a.i./6000 cm^2 * .5 (= 50 % saliva extraction factor)* 20 cm^2/event * 1 event/day ÷ 15 kg bw = 0.0003. MOE = NOAEL ÷ DOSE or 10 mg a.i./kg bw/day ÷ 0.0003mg a.i./kg bw/day = **33,000**

The data indicate that imidacloprid rapidly biologically disperses from the specific application loci. HED believes it is unlikely that a toddler would consistently "stroke" a pet exactly on the application loci. This assessment addresses the maximum dose that would be applied to a large dog. A toddler is expected to more likely touch areas of a pet to which imidacloprid has not dispersed (immediately upon treatment) such as the sides of shoulders or flanks. In the case of imidacloprid, the dermal absorption is 7%. The use of highly absorbent cotton gloves as dosimeters, is expected to result in **over-estimation** of actual dermal exposure.

As cotton is much more absorptive than human skin and the surface area of an adult hand is much greater than that of a toddler, it is unlikely that a toddler could absorb the "dose" measured by absorption to a cotton glove purposefully moved directly over the point of treatment, essentially at the time of treatment.

HED believes that the MOEs > 100, based upon the study data, are conservative i.e., overestimate the actual exposure and risk. Therefore, this use is not of concern to HED.

Toddler Dermal Exposure From Touching Treated Pet (Pet Hug): Toddler dermal exposure from touching treated pet (pet hug) was estimated according to the HED SOPs for Residential Exposure Assessments (12/18/97) as follows:

$$D = (((AR*F_{AR})/SA_{pet}) * (1 - DR)^{t} * SA_{hug} * (1\ mg/1000\mu g)) * DA$$

where:	D	=	dose from dermal pet contact (mg/day);
	AR	=	application rate or amount applied to animal in a single treatment (mg ai/animal);
	F_{AR}	=	fraction of the application rate available for dermal contact as transferable residue (20%)
	SA_{pet}	=	surface area of a treated dog (5,986cm^2/animal);
	t	=	time after application (days);
	DR	=	fractional dissipation rate per day (5% per day/100); and
	SA_{hug}	=	surface area of a child hug (1,875cm^2 contact/hug).
	DA	=	Dermal absorption factor (7 %)

In this case, actual compound-specific study data are used in place of the expression ($AR*F_{AR}$), which is the assumption that 20% of the application rate is available as dislodgeable residue. The ExpoSAC believes it is appropriate to use the dislodgeable residues from the 10 min post-application observations in the dog wipe study. Therefore, the estimate of exposure and risk are expressed as:

24.0 mg a.i. ÷ 5986 cm²/surface area dog * $(1 - DR)^{0day}$ * 1875 cm²/surface area child hug * 7 % DA ÷ 15 kg bw = 0.036 mg a.i./kg bw/day. MOE = NOAEL/DOSE ∴ 10 mg a.i./kg bw/day ÷ 0.036 mg a.i./kg bw/day = **280**

Adult and Toddler Dermal Post-Application Exposure to Treated Turf: Adult and toddler dermal post-application exposure to treated turf was assessed using HED SOPs, which state the following:

PDR = DFR * TC * hours/day * 0.001 mg/µg ÷ body weight

where:	PDR	=	Potential Dose Rate
	DFR	=	Dislodgeable Foliar Residue
	TC	=	Transfer Coefficient
	body weight	=	70 kg for adult, 15 kg for toddler

DFR and Transfer Coefficients (TCs) are utilized from the study reviewed and found acceptable by L. LaSota (Memo, 11/14/96, D223276, MRID 439239-01). The combined arithmetic mean of imidacloprid transferable residues from three study locations was 79.8 ng/cm², which was determined using the turf roller technique. The study was conducted at an application rate of 0.5 lb a.i./A and the maximum label rate for commercial application to residential lawns and turf is

0.4 lb a.i./A. Data were collected as soon as sprays had dried. The TCs were determined using "inner" and "outer" whole body dosimeters to simulate the use of a sleeveless shirt, short pants and shoes and adjusted to simulate 4 hours of foliar contact/day. The TC for adults is 3,343 cm^2/hr and 1,397 cm^2/hr for toddlers.

0.0798 $\mu g/cm^2$ * 3.343 cm^2/hr * 0.001 mg/μg * 2 hr/day * 7 % dermal absorption ÷ 70 kg bw = 0.00053 mg a.i./kg bw/day for adults. MOE = 10 mg a.i./kg bw/day ÷ 0.00053 mg a.i./kg bw/day = **19,000 for adults.**

0.0798 $\mu g/m^2$ * 1,397 cm^2/hr * 0.001 mg/μg * 2 hr/day * 7 % dermal absorption ÷ 15 kg bw = 0.001 mg a.i./kg bw/day. MOE = 10 mg a.i./kg bw/day ÷ 0.001 mg a.i./kg bw/day = **10,000 for toddlers.**

Adult and Adolescent Golfer Post-Application Dermal Exposure: Adult and adolescent golfer post-application dermal exposure was estimated using the ExpoSAC draft Policy regarding "Golfer Exposure Assessment For Adults and Children" (24 August 2000) as follows:

$DE_{(t)}$ (mg a.i./kg bw/day) = ($TTR_{(t)}$ ($\mu g/cm^2$)) * TC (cm^2/hr) * hr/day/1000 μg/mg * BW (body weight (kg))

where: $DE_{(t)}$ = dermal exposure at time (t) attributable to golfing on previously treated turf (mg a.i./kg bw/day).

$TTR_{(t)}$ = turf transferable residue at time $_t$ ($\mu g/cm^2$)

TC = Transfer Coefficient (500 cm^2/hr)

hr = exposure period (4 hours)

BW = body weight (kg) (70 kg for adult; adjusted (multiplied) by a factor of 1.7 for adolescent golfers)) A BW of 60 kg is utilized if the toxicological endpoint is derived from a developmental study and there are fetal effects.

DE = 0.0798 $\mu g/cm^2$ * 500 cm^2/hr * 4 hr/day/1000μg/mg * 7 % dermal absorption ÷ 70 kg bw = 0.00016 mg a.i./kg bw/day

MOE for adult golfer is 10 mg a.i./kg bw/day ÷ 0.00016 mg a.i./kg bw/day = 63,000

The adult dose level is adjusted by a factor of 1.7 to estimate adolescent golfer exposure.

0.00016 mg a.i./kg bw/day * 1.7 = 0.000272 mg a.i./kg bw/day

MOE for adolescent golfer is 10 mg a.i./kg bw/day ÷ 0.000272 = 37,000

4.4.1.3 Combined Residential Exposure

FQPA requires that all exposures that could reasonably be expected to occur on the same day be combined and compared to the appropriate toxicity endpoint. The residential scenarios that can reasonably be expected to occur on the same day for toddlers/children are listed in Table 11.

Table 11. Exposure Potential for Adult and Child Short-term Aggregate Risk Estimates for Imidacloprid.

Exposure Scenario		Exposure (Dose) mg a.i./kg bw/day	MOE	Combined Exposure (Dose) mg a.i./kg bw/day	COMBINED MOE[1]
Toddler - Treated Turf	Oral hand-to-mouth post-application exposure from contacting treated turf	0.0059	1,700	0.00692	1,500
	Incidental oral post-application exposure from ingestion of treated soil	0.00002	500,000		

Table 11. Exposure Potential for Adult and Child Short-term Aggregate Risk Estimates for Imidacloprid.

Exposure Scenario		Exposure (Dose) mg a.i./kg bw/day	MOE	Combined Exposure (Dose) mg a.i./kg bw/day	COMBINED MOE[1]
	Dermal post-application exposure from contacting turf	0.001	10,000		
Toddler - Treated Pet	Incidental oral post-application exposure from contacting treated pet	0.00276	3,600	0.03876	260
	Dermal post-application exposure from pet "hug"/ contacting treated pet	0.036	280		
Adult - Treated Turf	Handler dermal and inhalation exposure from applying imidacloprid using granular/push-type spreader	0.0000162	72,000	0.0005462	15,000
	Dermal post-application exposure from contacting treated turf	0.00053	19,000		
Adult - Treated Pet	Handler dermal and inhalation exposure from applying imidacloprid to pet with pet spot-on	0.025	400 [2]		
	Dermal post-application exposure from contacting treated pet				

[1] Combined MOEs are presented for toddler oral + dermal exposure to treated turf, and oral + dermal exposure to a treated pet. Combined MOEs are expressed as: $MOE_{DERMAL} + MOE_{ORAL}$. Combined MOEs are presented for an adult who applies the material to his/her lawn and then experiences post-application exposure. MOEs combined from different sources of exposure (i.e., application + post-application) are expressed as: $MOE_{applicator} + MOE_{post\text{-}application}$.

