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

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM **September 5, 2012**

Subject: Registration Review – Preliminary Problem Formulation for Ecological Risk and Environmental Fate, Endangered Species, and Drinking Water Assessments for Acetamiprid (PC Code 099050; DP Barcode D401171)

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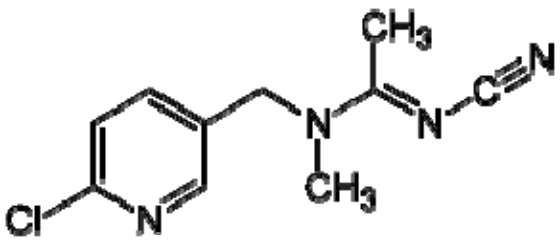
The Environmental Fate and Effects Division (EFED) has completed the preliminary problem formulation (attached) for the ecological risk, environmental fate, endangered species, and drinking water assessments to be conducted as part of the Registration Review of the neonicotinoid insecticide acetamiprid (PC Code 099050). The problem formulation draws on studies submitted by the technical registrant in response to data requirements, studies available in the open literature, and other supporting documents (*e.g.*, guidance documents, white papers). This document is intended to provide an overview of what is currently known about the environmental fate and ecological effects associated with acetamiprid and its degradates, and outlines uncertainties regarding attributes of the parent compound and its transformation products. It describes the preliminary ecological risk hypothesis and the processes that will be used during the completion of drinking water and ecological risk assessments in support of Registration Review. This document also recommends studies that should be included in a data call-in (DCI) to address uncertainties surrounding the environmental fate and potential ecological effects of acetamiprid.

United States Environmental Protection Agency

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

Problem Formulation for the Environmental Fate and Ecological Risk, Endangered Species, and Drinking Water Assessments in Support of the Registration Review of Acetamiprid



(E)-N^1-[(6-chloro-3-pyridyl)methyl]-N^2-cyano-N^1-methylacetamidine
CAS No. 135410-20-7
PC Code: 099050

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1. Purpose

The purpose of this problem formulation is to provide an understanding of the environmental fate and ecological effects of the registered uses of acetamiprid ((E)-N1-[(6-chloro-3-pyridyl)methyl]-N2-cyano-N1-methylacetamidine). Acetamiprid is a neonicotinoid insecticide registered for the following agricultural crops: alfalfa, apple, beans, blueberry, bushberry, caneberry, bulb vegetables, cole crops, cucurbit vegetables, fruiting vegetables, leafy vegetables, citrus, clover, cotton (unspecified), crabapple, cranberry, deciduous fruit trees (unspecified), grapes, leafy vegetables, legume vegetables, onion, ornamental herbaceous plants, ornamental nonflowering plants, ornamental wood shrubs and vines, pear, pine seedlings, pome fruits, Irish white potato, root and tuber vegetables, small fruits, soybeans, strawberry, tobacco, tomato, and tree nuts. Acetamiprid is registered for the following residential/commercial use areas/sites: ornamental and flowering plants, ornamental shrubs, ornamental trees, houseplants, gardens, poplar trees, preconstruction sites, households, outdoor building perimeters, residential areas, greenhouses, shadehouses, and lathouses. It is also registered to control ants, cockroaches, termites, and various other insects indoors and outdoors. This document will provide a plan for analyzing data relevant to acetamiprid and for conducting environmental fate and ecological risk, endangered species, and drinking water assessments for its registered uses. Additionally, this problem formulation is intended to identify data gaps, uncertainties, and potential assumptions used to address those uncertainties relative to characterizing the ecological risk associated with the registered uses of acetamiprid.

2. Description of Regulatory Action

The Food Quality Protection Act (FQPA) of 1996 mandated the Environmental Protection Agency (EPA) implement a new program for assessing the risks of pesticides, *i.e.*, Registration Review[1]. All pesticides distributed or sold in the United States (U.S.) generally must be registered by EPA. The decision to register a pesticide is based on the consideration of scientific data and other factors showing that it will not cause unreasonable risks to human health, workers, or the environment when used as directed on product labeling. The Registration Review program is intended to ensure that, as the ability to assess risk evolves and as policies and practices change, all registered pesticides continue to meet the statutory standard of no unreasonable adverse effects to human health and the environment. Changes in science, public policy, and pesticide use practices will occur over time; through the new Registration Review program, the Agency periodically reevaluates pesticides to ensure that as change occurs, products in the marketplace can be used safely.

As part of the implementation of the Registration Review program pursuant to Section 3(g) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), the Agency is beginning its evaluation to determine whether acetamiprid continues to meet the FIFRA standard for registration. This problem formulation for the environmental fate and ecological risk assessment chapter in support of the Registration Review is intended for the initial docket opening the public phase of the review process.

[1] http://www.epa.gov/oppsrrd1/registration_review

3. Conclusions from Previous Risk Assessments

3.1. Ecological Risk Assessments

Acetamiprid is used in outdoor sites and thus has the potential to result in exposures to wildlife. The Agency conducted a new chemical ecological risk assessment and drinking water assessment on acetamiprid in 2002. New use requests prompted five additional assessments completed in 2004, 2005, 2007, 2009, and 2011. These assessments serve as a basis for this problem formulation. The assessments are briefly discussed below.

A Section 3 new chemical ecological risk assessment was conducted for acetamiprid use on flowers and ornamentals, leafy vegetables, cole crops, cotton, fruiting vegetables, citrus, pome fruits, grapes and seeds (USEPA, 2002, D270368). The highest proposed maximum seasonal application rate for any crop was 0.6 pounds active ingredient per acre (lbs ai/A) for pome fruits. Acetamiprid was characterized as posing low risk to the environment relative to most other insecticides based on its selective toxicity, low use rates, and relatively rapid rate of degradation. Direct acute risk to aquatic invertebrates with direct application into shallow water bodies was predicted, and chronic risks to some species of aquatic invertebrates (due to the selectivity of acetamiprid) were predicted for other uses. Direct risk to Federally-listed threatened or endangered species (hereafter referred to as "listed species") of terrestrial wildlife, terrestrial plants, and saltwater invertebrates were also predicted. Direct effects on terrestrial invertebrates were presumed based on acetamiprid being an insecticide; however, actual risk to terrestrial invertebrates was not quantified. The only residue of concern evaluated was the parent acetamiprid.

Subsequent new use assessments were conducted for tobacco, potatoes, and residential uses in 2004 (USEPA, 2004, D304025) and for cucurbits, stone fruits, and tree nuts in 2005 (USEPA, 2005, D319610). The 2004 assessment indicated that acetamiprid may pose direct acute risks to non-listed and listed freshwater invertebrates, listed mammals, and listed terrestrial plants while the 2005 assessment indicated additional chronic risks to non-listed and listed aquatic invertebrates and non-listed and listed mammals and both acute and chronic risks to non-listed and listed birds. Additionally, direct risk to listed terrestrial plants was indicated. The maximum seasonal application rate for tree nuts (0.72 lbs ai/A) assessed in 2005 was higher than the highest rate previously evaluated. The risk assessments also noted that acetamiprid was moderately toxic to bees and belonged to a class of chemicals that has been associated with causing behavioral effects in bees. Potential for indirect effects to fish was also identified. The only residue of concern evaluated in the risk assessment was parent acetamiprid.

A 2007 assessment (USEPA, 2002, D270368) for new uses on berries, bulb vegetables, succulent legumes, and strawberries concluded that the proposed application rates were lower than those previously assessed, resulting in lower risk quotients (RQs); however, RQ values still exceeded the Agency's levels of concern (LOCs) for the same previously identified taxa. The only residue of concern evaluated in the risk assessment was the parent acetamiprid.

A 2009 new use assessment (Morrica *et al.*, 2005) for new uses on red clover and the climbing

vine small fruit subgroup (crop subgroup 13-07F, except fuzzy kiwifruit) indicated that the proposed uses could result in direct effects to birds (and to reptiles and terrestrial-phase amphibians for which birds serve as surrogates) on both an acute and chronic exposure basis (USEPA, 2009, D364328). Listed freshwater and estuarine/marine aquatic invertebrates and mammals may be affected by acute exposures to acetamiprid, and freshwater and estuarine/marine aquatic invertebrates may be directly affected by chronic exposures. Finally, the assessment also indicated that listed dicotyledonous plants could be adversely affected by spray drift from aerial applications to grapes and climbing vine small fruits. Indirect effects were predicted for aquatic plants, fish (and aquatic-phase amphibians for which fish serve as surrogates), estuarine/marine fish and aquatic invertebrates. The assessment considered the parent and the degradate, IM 1-4, as residues of concern and risk was evaluated using a total toxic residue approach.[2] Overall, the inclusion of IM-1-4 did not affect the risk conclusions.

In 2011, an assessment was completed for both existing and newly proposed agricultural uses of acetamiprid (described in **Table 3-1**); the uses that have been approved are included in this document, while uses that are still pending are not discussed. The existing uses were re-evaluated for aquatic organisms because the degradate IM 1-4 and unextracted residues were assumed to also be residues of concern; therefore, a total toxic residues approach was used to assess risk of both existing and proposed uses. IM-1-4 was considered as a residue of concern in this assessment because it has a considerably longer half-life than the parent compound and available data suggest it is as toxic as the parent compound to aquatic animal species. The screening-level risk assessment concluded that all proposed uses of acetamiprid have the potential for direct acute effects to listed aquatic invertebrates. There was also the potential for direct acute effects to non-listed aquatic invertebrates for five of the seven crop uses (including fruiting vegetables, citrus, and pome fruit). The Agency's chronic LOC for aquatic invertebrates was also exceeded for all proposed crop uses of acetamiprid.

The assessment in 2011 also indicated that for terrestrial organisms, there was a potential for direct acute effects to both listed and non-listed birds (reptiles and terrestrial-phase amphibians) for all of the proposed crop uses of acetamiprid. The higher risk estimates for birds compared to previous assessments were based on a recently study in zebra finches (*Taeniopygia guttata*) where acetamiprid was shown to be very highly toxic to passerine birds on an acute exposure basis. The assessment also indicated that acetamiprid had the potential to cause direct acute effects to listed mammals and terrestrial plants for all uses evaluated except for soybeans. In addition, there was also potential for direct effects to non-listed terrestrial plants for assessed uses on citrus and pome fruit.

Although the 2011 assessment did not predict direct risk to fish and aquatic plants for any assessed uses, the assessment noted that indirect effects to all taxa except aquatic non-vascular plants could occur due to effects on prey or habitat.[3]

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[2] The residues of concern for ecological risk assessment are defined by the Environmental Fate and Effects Division. The residues of concern for human health drinking water are the parent only and these are determined by the Health Effects Division.

[3] Indirect effects to terrestrial and aquatic vascular plants may occur due to effects on birds and mammals that are

Table 3-1. Existing Uses Assessed in the Completed Ecological Risk Assessments

Use Site/ Source	Year Assessed	Single App. Rate (lbs. ai/A)	Number of Apps.	Seasonal App. Rate (lbs. ai/A)	Interval Between Apps. (days)	Comments
Ready to Use Hand spray on Ornamentals, Citrus, Vegetables, and Fruits	2002	NS	NS	NS	7	--
Residential Uses	2004	2.2	NS	NS	NS	--
Ornamental and Flowering Plants	2002	0.15 lbs ai	NS	0.55 lbs ai	7	--
Cotton	2002, 2011	0.1	4	0.4	7	--
Leafy Vegetables within Crop Group 4	2002, 2011	0.075	5	0.375	7	--
Head and Stem Cole Crops	2002, 2011	0.075	5	0.375	7	--
Fruiting Vegetables (within Crop Group 8-10)	2002, 2011	0.075	4	0.3	7	--
Canola	2002	0.03 (5.0 g ai/kg seed; 6 lbs treated seed/A)	1	NA	NA	--
Citrus (within Crop Group 10-10)	2002, 2011	0.25	5	0.55	7	--
		0.25 (assumed[2])	2 (assumed[2])		7	--
		0.11 (assumed[2])	5	0.55	7	--
Pome Fruit (within Crop Group 11-10)	2002, 2011	0.15	4	0.60	12	--
Tuberous and Corm Vegetables (within Crop Sub-group 1C)	2004, 2011	0.075	4	0.3	7	--
Tobacco[2]	2004, 2011	0.075	4	0.3	7	None
Grapes and Other Climbing Small Fruits (except Fuzzy Kiwifruit, within Crop Sub-group 13-07F)	2002, 2009, 2011	0.1	2	0.2	14	None
Stone Fruit (within crop Group 12)	2005, 2011	0.15	4	0.6	10	None
Cucurbits (within Crop Group 9)	2005, 2011	0.10	5	0.5	5	Multiple seasons per year
Tree Nuts (within Crop Group 14, including Pistachio)	2005, 2011	0.18	4	0.72	7 in 2005 14 in 2011	--
Edible Podded Legume (within Crop Subgroup-6A)	2007, 2011	0.1	3	0.3	7	--

pollinators or important in seed dispersal of the species.

Use Site/ Source	Year Assessed	Single App. Rate (lbs. ai/A)	Number of Apps.	Seasonal App. Rate (lbs. ai/A)	Interval Between Apps. (days)	Comments
and Succulent Shelled Peas and Beans (within Crop Sub-Group 6B)						
Strawberries and Other Low Growing Berries (within Crop Sub-group 13-07G)	2007, 2011	0.13	2	0.26	7	--
Blueberries and Other Bush Berries (within Crop Sub-Group 13-07B) and Cane Berries (within Crop Sub-group 13-07A)	2007, 2011	0.085	5	0.5	7	--
Onions and Other Bulb Vegetables (within Crop Group 3-07)	2007, 2011	0.15	4	0.6	7	--
Clover (for use in OD, OR, and WA only)	2009, 2011	0.075	1	0.075	NA	--
Mustard	2002	0.03 (5.0 g ai/kg seed; 6 lbs treated seed/A)	1	NA	NA	--
Soybean	2011	0.04	2	0.078 (0.08 assumed[1])	7	150 foot buffer
						25 foot buffer

Abbreviations: App=Application

[1] Assumed for Tier I aquatic exposure modeling and terrestrial exposure modeling because it is not possible to model multiple applications at different rates.

[2]Scenarios were assumed for modeling purposes because the five applications of the single maximum application rate cannot be made according to the maximum seasonal application rate.

3.2. Drinking Water Assessments

The outdoor uses of acetamiprid potentially contribute residues to drinking water. The most recent Tier I drinking water assessment to support a human health risk assessment was completed in 2011 (USEPA, 2011, D394234, D394479). The assessment analyzed the drinking water concentrations for a number of proposed and existing agricultural uses assessed in the 2011 Ecological Risk Assessment (see **Table 3-1**). The Metabolism Assessment Review Committee (MARC) reported that the residue of concern for acetamiprid is the parent only (USEPA, 2001). Unextracted residues were observed in aerobic soil and aerobic aquatic metabolism studies and in some studies it was uncertain whether some of the unextracted residues contained parent compound (MRIDs 46255603, 44651881, 44699101, 44651879, 44988513, and 44988512).[4] Additionally, the extraction techniques were not exhaustive and it is

[4] If unextracted residues formed along with loss of the parent compound it is possible that some of the unextracted residues are the parent compound; however, if the parent degraded significantly in the beginning of the study and

likely that if different extraction techniques were used, a higher percentage would be extracted. Therefore, when it was uncertain, half-lives used in surface water and ground water modeling were estimated assuming that the unextracted residues were the parent compound. Then these new half-life values based on residues of parent and unextracted residues were used in modeling to estimate drinking water concentrations.[5] When the parent was shown to degrade at the beginning of the study and unextracted residues did not appear until the end of the study, it was assumed that the unextracted residues were not the parent compound.[6] Estimated drinking water concentrations (EDWCs) in surface water were derived using FQPA Index Reservoir Screening Tool (FIRST version 1.1.1, March 25, 2008) and ground water concentrations were estimated using the Screening Concentration in Ground Water (SCI-GROW version 2.3, July 29, 2003). For existing uses, the highest acute EDWC (estimated for acetamiprid use on tree nuts) was 42.8 µg acetamiprid+unextracted residues/L water and the annual average concentration was 12.2 µg acetamiprid+unextracted residues/L water. The highest estimated ground water concentration for existing uses was 0.013 µg/L. Whether EDWC will result in a human health risk concern is determined by considering EDWC as a part of aggregate dietary exposure (food and water) and comparing dietary exposure estimates to mammalian toxicity endpoints (modified by the necessary uncertainty and/or safety factors) to determine whether the LOC is exceeded for the dietary exposure pathway. Because of the absence of data on acetamiprid, the potential effects of drinking water treatment (*e.g.*, chlorination, ozonation) were not considered in the assessment.

4. Mechanism of Action

Acetamiprid is a chloronicotinyl insecticide belonging to the cyano-substituted sub-class of the neonicotinoid pesticides, which also includes thiacloprid (CAS No. 111988-49-9). Similar to other neonicotinoids including nitroguanidine-substituted compounds such as imidacloprid, clothianidin, dinotefuran and thiamethoxam, acetamiprid is a systemic, broad-spectrum insecticide that acts as a stomach poison against sucking and some biting insects (Sur and Stork, 2003). The compound acts as an agonist of the nicotinic acetylcholine receptor (nAChR) at the postsynaptic membrane of nerve cells. The active ingredient interrupts the function of the insect nervous system. As reported in the original Section 3 risk assessment, biochemical radio-ligand binding studies show that acetamiprid interacts with high affinity at the nAChR binding site in insects, and with low affinity at the nAChR in vertebrates (USEPA, 2002, D270368). The cyano-substituted neonicotinoids exhibit a lower toxicity to honeybees (LD_{50} values of <12.5 to 14.6 µg/bee) than the nitro-substituted neonicotinoids (18 to 138 ng/bee) (Iwasa *et al.*, 2004). Inhibition of cytochrome P450 activity in honeybees (*Apis mellifera*) resulted in increased toxicity of acetamiprid, indicating that P450 metabolism is an important detoxifying pathway for insects (Iwasa *et al.*, 2004).

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unextracted residues did not form until the end of the study, the unextracted residues are unlikely to be the parent compound.

[5] Half-lives including unextracted residues were calculated and used in modeling for the aerobic soil metabolism studies (MRID 46255603, 44651881 for clay loam soil, MRID 44651879) and aerobic aquatic metabolism studies (MRID 44988513), and anaerobic aquatic metabolism studies (MRID 44988512).

[6] This occurred in two soils (sandy loam and silty clay loam) in an aerobic soil metabolism study (MRID 44651881).

5. Overview of Pesticide Usage

5.1. Summary of Products and Overview of Usage

Acetamiprid was first registered in 2002 (USEPA, 2012). It is an insecticide used to control a variety of insects including aphids, beetles, caterpillars, leafhoppers, stinkbugs, thrips, whiteflies, boll worms, fleahoppers, earwigs, silverfish, termites, ants, cockroaches, weevils, Colorado potato beetles, potato psyllids, wireworms, household pests, bedbugs, Lygus bug, carpenterworm, apple maggots, borers (excluding the Emerald ash borer) and scale insects. There are currently 37 Section 3 registrations containing acetamiprid and 14 Section 24C (Special Local Needs) registrations (**Table 5-1**). Some formulated end products of acetamiprid contain other active ingredients in addition to acetamiprid; a flowable concentrate (Reg. No. 8033-116) and two termiticides (Reg. No. 8033-96 and 8033-109[7]) also contains the synthetic pyrethroid insecticide bifenthrin (CAS No. 82657-04-3) and one homeowner product (Reg. No. 8033-108) contains the conazole fungicide triticonazole (CAS No. 131983-72-7). Use sites include agriculture, residential, commercial, industrial, and nursery use sites. All use sites are described in more detail in the following sections.

Formulations include water dispersible granules (WDG), emulsifiable concentrates (EC), soluble concentrates (SC), liquids, water soluble packets (WSP), impregnated stickers, impregnated bait stations, gels, and an attract-and-kill device. Water dispersible granules, EC, SC, and WSP are applied as ground or aerial sprays and may result in spray drift. Gels are used as spot treatments, beads, and thin films to control ants and cockroaches. Water dispersible granules are all applied as a liquid. There are also seed treatment uses on potatoes, canola, and mustard. Some liquid formulations are injected into trees. Termiticides may be applied as a liquid or foam. They may be applied on soil surfaces as a perimeter treatment, crack and crevice treatment, or brush and spray. The may also be applied into soil using trenching, rodding, sub slab injection, and soil excavation techniques. Some termiticide products are applied to subsurfaces into piping, injections, and reticulation delivery systems. The impregnated materials are generally stickers used to control flies. The attract-and-kill device is a pheromone mixed with acetamiprid that is hung in trees.

Table 5-1. Summary of Section 3 and Section 24C (Special Local Need) Registrations for Acetamiprid (completed 04/12/2012)

Reg. Number	Registration Name	Percent Acet.	Form.	General Summary of Use Sites	Target pests
Agricultural Use Patterns That Are not Seed Treatments					
8033-20	Acetamiprid Technical	99.5			
8033-22	Tristar 70WSP Insecticide	70	WSP	Ornamentals[j]	Many: aphids, beetles, caterpillars, thrips, etc.
8033-23	Assail 70WP Insecticide	70	WP	Many: cotton, fruits, vegetables, tobacco, tree nuts, clover, *etc.*	Many: aphids, whitefly, weevils, thrips, *etc.*

[7] These are the parent labels for SLN registration numbers OK110002 and OK100003.

Reg. Number	Registration Name	Percent Acet.	Form.	General Summary of Use Sites	Target pests
8033-24	Intruder Brand Insecticide	70	WP	Cotton	Aphids, whitefly, plant bugs, fleahopper, boll worm
8033-36[c]	Assail 30 SG Insecticide	30	WDG	Many: cotton, fruits, vegetables, tobacco, tree nuts, clover, *etc.*	Many: aphids, whitefly, weevils, thrips, *etc.*
8033-26[a]	Acetamiprid 70 WSP Insecticide	70	WSP	Outdoor use only	Ants, termites
8033-94	Tristar 30 SG Insecticide	30	SC	Ornamentals and vegetables	Many: aphids, whitefly, thrips, *etc.*
8033-101[f]	Acetamiprid SL Insecticide	8.5	SC	Cotton	Aphids, whiteflies
8033-106	TRISTAR 8.5 SL INSECTICIDE	8.5	SC	Ornamentals, transplants of leafy & fruiting vegetables, greenhouse tomatoes	Broad range, including aphids, whiteflies, scales, caterpillars, weevils, leafminers
8033-116[h]	Justice OF Insecticide	13 10[e]	FC	Soybean	Many, including aphids, beetles, earworm, rootworm, grasshoppers
ID070011	Assail 70 WP Insecticide	70	WP	Alfalfa	Lygus bug
ID090014	Assail 30 SG Insecticide	30	WDG	Alfalfa seed crop	Lygus bug
NV070004	Assail 70 WP Insecticide	70	WP	Alfalfa seed crop	Lygus bug
OR070017	Assail 70 WP Insecticide	70	A&K	Alfalfa seed crop	Lygus bug
OR090005	Assail 70 WP Insecticide	70	WP	Poplar (hybrid)	Carpenterworm
UT090001	Assail 70 WP Insecticide	70	WP	Alfalfa seed crop	Lygus bug
WA060009	Tristar 30 SG insecticide	30	SC	Fruit and nut trees (non-bearing), apples, crabapples, pears, ornamental plants and trees	Apple maggot
WA060011	Tristar 70 WSP Insecticide	70	WSP	Crabapples, pears, fruit trees, crops, ornamental plants, ornamental trees, residential areas, nonag areas (public health) (outdoor)	Apple maggot
WA070006	Assail 70 WP Insecticide	70	WP	Alfalfa seed crop	Lygus bug
WA110010	Tristar 8.5 SL Insecticide	8.5	SC	Apples, crabapples, pears, ornamental plants and trees, non-bearing fruit and nut trees in non-agricultural quarantine and pest-free areas (including residential areas)	Apple maggot
WY080010	Assail 70 WP Insecticide	70	WP	Alfalfa seed crop	Lygus bug
Seed Treatments					

Reg. Number	Registration Name	Percent Acet.	Form.	General Summary of Use Sites	Target pests
8033-95[d]	Acetamiprid 50 FS Insecticide Seed Treatment	40	RTU liquid	Canola and mustard seed, potato seed piece	Aphids, Colorado potato beetle, flea beetle, leaf hopper, potato psyllid, wireworm
Ready To Use Products/Homeowner Use That are not Ant Baits or Impregnated Materials					
8033-21	Acetamiprid RTU Insecticide	.006	RTU spray	Ornamentals, vegetables, citrus, pome fruits	Many: aphids, beetles, caterpillars, leafhoppers, stinkbugs, etc.
8033-25	Acetamiprid 70 WSP Insecticide For Homeowner Use	70	WSP	Outdoor building perimeters	Ants, earwigs, silverfish, termites etc.
8033-107[g]	Acetamiprid Concentrate Insecticide	0.5		Ornamentals, vegetables, fruits, houseplants	Many: aphids, whitefly, thrips, etc.
8033-108	Acetamiprid + Triticonazole Concentrate	0.26 0.78[i]		Ornamentals, roses, flowers, trees, shrubs, houseplants	Many: aphids, whitefly, thrips, etc.
8033-107[g]	Acetamiprid Concentrate Insecticide	0.5		Ornamentals, vegetables, fruits, houseplants	Many: aphids, whitefly, thrips, etc.
Ant and Cockroach Baits and Gels					
8033-28	Acetamiprid (F5025) 0.15% Sweet Bait Gel-Ants OTC	0.15	Gel	Indoor/outdoor	Sweet and grease eating ants
8033-29[b]	Acetamiprid (F5025) 0.15% Sweet Bait Gel Ants PMP	0.15	Gel	Indoor/outdoor	Ants
8033-30	Acetamiprid (F5025) 0.15% Sweet Bait Gel Cockroach OTC	0.15	Gel	Indoor/outdoor	Cockroaches
8033-31	Acetamiprid (F5025) 0.15% Sweet Bait Gel Cockroaches	0.15	Gel	Indoor/outdoor	Cockroaches
8033-32	Acetamiprid (F5025) Bait Station Cockroaches-OTC	0.35	IM-BS in child-resistant container	Indoor/outdoor	Cockroaches
8033-33	Acetamiprid (F5025) Bait Station Cockroaches-PMP	0.35		Indoor/outdoor	Cockroaches
8033-34	Acetamiprid (F5025) 0.35%	0.35	Gel	Indoor/outdoor	Cockroaches

Reg. Number	Registration Name	Percent Acet.	Form.	General Summary of Use Sites	Target pests
	Protein Bait Gel Cockroach OTC				
8033-35	Acetamiprid (F5025) 0.35% Protein Bait Gel PMP Cockroaches PMP	0.35	Gel	Indoor/outdoor	Cockroaches
8033-90	Acetamiprid (F5025) 0.35% Cockroach Bait Gel-OTC	0.35	Gel	Indoor/outdoor	Cockroaches
8033-91	Acetamiprid (F5025) 0.35% Cockroach Bait Gel-PM	0.35	Gel	Indoor/outdoor	Cockroaches
8033-92	Acetamiprid (F5025) 0.35% Cockroach Bait Station OTC	0.35	IM- BS	Indoor/outdoor	Cockroaches
8033-93	Acetamiprid (F5025) 0.35% Cockroach Bait Station PMP	0.35	IM- BS	Indoor/outdoor	Cockroaches
8033-97	Acetamiprid (F5025) 0.075% Sweet Bait Gel - Ants OTC	0.075	Gel	Indoor/outdoor	Ants
8033-98	Acetamiprid (F5025) 0.075% Sweet Bait Gel-Ants-PMP	0.075	Gel	Indoor/outdoor	Ants
8033-99	Acetamiprid (F5025) 0.075% Gel Bait Station Ants - OTC	0.075	IM- BS	Indoor/outdoor	Ants
8033-100	Acetamiprid (F5025) 0.075% Gel Bait Station Ants - PMP	0.075	IM- BS	Indoor/outdoor	Ants
8033-105	Acetamiprid 0.075% Protein Ant Bait Station OTC	0.075	IM- BS	Indoor/outdoor	Ants
Termiticides					
8033-96	F4688 50 WSP Insecticide Termiticide	22.73 27.27[e]	WSP	Indoor/outdoor, food/feed handling establishments; mattresses	Termites, household pests (ants, bees, wasps, biting flies, centipedes, chiggers, cockroaches, crickets, earwigs, fleas, ticks, flies, mosquitoes, spiders,

Reg. Number	Registration Name	Percent Acet.	Form.	General Summary of Use Sites	Target pests
					scorpions, silverfish, sowbugs, stink bugs, *etc.*) , bedbugs
8033-109	F5688 11% ME Insecticide Termiticide	5 6[e]	EC	Indoor/outdoor, food/feed handling establishments	Termites, household pests (ants, bees, wasps, biting flies, centipedes, chiggers, cockroaches, crickets, earwigs, fleas, ticks, flies, mosquitoes, spiders, scorpions, silverfish, sowbugs, stink bugs, *etc*.), bedbugs
OK100001	F4688 50 WSP Insecticide Termiticide	22.73 27.27[e]	WSP	Outdoors	Termites
OK110002	F5688 11% ME Insecticide Termiticide	5 6[e]	EC	New or post-construction sub-concrete slab treatments through piping or similar delivery systems	Termites
OK100003	Transport Termiticide Insecticide	22.73 27.27[e]	WSP	Outdoors	Termites
Impregnated Materials					
8033-114	F7180-8 Fly Sticker Insecticide - PMP	4.4	IM-sticker	Indoor/outdoor	House flies, little house flies, blow flies, bottle flies, flesh flies, phorid flies, fungus gnats, and vinegar (fruit) flies.
8033-115	F7180-8 Fly Sticker Insecticide OTC	4.4	IM-sticker	Indoor/outdoor	

WP=wettable powder; SC=soluble concentrate; WSP=water soluble packet; RTU-ready to use; EC=emulsifiable concentrate; WDG=water dispersible granules; IM=impregnated material; FC=flowable concentrate; BS=bait station; Acet.=acetamiprid; reg=registration; OTC=over the counter; PMP=pest management professionals; A&K=attract-and-kill device

[a] Only for Sale to, and for Use and Storage by Pest Management Professionals

[b] Inject into cracks & crevices w/syringe or bait injector

[c] Geographical restrictions for certain use sites; chemigation permitted for cranberries & potatoes only

[d] Must not subsequently apply to potato plants grown from treated seed pieces; for canola & mustard, use only in commercial seed treatment facilities; all treated seed must be dyed; do not treat seed for fall planting

[e] Percent bifenthrin

[f] Chemigation prohibited

[g] For residential use sites only; not for commercial production

[h] Buffer is required with use

[i] Percent triticonazole

[j] Not for woodlands or forest management, not for homeowner use

5.2. Agricultural Uses and Residential Uses on Plants

BEAD prepares a Label Use Information System (LUIS) Report summarizing all registered uses of a product. The EFED Table 1 report was used as the source to summarize all relevant uses of acetamiprid. The report was completed on April 16, 2012. **Table 5-2** summarizes all agricultural uses with maximum single application rates provided in lbs ai/A. These uses include aerial or ground broadcast applications of liquids to alfalfa, apple, beans, blueberry, bushberry, caneberry, bulb vegetables, cole crops, cucurbit vegetables, fruiting vegetables, leafy vegetables, citrus, clover, cotton (unspecified), crabapple, cranberry, deciduous fruit trees (unspecified), grapes, leafy vegetables, legume vegetables, onion, ornamental herbaceous plants, ornamental nonflowering plants, ornamental wood shrubs and vines, pear, pine seedlings, pome fruits, Irish white potato, root and tuber vegetables, small fruits, soybeans, strawberry, tobacco, tomato, and tree nuts. Seed treatments are also allowed on potatoes, canola/rape, and mustard. The maximum number of applications per year was not specified on the labels.

Table 5-2. Summary of Use Patterns of Acetamiprid with Well Defined Use Rates for Agricultural Crops

Use Site	Application Method, Timing	Form	Max Single App. Rate (lbs ai/A)	Max # Apps / CC	Max App Rate/CC (lbs ai/A)	Max App Rate/Year (lbs ai/A)	Minimum Treatment Interval (days)
ALFALFA[1]	Broadcast, Foliar	WP	0.0744	NS	NS	NS	NS
ALFALFA[2]	Broadcast, Foliar	WP	0.074-0.075	3, 44	0.225-.2975	NS	7, 14
APPLE	Broadcast, Foliar	SC	0.15	NS	NS	NS	12
BEANS	Broadcast, Foliar	WDG	0.0994-0.1006	3	0.3-0.3019	NS	7
BLUEBERRY	Broadcast, Foliar	L-RTU	0.0005	5	NS	NS	7
BLUEBERRY, BUSHBERRY, CANEBERRY	Broadcast, Foliar	WDG, WP	0.0994-0.1006	NS, 5	0.4988-0.5006	NS	7
BULB VEGETABLES	Broadcast, Foliar	WP	0.1488-0.15	4	0.5994-0.6	NS	7
BULB VEGETABLES, COLE CROPS, CUCURBIT VEGETABLES, FRUITING VEGETABLES, LEAFY VEGETABLES	Broadcast, Pretransplant, Foliar	L	0.1529	NS	0.1529	NS	NS
CANOLA\RAPE	Seed Treatment	L-RTU	0.5039 lbs ai/lbs seed	NS	NS	NS	NS

Use Site	Application Method, Timing	Form	Max Single App. Rate (lbs ai/A)	Max # Apps / CC	Max App Rate/CC (lbs ai/A)	Max App Rate/Year (lbs ai/A)	Minimum Treatment Interval (days)
CITRUS	Broadcast, Foliar, Petal Fall	WDG, WP	0.2494	NS	0.5494	NS	7
CLOVER	Broadcast, Foliar	WP, WDG	0.0744-0.075	1	0.0744	NS	NS
COLE CROPS	Broadcast, Foliar	WP	0.0744-0.075	5	0.3719	NS	7
COTTON (UNSPECIFIED)[3]	Broadcast, Foliar	WDG, WP, L	0.0994-0.1006	NS, 4	0.3994-0.04061	NS	7
CRABAPPLE[4]	Broadcast, Foliar	SC, Solid	0.1488 - 0.15	NS	NS	NS, 0.5438	12
CRANBERRY	Broadcast, Foliar	WDG, WP	0.1294-0.1313	2	0.2588-0.2625	NS	7
CUCURBIT VEGETABLES	Broadcast, Foliar, Bloom	WDG, WP	0.0994-0.1006	5	0.4969-0.5031	NS	5
DECIDUOUS FRUIT TREES (UNSPECIFIED)[4]	Broadcast, Foliar	SC-Solid, L	0.1488-0.1529	NS	NS	NS, 0.5438	7, 12
FRUITING VEGETABLES	Broadcast, Foliar	WP, WDG	0.0744-0.075	4	0.2975-0.3	NS	7
GRAPES	Broadcast, Foliar	WDG	0.0994-0.1006	2	0.1988-0.2013	NS	14
LEAFY VEGETABLES	Broadcast, Foliar	WP, WDG	0.0744-0.075	5	0.3719-0.375	NS	7
LEGUME VEGETABLES	Broadcast, Foliar	WDG, WP	0.0994-0.1006	3	0.3-0.3019	NS	7
MUSTARD	Seed Treatment	L-RTU	0.5039 lbs ai / lbs seed	NS	NS	NS	NS
ONION	Broadcast, Foliar	WDG, WP	0.1488 -0.15	4	0.5994-0.6	NS	7
ORNAMENTAL AND/OR SHADE TREES, HERBACEOUS PLANTS	Broadcast, Foliar	L, SC-solid	0.1488-0.1529	NS	NS	NS, 0.5494	7, 12
ORNAMENTAL WOODY SHRUBS AND VINES	Broadcast, Foliar	L	0.1529	NS	NS	NS	7
PEAR[4]	Broadcast, Foliar	SC-solid	0.1488-0.15	NS	NS	NS, 0.5438	12
PEAS, SUCCULENT	Broadcast, Foliar	WDG, WP	0.0994- 0.1006	3	0.3-0.3019	NS	7
PINE SEEDLINGS	Broadcast, Foliar	L	0.1529	NS	NS	NS	7
POME FRUITS	Broadcast, Foliar, Pink to Bloom,	WP, WDG	0.1488-0.15	NS, 4	0.5906-0.6	NS	12

Use Site	Application Method, Timing	Form	Max Single App. Rate (lbs ai/A)	Max # Apps / CC	Max App Rate/CC (lbs ai/A)	Max App Rate/Year (lbs ai/A)	Minimum Treatment Interval (days)
	Petal Fall						
POTATO, WHITE/IRISH	Seed Treatment	L-RTU	0.0098 lbs ai / lbs seed	NS	0.2945	NS	NS
POTATO, WHITE/IRISH, ROOT AND TUBER VEGETABLES	Broadcast, Foliar	WDG, WP	0.744-0.075	4	0.3-0.3063	NS	7
SMALL FRUITS	Broadcast, Foliar	WDG, WP	0.0994-0.1006	2	0.1988-0.2013	NS	14
SMALL FRUITS	Broadcast, Foliar	WDG, WP	0.1294-0.1313	2	0.2588-0.2625	NS	7
SOYBEANS (UNSPECIFIED)[6]	Broadcast, Foliar	FC	0.0407	2	0.0814	NS	7
STONE FRUITS	Broadcast, Foliar, Dormant, Delayed Dormant, Petal Fall	WDG, WP	0.1488-0.15	4	0.595-0.6	NS	10
STRAWBERRY	Broadcast, Foliar	WDG, WP	0.1294-0.1313	2	0.2588-0.2625	NS	7
TOBACCO	Broadcast, Foliar	WDG, WP	0.0744-0.075	4	0.2975-0.3	NS	7
TOMATO	Chemigation, Soil drench treatment	L, SC-solid	0.0075-0.0076 lbs/plant	NS, 1	NS	NS	NS
TREE NUTS	Broadcast, Foliar	SC-solid	0.1488-0.15	NS	NS	NS, 0.5438	12
TREE NUTS	Broadcast, Foliar, Dormant, Delayed Dormant	WP, WDG	0.1794-0.18	4	0.7175-0.72	NS	14

Max.=maximum; form=formulation, App=application; WDG=water dispersible granule, FC=flowable concentrate; WP=wettable powder; EC=emulsifiable concentrate; L-RTU=liquid-ready to use; SC-Solid=soluble concentrate/solid; L=liquid; cc=crop cycle; NS=not specified; A&K=attract-and-kill device

*Can be applied to all uses sites using aerial, airblast, or ground equipment, except for the seed treatment uses. The maximum number of applications per year was not specified on labels.

[1] May only be used in ID, UT, WY.

[2] May only be used in NV, WA, ID.

[3] Some labels restrict use to CA, FL, GA, NC, SC, VA.

[4] Only allowed for use in WA.

[5] SC-solid may only be used in WA.

[6] Buffer Restrictions

[7] May only be used in OR.

EPA registration number WA110010 allows for control of apple maggot in non-agricultural quarantine and pest free areas (including residential areas) under order for Apple Maggot as Specified under WAC 16-470. The product is used on apples, crabapples, pears, ornamental plants and trees, and non-bearing fruit and nut trees. The product is applied to give the tree uniform spray coverage of the plant. The label does not have a maximum single application rate. It does indicate that the product may be applied every 12 days, up to 4 times a year, with a maximum of 0.55 lbs ai/A per year.

There are several products registered for use on a variety of sites without a specified maximum single application rate, maximum number of applications per crop cycle or year, maximum number of applications, or minimum retreatment interval.

