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

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM **May 15, 2013**

Subject: Registration Review – Preliminary Problem Formulation for Ecological Risk and Environmental Fate, Endangered Species, and Drinking Water Assessments for Fenhexamid (PC Code 090209; DP Barcode 407836)

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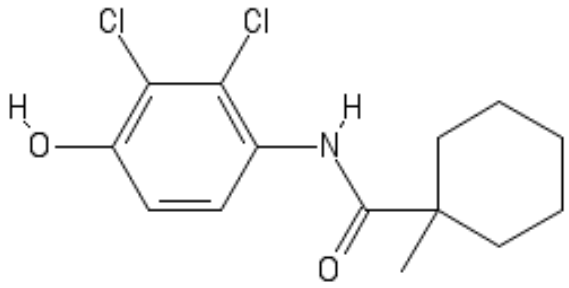
The Environmental Fate and Effects Division (EFED) has completed the preliminary problem formulation (attached) for the ecological risk, environmental fate, endangered species, and drinking water assessments to be conducted as part of the Registration Review of the hydroxyanilide fungicide fenhexamid (PC Code 090209). The problem formulation draws on studies submitted by the technical registrant (Bayer CropScience) in response to data requirements, studies available in the open literature, and other supporting documents (*e.g.*, guidance documents, white papers). This document is intended to provide an overview of what is currently known about the environmental fate and ecological effects associated with residues of fenhexamid and its degradates, and outlines uncertainties regarding attributes of the parent compound and its transformation products. It describes the preliminary ecological risk hypothesis and the processes that will be used during the completion of drinking water and ecological risk assessments in support of Registration Review. This document also recommends studies that should be considered in a data call-in (DCI) to address uncertainties surrounding the environmental fate and potential ecological effects of fenhexamid.

United States Environmental Protection Agency

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

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



N-(2,3-dichloro-4-hydroxyphenyl)-1-methylcyclohexanecarboxamide
CAS No. 126833-17-8
PC Code: 090209

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1. Introduction

EFED evaluated the most recent ecological risk and drinking water assessments for fenhexamid in association with the updated toxicity, exposure, and usage information to determine if sufficient data are available and if further updates are needed to support Registration Review. Recent risk assessments include a 2007 assessment for the use of fenhexamid on asparagus (Sutton and Steeger, 2007, D340419) In addition, EFED considered the latest Agency science policies and risk assessment methodologies. The structure, chemical name, and other identifiers of fenhexamid and its major transformation products can be found in the chemical identity table attached to this document (**Appendix A**).

Fenhexamid (CAS No. 126833-17-8) is an hydroxyanilide fungicide, and its mode of action is as a sterol biosynthesis inhibitor in fungi (Orton *et al.*, 2011).

Fenhexamid is currently registered for the following agricultural uses: almonds, asparagus, bushberries, caneberries, cherries, cucumbers, flavoring and spice crops, forest conifers, fruiting vegetables, ginseng, grapes, kiwi fruit, leafy greens (except spinach), pears, pistachios, pomegranates, raspberries, stone fruits, strawberries, and tomatoes. Non-agricultural uses include ornamental plants.

The chemical can be applied by chemigation, airblast, foliar ground spray, and as a dip treatment. All end-use products are formulated as water dispersible granules. There are three end-use products. Two products only contain fenhexamid and one contains fenhexamid (14.3%) and captan (53.6%), a phthalamide fungicide.[1] **Appendix F** summarizes currently registered products containing fenhexamid. The most recent assessment evaluated use on asparagus at 0.75 lbs a.i./A with two consecutive applications and a minimum retreatment interval of 7 days. Based on the Label Use Information System (LUIS) EFED Table 1 Report completed on October 30, 2012, the maximum single application rate is 0.75 lbs a.i./A, with a maximum seasonal application rate of 3 lbs a.i./A. When the minimum retreatment interval is specified, it is seven days. There is some uncertainty with the maximum single application rate for uses on ornamentals and forest conifers. The chemical use profile produced by the Biological and Economic Assessment Division (BEAD), located in the docket, lists the maximum single application rate, minimum retreatment interval, and maximum annual or seasonal application rates for the current uses of fenhexamid. The Screening Level Usage Analysis (SLUA) developed by BEAD is provided in **Appendix B**. According to the SLUA, most fenhexamid used on agricultural use sites is applied to strawberries and grapes.