2. HED believes handler exposure will be negligible. However, the results from an unpublished study (see residential post-application exposure to treated pets) were use to measure possible post-application exposure. HED herein used the data from sampling at ten minutes post-application and assumes that a pesticide handler would not receive a greater dose if applied according to label directions than what was measured via cotton glove dosimetry from purposeful stroking of treatment loci (see Section 4.4.1.1 Residential Handler of this risk assessment).

4.4.2 Non-occupational Off-Target Exposure

Spray drift is always a potential source of exposure to residents nearby to spraying operations. This is particularly the case with aerial application, but, to a lesser extent, could also be a potential source of exposure from groundboom application methods. The Agency has been working with the Spray Drift Task Force, EPA Regional Offices and State Lead Agencies for pesticide regulation and other parties to develop the best spray drift management practices. The Agency is now requiring interim mitigation measures for aerial applications that must be placed on product labels/labeling. The Agency has completed its evaluation of the new database submitted by the Spray Drift Task Force, a membership of U.S. pesticide registrants, and is developing a policy on how to appropriately apply the data and the AgDRIFT computer model to its risk assessments for pesticides applied by air, orchard airblast and ground hydraulic methods. After the policy is in place, the Agency may impose further refinements in spray drift management practices to reduce off-target drift and risks associated with aerial as well as other

application types where appropriate.

5.0 AGGREGATE RISK ASSESSMENTS AND RISK CHARACTERIZATION

Aggregate exposure risk assessments were performed for the following scenarios: acute aggregate exposure (food + drinking water), short-term aggregate exposure (food + drinking water + residential), and chronic aggregate exposure (food + drinking water). Intermediate- and long-term aggregate risk assessments were not performed because, based on the current use patterns of imidacloprid, HED does not expect exposure durations that would result in intermediate- or long-term exposures. A cancer aggregate risk assessment was not performed because imidacloprid is not carcinogenic. All potential exposure pathways were assessed in the aggregate risk assessment. Dietary (food and drinking water), handler and post-application residential exposures were considered, as necessary, because there is a potential for individuals to be exposed concurrently through these routes.

Since HED does not have ground and surface water monitoring data to calculate a quantitative aggregate exposure, DWLOCs were calculated. A DWLOC is a theoretical upper limit on a pesticide's concentration in drinking water in light of total aggregate exposure to a pesticide in food, drinking water, and through residential uses. A DWLOC will vary depending on the toxicity endpoint, drinking water consumption, body weights, and pesticide uses. Different populations will have different DWLOCs. HED uses DWLOCs in the risk assessment process to assess potential concern for exposure associated with pesticides in drinking water. DWLOC values are not regulatory standards for drinking water.

To calculate DWLOCs, the dietary food estimates (from DEEM-FCID™) were subtracted from the PAD value to obtain the maximum water exposure level. DWLOCs were then calculated using the standard body weights and drinking water consumption figures: 70kg/2L (US Population, adult male, and youth), 60 kg/2L (adult female), and 10kg/1L (infants and children).

For acute and chronic dietary exposure, HED is concerned when estimated dietary risk exceeds 100% of the aPAD and cPAD, respectively. HED's level of concern for residential oral, dermal and inhalation exposures are for MOEs <100. For imidacloprid, short-term oral, dermal and inhalation exposures estimates can be aggregated due to the use of oral equivalents and a common toxicity endpoint (decreased body weight gain).

5.1 Acute Aggregate Risk Assessment (Food and Drinking Water)

The acute aggregate risk assessment takes into account exposure estimates from dietary consumption of imidacloprid (food and drinking water). The dermal, inhalation, and incidental oral exposures resulting from short-term residential applications are assessed separately.

The Tier 1 [conservative, deterministic assessment using tolerance level residues and 100% CT information for registered and proposed commodities; and modified DEEM™ (version 7.76) processing factors for some commodities based on guideline processing studies] acute dietary exposure estimates are below HED's level of concern (<100% aPAD) at the 95th exposure

percentile for the general U.S. population (25% of the aPAD) and all other population subgroups. The most highly exposed population subgroup is children 1-2 years old, at 64% of the aPAD. The EECs generated by EFED are less than HED's calculated DWLOCs for acute exposure to imidacloprid and its degradates (imidacloprid urea, imidacloprid guanidine, and imidacloprid olefin) in drinking water. Therefore, the acute aggregate risk associated with the proposed use of imidacloprid does not exceed HED's level of concern for the general U.S. population or any population subgroups. Table 12 summarizes the acute aggregate exposure estimates to imidacloprid residues.

Table 12. Acute Aggregate Exposures to Imidacloprid Residues.

Population Subgroup	aPAD (mg/kg/day)	Acute Food Exposure (mg/kg/day)	Maximum Acute Water Exposure [1] (mg/kg/day)	Ground Water EEC [2] (µg/L)	Surface Water EEC [2] (µg/L)	Acute DWLOC [3] (µg/L)
U.S. Population	0.14	0.035373	0.104627	2.09	36.04	3700
All infants (< 1 year old)	0.14	0.075240	0.064760	2.09	36.04	650
Children (1-2 years old)	0.14	0.089369	0.050631	2.09	36.04	510
Children (3-5 years old)	0.14	0.066219	0.073781	2.09	36.04	740
Children (6-12 years old)	0.14	0.041805	0.098195	2.09	36.04	980
Youth (13-19 years old)	0.14	0.026434	0.113566	2.09	36.04	4000
Adults (20-49 years old)	0.14	0.023241	0.116759	2.09	36.04	4100
Females (13-49 years old)	0.14	0.023679	0.116321	2.09	36.04	3500
Adults (50+ years old)	0.14	0.024073	0.115927	2.09	36.04	4100

[1] maximum water exposure (mg/kg/day) = aPAD (mg/kg/day) - food exposure (mg/kg/day)
[2]The crop producing the highest level was used.
[3] DWLOC calculated as follows:

$$\text{DWLOC} = \frac{(\text{maximium water exposure (mg / kg / day)}) * (\text{body weight (kg)}) * (1000\ \mu\text{g / mg})}{\text{water consumption (liter / day)}}$$

5.2 Short-Term Aggregate Risk Assessment

The short-term aggregate risk assessment estimates risks likely to result from 1- to 30-day exposure to imidacloprid residues from food, drinking water, and residential pesticide uses. High-end estimates of the residential exposure are used in the short-term assessment, and average values are used for food and drinking water exposures.

Short-term aggregate risk assessments are required for adults as there is potential for both dermal and inhalation handler exposure, and dermal post-application exposure from the residential uses of imidacloprid on turf and pets. In addition, short-term aggregate risk assessments are required for children/toddlers because there is a potential for oral and dermal, post-application exposure resulting from the residential uses of imidacloprid on turf and pets. The short-term residential exposure potential from the turf and pet uses for adults and children/toddlers can be found in Table 11. The pet-treatment scenario resulted in the lowest combined MOE for adults (MOE = 400; handler and post-application) and children (MOE = 260; post-application). The turf-treatment resulted in much lower exposures for both adults (MOE = 15,000; handler and post-

application) and children (MOE = 1,500; post-application). Therefore, the pet-treatment exposure estimates were aggregated with the chronic dietary (food) to provide a worst-case estimate of short-term aggregate risk for the U.S. population and children 1-2 years old (the child population subgroup with the highest estimated chronic dietary food exposure) (see Table 13).

As the MOEs are greater than 100, the short-term aggregate risks are below HED's level of concern. For surface and ground water, the estimated average concentrations of imidacloprid and degradates (imidacloprid urea, imidacloprid guanidine, and imidacloprid olefin) are less than HED's calculated DWLOCs for imidacloprid in drinking water as a contribution to short-term aggregate exposure. Therefore, HED concludes with reasonable certainty that residues of imidacloprid in drinking water do not contribute significantly to the short-term aggregate human health risk at the present time.

Table 13. Short-Term Aggregate Risk and DWLOC Calculations for Imidacloprid.