5.3. Use on Trees

Three different labels allow for use as tree injections or basal bark treatments (EPA Reg No. 8033-94 and 8033-106) on ornamental and non-bearing fruit and nut trees. One of the labels (EPA Reg No. OR09005) is an attract-and-kill device to control carpenter worm in poplar trees. The device is applied with a string to trees where acetamiprid wettable powder is mixed with a grease and pheromone. This use is assumed to result in minimal exposure to aquatic organisms. Tree injection uses allow for 0.0024 – 0.0025 lbs ai per inch diameter at breast height (DBH). Basal bark treatments involve wetting the bark of the tree starting from a height of approximately eight feet downwards to the exposed root flair with a directed spray to completely wet the application area. Basal bark treatments recommend applications at 0.004 lbs per inch DBH of the intended target. Also recommend use of 0.15 lbs ai/36-42 total inches of treatment DBH, depending on the bark. Only single application rates are provided on the labels.

Table 5-3. Summary of Use Pattern Recommended for Control of Borers, Scale Insects, and Hemlock Wooly Adelgids in Ornamental or Non-Bearing Fruit and Nut Trees

Use Site	Application Method	Timing	Formulation	Single Application Rate Recommendations
Hybrid Poplar	Device applied to tree with string	Spring and Summer	Attract-and-kill Device	0.00000265 lbs ai/A
Ornamental and Non-bearing Fruit and Nut Trees	Tree injection treatment	Bud break through foliar	L, SC-solid	0.0024 - 0.0025 lbs ai/DBH
	Basal bark treatment	Bud break through foliar (Mid Spring)	L	NS, 0.004 lbs ai/DBH 0.15 lbs ai/ gal/36-42 DBH

L=liquid; SC-solid=soluble concentrate, solid; DBH=diameter breast height in inches; gal=gallon

5.4. Termiticide, Ants Control, and Control of Pests

A number of products are registered for use of control of termites, ants, and various other insects

around homes, buildings, eating establishments, animal production sites, equipment, ships and boats, transportation facilities, paths, patios, and wood protection treatment, *etc.* The uses involve surface application to soils, mound treatments, drench treatments, perimeter treatments, soil injection, trenching, rodding, void treatments, spot treatments, soil excavation treatments, crack and crevice treatments, drench, bait applications, mound treatments, and insecticidal strip treatments. Some termiticide products are applied to subsurfaces into piping and reticulation delivery systems. Soil excavation involves digging up soil, treating it, and then reapplying it. Rodding involves drilling a series of holes (no more than 12 inches apart) into the ground, injecting the pesticide, and then covering the hole. Trenching (may be 6 inches deep and wide) involves digging a trench around a structure and treating the trench, Often trenching and rodding are both used in treatments. Perimeter treatment may be up to 10 feet wide around the structure and up to 3 feet high on the structure. No information was available on application intervals or maximum number of applications per year.

Table 5-4. Summary of Uses Around Buildings, Paths, Wood, and Equipment

Application Method	Application Timing	Formulation	Maximum Single Application Rate
Application Rates in lbs ai/A			
Crack and crevice and/or spot treatment	When needed	SC-Solid	0.3659 lbs ai/A
Soil drench treatment, spray, crack and crevice treatment, spot treatment, void treatment, perimeter treatment	When needed	SC-solid, WP, EC	0.1829 - 0.189 lbs ai/A
Barrier treatment	When needed	SC-Solid	1.1 lbs ai/A
Barrier treatment, soil surface treatment, barrier treatment	Postconstruction, preconstruction	WP, EC	18.6-18.7 lbs ai/A
Drench	When needed	EC	23.4 lbs ai/A
Application Rate per Spot			
Crack and crevice and/or spot treatment	When needed	Bait	0.00000083 lbs ai/ spot
		Bait	0.00000165 lbs ai/ spot
		Bait	0.00000386 lbs ai/ spot
Applications Rates for Baits in Bait Stations			
Bait application	When needed	Bait	0.00001531 lbs ai/ bait station
		Bait	0.00002344 lbs ai/bait station
Application Rates in lbs ai per linear foot			
Soil treatment (subslab injection, trenching), soil excavation, spray, void treatment	When needed, postconstruction, preconstruction	EC, WP	0.0009 lbs ai/ linear ft
		EC, WP	0.0017 lbs ai/linear ft
Application Rates in lbs ai/gallon			
Crack and crevice treatment, void treatment, spot treatment, foam application, void treatment, soil injection	When needed	EC, WP, WDG	0.0043 lbs ai / 1 gal
		SC-Solid, WP	0.105 lbs ai / 25 gal 0.1065 lbs ai /25 gal
Other Application Rates			
Mound Drench	Cool weather (65 - 80	WP, EC	0.0043 lbs ai / mound

Application Method	Application Timing	Formulation	Maximum Single Application Rate
	F)		0.0086 lbs ai / mound
Spray, spot treatment, perimeter treatment	When needed	L-RTU, SC-solid	No dosage conversion
Bait application	When needed	Bait	No dosage conversion
Insecticidal strip treatment	When needed	IM	No dosage conversion

L-RTU=liquid-ready to use; SC-solid=soluble concentrate-solid; IM=impregnated material; EC=emulsifiable concentrate; WP=wettable powder; gal=gallon

5.5. Usage Data

Based on market usage data from 2000-2010, usage averaged approximately 60,000 lbs ai for 900,000 acres treated resulting in an overall average application rate of 0.067 lbs ai/A (USEPA, 2012) (**Table 5-5**). The screening-level use assessment (SLUA) estimate, which only considers agricultural use, indicate that 33% of the acetamiprid used is applied to apples and cotton (20,000 lbs ai/year on average). On average 2000 to 5000 lbs of acetamiprid per year is applied to pears, oranges, lettuce, strawberries, and grapes. Based on the maximum amount of crop treated, acetamiprid is important for pears, celery, strawberries, apples, grapes, and lettuce where on average greater than 15% of these crops are treated with acetamiprid. Values are calculated by merging pesticide usage data sources together, averaging across all observations, and then rounding.

Table 5-5. Screening Level Estimates of Agricultural Uses of Acetamiprid (099050), Sorted Alphabetically

Crop	Average Annual Pounds Active Ingredient Used on Crop	Percent Crop Treated	
		Average	Maximum
Alfalfa	<500	<1	<2.5
Almonds*	<500	<1	<2.5
Apples	20,000	25	40
Artichokes*	<500	N/C	N/C
Beans, Green	<500	<1	<2.5
Broccoli	1,000	10	15
Brussels Sprouts*	<500	N/C	N/C
Cabbage	1,000	10	15
Caneberries	<500	<2.5	5
Cantaloupes	<500	5	15
Cauliflower	<500	10	20
Celery	1,000	35	45
Cherries	1,000	5	15
Chicory*+	<500	N/C	N/C

Crop	Average Annual Pounds Active Ingredient Used on Crop	Percent Crop Treated	
		Average	Maximum
Cotton	20,000	5	5
Cucumbers	<500	<2.5	<2.5
Grapefruit	<500	<2.5	5
Grapes (all)	2,000	20	30
Lemons	<500	<2.5	5
Lettuce	3,000	15	30
Lima Beans	<500	<1	<2.5
Nectarines*	<500	N/C	N/C
Olives*+	<500	N/C	N/C
Onions	<500	5	5
Oranges	4,000	<2.5	10
Peaches	1,000	5	10
Pears	5,000	35	60
Pecans	<500	<1	<2.5
Peppers	<500	5	15
Pistachios	<500	<1	<2.5
Potatoes	1,000	<2.5	<2.5
Prunes	<500	5	5
Pumpkins	<500	5	5
Spinach	<500	10	20
Squash	1,000	<2.5	<2.5
Strawberries	3,000	30	50
Tobacco	<500	<1	<2.5
Tomatoes	1,000	5	10
Walnuts	1,000	5	10
Watermelons	<500	<1	<2.5

All numbers rounded.

<500 Less than 500 pounds of active ingredient
<2.5 Less than 2.5 percent of crop treated
<1 Less than 1 percent of crop treated
N/C Only lbs.ai available
* Based on CA DPR data only (valid because 95% or more of U.S. acres grown are in California)
+ Crops not known to be listed on active end use product registrations or as Section 18 emergency exemptions when this report was run

SLUA data sources include:
USDA-NASS (United States Department of Agriculture's National Agricultural Statistics Service)
Private Pesticide Market Research
California DPR (Department of Pesticide Regulation)

Figure 5-1 spatially represents acetamiprid agricultural use intensity in the U.S.; use intensity is highest in parts of the Southwest (CA and AZ), Northwest (WA and OR), and Northeast (NY, PA, and MI).

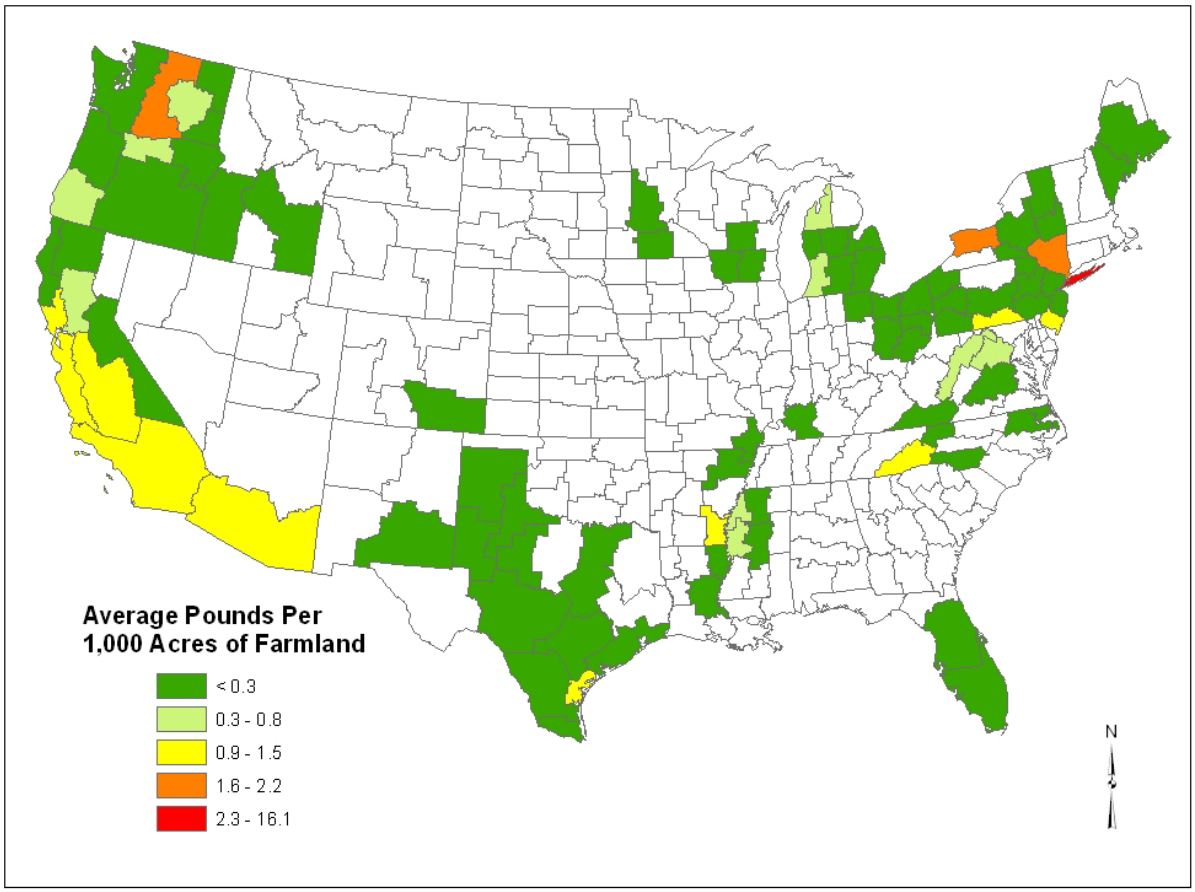


Figure 5-1. Average Pounds Acetamiprid Used by Crop Reporting District (2006-2010).[8]

[8] This map was developed by BEAD (USEPA, 2012). This is a map of agricultural pesticide usage at the Crop Reporting District (CRD) level; CRDs are aggregates of counties created by USDA NASS (USDA, 2010). Pesticide usage is displayed as average pounds (for the years 2006-2010) per 1,000 acres of farmland in a CRD to normalize for the variation in farmland between CRDs. Farmland acreage was obtained from USDA (2007).

Usage is based on private market surveys of pesticide use in agriculture (Proprietary Data, 2006-2010). The survey data are limited to the states that represent the top 80-90% of acreage for the individual crops; therefore, use may be occurring in regions outside the scope of the survey. CRDs showing no usage of pesticides may be due to either the lack of pesticide use in the region or non-participation in the agricultural surveys. In addition, across the years, there may be variations in the specific crops included in the CRD survey. This may result in a lower annual average for the CRD.

Sources: Proprietary Data, 2006-2010; USDA NASS Crop Reporting Districts, 2006-2010; USDA Census of Agriculture, 2007.

6. Environmental Fate and Transport

6.1. Summary

Acetamiprid may enter the environment via spray directly onto soil or foliage, via spreading of bait on surfaces, or via injection into soil and building foundations. It may move off-site via spray drift, leaching, and runoff. Acetamiprid is considered nonvolatile from dry non-adsorbing surfaces, water, and moist soil. It is not likely to bioconcentrate in aquatic or terrestrial organisms. Chemicals with half-lives greater than 60 days in soil, water, and sediment are considered persistent (USEPA, 2008b); therefore, aerobic aquatic and soil metabolism half-lives for acetamiprid indicate that acetamiprid is not persistent. However, there is uncertainty in the half-lives due to significant amounts of unextracted, unidentified residues in the metabolism studies. If these unidentified residues were found to be parent, then the compound would be classified as persistent.[9] Primary routes of degradation are via aerobic soil and aerobic aquatic metabolism. Acetamiprid is stable to hydrolysis at 25^{o}C and aqueous photolysis is not an important degradation pathway. Acetamiprid is classified as moderately mobile using the FAO classification system (K_{oc}s = 157-298 L/kg organic carbon) and may be transported into surface and ground water. Acetamiprid has nine (excluding carbon dioxide) identified degradates, five of which are major degradates. Four of the five major degradates have the pyridylmethylamine structure and one minor degradate contains both the pyridylmethamine structure and the cyano group of the parent. Residues of concern for human health drinking water were identified by the Health Effects Division to be the parent only. Residues of concern for aquatic organisms were determined to be the parent and IM 1-4[10] by the Environmental Fate and Effects Division. As some of the unextracted residues may be the parent compound or IM 1-4, unextracted residues were determined to be a residue of concern for both human health drinking water and aquatic organisms by the Environmental Fate and Effects Division.

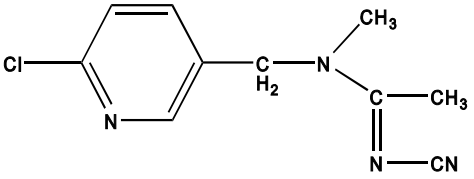
Acetamiprid has a log dissociation constant (pK_a) of 0.7 for the protonated form, indicating that its form will not change significantly at environmentally relevant pH values. The vapor pressure, air-water partition coefficient (K_{AW}), and ratio of acetamiprid concentration in moist soil to acetamiprid concentration in air ($C_{water+soil}/C_{air}$) indicate that it is nonvolatile from dry non-adsorbing surfaces, water, and moist soil using OPPTS[11,12] Guideline 835.6100 classifications. The log octanol-water partition coefficient (log K_{ow}) is 0.08 at 25^{o}C and the log octanol-air partition coefficient (log K_{OA}) is 12.5 indicating it is not likely to bioconcentrate in aquatic or terrestrial organisms (Armitage and Gobas, 2007; Gobas *et al.*, 2003; USEPA, 2009c).

Table 6-1 summarizes the identity information and physical-chemical properties of acetamiprid. **Table 6-2** summarizes other environmental fate data for the parent and provides half-lives for the

[9] Data indicates that some of the unextracted residues are unlikely to be parent; however, it is unknown what portion is parent and what portion is not.
[10] IM-1-4 retains the pyrimidylmethylamine structure of the parent.
[11] Office of Prevention, Pesticides, and Toxic Substances (OPPTS) is now the Office of Chemical Safety and Pollution Prevention (OCSPP); however, the guidelines still reference OPPTS and so the guidelines are referenced with OPPTS in this document.
[12] A list of all OPPTS Guidelines discussed in this document is available in Appendix D.

parent and unextracted residues. **Table 6-6** summarizes half-lives for the parent alone, residues of acetamiprid and IM 1-4, and residues of acetamiprid, IM 1-4, and unextracted residues. All of these half-life values are used to characterize estimated environmental concentrations (EECs) in water.

Table 6-1. Summary of physical-chemical properties of acetamiprid

Parameter	Value	Source	Comments
PC Code	099050	None	None
CAS Number	135410-20-7	(USNLM, 2009)	None
Structure			None
Chemical Name	N^1-[(6-chloro-3-pyridyl)methyl]-N^2-cyano-N^1-methylacetamidine	MRID 44651803	None
Molecular Weight	222.68	MRID 44651803	None
Water Solubility	4250 mg/L (25°C)	MRID 44651811	None
Vapor Pressure	<1 x 10^{-8} Torr at 25°C	MRID: 46235701	Nonvolatile from dry non-adsorbing surfaces (USEPA, 2010a)
	7.50 x 10^{-10} Torr at 25°C 1 X 10^{-4} mPa at 25°C	(AERU, 2012)	
Henry's Law constant	5.2 x 10^{-14} atm-m^3/mol at 25°C (estimated)	(Estimated from vapor pressure and water solubility at pH 7 and 20°C)	Calculated with vapor pressure reported by AERU (2009).
Dissociation Constant (pKa)	0.7 at 25°C	(USEPA, 2002)	None
Log K_{OW}	0.8 at 25°C	MRID 44651883	Not likely to bioconcentrate (USEPA, 2010a)
Air-water partition coefficient (K_{AW})	2.11 x 10^{-12} (log K_{AW} = -11.68)	Calculated[1]	Non-volatile from water (USEPA, 2010a)
Octanol-air partition coefficient (K_{OA})	3.0 x 10^{12} (log K_{OA} = 12.5)	Calculated[1]	Not likely to biomagnify in terrestrial food chains[2] (Gobas *et al.*, 2003; USEPA, 2009c)
$C_{water+soil}/C_{air}$	2.63 x 10^{11} to 2.02 x 10^{12}	Calculated[1]	Non-volatile from moist soil (USEPA, 2010a)

[1]All estimated values were estimated according to "*Guidance for Reporting on the Environmental Fate and Transport of the Stressors of Concern in Problem Formulations for Registration Review, Registration Review Risk Assessments, Listed Species Litigation Assessments, New Chemical Risk Assessments, and Other Relevant Risk*

Assessments" (USEPA, 2010a).

[2] A recent FIFRA Scientific Advisory Panel (SAP) reported, "Gobas *et al* (2003) concluded that chemicals with a log K_{OA} >5 can biomagnify in terrestrial food chains if log K_{OW} >2 and the rate of chemical transformation is low. However, further proof is needed before accepting these limits without reservations" (USEPA, 2009c). This was also supported by Armitage and Gobas's work completed in 2007 (Armitage and Gobas, 2007).

Table 6-2. Summary of environmental fate and transport properties of acetamiprid[6]

Parameter	Value(s)	Source / Study Classification	Comments
Hydrolysis[3] (days)	Half-life, linear regression[1]: Stable (pH 5, 7, 9 at 25°C) 50.8 (pH 9 at 35°C) 12.8 (pH 9 at 45°C)	MRID 44651876 Acceptable	None
Atmospheric Degradation (days)	Half-life: 0.140 (estimated)	(USEPA, 2009b) NA	Estimated Hydroxyl Radical Reaction Half-life for a 12-hour day; $1.5x10^6$ OH molecules/cm^3 Using EPIWeb Version 4.0
Aqueous Photolysis Half-life (days)	Half-life, linear regression[1]: 34[2] (pH 7, 25°C)	MRID 44988509 Acceptable	None
Soil Photolysis Half-life[4]	No half-lives available	MRID 48563501 Supplemental – not for use in modeling	Microbial activity was higher in the dark control than in the irradiated samples and the degradation was faster in the dark control. As soil photolysis did not occur at a faster rate than microbial degradation, photolysis will not be a major route of degradation when microbial degradation is occuring. It is not known whether degradation was faster in the dark control due to the differences microbial activity. The study provides evidence on degradation products that may be observed with irradiation.
Aerobic Soil Metabolism Half-life (days)	Half-life, nonlinear regression[1] at 20°C: Parent Only: 1.1, sandy loam 1.2, clay loam 1.0, clay loam Parent+Unextracted Residues 76, sandy loam 75, clay loam 99, clay loam	MRID 46255603 Supplemental – May be used in modeling	Only one replicate. Unextracted residues made up <1 to 31 % of applied radioactivity.

Parameter	Value(s)	Source / Study Classification	Comments
	Half-life, nonlinear regression[1] at 20°C: Parent Only: 2.8, sandy loam 0.90, silty clay loam 6, clay loam Parent+Unextracted Residues: 10, clay loam	MRID 44651881 Supplemental – May be used in modeling	Unextracted residues made up approximately 20-40% at the end of the study (182 days); however, unextracted residues were not observed until most of the parent had degraded in the silty clay loam and sandy loam suggesting that the unextracted residues were not the parent compound.[5]
	Half-life, nonlinear regression[1] at 20°C: Parent Only: 1.4, loamy sand Parent+Unextracted Residues: 2.0, loamy sand	MRID 44699101 Supplemental – May be used in modeling	Unextracted residues ranged from 2 to 17% of applied radioactivity. The identity of the unextracted residues is not known.
	Half-life, linear regression[1] at 25°C: Parent Only: 0.3, loamy sand	MRID 44651880 Supplemental – Not for use in modeling	Not conducted under GLP. Unextracted residues were high (up to 14%)
	Half-life, linear regression[1] at 25°C: Parent Only: 3.5, loamy sand Parent+Unextracted Residues: 6.4, loamy sand	MRID 44651879 Acceptable	Biphasic degradation was observed with an initial 3.6 day half-life followed by a 75 day half-life. Unextracted residues were up to 20%.
Anaerobic Soil Metabolism Half-life (days)	No half-lives available	MRID 48554501 Supplemental-Not for use in modeling	Dissolved oxygen concentrations ranged from 1.87-1.94 mg/L, indicating system was not fully anaerobic. Data on degradates can be used as the environment is expected to occur in natural systems.[7]
Aerobic Aquatic Metabolism Half-life (days)	Half-life, nonlinear regression[1] at 25°C:Parent Only: 25, loamy sand sediment Parent+Unextracted Residues: 74, loamy sand sediment	MRID 44988513 Acceptable	Maximum of 38% unextracted residues. The identity of the unextracted residues is not known. Data available for only one sediment.

Parameter	Value(s)	Source / Study Classification	Comments
Anaerobic Aquatic Metabolism Half-life (days)	Half-life, linear regression[1] at 25°C: Parent Only: 325, loamy sand sediment Parent+Unextracted Residues: 568, loamy sand sediment	MRID 44988512 Acceptable	Data available for only one sediment.
Solid-water distribution coefficient (K_d) in L/kg	Average K_d at 20°C 0.39, loamy sand, pH 4.4 3.9, loamy sand II, pH 6.2 1.1, silt loam, pH 6.6 3.5, clay, pH 7.5 4.1, sandy loam sediment, pH 5.6 Mean = 2.60 (standard deviation=1.72)	MRID 44651883 Acceptable	Coefficient of variation is 66%.
Freundlich solid-water distribution coefficient (K_F) in L/kg	K_F (1/n) at 20°C Parent: 0.33 (0.85), loamy sand, pH 4.4 3.0 (0.82), loamy sand II, pH 6.2 1.0 (0.90), silt loam, pH 6.6 3.2 (0.91), clay, pH 7.5 3.2 (0.83), sandy loam sediment, pH 5.6	MRID 44651883 Acceptable	Sorption was dependent on concentration in some soils.
Organic-carbon normalized distribution coefficient (K_{oc}) in $L/kg_{organic\ carbon}$	Average K_{oc} at 20°C 157, loamy sand, pH 4.4 266, loamy sand II, pH 6.2 251, silt loam, pH 6.6 298, clay, pH 7.5 164, sandy loam sediment, pH 5.6 Mean = 227 (standard deviation=63.26)	MRID 44651883 Acceptable	Coefficient of variation is 28%. The coefficient of variation is less than that for K_d values indicating that K_{oc} values will be better at predicting sorption across soils than K_d values. Moderately mobile according to FAO classification.
Terrestrial Field Dissipation Half-life (days)	Half-life, nonlinear regression[1]: 2.8, CA, Gilman loamy fine, Vinca rosea 14.1, FL, Astatula fine, tree ferns 4.2, NJ, Penn silt loam, garden mums	MRID 44988514 Supplemental	Wettable powder 70% ai (EXP80667A 70WP). Degradate IM 1-2 converted to IM 1-4 in storage stability study and IM 1-4 was not stable. Residues in plants were not reported. Broadcast at 0.15 lbs ai/A with four applications. Parent was not detected below 15 cm. ECM/ILV for soil are 44988516/44988517.

Parameter	Value(s)	Source / Study Classification	Comments
	Half-life, linear regression[1]: 3, WA, Timerman coarse sandy loam, apples 6, FL, Candler sand soil, oranges 13, NY, Oakville loamy fine sand, cabbage 6, CA, Romona loam soil, cotton	MRID 44988515 Supplemental	Wettable powder 70% ai (EXP80667A 70WP). Degradate IM 1-2 converted to IM 1-4 in storage stability study and IM 1-4 was not stable. Residues in plants were not reported. Broadcast at 0.15 lbs ai/acre with four applications. Parent was not detected below 15 cm. Conditions not favorable to leaching. Subset of data used to estimate half-life for FL and WA site. ECM/ILV for soil are 44988516/44988517.
	Half-life, linear regression[1]: 10.1, Prince Edward Island, Alberry sandy loam 5.2, Ontario, London loam 17.8, Manitoba, Ryerson clay loam	MRID 44988625 Supplemental	Wettable powder 70% ai (EXP61486A). Pan evaporation data were not reported so water balances could not be determined. Storage stability data were not submitted for the test site soils. Acetamiprid was applied four times at 168 g ai/ha with a 7 day interval to bare plots in Canada. Parent not detected below 15 cm depth. ECM/ILV for soil are 44988516/44988517.
Environmental Chemistry Methods and Independent laboratory Validation	LC/MS/MS for detection of acetamiprid, IM 1-2, IC-0 in soil	MRID 44988516/ 44988517 Satisfactory	Acetamiprid, IC-0, IM 1-4 LOD = 3.33 µg/kg-soil Acetamiprid, IM 1-2, IC-0, 1M-1-4 LOQ = 10 µg/kg-soil
	HPLC-UV for parent, IC-0, IM 1-4, IM 1-2 in water	MRID 44988536	LOD = 0.033 µg/L LOQ=0.1 µg/L

[1] Degradation kinetics were calculated using the single first order decay equation using either nonlinear regression of non-transformed data or linear regression of natural log transformed data.
[2] Value corrected to represent natural sunlight at 40°N latitude.
[3] MRID 44651877 is supplemental. A material balance was not conducted in the study; however, the results suggest that degradates IM-1-4 and IC-0 are stable.
[4] MRID 44988508 is unacceptable.
[5] This indicates that the unextracted residues were not the parent compound. Unextracted residues in the clay loam appeared as the parent was lost the identity of unextracted residues is unknown.
[6] This table shows half-lives for the parent and parent plus unidentified unextracted residues which may or may not be the parent. These values are relevant in understanding the uncertainty in data due to unextracted residues. **Table 6-6** summarizes half-lives calculated for acetamiprid plus IM 1-4 plus unextracted residues which will be used in the calculation of modeling inputs in the ecological risk assessment.
[7] Unextracted residues were at a maximum of 36.1% in the clay loam and 30% in the sandy loam soil. The identity of the unextracted residues is not known. Data only available on two soils. Results on four soils are recommended.

6.2. Degradation/Transformation of Parent

The persistence of acetamiprid is uncertain because a large portion of residues in the metabolism studies were unidentified; however, the overall evidence suggests it is not persistent in aerobic systems. Aerobic soil metabolism rates for the parent alone and for the parent and unextracted

residues in some soils indicate acetamiprid is not persistent.[13] However, if it is assumed that all of the unextracted residues are the parent compound, acetamiprid would be considered persistent in some systems. Evidence suggests that not all of the unextracted residues are the parent compound; however, it is unknown what portion of the unextracted residues are parent and what portion are not. As many of the values considering both parent and unextracted residues are lower than 10 days; it is likely that acetamiprid is not persistent in aerobic systems. Under anaerobic aquatic conditions acetamiprid is persistent.

Acetamiprid was stable to hydrolysis at 25°C and pH 5, 7, and 9; however, hydrolysis was observed at pH 9 at 35 and 45°C (MRID 44651876). The aqueous photolysis half-life of 34 days indicates that aqueous photolysis is a minor degradation pathway (MRID 44988509). Rates of soil photodegradation are not available.[14]

The primary route of degradation for the parent compound is aerobic soil metabolism. There is uncertainty in the degradation of acetamiprid due to high levels of unextracted residues in metabolism studies. Therefore, to assess the impact of this uncertainty on the risk assessment, degradation rates were estimated in two ways: for the measured parent by itself, and for measured parent plus unextracted residues under the assumption that unextracted residues are also parent compound or are a residue of concern. Half-lives were also calculated for these combinations along with N-methyl(6-chloro-3-pyridyl)methylamine (IM 1-4) because the IM 1-4 degradate is considered a residue of concern for aquatic organisms; IM 1-4 is not considered a residue of concern for human health drinking water residues. In nine soils, aerobic soil metabolism rates for the parent ranged from <1 day to 6 days for the parent alone, and from 2 to 99 days for the parent plus unextracted residues. This difference in half-lives is environmentally relevant and impacts the EECs and EDWCs (see Section 14.1.B for more discussion). Anaerobic soil metabolism half-lives are not available. Aerobic aquatic metabolism rates were slower than aerobic soil metabolism rates. The aerobic aquatic half-life was 25 days for the parent, and 74 days for parent plus unextracted residues in one sediment (MRID 44988513). Anaerobic aquatic metabolism was much slower, with a half-life of 325 days in a loamy sand sediment (MRID 44988512). Examination of aerobic aquatic and anaerobic aquatic metabolism in two sediments representative of intended use sites are recommended by OPPTS Guideline 835.4300; however, data are only available on one sediment for both of the studies.

6.3. Field Dissipation

The terrestrial field dissipation of acetamiprid was studied at seven U.S. sites on various crops, and on bare ground plots at three sites in Canada. The application rate used in all studies was 0.15 lbs ai/A. This is lower than the maximum single application rate for use on citrus--0.25 lbs ai/A/single application, which has the highest single application rate among agricultural uses, a maximum of five applications/season, and a maximum of 0.55 lbs ai/A/season (several other

[13] International half-lives that are considered persistent in soil, water, and sediment range from greater than 60 days to greater than 365 days (USEPA, 2008b).

[14] A soil photolysis study (MRID 48563501) is available; however, data were insufficient to determine the rate of soil photolysis.

fruit and nut tree crops have similar or slightly higher seasonal application rates). The dissipation half-lives for acetamiprid applied to domestic food, fiber and ornamental crops ranged from three to 14 days for residues in 0 to 15 cm (MRIDs 44988514, 44988515). The dissipation half-lives for acetamiprid applied to bare ground plots (determined in Canadian soils) ranged from five to18 days (MRID 44988625). The submitted studies generally met guideline requirements. However, because the degradate IM 1-2 converts to IM 1-4 in frozen storage within a short period of time (approximately 1 month), and many of the samples were stored for much longer periods of time (over 600 days, lengths of storage for which storage stability data were not reported) prior to analysis, the patterns of formation and decline could not be determined accurately for these major degradates. Also, at several of the study sites, negative water balances (*i.e.*, greater evaporation/total water loss from the soil than the total water input) following the final application likely precluded the possibility of significant leaching. Soil characteristics and results of the field studies are presented in **Table 6-3**. All reported maximum values for degradates in **Table 6-3** are for the period following the final application and represent individual replicates (U.S. sites) or replicate means (Canadian sites) from the 0- to 15-cm depth. The degradate IM 1-4 frequently had higher maximum concentrations in soils than the parent. In the studies conducted on cropped sites, IM 1-4 was detected at its maximum levels generally within two weeks of application. These IM-1-4 conclusions are uncertain because of the storage stability issue.

Table 6-3. Summary of Terrestrial Field Dissipation Study Results For Acetamiprid

MRID	Soil Texture	Study Site, Crop	Half-life in days	Max. Depth of Leaching	Maximum Concentration Observed in Soil (µg/kg-soil)			
					Acet.	IM 1-4[2]	IM 1-2[2]	IC-0
44988515	sandy loam	WA, apples	3	0-15 cm (a,b,c)[3]	148	149	29	ND[4]
44988515	sand	FL, oranges	6	0-15 cm (a, b)	77	60	ND	ND
44988515	loamy sand	NY, cabbage	13	0-15 cm (a, b)	107	197	ND	ND
44988515	loam	CA, cotton	6	0-15 cm (a, b, c); 15-30 cm (d)	68	202	20	18
44988514	loamy sand	CA, vincarosea	3	0-15 cm (a, b, c); 30-45 cm (d)	46	425	26	45
44988514	sand	FL, tree ferns	14	0-15 cm (a, b, d)	151	147	ND	12
44988514	silt loam	NJ, garden mums	4	0-15 cm (a, b, d)	96	191	ND	23

MRID	Soil Texture	Study Site, Crop	Half-life in days	Max. Depth of Leaching	Maximum Concentration Observed in Soil (µg/kg-soil)			
44988625	sandy loam	Prince Ed. Isl., CAN., Bare ground	10	0-15 cm (a, b, c, d)	331	135.0	17.0	14.5
44988625	loam	Ontario, CAN.	5	0-15 cm (a, b, c, d)	202.5	82.0	87.5	34.5
44988625	clay loam	Manitoba, CAN., bare ground	18	0-15 cm (a, b, c, d)	209.0	41.0	68.0	17.5

[1] Acetamiprid was applied at all sites using four applications at intervals ranging from 6 to 9 days.
[2] IM 1-2 converts to IM 1-4 under storage conditions. IM 1-2 concentrations shown are likely to be lower than those that occurred in the field.
[3] a = parent; b = IM-1-4; c = IM-1-2; d = IC-0.
[4] ND = not detected.

6.4. Degradates/Transformation Products

Transformation products resulting from the environmental degradation of acetamiprid are:

- N-methyl(6-chloro-3-pyridyl)methylamine (IM 1-4)
- (E)-N1-[(6-chloro-3-pyridyl)-methyl]-N2-cyano-N1-methylacetamidine (IM 1-5)
- 6-chloronicotinic acid (IC-0)
- N^2-carbamoyl-N^1-((6-chloro-3-pyridyl)-methyl)-N^1-methylacetamidine (IM 1-2)
- 6-chloro-3-pyridylmethano (IM-0)
- N-((6-chloro-3-pyridyl)methyl)-N-methylacetamide (IM 1-3)
- N-[(6-chloro-3-pyridyl)methyl]acetamide (IM 2-3)
- N^1-[(6-chloro-3-pyridyl)methyl]-N^2-cyanoacetamidine (IM 2-1)
- Carbon dioxide

Structures of these degradates and the maximum percent of applied radioactivity present as the specified degradate is shown in are shown in **Table 6-4** with additional information in **Appendix A**. **Figure 6-1** provides structures and a proposed degradation pathway. In the studies containing soil or sediment, there was a significant amount of unextracted residues in many of the studies. As indicated earlier, this could result in an underestimation of the maximum amount for degradates. The degradates IM 1-4, IM 1-5, IC-0, IM 1-2, and IM 1-3 were present at greater than 10% applied radioactivity and are considered major degradates. All of these degradates except IC-0 contain the pyridylmethylamine in acetamiprid that is similar to other pyridylmethylamine nicotinoid insecticides (depicted in **Figure 6-2**) and observed in nicotine, which acts on the nicotinic acetylcholine receptor (Tomizawa and Casida, 2005). Degradates IM 1-4, IM 1-5, and IM 1-3 were also relatively stable with peaks observed at the final sampling interval or high levels observed in studies over long durations. While IM-1-3 is relatively stable and is considered a major degradate based on the hydrolysis study (pH 9 with 35°C and 45°C), it was only detected at maximums of 3-8% in the metabolism studies. Maximum concentrations of IM 1-4 were often higher than maximum concentrations of parent observed in the terrestrial field

dissipations studies (see **Table 6-3**). Toxicity data on transformation products are discussed in Section **Table 8-4** and **Table 8-7**. Stressors of concern are identified in Section 9.

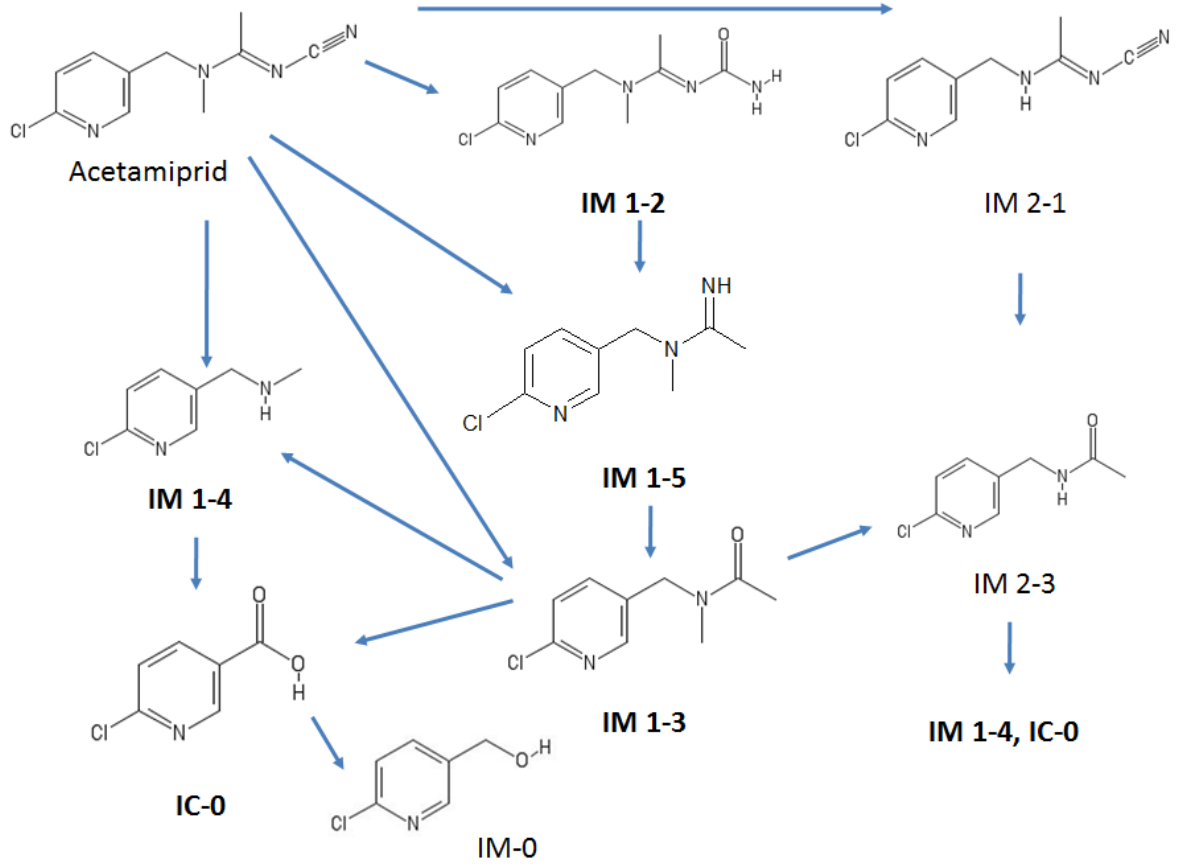
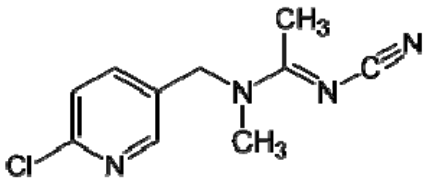
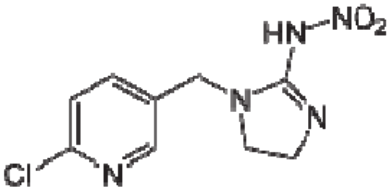


Figure 6-1. Potential Degradation Pathway for Acetamiprid. Bold degradates had greater than 10% applied radioactivity associated with the compound in at least one submitted fate study.