2. Conclusions from Previous Risk Assessments

2.1. Ecological Risk Assessments

Ecological risk assessments completed on fenhexamid on uses are summarized in **Table 1**. These risk assessments, along with studies submitted to support the registration of fenhexamid,

[1] The TEP containing multiple active ingredients does have agricultural use patterns and may be applied using ground boom equipment. Thus, it may result in spray drift to adjacent water bodies.

were used to develop this problem formulation. Potential risks identified in these assessments are briefly summarized in **Table 2** and **Table 3** below.

Table 1. Summary of Drinking Water and Ecological Risk Assessments Completed for Fenhexamid

Use Site(s)	Type of Action	Year	Drinking Water	Ecological
Grapes, strawberries, ornamentals	New Chemical	1999	(Cowles, 1999)	(Cowles and Spatz, 1999, D244921+; Cowles and Steeger, 1999, D244921)
Pears	Section 18 CA	1999	(Cowles and Steeger, 1999, D257742)	(Cowles and Steeger, 1999, D257742)
Almonds, Stone Fruit	Section 3	2000	(Felthousen, 2000, D259999)	(Felthousen, 2000, D259999)
Blueberries, Caneberries, Pistachios	Section 3	2002	(Sutton, 2002, D279884+)	(Sutton, 2002, D279884+)
Kiwi	Section 18 CA	2003	(Sutton, 2003, D285210+)	(Costello, 2003, D293198)
Kiwifruit, Leafy Greens, Fruiting Vegetables, Cucumber	Section 3	2003	(Sutton, 2003, D285210+)	(Sutton, 2003, D285210+)
Pome Fruit	Section 3	2004 2006	(Sutton and Steeger, 2006, D326293+)	(Phillips and Costello, 2004, D297963) (Sutton and Steeger, 2006, D326293+)
Ginseng, Pomegranate, Non-bell Pepper, Cilantro	Section 3	2005 2006	(Phillips and Costello, 2004, D297963; Sutton and Steeger, 2006, D326293+)	(Phillips and Costello, 2005, D312268+; Sutton and Steeger, 2006, D326289+)
Asparagus	Section 3	2007	(Sutton, 2007, D338651)	(Sutton and Steeger, 2007, D340419)

Fenhexamid was characterized in previous assessments as stable to hydrolysis, though non-persistent in aerobic environments and slightly persistent in anaerobic environments. Fenhexamid has low to moderate mobility in most soils. Fenhexamid's low persistence in aerobic environments will limit the amount of the chemical that is able to migrate into surface and ground water (Sutton and Steeger, 2007, D340419).

The only Agency levels of concern (LOC) exceeded in previous risk assessments are those for chronic risk to mammals including Federally-listed threatened and endangered species (hereafter referred to as "listed") (Phillips and Costello, 2005, D312268+; Sutton and Steeger, 2006, D326289+)[2]. The LOC exceedances were identified for applications ranging from two applications of 0.375 lbs a.i./A (pome fruit; D326293) to four applications of 0.75 lbs a.i./A (ginseng; D312268+). Based on uncertainties regarding potential adverse effects to plants (no terrestrial plant data are available) and on chronic effects to terrestrial organisms, 16-23 foot buffers from naturally vegetated aquatic habitats were previously recommended (Cowles and Spatz, 1999, D244921+; Cowles and Steeger, 1999, D257742) (Sutton, 2002, D279884+).

The following uncertainties were identified in previous risk assessments:

[2] Chronic LOCs for mammals were not exceeded in the earliest completed risk assessments but were exceeded in those completed in 2005 and later.

- Chronic exposure to fenhexamid resulted in decreased neonatal body weights in rats and was associated with diminished feed consumption in birds. Feed consumption rates decreased (*i.e.*, less food consumed with increasing dietary concentration of fenhexamid) in avian subacute dietary studies and a chronic avian reproduction study. Whether the reduced feed consumption was related to palatability or reflected a chemically-induced anorexia is not known; however, the potential to affect feed consumption and neonatal body weights is a concern.
- Although none of the LOCs were exceeded for aquatic plants, fenhexamid treatment was associated with both chlorosis (loss of color) and necrosis (cell death) in aquatic vascular plants. No terrestrial plant studies were required, and EFED is not aware of any that have been submitted. Therefore, there is uncertainty regarding potential effects on terrestrial plants.
- In preliminary assessments, there was uncertainty in whether solvents used in fate studies increased polymerization of the parent. In 2003 (Sutton, 2003, D274862) data were reviewed that indicated that acetonitrile did not significantly affect either the formation of metabolites or the behavior (including binding) of fenhexamid in soil as compared with the behavior of the compound following application in aqueous solution. Additional data on aerobic soil metabolism studies were waived. Conditional registrations were made pending additional information on bioconcentration factors and terrestrial field dissipation studies are still outstanding.