Population Subgroups	Short-Term Scenario									
	NOAEL (mg/kg/day)	Level of Concern[1]	Max Exposure[2] (mg/kg/day)	Average Food Exposure (mg/kg/day)	Residential Exposure[3] (mg/kg/day)	Aggregate MOE (food and residential)[4]	Max Water Exposure[5] (mg/kg/day)	Ground Water EEC[6] (ug/L)	Surface Water EEC[6] (ug/L)	Short-Term DWLOC[7] (µg/L)
US Population	10	100	0.1	0.006514	0.025	320	0.068486	2.09	17.24	2400
Children 1-2 years old	10	100	0.1	0.019898	0.03876	170	0.041342	2.09	17.24	410

[1] The level of concern (target MOE) includes 10X for interspecies extrapolation and 10X for intraspecies variation.

[2] Maximum Exposure (mg/kg/day) = NOAEL/Target MOE

[3] Residential Exposure = [Oral exposure + Dermal exposure + Inhalation Exposure]. The pet-treatment scenario resulted in the lowest combined residential MOE for adults (handler and post-application) and children (post-application). The combined MOEs for the pet-use scenario were used to calculate the short-term risk (see Table 11).

[4] Aggregate MOE = [NOAEL ÷ (Avg Food Exposure + Residential Exposure)]

[5] Maximum Water Exposure (mg/kg/day) = Target Maximum Exposure - (Food Exposure + Residential Exposure)

[6] The crop producing the highest level was used.

[7] DWLOC calculated as follows:

$$\text{DWLOC} = \frac{\left(\text{maximium water exposure (mg / kg / day)}\right) * \left(\text{body weight (kg)}\right) * \left(1000\ \mu\text{g / mg}\right)}{\text{water consumption (liter / day)}}$$

5.3 Chronic Aggregate Risk Assessment (Food and Drinking Water)

The chronic aggregate risk assessment takes into account average exposure estimates from dietary consumption of imidacloprid (food and drinking water) and residential uses. However, due to the use patterns, no chronic residential exposures are expected. Therefore, the chronic aggregate risk assessment will consider exposure from food and drinking water only.

The Tier 2 [partially refined, deterministic assessment using tolerance-level residue and average weighted % CT information and modified DEEM™ (version 7.76) processing factors for some commodities based on guideline processing studies] chronic dietary exposure estimates are below HED's level of concern (<100% cPAD) for the general U.S. population (11% of the cPAD) and all population subgroups. The most highly exposed population subgroup is children 1-2 years old, at 35% of the cPAD. The Tier 1 EECs generated by EFED are less than HED's calculated chronic DWLOCs for chronic exposure to imidacloprid and its degradates (imidacloprid urea, imidacloprid guanidine, and imidacloprid olefin) in drinking water. Therefore, the chronic aggregate risk associated with the proposed use of imidacloprid does not exceed HED's level of concern for the general U.S. population or any population subgroups. Table 14 summarizes the chronic aggregate exposure estimates to imidacloprid residues.

Table 14. Chronic Aggregate Exposures to Imidacloprid Residues.

Population Subgroup	cPAD (mg/kg/day)	Chronic Food Exposure (mg/kg/day)	Maximum Chronic Water Exposure[1] (mg/kg/day)	Ground Water EEC[2] (µg/L)	Surface Water EEC (µg/L)	Chronic DWLOC[3] (µg/L)
U.S. Population	0.057	0.006514	0.050486	2.09	17.24	1800
All infants (< 1 year old)	0.057	0.015037	0.041963	2.09	17.24	420
Children (1-2 years old)	0.057	0.019898	0.037102	2.09	17.24	370
Children (3-5 years old)	0.057	0.014076	0.042803	2.09	17.24	430
Children (6-12 years old)	0.057	0.008560	0.048440	2.09	17.24	480
Youth (13-19 years old)	0.057	0.004793	0.052207	2.09	17.24	1800
Adults (20-49 years old)	0.057	0.004858	0.052142	2.09	17.24	1800
Females (13-49 years old)	0.057	0.004753	0.052247	2.09	17.24	1600
Adults (50+ years old)	0.057	0.005737	0.051263	2.09	17.24	1800

[1] maximum water exposure (mg/kg/day) = cPAD (mg/kg/day) - food exposure (mg/kg/day)

[2] NR = not recorded.

[3] DWLOC calculated as follows:

$$\text{DWLOC} = \frac{(\text{maximium water exposure (mg / kg / day)}) * (\text{body weight (kg)}) * (1000\ \mu\text{g / mg})}{\text{water consumption (liter / day)}}$$

6.0 CUMULATIVE RISK

FQPA (1996) stipulates that when determining the safety of a pesticide chemical, EPA shall base its assessment of the risk posed by the chemical on, among other things, available information concerning the cumulative effects to human health that may result from dietary, residential, or other non-occupational exposure to other substances that have a common mechanism of toxicity. The reason for consideration of other substances is due to the possibility that low-level exposures to multiple chemical substances that cause a common toxic effect by a common mechanism could lead to the same adverse health effect as would a higher level of exposure to any of the other substances individually. A person exposed to a pesticide at a level that is considered safe may in fact experience harm if that person is also exposed to other substances that cause a common toxic effect by a mechanism common with that of the subject pesticide, even if the individual exposure levels to the other substances are also considered safe.

HED did not perform a cumulative risk assessment as part of this tolerance action for imidacloprid because HED has not yet initiated a review to determine if there are any other chemical substances that have a mechanism of toxicity common with that of imidacloprid. For purposes of this tolerance action, EPA has assumed that imidacloprid does not have a common mechanism of toxicity with other substances.

On this basis, the Registrant must submit, upon EPA's request and according to a schedule determined by the Agency, such information as the Agency directs to be submitted in order to evaluate issues related to whether imidacloprid shares a common mechanism of toxicity with any other substance and, if so, whether any tolerances for imidacloprid need to be modified or revoked. If HED identifies other substances that share a common mechanism of toxicity with imidacloprid, HED will perform aggregate exposure assessments on each chemical, and will begin to conduct a cumulative risk assessment.

HED has recently developed a framework that it proposes to use for conducting cumulative risk assessments on substances that have a common mechanism of toxicity. This guidance was issued for public comment on January 16, 2002 (67 FR 2210-2214) and is available from the OPP Website at: http://www.epa.gov/pesticides/trac/science/cumulative_guidance.pdf. In the guidance, it is stated that a cumulative risk assessment of substances that cause a common toxic effect by a common mechanism will not be conducted until an aggregate exposure assessment of each substance has been completed.

Before undertaking a cumulative risk assessment, HED will follow procedures for identifying chemicals that have a common mechanism of toxicity as set forth in the "*Guidance for Identifying Pesticide Chemicals and Other Substances that Have a Common Mechanism of Toxicity*" (64 FR 5795-5796, February 5, 1999).

7.0 OCCUPATIONAL EXPOSURE

An occupational exposure assessment for imidacloprid was prepared in an HED memorandum dated 2/26/03 (Memo, M. Dow; D281610).

7.1 Occupational Handler

Based primarily on the proposed new use patterns, commercial and private (i.e., grower operators) pesticide handlers are typically expected to have short-term exposures (i.e., 1-30 days). Table 5 lists a summary of proposed use patterns for imidacloprid. The acreages involved with the crops in this assessment are relatively small. Typically, if the maximum rate for soil application is applied, only one application will be made per season. The treatment intervals for foliar applications are generally 5-7 days. However, the HED ExpoSAC asserts that there is a possibility that commercial handlers might be exposed to intermediate-term exposures (1-6 months). Therefore, the estimated MOEs presented in Table 15 represent short/ intermediate-term (1 day-6 months) exposures/risks (short-term NOAEL is 10 mg a.i./kg bw/day and intermediate-term NOAEL is 9.3 mg a.i./kg bw/day).

The methods of application used to treat the proposed crops are variable. Generally speaking, aerial application is not specifically mentioned on the proposed labels. However, it is not prohibited. Other likely methods of application include airblast, ground boom (note that the soil applications are generally applied with specially "directed" sprays such as banded, side-dress, or in-furrow sprays, etc.), chemigation (cranberry and watercress), "hand-held irrigation" equipment (greenhouse cucumber and tomato), and possibly high-pressure hand-wand for crops such as passionfruit. Backpack sprayers may be used for "spot treatments" of watercress and possibly cranberry. Since all formulations are liquid emulsifiables, HED has assessed a mixer/loader using open-pour techniques in support of aerial operations. HED believes this is the most highly exposed loader work activity.

