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OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

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MEMORANDUM

Subject: Registration Review: Problem Formulation for the Environmental Fate, Ecological Risk, Endangered Species, and Drinking Water Assessments for Acequinocyl

To: Meg Hathaway, Chemical Review Manager
Dana Friedman, Acting Team Leader/Cathryn Britton, Team Leader
Kevin Costello, Branch Chief
Risk Management and Implementation Branch II
Pesticide Re-Evaluation Division (7508P)

From: Freeborn Jewett, M.S., Biologist 5/18/15
Michael Lowit, Ph.D., Ecologist 5/18/15
Sujatha Sankula, Ph.D., Branch Chief 5/18/15
Environmental Risk Branch I
Environmental Fate and Effects Division (7507P)

1. Executive Summary:

The Environmental Fate and Effects Division (EFED) has completed the problem formulation for the environmental fate, ecological risk, endangered species, and drinking water exposure assessments to be conducted as part of the Registration Review of the miticide acequinocyl. Functioning as the first stage of the risk assessment process for Registration Review, this problem formulation provides an overview of what is currently known about the environmental fate and ecological effects associated with acequinocyl and its degradates. It also describes the preliminary ecological risk hypothesis and analysis plan for evaluating and characterizing drinking water exposure and risk to non-target species and the environment in support of the Registration Review of acequinocyl. 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 acequinocyl.

Recommended Studies:

Ecological Effects

- Guideline 850.1025- Estuarine/marine invertebrate acute toxicity using mollusk (TGAI)
- Guideline 850.2100: Avian acute oral toxicity- with a passerine species (TGAI)
- Guideline 850.1400- Freshwater fish early-life stage (TGAI)
- Guideline 850.1400- Estuarine/marine fish early-life stage (TGAI)
- Guideline 850.4400- Aquatic vascular plant toxicity test (TEP)
- Guideline 850.4500- Estuarine/marine diatom toxicity test using *Skeletonomea costatum* (TEP)
- Guideline 850.4500- Freshwater diatom toxicity test using *Navicula pelliculosa* (TEP)
- Guideline 850.4550- Blue green algae toxicity test using *Anabaena flos-aquae* (TEP)
- Non Guideline- Whole sediment chronic invertebrates- freshwater midge *Chironomus dilutus*, freshwater amphipod *Hyalella azteca*, and estuarine/marine amphipod *Leptocheirus plumulosus*[1] (TGAI)[2]
- Non Guideline Tier I: Honeybee adult chronic oral exposure (TGAI)
- Non Guideline Tier I: Honeybee larval acute and chronic oral exposure (TGAI)
- Non-Guideline Tier II: Residue in pollen and nectar (recommendation pending risks identified in Tier I studies) (TEP)
- Guideline 850.3040: Tier II semi-field testing for pollinators (tunnel and feeding studies) (recommendation pending risks identified in Tier I studies) (TEP)
- Guideline 850.3040: Tier III full-field testing for pollinators (recommendation pending risk identified in Tier II studies) (TEP)

[1]EFED acknowledges that acequinocyl stability issues have been reported in estuarine/marine invertebrate tests that resulted in a waiver for the chronic estuarine/marine invertebrate study (USEPA, 2010). If chemical stability is an issue during the chronic testing with a marine/estuarine amphipod species, consulting with EFED scientists about other testing options may be possible.
[2]As indicated in 40 CFR Part 158, the registrant is required to submit a protocol for approval prior to initiating studies with each of the three invertebrate species.

Fate

Although fate data are available, there are data gaps for all guideline requirements triggered for acequinocyl uses (except terrestrial field dissipation) because of the numerous issues with the available studies (*described in Section 11*). In general, there is uncertainty for most of the studies about whether or not degradation rates were overestimated because there are unresolved questions about the potential contribution of non-experimental related sources of degradation that may have occurred during the course of the studies. It would be ideal to collectively address the data gaps (outlined in **Table 7)** for all of the fate studies; however, the ecological risk assessment and drinking water assessment (DWA) may proceed based on the available data by making conservative assumptions as in past risk assessments. Two approaches may be used to bound aquatic estimated environmental concentrations (EECs):

- In *Approach 1*, acequinocyl will conservatively be assumed to be stable to all routes of degradation because of the uncertainties associated with the environmental fate data, mainly the lack of validation of the analytical methods and the lack of storage stability data.
- In *Approach 2*, it will be assumed that the half-lives of acequinocyl and the degradation product 2-dodecyl-3-hydroxy-1,4-naphthalenedione aka 2-dodecyl-3-hydroxy-1,4-naphthoquinone or R1 (hereinafter R1) are accurate and total toxic residues (acequinocyl + R1) will be modeled to address toxicity concerns with R1. Uncertainties about degradation rates would need to be addressed for all studies in order to move away from conservative assumptions such as those outlined above (i.e., approach 1). Addressing other issues such as testing on additional soils (e.g. aerobic soil metabolism) is expected to have little impact on the risk assessment unless issues with the existing studies surrounding potential overestimation of degradation rates are addressed first; thereby, potentially allowing the risk assessment to move away from the assumption of stability (upper bound EEC). Despite uncertainties in the fate data, EECs based on both approaches led to the same conclusions in past risk assessments; that is, the greatest risk to the aquatic environment from use of acequinocyl is direct effects on invertebrate species. On the other hand, reliance on potentially conservative assumptions may lead to overly conservative mitigation measures to protect endangered aquatic species.

2. Introduction

The purpose of this problem formulation is to provide an understanding of what is known about the environmental fate and ecological effects of acequinocyl, considering its currently registered uses. This document will provide a plan for analyzing data relevant to acequinocyl and for conducting ecological risk, endangered species, and drinking water exposure assessments for its registered uses. 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 acequinocyl.

Acequinocyl (CAS: 57960-19-7; PC Code: 006329; (2-(acetyloxy)-3-dodecyl-1,4-naphthalenedione)) is a miticide belonging to the quinoline class of chemicals. Acequinocyl is registered for commercial use under the name of Kanemite 15 SC (15.8% a.i.) (EPA reg. #66330-38) for the control of various mite species (USEPA, 2014a). In the U.S., acequinocyl is labeled for use on tree nuts, pistachios, citrus, climbing vine fruits, pome fruits, fruiting vegetables, low growing berries, caneberries, cherries,

succulent shelled beans, melons, cucumbers, okra, edible podded beans, succulent soybean, hops, and landscape ornamentals. Acequinocyl is applied by foliar spray application using ground equipment at a maximum single application rate of 0.3 lbs a.i./A with a maximum of two applications annually.

3. Use Characterization

a. Mode of Action

Acequinocyl belongs to the quinoline class of chemicals. Upon application, acequinocyl hydrolyzes to hydroxy-acequinocyl (R1) in the mite body and binds to the Qo center at complex III in mitochondria. The net result is the blockage of cellular respiration and other adverse metabolic effects in mites, although it is not clear at this point what proportion of the miticidal action is through the parent and which is through the metabolite R1. Acequinocyl has no systemic activity but provides contact control of all life stages of mites.

b. Overview of Pesticide Use and Usage

The Biological and Economic Analysis Division (BEAD) provided a Screening Level Usage Analysis (SLUA) (USEPA, 2014a) to provide estimates of the actual usage of acequinocyl on agricultural crops.

The screening level usage profile (SLUA) produced by BEAD and located in the docket (USEPA, 2014a) and summarized in **Table 1**, lists the use patterns for the current uses of acequinocyl. Primary uses in terms of average weight of applied product of acequinocyl are almonds, apples, oranges, and strawberries. These data represent annual data from 2004-2012.

Appendix 2 summarizes the application rates of acequinocyl for all labeled uses.

Table 1: Estimates of the Actual Usage of Acequinocyl on Agricultural Crops.

Crop	Average Annual Lbs. A.I.	Percent Crop Treated	
		Average	Maximum
Almonds	1,000*	<1	<2.5
Apples	1,000	<2.5	<2.5
Grapefruit	<500	<2.5	<2.5
Grapes	<500	<1	<2.5
Lemons	<500	<2.5	<2.5
Oranges	1,000	<1	<2.5
Pears	<500	<1	<2.5
Strawberries	10,000	5	10
Tangerines	<500	<2.5	5
Walnuts	<500	<1	<2.5

*All numbers rounded.

4. Conclusions from Previous Risk Assessments

a. Ecological Risk Assessment

Acequinocyl was first assessed in 2003. Since then, the Agency has conducted multiple ecological risk assessments on acequinocyl. The most recent risk assessment was carried out in 2011 in Succulent Soybean, Low Growing Berry, Small Fruit Vine Climbing (except kiwifruit), Succulent Shelled Beans, Cowpea Forage, Caneberry, Melon, Cucumber, and Cherry (D448205). A full list of previous acequinocyl risk assessments is available in **Appendix 1**. The direct risk concerns identified in past assessments are:

- Freshwater Invertebrates (Acute listed and non-listed and Chronic listed and non-listed)
- Estuarine/Marine Invertebrates (Acute listed and non-listed and Chronic listed and non-listed)
- Mammals (Chronic listed and non-listed)
- Terrestrial Invertebrates (Assumed based on lack of acceptable endpoints)
- Birds (Chronic listed and non-listed)

b. Drinking Water Exposure Assessments

The most recent DWA was conducted in 2011 (DP389520). Two approaches were used to estimate drinking water concentrations (EDWCs) due to uncertainties associated with the available environmental fate data. In *Approach 1*, acequinocyl was assumed to be stable to all routes of degradation. In *Approach 2*, it was assumed that the half-lives of acequinocyl and the degradation product R1 were accurate and total toxic residues (acequinocyl + R1) were modeled to address toxicity concerns with both acequinocyl and R1.

Some EDWCs exceed the solubility limit of acequinocyl (6.69 µg/L at 20°C); therefore, in those cases the recommended EDWCs are equal to the solubility limit. The acute EDWC = 6.69 µg/L (*Approach 1)* and 5.59 µg/L (*Approach 2)*. The annual mean (chronic) EDWC = 6.69 µg/L (*Approach 1)* and 1.36 µg/L (*Approach 2*). The 30-year annual mean EDWC = 6.69 µg/L (*Approach 1)* and 0.27 µg/L (*Approach 2*). The ground water concentration = 3.6 x 10-3 µg/L (acute and chronic).

c. Clean Water Act Programs

Acequinocyl is not identified as a cause of impairment for any bodies listed as impaired under section 303(d) of the Clean Water Act (as of 11/2014).[1] A Total Maximum Daily Load (TMDL) has not been developed.[2] 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 Registration Review Risk Assessment and Management Process*[3], in order to ensure they can be used quantitatively or qualitatively in pesticide risk assessments.