Table 2. Potential risk concerns identified in previous assessments for fenhexamid[1]

	Birds[2]	Mammals	Terrestrial Invertebrates	Aquatic Vertebrates[3]	Aquatic Invertebrates	Terrestrial Plants	Aquatic Plants
Non-listed	--	C	--	--	--	No data	--
Listed	--	C	--	--	--	No data	--

A = Acute risk; C = Chronic risk; -- = No risk

[1] Risk concerns were identified when the RQ exceeded the corresponding level of concern in a previous risk assessment.

[2] Birds serve as surrogates for terrestrial-phase amphibians and reptiles

[3] Fish serve as surrogates for aquatic-phase amphibians

Table 3. Potential environmental concerns identified in previous assessments for fenhexamid

Bioaccumulation[1]	Groundwater Contamination[2]	Sediment	Persistence	Degrades of Concern
Not assessed	No	Not assessed	No	None

[1] Based on whether previous assessments indicated this was a risk concern or if previous assessments ran K_{ow} Based Aquatic Bioaccumulation Model (KABAM) for chemicals with a log K_{ow} greater than three.

[2] Previous risk assessments did not indicate that residues in ground water were high enough to result in a risk concern.

2.2. Drinking Water Exposure Assessments

A drinking water exposure assessment for the use of fenhexamid on asparagus was conducted in 2007 (Sutton and Steeger, 2007, D340419). Maximum Tier I Estimated Drinking Water Concentrations (EDWC) were developed using the Food Quality Protection Act Index Reservoir Screening Tool (FIRST, version 1.1.0; dated 12/12/2005) and the regression model Screening

Concentration in Ground Water (SCI-GROW, version 3.2, dated 7/29/2003). Exposure estimates were for fenhexamid (parent only), and were estimated for applications of 0.75 lbs a.i./A applied with a 7-day interval and a maximum yearly application rate of 3.0 lbs a.i./A/year. Monitoring data were not summarized in the drinking water assessment.

Table 4. Maximum EDWC for fenhexamid

Drinking Water Source	EDWC (µg/L)	
	Acute	Chronic
Groundwater	0.0007	0.0007
Surface Water	29	1.1

2.3. Clean Water Act Programs

Fenhexamid is not identified as a cause of impairment for any water bodies listed as impaired under section 303(d) of the Clean Water Act.[3] No Total Maximum Daily Loads (TMDL) or section 304(a) ambient water quality criteria have been developed for fenhexamid.[4] Aquatic life benchmarks[5] have not been established for fenhexamid. Any data submitted or otherwise located as part of the Registration Review process may be used to prepare aquatic life benchmarks if applicable.

3. Environmental Fate and Transport

3.1. Physical-Chemical Properties, BCF, and Mobility

Table 5 summarizes the identity information and physical-chemical properties of fenhexamid. Fenhexamid, a weak acid, has a log dissociation constant (pK_a) of 7.3, and will therefore be present in both a conjugate base (anionic) form[6], and in neutral form in the environment. The water solubility of fenhexamid is a function of the relative amounts of each of these forms as influenced by pH. Increasing pH from 5 to 9 resulted in roughly a 50-fold increase in water solubility, *i.e.*, from 20 to 1000 mg/L. Fenhexamid is considered nonvolatile from dry non-adsorbing surfaces, water, and moist soil.[7] The measured log octanol-water partition coefficient (log K_{ow}) decreases with increasing pH and is 3.62, 3.51, and 2.23 at pH 4, 7, and 9 (25°C), respectively. Estimated log octanol-air partition coefficients (log K_{OA}) range from 12 to 13. These partition coefficients indicate that fenhexamid has the potential to biomagnify in terrestrial organisms (Armitage and Gobas, 2007; Gobas *et al.*, 2003; USEPA, 2009c), or to bioconcentrate/bioaccumulate in aquatic organisms under some conditions. However,