HED believes that a "loader" (i.e., applicator in this sense) for chemigation will not likely be exposed more than a loader supporting aerial operations. Chemigation typically involves minibulk containers which have siphon tubes attached to the irrigation equipment and that "mixing and loading" in the typical sense of pouring liquids, does not occur. Therefore, a "chemigator" is not assessed, with the assumption that the work activity is represented by the mixer/loader supporting aerial operations.

The application techniques that are assessed include aerial, ground-boom open-cab, air-blast open cab, and high-pressure hand-wand. The later is representative of "hand-held irrigation equipment" as listed in the proposed labels and is typical of powered hand-held sprayers used to treat trees, shrubs, vines and nursery-greenhouse crops. For "hand-held" application machinery, it is HED policy to assess one individual who mixes, loads and applies the material (i.e., mixer/loader/applicator). HED believes the aforementioned pesticide handler work activities are representative of the kinds of activities associated with treatment of the proposed new crop uses.

The available exposure data for combined mixer/loader/applicator scenarios are limited in comparison to the monitoring of these two activities separately. These exposure scenarios are outlined in the PHED Surrogate Exposure Guide (August 1998). HED has adopted a methodology to present the exposure and risk estimates separately for the job functions in some scenarios and to present them as combined in other cases. Most exposure scenarios for hand-held equipment (such as hand wands, backpack sprayers, and push-type granular spreaders) are assessed as a combined job function. With these types of handheld operations, all handling activities are assumed to be effected by the same individual. The available monitoring data support this. Conversely, for equipment types such as fixed-wing aircraft, groundboom tractors, or air-blast sprayers, the applicator exposures are assessed and presented separately from those of the mixers and loaders. By separating the two job functions, HED determines the most appropriate levels of PPE for each aspect of the job without requiring the applicator to wear unnecessary PPE that may be required for a mixer/loader (e.g., chemical resistant gloves may only be necessary during the pouring of a liquid formulation).

No chemical-specific data are available with which to assess potential exposure to pesticide handlers. The estimates of exposure to pesticide handlers are based upon surrogate study data available in PHED (v. 1.1, 1998). For pesticide handlers, it is HED policy to present estimates of dermal exposure for "baseline" (i.e., with a single layer of work clothing consisting of a long-sleeved shirt, long pants, shoes plus socks and no protective gloves and with a single layer of work clothing and **the use of** protective gloves or other PPE as might be necessary). The four product labels involved in this assessment direct pesticide handlers to wear long-sleeved shirt, long pants, chemical resistant gloves (polyvinyl chloride or polyethylene for the 4.0 and 2.0 formulations), waterproof gloves for the 1.6 formulation and shoes plus socks.

There are no chemical-specific data with which to assess exposure to persons involved in the commercial treatment of seeds using imidacloprid. Therefore, HED uses a surrogate study: "Determination of Inhalation and Dermal Exposure to Mixer-Loaders, Baggers, and Clean-up Workers from Fipronil During and After the Application of Icon™ 6.2FS Insecticide to Rice Seed." ***The study is a proprietary study however due to the merger of Aventis CropScience with Bayer Corporation (Bayer Corporation, Crop Protection Products), HED herein uses the data to assess exposure to imidacloprid. The study data may not be used for assessing exposure to compounds other than those which are proprietary to what is currently Bayer Crop Science.***

The proprietary study, (MRID 454427-01) has been reviewed and is acceptable to HED (Memo, M. Dow, 11/26/01; D276181). The study was designed to determine the total exposure to workers during the course of a work day which involves mixing and loading, bagging, sewing filled bags closed, and "clean-up" and the end of a day. The study includes the use of, or lack of use of, a variety of PPE. Dermal exposure is presented as the arithmetic and geometric means of **Total** exposure. The data includes many observations of "unprotected" workers together with those workers who utilized varying "levels" of PPE. Dermal exposure was measured using whole body dosimeters. Inhalation exposure was estimated using personal air monitors and therefore simulates **unprotected respiratory exposure.**

An MOE ≥100 is adequate to protect pesticide handlers and for post-application exposures to agricultural workers or residents. See Table 15 for summary of commercial pesticide handler exposures and risks, using acres/day from "Standard Values for Daily Acres Treated in Agriculture"; Policy No. 9.1. Although the "average" field acreages of the proposed crops is relatively small as compared to corn, cotton, small grains, soybeans etc, HED assesses aerial application using the default assumption of 350 acres treated per day.

Table 15. Estimated Handler Exposure and Risk from Use of Imidacloprid on the Proposed New Fruit and Vegetable Crops.

Unit Exposure [1] (mg a.i./lb handled)	Applic. Rate [2]	Units Treated [3] Per Day	Average Daily Dose[4] (mg a.i./kg bw/day)	COMBINED MOE [5]	
				ST	IT
Mixer/Loader - Liquid - Open Pour - Supporting Aerial Operation (Artichoke)					
Dermal: SLNG 2.9 HC SLWG 0.023 HC Inhal 0.0012 HC	0.25 lb a.i./A	350 A	Dermal: NG 0.25 WG 0.002 Inhal 0.001	NG 40 WG 2,900	NG 37 WG 2,700
Applicator - Aerial (Artichoke)					
Dermal: SLNG 0.0050 HC SLWG 0.0022 HC Inhal 0.000068 MC	0.25 lb a.i./A	350	Dermal: NG 0.00044 WG 0.00019 Inhal 0.000085	NG 20,000 WG 36,000	NG 18,000 WG 34,000
Applicator - Ground-boom - Open Cab (Max Rate Soil Application)					
Dermal: SLNG 0.014 HC SLWG 0.014 MC Inhal 0.00074 HC	0. 5 lb a.i./A	80 A	Dermal: NG 0.00056 WG 0.00056 Inhal 0.00042	NG 10,000 WG 10,000	NG 9,500 WG 9,500
Applicator - Air-blast - Open Cab (Tropical fruits)					
Dermal: SLNG 0.36 HC SLWG 0.24 HC Inhal 0.0045 HC	0.1 lb a.i./A	40 A	Dermal: NG 0.0014 WG 0.00096 Inhal 0.00026	NG 6,000 WG 8,200	NG 5,600 WG 7,600
Mix/Load/Applicator - High Pressure Hand-wand (Hand Held Irrigation-Greenhouse - Cucumber & Tomato*)*					
Dermal SLNG no data SLWG 2.5 LC Inhal 0.12 LC	0.5 lb a.i./A	2.0 A	Dermal: NG no data WG 0.0025 Inhal 0.00171	NG no data WG 2,400	NG no data WG 2,200
Mixer/Loader/Applicator - Backpack - Liquid - Open Pour (Rate for Watercress Foliar Application)					
Dermal: SLNG no data SLWG 2.5 LC Inhal 0.03 LC	0.0469 lb a.i./A	0.18 A	Dermal: NG - no data WG 0.000021 Inhal 0.0000036	NG no data WG 410,000	NG no data WG 380,000

Table 15. Estimated Handler Exposure and Risk from Use of Imidacloprid on the Proposed New Fruit and Vegetable Crops.

Unit Exposure [1] (mg a.i./lb handled)	Applic. Rate [2]	Units Treated [3] Per Day	Average Daily Dose[4] (mg a.i./kg bw/day)	COMBINED MOE [5]	
				ST	IT
Dermal: geomet mean 0.0169 Inhalation: geomet. mean 0.00139	0.25 lb/cwt	99,000 lb/day (= 990 "cwt")	Dermal: geomet mean 0.0042 Inhalation: geomet mean 0.0049	1,100	1,000