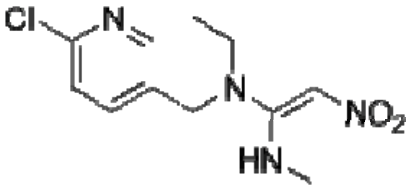
Acetamiprid



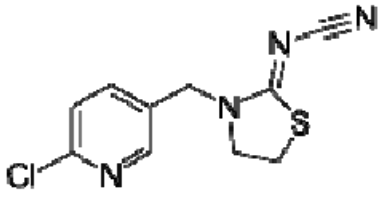
Imidacloprid



Nitenpyram



Thiacloprid



Nicotine

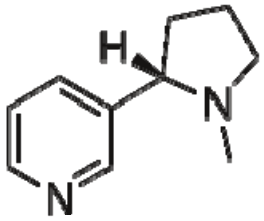


Figure 6-2. Structure of Pyridylmethylamine Nicotinoid Insecticides and Nicotine

The 2009 new use assessment for acetamiprid identified IM 1-4 as a residue of concern for aquatic animals and it was assumed to have similar toxicity to the parent (USEPA, 2009, D364328). The only residue of concern for human health drinking water is the parent compound. **Table 6-6** provides the half-lives estimated for parent with IM 1-4 and parent with IM 1-4 plus unextracted residues. Hydrolysis and aqueous photolysis data for IM 1-4 indicate it is stable to these degradation processes and that IM 1-4 has sorption coefficients similar to those of the parent (**Table 6-2**). Aerobic soil metabolism data show that residues of IM 1-4 were detected at high levels throughout the study for many of the soils with residues in three soils indicating that IM 1-4 was stable to aerobic soil metabolism.[15] The maximum depth that IM 1-4 was detected in terrestrial field dissipation studies was 15 cm. **Appendix A** contains additional environmental fate data submitted on IC-0.

[15] Three studies indicate that IM-1-4 is relatively stable to aerobic soil metabolism in some soils. In the aerobic soil metabolism study discussed in MRID 44651879, percent applied radioactivity associated with IM-1-4 was 73% at 120 days and 60% at 365 days. In the aerobic soil metabolism study discussed in MRID 44651881 on a clay loam soil at 10°C, percent applied radioactivity associated with IM-1-4 was 73% at 30 days and 54% at 178 days. In the same study (MRID 44651881) and soil (clay loam) at 20°C, percent applied radioactivity was 56% at 14 days and 37 at 182 days.

Table 6-4. Summary of Maximum Degradate Amounts in Environmental Fate Studies of Acetamiprid[d]

Compound	Maximum Degradate % of Applied Radioactivity Associated with Compound (Time of Peak) Amount Detected at Final Sampling Interval in Corresponding Study							Maximum Concentration in Terrestrial Field Dissipation (µg/kg soil)
	Hydrolysis	Aqueous Photolysis	Soil Photolysis	Aerobic Soil	Anaerobic Soil	Anaerobic Aquatic	Aerobic Aquatic	
IM 1-4	15 (35 d)a 15 (35 d)a	ND	32 (24 d)a 32 (24 d)a	73 (120 d)c 61 (365 d)c	64 (61 d) 61 (125 d)	27 (270 d)a 27 (270 d)a	64 (60 d)c 34 (300 d)c	425
IM 1-5	NA	ND	NA	22 (13 d)a 13 (182 d)b	NA	NA	NA	NA
IC-0	NA	ND	16 (24 d)a 16 (24 d)a	12 (7 d) ND (182 d)	3 (125 d)a 3 (125 d)a	ND	19 (180 d) ND (300 d)	45
IM 1-2	NA	ND	1 (7 d) ND (24 d)	55 (7 d) ND (182 d)	4 (5 d) ND (125 d)	1 (90 d) ND (365 d)	21 (30 d) <1 (300 d)	88
IM-0	NA	ND	ND	2.21 (7 d) ND (187 d)	2 (1 d) ND (125 d)	NA	NA	NA
IM-1-3	61 (35 d)a 61 (35 d)a	ND	4 (24 d)a 4 (24 d)a	3 (60 d) <1 (365 d)	3 (5 d) 3 (125 d)a	8 (180 d) 6 (365 d)	1 (90 d) ND (300 d)	NA
IM-2-1	NA	NA	3 (17 d) 2 (24 d)	NA	ND	NA	NA	NA
IM-2-3	NA	NA	ND	NA	2 (5 d) ND (125 d)	NA	NA	NA

NA=not analyzed; ND=not determined
a Peak at final sampling interval in some studies
b Peak at final sampling interval in some soils
c High levels observed for > 100 days.
d See **Appendix A** for more information on source of information in this table.

Table 6-5. Summary of environmental fate and transport properties of the acetamiprid degradate IM-1-4

Parameter	Value(s)	Source/ Study Classification	Comments
Hydrolysis (days)	Stable (pH 4, 7, 9 at 50°C)	MRID 44651877 Supplemental	Study duration was five days and at 50°C. Greater than 99% of applied residues were IM-1-4 at the end of the study.
Aqueous Photolysis Half-life (days)	Stable (pH 7, 25°C)	MRID 44988511 Valid	None
Aerobic Soil Metabolism	Slow degradation	See results from studies conducted on parent	High levels observed for > 100 days
Aerobic Aquatic Metabolism	Slow degradation		Peak observed at study termination
Anaerobic Soil Metabolism	Stable		Little degradation over more than 60 days
Anaerobic Aquatic Metabolism	Stable		
Solid-water distribution coefficient (K_d) in L/kg	Average K_d at 20°C 0.38, loamy sand , pH 4.4 6.48, loam sand II, pH 6.4 5.63, silt loam, pH 6.6 21.9, clay, pH 7.5 4.08, sandy loam sediment, pH 5.6 Mean = 7.69 (standard deviation=8.28)	MRID 44651885 Valid	Coefficient of variation is 108%.
Freundlich solid-water distribution coefficient (K_F) in L/kg	K_F (1/n) at 20°C 0.29, loamy sand , pH 4.4 5.35, loam sand II, pH 6.4 4.34, silt loam, pH 6.6 17.0, clay, pH 7.5 2.84, sandy loam sediment, pH 5.6 Mean = 5.97 (standard deviation=6.45)	MRID 44651885 Valid	Sorption was dependent on concentration in some soils. All 1/n values were less than 0.90.

Parameter	Value(s)	Source/ Study Classification	Comments
Organic-carbon normalized distribution coefficient (K_{oc}) in $L/kg_{organic\ carbon}$	Average K_{oc} at 20°C 153, loamy sand , pH 4.4 440, loam sand II, pH 6.4 1278, silt loam, pH 6.6 1842, clay, pH 7.5 163, sandy loam sediment, pH 5.6 Mean = 775 (standard deviation=753)	MRID 44651885 Valid	Coefficient of variation is 97%. The coefficient of variation is less than that for K_d values indicating that K_{oc} values will be better at predicting sorption across soils than K_d values. Moderately mobile to slightly mobile according to FAO classification.

Table 6-6. Summary of half-lives estimated for residues of parent, IM-1-4, and Unextracted residues in metabolism studies

Type of Study (MRID)	Study System	Half-life (days)*		
		Parent Only	Parent + IM-1-4	Parent+IM-1-4+Unextracted Residues
Aerobic Soil (44651881)	Silty Clay Loam, 20°C	0.9	1.1	1.1
	Clay Loam, 20°C	6	104	392
	Sandy Loam, 20°C	2.8	118	299
Aerobic Soil (46255603)	Sandy Loam, 20°C	1.1	2.4	72
	Clay Loam, 20°C	1.2	2.4	67
	Clay Loam, 20°C	1.0	1.7	84
Aerobic Soil (44699101)	Loamy Sand, 20°C	1.4	20	53
Aerobic Soil (44651879)	Loamy Sand, 25°C	3.5	430	895
Aerobic Aquatic (44988513)	Loam Sand, 25°C	25	215	658
Anaerobic Aquatic (44988512)	Loamy Sand, 25°C	325	590	1372

*All values were estimated using nonlinear regression and the single first order equation.

6.5. Mobility/Sorption

Acetamiprid is classified as moderately mobile with organic carbon normalized soil-water distribution coefficients (K_{oc}) ranging from 157 to 298 $L/kg_{organic\ carbon}$ measured in four soils and

one sediment (MRID 44651883)[16]. The mean K_{oc} was 227 L/kg-organic carbon and the coefficient of variation for K_{oc} values (28%) is less than that for K_d values (66%) indicating that K_{oc} values will be better at predicting sorption across soils than K_d values. Additionally, K_ds tend to be higher as the percent organic carbon increases. There was no relationship with K_ds and pH or percent clay. Based on the sorption coefficients and persistence, acetamiprid has the potential to reach ground water, especially in vulnerable sandy soils with low organic-carbon content and/or the presence of shallow ground water. However, the maximum depth at which it was detected in terrestrial field dissipation studies was 15 cm. The mobility of the degradate IM 1-4, which is a residue of concern for aquatic organisms, is similar to the mobility of the parent. K_d values ranged from 0.38 to 21.9 L/kg-soil in four soils and one sediment and K_{oc} values ranged from 153 – 1842 L/kg-organic carbon. The mean K_{oc} for IM 1-4 (775 L/kg-organic carbon) was slightly higher than the mean K_{oc} for the parent (227 L/kg-organic carbon). Therefore, the sorption coefficients for the parent will be used in modeling.

6.6. Monitoring Data

The following databases and sources were searched on May 4, 2012 for monitoring information on acetamiprid:

- The United States Environmental Protection Agency (USEPA) STORET Database (http://www.epa.gov/storet/dbtop.html)
- The United States Geological Survey (USGS) National Water-Quality Assessment (NAWQA) Program Data Warehouse (http://infotrek.er.usgs.gov/traverse/f?p=NAWQA:HOME:1405517206944567)
- The USGS National Stream Quality Accounting Network (NASQAN) program (http://water.usgs.gov/nasqan/)

No monitoring data are available as none of the databases reported looking for acetamiprid.

7. Clean Water Act

Acetamiprid is not identified as a cause of impairment for any water bodies listed as impaired under section 303(d) of the Clean Water Act, based on information provided at http://iaspub.epa.gov/tmdl_waters10/attains_nation_cy.cause_detail_303d?p_cause_group_id=885. In addition, no Total Maximum Daily Loads (TMDL) have been developed for acetamiprid, based on information provided at http://iaspub.epa.gov/tmdl_waters10/attains_nation.tmdl_pollutant_detail?p_pollutant_group_id=885&p_pollutant_group_name=PESTICIDES. More information on impaired water bodies and TMDLs can be found at http://www.epa.gov/owow/tmdl/.

The Agency invites submission of water quality data for this pesticide. To the extent possible, data should conform to the quality standards in Appendix A of the *OPP Standard Operating Procedure: Inclusion of Impaired Water Body and Other Water Quality Data in OPP's*

[16] Classification is based on the FAO classification system (USEPA, 2010a)

Registration Review Risk Assessment and Management Process (see: http://www.epa.gov/oppfead1/cb/ppdc/2006/november06/session1-sop.pdf), in order to ensure they can be used quantitatively or qualitatively in pesticide risk assessments.

8. Receptors

Consistent with the process described in the Overview Document (USEPA, 2004b), the risk assessment for acetamiprid will rely on a surrogate species approach. Toxicological data generated from surrogate test species, which are intended to be representative of broad groups of organisms, are used to extrapolate potential effects on a variety of species (receptors) within these groups. Categories of organisms evaluated include: fish, arthropods (insects, crustaceans), mollusks, birds, mammals, aquatic vascular and nonvascular plants, and terrestrial plants.

Acute and chronic toxicity data from studies submitted by the pesticide registrant, along with studies available in the open literature, will be used to evaluate the potential direct and indirect effects of acetamiprid on aquatic and terrestrial receptors. This includes toxicity of the technical grade active ingredient, degradates, and formulated products (*e.g.* "six-pack" acute toxicity studies). Open literature studies are identified using EPA's publically available ECOTOX database (USEPA, 2009a)[17], which employs a literature search engine for locating chemical toxicity data for aquatic life, terrestrial plants, and wildlife. The evaluation of both data sources may also provide insight into the direct and indirect effects of acetamiprid usage on biotic communities from loss of sensitive species and from changes in community structure or function.

The most sensitive endpoint for each group of organisms is used in risk assessment. Assessment endpoints include direct toxic effects on the survival, reproduction, and growth of terrestrial and aquatic life, as well as indirect effects, such as reduction in prey base and/or modification of habitat. A brief summary of the aquatic and terrestrial toxicity data available for acetamiprid and its degradates is provided in Sections 8.1 and 8.2, respectively. A more complete summary of the available data is presented in **Appendix B**. In addition, a summary of ecological incidents associated with acetamiprid is provided in Section 8.3. Additional information on degradate toxicity is discussed in Section 9.

Toxicity to fish and aquatic invertebrates is categorized using the system shown in **Table 8-1** (USEPA, 2004a). Toxicity to terrestrial fauna (birds and mammals) is categorized using the system shown in **Table 8-2**. Toxicity categories for plants have not been defined.

Table 8-1. Categories of Acute Toxicity for Aquatic Animals

LC_{50} (ppm)	Toxicity Category
< 0.1	Very highly toxic
> 0.1 - 1	Highly toxic
> 1 - 10	Moderately toxic
> 10 - 100	Slightly toxic

[17] http://cfpub.epa.gov/ecotox/

> 100	Practically nontoxic

Table 8-2. Categories of Acute Toxicity for Terrestrial Animals

LD_{50} (mg/kg)	LC_{50} (ppm)	Toxicity Category
<10	<50	Very highly toxic
10-50	50-500	Highly toxic
51-500	501 - 1000	Moderately toxic
501-2000	1001 - 5000	Slightly toxic
>2000	>5000	Practically nontoxic

8.1. Effects to Aquatic Organisms

The most sensitive aquatic toxicity endpoints resulting from acetamiprid (parent) and degradate exposure based on registrant-submitted studies are provided in **Tables 8-3** and **8-4**, respectively. As long as additional information is not submitted or available in the open literature, these endpoints will be used to calculate RQ values for acetamiprid. A single aquatic toxicity study (Beketov and Liess, 2008) was available in ECOTOX as of April 20, 2012; this study will be evaluated for utility in risk assessment during the Registration Review process.

8.1.A. Acetamiprid (Parent)

(a) Fish and Aquatic-Phase Amphibians

Two acute toxicity studies of the effect of acetamiprid on freshwater fish species were submitted. The 96-hr LC_{50} values are greater than 100 and 119 mg ai/L for the rainbow trout (*Oncorhynchus mykiss*; MRID 44651864) and bluegill sunfish (*Lepomis macrochirus*; MRID 44651863), respectively. Acetamiprid is therefore classified as practically non-toxic to freshwater fish on an acute exposure basis. Sublethal effects were noted in both studies. In rainbow trout, darkened body pigmentation, swollen abdomen, and loss of equilibrium were reported at the three highest concentrations (50, 70, 100 mg ai/L). In bluegill sunfish, darkened body pigmentation was observed in all fish at all treatments (11.8, 20.0, 35.4, 65.0, 119.3 mg ai/L). Unless more sensitive data is found in the open literature, the acute toxicity estimate for trout will be used to assess potential acute risk to freshwater fish (and aquatic-phase amphibians for which they serve as surrogates) during risk assessment.

In the only acute estuarine/marine fish study involving acetamiprid, the 96-hr LC_{50} for the sheepshead minnow (*Cyprinodon variegatus*; MRID 44988411) is 100 mg ai/L, and lethargy was observed in all surviving fish at 90 mg ai/L. Acetamiprid is classified as slightly toxic to estuarine/marine fish on an acute exposure basis. Unless more sensitive data is found in the open literature, the acute toxicity estimate for the sheepshead minnow will be used to assess potential acute risk to estuarine/marine fish during risk assessment.

A 35-day early life stage toxicity study (MRID 44651872) of fathead minnows (*Pimephales promelas*) was submitted to evaluate the chronic effects of acetamiprid on freshwater fish. The lowest observed adverse effect concentration (LOAEC) for the study is 38.4 mg ai/L based on both decreased survival and growth (measured by weight). The no-observed-adverse-effect concentration (NOAEC) is 19.2 mg ai/L, and this will be used to estimate potential chronic risk to freshwater fish (and aquatic-phase amphibians for which they serve as surrogates) during risk assessment.

No chronic toxicity data were submitted for estuarine/marine fish. However, given the low acute toxicity to both freshwater and estuarine/marine fish and the low likelihood of adverse chronic effects to freshwater fish identified in previous assessments, the need for chronic toxicity data for estuarine/marine fish is considered low.

(b) Aquatic Invertebrates

The non-biting midge (*Chironomus riparius*; MRID 45916201) is the most sensitive freshwater aquatic invertebrate species in which acetamiprid was tested. The 48-hr LC_{50} for the midge is 0.021 mg ai/L, and acetamiprid is therefore considered very highly toxic to freshwater invertebrates on an acute exposure basis. Acetamiprid is approximately three orders of magnitude more toxic to chironomids than to the freshwater cladoceran *Daphnia magna* (48-hr LC_{50} =50 mg ai/L; MRID 44651866) on an acute exposure basis. Therefore, the chironomid endpoint value will represent freshwater invertebrates during risk assessment.

Acetamiprid is also very highly toxic to mysid shrimp (*Americamysis bahia*; MRID 44651869), an estuarine/marine invertebrate, on an acute exposure basis (48-hr LC_{50} =0.066 mg ai/L). Sublethal effects (*e.g.*, lethargy) were observed among all the surviving mysids exposed to the 0.064 and 0.110 mg ai/L treatment levels and in at least one individual at all concentrations except the lowest (0.013 mg ai/L).

Chronic toxicity data for acetamiprid is available for *D. magna* (MRID 44651871). Survival was reduced in this species by 57%, compared to controls, at the highest test concentration (74 mg ai/L). Significant reductions in length (8%), weight (24%), and mean number of offspring (50%) were observed at 9 mg ai/L, resulting in a NOAEC of 5 mg ai/L based on reduced growth and reproduction. However, since acetamiprid is approximately three orders of magnitude more toxic to chironomids (LC_{50} =0.021 mg ai/L) than to daphnids (LC_{50} =50 mg ai/L) on an acute exposure basis, the available chronic endpoint for *D. magna* may not adequately represent chronic toxicity to more sensitive freshwater invertebrates. Therefore, an acute-to-chronic ratio (ACR) approach is used for this assessment. Since the acute daphnid endpoint is 50 mg ai/L and the chronic NOAEC is 5 mg ai/L, the ACR is for this species is 10. Applying the ACR to the chironomid acute toxicity endpoint results in an estimated chronic toxicity endpoint of 0.0021 mg ai/L. This ACR value will be used to calculate chronic RQ values for freshwater invertebrates unless more sensitive data is identified in the open literature.

A chronic study with acetamiprid (MRID 44651873) was also carried out on mysid shrimp as a representative of estuarine/marine invertebrates. Reduction in male dry body weight was the

most sensitive endpoint, yielding a NOAEC of 0.0025 mg ai/L and a LOAEC of 0.0047 mg ai/L. The percent reduction in male dry weight ranged from 11 to 36% in test levels that significantly differed from the dilution control.

Although acetamiprid is registered for use as an insecticide, the high sensitivity of amphipods (acute; see **Appendix B** for endpoint data) and mysid shrimp (acute and chronic) to the chemical suggests that there is the potential for concern to a variety of aquatic invertebrates, not just insects. Characterization of the taxonomic breadth and magnitude of this potential risk will be addressed during the upcoming risk assessment.

(c) Aquatic Plants

Tier 1 toxicity testing with aquatic plants indicates that acetamiprid is not toxic at the concentrations tested (**Table 8-3**). Exposure to acetamiprid did not significantly affect growth in the single aquatic vascular plant species (*Lemna gibba*, 14-day test) and four nonvascular plants species at limit concentrations tested ranging from 1.0 to 1.3 mg ai/L.

Table 8-3. Most Sensitive Aquatic Toxicity Endpoints for Acetamiprid

Species	Measured Effect	Duration	Endpoint	Toxicity Value mg ai/L	Test Substance % ai	MRID (Study Classification)
Freshwater Fish						
Oncorhynchus mykiss (Rainbow Trout)	Mortality	96 hours	LC_{50}	>100* (Practically non-toxic)	>99%	44651864 (Acceptable)
Pimephales promelas (Fathead Minnow)	Embryo and larval survival, larval growth (wet-weight and length)	35 days	NOAEC LOAEC	19.2 38.4	100%	44651872 (Supplemental)
Freshwater Invertebrates						
Chironomus riparius (Non-biting Midge)	Mortality	48 hours	LC_{50}	0.021 (Very highly toxic)	99.3	45916201 (Supplemental)
	Calculated Value	--	NOAEC	0.0021†	Acute-to-chronic Ratio	--
Estuarine/Marine Fish						
Cyprinodon variegatus (Sheepshead minnow)	Mortality	96 hours	LC_{50}	100 (Slightly toxic)	99.9%	44988411 (Acceptable)
Estuarine/Marine Invertebrates						
Americamysis bahia (Mysid shrimp)	Mortality	96 hours	LC_{50}	0.066 (Very highly toxic)	99.9%	44651869 (Acceptable)
	Reduced body weight in males	28 days	NOAEC LOAEC	0.0025 0.0047	99.9%	44651873 (Acceptable)

Species	Measured Effect	Duration	Endpoint	Toxicity Value mg ai/L	Test Substance % ai	MRID (Study Classification)
Aquatic Vascular Plants						
Lemna gibba (duckweed)	Frond number	14 days	EC_{50}	>1.0*	99.9%	44988415 (Acceptable)
			NOAEC	1.0		
Aquatic Non-Vascular Plants						
Navicula pelliculosa (Freshwater diatom)	Cell density	5 days	EC_{50}	>1.1*	99.9%	44988417 (Acceptable)
			NOAEC	1.1		
Skeletonema costatum (Marine diatom)	Cell density	5 days	EC_{50}	>1.0*	99.9%	44988418 (Acceptable)
			NOAEC	1.0		

* Non-definitive study endpoint; cannot be used to calculate RQs.

† Endpoint is estimated using the ACR of 10 calculated for *D. magna* (acute LC_{50} of 50 mg ai/L divided by chronic NOAEC of 5 mg ai/L = 10); applying ACR to the midge acute 48-hr LC_{50} of 0.021 mg ai/L results in estimate NOAEC of 0.0021 mg ai/L; unless additional data becomes available, this value will be used to estimate risk in upcoming Registration Review Ecological Risk Assessment.

8.1.B. Degradate Effects to Aquatic Organisms

An acute toxicity study of the degradate IM 1-4 on rainbow trout (MRID 44651865) was conducted at concentrations ranging from 4.3 to 69.3 mg ai/L (**Table 8-4**). No mortalities were reported except at the 69.3 mg ai/L test level, but this may have been due to buffering problems in the test solution, as pH levels ranged from 9.0-9.3. An additional concentration was subsequently tested under buffered conditions at 98.1 mg ai/L, and no mortality was observed. Sublethal effects, including darkened body pigmentation and surface swimming, were observed at concentrations above 4.3 mg ai/L. The 96-hr LC_{50} is >98.1 mg ai/L, classifying the degradate IM 1-4 as either slightly toxic or practically nontoxic to freshwater fish on an acute exposure basis. The 96-hr LC_{50} for the parent in rainbow trout (96-hr LC_{50}>100 mg acetamiprid/L) was also non-definitive.

Acute toxicity to aquatic invertebrates was evaluated for several degradates of acetamiprid. Toxicity tests on *D. magna* with degradates IC-0 (MRID 44988409), IM-1-2 (MRID 44651867), and IM 1-4 (MRID 44651868) resulted in 48-hr LC_{50} values of >95.1, >99.8, and 43.9 mg ai/L, respectively, while the *D. magna* 48-hr LC_{50} for the parent compound is 50 mg ai/L (MRID 44651866). This indicates that IM 1-4 has similar toxicity to the parent for freshwater aquatic invertebrates. The 48-hr LC_{50} of IM 1-5 for the non-biting midge (MRID 46255610) is 68 mg ai/L as compared to 0.021 mg ai/L for the parent, acetamiprid.

For estuarine/marine invertebrates, the only acute toxicity test with a degradate was with IM 1-4 on mysid shrimp (MRID 44651870), resulting in a 96-hr LC_{50} of 19 mg ai/L, which is two orders of magnitude less sensitive than the parent compound endpoint value of 0.066 mg ai/L for the same species.

A single chronic toxicity study with acetamiprid degradates was carried out with the IM 1-5 degradation product in *D. magna* (MRID 44651871). Significant reduction in mean number of offspring (30%) was observed at 51 mg ai/L, the LOAEC, resulting in a NOAEC of 26 mg ai/L based on impaired reproduction.

Overall, the data suggest that degradation products of acetamiprid have low toxicity to aquatic invertebrates, although similar toxicity of IM 1-4 to *D. magna* relative to the parent compound indicates that they may be equally toxic to some aquatic animal taxa. Given this uncertainty, a total toxic residues (TTR) approach is recommended for risk assessment for aquatic animals, where combined exposure values for parent and IM 1-4 degradate are compared to study endpoints for the purpose of estimating risk. An additional rationale for considering IM 1-4 in a TTR approach is that many degradates ultimately transform into IM 1-4 and IM 1-4 was observed at high levels in both field and lab studies. Identification and discussion of acetamiprid degradates that will be considered as residues of concern for risk assessment is provided in the portion of the document dealing with stressors or concern (Section 9).

Table 8-4. Aquatic Toxicity Endpoints for Degradates of Acetamiprid

Species (Degradate)	Measured Effect	Duration	Endpoint	Toxicity Value mg ai/L	Degradate % ai	MRID (Study Classification)
Freshwater Fish						
Oncorhynchus mykiss (Rainbow Trout)	Mortality	96 hours	LC_{50}	>98.1* (Slightly to practically non-toxic)	IM 1-4 96.7%	44651865 (Acceptable)
Freshwater Invertebrates						
Daphnia magna (Water flea)	Immobility	48 hours	EC_{50}	>95.1* (Practically non-toxic)	IC-0 99.7%	44988409 (Acceptable)
	Immobility	48 hours	EC_{50}	>99.8* (Practically non-toxic)	IM 1-2 99.6%	44651867 (Acceptable)
	Immobility	48 hours	EC_{50}	43.9 (Slightly toxic)	IM 1-4 98.7%	44651868 (Acceptable)
Chironomus riparius (Non-biting Midge)	Mortality	48 hours	LC_{50}	68 (Slightly toxic)	IM 1-5 98.9%	46255610 (Acceptable)
Daphnia magna (Water flea)	Number of young per female	21 days	NOAEC LOAEC	26 51	IM 1-5 98.9%	46255609 (Supplemental)
Estuarine/Marine Invertebrates						
Americamysis bahia (Mysid shrimp)	Mortality	96 hours	LC_{50}	19 (Slightly toxic)	IM 1-4 99.6%	44651870 (Acceptable)

* Non-definitive study endpoint; cannot be used for risk estimation during risk assessment.

8.2. Effects to Terrestrial Organisms

The most sensitive toxicity endpoint values associated with acetamiprid exposure to terrestrial organisms are shown in **Tables 8-5** and **8-6**. These endpoints will be used to calculate RQs for acetamiprid. The ECOTOX database was searched on April 20, 2012 for terrestrial organism toxicity data, and relevant studies are preliminarily discussed in the sections below.

8.2.A. Acetamiprid (Parent) Toxicity

(a) 4.2.1.1. Birds

Acute oral toxicity studies have been submitted for two avian species: the zebra finch (*Taeniopygia guttata*; MRID 48407701) and the mallard duck (*Anas platyrhynchos*; MRID 44651859). The former study was submitted in 2011 in order to represent toxicity to passerine birds. Acetamiprid is very highly toxic to zebra finches (14-day LD_{50} =5.68 mg ai/kg-bw) and moderately toxic to mallards (LD_{50} of 84.4 mg ai/kg-bw) on an acute oral exposure basis. Zebra finches are the most sensitive species for acute oral toxicity and their endpoint will be used for risk assessment. In both studies, at least one sublethal effect (*e.g.*, ruffled appearance, lethargy, loss of coordination) was observed at all doses.

Subacute dietary toxicity studies were performed on both the mallard duck (MRID 44651861) and the northern bobwhite quail (*Colinus virginianus*; MRID 44651860). The mallard and bob-white quail studies tested three and two concentrations, respectively. The 5-day dietary LC_{50} reported in both of these studies was >5000 mg ai/kg-diet since less than 50% mortality was observed at all concentrations tested. Both studies reported mortalities and sublethal effects at one or more test levels. The lowest concentration where no effects were observed was 200 mg ai/kg-diet in the mallard study based on reduced survival, behavioral effects, and decreased food consumption and 1000 mg ai/kg-bw in the quail study based on reduced survival and decreased food consumption. According to OPPTS 850.2200 guidance, a minimum of five test substance concentrations should be used during definitive avian dietary toxicity tests. Moreover, when mortalities are observed at one or more concentration levels, as is the case in both of these studies, a full definitive study (*i.e.*, with five test concentrations) is recommended according to EFED's non-definitive endpoint guidance policy. Since a definitive endpoint was not established in either of these studies, they will not be used to calculate RQs but may be used to characterize effects to birds based on sub-acute dietary exposure. It should also be noted that an avian dietary toxicity study (MRID48844901) of acetamiprid in the zebra finch has recently been submitted and is currently under review.

Chronic toxicity to birds was initially evaluated in the form of two reproduction studies using mallards (MRID 44988408) and northern bobwhite quail (MRID 44988407). However, there were uncertainties regarding major endpoints in both studies resulting in submission of two new studies in the same two species (MRIDs 46369201, 46555601). In the more recent mallard study, reduced male body weight was the most sensitive endpoint and was observed at all treatment levels (treatment range: 60.2 to 461 mg ai/kg-diet). Number of eggs laid, eggs set, viable embryos, and hatchling body weights were all affected at the 461 mg ai/kg-diet level. In

the more recent bobwhite quail study, the most sensitive endpoint was reduced hatchling body weight, which was observed at all test concentrations except the lowest, resulting in NOAEC and LOAEC values of 89.7 and 184 mg ai/kg-diet, respectively. Number of eggs laid, eggs set, viable embryos, and hatchling body weights were all reduced relative to controls at the 771 mg ai/kg-diet level. Since the mallard duck showed higher sensitivity than the bobwhite quail but yielded a non-definitive endpoint, chronic risk will be assumed for birds (as well as reptiles and terrestrial-phase amphibians) during risk assessment unless an additional study is submitted.

(b) Mammals

Studies evaluating the toxicity of acetamiprid to mammals were reviewed by the OPP Health Effects Division (HED); based on those reviews, acetamiprid is classified as highly toxic to mammals on an acute oral exposure basis. During initial testing in male and female rats (*Rattus norvegicus*) at acetamiprid doses ranging from 100 to 510 mg/kg-bw, more than half of the females died at all test levels except the lowest (*i.e.*, 100 mg/kg-bw) (MRID 44651833). Therefore, additional testing was carried out, with female rats only, at doses ranging from 80 to 160 mg/kg-bw. Based on the additional testing, the 14-day LD_{50} for female rats was 146 mg ai/kg-bw. Clinical signs of toxicity included crouching, tremors, low sensitivity, lateral position, prone position, salivation, and ataxia. All surviving animals returned to normal appearance and behavior by day 2 of the study.

Consistent results were reported in rats for a two-year chronic feeding study (MRIDs 44988429 and 45245304), a two-generation reproduction study (MRID 44988430), and a 13-week subchronic study (MRID 44651843) with acetamiprid. Reduction in growth, as measured by body weight, weight gain, and food consumption, was observed at test concentrations of 400-800 mg ai/kg-diet and greater; whereas test concentrations of 160-280 mg ai/kg-diet caused no significant adverse effects. In addition to growth endpoints, reproductive effects (*e.g.*, pup weight, litter size, viability) were also observed at 280 mg ai/kg-diet in the two-generation reproduction study (MRID 44988430). The NOAEC (160 mg/kg diet) that will be used for risk assessment will be based on the growth endpoints from the 2-year chronic feeding study.

(c) Terrestrial Invertebrates

An acute contact toxicity test with technical acetamiprid was conducted on young adult European honeybees (MRID 44651874). In this study, percent mortality was 40, 66.7, 46.7, 63.3, and 60% for the 6.25, 12.5, 25, 50, and 100 µg ai/bee test groups, respectively. The LD_{50} for the contact study was reported as 8.1 µg/bee. However, there is uncertainty in this LD_{50} value since no clear dose-response relationship was apparent. Since percent mortality was 66.7% at 12.5 µg ai/bee, the median mortality dose is considered to be below this value (*i.e.*, <12.5) suggesting that acetamiprid should be considered moderately toxic to honeybees on an acute contact exposure basis (Atkins *et al.*, 1976). In the ECOTOX database, Iwasa *et al.* (2004) report an acute contact 24-hr LD_{50} of 7.07 µg ai/bee. Although this endpoint was based on nominal concentrations and the exposure period was half that of a typical guideline acute contact study (*i.e.*, 48 hrs), it does generally support the registrant-submitted study finding that acetamiprid is moderately toxic to honeybees on a contact exposure basis. A full open-literature

review of Iwasa *et al.* (2004) will be conducted during the upcoming risk assessment.

An acute oral study was also carried out in honeybees (MRID 44651874), as well as oral and contact studies in bumble bees (*Bombus terrestris*; MRID 45932503), but endpoint values were greater than those from the guideline honeybee acute contact toxicity study.

EPA currently relies on a tiered approach for evaluating the potential effects of pesticides on honeybees. If an acute contact toxicity test (Tier 1) results in a 48-hr LC_{50} value less than 11 µg ai/bee, then honeybee toxicity of residues on foliage studies (Guideline 850.3030)[18] can be required (Tier 2). However, if the 48-hr LC_{50} is less than 11 µg ai/bee and there are data indicating potential effects to honeybee colonies, then field testing of pollinators (Tier 3) may be requested consistent with (Guideline 850.3040)[19].

Since the reported 48-hr LD_{50} of the honeybee acute contact toxicity study was <12.5 µg/bee, a toxicity of residues on foliage study was submitted (MRID 44651875) but was deemed unacceptable due to low recovery of acetamiprid on treated foliage. A second residues on foliage toxicity study was submitted, but has not yet been reviewed by EFED (MRID 45346901). Two semi-field studies conducted to evaluate the possible effect of acetamiprid on honeybee behavior were also submitted (MRIDs 45932504; 45932505), and were classified as supplemental[20]. Both studies used tents to expose honeybees via contact with forage and/or overspray, and applications rates were equivalent to 0.15 and 0.09 lbs ai/A, which is in line with single application rates for many registered and proposed crop uses. Mortality, flight frequency, and foraging behavior were evaluated relative to a control and a known toxic standard. No significant effects on any endpoints were observed in either study from acetamiprid treatments.

Several open literature studies of acetamiprid effects on honeybees are available for acetamiprid. These studies will be thoroughly reviewed as part of the upcoming Registration Review risk assessment.

Table 8-5. Most Sensitive Terrestrial Animal Toxicity Endpoints for Acetamiprid

Species	Measured effect	Endpoint	Test Duration	Toxicity Value (Acute Toxicity Category)	Test Substance % ai	MRID (Study Classification)
Birds						
Taeniopygia guttata (Zebra finch)	Mortality	LD_{50}	14 days	5.68 mg ai/kg-bw (Very highly toxic)	99.9%	48407701 (Acceptable)

[18] USEPA. 1996. Ecological Effects Test Guidelines. OPPTS 850.3030. Honeybee Toxicity of Residues on Foliage. EPA 712–C–96–148. April 1996. http://www.epa.gov/ocspp/pubs/frs/publications/OPPTS_Harmonized/850_Ecological_Effects_Test_Guidelines/Drafts/850-3030.pdf

[19] USEPA. 1996. Ecological Effects Test Guidelines. OPPTS 850.3040. Field Testing for Pollinators. EPA 712–C–96–150. April 1996. http://www.epa.gov/ocspp/pubs/frs/publications/OPPTS_Harmonized/850_Ecological_Effects_Test_Guidelines/Drafts/850-3040.pdf

[20] Note: non-guideline studies cannot be rated "acceptable" since there are no guideline standards

Species	Measured effect	Endpoint	Test Duration	Toxicity Value (Acute Toxicity Category)	Test Substance % ai	MRID (Study Classification)
Bobwhite quail (*Colinus virginianus*)	Mortality	LC_{50}	5 days	>5,000 mg/kg-diet* (Practically non-toxic)	>99%	44651860 (Supplemental)
Anas platyrhynchos (mallard duck)	Growth (body weight; weight gain; food consumption)	NOAEC LOAEC	22 weeks	<60.2 mg ai/kg-diet* 60.2 mg ai/kg-diet	100%	46369201 (Supplemental)
Mammals						
Rattus norvegicus (laboratory rat)	Mortality	LD_{50}	14 days	146 mg/kg-bw; females† (Highly toxic)	99.5%	44651833 (Acceptable: Reviewed by HED)
	Growth (female body weight; female weight gain)	NOAEC LOAEC	24 months	160 mg/kg-diet (7.1 mg/kg-bw/day) 400 mg/kg-diet	Not stated in DER	44988429
Terrestrial Arthropods						
Apis mellifera (Honeybee)	Mortality	LD_{50}	72 hours	Acute contact <12.5 µg ai/bee Acute oral >10.21 µg ai/bee	99%	44651874 (Acceptable)

***** Non-definitive study endpoint; cannot be used for risk estimation.

(d) Terrestrial Plants

The most sensitive terrestrial plant toxicity data are presented in **Table 8-6**. Seedling emergence and vegetative vigor studies (MRID 44988413) were conducted on ten plant species with a test substance that was listed as 71.1% acetamiprid as wettable powder. Seedling emergence results were classified as supplemental because only shoot length, and not plant weight, was measured as an endpoint for growth. Based on shoot length, the most sensitive monocotyledonous (monocot) species was onion (*Allium cepa*; EC_{25}=0.23 lbs ai/A; NOAEC=0.077 lbs ai/A), and the most sensitive dicotyledonous (dicot) species was cucumber (*Cucumis sativus*; EC_{25}=0.16 lbs ai/A; NOAEC=0.077 lbs ai/A). The vegetative vigor study was classified as core (*i.e.*, acceptable) for all plants except for lettuce (*Lactuca sativa*), which was classified as supplemental because adverse (phytotoxic) effects were observed in control plants. The most sensitive monocot and dicot species were ryegrass (*Lolium perenne*; EC_{25}=0.46 lbs ai/A; NOAEC=0.31 lbs ai/A) and lettuce (EC_{25}=0.0087 lbs ai/A; NOAEC=0.0046 lbs ai/A), respectively. Since lettuce was particularly sensitive to acetamiprid but the study was classified as supplemental, an additional vegetative vigor study was carried out on lettuce alone (MRID 45921401). The results of this study support the previous finding that lettuce is relatively sensitive (EC_{25}=0.0056 lbs ai/A; NOAEC=0.0025 lbs ai/A) compared to other plant species tested. Since lettuce serves as a surrogate for broadleaf dicots, potential toxicity to this larger group of plants is possible. Two nonguideline studies were also carried out to more closely examine the effects of acetamiprid on lettuce. Both studies (MRIDs 46229601 and 46229602) reported that the variety of lettuce (*i.e.*, buttercrunch) used in the first two studies, accounted for

the greater sensitivity of lettuce relative to other species tested, and that other varieties of lettuce exhibited reduced sensitivities.