[1] http://iaspub.epa.gov/tmdl_waters10/attains_nation_cy.cause_detail_303d?p_cause_group_id=885

[2] http://iaspub.epa.gov/tmdl_waters10/attains_nation.tmdl_pollutant_detail?p_pollutant_group_id=885&p_pollutant_group_name=PESTICIDES

[3] http://www.epa.gov/oppfead1/cb/ppdc/2006/november06/session1-sop.pdf

5. Environmental Fate and Transport

Acequinocyl appears to undergo fairly rapid transformation in most aquatic and terrestrial environments. Acequinocyl undergoes rapid hydrolysis under neutral and alkaline pH conditions with a half-life of 1.26 hours to less than 2 days. However, it is more stable under acidic pH conditions (e.g., 75 days at pH 4). Photodegradation in water appears to occur even more quickly with half-lives of less than 15 minutes in sterile lab and river water. In contrast, available data provides no evidence of photodegradation in soil. Aerobic biotransformation in soil was also rapid with half-lives less than 2 days under laboratory conditions. Acequinocyl also dissipated quickly in aquatic metabolism studies (half-lives < 1 day); however, hydrolysis may have contributed to the observed degradation. Under field conditions, acequinocyl applied to bare plots dissipated with half-lives ranging from 2 hours in California to 14 hours in New York. In contrast, magnitude of residue studies showed longer half-lives (mean half-life of 20 days based on apples, pears, oranges, grapefruit, lemon, and almonds; USEPA, 2004a).

Vapor pressure (1.69 x 10-6 Pa at 25 °C) and Henry's Law Constant (9.59 x10-7 atm x m3/mol) indicate a low possibility of volatilization of acequinocyl from soil and water.

Acequinocyl is expected to exhibit low mobility in soil. The soil adsorption Kd for acequinocyl ranged from 678 ml/g in sandy loam soil to 1,620 ml/g in silty clay loam soil. One of the major degradation products, R1, is slightly more mobile than acequinocyl under some conditions (Kd ranged from 27 ml/g in silt loam to 3,400 ml/g in sandy loam soil). In the field studies, acequinocyl and the observed degradates (R1 and AKM-18) were not detected below 0-15 cm soil depth.

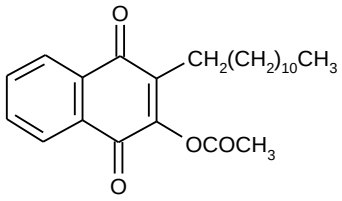
Acequinocyl has a tendency to bioconcentrate based on the bioconcentration factor (BCF) in fish (307 to 387) and high octanol/water partition coefficient (Log Pow ≥ 6.2). However, the depuration half-life is less than 1 day. The physical, chemical, and environmental fate properties of acequinocyl are summarized in **Table 2**.

a. Transformation Products

The major degradation products (formation > 10% of applied acequinocyl) most often detected in the laboratory and field studies were R1 (2-dodecyl-3-hydroxy-1, 4-napthoquinone) and AKM-18 (2-(1,2-dioxotetradecyl) benzoic acid). AKM-08 (2-(2-oxo-dodecyl)-3-hydroxy-1,4-naphthoquinone), o-phthalic acid, and phenol were major degradates only in the aqueous photolysis study. CBAA (2-carboxy-α-oxo-benzene acetic acid) was a major degradate only in the aerobic aquatic metabolism study. Fate data are not available for the major degradation products with the exception of the batch equilibrium study for R1. **Appendix 3** summarizes the maximum formation of major acequinocyl degradation products.

Table 2. Physical, Chemical, and Environmental Fate Properties of Acequinocyl

Parameter	Value	Reference	Comments
Chemical	Acequinocyl		
Chemical Name	2-(acetyloxy)-3-dodecyl-1,4-naphthalenedione		
Empirical Formula	$C_{24}H_{32}O_4$	MRID 45434901	
CAS Number	57960-19-7		

Parameter	Value	Reference	Comments
Structure		MRID 45434909	
SMILES	C(CCCCCCCCCCC)C1=C(C(=O)(c2c(cccc2)C1(=O)))OC(=O)C	EPI Suite v 4.1[1]	
Selected Physical/Chemical Parameters			
Molecular mass	384.5	MRID 45434901	
Water Solubility (20°C)	6.69 µg/L	MRID 45434906	
Log Pow	≥6.2		
Vapor pressure (25°C)	1.69 x 10^{-6} Pa	MRID 45434905	
Henry's law constant	9.59 x10^{-7} atm·m^3/mol		Calculated
Persistence[2]			
Hydrolysis (t ½)	19 days (pH 1.2) 75 days (pH 4) 1.6 days (pH 7) 1.26 hours (pH 9)	MRID 45434908 Supplemental	
Aqueous Photolysis (t ½)	14 minutes (buffer solution, pH 5) 12 minutes (sterile river water, pH 7.8)	MRID 45434909 Supplemental	
Soil Photolysis (t ½)	Stable*	MRID 45434910 Supplemental	*Rate of degradation was the same in irradiated samples (t ½ = 2.0 days) and dark controls (t ½ = 1.9 days)
Aerobic Soil Metabolism (t ½)	< 2 days (visual)	MRID 45434911 Supplemental	
Aerobic Aquatic Metabolism (t ½)	8.5 and 9.8 hours (total system)	MRID 45434914 Supplemental	Degradation likely driven by hydrolysis given that the system pH ~ 8.
Anaerobic Aquatic Metabolism (t ½)	< 1 day (visual, total system)	MRID 45434913 Supplemental	
Mobility			
Kd	678-1620 mL/g (acequinocyl) 27-3400 mL/g (R1)	MRID 45531902 Supplemental MRID 45434907 Supplemental	
Field Dissipation			
Terrestrial Field Dissipation (t ½)	2-14 hours	MRID 45651601 Acceptable	

Parameter	Value	Reference	Comments
Bioaccumulation			
Bioaccumulation in Common Carp (Depuration t ½) (BCF)	 < 1 day* (whole fish) 307-387 (whole fish)		* 80% depuration after 1 day

[1] http://www.epa.gov/opptintr/exposure/pubs/episuite.htm

[2] Half-lives based on acequinocyl + R1 residues may be recalculated at the time of risk assessment using the most up-to-date guidance (acequinocyl + R1 residue half-lives are presented in DP285811+, USEPA, 2004a).

6. Receptors

Consistent with the process described in the Overview Document (USEPA, 2004a), the risk assessment for acequinocyl relies on a surrogate species approach. Toxicological data generated from surrogate test species, which are intended to be representative of broad taxonomic groups, will be used to extrapolate the potential effects on a variety of species (receptors) included under these taxonomic groupings. **Table 3** and **Table 4** provide a summary of the aquatic and terrestrial taxonomic groups, respectively, and the most sensitive surrogate species tested to characterize the potential acute and chronic effects of acequinocyl. **Appendix 4** provides a full listing of the aquatic animal and plant toxicity endpoints for acequinocyl, as well as expanded explanations about the validity of the endpoints for risk assessments. **Table 5** provides information for the degradate R1. Empirically-measured toxicity data were not provided for major degradates AKM 18, AKM-08, o-Phthalic acid, Phenol, and CBAA. Estimates of the toxicities of these degradates are available in **Table 6**. Based on available ecotoxicity information, acequinocyl is very highly toxic to freshwater aquatic invertebrates. Acequinocyl is highly toxic to estuarine/marine fish and invertebrates, moderately toxic to freshwater fish, and slightly toxic to rats via inhalation. Acequinocyl is practically nontoxic to rats (acute oral exposure), birds, and honeybees (adult contact).

a. Effects to Aquatic Organisms

Aquatic invertebrates are the most sensitive taxa to acequinocyl exposure. Chronic toxicity data are available for freshwater invertebrates, but are not available for estuarine/marine invertebrates. A waiver request was granted for assessing chronic exposure to estuarine/marine invertebrates under chronic, flow-through conditions due to the fact that under experimental conditions, acequinocyl was not sufficiently stable to ensure desired exposure concentrations (USEPA 2010). This waiver applies to chronic studies, as stability was not as prevalent of an issue in acute studies. As a result, for the purposes of risk assessment, an estimated chronic toxicity value for estuarine/marine invertebrates will be estimated by taking an acute to chronic ratio (ACR) for water flea endpoints (MRIDs 46372101; 45434922) (2.4µg/L/0.98µg/L=2.45) and applying it to the most sensitive acute endpoint for an estuarine/marine invertebrate species, which is mysid shrimp (MRID 45434917) (0.94 µg/L/2.45=0.38 µg/L).

Several studies presented in **Table 3** were classified as supplemental because of low % recovery of the chemical. Unless specified otherwise in the "MRID & status" column of **Table 3,** these studies may be used quantitatively in risk assessments, as the low % recovery was consistent across all aquatic studies and degradation is presumed to result in conversion to major degradate R1. The R1 degradate is assumed to be of equal toxicity to acequinocyl to aquatic taxa, based on available aquatic toxicity data and results of ECOSAR toxicity modeling shown in **Table 5** and **Table 6**.

Part of the registration review process involves reviewing previously submitted studies to ensure that the study classifications reflect current guideline requirements. Three studies were submitted that tested the acute toxicity of acequinocyl TEP to bluegill sunfish (*Lepomis macrochirus*) (MRID 45428605), rainbow trout (*Oncorhynchus mykiss*) (MRID 45530601) and sheepshead minnows (*Cyprinodon variegatus*) (MRID 45428606). These studies were initially classified as acceptable, but will be downgraded based on the presence of a precipitate that was not centrifuged or filtered prior to analysis. The study measuring acute toxicity to rainbow trout (*Oncorhynchus mykiss*) (MRID 45530601) will be downgraded to invalid because a dose response was observed, but endpoints could not be determined because of uncertainty related to the bioavailability of the exposure concentrations. The studies measuring acute toxicity to sheepshead minnows (*Cyprinodon variegatus*) (MRID 45428606) and bluegill sunfish (*Lepomis macrochirus*) (MRID 45428605) will be downgraded to supplemental because no effects were observed at any concentrations, and exposure concentrations are assumed to be the limit of solubility (6.69 ppb). DERs for these studies will be modified to reflect these classification changes.