1. Unit Exposures are taken from "PHED SURROGATE EXPOSURE GUIDE", Estimates of Worker Exposure from The PHED Version 1.1, August 1998. SLNG = Dermal Single Layer Work Clothing **No Gloves**; SLWG = Dermal Single Layer Work Clothing **With Gloves**; Inhal. = Inhalation. Units = mg a.i./pound of a.i. handled. Data Confidence: LC = Low Confidence, MC = Medium Confidence, HC = High Confidence.
2. Applic. Rate. = Taken from Sections A & B (proposed labeling) of IR-4 submission for each crop. **Footnotes cont'd.**
3. Units Treated are taken from "Standard Values for Daily Acres Treated in Agriculture"; Policy No. 9.1. Science Advisory Council for Exposure; Revised 5 July 2000; PHED v 1.1, May 1997 (for greenhouse area); based on Stamper, J.H. et al., 1989, Pesticide Exposure to Greenhouse Handgunners; Arch. Environment. Contam. Toxicol. 18: 515-529. Backpack area treated adapted from Science Advisory Council for Exposure Policy 11, revised 22 FEB 2002 and Policy 9.1. Policy 11 indicates a backpack sprayer will utilize 5 gallons of spray to treat 1000 ft^2. Policy 9.1 indicates a worker may spray 40 gallons/day with a backpack sprayer. Therefore 40 gal/day ÷ 5 gal/1000 ft^2 = 8000 ft^2/day treated by backpack. 8000 ft^2 ÷ 43,560 ft^2/A = 0.18A/day
4. Average Daily Dose = Unit Exposure * Applic. Rate * Units Treated * 0.07 (7 % dermal absorption) ÷ Body Weight (70 kg).
5. MOE = Margin of Exposure = No Observable Adverse Effect Level (NOAEL) ÷ ADD. Short-term dermal and inhalation NOAEL = 10 mg a.i./kg bw/day and are identified from developmental study in the rat where maternal effects (↓ body weight gain) were observed. Intermediate-term dermal and inhalation NOAEL = 9.3 mg a.i./kg bw/day and are identified from subchronic neurotoxicity study in the rat where decreased body weight gain were observed. MOEs are "combined" that is, Dermal + Inhalation, since the toxicological effects are the same and are identified from the same study. **ST** = Short-term combined MOE; **IT** = Intermediate-term combined MOE
6. Unit exposures for seed treaters are taken from **proprietary study**.

Provided commercial pesticide handlers use label-prescribed PPE (i.e., long pants, long-sleeved shirt, shoes + socks and the respective protective gloves), all MOEs are >100, and, therefore, do not exceed HED's level of concern.

7.2 Occupational Post-application Exposure

There were no chemical-specific data with which to estimate post-application exposure of agricultural workers to dislodgeable residues of pesticide. Therefore, theoretical estimates of exposure, based on surrogate studies, have been conducted. The ExpoSAC (Policy 003.1, Rev. 7 Aug. 2000, Regarding Agricultural Transfer Coefficients; Amended ExpoSAC Meeting notes - 13 Sept 01) lists a number of possible post-application agricultural activities relative to some of the subject crops that result in potential pesticide exposure to agricultural workers. TCs expressed as cm^2/hr are identified for each of the post-application, agricultural activities. The TCs are derived from data in surrogate exposure studies conducted during the various activities listed.

The highest (i.e., most conservative) TCs relative to the subject crops appear to be for activities related to high-bush blueberries. The activities are hand harvest, pruning and training vines. The TC is 5,000 cm^2/hr. The maximum rate of application for high-bush blueberries, salal, and Juneberry is 0.5 lb a.i./A (the highest of all proposed uses).

HED expects post-application agricultural exposures to workers would typically be short-term

(1-30 days). However, the HED ExpoSAC asserts that there is a possibility for intermediate-term (1-6 months) post-application agricultural exposures to workers. Therefore, the estimated MOEs presented below represent short/ intermediate-term (1 day-6 months) exposures/risks (short-term NOAEL is 10 mg a.i./kg bw/day and intermediate-term NOAEL is 9.3 mg a.i./kg bw/day). The majority of the crops are "specialty" crops and none are expected to be planted in large acreage blocks as might be typical for some field crops like corn, cotton or soybeans. It is expected that post-application agricultural "duties" are more variable for small acreage crops and that it is not likely that workers would be performing the same tasks for more than 30 consecutive days at a time. Many of the proposed applications are soil directed and as such are typically at the maximum rate hence one application per season. Those crops that may receive multiple applications are not expected to result in intermediate-term exposures (i.e., more than 30 days).

The TCs used in this assessment are from an interim transfer coefficient policy developed by HED's ExpoSAC using proprietary data from the Agricultural Re-Entry Task Force (ARTF) database (policy # 3.1). It is the intention of HED's ExpoSAC that this policy will be periodically updated to incorporate additional information about agricultural practices in crops and new data on TCs. Much of this information will originate from exposure studies currently being conducted by the ARTF, from further analysis of studies already submitted to the Agency, and from studies in the published scientific literature.

Since no chemical-specific DFR data are available, post-application worker exposure is estimated using HED procedure that assumes 20% of the application rate is available as dislodgeable foliar residue on the day of treatment. The following convention is used to estimate post-application agricultural worker exposure:

PDR_t	=	DFR_t * CF1 * Tc * ET where:
PDR_t	=	potential dose rate on day "t" (mg/day)
DFR_t	=	dislodgeable foliar residue on day "t" (µg/cm^2)
CF1	=	weight unit conversion factor to convert µg units in DFR value to mg for the daily dose (0.001 mg/µg)
Tc	=	transfer coefficient (cm^2/hr) (In this case 5,000 cm^2/hr; ExpoSAC Policy 003.1 Rev. 7 Aug. 2000; amended 13 Sept 01 ExpoSAC meeting Notes).
ET	=	Exposure Time (hrs) (8)

and DFR_t = AR * F * $(1\text{-}D)^t$ * CF2 * CF3 where:

AR	=	Application rate (lb a.i./A) (0.5 lb a.i./A)
F	=	fraction of a.i. retained on foliage (unitless)
D	=	fraction of residue that dissipates daily (unitless)
t	=	post-application day on which exposure is being assessed
CF2	=	weight unit conversion factor to convert the lbs a.i. in the application rate to µg for the DFR value (4.54E8 µg/lb)
CF3	=	Area unit conversion factor to convert the surface area units (ft^2) in the application rate to cm^2 for the DFR value (1.08E-3 ft^2/cm^2 or 2.47E-8 acre/cm^2 if the application rate is per acre).

Therefore, DFR = 0.5 lb a.i./A * .20 * $(1\text{-}0)^0$ * 4.54E8 µg a.i./lb * 2.47E-8A/cm^2 = 1.12 µg/cm^2

PDR = 1.12 µg/cm^2 * 0.001 mg/µg * 5,000 cm^2/hr * 8 hr/day = 44.8 mg a.i./day * 0.07 (% dermal absorption ÷ 70 kg bw = 0.045 mg a.i./kg bw/day

MOE = NOAEL ÷ PDR
10 mg a.i./kg bw/day ÷ 0.045 mg a.i./kg bw/day = **220** = Short Term MOE
and
9 .3 mg a.i./kg bw/day ÷ 0.045 mg a.i./kg bw/day = **210** = Intermediate Term MOE

This estimate is for short/intermediate-term dermal exposures (1 day-6 months), and is considered to be a screening level estimate i.e., conservative (protective). HEDs level of concern for dermal exposure is for MOEs <100. In this case, MOEs are >100; therefore, post-application dermal exposure is not of concern for agricultural workers.

REI

Imidacloprid is classified in Toxicity Category IV for acute dermal, acute inhalation, primary eye irritation and primary skin irritation. Therefore, the interim WPS REI of 12 hours is sufficient to protect workers from excessive exposure.

7.3 Incidents

According to OPP's Incident Data System there is a number of unconfirmed incidents regarding imidacloprid. The State of California sent a report in 1999 of 56 cases involving imidacloprid the majority of which involved pesticide mixtures. In only one case was imidacloprid considered the cause of the illness (a kennel worker splashed a drop in his eye which began burning and had a corneal abrasion) [personal e-mail communication from Dr. Jerome Blondell (10/31/02)].

8.0 NATIONAL RESOURCE DEFENSE COUNCIL (NRDC) OBJECTIONS

In a letter dated 3/19/02 to James Hollins (EPA/OPP/IRSD), NRDC objected to the establishment of tolerances for various pesticide chemicals, including imidacloprid. Specifically, NRDC objected to the regulation issued under 21 U.S.C. 346a(l)(6), establishing a time-limited tolerance for pesticide chemical residues of imidacloprid on blueberries (67 Fed. Reg. 2580 - 1/18/02).

EPA has addressed the objections that are chemical specific to imidacloprid below.