Table 8-6. Most Sensitive Terrestrial Plant Toxicity Endpoints for Acetamiprid.

Species (Plant Group)	Test Substance	Study Type	EC_{25} (lbs ai/A)	NOAEC (lbs ai/A)	Endpoints Affected	MRID	Study Classification
Onion (monocot)	Wettable powder formulation (71.1% ai)	Seedling emergence	0.23	0.077	Shoot length	44988413	Supplemental
Cucumber (dicot)			0.16	0.077			
Perennial ryegrass (monocot)		Vegetative vigor	0.46	0.31	Plant weight		Acceptable
Lettuce (dicot)	Wettable powder formulation (70.04 % ai)		0.0056	0.0025	Shoot length	45921401	Supplemental

8.2.B. Degradate Toxicity to Terrestrial Organisms

The only available acute or subacute avian study on an acetamiprid degradate is a subacute dietary toxicity study of the compound IM 1-4 with the mallard duck (MRID 44651862) (**Table 8-7**). The 5-day dietary LC_{50} was >5000 mg ai/kg-diet, indicating that similar to the parent compound, IM 1-4 is practically non-toxic to mallards on a subacute dietary exposure basis. No mortalities were observed at any concentration in this study.

Acute oral toxicity tests with mammals were conducted on several metabolites and degradation products of acetamiprid (MRIDs 44988420, 44988421, 44988422, 44651834, 44651835). Results of these tests show that these compounds are considerably less toxic than the parent compound, and are classified as slightly toxic or practically nontoxic to mammals on an acute oral exposure basis.

Table 8-7. Available Terrestrial Animal Toxicity Endpoints for Degradates.

Species	Measured effect	Endpoint	Toxicity Value (Acute Toxicity Category)	Test Substance % ai	MRID (Study Classification)
Birds					
Anas platyrhynchos (Mallard duck)	Mortality	5-day LC_{50}	>5000 mg ai/kg-diet* (Practically non-toxic)	IM 1-4	44651862 (Acceptable)
Mammals					
Laboratory Rat	Mortality	LD_{50}	1792 mg ai/kg-bw (Practically nontoxic)	IM-0	44988421 (Acceptable)

Species	Measured effect	Endpoint	Toxicity Value (Acute Toxicity Category)	Test Substance % ai	MRID (Study Classification)
	Mortality	LD_{50}	>5000 mg ai/kg-bw (Practically nontoxic)	IC-0	44988420 (Acceptable)
	Mortality	LD_{50}	2176 mg ai/kg-bw (Practically nontoxic)	IM 2-2 99.9%	44988422 (Acceptable)
	Mortality	LD_{50}	>5000 mg ai/kg-bw (Practically nontoxic)	IM 1-2 99.6%	44651835 (Acceptable)
	Mortality	LD_{50}	1088 mg ai/kg-bw (Slightly toxic)	IM 1-4 99.6%	44651834 (Acceptable)

***** Non-definitive study endpoint; cannot be used for risk estimation.
† Endpoint value will be used for risk estimation

8.3. Incident Database Review

Since the time of the last risk assessment of acetamiprid in 2011, four incidents have been entered into U.S. EPA's Ecological Incident Information System (EIIS), which was last checked on August 28, 2012. One aquatic incident (I022234-001) took place in 2010 that involved a fire in a chemical warehouse containing Assail 70 WP insecticide (TGAI: acetamiprid) as well as an unreported list of other pesticides and fertilizers; water used to extinguish the fire resulted in runoff into a river that was ultimately linked to a fish kill of 700 to 1000 fish of unknown species. Since it is not possible to link any one chemical to this incident, the role of acetamiprid has been designated as "possible." Three incidents have been reported for acetamiprid related to honeybees. The first incident (I023702-003) spanned the years 2004-2006 and attributed hive population losses of 75-80% to Assail (acetamiprid) or Admire (imidacloprid). However, this information was published in the form of a newsletter and insufficient information was provided to determine the likelihood that acetamiprid was responsible. Another incident (I024270-001), which took place in May, 2012, reported dead bees in 48 colonies while pollination services were being provided to an orchard containing apple, apricot, and plum trees. Apparently, Assail was not applied until bees were removed from the area. It is unknown which other pesticides were applied during the bee kill incident. Based on this information, the role of acetamiprid in this incident is considered "unlikely." The final honeybee incident (I023979-002) took place on August 25, 2011 and was submitted in the form of an online news article. The incident occurred when a cotton field near the area where bees were being kept was sprayed with Assail 70WP at 8:30 am. All of the honeybees were reported to have died. This incident occurred 10 days after a similar bee kill incident attributed to Lorsban (chlorpyrifos); a 60-80 percent loss of the beekeeper's honeybees were reported to have died across the two incidents. Given that a spraying of Assail 70 WP was specifically associated with the bee kill, this incident is classified as "highly probable."

A total of 60 aggregated incidents have been reported in the Office of Pesticide Programs

Incident Data System (IDS) as of September 5, 2012. Forty-one (68%) of these incidents involved damage to plants, two (3%) incidents were reported for wildlife, and 18 (30%) were reported for domestic animals. Incident reports for non-target organisms typically provide information only on mortality events and plant damage. Sublethal effects in organisms such as abnormal behavior, reduced growth, or impaired reproduction are rarely reported, except for phytotoxic effects in terrestrial plants. EPA's changes in the registrant reporting requirements for incidents in 1998 may have further reduced the likelihood of incident reports. Registrants are now only required to submit detailed information on "major" fish, wildlife, and plant incidents. Minor fish, wildlife, and plant incidents, as well as all other non-target incidents, are generally reported in aggregate and are not included in EIIS. During the risk assessment associated with Registration Review of acetamiprid, these databases will be checked again and any additional incidents will be evaluated to determine if they represent current use patterns of acetamiprid.

The Avian Incident Monitoring System (AIMS; American Bird Conservancy 2009) was also queried on August 28, 2012, and did not list any bird incidents associated with acetamiprid.

9. Identification of Stressors of Concern

All major degradates of acetamiprid identified in fate studies have a similar pyridylmethylamine backbone as the parent and cannot be eliminated from scrutiny based on structural properties alone. Additionally, IM 1-2, IM-1-3, IM 1-4, IM 1-5, and IC-0 are all considered major degradates as they were observed with greater than 10% applied radioactivity associated with the degradate in some studies. Degradates IM-1-3, IM 1-4, and IM 1-5 were also relatively stable with peaks observed at the final sampling interval or high levels observed in studies over many days. While IM 1-3 is relatively stable, it was only a major degradate in the hydrolysis study (pH 9 at 35^{o}C and 45^{o}C and biotic metabolism is expected to be its predominant degradation pathway. Fate data suggest that exposure to these degradates (especially IM 1-4) could be significant compared to exposure to the parent.

Empirical toxicity data were used to determine whether degradates should be considered a residue of concern. Based on empirical toxicity data (**Table 9-1**), degradates IM 1-2, IM 1-5, IC-0, and IM-0 only have one or two established endpoints that can be compared with parent data from the same species. In these cases, these degradates appear to be less toxic than the parent. It should be noted that of the four degradates listed above, only IM 1-5 has data for any taxon that is considered to be highly sensitive to the parent (*i.e.*, chironomids, mysid shrimp). In this case, IM 1-5 is several orders of magnitude less sensitive to the non-biting midge than the parent compound. None of the above listed degradates have available data for mysid shrimp, which is the most sensitive estuarine/marine organism to acetamiprid. There is somewhat more data for IM 1-4 compared to the other degradates. IM 1-4 is similarly toxic to daphnids as the parent, but is considerably less toxic to mysid shrimp. In fish, it is not possible to make an adequate comparison since both acetamiprid and IM 1-4 endpoints are non-definitive. In insects, acute toxicity data indicate that the presence of an electron-withdrawing moiety (either a nitro or cyano group) is important for insecticidal activity, and the nitro group has been shown to result in higher toxicity to honey bees (Iwasa *et al.*, 2004). None of the degradates have the cyano or

nitro group. The assumption will be made in the assessment that IM 1-4 is a residue of concern for all aquatic animals as very limited data are available to evaluate sensitivity across species for this degradate; the impact of including IM-1-4 and unextracted residues on quantitation of risk values will be explored further during the risk assessment.

Table 9-1. **Comparison of Available Empirical Toxicity Data for Acetamiprid and Degradates**

Compound	Empirical (Measured) Toxicity Endpoints						
	Rainbow Trout 96-hr LC_{50}	Daphnid 48-hr LC_{50}	Mysid Shrimp 96-hr EC_{50}	Non-biting Midge 96-hr LC_{50}	Daphnid Chronic NOAEC	Mallard Subacute Dietary LC_{50}	Rat Acute Oral LD_{50}
Units*	**mg/L**	**mg/L**	**mg/L**	**mg/L**	**mg/L**	**mg/kg-diet**	**mg/kg-bw**
Acetamiprid	>100	50	0.066	0.021	5.0	>5000	146
IM-1-2	--	>99.8	--	--	--	--	2176
IM-1-4	>98.1	43.9	19	--	--	>5000	1088
IM-1-5	--	--	--	68	25	--	--
IC-0	--	>95.1	--	--	--	--	>5000
IM-0	--	--	--	--	--	--	1792

* All units are expressed in terms of the parent or degradate (*e.g.*, mg acetamiprid/L water or mg degradate/L water)

In an attempt to supplement available empirical toxicity data for acetamiprid transformation products, estimated toxicity data for degradates were generated using quantitative structure-activity relationships (QSAR) derived in the program ECOSAR[21] (version 1.00). ECOSAR is only used to prioritize the need for additional data on degradates, not to derive endpoint values for use in estimating risk. ECOSAR estimates were compared to measured toxicity information for parent and degradates (**Table 9-2;** an example ECOSAR output is provided in **Appendix C**). QSAR estimates specific to the parent compound class (*i.e.*, halopyridines) were not accurate when compared to measured data. Moreover, ECOSAR estimates for degradates were also not accurate compared to the empirical degradate dataset. Therefore, ECOSAR estimates appear to be of limited use in predicting degradate toxicity for these degradates. ECOSAR did, however, predict increased chronic toxicity of IM-1-4 in daphnids (0.025 mg IM 1-4/L) compared to that of the parent (0.097 mg acetamiprid /L) (**Table 9-2**) when using the aliphatic amine chemical class as the basis for analysis.

Based on the available information, none of the identified degradates appear to be more toxic than the parent. There is some evidence that acetamiprid and IM 1-4 may be similarly toxic to daphnids; conversely, mysid shrimp are approximately two orders of magnitude more sensitive to acetamiprid than to IM-1-4. Based on toxicity results for these two species, the extent of IM 1-4 toxicity to aquatic animals besides mysid shrimp is uncertain. Therefore, unless additional data on toxicity of IM 1-4 to other aquatic animals become available prior to risk assessment, total residues of parent plus IM 1-4 will be compared to the most sensitive acute and chronic aquatic animal endpoints for the parent or IM 1-4, whichever is more sensitive. In addition, unextracted residues will also be included in the TTR exposure calculations since it is uncertain how much of these unidentified residues are parent or IM 1-4. No specific additional studies to address

[21] http://www.epa.gov/oppt/newchems/tools/21ecosar.htm

degradate toxicity are recommended at this time.

Table 9-2. ECOSAR Quantitative Structure-Activity Relationship (QSAR) Toxicity Predictions for Acetamiprid and Degradates

Compound (compounds class used by ECOSAR)	Estimated Toxicity Endpoint (mg/L)				
	96-hr FW Fish LC_{50}	48-hr Daphnid LC_{50}	96-hr EC_{50} Green Algae	Fish Chronic Value	Daphnid Chronic Value
ECOSAR TOXICITY PREDICTIONS					
Acetamiprid (Parent)					
Empirical (*Measured*)	>100	50	>1.3	19.2	5.0
Halopyridines	0.21	0.73	--	0.30	0.97
Neutral SAR	59	36	19	5.5	3.7
IM 1-2					
Empirical (*Measured*)	--	>99.8	--	--	--
Amides	771	236	1.6	4.6	--
Halopyridines	0.225	1.4	--	8.9	--
Neutral SAR	5774	2692	563	570	182
IM 1-3					
Amides	284	101	1.0	1.7	--
Halopyridines	0.19	1.0	--	3.9	--
Neutral SAR	2008	988	248	196	72
IM 1-4					
Empirical (*Measured*)	>98.1	43.9	--	--	--
Aliphatic Amines	182	14	3.8	2.8	0.025
Halopyridines	0.15	0.80	--	3.3	--
Neutral SAR	1724	843	208	169	61
IM 1-5					
Empirical (*Measured*)	--	--	--	--	25
Halopyridines	0.184	1.369	--	27.067	0.752
Neutral Organic	28011	11695	1682	2821	673
IC-0					
Empirical (*Measured*)	--	>95.1	--	--	--
Halopyridines-acid	1.5	6.9	--	12	1.1
Neutral SAR	447	238	78	43	20
IM-0					
Halopyridines	0.13	0.75	--	--	--
Benzyl Alcohols	360	194	--	--	--
Neutral SAR	1934	934	221	190	67

Method of Estimating Exposure and Evaluating Risk for Degradates

To estimate exposure to compounds assumed to have a similar toxicity to the parent (*e.g.,* IM 1-4 for aquatic organisms), a TTR approach will be used by summing the residues observed in fate studies and then estimating degradation rates based on the total summed residues. The TTR

degradation rates will then be used to estimate exposure in place of degradation rates for the parent alone. As stated previously, the residues used to estimate degradation rates to estimate exposure for aquatic organisms will be parent, IM-1-4, and unextracted residues. The modeled TTR amounts will then be compared to toxicity endpoints for the parent or IM-1-4, whichever is more sensitive for each taxon. For human health drinking water, residues of concern are assumed to be the parent and unextracted residues and these residues will be combined to calculate degradation rates to arrive at a final estimated drinking water concentration (EDWC).

For terrestrial organisms, only the parent is considered a residue of concern as previously identified for human health. Unextracted residues are still considered a residue of concern for terrestrial organisms since these residues could consist of the parent compound. However, the T-REX program, which is used to model exposure of terrestrial organisms to acetamiprid, does not use fate data for modeling, except in the case of foliar dissipation data (which is not available for acetamiprid). Therefore, even though a TTR approach (parent plus unextracted residues) is relevant for terrestrial vertebrates, it does not influence exposure estimates. For terrestrial invertebrates, a standard procedure is not available to estimate exposure at this time, and may be addressed further at the time of the risk assessment. For terrestrial plants, the program TERRPLANT, which estimates exposure through spray drift and runoff, is also not influenced by fate parameters. SCIGROW and PRZM/EXAMS may be used to estimate exposure to residues in irrigation water and parent and unextracted residues will be included in the degradation rates used to estimate exposure.

Table 9-3 summarizes the different approaches for assessing risk to degradates for each taxon.

Table 9-3. Summary of Residues of Concern and Methods of Estimating Exposure for Different Classes of Organisms

Taxa	Residues of Concern[1]	Toxicity Assumption/ Exposure Assumption	Method of Estimating Exposure
Aquatic Animals Aquatic Plants	Acetamiprid, IM 1-4, unextracted residues	Similar Toxicity TTR	PRZM/EXAMs
Terrestrial Vertebrates[2]	Parent and Unextracted Residues	Similar Toxicity TTR	T-REX , unextracted residues will not influence results
Human Drinking Water	Parent and Unextracted Residues	Similar Toxicity TTR	PRZM/EXAMs, unextracted residues will influence results
Terrestrial Invertebrates	Parent and Unextracted Residues	Similar Toxicity TTR	Exposure not currently estimated
Terrestrial Plants	Parent and unextracted residues	Similar Toxicity TTR	TERRPLANT, unextracted residues will not influence results SCIGROW and PRZM/EXAMs for irrigation water, unextracted residues will influence results

Abbreviation: TTR= Total toxic residue approach

[1] Unextracted residues are only relevant residues of concern for terrestrial organisms when exposure is estimated for drinking water or for residues in irrigation water.

[2] Residues included in the TTR approach for these taxa are based on HED analysis of residues of concern for

humans and analysis of available toxicity data on degradates for birds.

Mixtures

Evaluation of pesticide environmental mixtures is beyond the scope of this assessment because of the myriad factors that cannot be quantified based on the available data. Those factors include identification of other possible co-contaminants and their concentrations, differences in the pattern and duration of exposure among contaminants, and the differential effects of other physical/chemical characteristics of the receiving waters (*e.g.* organic matter present in sediment and suspended water). Evaluation of factors that could influence additivity/synergism is beyond the scope of this assessment and the capabilities of the available data to allow for an evaluation. However, it is acknowledged that not considering mixtures could over- or under-estimate risks depending on the type of interaction and factors discussed above. The assessment will, however, analyze the toxicity of formulated products (including formulations involving more than one active ingredient) and will determine whether formulated products are more toxic than the technical grade active ingredient data used for assessing both direct and indirect risks. There are four registered Section 3 products that contain more than one active ingredient. Three contain acetamiprid and bifenthrin and one contains acetamiprid (0.26%) and triticonazole (0.78%). Available data on rat oral LD_{50}s for these formulations do not indicate that the formulations are more toxic to mammals than the active ingredient alone. Therefore, it is assumed that formulation toxicity is similar to the parent toxicity for terrestrial organisms. For aquatic organisms, exposure to entire formulations may occur with spray drift into a water body or when a product is applied directly to water. Products applied to cranberries may be directly applied to water. The only other product that is applied in an agricultural setting that could result in spray drift is for the product containing acetamiprid (13%) and bifenthrin (10%) (EPA Reg. No. 8033-116) that is used on soybean. Additional data on the aquatic toxicity of the product used on soybeans and representative typical end-use products used on cranberries are needed.

10. Ecosystems Potentially At Risk

The ecosystems at risk are often extensive in scope, and as a result it may not be possible to identify specific ecosystems during the development of a baseline risk assessment. However, in general terms, terrestrial ecosystems potentially at risk could include the treated field and areas immediately adjacent to the treated field that may receive drift or runoff. Areas adjacent to the treated field could include cultivated fields, fencerows and hedgerows, meadows, fallow fields or grasslands, woodlands, riparian habitats and other uncultivated areas.

Aquatic ecosystems potentially at risk include water bodies adjacent to, or downstream from, the treated field and might include impounded bodies such as ponds, lakes and reservoirs, or flowing waterways such as streams or rivers. For uses in coastal areas, aquatic habitat also includes marine ecosystems, including estuaries.

11. Assessment Endpoints

Assessment endpoints are defined as "explicit expressions of the actual environmental value that

is to be protected." Selection of the assessment endpoints is based on valued entities (*e.g.*, fish, birds), the ecosystems potentially at risk (*e.g.*, water bodies, riparian vegetation, and upland habitats), the migration pathways of acetamiprid (*e.g.*, runoff, drift, *etc.*), and the routes by which ecological receptors are exposed to acetamiprid (*e.g.*, direct contact, *etc.*). Assessment endpoints for acetamiprid include direct adverse effects on the survival, reproduction, and growth of the receptors, as well as indirect effects, such as reduction of the prey base or modification of habitat. Each assessment endpoint requires one or more "measures of ecological effect," defined as changes in the attributes of an assessment endpoint or changes in a surrogate entity or attribute in response to exposure to a pesticide. Specific measures of ecological effect are generally evaluated based on acute and chronic toxicity information from registrant-submitted guideline tests that are performed on a limited number of organisms. Additional ecological effects data from the open literature will also be considered.

12. Conceptual Model

For a pesticide to pose an ecological risk, it must reach ecological receptors in biologically significant concentrations. An exposure pathway is the means by which a pesticide moves in the environment from a source to an ecological receptor. For an ecological pathway to be complete, it must have a source, a release mechanism, an environmental transport medium, a point of exposure for ecological receptors, and a feasible route of exposure.

The conceptual model for acetamiprid provides a written description and visual representation of the predicted relationships between acetamiprid and degradates, potential routes of exposure, and the predicted effects for the assessment endpoint. A conceptual model consists of two major components: risk hypothesis and a conceptual diagram (USEPA, 1998).

12.1. Risk Hypothesis

A risk hypothesis describes the predicted relationship among the stressor, exposure, and assessment endpoint response along with the rationale for their selection (USEPA, 2004). For assessment of acetamiprid, the risk is stressor-initiated, where the stressor is acetamiprid and a major degradate IM-1-4 which was identified in the previous risk assessment as having a similar toxicity to that of the parent (USEPA, 2009, D364328). The risk hypothesis for this risk assessment is provided below:

Given the uses of acetamiprid and its environmental fate properties, there is a likelihood of exposure to non-target terrestrial and/or aquatic organisms. When used in accordance with the label, acetamiprid results in potential adverse effects upon the survival, growth, and reproduction of non-target terrestrial and aquatic organisms. Based on previous risk assessments there are potential direct risks to birds, mammals, freshwater invertebrates, estuarine/marine invertebrates, and terrestrial dicotyledonous plants.

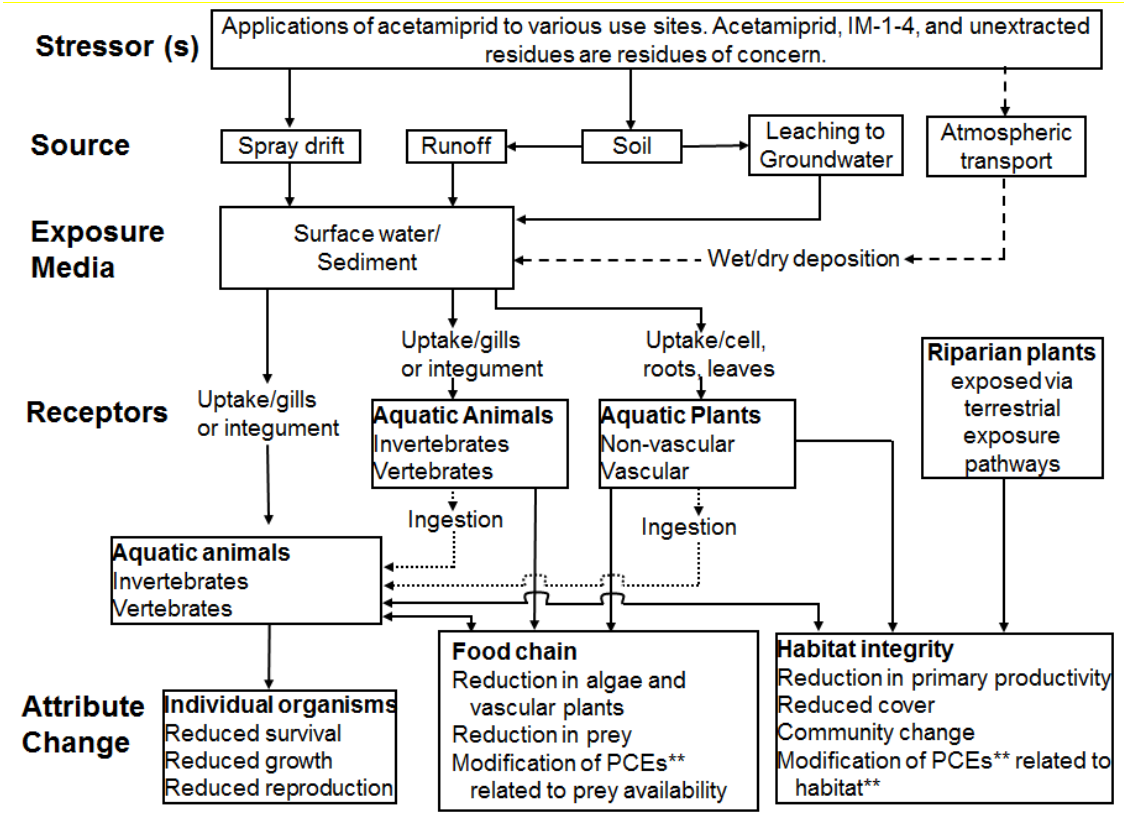
12.2. Conceptual Diagram

The conceptual model depicts the potential pathways for ecological risk associated with acetamiprid use on a variety of use sites. The conceptual model provides an overview of the expected exposure routes for terrestrial and aquatic organisms. In assessments, determinations are made on whether direct and indirect effects are likely to occur and on whether habitat modification may occur. The potential for habitat modification is determined based on primary constituent elements (PCEs) (as defined in 50 CFR 414.12(b)) for listed species. Although the conceptual models for direct/indirect effects and modification of designated critical habitat (PCE)s are shown on the same diagrams, the potential for direct/indirect effects and modification of PCEs will be evaluated separately in the assessment.

The potential exposure pathways and effects of acetamiprid on aquatic environments are depicted in **Figure 12-1** and for terrestrial environments in **Figure 12-2**. **Figure 12-3** depicts exposure from drinking water and inhalation to terrestrial vertebrates and invertebrates. Stressors of concern for aquatic animals and plants include parent acetamiprid, IM-1-4, and unextracted residues. Stressors of concern for terrestrial animals and terrestrial plants include acetamiprid alone. Unextracted residues are also included in the exposure assessment to terrestrial organisms when applicable (*e.g.*, when estimating exposure to residues in irrigation water for terrestrial plants). Solid arrows depict the most likely routes of exposure and effects; dashed lines depict potential routes of exposure that are not considered likely for acetamiprid. Applications to individual trees can result in absorption and translocation of acetamiprid from the site of application throughout the tree. Birds, mammals, and terrestrial invertebrates may be exposed through ingestion of leaves, seeds, pollen, or other edible portions of the tree. These exposure pathways are depicted in the conceptual model in **Figure 12-4**, along with the receptors of concern and the potential attribute changes in the receptors due to exposures of acetamiprid.

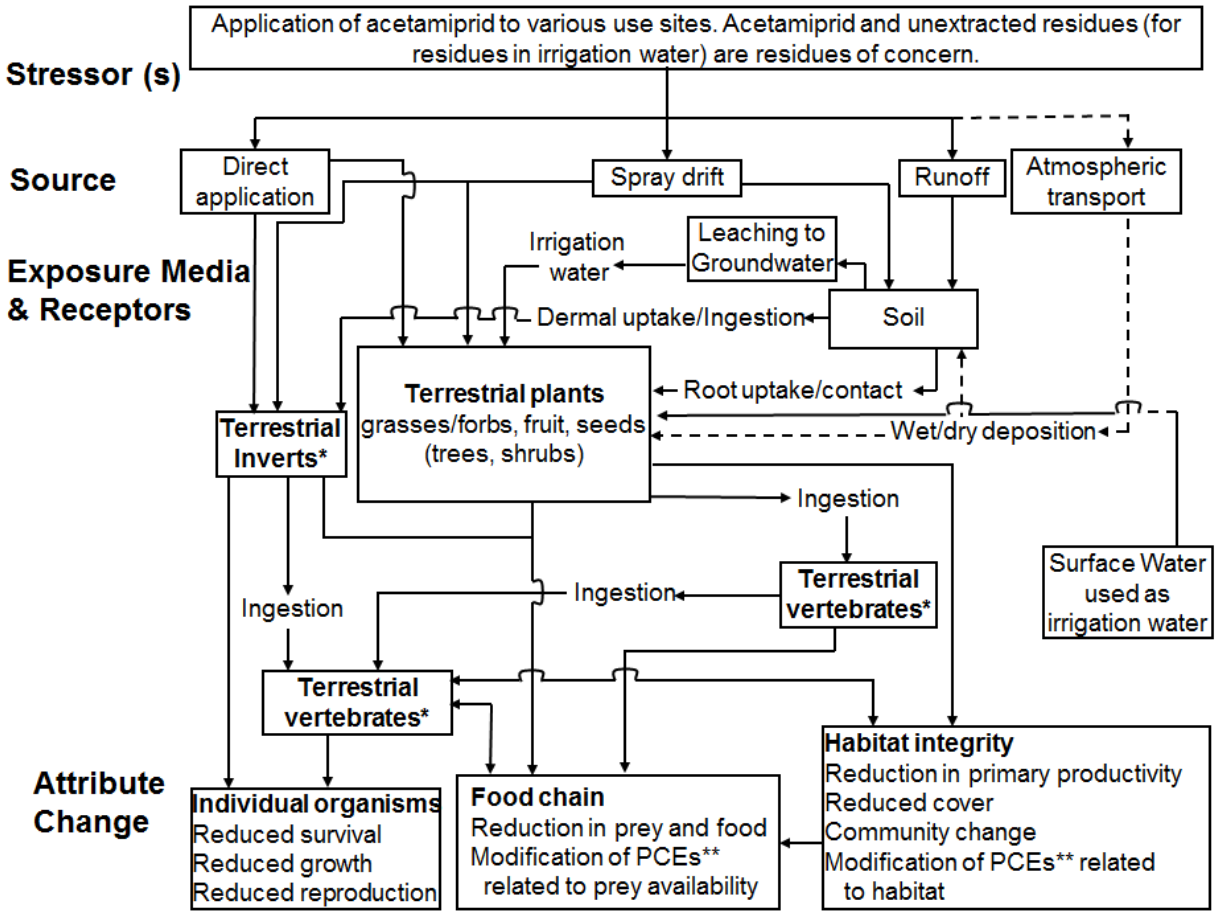
Acetamiprid will enter the environment via direct application to terrestrial environments. It may move off site via spray drift, runoff, and leaching. Acetamiprid is considered non-volatile from dry non-adsorbing surfaces, water, and soil. Additionally, the Screening Tool for Inhalation Risk (STIR) version 1.0 (November 23, 2010) indicates that exposure via inhalation is not likely to be a risk concern for birds and mammals (**Appendix E**). These results combined with the estimated atmospheric half-life of less than two days indicate that long-range transport in the vapor phase is not an exposure pathway of concern. Additionally, the K_{OA}, K_{OW}, and BCF suggest that acetamiprid is not likely to bioconcentrate or bioaccumulate in aquatic or terrestrial organisms. Organic-carbon normalized sorption coefficient (K_{OC}) values range from 157 to 300 L/kg-$_{OC}$ indicating that acetamiprid is classified as moderately mobile under the FAO mobility classification system. The Screening Imbibition Program (SIP) version 1.0, August 19, 2010 identifies that acetamiprid has the potential to be present in drinking water at high enough concentrations to result in a risk concern (**Appendix E**). This is a highly conservative evaluation as SIP assumes that concentrations in drinking water could be at the level of solubility. Acetamiprid may be applied as a flowable, as a gel, or in bait stations. Spray drift is only expected to result in significant exposure with broadcast applications (both aerial and ground boom spray) of liquids. Spray drift is assumed to be negligible for applications of liquids with a

hand held sprayer. When acetamiprid is placed into a bait station, runoff into the aquatic environment will likely be negligible; however, consumption of bait by non-target insects and terrestrial vertebrates may still occur. Aquatic exposure to residues injected into trees will be assumed to be minimal/negligible based on a communication with the technical registrant that acetamiprid is only injected into high value trees in residential areas. Finally, when acetamiprid is applied underground as for some of the termiticide uses, leaching to ground water may occur while spray drift and runoff are not likely to occur.



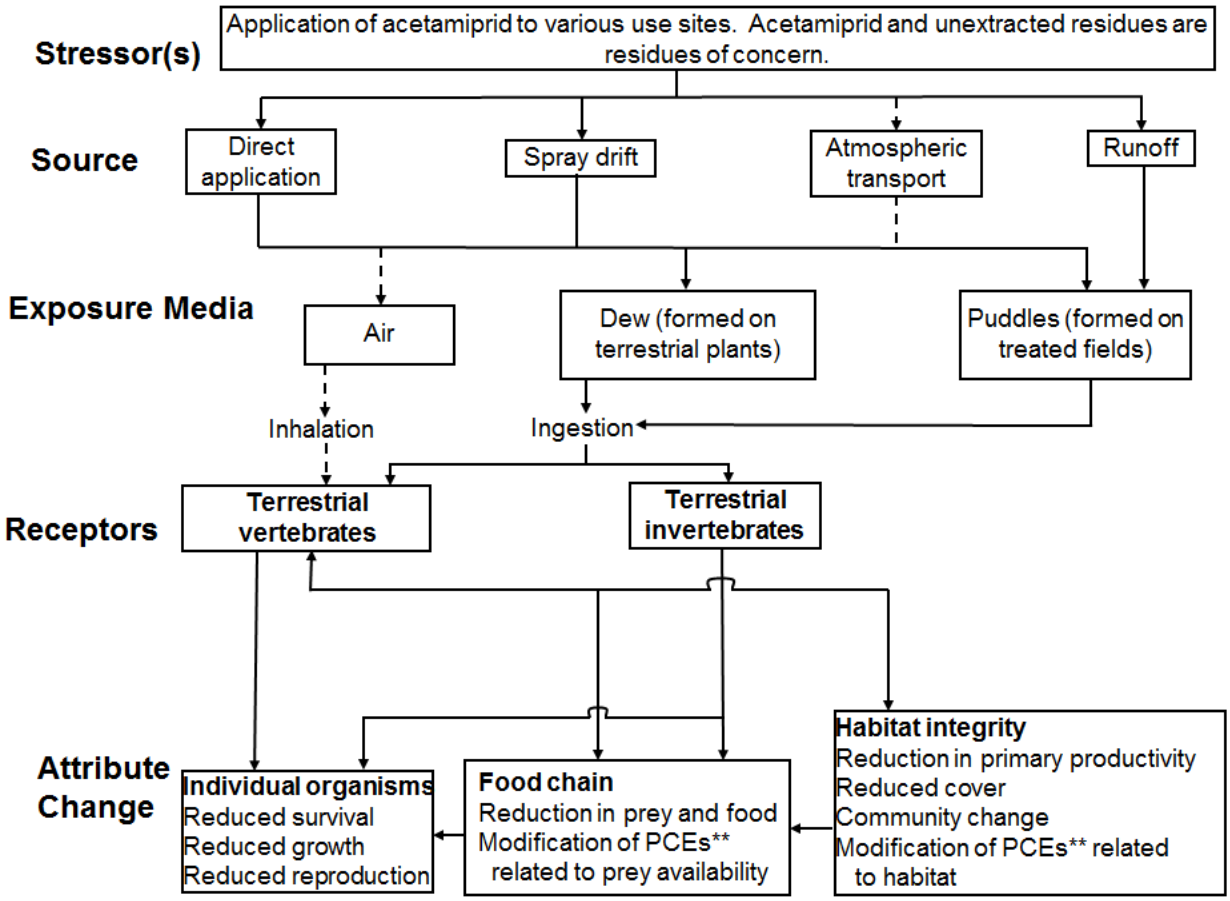
*Spray drift is not expected to be a significant pathway of exposure for applications of granular materials, seed treatments, and for applications of liquids with a hand held sprayer.
**PCE stands for primary constituent elements and are used to determine whether habitat modification may occur.

Figure 12-1. Conceptual model depicting stressors, exposure pathways, and potential effects to aquatic organisms and their habitat from the use of acetamiprid



*Spray drift is not expected to be a significant pathway of exposure for applications of granular materials, seed treatments, or applications of liquids with a handheld sprayer. See **Figure 12-3** for drinking water and inhalation exposure pathways for terrestrial vertebrates and ingestion of residues in dew by terrestrial invertebrates.
**PCE stands for primary constituent elements and are used to determine whether habitat modification may occur.

Figure 12-2. Conceptual model depicting stressors, generic exposure pathways, and potential effects to terrestrial organisms (terrestrial plants, terrestrial invertebrates, and dietary routes of exposure for terrestrial vertebrates) and their habitat from the use of acetamiprid



*Spray drift is not expected to be a significant pathway of exposure for applications of granular materials, seed treatments, or applications of liquids with hand held sprayers.

**PCE stands for primary constituent elements and are used to determine whether habitat modification may occur.

Figure 12-3. Conceptual model depicting stressors, drinking water and inhalation exposure pathways, and potential effects to terrestrial animals from the use of acetamiprid

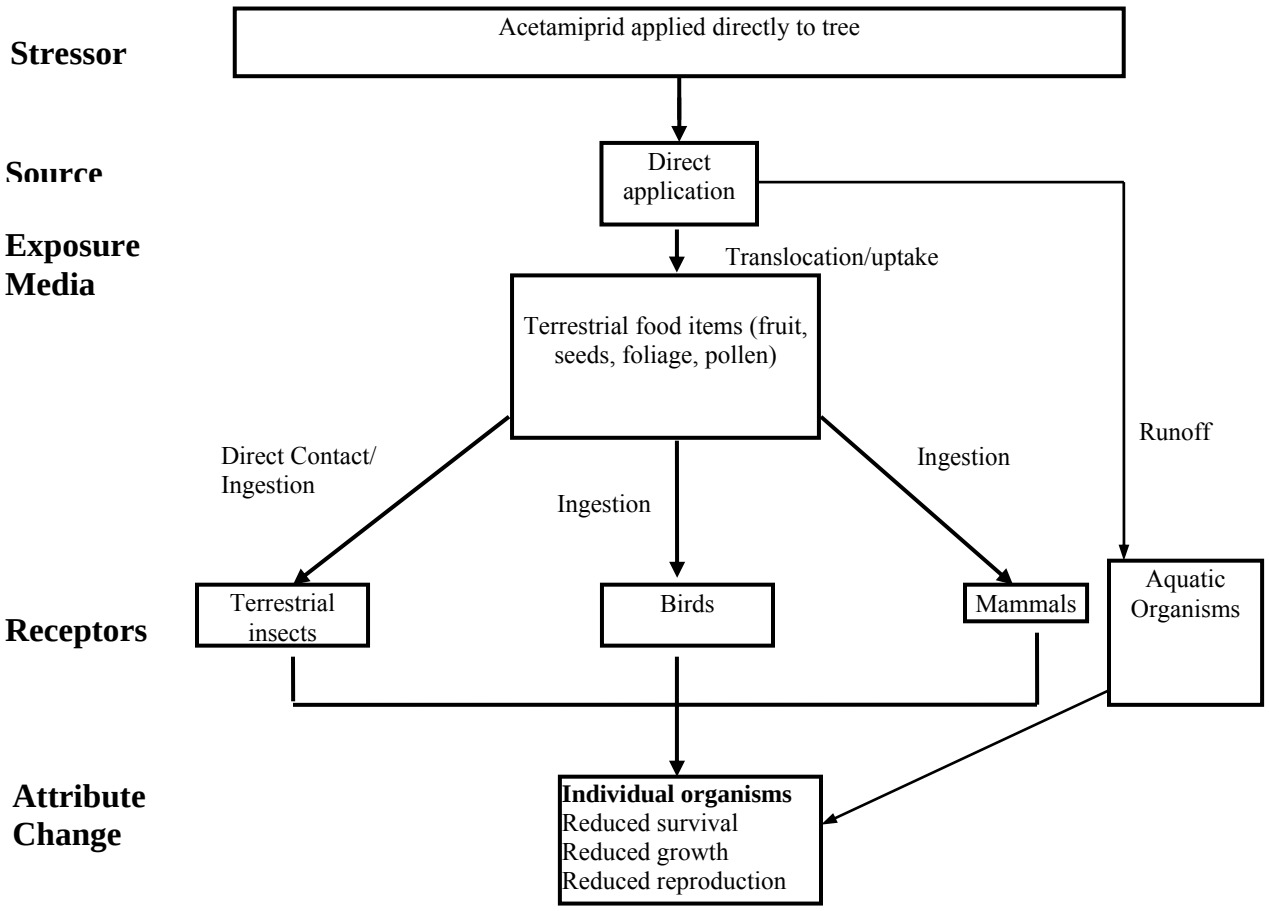


Figure 12-4. Conceptual model depicting stressors, exposure pathways, and potential effects to aquatic and terrestrial organisms from applications of acetamiprid to individual trees.