Table 3: Most Sensitive Aquatic Toxicity Endpoints for Acequinocyl

Taxa	Study Type	% ai	Species	Toxicity Value & Category	MRID & Status	Endpoints Affected
Freshwater Fish	Acute 850.1075	97.1	**Bluegill Sunfish** *Lepomis macrochirus*	LC50>1.1 mg ai/L NOAEC= 1.1 mg ai/L Moderately toxic	45434918 Supplemental Endpoints are valid for risk assessment.	None
Freshwater Invertebrates	Acute 850.1010	98.3	**Water Flea** *Daphnia magna*	LC50= 2.7 µg ai/L NOAEC= 0.66 µg ai/L Very highly toxic	46372101 Acceptable	Mortality and sublethal effects (lethargy)
	Chronic 850.1300	98.3	**Water Flea** *Daphnia magna*	NOAEC= 0.98 µg ai/L LOAEC= 1.8 µg ai/L	45434922 Supplemental Endpoints valid for risk assessment	Number of young, length and dry weight
Estuarine/ Marine Fish	Acute 850.1075	97.1	**Sheepshead minnow** *Cyprinodon variegatus*	LC50> 0.19 mg ai/L NOAEC= 0.19 mg ai/L Highly Toxic	45434921 Supplemental Endpoints valid to quantitatively assess risk.	None
Estuarine/ Marine Invertebrates	Acute 850.1035	97.1	**Mysid shrimp** *Americamysis bahia*	LC50=0.94 µg ai/L NOAEC= 0.27 µg ai/L Highly Toxic	45434917 Supplemental Endpoints valid to quantitatively assess risk.	Lethargic swimming, loss of equilibrium

Taxa	Study Type	% ai	Species	Toxicity Value & Category	MRID & Status	Endpoints Affected
	Chronic 850.1350	NA	**Mysid Shrimp** *Americamysis bahia*	NOAEC: 0.38 µg ai/L (Estimated using Acute to Chronic Ratio (ACR))	NA	NA
Aquatic Plants	Non Vascular 850.4400	97.1	**Green Algae** *Pseudokirchneriella subcapitata*	72-hour EC50=0.96 mg a.i./L NOAEC = 0.0017 mg ai/L	45435008 Supplemental Endpoints can be used to quantitatively assess risk to non-vascular aquatic plants. Study was conducted for 72 hours, shorter than the recommended 96-120 hour, yet the toxicity endpoint is several orders of magnitude above the limit of solubility for this chemical, so a new study would be unlikely to change risk conclusions.	None

a. Effects to Terrestrial Organisms

Table 4: Most Sensitive Terrestrial Toxicity Endpoints for Acequinocyl

Taxa	Study Type	% ai	Species	Toxicity Value & Category	MRID & Status	Endpoints Affected
Mammals	Acute oral 870.1100	96.8	**Rat** *Rattus norvegicus*	LD50> 5000 mg/kg-bw (Males and Females) Practically nontoxic	45435011 Acceptable	None

Taxa	Study Type	% ai	Species	Toxicity Value & Category	MRID & Status	Endpoints Affected
	Chronic 870.3800	97.1	**Rat** *Rattus norvegicus*	Parental NOAEL (m)= 100 mg/kg-diet LOAEL (m)= 800 mg/kg-diet Offspring NOAEL= 100 mg/kg-diet LOAEL= 800 mg/kg-diet	45531909 Acceptable	None
	Acute Inhalation	96.5	**Rat** *Rattus norvegicus*	LC50> 0.84 mg/L Males and Females Slightly Toxic	45435013 Acceptable	Mortality
Birds	Acute Oral 850.2100	98.4	**Mallard Duck** *Anas platyrhynchos*	LD50> 2000 mg ai/kg-bw NOAEL= 2000 mg ai/kg-bw Practically nontoxic	48660601 Acceptable	None
	Acute Dietary 850.2200	15.6	**Northern Bobwhite Quail** *Colinus virginianus*	LC50> 5970 mg ai/kg diet NOAEC= 5970 mg ai/kg diet Practically nontoxic	46622701 Acceptable	None
	Chronic 850.2300	97.1	**Mallard Duck** *Anas platyrhynchos*	NOAEC= 100 mg/kg-diet LOAEC= 500 mg/kg-diet	45435005 Acceptable	Female body Weight gain-
Terrestrial Invertebrates	Adult Acute Contact 850.3020	97.1	**Honeybee** *Apis mellifera*	48-hr LD50> 100 µg ai/bee NOAEL= 100 µg ai/bee Practically Nontoxic	45435007 Acceptable	None
	Adult Acute Oral	15.4	**Honeybee** *Apis mellifera*	72-hr LD50> 315 µg ai/bee NOAEL= 43.8 µg ai/bee	45428608 Supplemental Acceptable for use in risk assessment	None
Terrestrial Plants	Seedling Emergence Monocot 850.4100	15.3	**Oat** (*Avena sativa*) **Onion** (*Allium cepa*) **Corn** *(Zea mays*)	EC25>0.9 lb ai/a NOAEC= 0.9 lb ai/a No effect for all species	45428609 Acceptable	None

Taxa	Study Type	% ai	Species	Toxicity Value & Category	MRID & Status	Endpoints Affected
			Ryegrass (*Lolium perenne*)			
	Seedling Emergence Dicot 850.4100	15.3	**Carrot** (*Daucus carota*) **Rapeseed** (*Brassica napus*) **Sugarbeet** (*Beta vulgaris)* **Tomato** (*Solanum Lycopersicum*) **Cabbage** (*Brassica oleracea*) **Soybean** *(Glycine max*)	EC25= 0.7 lb ai/a NOAEC= 0.3 lb ai/a <u>Most sensitive species</u>: Carrot	45428609 Acceptable	Shoot Height
	Vegetative Vigor Monocot 850.4150	15.3	**Oat** (*Avena sativa*) **Onion** (*Allium cepa*) **Corn** (*Zea mays*) **Ryegrass** (*Lolium perenne*)	EC25> 0.9 lbs ai/a NOAEC= 0.9 lbs ai/a No effect for all species	45428610 Acceptable	None
	Vegetative Vigor Dicot 850.4150	15.3	**Carrot** (*Daucus carota*) **Rapeseed** (*Brassica napus*) **Sugarbeet** (*Beta vulgaris*) **Tomato** (*Solanum Lycopersicum*) **Cabbage** (*Brassica oleracea*) **Soybean** *(Glycine max*)	EC25> 0.9 lbs ai/a NOAEC= 0.3 lbs ai/a <u>Most sensitive species</u>: Beets, cabbage	45428610 Acceptable	Shoot Height

b. Degradate toxicity

Two studies were submitted that compared the acute toxicity of acequinocyl and R1 to the most sensitive aquatic species, the water flea (*Daphina magna*) (LC_{50} acequinocyl= 2.7 µg ai/L; LC50 R1= 2.4 µg ai/L). The results of these studies (**Table 5**) indicate that acute exposure of acequinocyl and the R1 degradate are of equal toxicity to aquatic freshwater invertebrates. A study carried out with the common carp (*Cyprinus carpio*) (MRID 46370502) did not observe toxicity effects for acequinocyl or R1 up to a maximum concentration of 1.1 mg ai/L. Toxicity data were not available for major degradates AKM 18, AKM 08, o-Phthalic acid, Phenol, CBAA. A full list of the major degradates and their chemical properties is available in **Appendix 3**.

Table 5: Toxicity Endpoints of Acequinocyl and the Major Acequinocyl Degradate H-Acequinocyl (R1)

Taxa	Study Type	Compound	Species	Toxicity Value & Category	MRID & Status
Freshwater Invertebrate	Acute 850.1010	Acequinocyl 97.0%	**Water Flea** *Daphnia magna*	LC50= 2.7 µg ai/L NOAEC= 0.66 µg ai/L Very highly Toxic	46372101 Acceptable
Freshwater Invertebrate	Acute 850.1010	R1 96.9%	**Water Flea** *Daphnia magna*	LC50= 2.4 µg ai/L NOAEC= 1.7 µg ai/L Very Highly Toxic	46372101 Acceptable
Freshwater Invertebrate	Acute 850.1010	Mixture composed of equal parts: Acequinocyl 97.0% + R1 96.9%	**Water Flea** *Daphnia magna*	LC50= 5.2 µg ai/L NOAEC= 1.5 µg ai/L Very Highly Toxic	46372101 Acceptable
Freshwater Fish	Acute 850.1075	R1 99.3%	**Common Carp** *Cyprinus carpio*	LC50>2.3 mg ai/L NOAEC= 2.3 mg ai/L Moderately Toxic	46370502 Supplemental-Non guideline test species and was conducted as a limit test. Endpoint can be used to quantitatively assess risk.

ECOSAR was used to predict toxicity of the major degradates (>10% formation) R1, AKM 18, AKM 08, o-Phthalic acid, Phenol, and CBAA. ECOSAR uses quantitative structure activity relationships (QSAR) to predict effects of acute exposure to aquatic species. Reliability of the predictive capacity of ECOSAR modeling is determined based on how closely the modeling program can estimate the toxicity of the parent compound.

Similarities between empirically-derived toxicity values for the parent or the R1 degradate and the toxicity values predicted by ECOSAR indicated that predicted toxicity values provided meaningful indications of acute and chronic exposure toxicity of acequinocyl degradates to the most sensitive

aquatic taxa, *Daphnia magna,* as well as exposure to green algae. Based on a similar comparison of ECOSAR-predicted toxicity values of acequinocyl to freshwater and estuarine/marine fish with the predicted values generated by ECOSAR, there was no confidence in these predicted values. The ECOSAR output for daphnia and green algae are available in **Table 6.**

Table 6: Acute and Chronic Values (µg ai/L) Predicted through ECOSAR Modeling

Exposure (Acute/ Chronic)	Taxa	Parent		Degradate						
		Acequinocyl Toxicity (from studies)	Acequinocyl (Predicted)	R1 (From studies)	R1 (predicted)	AKM 18	AKM 08	o-Phthalic acid	Phenol	CBAA
Acute	*Daphnia magna* **LC_{50}**	2.7	8	2.4	12	540	59	4,858,623	9,295	365,026
Chronic	*Daphnia magna* **NOAEC**	0.98	9	--	3	149	45[1]	373,177	1,770	43,360
Acute	Green Algae	960	34	--	34	1889	15	2,538,352	44,824	1,028,138

[1]Estimated by ECOSAR program using Acute to Chronic toxicity ratio

ECOSAR modeling does not provide evidence that major degradates R1 and AKM 08 are more or less toxic than acequinocyl, as the predicted toxicities of these degradates are similar to the measured toxicity endpoints of acequinocyl. In the case of R1, this was verified empirically, as discussed above. The degradates AKM-18, o-Phthalic acid, phenol and CBBA are predicted to be several orders of magnitude less toxic than acequinocyl.

c. Ecological Incidents

The Ecological Incident Information System or EIIS maintained by the Environmental Fate and Effects Division, and the Avian Incident Monitoring System (AIMS) maintained by the American Bird Conservancy, were searched on February 26, 2015 and no ecological incidents were recorded resulting from the use of acequinocyl.

In addition to the incidents recorded in EIIS and AIMS, additional incidents are reported to the Agency in aggregated form. Pesticide registrants report certain types of incidents to the Agency as aggregate counts of incidents occurring per product per quarter. Ecological incidents reported in aggregate reports include those categorized as 'minor fish and wildlife' (W-B), 'minor plant' (P-B), and 'other non-target' (ONT) incidents. 'Other non-target' incidents include reports of adverse effects to insects and other terrestrial invertebrates. For acequinocyl, there have been no reported incident summaries as of January 8, 2015.

7. Exposure Pathways of Concern

EFED's environmental exposure models estimate the potential exposure of plants and animals to pesticide residues in aquatic and terrestrial environments based on registered labels including maximum acequinocyl application rates and intervals. Some of the aquatic models can also be utilized to estimate pesticide residues in drinking water for use in the dietary exposure models. A more detailed description of aquatic and terrestrial models can be found at the following website: http://www.epa.gov/pesticides/science/models_db.htm.