Issue #1: <u>EPA relied on national consumption data which is averaged throughout the year when the section 18 was issued to NJ and MI, which underestimates exposure</u>

<u>Background:</u> NRDC is contending that, for imidacloprid, EPA relied on estimates of national consumption of blueberries and not regional or state-specific data for its granting of Section 18 petitions for blueberries for the states of New Jersey and Michigan. NRDC states that the fresh nature of the food and the potential for heavy local consumption with a strong seasonal component strongly suggests that national consumption data may underestimate consumption in localized areas in NJ and MI. The FQPA, NRDC continues, therefore requires that an additional uncertainty factor be applied to account for any potential inadequacies arising from the use of a distribution of national estimates of consumption as a surrogate for what potentially could be much higher local consumption. NRDC states that by using national data, EPA will underestimate dietary exposures to consumers in NJ and MI because consumers in NJ and MI are likely to eat more blueberries than the national average because of their ready availability, cost, proximity to market, and freshness; further, these consumers are more likely to eat locally grown blueberries containing imidacloprid residues than the average U.S. consumer. They provide a

specific example: A child eating blueberries in one of these two high imidacloprid use states will certainly stand a greater chance of consuming greater amounts of imidacloprid when local blueberries are ripe and plentiful than national consumption data would suggest.

EPA Response: EPA is confident that the methodologies used in its estimation of exposure and the percentile of regulation selected do not systematically underestimate exposures to significant subpopulations. This is based, in part, on the extensive food consumption survey data from USDA (its Continuing Survey of Food Intake by Individuals or CSFII) which surveyed more than 20,000 individuals from all states and results in more than 40,000 unique person-days of consumption. We note that, contrary to the assertion by NRDC, consumption is not *averaged* throughout the year, but instead each reported consumption amount is an actual recorded amount at the time of the CSFII survey interview, and is not "averaged throughout the year." As such, it represents a distribution of actual reported single-day reported consumptions. Overall, then, EPA considers this to be an extensive database which can be relied upon to give a very good approximation of high-end food consumption on a national basis in the U.S.

NRDC is apparently concerned that there may be areas or the U.S., or areas of the U.S. at certain times of the year, where high-end consumption may not be adequately reflected in the USDA CSFII data. Specifically, there may be localized areas in the U.S. where a very high end consumption level on a national scale represents only a moderately-high end consumption on a local temporo-spatial scale. NRDC cites number of potential reasons for this which relates to local availability of produce, and its cost, proximity to market, and freshness. These, they state, may tend to cause localized increases in consumption (potentially during certain seasons) that are not fully reflected in a probabilistic manner in the national CSFII database. In other words, NRDC states that there may be specific temporo-spatial subpopulations that consume large amounts of specific commodities at specific times of the year and that the consumption patterns of these subpopulations are not adequately or appropriately reflected in national consumption statistics. These subpopulations, NRDC contends, should be examined separately in any EPA assessment. Absent this, NRDC believes that an FQPA uncertainty factor should be added to the assessment to address this uncertainty/lack of knowledge.

EPA believes that the CSFII survey is adequate to capture the high-end consumers about which NRDC raises concerns. The survey is statistically designed to be representative of the U.S population and reflects variability in consumption over all seasons and geographic regions. Due in part to this design and the fact that fresh blueberries are widely available in season in states where they are not grown, EPA does not believe that the high-end consumption estimates present in the USDA CSFII survey materially or systematically underestimate the consumption patterns of consumers in blueberry-producing states (either overall or during harvest and other "high-availability" seasons). Further, NRDC has presented no evidence that any sizable differential consumption is linked to price or freshness or that consumers will consume unusually high amounts in direct response to cost or availability.

NRDC cites a specific example with respect to the Section 18's issued for imidacloprid in NJ and MI. They consider the case of a child eating blueberries in one of these two high imidacloprid use states. HED examined the general pattern of blueberry consumption by children 1-2 and a number of its associated statistics. Among the 1243 reported blueberry consumption events by

children 1-2 years old in the 1994-96/1998 CSFII, the highest reported consumption was 310 grams (almost 3/4 lb or 2 ¼ cups) by an 2 year old female who weighed 12.7 kg. The next three highest consumption values are 181 grams, 79.6 grams and 77.5 grams. The estimated 99th percentile consumption is 36 grams.

Issue #2: NRDC is objecting to regulating acute dietary exposure at the 95th percentile of exposure, contending that it would be more appropriate to regulate at the 99.9th percentile of exposure.

Background: Standard OPP policy is to perform risk assessments using a "tiered" approach. That is, initial exposure and risk assessments are done using worst-case (or near worst case) assumptions which rarely, if ever, produce estimates of risk which underestimate actual exposures. Since these assessments are done by using a combination of multiple conservative assumptions (e.g, 100% crop treated, tolerance level residues, etc.), decisions typically consider a lower percentile (95th) instead of the 99.9th percentile which is considered when considerably more realistic data is inserted. NRDC is objecting to the use of the 95th percentile in this case, despite the fact that the risk assessment was performed using multiple conservative assumptions.

EPA Response: This issue was directly addressed earlier in our Guidance Document entitled "Choosing a Percentile of Acute Dietary Exposure" and its associated response document[2]. Both are available on the web (http://www.epa.gov/pesticides/trac/science/trac2b054.pdf, see page 16-17 and http://www.epa.gov/pesticides/trac/science/trac2b055.pdf, see page 19-23). Briefly, a Tier 1 or Tier 2 assessment (for which a 95th percentile point of regulation is used) reflects worst (or near-worst) case exposure scenarios: for example, 100% of the crop is assumed to be treated and to contain residue levels either at tolerance or characteristic of field trials in which maximum application rate and minimum preharvest interval conditions apply. It is designed to be an assessment which overestimates (and quite drastically) actual exposures. A "95th percentile" Tier 1 assessment will (in the vast majority of instances) produce exposure estimates which are *greater* than (the more refined) exposure estimates produced in a Tier 3 or 4 assessment at the 99.9th percentile. Thus, the 95th percentile Tier 1 exposure estimate used as a basis for granting a Section 18 is a screening tool and is fully expected to provide a higher estimate of exposure than any more refined procedure (using more realistic inputs) would at a nominally higher (99.9) percentile.

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[2] Specifically, a direct comparison of results of a Tier 1 assessment and a Tier 3 assessment are provided in which the Tier 1 assessment provided exposure estimates roughly an order of magnitude higher than that produced at Tier 3 – using the same data set that is adjusted only for the methodological differences between a Tier 1 and a Tier 3 assessment. We have found that this order of magnitude difference provides a good "rule of thumb" for estimating the difference between the lower Tier (Tier 1 and 2) and higher Tier (Tier 3) assessments.

Issue #3: In spite of imidacloprid having many residential uses, EPA failed to calculate residential risks for some scenarios, based on low toxicity (no endpoints were chosen).

EPA Response: On October 8, 2002, the Health Effects Division (HED) Hazard Identification Assessment Review Committee (HIARC) reviewed the hazard database for imidacloprid and established new endpoints. The following endpoints were chosen: acute dietary, chronic dietary, short-term oral, intermediate-term oral, short-term dermal, intermediate-term dermal, long-term dermal, short-term inhalation, intermediate-term inhalation, and long-term inhalation. In the current risk assessment dated 3/4/03, EPA calculated short-term residential risks (oral, dermal, and inhalation) for both adults and children for a wide-range of representative scenarios, including applications to lawns, ornamental plantings, indoor and outdoor potted plants, and dogs and cats. Based on current residential use patterns for imidacloprid, EPA expects the duration of exposure to be short-term (1-30 days), and would not result in intermediate or long-term exposure. EPA also conducted human health aggregate risk assessments for the following exposure scenarios: acute aggregate (food + drinking water), short-term aggregate exposure (food + drinking water + residential), and chronic aggregate exposure (food + drinking water).

Issue #4: EPA failed to regulate on the basis of a NOEL, and relied on a LOAEL for acute and chronic toxicity.

EPA Response: On October 8, 2002, the Health Effects Division (HED) Hazard Identification Assessment Review Committee (HIARC) reviewed the hazard database for imidacloprid and established new endpoints. The acute dietary endpoint was chosen from an acute neurotoxicity study performed in rats. The LOAEL was 42 mg/kg-day based upon the decrease in motor and locomotor activities observed in females; a NOAEL was not established. HIARC believes that this endpoint is appropriate, since these effects were seen following a single dose, and is applicable to the general population, including infants and children and is also protective of developmental effects which may occur in the population subgroup females 13-50. The maternal and developmental effects in the rabbit study, though severe, occurred at higher doses, and this endpoint is adequately protective of those effects.