13. Analysis Plan

In order to address the risk hypothesis, the potential for adverse effects on the environment is estimated. The use, environmental fate, and ecological effects of acetamiprid are characterized and integrated to assess the risks. This is accomplished using a risk quotient (ratio of exposure concentration to effects concentration) approach. Although risk is often defined as the likelihood and magnitude of adverse ecological effects, the risk quotient-based approach does not provide a quantitative estimate of likelihood and/or magnitude of an adverse effect. However, as outlined in the Overview Document (USEPA, 2004b), the likelihood of adverse effects to individual organisms from particular uses of acetamiprid is estimated using the probit dose-response slope and either the level of concern (discussed below) or actual calculated risk quotient value.

This analysis plan will be revisited and may be revised depending upon the information

submitted by the public in response to the opening of the Registration Review docket for acetamiprid.

13.1. Measures of Exposure

In order to estimate risks of acetamiprid exposure in aquatic and terrestrial environments, all exposure modeling and resulting risk conclusions will be based on current label information on the maximum application rates and will be estimated for each use of acetamiprid. Measures of exposure are based on aquatic and terrestrial models that predict EECs of acetamiprid.

13.1.A. Exposure in the Aquatic Environment

Concentrations of acetamiprid and associated residues (IM-1-4 and unextracted residues) in surface waters (EECs) will be estimated using PRZM (Pesticide Root Zone Model version 3.12.2; May 12, 2005) and EXAMS (Exposure Analysis Modeling System version 2.98.04.06; April 25, 2005) (Burns, 2000; Carsel *et al.*, 1997). The PRZM model simulates pesticide movement from and transformation on an agricultural field following application. The EXAMS model simulates resulting concentrations in a receiving water body. The PRZM and EXAMS models and their user manuals may be downloaded from the EPA Water Models web-page (USEPA, 2011b). Percent Cropped Area (PCA) adjustment factors are used to account for the maximum fractional area within a watershed that may be planted with a modeled crop, and are used to modify human health drinking water concentrations predicted by PRZM and EXAMS (Echeverria *et al.*, 2012). Acetamiprid has uses in agricultural, commercial, and residential uses sites; therefore, a PCA of 1.0 will be used.

EFED is currently exploring methods to assess urban and residential uses on a national basis. At the present time, EFED considers the use of the impervious scenario (a Pesticide Root Zone Model (PRZM) modeling scenario) as the most suitable available modeling approach for impervious runoff. The PRZM impervious scenario may be used in the tier II coupled aquatic models PRZM/EXAMS along with a residential or other suitable scenario such as rights-of-way (ROW) to obtain EECs. The conceptual model for the residential scenario integrates simultaneous modeling of the individual use scenario with an impervious scenario. This approach assumes that no watershed is completely covered by either the ¼ acre lot (the basis for the residential scenario) or undeveloped land (the basis for the ROW scenario) for residential and ROW use patterns; therefore, differential amounts of runoff will occur within the watershed. The impervious scenario was developed to represent the paved areas within a watershed not including roads, parking lots, sidewalks, and buildings outside the ¼ acre lot (the ¼ acre lot scenario accounts for impervious surfaces such as buildings within the represented area). By modeling a separate scenario for impervious surfaces, it is also possible to estimate that amount of exposure that could occur when the pesticide is oversprayed onto this surface. Using two scenarios in tandem requires post-processing of the modeled output in order to derive a weighted EEC that represents the contribution of both the pervious (*i.e.*, residential and ROW scenarios) and the impervious surfaces. Exposure from both scenarios can also be weighted and aggregated. The daily time series from each model run from the times series file

(NAME_TS.out) generated from the PRZM graphical user interface (PE5.pl) residential and impervious surface scenarios are combined using EXCEL. The time series data are weighted based on percentage of impervious surface, the percentage of the pervious surface treated, and an adjusted time series is created. Rolling averages for the relevant durations of exposure (*e.g.*, 21 day and 60 day averages) are calculated, and the relevant one-in-ten year return EEC is generated from these distributions.

Concentrations of acetamiprid and associated residues (IM-1-4 and unextracted residues) in ground water will be estimated using EFED's Tier I aquatic model SCIGROW (Screening Concentration In Ground Water, version 2.3; 8/8/2003). SCIGROW is a regression model used as a screening tool to estimate pesticide concentrations found in ground water used as drinking water. The output of SCIGROW represents concentrations that might be expected in shallow unconfined aquifers under sandy soils, and therefore represents ground water that is most potentially vulnerable to pesticide contamination. The SCIGROW model and user's manual may also be downloaded from the EPA Water Models web-page (USEPA, 2011b). Aerobic soil metabolism may be assumed to be negligible for uses that are applied at depths where microbial activity is minimal.

The exposure assessment for house perimeter treatment required a modification in the standard modeling approach to account for the lack of uniform pesticide application in a small watershed such as yard, housing development, etc. The recommended perimeter treatment requires a 10 feet treated area around the perimeter of the house and allows for treatment of 3 feet up the side of the building. A treated area factor was estimated using a housing density of four 2000 ft^2 houses per acre. Each house has a perimeter of 180 ft and treated area of 2,340 ft^2 (180 ft × 13 ft). The estimated treated area per acre is then 9,360 ft^2 which results in an estimated 21% of an acre (9,360ft^2/43,560ft^2/acre). The application rate may be assumed to be 21% of the actual for the perimeter treatment scenario.

In addition to modeling estimates, available monitoring data will be evaluated. Monitoring data will include those collected/reported by states as well as other federal departments/agencies (*e.g.*, USGS National Water Quality Assessment; http://water.usgs.gov/nawqa).

A downstream dilution model (under development) may be used to identify areas downstream from a use area that may have EECs high enough to result in a risk concern. This analysis will be used to define the potential area of effects for endangered species.

13.1.B. Exposure to Terrestrial Animals via Residues on Food Items

Exposure estimates for terrestrial animals assumed to be in the target area or in an area exposed to spray drift are derived using the T-REX model (version 1.4.1, 10/09/2008) (USEPA, 2008a). This model incorporates the Kenaga nomograph, as modified by Fletcher *et al.* (1994), which is based on a large set of field residue data. The upper-limit values from the nomograph represent the upper bound of residue values from actual field measurements (Hoerger and Kenaga, 1972). The Fletcher *et al.* (1994) modifications to the Kenaga nomograph are based on measured field residues from 249 published research papers, including information on 118 species of plants, 121

pesticides, and 17 chemical classes (Fletcher *et al.*, 1994). Based on these data, T-REX assumes a 35-day foliar dissipation half-life in the absence of other data.

For applications of gels containing acetamiprid, acute exposure and risks to terrestrial wildlife are estimated with the conceptual approach and the LD_{50}/ft^2 method given in the model T-REX. Terrestrial EECs are calculated based on an estimation of loadings of pesticide per unit area (expressed in terms of mg ai/ft^2) for a single application (multiple applications are not accounted for in this analysis); the available mass of pesticide per square foot is then compared to the acute oral dose for toxicity (LD_{50} values adjusted for body weight and percent body weight consumed) to derive risk quotients for birds and/or mammals.

The T-REX model is used to estimate exposures and risks to avian and mammalian species resulting from acetamiprid seed treatment. T-REX approximates acute exposure from seed treatment using avian and mammalian Nagy doses (mg ai bw^{-1} day^{-1}), and also utilizes an approach analogous to the LD_{50}/ft^2 analyses done for granular applications. Chronic exposures are estimated based on the maximum seed application rate (mg ai/kg seed), which can be compared directly to estimated dietary-based chronic dietary toxicity endpoints to estimate risks.

13.1.C. Exposure to Terrestrial Plants

EECs for terrestrial plants inhabiting dry and wetland areas are derived using the program TERRPLANT (version 1.2.2, 12/26/2006) (USEPA, 2006). This model uses estimates of pesticides in runoff and spray drift to calculate EECs. EECs are based upon solubility, application rate and minimum incorporation depth. AgDRIFT may also be used to assess exposure to spray drift.

13.1.D. Exposure to Spray Drift

Two spray drift models, AgDISP and AgDRIFT, are used to assess exposures of aquatic and terrestrial organisms to acetamiprid deposited in terrestrial and aquatic habitats by spray drift. AgDrift (version 2.01; dated 5/24/2001)(Spray Drift Task Force Spray Software) is the model most commonly used to simulate spray drift into terrestrial and aquatic environments. AgDISP (version 8.13; dated 12/14/2004) (Teske and Curbishley, 2003) is used when a parameter needs to be modeled that is not available in AgDRIFT. Spray drift analysis will be an important part of the analysis in defining the potential area of effects for endangered species.

13.1.E. Exposure to Terrestrial Plants from Residues in Irrigation Water

Non-target crops may be exposed to contaminated irrigation waters from surface water or shallow ground water containing acetamiprid. The potential risks to plants when exposed to irrigation water contaminated with acetamiprid will be estimated for both ground water and surface water irrigation sources. The EECs for ground water and surface water will be calculated using SCIGROW and PRZM/EXAMs, respectively. Comparisons will be made to the most sensitive endpoint from the vegetative vigor study assuming that runoff of irrigation water does not occur.

13.1.F. Exposure from Applications to Individual Trees

There is no currently approved model for estimating potential exposure to organisms from tree injection or bark treatment. A screening-level estimate of exposure will be used in the assessment to determine whether a more in-depth analysis of this use pattern is needed due to the potential for risk to organisms. The method used to estimate exposure in the terrestrial environment is discussed in a recently completed assessment in EFED and the screen is based on the following assumptions (USEPA, 2010b). The aquatic risk assessment methodology was developed for this problem formulation.

(1) Aquatic Risk Assessment
   a. The total mass of chemical applied to the trees on one acre is assumed to be an application rate. PRZM/EXAMs will be used to estimate potential exposure from applications to bark of trees. Spray drift will be assumed to be minimal. Aquatic exposure due to tree injections will be assumed to be minimal.

(2) Concentration of chemical in leaves for Terrestrial Risk Assessment
   a. Leaf concentration was estimated by assuming that 100% of the chemical was translocated to the leaves. Leaf mass was estimated using allometric equations developed for blue oak trees presented by the USDA Forest Service (Karlick and McKay, 2002). The following equations are used to evaluate risk to terrestrial organisms.

      EEC = total mass of chemical applied / leaf mass on tree.

      Leaf mass (g) = $1.78x^2 - 12.4x - 108.5$
      x = tree circumference at breast height (cm)

   Pesticide concentration on leaves was converted to dose by assuming that birds consume 114% and mammals consume 95% of their body weight daily using the following equation:

      Body weight adjusted EEC for residues on leaves mg/kg bw
      = X mg/kg leaf × 1.14 or 0.95 kg leaf/kg-bw

13.2. Measures of Effect

Ecological effects data are used as measures of direct and indirect effects to biological receptors. Effects data are obtained from registrant-submitted studies or from literature studies identified by the ECOTOX database. The acute measures of effect used for animals in this assessment are the LD_{50}, LC_{50} and EC_{50}. LD stands for "Lethal Dose", and LD_{50} is the amount of a material, given all at once, that is estimated to cause the death of 50% of the test organisms. LC stands for "Lethal Concentration" and LC_{50} is the concentration of a chemical that is estimated to kil1 50% of the test organisms. EC stands for "Effect Concentration" and the EC_{50} is the concentration of a

chemical that is estimated to produce a specific effect in 50% of the test organisms. Endpoints for chronic measures of exposure for listed and non-listed animals are the NOAEL/NOAEC. NOAEL stands for "No Observed-Adverse-Effect-Level" and refers to the highest tested dose of a substance that has been reported to have no harmful (adverse) effects on test organisms. The NOAEC (*i.e.*, "No-Observed-Adverse-Effect-Concentration") is the highest test concentration at which none of the observed effects were statistical1y different from the control. For non-listed plants, only acute exposures are assessed (*i.e.*, EC_{25} for terrestrial plants and EC_{50} for aquatic plants); for listed plants either the NOAEC or EC_{05} is used.

Where available, sublethal effects observed in both registrant-submitted and open literature studies wil1 be evaluated qualitatively. Such effects may include behavioral changes (*e.g.*, lethargy and changes in coloration). However, quantitative assessments of risks are limited to those endpoints that can be directly linked to the Agency's assessment endpoints of impaired survival, growth and reproduction.

In the absence of taxa-specific data, the assessment of risk for direct effects to non-target organisms makes the assumption that toxicity of acetamiprid to birds is similar to terrestrial-phase amphibians and reptiles. The same assumption is made for fish and aquatic-phase amphibians. In the absence of data for either acute or chronic effects, the conservative assumption wil1 be to presume that acetamiprid is toxic.

13.3. Integration of Exposure and Effects

Risk characterization is the integration of exposure and ecological effects characterizations to determine the potential ecological risk from the registered uses of acetamiprid and the likelihood of direct and indirect effects to non-target organisms in aquatic and terrestrial habitats. The exposure and toxicity (effects) data are integrated in order to evaluate the risks of adverse ecological effects on non-target species. For the assessment of acetamiprid, the risk quotient (RQ) method is used to compare exposure and measured toxicity values. EECs are divided by acute and chronic toxicity values. The resulting RQs are then compared to the Agency's Levels of Concern (LOCs) (USEPA, 2004b)(**Appendix F**). These criteria are used to indicate when acetamiprid use, as directed on the labels, has the potential to cause adverse direct or indirect effects to non-target organisms. In addition, incident data from the EIIS will be considered as part of the risk characterization.

13.3.A. Deterministic and Probabilistic Assessment Methods

The quantitative assessment of risk will primarily depend on the deterministic point-estimate (RQ) based approach described in the risk assessment. Depending on the extent of refinement needed by the risk manager, risk estimates may be further refined using probabilistic tools that the Agency has developed. These tools have been reviewed by FIFRA Scientific Advisory Panels[22] and have been deemed as an appropriate means of refining assessments where deterministic approaches have identified risks. Newer tools may be available to assess the routes

[22] http://vvww.epa.gov/scipoly/sap/index.htm

of exposure and will be applied as appropriate in Registration Review.

13.3.B. Endocrine Disruptor Screening Program

As required by FIFRA and FFDCA, EPA reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. Collectively, these studies include acute, sub-chronic and chronic toxicity, including assessments of carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity. These studies include endpoints which may be susceptible to endocrine influence, including effects on endocrine target organ histopathology, organ weights, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. For ecological hazard assessments, EPA evaluates acute tests and chronic studies that assess growth, developmental and reproductive effects in different taxonomic groups. As part of its most recent registration decision, EPA reviewed these data and selected the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database. However, as required by FFDCA section 408(p), acetamiprid is subject to endocrine screening as part of the Endocrine Disruptor Screening Program (EDSP).

EPA has developed the EDSP to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Under FFDCA section 408(p), the Agency must screen all pesticide chemicals. Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. Acetamiprid is not among the group of 58 pesticide active ingredients on the initial list to be screened under the EDSP. Accordingly, as part of Registration Review, EPA will issue future EDSP orders/data call-ins, requiring the submission of EDSP screening assays for acetamiprid. For further information on the status of the EDSP, the policies and procedures, the list of 67 chemicals, future lists, the test guidelines and the Tier 1 screening battery, please visit our website.[23]

13.3.C. Endangered Species Assessment

Consistent with the Agency's responsibility under the Endangered Species Act (ESA), the Agency will evaluate risks to Federally-listed threatened and/or endangered (listed) species from registered uses of acetamiprid. This assessment will be conducted in accordance with the

[23] http://www.epa.gov/endo/

Overview Document (USEPA, 2004b), provisions of the ESA, and the Services' Endangered Species Consultation Handbook (USFWS/NMFS, 1998).

The action area is used to identify all listed (threatened and endangered) species and designated critical habitat that could be affected by the Federal action. The Federal action is the authorization or registration of pesticide use or uses as described on the label(s) of pesticide products containing a particular active ingredient. The action area is defined by the Endangered Species Act as, "all areas to be affected directly or indirectly by the Federal action and not merely the immediate area involved in the action" (50 CFR §402.2). Based on an analysis of the Federal action, the action area is defined by the actual and potential use of the pesticide.

In the case of nationwide ecological risk assessment conducted for acetamiprid under Registration Review, the action area will encompass the entire United States and its territories. The purpose of defining the action area as the entire US and its territories is to ensure that the initial area of consideration encompasses all areas where acetamiprid may be used now and in the future, including the potential for off-site transport via spray drift and downstream dilution. Additionally, the concept of a nationwide action area takes into account the potential for direct and indirect effects and any potential modification to critical habitat based on ecological effect measures associated with reduction in survival, growth, and reproduction, as well as the full suite of sublethal effects available in the effects literature. It is important to note that the nationwide action area does not imply that direct and/or indirect effects and critical habitat modification are expected to or are likely to occur over the full extent of the action area, but rather to identify all listed species and critical habitat that may potentially be affected by the action. The Agency will use more rigorous analysis including consideration of available land cover data, toxicity data, and exposure information to determine areas where individual listed species and designated critical habitat may be affected or modified via endpoints associated with reduced survival, growth, or reproduction.

13.3.A. Risk Assessment of Pollinators

The EPA is aware of registrant-submitted studies and other open literature studies regarding the potential effects of neonicotinoid insecticides on insect pollinators and specifically on honey bees. EPA is also aware of concerns regarding the potential association between the use of nitroguanidine-substituted neonicotinoids and honey bee losses characterized as Colony Collapse Disorder (CCD) and the broader phenomenon of declining honey bee health globally. While a number of factors (*e.g.*, nutrition, habitat loss, disease, parasites, bee management practices, and pesticides) have been hypothesized, no single factor has yet to be identified as the "cause" of declines.

As part of the review process, EPA examines the effects of chemicals on bees based on both laboratory and when appropriate, field studies to determine whether individual bees and entire bee colonies may be affected by the use of a compound and to support risk mitigation decisions. EPA is currently revising its process for assessing pesticide risks to bees to reflect advancements in the state of the science that underlie bee exposure and effects assessments. Interim guidance

(USEPA 2011[24]) on factors to consider when evaluating exposure and effects to bees is available to ecological risk assessors. In 2012, EPA will present to a FIFRA Scientific Advisory Panel (SAP) a proposed process for quantifying risks to honeybees and identifying exposure and effect studies needed to inform that process. Based on input from the SAP, EPA will incorporate its revised assessment process to quantify risks to bees in a similar manner as that used to evaluate risks to other taxa.

As EPA's understanding of the science evolves, its need for data and its evaluation of those data will evolve as well. Therefore, as with all taxa, EPA reserves the right to require additional data it deems necessary to inform its understanding of potential ecological risks and support its associated risk management decisions. Additional data requirements for pollinators may extend beyond those identified in problem formulations and preliminary work plans written in support of the Registration Review process.

13.3.B. Human Health Drinking Water Assessment

In order to bring the drinking water assessment up to date with current data, models and simulation model guidance, a new drinking water assessment will be conducted to support future human health dietary risk assessments of acetamiprid. The drinking water assessment will incorporate model estimates of acetamiprid and unextracted residues in surface water and groundwater. Concentrations of acetamiprid and unextracted residues in surface waters will be estimated using PRZM and EXAMs (see description in Section 13.1.A), and concentrations in ground water will be estimated using SCIGROW (see description in Section 13.1.A).

The drinking water assessment will also include available surface and ground water monitoring data with consideration of changes in use patterns that may have occurred. States are encouraged to submit monitoring data for review.

14. Preliminary Identification of Data Gaps

14.1. Fate

Several fate studies are needed to better characterize the environmental fate and transport of acetamiprid. The studies listed below will decrease the uncertainty in determining the potential exposure to the pesticide. EFED recommends the following studies be required:

- Aerobic Aquatic Metabolism (OPPTS Guideline 835.4300); test substance acetamiprid, data needed for one sediment
- Anaerobic Aquatic Metabolism (OPPTS Guideline 835.4400); test substance acetamiprid, data needed for one sediment
- Column and Aged Column Leaching Study (OPPTS Guideline 835.1240); Parent and

[24] USEPA. 2011. Pesticides: Science and Policy. Interim Guidance on Honey Bee Data Requirements. http://www.epa.gov/pesticides/science/efed/policy_guidance/team_authors/terrestrial_biology_tech_team/honeybee_data_interim_guidance.htm

representative TEP for formulations applied using trenching, rodding, soil injection, and soil excavation techniques

- Aquatic Field Dissipation (OPPTS Guidelines 835.6200); test substance is representative end-use product used on cranberries
- Aerobic Soil Metabolism (OPPTS Guideline 835.4100), Test substance acetamiprid additional information on MRIDs 46255603, 44651881, 44699101, 44651879 or identity of unextracted residues
- Aerobic Aquatic Metabolism (OPPTS Guideline 835.4300), Test substance acetamiprid, additional information for MRID 44988513 or identity of unextracted residues
- Anaerobic Aquatic Metabolism (OPPTS Guideline 835.4400), Test substance acetamiprid additional information for MRID 44988512 or identity of unextracted residues
- Environmental Chemistry Methods: Water (OPPTS Guideline 850.7100), parent and major degradates IM 1-2, IM 1-5, IM 1-4, IM 1-3, and IC-0

In addition to the above studies, the following studies would provide additional information that would reduce uncertainty in the risk assessment or assist the public in monitoring:

- Terrestrial Field Dissipation (OPPTS Guideline 835.6100); test substance acetamiprid

Table 14-1 summarizes the fate data requirements for acetamiprid. A rationale discussing the need for each study is also provided below.

Table 14-1. Summary of Submitted Environmental Fate Studies, Study Classifications and Data Gaps for Acetamiprid and Its Degradates

OPPTS Guideline	MRID Test Material	Study Classification	Comments on Study Classification	Data Gap?	Are additional data needed for risk assessment?	Comments
Hydrolysis 835.2120 (161-1)	44651876 Parent	Acceptable	Values may be used in risk assessment.	No	No	--
	44651877	Supplemental	Screening study at 50°C. Shown to be stable.			
Aqueous Photolysis 835.2240 (161-2)	44988509 Parent	Acceptable	Values may be used in risk assessment	No	No	--
	44988511 Parent	Valid	--			

OPPTS Guideline	MRID Test Material	Study Classification	Comments on Study Classification	Data Gap?	Are additional data needed for risk assessment?	Comments
Soil Photolysis 835.2410 (161-3)	48563501 Parent	Supplemental	Unable to calculate half-lives due to microbial activity being higher in dark control than in irradiated sample.	Yes	No	When microbial degradation is present it is expected to be a more important degradation pathway than photolysis. Additional data are not expected to impact the risk assessment.
Aerobic Soil Metabolism 835.4100 (162-1)	46255603 Parent	Supplemental	High unextracted residues	Yes	Yes	All of the studies contained high levels of unextracted residues and maximum amounts of residues observed may be higher than observed. In absence of additional data, unextracted residues will be included when estimating half-lives for use in aquatic modeling.
	44651881 Parent	Supplemental				
	44699101 Parent	Supplemental				
	44651880 Parent	Supplemental – Not for use in modeling				
	44651879 Parent	Acceptable				
Anaerobic Soil Metabolism 835.4200 (162-2)	48554501 Parent	Supplemental-Not for use in modeling	Dissolved oxygen concentrations were 1.9 mg/L	Yes	No	While data are required by 40 CFR Part 158.1300, additional data are not expected to impact the risk conclusions.
Aerobic Aquatic Metabolism 835.4300 (162-4)	44988513 Parent	Acceptable	Data only available on one sediment. High levels of unextracted residues.	Yes	Yes	For the study available on one sediment there were significant unextracted residues. In the absence of additional data, unextracted residues will be included when estimating half-lives for use in aquatic modeling. If data are only available on one sediment the estimated value will be multiplied by three.

OPPTS Guideline	MRID Test Material	Study Classification	Comments on Study Classification	Data Gap?	Are additional data needed for risk assessment?	Comments
Anaerobic Aquatic Metabolism 835.4400 (162-3)	44988513 Parent	Acceptable	Data only available on one sediment. High levels of unextracted residues.	Yes	Yes	For the study available on one sediment there were significant unextracted residues. In the absence of additional data, unextracted residues will be included when estimating half-lives for use in aquatic modeling. If data are only available on one sediment the estimated value will be multiplied by three.
Adsorption/ Desorption 835.1230 (163-1)	44651883 Parent	Acceptable	Test material was parent	No	No	--
	44651885 IM-1-4	Valid	Test material was IM-1-4			
Leaching and Aged Column Leaching 835.1240	--	---	--	Yes	Yes	Data are needed to predict the risk of contamination of ground water from uses involving trenching, rodding, soil excavation, and subslab injection.
Terrestrial Field Dissipation 835.6100	44988514 Parent	Supplemental	IM-1-2 not stable, residues in plants not measured	Yes	No	Additional data are not expected to impact the risk assessment conclusions.
	44988515 Parent	Supplemental	IM-1-2 not stable. Residues in plants not measured			
	44988625 Parent	Supplemental	No storage stability data			
835.6200 Aquatic Field Dissipation	--	--	--	Yes	Yes	Acetamiprid may be used on cranberries and therefore, applied directly to water. Therefore, data on aquatic field dissipation of acetamiprid are needed.

OPPTS Guideline	MRID Test Material	Study Classification	Comments on Study Classification	Data Gap?	Are additional data needed for risk assessment?	Comments
Bioconcentration Factor 850.1730	--	--	--	No	No	Not required because K_{OW} is < 1000 (40 CFR Part 158.630)
Environmental Chemistry Method: Water 850.7100	44988536 Parent and Major Degradates	Satisfactory	--	No	No	An ECM and ILV are needed with a limit of quantitation (LOQ) for the parent below 2.5 µg/L that may be used in monitoring. Available methods have an LOQ of 0.1 µg/L.[1]
Environmental Chemistry Method: Soil and sediment 850.7100	44988516/44988517 Parent and Major Degradates	Satisfactory	--	No	No	

Abbreviations: ECM=Environmental Chemistry Method; ILV=independent laboratory Validation
[1] The LOQ was based on the NOAEC for mysid (NOAEC = 0.0025 mg ai/L) and an LOC of 1 (MRID 44651873).

14.1.A. Rationales for Requesting Fate Studies

- Anaerobic Aquatic Metabolism (OPPTS Guideline 835.4400); test substance acetamiprid, data needed for one sediment and additional data needed on the identity of unextracted residues for MRID 44988513
- Aerobic Aquatic Metabolism (OPPTS Guideline 835.4300); test substance acetamiprid, data needed for one sediment and additional data needed on the identity of unextracted residues for MRID 44988513
- Aerobic Soil Metabolism (OPPTS Guideline 835.4100), Test substance acetamiprid additional information on MRIDs 46255603, 44651881, 44699101, 44651879 regarding the identity of unextracted residues

Data on aerobic aquatic and anaerobic aquatic metabolism (OPPTS Guidelines 835.4300 and 835.4400) in two sediments each are recommended; however, data are only available for each type of test in one sediment. This could result in underestimation or overestimation of typical half-lives in such media. Because only a single data point (half-life) is available for each of these studies, model input half-lives are assumed to equal three times the measured values, in keeping with standard EFED procedure (USEPA, 2009b). Having half-lives from additional studies would allow estimation of 90th percentile confidence bounds on the mean half-lives for use in modeling, which would probably be less conservative. A total toxic residue (including parent, IM-1-4, and unextracted residues) approach is used in modeling for the ecological risk assessment. Half-life values used in modeling were high (*i.e.*, >1500 days), and as a

consequence EECs are conservative. These data gaps will also influence the estimated drinking water concentrations (EDWCs).

The identity of unextracted residues is unknown in a number of submitted studies where unextracted residues made up greater than 10% of applied radioactivity (<1 to 40%). This creates significant uncertainty for the risk assessment. Due to the uncertainty in the identity of these residues, in the absence of additional data, it will be assumed that the unidentified residues are residues of concern in estimating the half-lives of total residues of concern. It will be assumed that unextracted residues have similar toxicity to the parent compound. In a recently completed ecological risk assessment, the parent, IM-1-4, and unextracted residue risk quotients were up to twice the values of those for the parent and IM-1-4 only (USEPA, 2011a). For the drinking water assessment, inclusion of unextracted residues resulted in EDWCs that were 4 to 35 times the EDWCs based on parent alone (USEPA, 2011, D394234, D394479). If the identity of the unextracted residues were known, the degradate profile would likely change. Additional studies that make an effort to ensure that all residues that can be extracted from soil and sediment are extracted[25], and that those residues are identified, could significantly reduce the uncertainty resulting from having significant amounts of unextracted and unidentified residues in metabolism studies.

In all fate studies, efforts should be made to extract all residues from soil and sediment.

- Column and Aged Column Leaching Study (OPPTS Guideline 835.1240) and Aged Column Leaching; Parent and representative TEP for formulations used as termiticides

Acetamiprid may be used to control termites and is applied via trenching, rodding (boring a series of relatively evenly spaced holes in the soil adjacent to the structure and back-filling the holes with termiticide and soil), sub slab injection, soil excavation, or injected into piping or similar systems around buildings. There is a particular concern for leaching of pesticides applied under the soil surface as other chemicals have been found at high levels when applied in this manner (USEPA, 1999). The pesticide may be applied below levels where microbial activity is high, resulting in greater persistence. There is also a concern that the formulation may enhance the movement of the pesticide in soils as the entire formulation is applied under the soil surface. The environmental risk concern is that the increased mobility may potentially allow acetamiprid to reach drinking water wells and in-ground drainage systems such as French drains, which are used to drain water away from basement walls, and tile drains, which are used to lower the water table in residential and other areas. Both the French and tile drains typically convey water through storm-water drainage-ways to water bodies rather than to wastewater treatment facilities. In order to better understand the risk of these uses EFED requests column leaching studies be conducted on the parent and representative formulations (including a formulation that is applied in foam) that are used in this manner. If the formulation indicates that the formulation is more mobile than the parent, EFED believes it would be prudent to request a radio-labeled aged soil

[25] A reasonable effort to extract all residues would include employing a variety of extraction solvents and testing extraction efficiencies for known analytes. Use of acids and bases if they do not alter the chemical of interest may also be used.

column leaching study that determines how fast the formulation components lose their ability to enhance acetamiprid mobility and estimates the rate of decay in mobility enhancement. EFED envisions such a study consisting of a radio-labeled aged soil column leaching study using acetamiprid formulation aged for different lengths of time (for example, 0 months, 1 month, 3 months, 6 months, and 1 year). If such a study is performed, EFED recommends that acetamiprid and acetamiprid degradates be quantified. It would also be recommended that multiple soil types varying in organic matter content be studied including a loamy sand and a silt loam or sandy loam. Ideally, the studies would be conducted on soils where adsorption/desorption data for the parent were also available and the soils were shown to be vulnerable soils.

- Aquatic Field Dissipation (OPPTS Guidelines 835.6200); test substance is representative end-use product used on cranberries

Acetamiprid may be used on cranberries and applied directly to water. 40 CFR § 158.1300 recommends that aquatic field dissipation studies be available when products may be applied directly to water or when there is a potential for aquatic exposure. Data from aquatic field dissipation studies are needed to get a better understanding of the environmental fate of acetamiprid in aquatic systems. In the absence of additional data, EFED will use available data to predict the fate of acetamiprid in cranberry bogs.

14.1.B. Discussion of Additional Fate Data to Reduce Uncertainty or Aid in Monitoring

- Terrestrial Field Dissipation (OPPTS Guideline 835.6100), Test substance acetamiprid formulation

Terrestrial field dissipation studies are only available examining applications of wettable powders. Studies conducted using other formulations such as soluble concentrates, emulsifiable concentrates, and termiticide formulations would reduce the uncertainty on the effect of the formulation on the environmental transport of acetamiprid. This would be particularly helpful for termiticide formulations that are directly injected below the soil surface. Additionally, IM 1-2 was converted to IM 1-4 during storage and IM 1-4 was not stable for two of the studies with storage stability data. In a third study, storage stability data were not available. This results in uncertainty in the maximum residues of IM 1-2 and IM 1-4 that would occur in the environment. This is particularly important as concentrations of IM 1-4 were sometimes higher than concentrations of the parent. Additional data to resolve these uncertainties in the terrestrial field dissipation results would reduce the uncertainty in the risk assessment.

- Environmental Chemistry Methods (OPPTS Guideline 850.7100)

Environmental chemistry methods for parent and degradates using a variety of instruments would aid the public in being able to monitor for acetamiprid and its degradates in use areas. These methods could be specific to acetamiprid, or multiresidue methods for multiple

compounds that include acetamiprid and/or its degradates. These methods would add to the methods already available for monitoring.

14.2. Ecological Effects

Several ecological effects studies on acetamiprid are needed to better assess the potential risk of exposure to non-target organisms. **Table 14-2** summarizes the data that have been submitted for the parent compound and also highlights additional studies that are needed for risk assessment. Additional rationale for requesting specific studies is outlined below.

The following studies are needed to decrease uncertainty in risk estimation and characterization of acetamiprid:

Avian Toxicity

- *Avian Reproductive Toxicity Study with Mallard Duck – OCSPP 850.2300 [1 Study]*

An avian chronic reproductive toxicity study (MRID 46369201) yielded a non-definitive endpoint. A NOAEC value was not derived in the study and effects were recorded at all concentrations tested. Establishment of a NOAEC is essential if the study is to be used in risk assessment. Therefore the extent of possible chronic risk to birds cannot be determined until an additional avian reproduction study (OCSPP 850.2300) is submitted. EFED reviewed this avian reproduction study in August, 2005 and classified it as supplemental since it did not establish a NOAEC because statistically significant effects on male body weight gain were observed at all treatment levels. EFED issued an additional document in 2012 (D325745) reconfirming that the study remains classified as supplemental. Therefore, additional data on avian reproductive toxicity in mallard ducks are recommended.

Aquatic Invertebrate Toxicity

- *28-day Chironomid Toxicity Test – Non-guideline [1 Study]*

Based on a search of the European Pesticide Properties Database (PPDB), a 28-day chronic study with the non-biting midge (*Chironomidae*) exists. If this is a registrant-sponsored study, EFED would appreciate submission of this study to better assess toxicity to sensitive non-target arthropods. Submission of these data could potentially be used to avoid relying on an acute-to-chronic ratio for estimating chronic toxicity to chironomids. If this study is not available, a new study is not being requested for risk assessment.

- *Freshwater invertebrate, acute toxicity, Daphnia – OCSPP 850.1010 Test Substance EPA Registration Number 8033.116 and TEP for products used on cranberries*

40 CFR § 158.630 footnote 9 recommends that acute aquatic toxicity testing data be obtained when, “An ingredient in the end-use formulation other than the active ingredient is expected to

enhance the toxicity of the active ingredient or to cause toxicity to aquatic organisms." EPA Registration Number 8033-116 contains both acetamiprid and bifenthrin, which is toxic to aquatic organisms, and may be deposited directly into the aquatic environment via spray drift. Submission of these data will allow evaluation of the likelihood of risk to aquatic invertebrates exposed to this product via spray drift. Additionally, products with applications to cranberries may have direct applications to water. OCSPP 850.1010 on representative typical end-use products for these products are recommended.

Terrestrial Invertebrate Toxicity

- *Honeybee Toxicity on Foliage Residue Study – OCSPP 850.3030 [1 Study]*

Based on current Agency policy, an acceptable honeybee foliage residue study (OCSPP 850.3030) is recommended when the acute contact toxicity to bees is <11 µg/bee, as in the case of acetamiprid. A toxicity of residues on foliage study (MRID 44651875) was submitted for acetamiprid but was deemed unacceptable. While this study design does not address the systemic nature of acetamiprid, it is requested to provide a better understanding of the residual toxicity associated with foliar applications. It should be noted that a second foliage residue toxicity study was submitted in 2001 (MRID 45346901), but has not yet been reviewed by EFED.

- *Honeybee Larval Toxicity Study – Non-guideline [1 Study]*

Since at least one of the registered uses of acetamiprid is as an ovicide, potential effects to young bees could exist. Toxicity studies with acetamiprid have only been submitted for young adult bees and do not address possible effects on brood (larvae and pupae) survival. In addition, since acetamiprid is a systemic fungicide, it may be transferred to pollen and nectar and subsequently brought back to hive where larvae and pupae may be exposed. Honeybee brood studies are not currently a data requirement in the U.S., however, a non-guideline honeybee larval toxicity study is recommended as a special study (see **Appendix F** for DCI justification table).

- *Nectar and Pollen Residue Study – Non-guideline [1 Study]*

Acetamiprid is a systemic compound, and there is uncertainty as to the extent that residues may translocate to pollen and nectar, where honeybee larvae and pupae may be exposed. However, this route of exposure will only be considered a potential concern if acetamiprid exhibits significant toxicity to larval bees. Therefore, EFED recommends residue studies of pollen and nectar (and other plant products, as appropriate) of pollinator-attractive crops on which the compound is registered for use (see **Appendix F** for DCI justification tables) pending the results of the non-guideline larval toxicity test. If the screening-level acute RQ exceeds 0.4 (based on larval toxicity data), then the pollen and nectar residue study may be requested. EFED will also evaluate the HED magnitude of residue toxicity data to determine whether it can be used to supplement or replace studies estimating residues of acetamiprid on plant pollen and nectar.

- *Beneficial Insect Studies – Non-guideline [2 Studies]*

Two beneficial insect studies were identified in the European PPDB: one study with the parasitoid aphid (*Aphidius rhopalosiphi*) and one study with the predatory mite (*Typhlodromus pyri*). Both studies appear to report mortality endpoint data. If these studies were sponsored by the registrant, EFED would appreciate that they be submitted in order to characterize effects to terrestrial invertebrates.

Terrestrial Plant Toxicity

- *Tier II Seedling Emergence Study – OCSPP 850.4100 [1 Study]*

The Tier II seedling emergence study in terrestrial plants (OCSPP 850.4100; MRID 44988413) did not measure plant weight, which is one of the two major endpoints in this type of study, resulting in uncertainty regarding the effects of acetamiprid on plant growth. Therefore, an additional Tier II plant study should be submitted which includes both plant weight and shoot length endpoint data from all 10 recommended species.

Table 14-2. Summary of Submitted Aquatic and Terrestrial Effects Studies and Data Gaps for Parent Acetamiprid.

Guideline	Description—Test Substance	MRID(s)	Study Classification	Are additional data needed for risk assessment?	Comments
Avian and Mammalian Testing					
850.2100	Avian acute oral toxicity, waterfowl—TGAI	44651859	Acceptable	No	
850.2100	Avian acute oral toxicity, passerine species—TGAI	48407701	Acceptable	No	
850.2200	Avian dietary toxicity, waterfowl species—TGAI	44651861	Supplemental	No	Definitive study tested less than five concentrations; mortalities occurred. But available data suggest that dietary toxicity is low.
850.2200	Avian dietary toxicity, upland game bird—TGAI	44651860	Supplemental	No	Definitive study tested less than five concentrations; mortalities occurred. But available data suggest that dietary toxicity is low.
850.2300	Avian reproduction, waterfowl species—TGAI	46369201	Supplemental	**Yes**	NOAEC not established due to effects on male body weight gain at all test levels.
850.2300	Avian reproduction, upland game bird species—TGAI	46555601	Acceptable	No	
850.2400	Wild mammal toxicity—TGAI	None	N/A	No	Not triggered based on ecotoxicity data, predicted EECs, fate properties, and use pattern criteria.
850.2500	Simulated or actual field testing—TEP	None	N/A	No	Not triggered based on ecotoxicity data, predicted EECs, fate properties, and use pattern criteria.