The Screening Imbibition Program (SIP v.1.0) is used during the problem formulation phase of Registration Review to provide an upper-bound estimate of exposure of birds and mammals to pesticides through drinking water alone. SIP does not aggregate the drinking water exposure route with other exposure routes (*i.e.,* dietary, inhalation, dermal). Due to the lack of an observed toxicological effect at all levels, the risk from acequinocyl exposure from drinking water alone is presumed to be low. SIP readout for acequinocyl is available in **Appendix 5**

The Screening Tool for Inhalation Risk (STIR v.1.0) is used during the problem formulation phase of Registration Review to assess the potential for exposure to birds and mammals through inhalation. The exposure pathways that are assessed by this tool include both droplet inhalation and vapor phase inhalation. STIR is intended to determine if exposure is likely and not whether or not the potential for risk exists. If STIR predicts that exposure is likely, additional inhalation data may be necessary to adequately assess risk due to the inhalation exposure pathway. The STIR model predicted that exposure if not likely significant. STIR inputs and outputs for acequinocyl are available in **Appendix 6.**

8. Analysis Plan

a. Stressors of Concern

In order to estimate risks of acequinocyl exposures in aquatic and terrestrial environments, all exposure modeling and resulting risk conclusions will be based on registered labels including maximum application rates and methods for each use of acequinocyl. EFED's environmental exposure models estimate the potential exposure of plants and animals to pesticide residues in aquatic and terrestrial environments.

i. Ecological Risk Assessment

The stressors of concern for terrestrial taxa are acequinocyl and R1. Based on empirically-derived toxicity endpoints and predicted toxicity from ECOSAR, acequinocyl and R1 are predicted to be of equal toxicity. The stressors of concern for aquatic taxa are acequinocyl, R1, and the degradate AKM-08 which forms primarily during aqueous photolysis. Based on chemical similarities, empirically-derived toxicity endpoints, and the results of ECOSAR modeling results for aquatic taxa, these chemicals are presumed to be equally toxic to aquatic taxa. As in past risk assessments, conservative assumptions may be made for modeling aquatic EECs due to uncertainties about the available fate data. Two approaches may be used to address the uncertainty by bounding EECs. Approach 1 will assume parent compound stability, while Approach 2 (total toxic residues of acequinocyl + R1) will assume that the half-lives of acequinocyl and the R1 degradate were accurate. Approach 2 will assume equal toxicity for acequinocyl and R1. Approach 2 will not capture exposure to AKM-08 which is proposed as a degradation product of R1 and is assumed to be equally as toxic as R1 and acequinocyl. Approach 2 may be updated to include AKM-08 if it is determined that the available fate data are sufficient to address AKM-08 formation and decline. However, Approach 1 will account for any uncertainty in the formation of AKM-08 or any minor degradates which have similar structure to acequinocyl[4] and may have similar toxicity to acequinocyl and R1.

ii. Drinking Water

The last DWA was conducted in 2011 (DP389520). A new DWA will be conducted in registration review for all registered uses of acequinocyl. The DWA will include exposure estimates based on acequinocyl and the hydroxylated degradate, that is, R1 (residue of concern recommended by the Metabolism Assessment Review Committee (MARC) of the Health Effects Division (HED) (USEPA, 2004c) in surface and ground waters.

As in previous DWAs, two approaches may be used to calculate EDWCs due to uncertainties associated with the available environmental fate data. In *Approach 1*, acequinocyl will be conservatively assumed to be stable to all routes of degradation. In *Approach 2*, it will be assumed that the half-lives of acequinocyl and the degradation product R1 were accurate and the total toxic residues (acequinocyl + R1) will be modeled to address toxicity concerns with both acequinocyl and R1.

Surface water and ground water concentrations will be modeled using the most up-to-date models and guidance at the time of the risk assessment. The DWA will also include a summary of available surface and ground water monitoring data.

[4] Minor degradates with structures similar to acequinocyl formed in some of the available fate studies (e.g., aqueous photolysis and aerobic aquatic metabolism)

b. Measures of Exposure

EFED will use standard available models to evaluate potential exposures to aquatic and terrestrial organisms as described at http://www.epa.gov/pesticides/science/models_db.htm.

i. Available Monitoring Data

EFED will consider available monitoring data from federal and state agencies or other sources. The Agency welcomes submission of monitoring data.

c. Measures of Effect

Ecotoxicity data presented in **Tables 3-4** of this problem formulation will be used to calculate risk quotients. Any additional information submitted by the registrant or found in the open literature prior to conducting the risk assessment will also be considered. The open literature studies will be identified using EPA's ECOTOXicology database (ECOTOX[5]), which employs a literature search engine for locating chemical toxicity data for aquatic life, terrestrial plants, and wildlife.

9. Endangered Species Assessment

Consistent with EPA's responsibility under the Endangered Species Act (ESA), the Agency will evaluate risks to federally listed threatened and endangered (listed) species from registered uses of pesticides in accordance with the Joint Interim Approaches developed to implement the recommendations of the April 2013 National Academy of Sciences (NAS) report, *Assessing Risks to Endangered and Threatened Species from Pesticides*. The NAS report outlines recommendations on specific scientific and technical issues related to the development of pesticide risk assessments that EPA and the Services must conduct in connection with their obligations under the ESA and FIFRA. EPA will address concerns specific to acequinocyl in connection with the development of its final registration review decision for acequinocyl.

In November 2013, EPA, the U.S. Fish and Wildlife Service, National Marine Fisheries (the Services), and USDA released a white paper containing a summary of their joint Interim Approaches for assessing risks to listed species from pesticides. These Interim Approaches were developed jointly by the agencies in response to the NAS recommendations, and reflect a common approach to risk assessment shared by the agencies as a way of addressing scientific differences between the EPA and the Services. Details of the joint Interim Approaches are contained in the November 1, 2013 white paper, *Interim Approaches for National-Level Pesticide Endangered Species Act Assessments Based on the Recommendations of the National Academy of Sciences April 2013 Report.*

Given that the agencies are continuing to develop and work toward implementation of the Interim Approaches to assess the potential risks of pesticides to listed species and their designated critical habitat, this ecological problem formulation supporting the Preliminary Work Plan for acequinocyl does not describe the specific ESA analysis, including effects determinations for specific listed species or designated critical habitat, to be conducted during registration review. While the agencies continue to develop a common method for ESA analysis, the planned risk assessment for the registration review of acequinocyl will describe the level of ESA analysis completed for this particular registration review case. This assessment will allow EPA to focus its future evaluations on the types of species where the potential for effects exists, once the scientific methods being developed by the agencies have been fully vetted. Once the agencies have fully developed and implemented the scientific methods necessary to

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

complete risk assessments for listed species and their designated critical habitats, these methods will be applied to subsequent analyses of acequinocyl as part of completing this registration review.

10. Endocrine Disruptors Screening Program

Acequinocyl was not included in either the first or second group of chemicals issued an order to conduct Tier I EDSP testing, for more information on the EDSP program, visit http://www.epa.gov/endo/.

11. Preliminary Identification of Data Gaps

a. Fate

Table 7 lists the status of the fate and transport data requirements for acequinocyl. Although fate data are available, there are data gaps for all guideline requirements triggered for acequinocyl uses (except terrestrial field dissipation) because of the numerous issues with the available studies. These issues need to be addressed to upgrade the status of these studies. A common issue identified in most of the submitted fate studies is the necessity to determine whether the analytical methods were appropriate to accurately assess the rate of degradation of acequinocyl and to identify its major transformation products. Validation of all analytical methods used is required to address this issue. Another common deficiency is the lack of storage stability data to determine if the degradation of [^{14}C] acequinocyl and its transformation products occurred during storage before the analysis of samples. Storage stability data reflecting storage conditions for each study are required to address this issue. Although some data have been submitted to address these issues (e.g., method validation), they are insufficient to upgrade any of the studies.

It would be ideal to collectively address the data gaps for all of the fate studies; however, the ecological risk assessment and DWA may proceed based on the available data by making conservative assumptions as in past risk assessments. Two approaches may be used to bound aquatic EECs. In *Approach 1*, acequinocyl will conservatively be assumed to be stable to all routes of degradation because of the uncertainties associated with the environmental fate data, mainly the lack of validation of the analytical methods and the lack of storage stability data. In *Approach 2*, it will be assumed that the half-lives of acequinocyl and the degradation product R1 are accurate and total toxic residues (acequinocyl + R1) will be modeled to address toxicity concerns with R1.

Uncertainties about degradation rates would need to be addressed for all studies in order to move away from conservative assumptions such as those outlined above. Addressing other issues such as testing on additional soils (e.g. aerobic soil metabolism) is expected to have little impact on the risk assessment unless issues with the existing studies surrounding potential overestimation of degradation rates are addressed first; thereby, potentially allowing the risk assessment to move away from the assumption of stability. Despite uncertainties in the fate data, EECs based on both approaches led to the same conclusions in past risk assessments; that is, the greatest risk to the aquatic environment from use of acequinocyl is direct effects on aquatic invertebrate species. On the other hand, reliance on potentially conservative assumptions may lead to overly conservative mitigation measures to protect endangered aquatic species.

Table 7. Environmental Fate Data and Data Gaps for Acequinocyl

OCSPP Guideline	Data Requirement	MRID	Classification	Data Gap?	Comments
835.2120	Hydrolysis	45434908	Supplemental	Yes	It would be ideal to collectively address the data gaps for all of the fate studies; however, the ecological risk assessment and DWA may proceed based on the available data by making conservative assumptions as in past risk assessments. A detailed discussion about data gaps and assumptions that will be made in the absence of additional data are described above.
835.2240	Aqueous Photolysis	45434909	Supplemental	Yes	
835.2410	Soil Photolysis	45434910	Supplemental	Yes	
835.4100	Aerobic Soil Metabolism	45434911 45434912	Supplemental Invalid	Yes	
835.4200	Anaerobic Soil Metabolism	-	-	Yes	
835.4300	Aerobic Aquatic Metabolism	45434914	Supplemental	Yes	
835.4400	Anaerobic Aquatic Metabolism	45434913	Supplemental	Yes	
835.1230 835.1240	Leaching Adsorption/ Desorption	45531902 45434907	Supplemental Supplemental	Yes	
835.6100	Terrestrial Field Dissipation	45651601	Acceptable	No	
850.1730	Accumulation in Fish	45434923	Supplemental	Yes	

b. Effects

Tables 8-9 identify ecological effect studies by MRID that offer data for each guideline requirement. In the case that studies providing valid toxicity endpoints are not available, these will be recommended below. Rationale for additional data requests are presented in the table, and in the case that OCSPP test guidelines are not available for the data requirement, rationale for the additional data request is present in the comments.

Table 8: Data Gap Table of Aquatic Effect Data for Acequinocyl and Major Degradates

OCSPP Guideline	Data requirement	MRID	Classification	Data Gap?	Comments
850.1010	Freshwater Invertebrate Acute Toxicity	46372101	Acceptable	No	
850.1035 Mysid 850.1025 Oyster	Estuarine/Marine Invertebrate Oyster Acute Toxicity	45434917 45434916	Supplemental Supplemental	**Yes**	Guideline requirement for mysid shrimp is fulfilled. Study recorded high rate of degradation of the chemical throughout the experiment, however this recovery % is consistent with all aquatic studies.