[3] Specific state causes of impairment that make up the national pesticides cause of impairment group are listed at http://iaspub.epa.gov/tmdl_waters10/attains_nation_cy.cause_detail_303d?p_cause_group_id=885.
[4] Specific state pollutants that make up the National Pesticides Pollutant Group and have TMDLs are listed at http://iaspub.epa.gov/tmdl_waters10/attains_nation.tmdl_pollutant_detail?p_pollutant_group_id=885&p_pollutant_group_name=PESTICIDES.
[5] Aquatic Life Benchmarks are available at (http://www.epa.gov/oppefed1/ecorisk_ders/aquatic_life_benchmark.htm.
[6] Ionizes at the oxygen on the phenyl ring.
[7] Based on the volatility classification scheme in *Guidance for Reporting on the Environmental Fate and Transport of the Stressors of Concern in the Problem Formulation for Registration Review, Registration Review Risk Assessments, Listed Species Litigation Assessments, New Chemical Risk Assessments, and Other Relevant Risk Assessments* (USEPA, 2010b).

bioconcentration and biomagnification will likely be lower than predicted based on partition coefficients alone, since fenhexamid rapidly degrades in soil and aquatic environments, and is known to be metabolized in vivo as well (*e.g.*, conjugated with glucuronic acid), based upon studies on bluegill sunfish (*Lepomis macrochirus*). The maximum measured bioconcentration factor (BCF) based on total radioactivity observed in bluegill sunfish tissue was 540 L/kg-wet weight viscera. Depuration in one BCF study was rapid, with a half-life of less than 1 day. Available BCF values are uncertain, as they are based on total radioactivity rather than on parent compound alone.

Fenhexamid is classified as moderately mobile to slightly mobile, with organic-carbon normalized Freundlich soil-water distribution coefficients (K_{foc}) ranging from 446 to 1,226 L/kg-organic carbon measured in six soils (MRID 44342722)[8]. K_{foc} values for WAK 7004, a transformation product of fenhexamid, range from 2,324 to 5,037 L/kg-organic carbon in four soils (MRID 44346723) and the transformation product is classified as slightly mobile. Fenhexamid may move into surface water in water or sediment runoff. Fenhexamid may be transported into surface water (as indicated by the estimated environmental concentrations, EECs) and will also partition into sediment.

Table 5. Summary of physical-chemical properties of fenhexamid

Parameter	Value			Source or MRID	Comments
PC Code	090209			--	--
CAS Number	126833-17-8			(USEPA, 2012)	--
Molecular Formula	$C_{14}H_{17}Cl_2NO_2$			--	--
Chemical Name	N-(2,3-dichloro-4-hydroxyphenyl)-1-methylcyclohexanecarboxamide			--	--
Molecular Weight (g/mole)	302.20			--	--
Water Solubility at 20°C (mg/L)	pH	Solubility		44346719	--
	5-7	20			
	8.5	200			
	9.3	1000			
Vapor Pressure	°C	Vapor Pressure		44346720	Nonvolatile from dry non-adsorbing surfaces
		Pascal	Torr		
	20	4×10^{-7}	3×10^{-9}		
	25	9×10^{-7}	7×10^{-9}		
Henry's Law constant at 20°c (atm-m^3/mole)	pH	Henry's Law Constant		Calculated[1]	--
	5-7	6×10^{-11}			
	8.5	6×10^{-12}			
	9.3	1×10^{-12}			
Log Dissociation Constant (pKa)	7.3			44346714	Weak Acid
Octanol-Water Partition Coefficient (K_{ow}) at 20°C	pH	log K_{ow}	K_{ow}	44346717	Has the potential to bioconcentrate (USEPA, 2010a)
	4	3.62	4200		
	7	3.51	3200		
	9	2.23	170		
Air-water partition coefficient (K_{AW}) at 20°C	pH	Log K_{AW}	K_{AW}	Calculated[1]	Non-volatile from water
	5-7	-9	2×10^{-9}		