Guideline	Description—Test Substance	MRID(s)	Study Classification	Are additional data needed for risk assessment?	Comments
Aquatic Animal Testing					
850.1010	Freshwater invertebrate, acute toxicity, *Daphnia*—TGAI	44651866	Supplemental	No	Water hardness during test (216-219 mg/L $CaCO_3$ is higher than guideline recommended value of 180 mg/L)
850.1010	Freshwater invertebrate, acute toxicity, Daphnia—TEP			**Yes**	Data needed on products that could result in spray drift into aquatic water bodies that contain multiple active ingredients. EPA Registration Number 8033-116 is a liquid formulation that may be applied to soybean by aerial or ground spray. Additionally, products applied to cranberries may be applied directly to water.
850.1020	Freshwater invertebrate, acute toxicity, Amphipod—TGAI	45932501	Supplemental	No	
Non-guideline	Freshwater invertebrate, acute toxicity, Non-biting midge (Chironomidae)—TGAI	45916201	Supplemental	No	
850.1025	Estuarine/Marine Mollusk acute toxicity—TGAI	44988410	Acceptable	No	
850.1035	Estuarine/Marine crustacean acute toxicity—TGAI	44651869	Acceptable	No	
850.1075	Freshwater fish, acute toxicity, warm water species—TGAI	44651863	Acceptable	No	
850.1075	Freshwater fish, acute toxicity, cold water species—TGAI	44651864	Acceptable	No	
850.1075	Estuarine/Marine fish acute toxicity—TGAI	44988411	Acceptable	No	
850.1300	Freshwater invertebrate, reproduction test—TGAI	44651871	Acceptable	No	
850.1350	Estuarine/marine invertebrate, reproduction test—TGAI	44651873	Acceptable	No	
Non-guideline	28-day toxicity to non-biting midge (Chironomidae)—TGAI	None	N/A	No*	This study was identified in the European Pesticide Properties Database. If this is a registrant-sponsored study, submission of this study to EPA is requested. If this study is not available, a new study is not being recommended.
850.1400	Freshwater fish, early life stage test—TGAI	44651872	Supplemental	No	

Guideline	Description—Test Substance	MRID(s)	Study Classification	Are additional data needed for risk assessment?	Comments
850.1400	Saltwater fish, early life stage test—TGAI	None	N/A	No	Test not triggered under 40 CFR §158.630
850.1500	Freshwater fish life cycle test	None	N/A	No	Data requirement triggered because EEC >0.1 of NOAEC of mysid from life cycle tests (EEC = 0.7 mg/L and NOAEC=19.2 mg ai/L). However, EECs and the fish early life stage toxicity NOAEC (19.2 mg/L) are not similar. Additionally, NOAECs from early life stage and fish full life cycle studies on thiacloprid (a neonicotinoid with a similar structure to acetamiprid) were similar; also, the reproductive NOAECs and parental NOAECs from avian and mammalian studies with acetamiprid were similar. Weight of evidence suggests that this study will not provide any critical new information (see discussion below).
850.1500	Estuarine/marine fish life cycle test	None	N/A	No	
850.1950	Simulated or actual field testing for aquatic organisms	None	N/A	No	Higher tier testing to address risk uncertainties have not been identified at this time
Sediment Testing					
850.1735	Whole sediment 10-d freshwater invertebrate—TGAI	None	N/A	No	Data requirement not triggered: K_d <50 Log K_{OW} <3 K_{OC} <1,000
850.1740	Whole sediment 10-d estuarine/marine invertebrate—TGAI	None	N/A	No	Data requirement not triggered: K_d <50 Log K_{OW} <3 K_{OC} <1,000
Agency-wide guideline	Whole sediment chronic freshwater and/or marine invertebrate—TGAI	None	N/A	No	Data requirement not triggered: K_d <50 Log K_{OW} <3 K_{OC} <1,000

Guideline	Description—Test Substance	MRID(s)	Study Classification	Are additional data needed for risk assessment?	Comments
Terrestrial Invertebrates					
850.3020	Honeybee acute contact toxicity—TGAI	44651874	Supplemental	No	A definitive LD_{50} was not established due to lack of dose response; however, study is sufficient as a trigger for additional tiered bee studies
850.3030	Honeybee toxicity of residues on foliage—TEP	44651875	Invalid	**Yes**	While this study does not address the systemic nature of acetamiprid, it is recommended to provide a better understanding of the residual toxicity associated with foliar applications. Note: an additional foliage residue toxicity study was submitted (MRID 45346901), but has not yet been reviewed by EFED
		45346901	Not Reviewed	N/A	Review of this study could change the recommendation for additional foliage residue toxicity data
850.3040	Field testing for pollinators	None	N/A	No	
Non-guideline	Honeybee semi-field tunnel study—TEP	45932504 45932505	Supplemental	No	
Non-guideline	Honeybee larval toxicity study—TGAI	None	N/A	**Yes**	Recommended since acetamiprid is systemic and may be transferred to pollen and nectar and subsequently brought back to hive
Non-guideline	Honeybee pollen and nectar residue study—TEP	None	N/A	**Yes**	Recommended since acetamiprid is systemic and may be transferred to pollen and nectar and subsequently brought back to hive
Non-guideline	Toxicity to beneficial insects – parasitoid aphid and predatory mite (2 studies)	None	N/A	No*	These studies were identified in the European Pesticide Properties Database. If they are registrant-sponsored studies, their submission to EPA is requested. However, if these studies are not available, new studies are not being recommended.

Guideline	Description—Test Substance	MRID(s)	Study Classification	Are additional data needed for risk assessment?	Comments
Terrestrial Plants					
850.4100 Tier II	Seedling emergence (10 species) —TGAI	44988413	Supplemental	**Yes**[†]	Seedling weight was not measured. Additional study (with 10 recommended plant species) with seedling weight endpoint is recommended.
850.4150 Tier II	Vegetative vigor (10 species) — TGAI	44988413	Acceptable	No	Study was acceptable for all plant species tested except for lettuce. Additional data have since been submitted for lettuce.
850.4150 Tier II	Vegetative vigor (10 species) — TGAI	45921401	Supplemental	No	This study was submitted to supplement MRID 44988413
Aquatic Plants					
850.4400 Tier I and/or II	Tier II Aquatic plant growth, vascular plant — TGAI	44988415	Acceptable	No	If future proposed registrations result in surface water EECs greater/equal to the highest concentration tested in studies, additional toxicity testing may be recommended.
850.5400 Tier I and/or II	Tier II Aquatic Plant, freshwater green alga species — TGAI	44988414	Acceptable	No	
850.5400 Tier I and/or II	Tier II Aquatic Plant, freshwater diatom—TGAI	44988417	Acceptable	No	
850.5400 Tier I and/or II	Tier I Aquatic Plant, marine diatom — TGAI	44988418	Acceptable	No	
850.5400 Tier I and/or Tier II	Tier II Aquatic Plant, cyanobacterium — TGAI	44988416	Acceptable	No	

***** Study is being requested only if it has already been performed and is available from the registrant.

Table 14-3. Summary of Submitted Aquatic and Terrestrial Animal Effects Studies and Data Gaps for Degradates of Acetamiprid.

Guideline	Description—Test Substance	MRID(s)	Study Classification	Data Gap	Comments
Avian and Mammalian Testing					
850.2200	Avian dietary toxicity, waterfowl species—IM-1-4	44651862	Supplemental	No	
Aquatic Animal Testing					
850.1010	Freshwater invertebrate, acute toxicity, *Daphnia*—IC-0	44988409	Acceptable	No	

Guideline	Description—Test Substance	MRID(s)	Study Classification	Data Gap	Comments
850.1010	Freshwater invertebrate, acute toxicity, *Daphnia*—IM-1-2	44651867	Acceptable	No	
850.1010	Freshwater invertebrate, acute toxicity, *Daphnia*—IM-1-4	44651868	Acceptable	No	
Non-guideline	Freshwater invertebrate, acute toxicity, Non-biting midge—IM-1-5	46255610	Acceptable	No	
850.1035	Estuarine/Marine crustacean acute toxicity—IM-1-4	44651870	Acceptable	No	
850.1075	Freshwater fish, acute toxicity, cold water species—IM-1-4	44651865	Supplemental	No	
850.1300	Freshwater invertebrate, reproduction test—IM-1-5	46255609	Supplemental	No	

* Submission of additional data is recommended.

The following studies are technically data gaps but are not deemed necessary for risk assessment of acetamiprid at this time:

- *Avian Dietary Toxicity Studies – OCSPP 850.2200*

Two avian subacute dietary toxicity studies were submitted for acetamiprid (MRID 44651860, bobwhite quail; MRID 44651861, mallard duck). Both studies estimated the LC_{50} to be greater than the highest concentration tested (>5,000 mg/kg-diet). However, the bobwhite and mallard studies only tested two and three concentrations, respectively. OCSPP 850.2200 guidance states that a minimum of five concentrations of the test substance should be used during avian dietary toxicity definitive tests. Moreover, mortalities were observed at one or more concentration levels in both studies, which triggers full (*i.e.*, five concentrations) definitive tests in accordance with EFED's non-definitive endpoint guidance policy. Additionally, range-finding data were not submitted for the bobwhite quail study, which would help support the "greater than" LC_{50} result. The mallard duck study was conducted during two different time periods; initially, two test concentrations were evaluated followed by an additional test concentration two months later. However, given that the passerine oral toxicity data is at least one order of magnitude lower (more sensitive) than the avian sub-acute dietary data, requesting additional dietary studies is not likely to change the outcome of the risk assessment. It should also be noted that an avian dietary toxicity study (MRID48844901) of acetamiprid in the zebra finch has recently been submitted and is currently under review.

- *Freshwater Fish Life Cycle Test – OCSPP 850.1500*

40 CFR § 158.630 recommends that a freshwater fish life cycle test be conducted because EECs are greater than 0.1 multiplied by the NOAEC from mysid life cycle test (0.1 x NOAEC of Mysid shrimp 2.5 µg ai/L = 0.25; maximum EEC = 0.70 mg/L see **Appendix H**). However, reproductive and parental NOAECs in avian and mammalian reproduction studies were similar, suggesting that a reproductive endpoint in fish may also not be more sensitive than the parental endpoints. Additionally, when surface water EECs (0.00072 – 0.70 mg/L) generated in this problem formulation (**Appendix H**) and in previous assessments are compare to the fish early life stage toxicity endpoint for the fathead minnow (19.2 mg ai/L), it appears unlikely that effects to freshwater fish will occur with chronic exposure to acetamiprid at current use rates. In addition, NOAEC values from a fish early life-stage study on rainbow trout (NOAEC=0.918; MRID 44927829) and a fish full life cycle study on fathead minnows (NOAEC=0.718 mg ai/L; MRID 44927904) with another cyano-substituted neonicotinoid, thiacloprid, were similar, suggesting that a fish full life cycle with acetamiprid is not likely to yield a substantially lower NOAEC than the ELS study. Therefore, based on the weight of evidence, requesting a freshwater fish life cycle test is not likely to change the outcome of the risk assessment.

14.2.A. Testing on Typical End-Use Products (TEP)

A Typical End-Use Product is defined in the *Pesticide Assessment Guidelines Subdivision J Hazard Evaluation: Nontarget plants* on Part 120-2(1) on Page 18 as "a pesticide product that is representative of a major formulation category (*e.g*., emulsifiable concentrate, granular product, wettable powder) and pesticide group (*e.g*., herbicide, fungicide, insecticide *etc*.) and contains the active ingredient of the applicant's product." (Holst and Ellwanger, 1982) Page 5 of these guidelines provides additional information on what TEP data should be tested for toxicity testing in the following excerpt:

> "The Agency seeks to avoid imposing a burden of duplicative testing on applicants for registration. Therefore, where 40 CFR Part 158 specifies that the test substance should be a representative end-use product, testing may be performed using the formulation in question (end-use product being registered) or similar, yet representative, end-use product. It is not necessary to repeat the test using other similar products." (Holst and Ellwanger, 1982)

When TEP data are requested, data should be submitted for the different formulation types, *e.g*., wettable powder, emulsifiable concentrate, granular, along with a rationale as to why the TEP is representative of other similar end-use products.

14.3. Additional Information Needed on Specific Labels, Uses, and Formulation Types

Some of the labels do not contain enough information to estimate the exposure for particular uses without several assumptions. When such information is not provided, the Agency must rely on

standard assumptions. Such assumptions may be high-end, so that the Agency does not run the risk of underestimating risks. The information in question is discussed briefly below:

- EPA Registration Number WA110010

The label for EPA registration number WA110010 allows for control of apple maggots in non-agricultural quarantine and pest free areas (including residential areas) on apples, crabapples, pears, ornamental plants and trees, and non-bearing fruit and nut trees. The product is applied to give the tree uniform spray coverage of the plant. The label does not have a maximum single application rate. It does indicate that the product may be applied every 12 days, up to 4 times a year, with a maximum of 0.55 lbs ai/A/year.

- EPA Registration Number 8033-22

The label for EPA Registration Number 8033-22 does not have a maximum single application rate for any of the uses on ornamental and flowering plants grown outdoors and in greenhouses, shadehouses, and lathouses. Use instructions give a number of water soluble packets per gallons. The following use restrictions are provided:

  - Do not make more than five applications per year
  - Do not reapply more than once every seven days
  - Do not apply more than 0.55 lbs ai per year

- EPA Registration Number 8033-21

EPA Registration Number 8033-21 is a liquid ready-to-use product that may be used on ornamentals, houseplants, vegetables, citrus fruits, and pome fruits. Neither a maximum single application rate nor a maximum number of applications per crop cycle or per year is provided on the label.

- EPA Registration Number 8033-108

EPA Registration Number 8033-108 is a product for homeowner use. Use sites include gardens and houseplants. No maximum single application rate, maximum number of applications, or maximum application rate per year or crop cycle are provided.

- EPA Registration Number 8033-107

EPA Registration Number 8033-107 is a homeowner product registered for use on gardens, vegetables, pome fruits, grapes and other climbing vine small fruit (except fuzzy kiwifruit), tuberous and corm vegetables, stone fruit, cucurbits, tree nuts, edible podded and legume vegetables, succulent shelled peas, beans, blueberries and other bush and cane berries, onions, bulb vegetables, and houseplants. No maximum single application rate, maximum number of applications, or maximum application rate per year or crop cycle are provided.

- Agricultural Uses

Many agricultural product labels do not specify maximum number of applications per crop cycle or year or maximum application rate per year or crop cycle. A few uses on transplants provide a use rate in lbs ai/plant. As a high number of plants may be planted, this results in a very high estimated application rate per acre. A maximum single application rate in lbs ai/A or maximum number of plants treated per acre is needed to estimate exposure. In the absence of this information, EFED will use estimates on the maximum number of plants that may be planted per acre to estimate a maximum single application rate for these uses.

- Uses on Trees

Labels of two products allow for use of tree injections or basal bark treatments (EPA Reg No. 8033-94 and 8033-106) on ornamental and non-bearing fruit and nut trees. The use parameters on the labels are not well-defined. Use rates for trees are provided only as recommendations on these labels. The maximum annual application rate is not specified for any of the uses for trees. No maximum single or annual rate is provided for bark treatment. Minimum application intervals and the maximum number of applications per year are not specified. In addition, applications to individual trees are also not well-defined; a maximum amount of acetamiprid that can be applied per diameter of the tree is needed to determine exposure and potential risks associated with applications to individual trees. Finally, it would also be helpful define a maximum amount of acetamiprid that can be applied to individual trees per acre or info on a maximum number of trees that could be treated per acre with various diameter at breast heights (DBH). It would also be useful to specify the types of sites for which the product is intended (*e.g.*, forest, tree production, residential, *etc.*).

- Termiticides, Ant Control, and Control of other Pests

For termiticide, ant control, and the control of other miscellaneous pests around buildings, structures, equipment, paths, wood products, etc., a maximum single application rate per acre, maximum number of applications, and maximum application per year should also be provided on labels. For mound treatments, in the absence of additional information, EFED will use estimates on the maximum number of mounds per acre that may occur to estimate an application rate. For perimeter treatments, a maximum distance from the edge of the building that may be treated should be provided. In the absence if additional information provided on the labels, EFED will make conservative assumptions for these uses.

- Bait Treatments (Gels)

Some labels provide an application rate per spot. A maximum single application rate per acre or other unit area, maximum number of applications, and maximum application per year should be provided on labels. In the absence of this information, EFED will use estimates on the maximum number of mounds per acre that may occur in order to estimate an application rate.

- Seed Treatments

Acetamiprid may be used to treat mustard, canola, and potato seed pieces. For seed treatment uses, the following information is needed:

  - Number of seeds (treated seeds, if encapsulated) per pound
  - Number of treated seeds per acre or pound of treated seed per acre
  - Amount of active ingredient per treated seed or cwt of seed
  - Minimum planting depth
  - Identify where the treatment is for commercial use only or commercial and "on farm" treatments can be made

- Uses on Cranberries

Acetamiprid may be used on cranberries. The use directions for cranberries are combined with use instructions for other berries that do not have a portion of the crop that is flooded. More information is needed on the labels describing use of acetamiprid on cranberries because cranberries are grown in cranberry bogs and may involve direct applications to water. For uses that may involve direct applications to water, it is recommended that the following information be included on the label so that exposure may be estimated.

  - The maximum target concentration in water must be specified on the label (specify if there is a requirement to test the water body for stratification to calculate the application rate)
  - Describe the period of time water must be held before it is released
- Granular Formulations

In order to assess the risk to terrestrial organisms exposed to baits or granules not in a container or bait station the weight of one granule or number of granules per unit weight for each granular formulation would be useful.

14.4. Other Information Needs

There is specific information that will assist the Agency in refining the ecological risk assessment, including any species-specific effects determinations. The Agency is very much interested in obtaining the following information:

- Confirmation on the following label information
  - Frequency of application, application intervals, and maximum number of applications per season
  - Geographic limitations on use
- Use or potential use distribution (*e.g.*, acreage and geographical distribution of relevant crops)
- Use history

- Median and 90th percentile reported use rates (lbs. ai/acre) from usage data – national, state, and county
- Application timing (date of first application and application intervals) by crop – national, state, and county
- Sub-county crop location data
- Directly acquired county-level usage data (not derived from state level data)
    - Maximum reported use rate (lbs. ai/acre) from usage data – county
    - Percent crop treated – county
    - Median and 90th percentile number of applications – county
    - Total pounds per year – county
    - The year the pesticide was last used in the county/sub-county area
    - The years in which the pesticide was applied in the county/sub-county area
- State or local use restrictions
- Ecological incidents (non-target plant damage and avian, fish, reptilian, amphibian and mammalian mortalities) not already reported to the Agency
- Monitoring data

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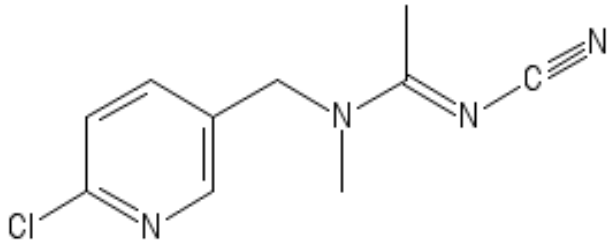
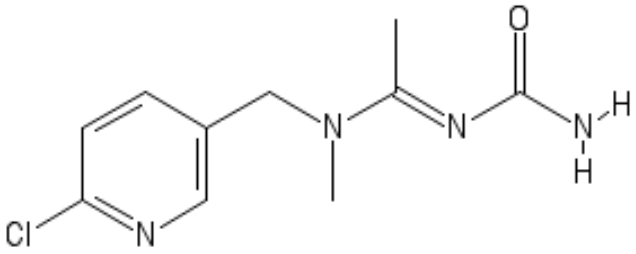
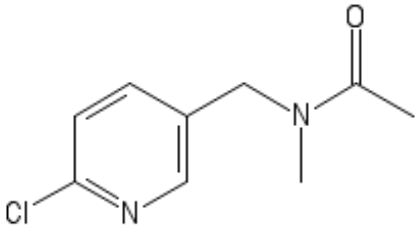
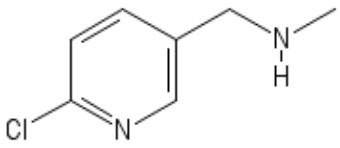
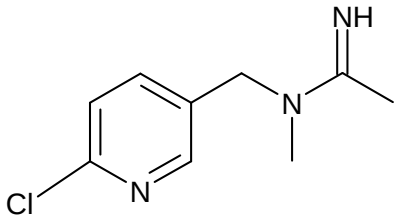
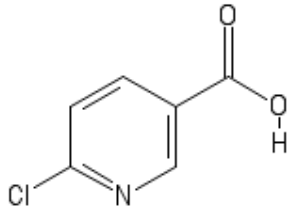
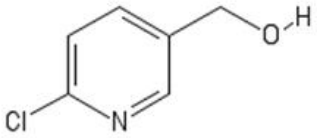
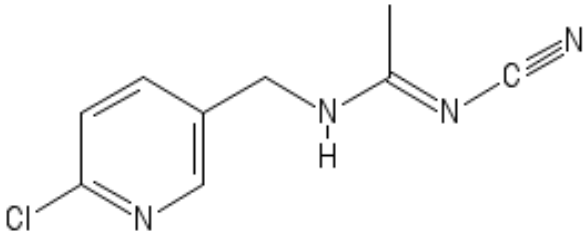
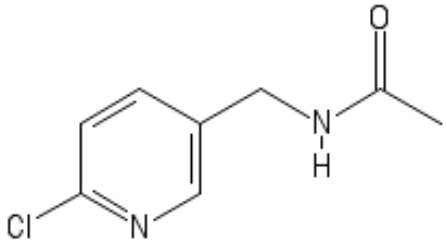
Appendix A. Supplemental Environmental Fate Information

Table A1. Structures of Acetamiprid and Its Environmental Transformation Products.

Code Name/ Synonym/ Chemical Name/ Formula/MW/ SMILES	Chemical Structure
Acetamiprid **IUPAC:** (E)-N^1-[(6-chloro-3-pyridyl)methyl]-N^2-cyano-N^1-methyl **CAS:** (1*E*)-*N*-[(6-chloro-3-pyridinyl)methyl]-*N*'-cyano-*N*-methylethanimidamide **CAS No.:** 135410-20-7 **Formula:** $C_{16}H_{11}CLN_4$ **MW:** 222.68 g/mol **SMILES:** Clc1ncc(cc1)CN(\C(=N\C#N)C)C	
IM-1-2 **IUPAC:** N^2-carbamoyl-N^1-[(6-chloro-3-pyridyl)methyl]-N^1-methylacetamidine **Formula:** $C_{10}H_{13}ClN_4O$ **MW:** 240.69 g/mol **SMILES:** C/C(=N\C(=O)N)/N(C)Cc1ccc(nc1)Cl	
IM-1-3 **IUPAC:** N-[(6-chloro-3-pyridyl)methyl]-N-methylacetamide **Formula:** $C_9H_{11}ClN_2O$ **MW:** 198.65 g/mol **SMILES:** CC(=O)N(C)Cc1ccc(nc1)Cl	
IM-1-4 **IUPAC:** N-methyl(6-chloro-3-pyridyl)methylamine **MW:** 155.5 g/mole **SMILES:** C1=C(C=CC(=C1)CN(C)[H])Cl	

Code Name/ Synonym/ Chemical Name/ Formula/MW/ SMILES	Chemical Structure
IM-1-5 **IUPAC:** (E)-N1-[(6-chloro-3-pyridyl)-methyl]-N2-cyano-N1-methylacetamidine SMILES: C1=CC(=NC=C1CN(C)C(C)=N)Cl	
IC-0 **IUPAC:** 6-Chloronicotinic acid **Formula:** $C_6H_4ClNO_2$ **MW:** 157.55 g/mol **SMILES:** c1cc(ncc1C(=O)O)Cl	
IM-0 **IUPAC: (**6-Chloro-3-pyridyl)methanol **Formula:** C_6H_6ClNO **MW:** 143.57 g/mol **SMILES:** c1cc(ncc1CO)Cl	
IM-2-1 **IUPAC:** N^1-[(6-chloro-3-pyridyl)methyl]-N^2-cyanoacetamidine **Formula:** $C_9H_9ClN_4$ **MW:** 208.65 g/mol **SMILES:** C/C(=N\C#N)/NCc1ccc(nc1)Cl	
IM-2-3 **IUPAC:** N-[(6-chloro-3-pyridyl)methyl]acetamide **Formula:** $C_8H_9ClN_2O$ **MW:** 184.62 g/mol **SMILES:** CC(=O)NCc1ccc(nc1)Cl	

Abbreviations MW =molecular weight; IUPAC: International Union of Pure and Applied Chemistry name; SMILES: Simplified Molecular-input Line-entry System

Table A2. Maximum amount of applied radioactivity present as a specified compound in environmental fate studies submitted on acetamiprid.

Compound	Max %AR (Sampling Interval)	Final %AR (Sampling Interval)	Comment	Study Type	MRID
Acetamiprid	Not Applicable	95 (35 days)	pH 4 all temps	Hydrolysis	44651876
		97. (35 days)	pH 5 all temps	Hydrolysis	44651876
		93 (35 days)	pH 7 all temps	Hydrolysis	44651876
		88 (35 days)	pH 9 all temps	Hydrolysis	44651876
		54 (30 days)	Water	Aqueous Photolysis	44688509
		27 (24 days)	Loamy sand	Soil Photolysis	48563501
		1 (187 days)	Sandy Loam 01/07	Aerobic Soil	46255603
		1 (187 days)	Clay loam 01/08	Aerobic Soil	46255603
		1 (187 days)	Clay loam 01/10	Aerobic Soil	46255603
		<1 (112 days)	Collumbey soil	Aerobic Soil	44699101
		<1 (365 days)	Loamy sand	Aerobic Soil	44651879
		nd (7 days)	Sandy Loam	Aerobic Soil	44651880
		46 (182 days)	Clay loam, 20°C	Aerobic Soil	44651881
		3 (182 days)	Sandy loam, 20°C	Aerobic Soil	44651881
		<1 (182 days)	Silty clay loam, 20°C	Aerobic Soil	44651881
		4 (178 days)	Clay loam, 10°C	Aerobic Soil	44651881
		2 (125 days)	Sandy loam	Anaerobic Soil	48554501
		17 (127 days)	Clay loam	Anaerobic Soil	48554501
		5 (300 days)	Sandy loam	Aerobic Aquatic	44988513
		52 (365 days)	Loamy sand	Anaerobic Aquatic	44988512
IM-1-4	<1 (0 days)	<1 (35 days)	pH 4 all temps	Hydrolysis	44651876
	<1 (0 days)	<1 (35 days)	pH 5 all temps	Hydrolysis	44651876
	<1 (35 days)	<1 (35 days)	pH 7 all temps	Hydrolysis	44651876
	15 (35 days)	15 (35 days)	pH 9 all temps	Hydrolysis	44651876
	nd	nd	Water	Aqueous Photolysis	44688509
	32 (24 d)	32 (24 d)	Loamy sand	Soil Photolysis	48563501
	21 (7 days)	1 (187 days)	Sandy Loam 01/07	Aerobic Soil	46255603
	21 (7 days)	<1 (187 days)	Clay loam 01/08	Aerobic Soil	46255603
	18 (7 days)	1 (187 days)	Clay loam 01/10	Aerobic Soil	46255603
	61 (7 days)	26 (112 days)	Collumbey soil	Aerobic Soil	44699101
	73 (120 days)	61 (365 days)	Loamy sand	Aerobic Soil	44651879
	16 (7 days)	16 (7 days)	Sandy Loam	Aerobic Soil	44651880
	56 (14 days)	37 (182 days)	Clay loam, 20°C	Aerobic Soil	44651881
	73 (14 days)	42 (182 days)	Sandy loam, 20°C	Aerobic Soil	44651881
	67 (3 days)	1 (182 days)	Silty clay loam, 20°C	Aerobic Soil	44651881
	73 (30 days)	54 (178 days)	Clay loam, 10°C	Aerobic Soil	44651881
	64 (61 days)	61 (125 days)	Sandy loam	Anaerobic Soil	48554501
	49 (93 days)	46 (127 days)	Clay loam	Anaerobic Soil	48554501
	64 (60 days)	34 (300 days)	Sandy loam	Aerobic Aquatic	44988513
	27 (270 days)	27 (270 days)	Loamy sand	Anaerobic Aquatic	44988512
IM-1-5	na	na	pH 4 all temps	Hydrolysis	44651876
	na	na	pH 5 all temps	Hydrolysis	44651876

Compound	Max %AR (Sampling Interval)	Final %AR (Sampling Interval)	Comment	Study Type	MRID
	na	na	pH 7 all temps	Hydrolysis	44651876
	na	na	pH 9 all temps	Hydrolysis	44651876
	nd	nd	Water	Aqueous Photolysis	44688509
	na	na	Loamy sand	Soil Photolysis	48563501
	16 (187 days)	16 (187 days)	Sandy Loam 01/07	Aerobic Soil	46255603
	12 (187 days)	12 (187 days)	Clay loam 01/08	Aerobic Soil	46255603
	13 (7 days)	8 (187 days)	Clay loam 01/10	Aerobic Soil	46255603
	na	na	Collumbey soil	Aerobic Soil	44699101
	na	na	Loamy sand	Aerobic Soil	44651879
	na	na	Sandy Loam	Aerobic Soil	44651880
	na	na	Clay loam, 20°C	Aerobic Soil	44651881
	nd	nd	Sandy loam, 20°C	Aerobic Soil	44651881
	22 (13 days)	13 (182 days)	Silty clay loam, 20°C	Aerobic Soil	44651881
	nd	nd	Clay loam, 10°C	Aerobic Soil	44651881
	na	na	Sandy loam	Anaerobic Soil	48554501
	na	na	Clay loam	Anaerobic Soil	48554501
	na	na	Sandy loam sediment	Aerobic Aquatic	44988513
	na	na	Loamy sand sediment	Anaerobic Aquatic	44988512
IC-0	na	na	pH 4 all temps	Hydrolysis	44651876
	na	na	pH 5 all temps	Hydrolysis	44651876
	na	na	pH 7 all temps	Hydrolysis	44651876
	na	na	pH 9 all temps	Hydrolysis	44651876
	nd	nd	Water	Aqueous Photolysis	44688509
	16 (24 days)	16 (24 days)	Loamy sand	Soil Photolysis	48563501
	5.2 (7 days)	nd (187 days)	Sandy Loam 01/07	Aerobic Soil	46255603
	7 (7 days)	nd (187 days)	Clay loam 01/08	Aerobic Soil	46255603
	10 (7 days)	nd (187 days)	Clay loam 01/10	Aerobic Soil	46255603
	11 (4 days)	1 (112 days)	Collumbey soil	Aerobic Soil	44699101
	5 (60 days)	3 (365 days)	Loamy sand	Aerobic Soil	44651879
	11 (2 days)	10 (7 days)	Collumbey Sandy	Aerobic Soil	44651880
	11 (120 days)	4 (182 days)	Clay loam, 20°C	Aerobic Soil	44651881
	4 (120 days)	3 (182 days)	Sandy loam, 20°C	Aerobic Soil	44651881
	12 (7 days)	nd (182 days)	Silty clay loam, 20°C	Aerobic Soil	44651881
	3 (178 days)	3 (178 days)	Clay loam, 10°C	Aerobic Soil	44651881
	3 (125 days)	3 (125 days)	Sandy loam	Anaerobic Soil	48554501
	1 (127 days)	1 (127 days)	Clay loam	Anaerobic Soil	48554501
	19 (180 days)	nd (300 days)	Sandy loam sediment	Aerobic Aquatic	44988513
	nd	nd (187 days)	Loamy sand sediment	Anaerobic Aquatic	44988512
IM-1-2	na	na	pH 4 all temps	Hydrolysis	44651876
	na	na	pH 5 all temps	Hydrolysis	44651876
	na	na	pH 7 all temps	Hydrolysis	44651876
	na	na	pH 9 all temps	Hydrolysis	44651876
	nd	nd	Water	Aqueous Photolysis	44688509
	0.7 (7 d)	nd (24 d)	Loamy sand	Soil Photolysis	48563501
	36 (1 day)	nd (187 days)	Sandy Loam 01/07	Aerobic Soil	46255603

Compound	Max %AR (Sampling Interval)	Final %AR (Sampling Interval)	Comment	Study Type	MRID
	29 (3 days)	nd (187 days)	Clay loam 01/08	Aerobic Soil	46255603
	28 (1 days)	nd (187 days)	Clay loam 01/10	Aerobic Soil	46255603
	8 (1 day)	nd (112 days)	Collumbey soil	Aerobic Soil	44699101
	nd	nd	Loamy sand	Aerobic Soil	44651879
	55 (1 day)	nd (7 day)	Collumbey Sandy	Aerobic Soil	44651880
	<LOQ (2 days)	nd (182 days)	Clay loam, 20°C	Aerobic Soil	44651881
	nd	nd	Sandy loam, 20°C	Aerobic Soil	44651881
	<LOQ (1 day)	nd (182 days)	Silty clay loam, 20°C	Aerobic Soil	44651881
	<LOQ (2 days)	nd (182 days)	Clay loam, 10°C	Aerobic Soil	44651881
	4 (5 days)	Nd (125 days)	Sandy loam	Anaerobic Soil	48554501
	3 (7 days)	Nd (127 days)	Clay loam	Anaerobic Soil	48554501
	21 (30 days)	0.74 (300 days)	Sandy loam sediment	Aerobic Aquatic	44988513
	1 (90 days)	nd (365 days)	Loamy sand sediment	Anaerobic Aquatic	44988512
IM-0	na	na	pH 4 all temps	Hydrolysis	44651876
	na	na	pH 5 all temps	Hydrolysis	44651876
	na	na	pH 7 all temps	Hydrolysis	44651876
	na	na	pH 9 all temps	Hydrolysis	44651876
	nd	nd	Water	Aqueous Photolysis	44688509
	nd	nd	Loamy sand	Soil Photolysis	48563501
	nd	nd	Sandy Loam 01/07	Aerobic Soil	46255603
	2.21 (7 days)	nd (187 days)	Clay loam 01/08	Aerobic Soil	46255603
	1 (14 days)	nd (187 days)	Clay loam 01/10	Aerobic Soil	46255603
	na	na	Collumbey soil	Aerobic Soil	44699101
	na	na	Loamy sand	Aerobic Soil	44651879
	na	na	Collumbey Sandy	Aerobic Soil	44651880
	na	na	Clay loam, 20°C	Aerobic Soil	44651881
	na	na	Sandy loam, 20°C	Aerobic Soil	44651881
	na	na	Silty clay loam, 20°C	Aerobic Soil	44651881
	na	na	Clay loam, 10°C	Aerobic Soil	44651881
	2 (1 day)	nd (125 days)	Sandy loam	Anaerobic Soil	48554501
	nd	nd	Clay loam	Anaerobic Soil	48554501
	na	na	Sandy loam sediment	Aerobic Aquatic	44988513
	na	na	Loamy sand sediment	Anaerobic Aquatic	44988512
IM-1-3	<1 (15 days)	<1 (35 days)	pH 4 all temps	Hydrolysis	44651876
	<1 (35 days)	<1 (35 days)	pH 5 all temps	Hydrolysis	44651876
	4 (22 days)	4 (35 days)	pH 7 all temps	Hydrolysis	44651876
	61 (35 days)	61 (35 days)	pH 9 all temps	Hydrolysis	44651876
	nd	nd	Water	Aqueous Photolysis	44688509
	4 (24 days)	4 (24 days)	Loamy sand	Soil Photolysis	48563501
	nd	nd	Sandy Loam 01/07	Aerobic Soil	46255603
	3 (7 days)	nd (187 days)	Clay loam 01/08	Aerobic Soil	46255603
	2 (7 days)	nd (187 days)	Clay loam 01/10	Aerobic Soil	46255603
	3 (4 days)	nd (112 days)	Collumbey soil	Aerobic Soil	44699101
	3 (60 days)	<1 (365 days)	Loamy sand	Aerobic Soil	44651879
	nd	nd (7 days)	Collumbey Sandy	Aerobic Soil	44651880

Compound	Max %AR (Sampling Interval)	Final %AR (Sampling Interval)	Comment	Study Type	MRID
	3 (28 days)	<1 (182 days)	Clay loam, 20°C	Aerobic Soil	44651881
	<LOQ (14 days)	<LOQ (14 days)	Sandy loam, 20°C	Aerobic Soil	44651881
	2 (7 days)	0.71 (182 days)	Silty clay loam, 20°C	Aerobic Soil	44651881
	2 (122 days)	2 (122 days)	Clay loam, 10°C	Aerobic Soil	44651881
	3 (5 days)	3 (125 days)	Sandy loam	Anaerobic Soil	48554501
	2 (24-127 days)	2 (127 days)	Clay loam	Anaerobic Soil	48554501
	1 (90 days)	nd (300 days)	Sandy loam sediment	Aerobic Aquatic	44988513
	8 (180 days)	6 (365 days)	Loamy sand sediment	Anaerobic Aquatic	44988512
IM-2-1	3 (17 days)	2 (24 days)	Loamy sand	Soil Photolysis	48563501
	nd	nd	Sandy loam	Anaerobic Soil	48554501
	nd	nd	Clay loam	Anaerobic Soil	48554501
IM-2-3	nd	nd	Loamy sand	Soil Photolysis	48563501
	2 (5 days)	nd (125days)	Sandy loam	Anaerobic Soil	48554501
	1 (11 days)	nd (127 days)	Clay loam	Anaerobic Soil	48554501
Unidentified Compound	3 (14 days)	nd (187 days)	Sandy Loam 01/07	Aerobic Soil	46255603
	1 (14 days)	nd (187 days)	Clay loam 01/08	Aerobic Soil	46255603
	4 (187 days)	4 (187 days)	Clay loam 01/10	Aerobic Soil	46255603
	4 (4 days)	nd (112 days)	Collumbey soil	Aerobic Soil	44699101
	2 (3 days)	nd (365 days)	Loamy sand	Aerobic Soil	44651879
	12 (7 days)	12 (7 days)	Collumbey Sandy	Aerobic Soil	44651880
	3 (56 days)	2 (182 days)	Clay loam, 20°C	Aerobic Soil	44651881
	<1 (56 days)	<1 (56 days)	Sandy loam, 20°C	Aerobic Soil	44651881
	<1 (7 days)	nd (182 days)	Silty clay loam, 20°C	Aerobic Soil	44651881
	<1 (182 days)	<1 (182 days)	Clay loam, 10°C	Aerobic Soil	44651881
Unextracted Residues	26 (118 days)	19 (187 days)	Sandy Loam 01/07	Aerobic Soil	46255603
	31 (28 days)	20 (187 days)	Clay loam 01/08	Aerobic Soil	46255603
	29 (14 days)	28 (187 days)	Clay loam 01/10	Aerobic Soil	46255603
	16 (112 days)	16 (112 days)	Collumbey soil	Aerobic Soil	44699101
	21 (365 days)	21 (365 days)	Loamy sand	Aerobic Soil	44651879
	14 (7 days)	14 (7 days)	Collumbey Sandy	Aerobic Soil	44651880
	40 (182 days)	40 (182 days)	Clay loam, 20°C	Aerobic Soil	44651881
	26 (182 days)	26 (182 days)	Sandy loam, 20°C	Aerobic Soil	44651881
	21 (28 days)	18 (182 days)	Silty clay loam, 20°C	Aerobic Soil	44651881
	25 (178 days)	25 (178 days)	Clay loam, 10°C	Aerobic Soil	44651881
	31 (91 days)	30 (125 days)	Sandy loam	Anaerobic Soil	48554501
	42 (93 days)	36 (127 days)	Clay loam	Anaerobic Soil	48554501
	38 (300 days)	38 (300 days)	Sandy loam sediment	Aerobic Aquatic	44988513
	17 (270 days)	17 (365 days)	Loamy sand sediment	Anaerobic Aquatic	44988512
CO_2	3 (16-24 days)	3 (24 days)	Loamy sand	Soil Photolysis	48563501
	52 (118 days)	50 (187 days)	Sandy Loam 01/07	Aerobic Soil	46255603
	54 (91 days)	54 (187 days)	Clay loam 01/08	Aerobic Soil	46255603
	57 (118 days)	51 (187 days)	Clay loam 01/10	Aerobic Soil	46255603
	<1 (30 days)	<1 (30 days)	Water	Aqueous photolysis	44688509
	56 (112 days)	56 (112 days)	Collumbey soil	Aerobic Soil	44699101
	19 (270 days)	12 (365 days)	Loamy sand	Aerobic Soil	44651879

Compound	Max %AR (Sampling Interval)	Final %AR (Sampling Interval)	Comment	Study Type	MRID
	44 (7 days)	44 (7 days)	Collumbey Sandy	Aerobic Soil	44651880
	1 (9 days)	0.3 (125 days)	Sandy loam	Anaerobic Soil	48554501
	0.6 (3 days)	0.4 (127 days)	Clay loam	Anaerobic Soil	48554501
	5 (300 days	5 (300 days)	Sandy loam	Aerobic Aquatic	44988513
	1 (365 days)	1 (365 days)	Loamy sand sediment	Anaerobic Aquatic	44988512

na=not analyzed; nd=not detected; AR=applied radioactivity
If a study is not listed under a specific analyte, it was not analyzed in the study.