OCSPP Guideline	Data requirement	MRID	Classification	Data Gap?	Comments
					Guideline requirement for mollusk remains unfulfilled. Poor performance of controls in the eastern oyster study (MRID 45434916) means that this study is only valid for qualitative use.
850.1300	Freshwater Invertebrate Life Cycle	45434922	Supplemental	No	The supplemental study is considered scientifically sound for use in the risk assessment, as the low recovery % was outside guideline recommendations but was consistent with other aquatic studies.
850.1350	Estuarine/Marine Invertebrate Life Cycle	None	NA	No	Waiver request was granted to exempt the registrant from this guideline requirement because of solubility issues with acequinocyl. This endpoint will be estimated using an Acute to Chronic Ratio (ACR).
850.1075	Freshwater Fish Acute Toxicity	45868502/ 45434920 (same study) Trout 45434918 Bluegill	Supplemental Supplemental	No	The supplemental study is considered scientifically sound for quantitative use in the risk assessment as the low chemical recovery % was outside guideline recommendations but was consistent with other aquatic studies.
850.1075	Estuarine/Marine Fish Acute Toxicity	45434921	Supplemental	No	The supplemental study is considered scientifically sound for use in the risk assessment, as this limit test measured no effect at levels that were several orders of magnitude above the limit of solubility. The chemical recovery % was outside guideline recommendations but was consistent with other aquatic studies.
850.1400	Freshwater Fish Early-Life Stage	45428607	Supplemental	**Yes**	Only two replicates per test concentration were included. As a result, the study may only be used to qualitatively assess risk of chronic exposure to freshwater fish. Study

OCSPP Guideline	Data requirement	MRID	Classification	Data Gap?	Comments
					must be repeated with the recommended four replicates. In the absence of these data, chronic freshwater fish toxicity data for surrogate pesticides – starting with data for closely related pesticides and proceeding to data for less related pesticides – may be used to characterize the chronic toxicity of acequinocyl to freshwater fish.
850.1400	Estuarine/Marine Fish Early-Life Stage	None	NA	**Yes**	In absence of data, chronic toxicity to estuarine/marine fish may be characterized using data for surrogate pesticides – starting with data for closely related pesticides and proceeding to data for less related pesticides. EFED acknowledges that previous chronic studies with estuarine/marine studies have encountered difficulties maintaining concentrations due to low solubility in salt water. If this problem continues to occur, this test can be conducted using TEP, as this is reported to have a higher solubility in salt water.
850.4400	Aquatic Vascular Plant Toxicity Test using *Lemna* spp.	None	NA	**Yes**	40 CFR Part 158 requires the submission of aquatic vascular plant toxicity data. Risk to this taxa will be presumed until data are submitted.
850.4500	Green Algae Toxicity *Pseudokirchneriella subcapitata*	45428611 TGAI 45435008 TEP	Supplemental	No	Both studies with green algae were conducted for less than the recommended 96 hours and as a result, are classified as supplemental. The toxicological endpoints derived from these studies for green algae are far above the limit of solubility of this
850.4500	Marine diatom *Skeletonema costatum*	None	NA	**Yes**	

OCSPP Guideline	Data requirement	MRID	Classification	Data Gap?	Comments
850.4500	Freshwater diatom *Navicula pelliculosa*	None	NA	**Yes**	chemical, so the submission of a new study on green algae would not impact the risk conclusion and is therefore not requested at this time. 40 CFR Part 158 requires the submission of toxicity data for nonvascular aquatic plant species Green Algae *Pseudokirchneriella subcapitata,* Marine diatom *Skeletonema costatum,* Freshwater diatom *Navicula pelliculosa,* and Blue Green Algae/Cyanobacterium *Anabaena flos-aquae*. Risk to this taxa will be presumed until valid studies are submitted for each taxa except green algae.
850.4550	Blue Green Algae/ Cyanobacterium *Anabaena flos-aquae*	None	NA	**Yes**	
Non Guideline	Whole sediment: chronic invertebrates- freshwater and estuarine/marine	None	NA	**Yes**	Chronic sediment invertebrate toxicity data are required under 40 CFR Part 158 and further clarified in Guidance for Benthic Invertebrates (USEPA, 2014) if: i. The half-life of the pesticide in sediment if > 10 days in either the aerobic soil or aquatic metabolism studies and if any of the following exist: A. The soil partition coefficient (Kd) is ≥ 50 B. The log Kow is ≥ 3. C. The Koc is ≥ 1,000. The average half-life of acequinocyl and major degradate R1 reported in the aerobic soil metabolism is 42 days; and the log Kow and Koc of acequinocyl are 6.69 and 1027-970 mL/g, respectively. Exposure duration for benthic invertebrates to acequinocyl and R1 is considered more relevant because available data suggest that the toxicity of the two compounds is equal for aquatic invertebrates. Therefore, chronic sediment tests with the midge *Chironomus dilutus*, freshwater amphipod *Hyalella azteca*,

OCSPP Guideline	Data requirement	MRID	Classification	Data Gap?	Comments
					and estuarine/marine amphipod *Leptocheirus plumulosus* are needed. In the absence of these data, sediment-dwelling invertebrate chronic toxicity data for surrogate pesticides – starting with data for closely related pesticides and proceeding to data for less related pesticides – may be used to characterize the chronic toxicity of acequinocyl to sediment-dwelling invertebrates. **As indicated in 40 CFR Part 158, the registrant is required to submit a protocol for approval prior to initiating the study.**

Table 9: Data Gap Table of Terrestrial Effects Data for Acequinocyl

OCSPP Guideline	Data requirement	Submitted Studies (MRID)	Study Classifications	Data Gap?	Comments
850.2100	Avian Acute Oral Toxicity (Upland game or waterfowl species)	45660601	Acceptable	No	--
850.2100	Avian Acute Oral Toxicity (Passerine species)	None	NA	**Yes**	Measures of effect from a non-passerine species could potentially underestimate acequinocyl toxicity to passerine species, consequently, additional information on acequinocyl toxicity to a passerine species is needed to reduce the uncertainty created by this analysis.
850.2200	Avian Dietary Toxicity	46622701 45435003	Acceptable Acceptable	No	--
850.2300	Avian Reproduction	45435005 45435006	Acceptable Acceptable	No	--
850.3020	Tier I- Honeybee Acute Adult Contact Toxicity	45435007	Acceptable	No	--
Non-Guideline (OECD 213)	Tier I- Honeybee Acute Adult Oral Toxicity	45428608	Supplemental	No	The supplemental study is considered scientifically sound for use in the risk assessment.
Non-Guideline	Tier I-Honeybee Adult Chronic Oral Exposure	None	NA	**Yes**	This study estimates the exposure to adult bees resulting from visits to contaminated flowers over an

OCSPP Guideline	Data requirement	Submitted Studies (MRID)	Study Classifications	Data Gap?	Comments
					extended period of time or through consumption of contaminated food in the hive.
Non-Guideline	Tier I- Honeybee Larval Acute and Chronic Oral Exposure	None	NA	**Yes**	These studies help characterize the effect of repeated exposure of the brood to pesticides that may enter the hive and be stored in food sources such as pollen, honey, royal or brood jelly.
850.3030	Tier II- Honeybee Toxicity of Residues on Foliage	None	NA	No	The acute contact 48-hr LD50 was above 100 µg ai/bee. This study is only triggered if contact toxicity is less than 11 µg ai/bee.
Non-Guideline	Tier II- Nectar and Pollen Residue Study for Insect Pollinators	(none)	NA	**Yes**	If risks are identified from Tier I risk estimation for honeybees, then Tier II risk estimations may need to be called in to identify more targeted routes of exposure. Exposure of acequinocyl through translocation to nectar and pollen could be a route of exposure to insect pollinators.
Non-Guideline (OECD 75)	Tier II- Semi-Field Testing for Honeybees	None	NA	**Yes**	If risks are identified from Tier I risk estimation for honeybees, then Tier II risk estimations may need to be called in to identify more targeted risk mitigation options. Typically semi-field studies are usually conducted under conditions that represent the worst-case exposure scenario of proposed uses to the entire colony.
850.3040	Tier III- Field Testing for Pollinators	None	NA	**Yes**	If risks are identified from Tier II risk estimation for honeybees, then Tier III field studies may need to be called in to identify more targeted risk mitigation options.
850.4100	Seedling Emergence and Seedling Growth	45428609	Acceptable	No	--
850.4150	Vegetative Vigor	45428610	Acceptable	No	

Justifications for non-guideline data requirements are below:

Study Title: Tier I- Pollinator Chronic Oral Toxicity, Adult
Rationale for Requiring the Data
Terrestrial invertebrates are likely to be impacted if exposed to pesticides in various use settings. Pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to the hive. Therefore, potential chronic effects to adult honeybees and other pollinators from oral exposure to some pesticides could exist. Currently available toxicity studies do not address possible lethal and sublethal effects of chronic oral exposure on adult terrestrial invertebrates and will assist in determining whether the sensitivity of adult bees differs from that of earlier life stages. Because of the potential for pollen and nectar to be contaminated with pesticide residues, and subsequently brought back to the hive, it is important to determine the chronic oral toxicity of this compound to adult honeybees and other pollinators. The Office of Pesticide Programs has made available a guidance regarding ecological testing for invertebrates with the honeybee. The guidance discusses Tier I laboratory-based chronic oral toxicity studies of individual adult honeybees as a critical component of the screening-level risk assessment process for examining potential risks from specific routes of exposure. The guidance can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance . Study design elements for the chronic 10-day oral toxicity test with honeybees are similar to the OECD Test Guideline 213 acute oral toxicity test http://www.oecd-ilibrary.org/environment/test-no-213-honeybees-acute-oral-toxicity-test_9789264070165-en .
Practical Utility of the Data
How will the data be used? The Tier I chronic oral toxicity data on adult bees serve as a foundation for the screening-level assessment of potential risk to non-target organisms including federally listed threatened or endangered species and non-listed terrestrial invertebrate insects, including pollinators, from chronic oral exposures to pesticides. The data will be used to reduce uncertainties associated with the risk assessment for terrestrial invertebrates and will improve EPA's understanding of the potential direct and indirect lethal and sublethal effects on a broad range of terrestrial species, particularly insect pollinators and to determine whether adult toxicity differs substantially from other life stages evaluated in other Tier I tests. If chronic oral effects data for adults are not available, risks to terrestrial insects from chronic oral exposure will be assumed. **How could the data impact the Agency's future decision-making?** The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect listed threatened or endangered species and/or their designated critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in use restrictions.

Study Title: Tier I- Pollinator Acute Oral Toxicity, Larvae
Rationale for Requiring the Data
Terrestrial invertebrates are likely to be impacted if exposed to pesticides in various use settings. Pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to the hive where larvae and pupae may be exposed. Therefore, potential adverse effects to developing bees and other insect pollinators could result from exposure to pesticide residues. Available toxicity studies do not address possible effects on brood (larvae and pupae) survival/development. Because of the potential for pollen and nectar to be contaminated with pesticide residues, and subsequently brought back to the hive, it is important to determine the acute oral toxicity of this compound to bee brood.

The Office of Pesticide Programs has made available a guidance regarding ecological testing for terrestrial invertebrates using the honeybee as a surrogate test species. The guidance discusses Tier I laboratory-based acute toxicity studies of individual honeybee larvae as a critical component of the screening-level risk assessment process for examining potential risks from specific routes of exposure. The guidance can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance . Additional guidance on larval honeybee toxicity test design can be found in OECD Test Guideline 237 http://www.oecd-ilibrary.org/environment/test-no-237-honey-bee-apis-mellifera-larval-toxicity-test-single-exposure_9789264203723-en .