A 3X uncertainty factor for the use of a LOAEL was judged to be adequate (as opposed to a 10X) because: **1)** the LOAEL (42 mg/kg-day) is comparable to the LOAELs seen in adults in the developmental rat study (30 mg/kg-day) and the two-generation reproduction study [47/52 mg/kg-day (male/female)] and in the offspring in the DNT (55 mg/kg-day); **2)** the extrapolated NOAEL of 14 mg/kg-day (42/3 = 14) is comparable to the NOAEL of 20 mg/kg-day established in the offspring in the DNT; and, **3)** the neurotoxic effects in this study showed a good dose response which resulted in minimal effects on motor activity and locomotor activity at the LOAEL.

All other endpoints (chronic dietary, short-term oral, intermediate-term oral, short-term dermal, intermediate-term dermal, long-term dermal, short-term inhalation, intermediate-term inhalation, and long-term inhalation) are regulated based on NOAELs (not LOAELS).

Issue #5: In light of the outstanding data requirement for prospective groundwater monitoring studies, EPA failed to retain a 10X FQPA factor for imidacloprid when using predictive models instead of "reliable data".

EPA Response: The imidacloprid exposure assessment is based on conservative models that provide screening concentrations that represent exposure levels that are highly unlikely to be exceeded under normal use conditions. Assuming that toxicity is also assessed in a similarly conservative fashion, the margin of safety in risk assessments for imidacloprid should be high since exposure at levels close to the screening concentration should be quite rare. From the standpoint of the exposure assessment alone (independent of considerations of the conservative assumptions with relationship to the toxicity endpoints and selection of a reference dose) the assumptions made greatly increase the probability that the screening concentrations overestimate human exposure.

The ground-water screening concentration is based upon measured concentrations in extremely vulnerable ground water. For imidacloprid, the screening concentration of 2.09 ppb far exceeds the highest concentrations observed in samples of vulnerable ground waters from the prospective ground-water monitoring studies (0.1 ppb) and also exceeds concentrations observed in field studies evaluating highly vulnerable ground water adjacent to treated fields in Long Island, New York (concentrations up to 1.0 ppb).

Two small-scale prospective ground-water monitoring studies were originally requested by the Agency in 1994 (EFED Memorandum to Registration Division dated 8/4/1994; associated DP Barcode is D200228). This request predates the development of EFED's Tier 1 ground-water screening model in 1997 and the Food Quality Protection Act of 1996. The field phase of these prospective ground-water monitoring studies commenced in 1996. The SCI-GROW model results were used for drinking water exposure via a ground-water source because this was a more conservative (i.e., higher than all field-measured values and therefore representing a worst case assumption) than measured values in vulnerable ground-water. SCI-GROW screening concentrations, under normal use patterns, only have the potential to be exceeded in drinking water for the very small percentage of the population that derives their drinking water from ground-water less than 30 feet deep, is overlain by highly permeable soils, and there is substantial annual recharge of an unconfined aquifer that serves as a drinking water source.

The surface water screening concentration is based upon measured concentrations in extremely vulnerable surface water - a small pond or reservoir without flow through. For imidacloprid, the screening concentration of 36.04 ppb (acute exposure) and 17.24 ppb (chronic exposure) is unlikely to be exceeded because of conservative assumptions such as

- 100% of the watershed was treated.
- Aqueous photolysis rate much slower than observed in the laboratory.
- Soil metabolism rate slower than appears to have occurred in majority of field studies and that represents a 90% upper-bound of the mean in laboratory studies.
- No flow-through in the receiving water body to dilute pesticide residues over time.
- The pesticide is applied to the treated crop at the maximum allowed application rate - every year or growing season.
- The pesticide is applied to a cropped site that is highly vulnerable to runoff.
- Rainfall occurs shortly after application to maximize runoff potential.

9.0 DATA NEEDS/LABEL REQUIREMENTS

9.1 Chemistry

PP#1E6225 - Artichoke; PP#1E6268 - Bushberry, Lingonberry, Juneberry and Salal; PP#2E6421 - Stonefuit; PP#2E6417 - Strawberry; PP#2E6403 - Legume Vegetables, Except Soybean; PP#s 2E06409 and 2E06506 - Root and Tuber Vegetables, Except Sugar Beets and Leaves of Root and Tuber Vegetables

- None

PP#1E06074 - Imported Banana

- Revised Section F to include: 1) the correct tolerance expression of "imidacloprid (1-[(6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine) and its metabolites containing the 6-chloropyridinyl moiety, all expressed as 1-[(6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine,..." and 2) the HED-recommended tolerance of 0.02 ppm.

PP#2E06414 - Corn, Pop

- Revised Section F to include: 1) the correct tolerance expression of "imidacloprid (1-[(6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine) and its metabolites containing the 6-chloropyridinyl moiety, all expressed as 1-[(6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine,..." and 2) the correct commodity definition for pop corn: corn, pop, grain.

PP#0E6203 - Cranberry; PP#2E06458 - Mustard, seed; PP#1E6254 - Okra; PP#0E6237-Watercress

- Revised Section F to include the correct tolerance expression of "imidacloprid (1-[(6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine) and its metabolites containing the 6-chloropyridinyl moiety, all expressed as 1-[(6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine,..."

PP#2E6406 - Avocado, Papaya, Star Apple, Black Sapote, Mango, Sapodilla, Canistel, Mamey Sapote, Lychee, Longan, Spanish Lime, Rambutan, Pulasan, and Persimmon

- Crop field trial data on lychee.
- Final report of crop field study on avocado.
- Revised Section B to include a 7-day PHI.

PP#2E6435 - Guava, Feijoa, Jaboticaba, Wax Jambu, Starfruit, Passionfruit, and Acerola

- Revised Section B to include a 7-day PHI

9.2 Toxicology

- The HED HIARC requested a 28-day inhalation toxicity study as a condition of registration. However, based on the low volatility and low inhalation toxicity (Category IV) of imidacloprid and inhalation MOEs >1000 for the proposed uses in this risk assessment, imidacloprid qualifies for a waiver of the 28-day inhalation toxicity study for the proposed uses [SOP 2002.01: *Guidance: Waiver Criteria for Multiple-Exposure*

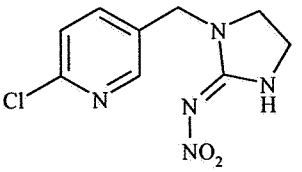
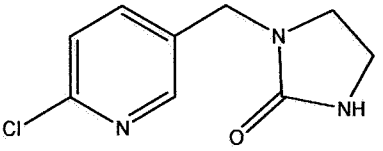
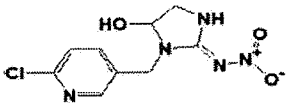
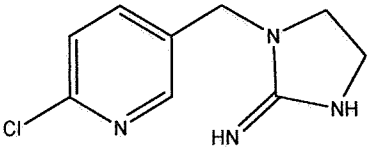
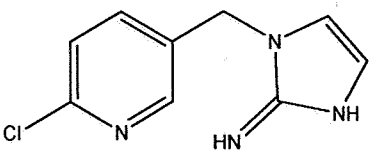
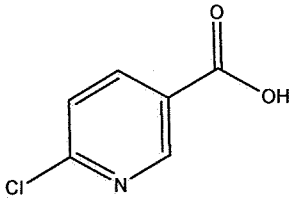
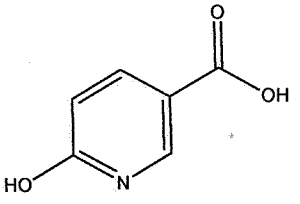
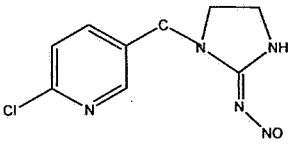
Inhalation Toxicity Studies, 08/15/02]. **The requirement for the 28-day inhalation toxicity study is waived for this action only.** If in the future, requests for new uses or formulations are submitted that may result in a significant change in either the toxicity profile or exposure scenarios, HED will reconsider this data requirement.

10.0 ATTACHMENTS

Attachment 1. Summary of Metabolites Discussed in Risk Assessment.
Attachment 2. Summary of Residues from the Crop Field Trials with Imidacloprid.
Attachment 3. Summary of Proposed and HED-Recommended Tolerances.

cc: J. Tyler (RAB1), M. Dow (RAB1)
RAB1 Branch (2/13/03), HED RARC (2/20/03), G. Herndon (3/4/03)
J. Tyler: 809B: CM#2: (703)305-5564: 7509C: RAB1

ATTACHMENT 1. Summary of Metabolites Discussed in Risk Assessment.