Table A3. Summary of environmental fate and transport properties of IC-0 (6-chloronicotinic acid), a degradate of acetamiprid

Parameter	Value(s)	Source	Study Classification	Comment
Aerobic Soil Metabolism Half-life	Half-life, linear regression[1]: 2.5 days (sandy loam soil at 20°C) 1.7 days (clay soil at 20°C) 6.6 days (loam soil at 20°C)	MRID 44651882	Supplemental	British soils and USDA classification could not be determined. Unextracted residues ranged from 3.1-20.7% of applied radioactivity. Half-lives calculated using a subset of data for clay and loam soils.
Solid-water distribution coefficient (Kd)	Average K_d in L/kg at 20°C: 0.44, loamy sand, pH 4.4 0.83, loam sand II, pH 6.2 0.28, silt loam, pH 6.6 0.28, clay, pH 7.5 2.36, sandy loam sediment, pH 5.6	MRID 44651884	Acceptable	
Freundlich solid-water distribution coefficient (KF)	K_F in L/kg (1/n) at 20°C: 0.40 (0.91), loamy sand, pH 4.4 0.79 (1.0), loam sand II, pH 6.2 0.26 (0.94), silt loam, pH 6.6 0.19 (0.82), clay, pH 7.5 1.81 (0.86), sandy loam sediment, pH 5.6	MRID 44651884	Acceptable	Freundlich exponents indicate that sorption was dependent on concentration in some soils.
Organic-carbon normalized distribution coefficient (KOC)	Average K_{OC} in L/kg OC at 20°C: 177, loamy sand, pH 4.4 56, loam sand II, pH 6.2 64, silt loam, pH 6.6 34, clay, pH 7.5 94, sandy loam sediment, pH 5.6	MRID 44651884	Acceptable	None

Appendix B. Summary of Available Effects Studies

Aquatic Organisms

Tables B1 to **B7** contain all available aquatic toxicity endpoints from registrant-submitted studies. Below is a brief summary of available aquatic toxicity studies.

Fish and Aquatic-Phase Amphibians

Two acute toxicity studies (**Table B1**) have been submitted examining the effect of acetamiprid on freshwater fish. A 96-hr flow-through study with the bluegill sunfish (*Lepomis macrochirus*; MRID 44651863) was conducted at measured concentrations of 0 (control), 11.8, 20.0, 35.4, 65.0 and 119.3 mg ai/L. No mortality was observed in any of the test concentrations with the LC_{50} >100 mg ai/L. Darkened body pigmentation was observed in all fish at all treatments, therefore the NOAEC for the study, based on alterations in fish coloration is <11.8 mg ai/L. A 96-hr flow-through study was conducted with rainbow trout (*Oncorhynchus mykiss*; MRID 44651864) at nominal concentrations of 0 (control), 25, 35, 50, 70 and 100 mg ai/L. Mortality was limited to 20% at the highest concentration, with the LC_{50}>100 mg ai/L. However, sublethal effects, including darkened body pigmentation, swollen abdomen and loss of equilibrium were reported in 20% of the fish at both the 50 and 70 mg ai/L concentrations and 90% at the 100 mg ai/L concentration. The NOAEC for the study is 35 mg ai/L. Acetamiprid is classified as practically nontoxic to freshwater fish on an acute exposure basis, however sublethal effects were noted.

A 96-hr static renewal acute exposure study of the effects of the degradate IM-1-4 on rainbow trout is available (MRID 44651865) (**Table B1**). The fish were exposed at measured concentrations of 4.3, 8.5, 16.9, 33.8, 69.3 and 98.1 mg ai/L. The 98.1 mg ai/L concentration was buffered and conducted separately after mortality of 100% was observed in the unbuffered 69.3 mg ai/L concentration. The pH of the 69.3 mg ai/L replicates ranged from 9.0 to 9.3, which may account for the mortality. No mortalities were reported in the other concentrations. Sublethal effects, including darkened body pigmentation and surface swimming were observed in all concentrations above 4.3 mg ai/L (the NOAEC for the study). The LC_{50} is >98.1 mg ai/L; the degradate IM-1-4 is classified as practically nontoxic to freshwater fish on an acute exposure basis.

Table B1. Acute toxicity of technical grade acetamiprid and degradate IM-1-4 to freshwater fish.

Species	Test substance	LC_{50} mg ai/L	Toxicity Category	MRID	Study Classification
Rainbow trout (*Oncorhynchus mykiss*)	Technical acetamiprid	>100	Practically non-toxic	44651864	Acceptable
Bluegill sunfish (*Lepomis macrochirus*)	Technical acetamiprid	>100	Practically non-toxic	44651863	Acceptable
Rainbow trout (*Oncorhynchus mykiss*)	94.5% IM-1-4 degradate	>98.1	Practically non-toxic	44651865	Supplemental

In a 96-h flow-through acute toxicity study (**Table B2**), estuarine/marine sheepshead minnows (*Cyprinodon variegatus*) were exposed to measured acetamiprid concentrations of 0 (control), 19, 32, 54, 90 and 150 mg ai/L. Mortality was 10% in the 90 mg ai/L and 100% in the 150 mg ai/L test concentrations. Lethargy was observed in all of the surviving fish at the 90 mg ai/L treatment level. No other sublethal effects were reported. The 96-hr LC_{50} is 100 mg ai/L, which classifies acetamiprid as slightly toxic to estuarine/marine fish on an acute exposure basis.

Table B2. Acute toxicity of technical grade acetamiprid to estuarine/marine fish.

Species	Test Substance	LC_{50} mg ai/L	Toxicity Category	MRID	Study Classification
Sheepshead minnow *(Cyprinodon variegatus)*	Technical acetamiprid	**100***	Slightly toxic	44988411	Acceptable

* Most sensitive endpoint

A 35-day flow-through fish early life stage toxicity study (MRID 44651872) was submitted to evaluate the effect of chronic exposure on freshwater fish. Fathead minnow (*Pimephales promelas*) were exposed to acetamiprid at measured concentrations of 9.9, 19.2, 38.4, 76.0, and 147.5 mg ai/L. Mortalities were reported at 5% 20% and 100% in concentrations 38.4, 76.0 and 147.5 mg ai/L, respectively. Weights were reduced 17% and 62% at concentrations 38.4 and 76.0 mg ai/L. The lowest observed adverse effect concentration (LOAEC) for the study is 38.4 mg ai/L based on decreased survival and growth. The NOAEC is 19.2 mg ai/L (**Table B3**).

No chronic toxicity data have been submitted for estuarine/marine fish.

Table B3. Early life-stage toxicity of technical grade acetamiprid to freshwater fish.

Species	Test Substance	NOAEC	LOAEC	Endpoints Affected	MRID	Study Classification
Fathead minnow *(Pimphales promelas)*	Technical acetamiprid	**19.2 mg ai/L***	38.4 mg ai/L	Embryo and larval survival, larval growth (wet-weight and length)	44651872	Supplemental

* Most sensitive endpoint

Aquatic Invertebrates

An acute toxicity study was submitted to assess the effect of acetamiprid on the water flea (*Daphnia magna*; MRID 44651866) at nominal concentrations of 0 (control), 12.5, 25, 50, 100 and 200 mg ai/L. Immobile daphnids were observed at 20%, 45%, 85% and 100% at concentrations of 25, 50, 100 and 200 mg ai/L. The LC_{50} for daphnids is 50 mg ai/L and the NOAEC, based on immobility, is 12.5 mg ai/L (**Table B4**).

A 96-hr acute toxicity study (MRID 45932501) was submitted for the freshwater amphipod, *Gammarus fasciatus*. Test organisms were exposed at measured concentrations of 0 (control), 9.4, 18, 33, 76 and 140 µg ai/L. Mortality was 5% in the control and 0, 10, 40, 35 and 70%, in the treatment groups respectively. Lethargy was observed at the 33 µg ai/L concentration and higher. The LC_{50} is 80 µg ai/L and the NOAEC is 18 µg ai/L based on lethargy. The slope of the dose-response curve is 1.89. Based on a 96-hr LC_{50} value of 80 µg ai/L, acetamiprid is classified as very highly toxic to freshwater invertebrates on an acute exposure basis.

The 48-hour acute toxicity of acetamiprid (technical) to the midge, *Chironomus riparius*, was studied under static conditions (MRID 45916201). Test organisms were exposed to negative control, solvent (acetone) control and test chemical at a single dosing nominal concentrations of 6.3, 13, 25, 50, and 100 µg/L (corresponding mean-measured concentrations were 6.0, 14, 26, 46 and 110 µg ai/L) in overlying water. Mortality was recorded at 0, 24 and 48 hours. After 48 hours of static exposure to acetamiprid in the presence of sediment, the 48-hr LC_{50} is 20.9 µg ai/L based on mean-measured concentrations. The NOAEC is 6 µg ai/L, based on mortality.

An aquatic invertebrate study with acetamiprid was identified in the ECOTOX database (Beketov and Liess, 2008). In this study, amphipods (*Gammarus pulex*), blackfly larvae (*Simulium latigonium*), and mayfly larvae (*Baetis rhodani*) were exposed to as single concentration of acetamiprid for 96 hours under static conditions; LC_{50} values were subsequently determined. The results and scientific soundness of this study will be evaluated prior to endpoint selection for the upcoming acetamiprid registration review risk assessment.

The 48-hr-acute toxicity of the IM-1-4 degradate to *Daphnia magna* was studied under static renewal conditions at mean measured concentrations of 6.9, 13.9, 28.0, 55.9 and 113.0 mg ai/L. The 48- hour EC_{50} was 43.9 mg ai/L. The NOAEC based on mortality/immobilization was 6.9 mg ai/L. Based on the results of this study, IM-1-4 is classified as slightly toxic to *Daphnia magna*. Two other acute exposure studies evaluating the toxicity of acetamiprid degradates IC-0 and IM-1-2 to daphnids are available, and resulted in EC_{50} values that were greater than the highest concentration tested; therefore, these degradates are classified as practically non-toxic to daphnids on an acute exposure basis.

In a 48-hour static acute toxicity study, effects of the acetamiprid degradate IM-1-5 to the sediment-dwelling freshwater midge, *Chironomus riparius*, were assessed (MRID 46255610). Test organisms were exposed to mean-measured concentrations (in the overlying water) of 0 (control), 6.0, 14, 26, 46 and 110 µg ai/L. The 48-hr LC_{50} is 68 mg ai/L based on mean-measured concentrations. The NOAEC is 49 mg ai/L, based on mortality. The acetamiprid degradate IM-1-5 is classified as slightly toxic to freshwater invertebrates on an acute exposure

basis.

Table B4. Acute toxicity of acetamiprid and degradates to freshwater invertebrates.

Species	Test substance	EC_{50}/LC_{50} mg ai/L	Toxicity Category	MRID	Study Classification
Waterflea *(Daphnia magna)*	Technical acetamiprid	50	Slightly toxic	44651866	Supplemental
Amphipod *(Gammarus fasciatus)*	Technical acetamiprid	0.08	Very highly toxic	45932501	Supplemental
Midge (*Chironomus riparius*)	Technical acetamiprid	**0.021***	Very highly toxic	45916201	Supplemental
Waterflea *(Daphnia magna)*	99.7% IC-0 degradate	>95.1	Practically non-toxic	44988409	Acceptable
Waterflea *(Daphnia magna)*	99.6%IM-1-2 degradate	>99.8	Practically non-toxic	44651867	Acceptable
Waterflea *(Daphnia magna)*	98.7% IM-1-4 degradate	43.9	Slightly toxic	44651868	Acceptable
Midge (*Chironomus riparius*)	98.9% IM-1-5 degradate	68	Slightly toxic	46255610	Acceptable

* Most sensitive endpoint

In a 96-hr acute flow-through toxicity study, mysid shrimp (*Americamysis bahia*) were exposed to mean measured concentrations of 0 (control), 13, 23, 36, 64 and 110 µg ai/L. Mortality was 5%, 10% and 35% and 90% in the 23, 36, 64 and 110 µg ai/L treatment levels respectively. Lethargy was reported in all of the surviving mysids exposed to the 64 and 110 µg ai/L treatment levels. The LC_{50} is 66 µg ai/L and the NOAEC is 13 µg ai/L based on lethargy; acetamiprid is classified as very highly toxic to mysid shrimp on an acute exposure basis (**Table B5**).

In a 96-hr-acute flow-through toxicity study, Eastern oysters (*Crassostrea virginica*) were exposed to mean measured concentrations of 0 (control), 14, 24, 38, 58 and 100 mg a.i/L. No mortality was observed. Shell growth among oysters exposed to the 24, 38, 58 and 100 mg ai/L test concentrations was 2.1, 1.7, 0.80 and 0.41 mm respectively, which was significantly reduced compared to control growth (2.9 mm). The 96-hr EC_{50} for shell growth inhibition is 41 mg a.i/L; therefore, acetamiprid is classified as slightly toxic to eastern oysters on an acute exposure basis.

In a 96-hr static acute toxicity study with the degradate IM-1-4, mysid shrimp (*A. bahia*) were exposed to mean measured concentrations of 0 (control), 3.2, 6.7, 14, 27, 55 and 110 mg a.i/L. Mortality was 5%, 35%, 65%, 95% and 100% in the 6.7, 14, 27, 55 and 110 mg a.i/L treatment levels, respectively. Lethargy was reported in all of the surviving mysids exposed to the 27 and 55 mg ai/L treatment levels. The LC_{50} is 19 mg a.i/L and the NOAEC is 3.2 mg a.i/L; IM-1-4 is classified as slightly toxic to estuarine/marine invertebrates on an acute exposure basis.

Table B5. Acute toxicity of acetamiprid and degradates to estuarine/marine invertebrates.

Species	Test substance	LC_{50} mg ai/L	Toxicity Category	MRID	Study Classification
Eastern oyster shell deposition *(Crassostrea virginica)* Flow-through	Technical acetamiprid	41	Slightly toxic	44988410	Acceptable
Mysid *(Americamysis bahia)*	Technical acetamiprid	**0.066***	Very highly toxic	44651869	Acceptable
Mysid *(Americamysis bahia)*	99.6% IM-1-4	19	Slightly toxic	44651870	Acceptable

* Most sensitive endpoint

A 21-day chronic toxicity study was conducted with daphnids at concentrations of 0 (control), 2, 5, 9, 18, 37 and 74 mg ai/L (MRID 44651871). Survival was reduced to 57% at the highest test concentration. Significant reduction in length (8%), weight (24%) and mean number of offspring (50%) were observed at 9 mg ai/L, the LOAEC. The NOAEC is 5 mg ai/L based on reduced growth and reproduction (**Table B6**).

A 21-day chronic toxicity study of degradate IM-1-5 was conducted with daphnids at nominal concentrations of 0 (control), 6.3, 13, 25, 50 and 100 mg ai/L (MRID 44651871). Significant reduction in mean number of offspring (30%) was observed at 50 mg ai/L, the LOAEC. The NOAEC is 25 mg ai/L based on impaired reproduction.

A 28-day flow-through chronic toxicity study was conducted with mysid shrimp exposed at mean measured concentrations of 0 (control), 0.93, 1.4, 2.5, 4.7, 10 and 20 µg ai/L. Survival rates of 85%, 80%, 92%, 93%, 93% and 63% was observed in the 0.93, 1.4, 2.5, 4.7, 10 and 20 µg ai/L treatment levels respectively. Only the 20 µg ai/L was statistically significant different from the control in terms of reduced survival, and further analyses were not conducted on this concentration. Reduction in male dry body weight was the most sensitive endpoint; the NOAEC is 2.5 µg ai/L and the LOAEC is 4.7 µg ai/L.

Table B6. Chronic toxicity of acetamiprid and degradates to aquatic invertebrates.

Species	Test Substance	NOAEC	LOAEC	Endpoints Affected	MRID	Study Classification
Waterflea *(Daphnia magna)*	Technical acetamiprid	5.0 mg ai/L	9.0 mg ai/L	Reduced offspring production	44651871	Acceptable
Waterflea *(Daphnia magna)*	98.9% IM-1-5 degradate	25 mg ai/L	51 mg ai/L	Number of young per female	46255609	Supplemental
Mysid *(Americamysis bahia)*	Technical acetamiprid	**0.0025 mg ai/L***	0.0047 mg ai/L	Reduced body weight in males	44651873	Acceptable

* Most sensitive endpoint

Aquatic Plants

Tier 1 toxicity testing with aquatic nonvascular plants indicates that acetamiprid had no effect on the growth of green algae *Pseudokirchneriella subcapitata*, cyanobacteria *Anabaena flos-aquae,* freshwater diatoms *Navicula pelliculosa* or marine diatoms *Skeletonema costatum* at the highest concentrations tested (range: 1.0 to 1.3 mg ai/L) (**Table B7**). Tier 1 toxicity testing with aquatic vascular plants indicates that acetamiprid had no effect on the growth of duckweed (*Lemna gibba*) at the highest concentration tested, *i.e*., 1.0 mg ai/L.

Table B7. Toxicity of acetamiprid to aquatic plant species.

Species	Test substance	NOAEC (mg ai/L)	EC_{50} (mg ai/L)	MRID	Study Classification
Aquatic Vascular Plants					
Duckweed (*Lemna gibba)*	Technical acetamiprid	1.0	>1.0	44988415	Acceptable
Aquatic Non-vascular Plants					
Green algae (*Pseudokirchneriella subcapitata*)	Technical acetamiprid	1.3	>1.3	44988414	Acceptable
Marine diatom *(Skeletonema costatum)*	Technical acetamiprid	1.0	>1.0	44988418	Acceptable
Freshwater diatom *(Navicula pelliculosa)*	Technical acetamiprid	1.1	>1.1	44988417	Acceptable
Cyanobacteria (*Anabaena flos-aquae*)	Technical acetamiprid	1.3	>1.3	44988416	Acceptable

Terrestrial Organisms

Tables B8 to **B15** contains all available terrestrial toxicity endpoints from registrant-submitted studies. Below is a brief summary of available terrestrial toxicity studies.

Birds

The acute oral toxicity of acetamiprid to 4-to-8-month-old zebra finches (*Taeniopygia guttata* aka *poephila guttata*) was assessed over 14 days. Acetamiprid was administered to birds at nominal doses of 1.8, 2.5, 3.6, 5, 7, and 10 mg ai/kg bw. The 14-day acute oral LD_{50} is 5.68 mg ai/kg bw (**Table B8**). At least one clinical sign of toxicity or observation of abnormal behavior was recorded in all treatment groups, but not in the control group. Symptoms ranged from transient ruffled appearance in the lowest dose group (1.8 mg ai/kg bw) to lethargy, wing droop, prostrate posture, loss of coordination, loss of righting reflex, depressed behavior, and minor muscle fasciculation in higher dose groups. Acetamiprid is therefore classified as very highly toxic to zebra finches on an acute oral exposure basis.

The acute oral toxicity of acetamiprid to mallard ducks (*Anas platyrhynchos*) was assessed over 14 days at measured doses of 0 (control), 43, 64, 85, 124, and 181 mg ai/kg-bw. Mortality was 0% in the control and 43 mg ai/kg-bw doses, and 40%, 40% 80% and 100% in the 64, 85, 124

and 181 mg ai/kg-bw doses. Sublethal effects, including abnormal behavior and loss of coordination, were reported at all doses. The 14-day LD_{50} is 84.4 mg ai/kg-bw; the NOAEL is <43 mg ai/kg-bw based on impaired behavior. Acetamiprid is classified as moderately toxic to mallard ducks on an acute oral exposure basis (**Table B8**).

Table B8. Acute oral toxicity of technical grade acetamiprid to birds.

Species	Test Substance	LD_{50} (mg ai/kg-bw)	Toxicity Category	MRID	Study Classification
Zebra finch (*Taeniopygia guttata*)	Technical acetamiprid	**5.68***	Very highly toxic	48407701	Acceptable
Mallard duck (*Anas platyrhynchos*)	Technical acetamiprid	84.4	Moderately toxic	44651859	Acceptable

* Most sensitive endpoint

The subacute dietary toxicity of acetamiprid to mallard duck was assessed at concentrations of 0 (control), 200, 1000 and 5000 mg a.i/kg-diet. Mortality was 10% at the 1000 mg ai/kg-diet concentration and 40% at the 5000 mg ai/kg-diet concentration. Sublethal effects including imbalance and reduced food consumption were reported at in all surviving birds at the 1000 and 5000 mg ai/kg-diet concentrations. The subacute dietary LC_{50} is >5000 mg ai/kg-diet. The NOAEC is 200 mg ai/kg-diet based on reduced survival, behavioral effects and reduced food consumption. Acetamiprid is classified as slightly toxic to birds on a subacute dietary exposure basis (**Table B9**).

The subacute dietary toxicity of acetamiprid to 10-day old bobwhite quail (*Colinus virginianus*) was assessed at concentrations of 0 (control), 1000 and 5000 mg ai/kg-diet. Mortality was 20% at the 5000 mg ai/kg-diet concentration, the only mortalities in the study. Food consumption was markedly depressed in the 5000 mg ai/kg-diet treatment group, the only sublethal effect reported. The LC_{50} is >5000 mg ai/kg-diet and the NOAEC is 1000 mg ai/kg-diet based on reduced survival and decreased food consumption. Acetamiprid is classified as practically nontoxic to bobwhite quail on a subacute dietary basis.

The subacute dietary toxicity of the acetamiprid degradate IM-1-4 to mallard duck was assessed at test concentrations of0 (control), 5, 50, 500, 2500 and 5000 mg ai/kg-diet. No mortalities or sublethal effects were reported. The subacute dietary LC_{50} is >5000 mg ai/kg-diet. The NOAEC is 5000 mg ai/kg-diet. IM-1-4 is classified as practically nontoxic to birds on a subacute dietary exposure basis.

Table B9. Subacute dietary toxicity of acetamiprid to birds.

Species	Test substance	LC_{50} (mg ai/kg-diet)	Toxicity Category	MRID	Study Classification
Mallard duck (*Anas platyrhynchos*)	Technical acetamiprid	>5000	Practically non-toxic	44651861	Supplemental
Bobwhite quail (*Colinus virginianus*)	Technical acetamiprid	>5000	Practically non-toxic	44651860	Supplemental
Mallard duck (*Anas platyrhynchos*)	IM-1-4 degradate	>5000	Practically non-toxic	44651862	Acceptable

Chronic toxicity to birds was uncertain in past risk assessments because of deficiencies in the avian reproduction studies with both the mallard (MRID 44988408) and the northern bobwhite quail (MRID 44988407). The initial mallard duck reproduction study provided an estimated NOAEC of 125 mg ai/kg diet based on reductions in adult female body weight. The previous bobwhite quail reproduction study showed significant reductions in hatchling body weights at all treatment concentrations and thus failed to establish a NOAEC; the LOAEC was 250 mg ai/kg-diet. Subsequent studies were submitted (**Table B10**).

In a one-generation reproductive toxicity study (MRID 46369204), acetamiprid was administered to mallard ducks at measured concentrations of 0 (control), 60.2, 134, 258, and 461 mg ai/kg-diet. Both male and female body weight gains were statistically-reduced compared to the controls; the male body weights were affected at all treatment levels (70% at lowest treatment), while female body weight gains were reduced at the 258 and 461 mg ai/kg-diet treatment levels (roughly 50%). No other effect on any adult parameter was observed. The number of eggs laid was statistically-reduced at the 461 mg ai/kg-diet level compared to the control (673 versus 896 eggs for 17 laying pairs). In addition, the number of eggs set, the number of viable embryos, and hatchling weights were statistically-reduced at the 461 mg ai/kg-diet level. No other effect on any reproductive endpoint was observed. Based on as statistically significant 3% decrease in male bodyweight gain in the lowest treatment group, a NOAEC was not established for the study, i.e., NOAEC<60.2 mg ai/kg diet; the LOAEC is 60.2 mg ai/kg-diet. The NOAEC for reproductive effects is 258 mg ai/kg-diet.

In a one-generation reproductive toxicity study (MRID 46555601), acetamiprid was administered to bobwhite quail at measured concentrations of 0 (control), 89.7, 184, 385 and 775 mg ai/kg-diet. No treatment-related effects were observed on adult survival or food consumption, or upon terminal necropsy of all decedent and surviving birds. There was a significant reduction (18%) in adult female body weight change at the highest treatment level. There were significant reductions in eggs set, viable embryos, viable embryos to eggs set, live embryos, number hatched, number of hatchlings to eggs laid, hatchling survival, hatchling survival to eggs set and hatchling survival to number hatched. The NOAEC and LOAEC for the study are 89.7 and 184 mg ai/kg-diet, respectively

Table B10. Reproductive chronic toxicity of technical grade acetamiprid to birds.

Species	Test Substance	NOAEC (mg ai/kg diet)	LOAEC (mg ai/kg-diet)	MRID	Study Classification
Mallard duck (*Anas platyrhynchos*)	Technical acetamiprid	**<60.2***	60.2	46369201	Supplemental
Northern bobwhite quail (*Colinus virginianus*)	Technical acetamiprid	89.7	184	46555601	Acceptable

* Most sensitive endpoint

Mammals

The available data indicate that acetamiprid is moderately toxic to mammals on an acute oral exposure basis (LD_{50}=146 mg ai/kg-bw). The original Section 3 risk assessment reported an LD_{50}=167 mg ai/kg. Acute oral toxicity tests were also conducted on several metabolites and degradation products of acetamiprid. Results of these tests show that these compounds are considerably less toxic than the parent compound, and are classified as slightly toxic or practically nontoxic to mammals (**Table B11**).

Table B11. Acute toxicity of acetamiprid and degradates to mammals.

Species	Test substance	LD_{50} (mg ai/kg-bw)	Toxicity Category	MRID	Classification
Laboratory rat *Rattus rattus*	Technical acetamiprid	146	Moderately toxic	44651833	Acceptable
Laboratory rat *Rattus rattus*	IM-1-4 (99.6%) degradate	1088	Slightly toxic	44651834	Acceptable
Laboratory rat *Rattus rattus*	IM-1-2 (99.9%) degradate	2176	Practically nontoxic	44988422	Acceptable
Laboratory rat *Rattus rattus*	IM-1-2 (99.6%) degradate	>5000	Practically nontoxic	44651835	Acceptable
Laboratory rat *Rattus rattus*	IM-0 degradate	1792	Practically nontoxic	44988421	Acceptable
Laboratory rat *Rattus rattus*	IC-0 degradate	>5000	Practically nontoxic	44988420	Acceptable

Consistent results were reported for two chronic studies and a 13-week subchronic study of acetamiprid in rats (**Table B12**). Reduction in growth, as measured by body weight, weight gain, and food consumption, were observed at test concentrations of 400-800 mg ai/kg-diet and greater, whereas test concentrations of 160-280 mg ai/kg-diet caused no significant effects. In

addition to growth endpoints, reproductive effects were also observed at 280 mg ai/kg-diet in a two-generation study (MRID 44988430). The NOAEC (160 mg/kg diet) that will be used for risk assessment will be based on the growth endpoints from the 2-year chronic feeding study (MRID 44988429).

Table B12. Chronic toxicity of acetamiprid to mammals.

Species (Test Type)	Test Substance	Measured Effect	NOAEC (mg ai/kg diet)	LOAEC (mg ai/kg-diet)	MRID
Laboratory Rat (Subchronic Dietary: 13 weeks)	Technical acetamiprid	Body weight, weight gain, and food consumption	200	800	44651843
Laboratory Rat (Chronic feeding: 24 months)	Technical acetamiprid	Female body weight, female weight gain	160	400	44988429; 45245304
Laboratory Rat (Two-generation reproduction)	Technical acetamiprid	Parental Toxicity: Body weight, weight gain, food consumption	280	800	44988430
		Offspring Toxicity: Pup weight, litter size, viability and weaning indices, age to maturation	280	800	
		Reproductive Toxicity: Litter size, pup weights	280	800	

Terrestrial Invertebrates

Supplemental acute oral and contact honeybee (*Apis mellifera*) toxicity tests are available (**Table B13**). Honeybees were exposed to acetamiprid in an oral study as follows: 0 (control), 1.38, 2.6, 4.9, 10.21, 20.0 and 39.17 µg ai/bee. Mortality at 48-hrs averaged 6.7, 26.7, 36.7, 40, 26.7 and 30.0%, respectively. The study was carried out to 72-hrs, when the mortality averaged 10, 30, 36.7, 46.7, 50.0 and 30.0%, respectively. Both the 48 and 72-hr mortality in the dimethoate toxic reference averaged 50%. Dimethoate is commonly used as a positive control in honeybee studies to ensure the population of bees in the study demonstrates expected susceptibility to a known toxicant. Since none of the concentrations had greater than 50% mortality, it is not possible to calculate an LD_{50} value for acetamiprid; however, roughly 50% mortality was observed in the 20 µg ai/bee treatment. The NOAEC is 1.38 µg ai/bee based on decreased survival. With an LD_{50} of greater than 10.21 µg ai/bee, acetamiprid is classified as practically non-toxic to honeybees on an acute exposure basis.

In the acute contact toxicity test, the percent mortality was 40, 66.7, 46.7, 63.3, and 60% for the 6.25, 12.5, 25, 50, and 100 µg ai/bee test groups, respectively. The LC_{50} for the contact study was reported as 8.1 µg/bee. However, there is uncertainty in this LC_{50} value since no clear dose-response relationship was apparent. Since percent mortality was 66.7% at 12.5 µg ai/bee, the median mortality concentration is considered to be below this value (*i.e.*, <12.5) suggesting that

acetamiprid should be considered moderately toxic to honeybees on an acute contact exposure basis.

In addition to honeybees, the effect of acetamiprid on bumble bees, *Bombus terrestris,* was investigated. Bumble bees were exposed to acetamiprid for 48 hours in both an acute oral and acute contact toxicity test. Measured concentrations in the oral toxicity test were 0 (control), 3.36, 6 76, 10.37, 21.36, and 31.78 µg ai/bee. By 48 hours in the oral test, there was 0.0, 18.2, 1.0, 37.5, and 100.0% mortality in the 3.36, 6.76, 10.37, 21.36, and 31.78 µg ai/bee concentrations and 8.3% in the control. The calculated LD_{50} is 22.32 µg ai/bee and the NOAEC is 10.37 µg ai/bee, despite the mortality noted in the 6.76 µg ai/bee test concentration. The contact nominal concentration was 100 µg ai/bee and a negative control. At 48-hrs there was 3.3% mortality in both groups. The contact LD_{50} is >100 µg ai/bee and the NOAEC is 100 µg ai/bee. Based on these results, acetamiprid is classified as practically nontoxic to bumble bees on both an acute oral and contact exposure basis.

Table B13. Acute toxicity of technical grade acetamiprid to non-target terrestrial invertebrates.

Species	Test substance	LD_{50} (µg ai/bee)	Toxicity Category	MRID	Study Classification
Honey bee (*Apis mellifera*)	Technical acetamiprid	>10.21 (oral)	Slightly-toxic	44651874	Supplemental
	Technical acetamiprid	<12.5 (contact)	Moderately toxic	44651874	Supplemental
Bumble bee (*Bombus terrestris*)	Technical acetamiprid	22.32 (oral)	Practically nontoxic	45932503	Supplemental
	Technical acetamiprid	>100 (contact)	Practically nontoxic	45932503	Supplemental

A toxicity of residues on foliage study for honeybees was submitted (MRID 44651875) but was deemed unacceptable due to low recovery of acetamiprid on treated foliage. A second residues on foliage toxicity study was submitted, but has not yet been reviewed by EFED (MRID 45346901). Two semi-field studies conducted to evaluate the possible effect of acetamiprid on honeybee behavior were also submitted (MRIDs 45932504; 45932505), and were classified as supplemental[26]. Both studies used tents to expose honeybees via contact with forage and/or overspray, and applications rates were equivalent to 0.15 and 0.09 lbs ai/A, which is in line with single application rates for many registered and proposed crop uses. Mortality, flight frequency, and foraging behavior were evaluated relative to a control and a known toxic standard. No significant effects on any endpoints were observed in either study from acetamiprid treatments.

In the ECOTOX database, Iwasa *et al.*, 2004, report an LD_{50} of 7.07 µg ai/bee in a 24 hr contact study. This endpoint was based on nominal concentrations, but indicates that acetamiprid is moderately toxic to honeybees. A seven day study with speckled cutworm moth larvae (*Lacanobia subjuncta*) in a leaf litter substrate, Doerr *et al*., 2004, reported an LC_{50} of 71.3 mg/L. These values are provided for qualitative risk characterization. DERs have not yet been generated, but the papers have been submitted for evaluation, and will be reviewed as needed for

[26] Note: non-guideline studies cannot be rated "acceptable" since there are no guideline standards

the upcoming registration review risk assessment.

Several open literature studies of acetamiprid effects on honeybees are available for acetamiprid. These studies will be thoroughly reviewed as part of the upcoming registration review risk assessment, but are briefly summarized here. El Hassani *et al.* (2008) exposed bees to 0.1, 0.5, and 1 µg of active ingredient, and recorded increases in sucrose responsiveness, locomotor activity (total length walked), and responsiveness to water (proboscis extension reflex after stimulation by water), which are all considered activating effects since they signify increases in specific functions. Conversely, the lowest dose of acetamiprid (*i.e.*, 0.1 µg/bee) also impaired olfactory-related learning performance. A follow-up study by Aliouane *et al*. (2009) supported the previous water responsiveness finding. Laurino *et al.* (2011) found increased mortality in bees that ingested 50 and 100 ppm (ng/µl) of a formulation containing acetamiprid (5% ai). Mortality attributed to acetamiprid in the higher dose group was 50.85% compared to the control group, but these effects were only seen in bees that were starved for two hours before dosing. In the same study, bees fed sugar did not show any significant mortality from oral or indirect contact exposure to acetamiprid over a 72-hour observation period. In the above studies, acetamiprid generally exhibited lower toxicity to bees than a small sample of other neonicotinoids insecticides (*e.g*., clothianidin). This supports a previous open literature laboratory study suggesting that nitroguanidine substituted neonicotinoids (*e.g.*, clothianidin, imidacloprid, thiamethoxam and dinotefuran) are more toxic to bees than their cyano-substituted neonicotinoids (*e.g.*, acetamiprid, thiacloprid) (Iwasa *et al.*, 2004). However, El Hassani *et al.* (2008) did show that acetamiprid, but not thiamethoxam, had a detectable impact on bee behavior at sublethal doses.

Effects of the acetamiprid degradate IM-1-5 on adult collembola, *Folsomia candida*, were examined at concentrations of 0 (control), 0.1, 0.5. 2.5, 12.5 and 62.5 mg/kg artificial soil over a 28- day exposure period (MRID 46255612). Reproduction was the measured endpoint. Reproduction was reduced by 15, 14, 8, 6 and 24% in the 0.1, 0.5, 2.5, 12.5 and 62.5 mg/kg treatments, respectively; reductions at the 2.5 and 12.5 mg/kg treatment levels were not statistically significant. The EC_{50} for the study is >62.2 mg/kg-soil and the NOAEC is <0.1 mg/kg-soil.

Rove beetles, *Aleochara bilineata*, were exposed to the degradate IM-1-5 at concentrations of 0 (control), 0.1, 2.5 and 62.5 mg/kg sand substrate over an 87-day period (MRID 46255611). Fly pupae (*Delia antique*) were introduced on days 7, 14 and 21(as food) to evaluate beetle reproduction. Adult beetles were removed on day 28, and fly pupae were removed on day 35. Beetle emergence was observed from day 39 to 87. Number of emerged beetles was the measurement endpoint. There was a 19% reduction in emergence at the highest test concentration. The EC_{50} for the study is >62.5 mg/kg substrate and the NOAEC is 2.5 mg/kg substrate.

In a 14-day acute toxicity study, earthworms (*Eisenia foetida*) were exposed to acetamiprid at 0 (control), 4, 8, 15, 30 or 60 mg ai/kg dry weight of artificial substrate (MRID 44988412). The reference chemical used was chloroacetamide at 37 mg ai/kg of the substrate. The 14-day LC_{50} was 9.12 mg ai/kg-substrate. The 7-day LC_{50} was 10 mg ai/kg substrate. The NOEC and LOEC values were not determined. Acetamiprid is considered to be toxic to earthworms up to/and above a concentration of 4 mg ai/kg substrate.

Earthworms (*Eisenia foetida*) were exposed to IM-1-5 at nominal test concentrations of 0 (control), 4, 8, 15, 30, and 1000 mg/kg (MRID46255613). By 14 days, there were no mortalities. Reductions in body weight by day 14 were 2.9% in the 1000 mg/kg treatment group. No body weight reductions were observed in the control or the 4, 8, 15, and 30 mg/kg treatment groups. The LC_{50} was >1000 ppm; a NOEC value was estimated at 1000 mg/kg.

Earthworms (*Eisenia foetida*) were exposed to the IM-1-5 degradate over an 8-week period at nominal test concentrations of 0 (control), 0.1, 0.5, 2.5, 12.5, and 62.5 mg/kg in artificial soil (MRID 46255614). By 28 days, there were no mortalities in the control or treatment groups. There were no significant differences in adult body weight changes or number of juveniles produced in any treatment group compared to the control. The LC_{50} was >62.5 mg/kg and the NOEC value was 62.5 mg/kg.