Practical Utility of the Data

How will the data be used?

The Tier I acute oral toxicity data on honeybee larvae serve as a foundation for the screening-level assessment of potential risk to non-target organisms such as federally listed threatened or endangered and non-listed terrestrial invertebrate insects, including pollinators, and/or modify their designated critical habitat from acute oral exposures to pesticides. The data will be used to reduce uncertainties associated with the risk assessment for terrestrial invertebrates and will improve EPA's understanding of the potential effects on terrestrial species and whether there is a differential sensitivity of larval bees relative to adult bees. If acute oral effects data for larvae are not available, risks to terrestrial insects from acute oral exposure will be assumed

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

The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect listed threatened or endangered species and/or modify their designated critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in use restrictions.

Study Title: Tier I- Pollinator Chronic Oral Toxicity, Larvae

Rationale for Requiring the Data

Terrestrial invertebrates are likely to be impacted if exposed to pesticides in various use settings. Pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to the hive where larvae and pupae may be exposed. Therefore, potential effects to developing bees could result from chronic oral exposure to pesticide residues. Available toxicity studies do not address possible chronic effects on brood (larvae and pupae) survival. Because of the potential for pollen and nectar to be contaminated with pesticide residues, and subsequently brought back to the hive, it is important to determine chronic larval/pupal toxicity and whether adult emergence is adversely affected. This study will provide information on whether honeybee larvae differ in sensitivity from adult bees following chronic exposure.

The Office of Pesticide Programs has made available a guidance regarding ecological testing for invertebrates with the honeybee. The guidance discusses Tier 1 laboratory-based chronic oral toxicity studies of individual honeybee larvae as a critical component of the screening-level risk assessment process for examining potential risks from specific routes of exposure. The guidance can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance.
Additional information on larval honeybee toxicity repeat exposure test design can be found in the oECD draft guidance
http://www.oecd.org/env/ehs/testing/Draft_GD_honeybees_rep_exp_for_2nd_CR_25_November_2013.pdf .

Practical Utility of the Data
How will the data be used? The Tier I chronic oral toxicity data on bee larvae serve as a foundation for the screening-level assessment of potential risk to non-target organisms including federally listed threatened or endangered and non-listed terrestrial invertebrate insects, including pollinators, from chronic oral exposures to pesticides. The data will be used to reduce uncertainties associated with the risk assessment for terrestrial invertebrates and will improve EPA's understanding of the potential direct and indirect lethal and sublethal effects on a broad range of terrestrial species, particularly insect pollinators. These data will also assist in determining whether early life stages of the bee differ in their sensitivity to pesticides relative to adults. If chronic oral effects data for larvae are not available, risks to terrestrial insects from chronic oral exposure will be assumed. **How could the data impact the Agency's future decision-making?** The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect listed threatened or endangered species and/or modify their designated critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in use restrictions.

Study Title: Tier II Semi-Field Toxicity Testing (tunnel/enclosure studies)
Rationale for Requiring the Data
Tier II studies are conditional on the outcome of the screening-level assessment where acute and/or chronic risk levels of concern have been exceeded for terrestrial invertebrates. Terrestrial invertebrates are likely to be impacted if exposed to pesticides in various use settings. Pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to the hive and may adversely affect developing brood (egg, larvae, and pupae) and adult bees. Screening-level (Tier I) studies of individual bees do not address possible effects and/or exposure to pesticide residues at the colony-level. Because of the potential for pollen and nectar to be contaminated with pesticide residues, and subsequently brought back to the hive, it is important to determine whether bee colonies may be negatively affected under relatively controlled exposure conditions of a semi-field study. In addition to providing effects data, these studies can provide data on exposure as pesticide residues in pollen/nectar of treated plants. The Office of Pesticide Programs has made available a guidance regarding ecological testing for invertebrates with the honeybee. The guidance describes the tiered testing process and can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance . Additional information on honeybee colony studies under semi-field conditions can be found in the OECD Guidance 75 http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono%28 .
Practical Utility of the Data
How will the data be used? Tier II colony-level data will be used to assess potential risk to non-target organisms including listed and non-listed terrestrial social invertebrate species and to determine whether effects observed in the screening-level (Tier I) laboratory-based studies of individual bees are evident in colony-level studies under semi-field conditions. The Tier II semi-field test of whole colonies is a relatively controlled study, *i.e.*, bees are confined to a specific area, that is designed to represent potential field-level exposure and account for hive dynamics, which are not achievable from other pollinator studies. This study will be used to determine whether adverse effects to insect pollinators at the whole colony level, may result for the use of pesticides and will help to refine risk estimates derived in the screening-level risk assessment for beneficial terrestrial

invertebrates. Measured residues in pollen/nectar can also be used to refine risk estimates derived from model-based or default values in the screening-level assessment.

How could the data impact the Agency's future decision-making?
The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect federally listed threatened or endangered species or their designated critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in significant use restrictions.

Study Title: Tier II Semi-Field Toxicity Testing (feeding studies)

Rationale for Requiring the Data

Pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to the hive, and may adversely affect developing brood (egg, larvae, and pupae) and adult bees. Tier II feeding studies are conditional on the outcome of the screening-level assessment where acute and/or chronic risk levels of concern have been exceeded for terrestrial invertebrates based on Tier I studies of individual bees. Feeding studies utilize free foraging bee colonies that are "dosed" with specific quantities of test material and represent a means of ensuring exposure to the test material through spiked pollen and/or sugar solutions fed to the colony while still allowing the bees to forage freely. Since bee colonies are not confined to enclosures, colonies can be exposed for longer duration periods without subjecting the bees to stress that typically results from Tier II tunnel studies. Available toxicity studies of individual bees (Tier 1) conducted to support screening-level assessments do not address possible effects and/or exposure to pesticide residues at the colony-level. Because of the potential for pollen and nectar to be contaminated with pesticide residues, and subsequently brought back to the hive, it is important to determine whether bee colonies may be negatively affected where bees are free foraging and have the option to collect/consume alternative forage items beyond the spiked food. Since multiple dose levels can be more readily tested, feeding studies can help to define dose-response relationships at the whole colony level.

The Office of Pesticide Programs has made available a guidance regarding ecological testing for invertebrates with the honeybee. The guidance describes the tiered testing process and can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance . Additional information on honeybee colony feeding studies can be found in the EPPO Guidance 170 at: http://www.nationalbeeunit.com/index.cfm?pageId=187 .

Practical Utility of the Data

How will the data be used?
Tier II colony feeding data will be used to assess potential risk to non-target organisms including listed and non-listed terrestrial social invertebrate species. The colony feeding study is designed to represent potential field-level exposure and account for hive dynamics using longer duration exposure periods than are possible in Tier II tunnel studies. The study will be used to determine whether potential adverse effects to insect pollinators at the whole colony level when bees are able to forage naturally beyond the spiked food. Results from the feeding study will help to refine the screening-level risk assessment for beneficial terrestrial invertebrates that were based on Tier I studies on individual bees. Since feeding studies can help to define a dose-response relationship at the colony level, the studies can provide a means of determining exposure thresholds below which the likelihood of adverse effects on colonies may be low.

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

Tier II colony-level data will be used to refine screening-level risk estimates derived using Tier I laboratory-based data on individual bees. The Tier II data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect federally listed threatened or endangered species or their designated critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in significant use restrictions.

Study Title: Residues in Pollen and Nectar

Rationale for Requiring the Data

Terrestrial invertebrates are likely to be impacted if exposed to pesticide residues in various use settings. Pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to hive where all life stages may be exposed. For some pesticides, the quantification of pollinator-relevant residues in treated flowering plants is needed, 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, including (where appropriate), but not limited to, guttation water, sap/resins, whole plant tissue (*e.g.,* leaves, stems), as well as blooming, pollen-shedding, and nectar producing parts (*i.e.*, flowers and, if present, extra-floral nectaries) of plants may inform the potential for risk. Studies should be designed to provide residue data for crops and application methods of concern.

The Office of Pesticide Programs has made available a guidance regarding ecological testing for invertebrates with the honeybee. The guidance can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance .

Practical Utility of the Data

How will the data be used?

Measured residue data will be used to refine conservative estimates of pesticide exposure and reduce uncertainties associated with the Tier I exposure assessment by providing direct measurements of pesticide concentrations resulting from actual use settings. Measured residues may provide a more realistic understanding of exposure through contact or ingestion with which to calculate risk quotients for individual bees as well as to characterize exposure to the colony. If measured residue data are not available, risk estimates for terrestrial insects will be based on model-generated or default values used to support the screening-level assessment.

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

The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect federally listed threatened or endangered species or their designated critical habitat. Without these data, EPA will have to rely on conservative estimates of exposure which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in use restrictions.

12. Bibliography

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Appendix 1: Previous Actions and Assessed Uses for Acequinocyl

Crop	Application Rate (lb ai/A)		Number of Applications (Application Interval in Days)	Action/DP Barcode/Date
	Single Lbs a.i./A	Seasonal/ Annual Lbs a.i./A		
Succulent Soybean, Low Growing Berry, Small Fruit Vine Climbing (except kiwifruit), succulent shelled beans, cowpea forage, Caneberry, Melon, Cucumber, and Cherry	0.3	0.6	2 (14-21)	IR-4 New Uses D389520, D390259 10/25/2011 Tier II Drinking Water Assessment D448205 9/7/2011
Fruiting Vegetables, Okra, Edible podded beans, Hop	0.3	0.6	2 (21)	IR-4 New Uses Registration/ Drinking Water Assessment D368579, D368426, D417967, D417966 4/29/2010
Citrus, Tree Nuts, Grapes, Pome Fruits, Strawberries	0.3	0.6	2 (21)	
Outdoor Ornamental	0.125	0.25	2 (14)	
Citrus, Tree Nuts, Grapes, Pome Fruits	0.3	0.6	2 (21)	Section 3 New Uses D337381, D330467, D330471 8/15/2007
Non-food outdoor uses (various ornamentals)	0.125	0.6	5 (14)	
Food Crops (citrus, tree nuts, grapes, pome fruits, strawberries)	0.3	0.6	2 (21)	Tier II Drinking Water Assessment DP337221 6/27/2007
Outdoor Residential Ornamentals (including roses)	0.125	0.625	5 (14)	
Pome Fruits Citrus Almonds Pistachios Strawberries	0.3	0.6	2 (21)	Section 3 New Uses D285811, D286428, D289153, D290010, D287269, D290009, D291174 2/3/2004
Outdoor Ornamentals	0.125	0.250	2 (14)	
Greenhouse, Shade House Ornamental, Floral, Foliage, Nursery Crops	0.125 lbs/100 gallons formulation	N/A	N/A	Section 3 New Uses D291707 8/7/2003

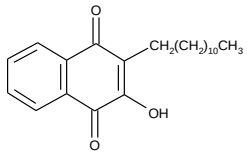
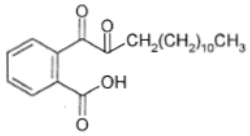
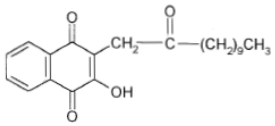
Appendix 2: Application Rates of Acequinocyl on Agricultural Crops (Based on Kanemite 15 SC Label).