Name	Structure
Imidacloprid 1-[(6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine	
Imidacloprid urea 1-[(6-chloro-3-pyridinyl)methyl]-2-imidazolidinoe	
Imidacloprid hydroxy (WAK 4103)	
Imidacloprid guanidine (WAK 4140) 1-[(6-chloro-3-pyridinyl)methyl]-4,5-dihydro-1H-imidazol-2-amine	
Imidacloprid olefin (WAK 3745) 1-[(6-chloro-3-pyridinyl)methyl]-4,5-dihydro-1H-imidazol-2H-imidazol-2-imine	
6-CNA 6-chloronicotinic acid	
6-hydroxynicotinic acid	
WAK 3839	

ATTACHMENT 2. Summary of Residues from the Crop Field Trials with Imidacloprid.

Crop Matrix	Applic. Rate (lb ai/A)/ Applic. Method	PHI [1] (days)	Residues (ppm)				
			Mean	Std. Dev.	HAFT [2]	Min.	Max.
ARTICHOKE [proposed use (foliar application) = 0.5 lb ai/A total application rate, 7-day PHI]							
Artichoke	0.247-0.267/foliar	7	1.39	NR	1.61	0.96	1.89
BLUEBERRY [proposed use (foliar application, highbush) == 0.2 lb ai/A, 3-day PHI); proposed use (soil application, highbush) = 0.5 lb ai/A, 7-day PHI proposed use (lowbush) = 0.2 lb ai/A, 21-day PHI]							
Highbush blueberry	0.094-0.112/foliar	3	1.10	NR	2.56	0.33	2.802
Highbush blueberry	0.497-0.789/soil	7	NA	NR	NA	<0.05	0.09
Lowbush blueberry	0.092-0.098/foliar	2	0.86	NR	1.03	0.54	1.04
CHERRY (proposed use = 0.5 lb ai/A total application rate, 7-day PHI)							
Cherry (sweet)	0.484-0.677/foliar	6-7	0.773	NR	0.627	0.218	0.630
Cherry (tart)	0.5-0.505/foliar	7-8	1.44	NR	2.47	0.876	2.54
PEACH (proposed use = 0.3 lb ai/A total application rate, 0-day PHI)							
Peach	0.3/foliar	7	0.17	NR	0.06	0.14	0.20
	0.3/foliar	0	0.346	NR	0.614	0.153	0.767
PLUM (proposed use = 0.5 lb ai/A total application rate, 7-day PHI)							
Plum	0.5-0.51/foliar	6-7	0.29	NR	0.67	0.077	0.70
STRAWBERRY [proposed use = 0.5 lb ai/A total application rate, 7-day PHI (foliar) and 30-day PHI (soil)]							
Strawberry	0.503-0.524/one soil, three foliar	6-7	0.177	NR	0.305	0.114	0.349
BEAN (DRY) [proposed use(seed treatment) = 0.25 lb ai/cwt total application rate; proposed use = 0.5 lb. ai/A total application rate, 7-day PHI (foliar) and 21-day PHI (soil)]							
Bean (dry)	0.25 (lb ai/cwt)/ seed treatment; 0.375/soil; 0.12/foliar	6-8	0.490	NR	1.002	0.118	1.12
Pea (Dry, Succulent, Edible-Podded) [proposed use (seed treatment) = 0.25 lb ai/cwt total application rate; proposed use (foliar and soil) = 0.5 lb. ai/A total application rate, 7-day PHI (foliar) and 21-day PHI (soil)]							
Pea (dry, shelled)	0.25 (lb ai/cwt)/ seed treatment; 0.375/soil; 0.12/foliar	7	0.24	NR	0.56	0.07	0.63
Pea (succulent, shelled)			0.24	NR	0.56	0.07	0.63
Pea (edible podded)			0.24	NR	0.56	0.07	0.63
BANANA (proposed use (soil application)= 0.31 lb ai/A total application rate, 0-day PHI)							
Whole Fruit (pulp and peel)	0.31/basal drench	7	0.0102	0.000755	0.0116	<0.010	0.0132
CRANBERRY (proposed use (foliar application) = 0.5 lb ai/A total application rate; 30-day PHI)							
Cranberry	0.50/foliar	20-36	<0.05	-	<0.05	<0.05	<0.05
PAPAYA (proposed use (foliar application) = 0.5 lb ai/A total application rate, 6-day PHI)							
Papaya	0.496-0.55/foliar	5-7	0.23	0.14	0.44	0.076	0.49
MAMEY SAPOTE (proposed use (foliar application) = 0.5 lb ai/A total application rate, 6-day PHI)							
Mamey Sapote	0.5/foliar	30	<0.05	NA [3]	<0.05	<0.05	<0.05

Crop Matrix	Applic. Rate (lb ai/A)/ Applic. Method	PHI [1] (days)	Residues (ppm)				
			Mean	Std. Dev.	HAFT [2]	Min.	Max.
MANGO (proposed use (foliar application) = 0.5 lb ai/A total application rate, 6-day PHI)							
Mango	0.4/foliar	30-80	0.036	0.032	0.15	<0.05	0.15
AVOCADO (proposed use (foliar application) = 0.5 lb ai/A total application rate, 6-day PHI)							
Avocado	0.5/foliar	60	<0.05	NA	<0.05	<0.05	<0.05
GUAVA (proposed use = 0.5 lb ai/A total application rate, 15-day PHI)							
Guava	0.5/foliar	14-15	0.260	0.098	0.375	0.126	0.400
GARDEN BEET (proposed use = 0.5 lb ai/A total application rate, 7-day PHI [4])							
Garden Beet Tops	0.414-0.507/one soil, three foliar	6-8	2.39	0.733	3.15	1.40	3.78
Garden Beet Roots			0.208	0.0985	0.292	<0.100	0.352
RADISH (proposed use = 0.5 lb ai/A total application rate, 7-day PHI [4])							
Radish Top	0.419-0.656/one soil, one foliar	6-8	1.259	0.923	2.737	0.472	2.744
Radish Root			0.0646	0.0310	0.123	<0.05	0.130
CARROT (proposed use = 0.5 lb ai/A total application rate, 7-day PHI)							
Carrot Root	0.514-0.760/one soil, one foliar	6-7	0.0554	0.0130	0.0826	<0.05	0.0896

[1] PHI = preharvest interval
[2] HAFT = highest average field trial
[3] NA = not applicable
[4] Minimum 21-day PHI for Admire 2F as a soil application; minimum 7-day PHI for Provado 1.6F as a foliar application.
[5] NR = Not Reported.

ATTACHMENT 3. Summary of Proposed and HED-Recommended Tolerances.

PP# or ID#	Proposed		HED-Recommended	
	Commodity	Tolerance	Commodity Definition	Tolerance
1E6225	Artichoke	2.5	Artichoke, globe	2.5
1E6074	Banana (Import only)	0.01	Banana	0.02
0E6203	Cranberry	0.05	Cranberry	0.05
2E6458	Mustard, seed	0.05	Mustard, seed	0.05
1E6254	Okra	1.0	Okra	1.0
2E6414	Corn, pop	0.05	Corn, pop, grain	0.05
	Corn, pop, stover	0.2	Corn, pop, stover	0.20
2E6417	Strawberry	0.5	Strawberry	0.50
1E6237	Watercress	3.5	Watercress	3.5
2E6435	Guava Feijoa Jaboticaba Wax jambu Starfruit Passionfruit Acerola	1.0	Guava Feijoa Jaboticaba Wax jambu Starfruit Passionfruit Acerola	1.0
2E6406	Avocado Papaya Star apple Black sapote Mango Sapodilla Canistel Mamey Sapote	1	Avocado Papaya Star apple Sapote, black Mango Sapodilla Canistel Sapote, mamey	1.0
	Lychee Longan Spanish Lime Rambutan Pulasan Persimmon	3	Lychee Longan Spanish Lime Rambutan Pulasan Persimmon	3.0
1E6268	Bushberry Juneberry Lingonberry Salal	3.5	Bushberry, subgroup 13B Juneberry Lingonberry Salal	3.5
2E6409	Vegetable, leaves of root and tuber, group 2	4.0	Vegetable, leaves of root and tuber, group 2	4.0
2E6506	Vegetable, root and tuber, except sugar beet, group 1	0.4	Vegetable, root and tuber, group 1,except sugar beet	0.40
2E6421	Fruit, stone, group 12	3.0	Fruit, stone, group 12	3.0
2E6403	Vegetable, Legume, Except Soybean, Group 6	4.0	Vegetable, legume, group 6, except soybean	4.0