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

Parameter	Value			Source or MRID	Comments
	8.5	-10	2×10^{-10}		
	9.3	-10	5×10^{-11}		
Octanol-air partition coefficient (K_{OA}) at 20°C (unitless)	pH	Log K_{OA}	K_{OA}	Calculated[1]	Potential to biomagnify in terrestrial food chains; however, this will likely be mitigated by rapid degradation rates.[2]
	5-7	12	$\sim2\times10^{12}$		
	8.5	12	7×10^{11}		
	9.3	13	3×10^{12}		
$C_{water+soil}/C_{air}$	1×10^{9} to 2×10^{11}			Calculated[1]	Non-volatile from moist soil
Freundlich Organic-carbon normalized soil-water distribution coefficients (L/kg-OC)	Soil	Parent	WAK 7004	44346722 for parent	Acceptable. 1/n range from 0.76-0.9. Sorption is influenced by pH and %OC
	Laacher	446	--		
	Borstel	888	--		
	Stanley	1024	2324		
	Howe	1025	2421		
	Vero	1226	5037		
	Napa	658	3212	44346723 for WAK 7004	Supplemental
Bioconcentration Factor for Total Radioactivity - steady state L/kg-wet weight	540 viscera			44346747	Supplemental, pH 6.5-7.1, 22°C. Parent made up ~43% of residues in fish. Values based on total radioactivity.
	36.7-60.1 edible 248-339 viscera 132-185 whole fish			44346746	Supplemental, pH 7.1-7.5. 20-23°C

[1]All estimated values were calculated according to "*Guidance for Reporting on the Environmental Fate and Transport of the Stressors of Concern in Problem Formulations for Registration Review, Registration Review Risk Assessments, Listed Species Litigation Assessments, New Chemical Risk Assessments, and Other Relevant Risk Assessments*" (USEPA, 2010a). Volatility classifications systems are also provided in the same source.

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

3.2. Laboratory Degradation Studies

Table 6 summarizes other environmental fate data for the parent, and provides half-lives for the parent and unextracted residues. Chemicals with half-lives greater than 60 days in soil, water, and sediment are considered persistent (USEPA, 2008); therefore, aerobic aquatic and soil metabolism half-lives for fenhexamid indicate that it is not persistent. However, there is uncertainty in the half-lives due to significant amounts of unextracted residues in the metabolism studies. If these unidentified residues were found to be parent, then the compound would be classified as persistent. More discussion on this issue is available in Section 3.3. Primary routes of degradation are via aerobic soil and aerobic aquatic metabolism. Time for decline in concentration/mass by 50% (DT_{50}) in four aerobic soils ranged from two hours to a little more than 24 hours for parent alone and 137 to 1239 days for parent and unextracted residues. Aerobic soil studies were considered to be supplemental because of the high amounts of unextracted residues observed and the uncertainty in whether the carrier solvent increased polymerization of the parent. The uncertainty with the carrier solvent causing polymerization is no longer an uncertainty because studies showed that there was no difference in results from studies conducted with and without the carrier solvent. DT_{50} values in two aerobic aquatic systems ranged from 16 to 17 days for parent and 454 to 734 days for parent and unextracted

residues. Aqueous photolysis may also be an important degradation mechanism when exposure to sunlight is significant, as the DT_{50} for this pathway was a few hours. Fenhexamid is stable to hydrolysis at 25°C pH 5, 7, and 9. Soil photolysis was assumed to be minimal in aerobic systems because the percent of applied radioactivity remaining as parent in dark control and irradiated samples was similar over time. The study was considered to be supplemental because the amount of loss due to soil photolysis alone could not be determined.