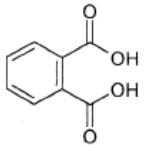
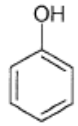
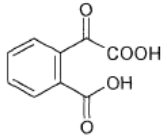
Use	Max single app rate (lbs./A)	Max # apps per year	Max app rate per year (lbs ai/A)	Minimum retreatment interval (days)
Tree Nuts and Pistachios	31 fl oz/A[1]	2	0.6	21
Citrus	31 fl oz/A	2	0.6	21
Small-Vine subgroup 13-07F (Except Kiwi)	31 fl oz/A	2	0.6	21
Pome Fruits	31 fl oz/A	2	0.6	21
Low-Growing Berries-Subgroup 13-07G	31 fl oz/A	2	0.6	21
Fruiting Vegetables (Except cucurbits)	31 fl oz/A	2	0.6	21
Melon Crop Group 9A and Cucumber	31 fl oz/A	2	0.6	21
Succulent Shelled Bean	31 fl oz/A	2	0.6	14
Caneberry Crop Subgroup 13-07A	31 fl oz/A	2	0.6	21
Cherry	31 fl oz/A	2	0.6	14
Okra	31 fl oz/A	2	0.6	21
Edible Potted Beans	31 fl oz/A	2	0.6	21
Succulent Soy Vegetable	31 fl oz/A	2	0.6	21
Hops	31 fl oz/A	2	0.6	21
Landscape Ornamentals	12.8 fl oz/A	2[2]	0.25	14

[1]Label states that Kanemite contains 1.25 lb ai/gal

[2]Inferred based on maximum single and annual application rates.

Appendix 3. Summary of Acequinocyl Major Degradates and Maximum Percent Formation Observed in the Laboratory and Field Studies

Degradate	Maximum Degradate Concentration (% of applied) and Time to Max Concentration						
	Hydrolysis[1]	Aqueous Photolysis	Soil Photolysis[4]	Aerobic Soil Metabolism	Aerobic Aquatic Metabolism[5]	Anaerobic Aquatic Metabolism[5]	Terrestrial Field Dissipation
R1 (2-dodecyl-3-hydroxy-1,4-naphthalenedione) 	pH 7: 54.7% (96 hr)	--[2]	--	Silt loam soil; phenyl-U-^{14}C label: 33.8% (2 days)	Total system: 12.2% (0 days)	Total system: 41.0-41.1% (3, 7, and 14 days)	NY: 37.8% (3 hr after 2nd application) GA: 37.8%[7] CA: 26.4%[7]
AKM 18 [2-(1,2-dioxotetradecyl)benzoic acid] 	pH 9: 10.9% (3 hr)	--	--[4]	--	Total system: 19.5% (1 day)	Total system: 23.2% (269 days)	NY: 16.5% [7,8]
AKM-08 [2-(2-oxo-dodecyl)-3-hydroxy-1,4-naphthoquinone] 	--	Buffer solution: 12.9% (2 hr)	--	--	--	--	--

Degradate	Maximum Degradate Concentration (% of applied) and Time to Max Concentration						
	Hydrolysis[1]	Aqueous Photolysis	Soil Photolysis[4]	Aerobic Soil Metabolism	Aerobic Aquatic Metabolism[5]	Anaerobic Aquatic Metabolism[5]	Terrestrial Field Dissipation
o-Phthalic acid 	--	Buffer solution: 12.7% (24 hr)[3] River water: 11.9% (24 hr)[3]	--	--	--	--	--
Phenol 	--	River water: 10% (24 hr)[3]	--	--	--	--	--
CBAA (2-carboxy-α-oxo-benzene acetic acid) 	--	--	--	--	Water layer: 11.3% (2 days)[6]	--	--

[1] "Unknown 1" was described as polar radioactive material consisting of one or more compounds. It was observed at pH 1.2, 4, 7, and 9 and represented a maximum of 41.6% of the applied radioactivity (pH 9, 0.75 hours).

[2] Although a maximum of 11.61% formed in the irradiated sample, formation can be predominately attributed to hydrolysis (9.07% formation in the dark control).

[3] There is uncertainty about the % formation. Detected in the aqueous eluate fraction which was only analyzed for the irradiated samples at 24 hours. Aqueous eluate fraction was 40.53% (buffer solution) and 43.90% (river water) for the irradiated samples and < 5.08% (buffer solution) and < 5.19% (river water) for the dark samples at 24 hours. Unknown if present in dark samples but must be less the ca. 5% of applied radioactivity in those samples. Only a portion of the aqueous eluate fraction was analyzed (60% of the buffer solution and 87% of the river water fraction applied to the column) due to loss during purification.

[4] AKM-18 and compound A (unidentified) formed greater than 10% in the irradiated samples; however, an equal or greater amount formed in the dark controls indicating that formation was not due to photolysis. Likewise, radioactive material designated as polar compounds was observed greater than 10% of the applied radioactivity (26.2% irradiated samples and 23.4% dark controls). However, it is uncertain if the irradiated polar peak represented photolytic degradation because the polar peaks may have represented more than one compound and those compounds may or may not have been present in both irradiated samples and dark controls.

[5] Degradates retaining the naphthoquinone structure formed less than 10% of applied acequinocyl.

[6] Sediment layer was not analyzed.

[7] Formed immediately after application.

[8] Formation based on a single replicate. The second replicate had a concentration below the LOD and the third replicate was not analyzed due to a lab error.

Appendix 4: Complete List of Toxicity Endpoints for Acequinocyl

Taxa	Study Type	% ai	Species	Toxicity Value & Category	MRID & Status	Endpoints Affected
Mammals	Acute oral 870.1100	96.8	**Rat** *Rattus norvegicus*	LD50> 5000 mg/kg-bw (Males and Females) Practically nontoxic	45435011 Acceptable	None
	Chronic Two Generation Reproductive Study 870.3800	97.1	**Rat** *Rattus norvegicus*	Male NOAEC= 100 mg/kg-diet Male LOAEC= 800 mg/kg-diet Female NOAEC> 1500 mg/kg-diet	45531909 Acceptable	None
	Acute Inhalation 870.1300	96.5	**Rat** *Rattus norvegicus*	LC50> 0.84 mg/L Males and Females Slightly Toxic	45435013 Acceptable	Mortality
Birds	Acute Oral 850.2100	97.1	**Japanese Quail** *Coturnix coturnix japonica*	8-Day LD50> 2000 mg/kg-bw 8-day NOAEL= 2000 mg/kg-bw Practically nontoxic	45435002 Supplemental-Japanese quail not a recommended species. May be used for quantitative assessment of risk.	No Effect
	Acute Oral 850.2100	98.4	**Mallard Duck** *Anas platyrhynchos*	LD50> 2000 mg ai/kg-bw NOAEL= 2000 mg ai/kg-bw Practically nontoxic	48660601 Acceptable	None
	Acute Oral 850.2100	15.6	**Northern Bobwhite Quail** *Colinus virginianus*	8-Day LC50> 2000 mg/kg-bw 8-Day NOAEL= 2000 mg/kg-bw Practically nontoxic	45530602 Acceptable	No Effect
	Acute Dietary 850.2200	97.1	**Japanese Quail** *Coturnix coturnix japonica*	8-Day LC50> 4952 mg/kg-diet NOAEC= 926 mg/kg-diet Slightly toxic	45435004 Supplemental-Japanese Quail not recommended test species. May be used for quantitative	Subacute toxicity= NOAEC based on weight loss

Taxa	Study Type	% ai	Species	Toxicity Value & Category	MRID & Status	Endpoints Affected
					assessment of risk.	
	Acute Dietary 850.2200	15.6	**Northern Bobwhite Quail** *Colinus virginianus*	LC50> 5970 mg ai/kg diet NOAEC= 5970 mg ai/kg diet Practically nontoxic	46622701 Acceptable	None
	Acute Dietary 850.2200	97.1	**Mallard Duck** *Anas platyrhynchos*	LC50> 5000 mg/kg-diet NOAEC= 488 mg/kg diet Practically nontoxic	45435003 Acceptable	Body Weight Gain
	Chronic (reproduction) 850.2300	97.1	**Northern Bobwhite Quail** *Colinus virginianus*	NOAEC= 2515 mg/kg ai-diet LOAEC> 2515 mg/kg ai-diet	45435006 Acceptable	None
	Chronic (reproduction) 850.2300	97.1	**Mallard Duck** *Anas platyrhynchos*	NOAEC= 100 mg/kg-diet LOAEC= 500 mg/kg-diet	45435005 Acceptable	Female body Weight gain-no mortality
Freshwater Fish	Acute 850.1075	97.1	**Rainbow Trout** *Oncorhynchus mykiss*	LC50> 33 mg ai/L NOAEC= 33 mg ai/L Slightly Toxic	45434920 and 45868502-Supplemental Recurring solubility issues led to questions about the exposure concentrations. As this study tested well above the solubility limit (>1000x) and saw no effect, this is satisfactory to fulfill guideline requirements for an acute study. Endpoints are valid for	None

Taxa	Study Type	% ai	Species	Toxicity Value & Category	MRID & Status	Endpoints Affected
					quantitative risk assessment	
	Acute 850.1075	15.4	**Rainbow Trout** *Oncorhynchus mykiss*		45530601 Invalid (formerly Acceptable)[2]	Mortality
	Acute 850.1075	97.1	**Bluegill Sunfish** *Lepomis macrochirus*	LC50> 1.1 mg ai/L NOAEC= 1.1 mg ai/L Moderately toxic	45434918 Supplemental-Conducted as a limit test. No effect was observed at concentrations far greater than solubility limit. As a result, endpoints are valid to quantitatively assess risk.	None
	Acute 850.1075	15.8	**Bluegill Sunfish** *Lepomis macrochirus*		45428605 Supplemental (Formerly Acceptable) [2]	None
	Acute 850.1075	97.1	**Zebrafish** *Brachydanio rerio*	LC50> 1.1 mg ai/L NOAEC= 1.1 mg ai/L	45434919 Supplemental-Not an acceptable species. Endpoints may only be used for quantitative risk analysis.	None
	Chronic 850.1400	15.8	**Rainbow Trout** *Oncorhynchus mykiss*	NOAEC= 0.52 mg ai/L ([1]Centrifuged NOAEC= 0.07 mg ai/L) LOAEC= 1.1 mg ai/L	45428607 Supplemental-Only two replicates per test concentration. Endpoints are may only be used to qualitatively	Post Hatch Survival