Terrestrial Plants

The effect of acetamiprid on the seedling emergence and vegetative vigor of monocot: corn (*Zea mays*), oat (*Avena sativa*), onion (*Allium cepa*), perennial ryegrass (*Lolium perenne*), and dicot: cabbage (*Brassica oleracea*), cucumber (*Cucumis sativus*), lettuce (*Lactuca sativa*), soybean (*Glycine max*), tomato (*Lycopersicon esculentum*), and turnip (*Brassica rapa*) crops was studied at nominal concentrations (MRID 44988413). For the seedling emergence study, nominal concentrations were as follows: cabbage, cucumber, onion and tomato: 0.041, 0.081, 0.16, 0.33 and 0.65 lbs ai/A; corn, lettuce, oat, perennial ryegrass, soybean and turnip: 0.65 lbs ai/A. For the vegetative vigor study, nominal concentration were as follows: cabbage, oat, onion, soybean and tomato: 0.65 lbs ai/A; corn and cucumber: 0.041, 0081, 0.16, 0.33 and 0.65 lbs ai/A; lettuce: 0.005, 0.01, 0.02, 0.041, 0.081 and 0.16 lbs ai/A; perennial ryegrass: 0.041, 0.081, 0.16, 0.33 and 0.65 lbs ai/A; and turnip: 0.02, 0.041, 0.081, 0.16, 0.33 and 0.65 lbs ai/A.

The seedling emergence part of this study was classified as supplemental because the weight of the seedlings was not measured. Measurement of both plant weight and plant height are required, but only plant height was measured in this study. The percent seedling emergence was not affected in all species tested after exposure to acetamiprid. There was, however, reduction in shoot length of cucumber, onion, and tomato exposed to acetamiprid at 0.15, 0.32 and 0.62 lbs ai/A. The most sensitive monocot species was onion with an EC_{25} of 0.23 lbs ai/A. The most sensitive dicot species was cucumber, with an EC_{25} of 0.16 lbs ai/A (**Table B14**). The NOEC based on the seedling emergence (shoot length) in cucumber (dicot) and onion (monocot) was 0.077 lbs ai/A.

The vegetative vigor part of this study was acceptable for all species except lettuce. The test with lettuce was classified as supplemental because significant adverse phytotoxic effects were observed in the control plants. In the vegetative vigor test, the shoot length in all species was not affected by acetamiprid treatment. Plant weight was also not affected in cabbage, corn, cucumber, oat, onion, soybean and tomato exposed to the compound. There was, however, a reduction in the plant weight of lettuce, perennial ryegrass, and turnip exposed to various concentrations of acetamiprid. The most sensitive monocot species in the vegetative vigor test was perennial ryegrass, with an EC_{25} of 0.46 lbs ai/A and a NOAEC of 0.31 lbs ai/A. The most sensitive dicot species was lettuce, with a EC_{25} of 0.016 lbs ai/A and a NOEC of 0.0094 lbs ai/A.

A subsequent study was submitted concerning the effect of acetamiprid on vegetative vigor on lettuce alone (MRID 45921401). In this study, the EC_{25} and NOAEC for plant weight were 0.012 and <0.0025 lbs ai/A, respectively. Shoot length was the more sensitive parameter with an EC_{25} of 0.0056 and a NOAEC of 0.0025 lbs ai/A. Two other studies more closely examined the phytotoxic effects of acetamiprid on lettuce. Both studies (MRID 46229601 and 46229602) reported that the variety of lettuce used in the first two studies, buttercrunch, accounted for the greater sensitivity of lettuce relative to other species tested, and other varieties of lettuce exhibited reduced sensitivities.

Table B14. Summary of endpoints (lbs ai/A) in terrestrial plant toxicity studies submitted for acetamiprid.

Species		Seedling emergence		Vegetative vigor	
		NOAEC	EC_{25}	NOAEC	EC_{25}
Monocots	Oat	0.62	>0.62	0.67	>0.67
	Corn	0.62	>0.62	0.59	>0.59
	Onion	**0.077***	**0.23***	0.65	>0.65
	Ryegrass	0.62	>0.62	**0.31***	**0.46***
Dicots	Cucumber	**0.077***	**0.16***	0.59	>0.59
	Soybean	0.62	>0.62	0.65	>0.65
	Turnip	0.62	>0.62	0.031†	0.2
	Lettuce	0.62	>0.62	**0.0025***	**0.0056***
	Tomato	0.077	0.16	0.65	>0.65
	Cabbage	0.62	>0.62	0.67	>0.67

* Most sensitive endpoint

† EC_{05} is used when calculated EC_{25} is less than derived NOAEC.

Appendix C. Example ECOSAR Output

Output for IM-1-5

SMILES : c1cc(ncc1CN(C)C(C)=N)CL
CHEM :
CAS Num:
ChemID1:
ChemID2:
ChemID3:
MOL FOR: C9 H12 CL1 N3
MOL WT : 197.67
Log Kow: -0.68 (KowWin estimate)
Melt Pt:
Wat Sol: 1.7E+005 mg/L (WskowWin estimate)

ECOSAR v1.00 Class(es) Found

Halopyrdines

ECOSAR Class	Organism	Duration	End Pt	Predicted mg/L (ppm)
Halopyrdines	: Fish	96-hr	LC50	0.184
Halopyrdines	: Daphnid	48-hr	LC50	1.369
Halopyrdines	: Fish	32-day	ChV	27.067
Halopyrdines	: Daphnid		ChV	0.752 !
Neutral Organic SAR	: Fish	96-hr	LC50	28010.680
(Baseline Toxicity)	: Daphnid	48-hr	LC50	11695.474
	: Green Algae	96-hr	EC50	1681.517
	: Fish		ChV	2821.084
	: Daphnid		ChV	672.943
	: Green Algae		ChV	373.311

Note: * = asterisk designates: Chemical may not be soluble enough to measure this predicted effect.

Note: ! = exclamation designates: The toxicity value was determined from a predicted SAR using established acute-to-chronic ratios and ECOSAR regression techniques which are documented in the supporting Technical Reference Manual. When possible, this toxicity value should be considered in a weight of evidence approach.

Halopyrdines :

For Fish and Daphnid Acute Toxicity Values: If the log Kow of the chemical is greater than 5.0, or if the compound is solid and the LC50 exceeds the water solubility by 10X, no effects at saturation are predicted for these endpoints.

For Green Algae Acute Toxicity Values: If the log Kow of the chemical is greater than 6.4, or if the compound is solid and the EC50 exceeds the water solubility by 10X, no effects at saturation are predicted for these endpoints.

For All Chronic Toxicity Values: If the log Kow of the chemical is greater than 8.0, or if the compound is solid and the ChV exceeds the water solubility by 10X, no effects at saturation are predicted for these endpoints.

ECOSAR v1.00 SAR Limitations:

Maximum LogKow: 5.0 (LC50)
Maximum LogKow: 6.4 (EC50)
Maximum LogKow: 8.0 (ChV)
Maximum Mol Wt: 1000

Baseline Toxicity SAR Limitations:

Maximum LogKow: 5.0 (Fish 96-hr LC50; Daphnid LC50)
Maximum LogKow: 6.4 (Green Algae EC50)
Maximum LogKow: 8.0 (ChV)
Maximum Mol Wt: 1000

Appendix D. Reference List for OPPTS 835 Guidelines

The Office of Prevention, Pesticides, and Toxic Substances (OPPTS) became the Office of Chemical Safety and Pollution Prevention (OCSPP) in 2011. The guidelines have not been updated since the name change and the titles still use OPPTS.

OPPTS Guideline	Citation
Hydrolysis 835.2120 (161-1)	USEPA. 2008. *Fate, Transport, and Transformation Guidelines. OPPTS 835.2120 Hydrolysis*. E. 712-C-08-012. October 2008. Office of Prevention, Pesticides, and Toxic Substances. United States Environmental Protection Agency. Available at http://www.epa.gov/ocspp/pubs/frs/publications/Test_Guidelines/series835.htm (Accessed May 5, 2012).
Aqueous Photolysis 835.2240 (161-2)	USEPA. 2008. *Fate, Transport, and Transformation Guidelines. OPPTS 835.2240 Photodegradation in Water*. E. 712-C-08-013. October 2008. Office of Prevention, Pesticides, and Toxic Substances. United States Environmental Protection Agency. Available at http://www.epa.gov/ocspp/pubs/frs/publications/Test_Guidelines/series835.htm (Accessed May 5, 2012).
Soil Photolysis 835.2410 (161-3)	USEPA. 2008. *Fate, Transport, and Transformation Guidelines. OPPTS 835.2410 Photodegradation in Soil*. E. 712-C-08-015. October 2008. Office of Prevention, Pesticides, and Toxic Substances. United States Environmental Protection Agency. Available at http://www.epa.gov/ocspp/pubs/frs/publications/Test_Guidelines/series835.htm (Accessed May 5, 2012).
Aerobic Soil Metabolism 835.4100 (162-1) Anaerobic Soil Metabolism 835.4200 (162-2)	USEPA. 2008. *Fate, Transport, and Transformation Guidelines. OPPTS 835.4100 Aerobic Soil Metabolism; OPPTS 835.4200 Anaerobic Soil Metabolism*. EPA712-C-08-016 & E. 712-C-08-017. October 2008. Office of Prevention, Pesticides, and Toxic Substances. United States Environmental Protection Agency. Available at http://www.epa.gov/ocspp/pubs/frs/publications/Test_Guidelines/series835.htm (Accessed May 17, 2012).
Aerobic Aquatic Metabolism 835.4300 (162-4) Anaerobic Aquatic Metabolism 835.4400 (162-3)	USEPA. 2008. *Fate, Transport, and Transformation Guidelines. OPPTS 835.4300 Aerobic Aquatic Metabolism; OPPTS 835.4400 Anaerobic Aquatic Metabolism*. EPA 712-C-08-018 & E. 712-C-08-019. October 2008. Office of Prevention, Pesticides, and Toxic Substances. United States Environmental Protection Agency. Available at http://www.epa.gov/ocspp/pubs/frs/publications/Test_Guidelines/series835.htm (Accessed May 17, 2012).
Sorption coefficients 835.1230 (163-1)	USEPA. 2008. *Fate, Transport, and Transformation Guidelines. OPPTS 835.1230 Adsorption/Desorption (Batch Equilibrium)*. E. 712-C-08-009. October 2008. Office or Prevention, Pesticides, and Toxic Substances. United States Environmental Protection Agency. Available at http://www.epa.gov/ocspp/pubs/frs/publications/Test_Guidelines/series835.htm (Accessed May 5, 2012).
Leaching and Aged Column Leaching 835.1240	USEPA. 2008. *Fate, Transport, and Transformation Guidelines. OPPTS 835.1240 Leaching Studies*. E. 712-C-08-010. October 2008. Office of Prevention, Pesticides, and Toxic Substances. United States Environmental Protection Agency. Available at http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0152-0007 (Accessed May 5, 2012).

OPPTS Guideline	Citation
Terrestrial Field Dissipation 835.6100	USEPA. 2008. *Fate, Transport, and Transformation Guidelines. OPPTS 835.1230 Adsorption/Desorption (Batch Equilibrium)*. E. 712-C-08-009. October 2008. Office or Prevention, Pesticides, and Toxic Substances. United States Environmental Protection Agency. Available at http://www.epa.gov/ocspp/pubs/frs/publications/Test_Guidelines/series835.htm (Accessed May 5, 2012).
Aquatic Field Dissipation 835.6200	USEPA. 2008. *Fate, Transport, and Transformation Test Guidelines. OPPTS Aquatic (Sediment) Field Dissipation*. EPA 712-C-08-021. October 2008. Office of Prevention, Pesticides, and Toxic Substances. United States Environmental Available at http://www.epa.gov/ocspp/pubs/frs/publications/Test_Guidelines/series835.htm (Accessed May 15, 2012).
Bioconcentration Factor 850.1730	USEPA. 1996. *Ecological Effects Test Guidelines. OPPTS 850.1730 Fish BCF*. E. 712-C-96-129. April 1996. Environmental Fate and Effects Division. Office of Pesticide Programs. United States Environmental Protection Agency. Available at http://www.epa.gov/opptsmnt/pubs/frs/publications/OPPTS_Harmonized/850_Ecological_Effects_Test_Guidelines/Drafts/850-1730.pdf (Accessed May 14, 2012).
Environmental Chemistry Method	USEPA. 1996. *Ecological Effects Test Guidelines. OPPTS 850.7100*. E. 712-C-96-348. April 1996. Office of Prevention, Pesticides, and Toxic Substances. Available at http://www.epa.gov/opptsmnt/pubs/frs/publications/OPPTS_Harmonized/850_Ecological_Effects_Test_Guidelines/Drafts/850-7100.pdf (Accessed May 17, 2012).

Appendix E. Results from Screening Imbibition Program (SIP) and the Screening Tool for Inhalation Risk Assessment (STIR)

The Screening Imbibition Program (SIP v.1.0, Released June 15, 2010) was used to calculate an upper bound estimate of exposure using acetamiprid's solubility (4250 mg/L, MRID 44651803), the most sensitive acute and chronic avian toxicity endpoints (Zebra finch with LD_{50} of 5.68 mg ai/kg-bw and Mallard duck NOAEC of less than 60.2 mg/kg-diet) and the most sensitive acute and chronic mammalian toxicity endpoints (Rat LD_{50} of 146 mg ai/kg-bw and NOAEC of 7.1 mg ai/kg-bw/day or 160 mg ai/kg-diet). Based on the output, exposure through drinking water alone is potential acute and chronic risk to small birds and a potential chronic risk to small mammals. Results from SIP are shown below.

Inhalation is another potential exposure route for terrestrial vertebrates. Based on the vapor pressure of acetamiprid (7.5×10^{-10} Torr at 25°C), acetamiprid is nonvolatile from dry nonadsorbing surfaces and non-volatile from water and moist surfaces, and therefore risk from inhalation is not expected (AERU, 2012). The 4-hr LC_{50} inhalation study using rats was greater than 1.15 mg/L (MRID 44651837). The STIR model (Screening Tool for Inhalation Risk) was used to evaluate inhalation risk to birds and mammals. The endpoints discussed above were used in the model. Results from STIR are shown below.

Results from SIP version 1.0

Table 1. Inputs

Parameter	Value
Chemical name	acetamiprid
Solubility (in water at 25°C; mg/L)	4250
Mammalian LD_{50} (mg/kg-bw)	146
Mammalian test species	laboratory rat
Body weight (g) of "other" mammalian species	
Mammalian NOAEL (mg/kg-bw)	160
Mammalian test species	laboratory rat
Body weight (g) of "other" mammalian species	
Avian LD_{50} (mg/kg-bw)	5.68
Avian test species	other
Body weight (g) of "other" avian species	12.1
Mineau scaling factor	1.15
Mallard NOAEC (mg/kg-diet)	60.2
Bobwhite quail NOAEC (mg/kg-diet)	
NOAEC (mg/kg-diet) for other bird species	
Body weight (g) of other avian species	
NOAEC (mg/kg-diet) for 2nd other bird species	
Body weight (g) of 2nd other avian species	

Enter body weight of 'other' avian species for LD50.

Table 2. Mammalian Results

Parameter	Acute	Chronic
Upper bound exposure (mg/kg-bw)	731.0000	731.0000
Adjusted toxicity value (mg/kg-bw)	112.2974	123.0657
Ratio of exposure to toxicity	6.5095	5.9399
Conclusion*	**Exposure through drinking water alone is a potential concern for mammals**	**Exposure through drinking water alone is a potential concern for mammals**

Table 3. Avian Results

Parameter	Acute	Chronic
Upper bound exposure (mg/kg-bw)	3442.5000	3442.5000
Adjusted toxicity value (mg/kg-bw)	6.1247	2.9867
Ratio of exposure to acute toxicity	562.0681	1152.6191
Conclusion*	**Exposure through drinking water alone is a potential concern for birds**	**Exposure through drinking water alone is a potential concern for birds**

*Conclusion is for drinking water exposure alone. This does not combine all routes of exposure. Therefore, when aggregated with other routes (*i.e.*, diet, inhalation, dermal), pesticide exposure through drinking water may contribute to a total exposure that has potential for effects to non-target animals.

Results from STIR Version 1.0.xlsx

Welcome to the EFED Screening Tool for Inhalation Risk

This tool is designed to provide the risk assessor with a rapid method for determining the potential significance of the inhalation exposure route to birds and mammals in a risk assessment.

Input

NOTE: When entering values, press the "Ent in order to update linked cells.

Application and Chemical Information	
Enter Chemical Name	Acetamiprid
Enter Chemical Use	Soybean
Is the Application a Spray? (enter y or n)	y
If Spray What Type (enter ground or air)	air
Enter Chemical Molecular Weight (g/mole)	222.68
Enter Chemical Vapor Pressure (mmHg)	7.50E-10
Enter Application Rate (lb a.i./acre)	0.25
Toxicity Properties	
Bird	
Enter Lowest Bird Oral LD_{50} (mg/kg bw)	5.68
Enter Mineau Scaling Factor	1.15
Enter Tested Bird Weight (kg)	0.012
Mammal	
Enter Lowest Rat Oral LD_{50} (mg/kg bw)	146
Enter Lowest Rat Inhalation LC_{50} (mg/L)	1.15
Duration of Rat Inhalation Study (hrs)	4
Enter Rat Weight (kg)	0.35

Output

Results Avian (0.020 kg)		
Maximum Vapor Concentration in Air at Saturation (mg/m^3)	8.99E-06	
Maximum 1-hour Vapor Inhalation Dose (mg/kg)	1.13E-06	
Adjusted Inhalation LD_{50}	3.74E-01	
Ratio of Vapor Dose to Adjusted Inhalation LD_{50}	3.02E-06	Exposure not Likely Significant
Maximum Post-treatment Spray Inhalation Dose (mg/kg)	2.40E-02	
Ratio of Droplet Inhalation Dose to Adjusted Inhalation LD_{50}	6.42E-02	Exposure not Likely Significant

Results Mammalian (0.015 kg)		
Maximum Vapor Concentration in Air at Saturation (mg/m^3)	8.99E-06	
Maximum 1-hour Vapor Inhalation Dose (mg/kg)	1.42E-06	
Adjusted Inhalation LD_{50}	6.85E+01	
Ratio of Vapor Dose to Adjusted Inhalation LD_{50}	2.07E-08	Exposure not Likely Significant
Maximum Post-treatment Spray Inhalation Dose (mg/kg)	3.02E-02	
Ratio of Droplet Inhalation Dose to Adjusted Inhalation LD_{50}	4.41E-04	Exposure not Likely Significant

Appendix F. Agency risk quotient (RQ) metrics and levels of concern (LOC) for Federally-listed (listed) threatened/endangered and non-listed species per risk class

Risk Class	Risk Description	RQ	LOC
Aquatic Animals (fish and invertebrates)			
Acute	Potential for effects to non-listed animals from acute exposures	Peak EEC/LC_{50}[1]	0.5
Acute Restricted Use	Potential for effects to animals from acute exposures Risks may be mitigated through restricted use classification	Peak EEC/LC_{50}[1]	0.1
Acute Listed Species	Listed species may be potentially affected by acute exposures	Peak EEC/LC_{50}[1]	0.05
Chronic	Potential for effects to non-listed and listed animals from chronic exposures	60-day EEC/NOEC (fish)	1
		21-day EEC/NOEC (invertebrates)	
Terrestrial Animals (mammals and birds)			
Acute	Potential for effects to non-listed animals from acute exposures	EEC[2]/LC_{50} (Dietary)	0.5
		EEC/LD_{50} (Dose)	
Acute Restricted Use	Potential for effects to animals from acute exposures Risks may be mitigated through restricted use classification	EEC[2]/LC_{50} (Dietary)	0.2
		EEC/LD_{50} (Dose)	
Acute Listed Species	Listed species may be potentially affected by acute exposures	EEC [2]/LC_{50} (Dietary)	0.1
		EEC/LD_{50} (Dose)	
Chronic	Potential for effects to non-listed and listed animals from chronic exposures	EEC [2]/NOAEC	1
Plants			
Non-Listed	Potential for effects to non-target, non-listed plants from exposures	EEC/ EC_{25}	1
Listed Plant	Potential for effects to non-target, listed plants from exposures	EEC/ NOEC	1
		EEC/ EC_{05}	

Appendix G. Data Call-In Justification Tables for Non-Guideline Ecological Effects Studies

Study Title: Pollinator Larval Toxicity Study **Guideline Number: Non-guideline** **Test Substance: Acetamiprid**
Rationale for Requiring the Data
Acetamiprid is a systemic insecticide and is moderately toxic to young adult honey bees on an acute contact exposure basis. Previously submitted studies of acetamiprid do not provide information on the potential toxicity to developing honeybee brood (larvae and pupae). Since acetamiprid is a systemic pesticide, there is the potential for pollen and nectar to be contaminated with the product and subsequently brought back to the hive where larvae may be exposed. Therefore, a non-guideline honeybee larval toxicity study is recommended. The registrant should submit a proposed protocol for review and approval by EFED prior to initiation of the study.
Practical Utility of the Data
How will the data be used? Data will be used to assess risk to non-target listed and non-listed terrestrial invertebrate species. This study would allow the Agency to refine the screening-level hazard assessment for beneficial terrestrial invertebrates. The effects data will be used to determine the potential for adverse effects on beneficial terrestrial invertebrates through direct effects on larval bees. **How could the data impact the Agency's future decision-making?** EPA is required by section 7(a)(2) of the Endangered Species Act (ESA) to ensure that any action it authorizes or takes "…is not likely to jeopardize the continued existence of any endangered or threatened species or result in the destruction or adverse modification of critical habitat" and "to use the best scientific data available" in carrying out this obligation. The data EPA intends to call in are necessary to inform the determination required by ESA as to whether continued registration of a pesticide is or is not likely to jeopardize the species or its critical habitat. The lack of these data will limit the flexibility that the Agency and registrants have in coming into compliance with ESA and could result in use restrictions that are unnecessarily severe. In addition, the lack of these data may result in an uncertain assumed risk and potential mitigation of acetamiprid formulations under FIFRA.

Study Title: Residues in Pollen and Nectar/Field Residue Analysis Study **Guideline Number: Non-guideline** **Test Substance: Acetamiprid**
Rationale for Requiring the Data
Acetamiprid is a systemic insecticide and is moderately toxic to young adult honey bees on an acute contact exposure basis. The systemic nature of the compound necessitates the quantification of pollinator-relevant residues in treated flowering plants, since pollinators will be exposed to residues from either current or prior season applications (due to the potential for residues to accumulate in plants and trees). Residues in edible/transportable-to-hive parts of treated trees and plants, particularly pollen-shedding and nectar producing parts (*i.e.*, flowers and, if present, extra-floral nectaries) of plants may inform the potential for risk.

The Agency will consider multiple crops based on certain selective criteria, including, but not limited to, the estimated usage, the application method, and whether the crop is attractive to pollinators. Furthermore, the Agency will consider a semi-field, full-field, or greenhouse-based protocol lasting at least two years with multiple sampling time-steps. The protocol will depend on application type and crop. The registrant should consult the Agency on the design of the protocol prior to the initiation of the study.

Practical Utility of the Data

How will the data be used?

To assess risk to non-target listed and non-listed terrestrial invertebrate species. These data would allow the Agency to refine the screening level risk assessment for beneficial terrestrial invertebrates. Exposure data is an integral part of determining the potential for risk to beneficial terrestrial invertebrates through direct exposure from their food sources.

How could the data impact the Agency's future decision-making?

EPA is required by section 7(a)(2) of the Endangered Species Act (ESA) to ensure that any action it authorizes or takes "…is not likely to jeopardize the continued existence of any endangered or threatened species or result in the destruction or adverse modification of critical habitat" and "to use the best scientific data available" in carrying out this obligation. The data EPA intends to call in are necessary to inform the determination required by ESA as to whether continued registration of a pesticide is or is not likely to jeopardize the species or its critical habitat. The lack of these data will limit the flexibility that the Agency and registrants have in coming into compliance with ESA and could result in use restrictions that are unnecessarily severe. In addition, the lack of these data may result in an uncertain assumed risk and potential mitigation of acetamiprid formulations under FIFRA.

Appendix H. Preliminary Estimate of Surface Water Concentrations for Ecological Risk Assessment

An EEC was estimated using the highest single application rate of 23.4 lbs a.i./A. An EEC for both a residential use setting and for perimeter treatment are both estimated using different assumptions. The perimeter treatment scenario resulted in higher EECs. The estimated application area for a perimeter treatment is up to 10 feet from the building and up to 3 foot on the surface of the building. A treated area factor was estimated using a housing density of four 2000 ft^2 houses per acre. Each house has a perimeter of 180 ft and treated area of 2340 ft^2 (180 ft x 13 ft). The estimated treated area per acre is then 9360 ft^2 which results in an estimated 21% of an acre (9360ft^2/43560ft^2/acre). The EEC from the residential scenario was multiplied by 0.21 to estimate an EEC to use as a screen for the perimeter treatment scenario. For other residential uses, it was assumed that half of a lot could be treated. Finally, the rice model was used to evaluate potential exposure for a cranberry use. Below are the output files from PRZM/EXAMs, GENEEC, and the rice model with EECs shown in Table H1.

Table H1. Preliminary Screening EECs for Acetamiprid Use in Residential Areas, Perimeter Treatments, and for Use on Cranberries

Scenario	Model	Area Treated Factor	Estimated Environmental Concentration (mg/L)		
			Peak	21-day	60-day
Residential	GENEEC	0.5	0.5	0.5	0.5
Perimeter	GENEEC	0.21	0.21	0.21	0.21
Residential	PRZM/EXAMS	**	0.72	0.71	0.70
Perimeter	PRZM/EXAMS	0.21	0.17	0.17	0.17
Cranberry	Rice Model	1.0	0.10	0.10	0.10

**PRZM/EXAMs was used to estimate exposure in a residential setting in California. The scenario was created specifically for California and it may not be conservative for the entire United States. The assumptions made were that there was half of the area was pervious and half impervious. It was assumed that half of the pervious surface was treated and 10% of the impervious surface was treated. Time series files from runs with an impervious surface scenario and residential scenario were combined to arrive at the final EEC.

```
RUN No.   1 FOR acetamiprid      ON   resident      * INPUT VALUES *
  ---------------------------------------------------------------------
   RATE (#/AC)   No.APPS &   SOIL  SOLUBIL   APPL TYPE NO-SPRAY INCORP
    ONE(MULT)    INTERVAL    Koc   (PPM )    (%DRIFT)   (FT)     (IN)
  ---------------------------------------------------------------------
23.400( 23.400)   1   1     227.0 4250.0   GRHIFI(  6.6)     .0    .0


  FIELD AND STANDARD POND HALFLIFE VALUES (DAYS)
  ---------------------------------------------------------------------
  METABOLIC  DAYS UNTIL  HYDROLYSIS   PHOTOLYSIS   METABOLIC  COMBINED
   (FIELD)   RAIN/RUNOFF   (POND)     (POND-EFF)    (POND)     (POND)
  ---------------------------------------------------------------------
   383.00        2          N/A     34.00- 4216.00   ******   1344.49


  GENERIC EECs (IN MILLIGRAMS/LITER (PPM))     Version 2.0 Aug 1, 2001
  ---------------------------------------------------------------------
      PEAK      MAX 4 DAY     MAX 21 DAY    MAX 60 DAY    MAX 90 DAY
      GEEC      AVG GEEC       AVG GEEC      AVG GEEC      AVG GEEC
  ---------------------------------------------------------------------
```

1.01 1.01 1.00 .98 .96

stored as acetres.out
Chemical: acetamiprid
PRZM environment: CAresidentialRLF.txt modified Tueday, 20 February 2007 at 13:04:34
EXAMS environment: pond298.exv modified Wedday, 15 November 2006 at 13:47:26
Metfile: w23234.dvf modified Wedday, 3 July 2002 at 10:04:22
Water segment concentrations (ppb)

Year	Peak	96 hr	21 Day	60 Day	90 Day	Yearly
1961	39.37	39.29	39.24	39.07	38.9	32.79
1962	124	123	122	120	119	106
1963	211	211	209	207	206	192
1964	273	272	269	266	265	256
1965	270	270	270	270	269	265
1966	280	279	279	279	279	274
1967	508	506	498	488	483	449
1968	494	494	491	489	489	476
1969	537	536	535	531	528	509
1970	562	561	559	554	553	535
1971	529	529	528	528	528	518
1972	507	507	507	507	506	499
1973	582	581	579	577	575	554
1974	561	561	560	559	558	548
1975	569	569	568	565	563	548
1976	554	553	552	552	551	540
1977	567	567	565	563	563	555
1978	619	618	616	612	611	592
1979	678	677	675	671	668	644
1980	682	682	680	678	675	655
1981	693	692	689	685	683	662
1982	923	920	909	900	896	864
1983	894	893	890	889	887	856
1984	821	821	819	818	817	802
1985	796	795	794	793	793	776
1986	825	824	822	817	815	786
1987	802	801	799	795	794	774
1988	759	758	757	755	755	741
1989	713	713	712	709	709	698
1990	692	692	690	689	688	674

Sorted results

Prob.	Peak	96 hr	21 Day	60 Day	90 Day	Yearly
0.032258064516129	923	920	909	900	896	864
0.0645161290322581	894	893	890	889	887	856
0.0967741935483871	825	824	822	818	817	802
0.129032258064516	821	821	819	817	815	786
0.161290322580645	802	801	799	795	794	776
0.193548387096774	796	795	794	793	793	774
0.225806451612903	759	758	757	755	755	741
0.258064516129032	713	713	712	709	709	698
0.290322580645161	693	692	690	689	688	674
0.32258064516129	692	692	689	685	683	662

```
0.354838709677419 682   682   680   678   675   655
0.387096774193548 678   677   675   671   668   644
0.419354838709677 619   618   616   612   611   592
0.451612903225806 582   581   579   577   575   555
0.483870967741936 569   569   568   565   563   554
0.516129032258065 567   567   565   563   563   548
0.548387096774194 562   561   560   559   558   548
0.580645161290323 561   561   559   554   553   540
0.612903225806452 554   553   552   552   551   535
0.645161290322581 537   536   535   531   528   518
0.67741935483871  529   529   528   528   528   509
0.709677419354839 508   507   507   507   506   499
0.741935483870968 507   506   498   489   489   476
0.774193548387097 494   494   491   488   483   449
0.806451612903226 280   279   279   279   279   274
0.838709677419355 273   272   270   270   269   265
0.870967741935484 270   270   269   266   265   256
0.903225806451613 211   211   209   207   206   192
0.935483870967742 124   123   122   120   119   106
0.967741935483871 39.37 39.29 39.24 39.07 38.9  32.79

0.1   824.6 823.7 821.7 817.9 816.8 800.4
                            Average of yearly averages:   546.026333333333

Inputs generated by pe5.pl - November 2006

Data used for this run:
Output File: acetres
Metfile:    w23234.dvf
PRZM scenario:    CAresidentialRLF.txt
EXAMS environment file: pond298.exv
Chemical Name:    acetamiprid
Description Variable Name     Value Units Comments
Molecular weight  mwt   222.68      g/mol
Henry's Law Const.      henry 5.2E-14     atm-m^3/mol
Vapor Pressure    vapr  7.5E-10     torr
Solubility  sol   4250  mg/L
Kd    Kd          mg/L
Koc   Koc   227   mg/L
Photolysis half-life    kdp   34    days  Half-life
Aerobic Aquatic Metabolism    kbacw 1974  days  Halfife
Anaerobic Aquatic Metabolism  kbacs 4116  days  Halfife
Aerobic Soil Metabolism asm   383   days  Halfife
Hydrolysis: pH 7  0     days  Half-life
Method:     CAM   1     integer     See PRZM manual
Incorporation Depth:    DEPI  0     cm
Application Rate: TAPP  26.22 kg/ha
Application Efficiency: APPEFF      0.99  fraction
Spray Drift DRFT  0     fraction of application rate applied to pond
Application Date  Date  01-01 dd/mm or dd/mmm or dd-mm or dd-mmm
Record 17:  FILTRA
      IPSCND      1
      UPTKF
Record 18:  PLVKRT
      PLDKRT
      FEXTRC      0.5
Flag for Index Res. Run IR    EPA Pond
```

Flag for runoff calc. RUNOFF none none, monthly or total(average of entire run)

stored as acetimp1.out
Chemical: acetamiprid
PRZM environment: CAImperviousRLF.txt modified Tueday, 20 February 2007 at 13:05:44
EXAMS environment: pond298.exe modified Wedday, 15 November 2006 at 13:47:26
Metfile: w23234.dvf modified Wedday, 3 July 2002 at 10:04:22
Water segment concentrations (ppb)

Year	Peak	96 hr	21 Day	60 Day	90 Day	Yearly
1961	13.94	13.84	13.43	12.65	12.22	10.08
1962	20.15	20.06	19.77	19.2	18.87	17.26
1963	36.5	36.33	35.63	34.45	33.78	30.14
1964	31.34	31.32	31.21	30.98	30.82	29.72
1965	51.3	51.14	50.46	49.09	48.31	44.99
1966	59.57	59.4	58.76	58.33	57.81	54.67
1967	96.46	96.12	94.63	91.86	90.34	82.55
1968	98.5	98.32	97.67	96.4	95.57	90.78
1969	94.55	94.49	94.13	93.5	93.01	89.44
1970	91.67	91.61	91.34	90.67	90.19	86.78
1971	86.87	86.81	86.55	86.01	85.65	82.77
1972	82.58	82.52	82.32	81.82	81.45	78.75
1973	105	105	104	102	101	95.05
1974	118	118	117	115	114	108
1975	109	109	108	108	107	104
1976	106	106	106	106	105	102
1977	113	113	112	111	110	105
1978	107	107	107	106	105	101
1979	104	104	103	103	102	98.21
1980	101	101	100	99.61	99.11	95.47
1981	92.38	92.34	92.16	91.87	91.64	88.68
1982	97.7	97.56	97	95.99	95.37	91.44
1983	102	102	102	101	99.84	95.19
1984	96.4	96.34	96.01	95.4	94.93	91.36
1985	97.17	97.04	96.57	96.12	95.64	91.79
1986	101	101	101	99.62	98.91	94.6
1987	104	104	103	102	102	97.12
1988	99.71	99.61	99.22	98.44	97.91	94.06
1989	100	99.96	99.52	98.7	98.13	94.09
1990	107	106	106	105	104	99.42

Sorted results

Prob.	Peak	96 hr	21 Day	60 Day	90 Day	Yearly
0.032258064516129	118	118	117	115	114	108
0.0645161290322581		113	113	112	111	110	105
0.0967741935483871		109	109	108	108	107	104
0.129032258064516	107	107	107	106	105	102
0.161290322580645	107	106	106	106	105	101
0.193548387096774	106	106	106	105	104	99.42
0.225806451612903	105	105	104	103	102	98.21
0.258064516129032	104	104	103	102	102	97.12
0.290322580645161	104	104	103	102	101	95.47
0.32258064516129	102	102	102	101	99.84	95.19
0.354838709677419	101	101	101	99.62	99.11	95.05

```
0.387096774193548 101   101   100   99.61 98.91 94.6
0.419354838709677 100   99.96 99.52 98.7  98.13 94.09
0.451612903225806 99.71 99.61 99.22 98.44 97.91 94.06
0.483870967741936 98.5  98.32 97.67 96.4  95.64 91.79
0.516129032258065 97.7  97.56 97    96.12 95.57 91.44
0.548387096774194 97.17 97.04 96.57 95.99 95.37 91.36
0.580645161290323 96.46 96.34 96.01 95.4  94.93 90.78
0.612903225806452 96.4  96.12 94.63 93.5  93.01 89.44
0.645161290322581 94.55 94.49 94.13 91.87 91.64 88.68
0.67741935483871  92.38 92.34 92.16 91.86 90.34 86.78
0.709677419354839 91.67 91.61 91.34 90.67 90.19 82.77
0.741935483870968 86.87 86.81 86.55 86.01 85.65 82.55
0.774193548387097 82.58 82.52 82.32 81.82 81.45 78.75
0.806451612903226 59.57 59.4  58.76 58.33 57.81 54.67
0.838709677419355 51.3  51.14 50.46 49.09 48.31 44.99
0.870967741935484 36.5  36.33 35.63 34.45 33.78 30.14
0.903225806451613 31.34 31.32 31.21 30.98 30.82 29.72
0.935483870967742 20.15 20.06 19.77 19.2  18.87 17.26
0.967741935483871 13.94 13.84 13.43 12.65 12.22 10.08

0.1   108.8 108.8 107.9 107.8 106.8 103.8
                            Average of yearly averages:   81.4803333333333

Inputs generated by pe5.pl - Novemeber 2006
Data used for this run:
Output File: acetimp1
Metfile:    w23234.dvf
PRZM scenario:    CAImperviousRLF.txt
EXAMS environment file: pond298.exv
Chemical Name:    acetamiprid
Description Variable Name     Value Units Comments
Molecular weight  mwt   222.68      g/mol
Henry's Law Const.      henry 5.2E-14     atm-m^3/mol
Vapor Pressure    vapr  7.5E-10     torr
Solubility  sol   4250  mg/L
Kd    Kd          mg/L
Koc   Koc   227   mg/L
Photolysis half-life    kdp   34    days  Half-life
Aerobic Aquatic Metabolism    kbacw 1974  days  Halfife
Anaerobic Aquatic Metabolism  kbacs 4116  days  Halfife
Aerobic Soil Metabolism asm   383   days  Halfife
Hydrolysis: pH 7  0     days  Half-life
Method:     CAM   2     integer     See PRZM manual
Incorporation Depth:    DEPI  0     cm
Application Rate: TAPP  0.2622      kg/ha
Application Efficiency: APPEFF      0.99  fraction
Spray Drift DRFT  0     fraction of application rate applied to pond
Application Date  Date  01-01 dd/mm or dd/mmm or dd-mm or dd-mmm
Record 17:  FILTRA
      IPSCND      1
      UPTKF
Record 18:  PLVKRT
      PLDKRT
      FEXTRC      0.5
Flag for Index Res. Run IR    EPA Pond
Flag for runoff calc.   RUNOFF      none  none, monthly or total(average of
entire run)
```

Tier I Rice Model v2.0

Equation: EEC = (App rate * 100 / (dw + (dsed * (θ + (ρ * Kd / 1000))))) * exp (-day * k_{AAM})

Inputs

Parameter	Value
Application rate (lbs/A)	0.13
Koc (L/kg)	227
If no Koc, enter Kd (L/kg)	
AAM t1/2 (d)	384

Model Parameters

Parameter	Value
Water column depth (m)	0.10
Sediment depth (m)	0.01
Organic fraction of sediment	0.01
Sediment bulk density (kg/m^3)	1300
Sediment porosity	0.509

Calculated Parameters

Parameter	Value
Kd input (L/kg)	2.27
AAM rate constant	0.001805
App. rate (kg/ha)	0.14573

Daily Output

Day	EEC (µg/L)
0	108.2689
1	108.0737
2	107.8788
3	107.6842
4	107.49
5	107.2962
6	107.1027
7	106.9095
8	106.7167
9	106.5243
10	106.3321
11	106.1404
12	105.949
13	105.7579
14	105.5672
15	105.3768
16	105.1867
17	104.997
18	104.8077
19	104.6187
20	104.43
21	104.2417
22	104.0537
23	103.866
24	103.6787
25	103.4917
26	103.3051
27	103.1188

Eco EECs

Holding Time	Peak	21-d Mean	60-d Mean	Annual Mean
Paddy	108.27	106.34	102.70	79.37
3-d Tail	107.68	105.76	102.15	78.94
21-d Tail	104.24	102.38	98.88	76.42

DW EECs

	100% PCA		85% PCA		67% PCA		56% PCA
Holding Time	Peak	Annual Mean	Peak	Annual Mean	Peak	Annual Mean	Peak
3-d Tail	107.68	78.94	91.53	67.10	72.15	52.89	60.30
21-d Tail	104.24	76.42	88.61	64.95	69.84	51.20	58.38