Taxa	Study Type	% ai	Species	Toxicity Value & Category	MRID & Status	Endpoints Affected
					characterize risk.	
Freshwater Invertebrates	Acute 850.1010	98.3	**Water Flea** *Daphnia magna*	LC50= 2.7 µg ai/L NOAEC= 0.66 µg ai/L Very highly Toxic	46372101 Acceptable	Mortality and sublethal effects (lethargy)
	Acute 850.1010	15.4	**Midge** *Chironomus riparius*	LC50 >13.23 mg a.i./L *Endpoint reported in study did not correct for % a.i. The endpoint reflected above reflects the corrected concentration. An addendum will be issued to correct this in the DER. Slightly Toxic	45782303 Supplemental-Concentrations not analyzed at all concentrations - Endpoints may be used to quantitatively assess risk to midges from exposure in water column.	Mortality
	Chronic 850.1300	98.3	**Water Flea** *Daphnia magna*	NOAEC= 0.98 µg ai/L LOAEC= 1.8 µg ai/L	45434922 Supplemental-Quick degradation of technical meant low recovery rate (37-41%). Endpoints valid for quantitative assessment or risk.	Number of young, length and dry weight
Estuarine/ Marine Fish	Acute 850.1075	97.1	**Sheepshead minnow** *Cyprinodon variegatus*	LC50> 0.19 mg ai/L NOAEC= 0.19 mg ai/L (Toxicity endpoints of centrifuged samples with mean measured concentrations) Highly Toxic	45434921 Supplemental-Limit test-Precipitate centrifuged and counted in toxicity endpoints calculation. No effect was observed at concentrations far exceeding the solubility	None

Taxa	Study Type	% ai	Species	Toxicity Value & Category	MRID & Status	Endpoints Affected
					limit of this chemical. Therefore, these endpoints are valid for quantitative risk assessment.	
	Acute 850.1075	15.8	**Sheepshead minnow** *Cyprinodon variegatus*	LC50> 68 mg ai/L NOAEC=68 mg ai/L Slightly Toxic	45428606 Supplemental (Formerly Acceptable) [2]	None
Estuarine/ Marine Invertebrates	Acute 850.1035	97.1	**Mysid shrimp** *Mysidopsis bahia*	96-hour LC50=0.94 µg ai/L NOAEC= 0.27 µg ai/L Highly Toxic	45434917 Supplemental-Environmental conditions (pH, salinity, vessel size, temperature) all outside recommended levels. Mean measured concentration were only 7.8-16% of nominal. Endpoints are valid for quantitative risk assessment.	Lethargic swimming, loss of equilibrium
	Acute 850.1025	97.1	**Eastern Oyster** *Crassostrea virginica*	96 Hour EC50= 0.59 µg ai/L NOAEC <0.11 µg ai/L	45434916 Supplemental-Shell deposition was lower than minimum 2.0 mm meaning there was uncertainty with the control quality. Results of this study can be	Shell Deposition

Taxa	Study Type	% ai	Species	Toxicity Value & Category	MRID & Status	Endpoints Affected
					used to qualitatively assess risk.	
	Chronic 850.1350	NA	**Mysid Shrimp** *Mysidopsis bahia*	NOAEC = 0.38 µg/L (Estimated using Acute/Chronic ratio)	Acequinocyl is extremely unstable in seawater (MRID 47914901). As a result, a waiver request was granted for studies assessing chronic exposure to estuarine /marine invertebrates under flow-through conditions (MRID 47256201). For the purposes of risk assessment, chronic effect endpoints will be estimated by taking the acute to chronic ratio of endpoints observed in freshwater invertebrates.[2]	
Aquatic Plants	Non Vascular 850.4400	15	**Green Algae** *Pseudokirchneriella subcapitata*	72-hour EC50= 0.96 mg ai/L NOAEC= 0.0017 mg ai/L LOAEC=0.0055 mg ai/L	45428611 Supplemental-72 hour study shorter than the recommended 96 hour. Endpoints may	Cell Density

Taxa	Study Type	% ai	Species	Toxicity Value & Category	MRID & Status	Endpoints Affected
					be used for quantitative risk assessment.	
	Non Vascular 850.4400	97.1	**Green Algae** *Pseudokirchneriella subcapitata*	72-hour EC50>78.0 mg ai/L NOAEC ≥ 78.0 mg ai/L	45435008 Supplemental-72 hour study shorter than the recommended 96 hour. Endpoints valid for quantitative use in risk assessment	none
Terrestrial Invertebrates	Adult Acute Contact 850.3020	97.1	**Honeybee** *Apis mellifera*	48-Hour LD50>100 µg ai/bee NOAEL= 100 µg ai/bee Practically Nontoxic	45435007 Acceptable	None
	Adult Acute Oral Non-Guideline	15.4	**Honeybee** *Apis mellifera*	72-Hour LD50> 315 µg ai/bee NOAEL= 43.8 µg ai/bee	45428608 Supplemental-study uses TEP. Endpoints can be used for quantitative assessment of risk to honeybees.	None
	Adult Acute Contact 850.3020	15.4	**Honeybee** *Apis mellifera*	72-Hour LD50> 350 µg ai/bee NOAEL= 175 µg ai/bee Practically nontoxic	45428608 Acceptable	None
	Earthworm Subchronic 850.6200	97.1	**Earthworm** *Eisenia fetida*	LC50> 1000 mg ai/kg NOAEC= 500 mg ai/kg LOAEC= 1000 mg ai/kg	45435009 Supplemental-Non Guideline study	Reductions in body weight gain
	Acute Toxicity Earthworm – 850.6200	15.6	**Earthworm** *Eisenia fetida*	LC50> 156 mg ai/kg NOAEC= 156 mg ai/kg LOAEC >156 mg ai/kg	45782304 Supplemental-Non Guideline study	Weight loss
Terrestrial Plants	Seedling Emergence Monocot	15.3	**Oat** *Avena sativa,* **Onion** *Allium cepa,* **Corn** *Zea mays,*	Most Sensitive Monocot: None EC25> 0.9 lb ai/a	45428609 Acceptable	None

Taxa	Study Type	% ai	Species	Toxicity Value & Category	MRID & Status	Endpoints Affected
	850.4100		**Ryegrass** *Lolium perenne*	NOAEC= 0.9 lb ai/a		
	Seedling Emergence Dicot 850.4100	15.3	**Carrot** *Daucus carota,* **Rapeseed** *Brassica napus,* **Beets** *Beta vulgaris,* **Tomato** *Lycopersicon esculentum,* **Cabbage** *Brassica Oleracea* **Soybean** *Glycine max*	Most sensitive dicot: Carrot EC25= 0.7 lb ai/a NOAEC= 0.3 lb ai/a	45428609 Acceptable	Shoot Height
	Vegetative Vigor Monocot 850.4150	15.3	**Oats** *Avena sativa,* **Onion** *Allium cepa,* **Corn** *Zea mays,* **Ryegrass** *Lolium perenne*	Most Sensitive Species: None EC25> 0.9 lbs ai/a NOAEC= 0.9 lbs ai/a	45428610 Acceptable	None
	Vegetative Vigor Dicot 850.4150	15.3	**Carrot** *Daucus carota,* **Rapeseed** *Brassica napus,* **Beets** *Beta vulgaris* **Cabbage** *Brassica Oleracea* **Tomato** *Lycopersicon esculentum,* **Soybean** *Glycine max*	Most Sensitive Species: Beets and Cabbage EC25> 0.9 lbs ai/a NOAEC= 0.3 lbs ai/a	45428610 Acceptable	Shoot Height

[1] Centrifuged samples yielded measured active ingredient concentrations of 13-19% of the uncentrifuged. For the purposes of risk assessment, the NOAEC will be 0.52 mg ai/L X 0.13 mg ai/L= 0.07 mg ai/L, and this adjusted value will be used to calculate Risk Quotients.

[2] For the purposes of risk assessment, an estimated chronic toxicity value for estuarine/marine invertebrates was assumed by taking the acute to chronic ratio (ACR) observed in freshwater invertebrate studies (MRIDs 46372101; 45434922) (2.4µg/L/0.98µg/L=2.45) and applying it to the most sensitive estuarine marine acute endpoint (MRID 45434917) (0.94 µg/L/2.45=0.38 µg/L).

Appendix 5- SIP Inputs and Outputs

Inputs

Parameter	Value
Chemical name	
Solubility (in water at 25°C; mg/L)	0.00669
Mammalian LD_{50} (mg/kg-bw)	5000
Mammalian test species	laboratory rat
Body weight (g) of "other" mammalian species	
Mammalian NOAEL (mg/kg-bw)	100
Mammalian test species	laboratory rat
Body weight (g) of "other" mammalian species	
Avian LD_{50} (mg/kg-bw)	2000
Avian test species	mallard duck
Body weight (g) of "other" avian species	
Mineau scaling factor	1.15
Mallard NOAEC (mg/kg-diet)	100
Bobwhite quail NOAEC (mg/kg-diet)	2515
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	

Table 2. Mammalian Results

Parameter	Acute	Chronic
Upper bound exposure (mg/kg-bw)	0.0012	0.0012
Adjusted toxicity value (mg/kg-bw)	3845.8028	76.9161
Ratio of exposure to toxicity	0.0000	0.0000
Conclusion*	**Drinking water exposure alone is NOT a potential concern for mammals**	**Drinking water exposure alone is NOT a potential concern for mammals**

Table 3. Avian Results

Parameter	Acute	Chronic
Upper bound exposure (mg/kg-bw)	0.0054	0.0054
Adjusted toxicity value (mg/kg-bw)	1038.4508	4.9613
Ratio of exposure to acute toxicity	0.0000	0.0011
Conclusion*	**Drinking water exposure alone is NOT a potential concern for birds**	**Drinking water exposure alone is NOT a potential concern for birds**

Appendix 6- STIR inputs and outputs for acequinocyl

Input		
Application and Chemical Information		
Enter Chemical Name	Acequinocyl	
Enter Chemical Use	Miticide	
Is the Application a Spray? (enter y or n)	y	
If Spray What Type (enter ground or air)	ground	
Enter Chemical Molecular Weight (g/mole)	335	
Enter Chemical Vapor Pressure (mmHg)	1.26E-08	
Enter Application Rate (lb a.i./acre)	0.3	
Toxicity Properties		
Bird		
Enter Lowest Bird Oral LD_{50} (mg/kg bw)	2000	
Enter Mineau Scaling Factor	1.15	
Enter Tested Bird Weight (kg)	1.58	
Mammal		
Enter Lowest Rat Oral LD_{50} (mg/kg bw)	5000	
Enter Lowest Rat Inhalation LC_{50} (mg/L)	0.84	
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)	2.27E-04	
Maximum 1-hour Vapor Inhalation Dose (mg/kg)	2.86E-05	
Adjusted Inhalation LD_{50}	1.35E+00	
Ratio of Vapor Dose to Adjusted Inhalation LD_{50}	2.11E-05	**Exposure not Likely Significant**
Maximum Post-treatment Spray Inhalation Dose (mg/kg)	3.17E-02	
Ratio of Droplet Inhalation Dose to Adjusted Inhalation LD_{50}	2.35E-02	**Exposure not Likely Significant**
Results Mammalian (0.015 kg)		
Maximum Vapor Concentration in Air at Saturation (mg/m^3)	2.27E-04	
Maximum 1-hour Vapor Inhalation Dose (mg/kg)	3.59E-05	
Adjusted Inhalation LD_{50}	5.00E+01	
Ratio of Vapor Dose to Adjusted Inhalation LD_{50}	7.18E-07	**Exposure not Likely Significant**
Maximum Post-treatment Spray Inhalation Dose (mg/kg)	3.98E-02	
Ratio of Droplet Inhalation Dose to Adjusted Inhalation LD_{50}	7.97E-04	**Exposure not Likely Significant**