Table 6. Summary of transformation studies conducted on fenhexamid

Study	System Details (Kinetic Equation)	Kinetic Equation Fitted Value[1]		Representative Half-life to Derive Model Input (days)[2]	Reference Or (MRID), Study Classification And Comments
		DT_{50} (days)	DT_{90} (days)		
Abiotic Hydrolysis	pH 5, 25°C pH 7, 25°C pH 9, 25°C	Stable		Stable	44346725, Acceptable
Atmospheric Degradation	Hydroxyl Radical (SFO)	0.61	2.03	Not applicable	Estimated using EPIWEB v.4.1 for 12-hour day, $1.5x10^6$ OH molecules/cm^3. k=1.13 $days^{-1}$; See **Appendix E**
Direct Aqueous Photolysis	pH 7, 25°C Sterile 40°N sunlight (SFO)	0.08	0.27	SFO $T_{1/2}$=0.08	MRID 44346726, Acceptable. Corrected for 40°N latitude. Phenyl ring labeled.
	pH 8, 25°C Natural water 40°N sunlight (SFO)	0.03	0.1	SFO $T_{1/2}$=0.1	MRID 44346732, Supplemental-May be used in modeling. Phenyl ring labeled.
Soil Photolysis	sandy loam, pH 7.1, 25°C	Not significant pathway when microbial degradation is occurring			44346728, Supplemental. Phenyl ring labeled. Portion of loss due to photolysis versus microbial degradation could not be determined. Up to 47% unextracted residues.
Aerobic Soil Metabolism (20°C)	IN sandy loam/ Howe pH 7.1, 1% OC (IORE, SFO*)	0.3 1239*	3.3 4115*	T_{IORE}=1.0 SFO $T_{1/2}$=1239*	MRID 44346729, Supplemental-May be used in modeling. Phenyl ring labeled. Some soils were foreign soils. WRB classifications were not provided, and it was not determined whether soils were representative of a U.S. use site. Up to 75, 58, 69, and 81% unextracted residues.
	German sand/ BBA2.1 pH 5.9, 0.7%OC (IORE, SFO*)	0.091 376*	2.12 1250*	T_{IORE}=0.637 SFO $T_{1/2}$=376*	
	German loam sand/ BBA 2.2 pH 6.6, 2.5%OC (IORE, DFOP*)	1.36 449*	11.2 1920*	T_{IORE}=3.4 DFOP slow DT_{50}=634*	
	German, sandy loam/ Laacher pH 7.0, 1.4%OC (IORE, DFOP*)	0.378 723*	2.86 2401*	T_{IORE}=0.9 SFO $T_{1/2}$=723*	
	IN sandy loam/ Howe pH 7.1, 1% OC (IORE, DFOP*)	0.125 188*	3.06 823*	T_{IORE}=0.922 DFOP slow DT_{50}=273*	MRID 44346730, Supplemental-May be used in modeling. Carboxamide ring labeled. No replicates. 1.43 mg/kg soil. WRB classifications were not provided, and it was not determined whether German soil was representative of a U.S. use site. Up to 60% unextracted residues.
	German, sandy loam/ Laacher pH 7.0, 1.4%OC	0.563 137*	5.00 749*	T_{IORE}=1.51 DFOP slow DT_{50}=263*	

Study	System Details (Kinetic Equation)	Kinetic Equation Fitted Value[1]		Representative Half-life to Derive Model Input (days)[2]	Reference Or (MRID), Study Classification And Comments
		DT_{50} (days)	DT_{90} (days)		
	(IORE, DFOP*)				
Aerobic Aquatic (20^oC)	German Lake pH5.6, 3.34% OC (SFO)	15.8 734*	52.6 2439*	SFO $T_{1/2}$= 15.8, 734*	MRID 44518701, Acceptable. Phenyl ring labeled. Up to 75 and 77% unextracted residues. Total system values reported. Multiple unidentified minor degradates.
	US Lake pH 7, 3.85% OC (SFO)	17.0 454*	56.5 1508*	SFO $T_{1/2}$= 17.0, 454*	
Anaerobic Soil (20^oC)	IN sandy loam/ Howe: DI water pH 7.1, 1% OC (SFO)	115 1026*	381 3408*	SFO $T_{1/2}$= 115, 1026*	44346731, Acceptable. Phenyl ring labeled. 10 unidentified minor degradates. Mixed with sucralose. Up to 73% unextracted residues. System treated with 300 mg $HgCl_2$ had 24% unextracted residues. Oxygen content reached 4-8% during experiment.

WRB=World Resources Base; OC=organic carbon; IN=Indiana; DTX=time for concentration/mass to decline by X percentage; SFO=single first order; DFOP=double first order in parallel; IORE=indeterminate order (IORE); SFO DT_{50}=single first order half-life; T_{IORE}=the half-life of a SFO model that passes through a hypothetical DT90 of the IORE fit; DFOP slow DT_{50}=slow rate half-life of the DFOP fit

* Value calculated for parent and unextracted residues which may or may not be parent. These values are relevant in understanding the uncertainty in data due to unextracted residues.

[1] DT50 and DT90 values were calculated using nonlinear regression and SFO, DFOP, or IORE equations. The equations can be found in the document, *Standard Operating Procedure for Using the NAFTA Guidance to Calculate Representative Half-life Values and Characterizing Pesticide Degradation* (Bohaty et al., 2012),

[2] The value used to estimate a model input value is the calculated SFO DT_{50}, T_{IORE}, or the 2nd DT_{50} from the DFOP equation. The model chosen is consistent with that recommended using the, *Guidance for Evaluating and Calculating Degradation Kinetics in Environmental Media* (USEPA and Canada, 2011). The same kinetic equation used to determine the representative model input value was used to describe the DT50 and DT90 results based on standard kinetic equations.

3.3. Transformation Products

Fenhexamid has twenty identified degradates (excluding carbon dioxide), three of which are major degradates (**Figure 2**). The maximum percent of applied radioactivity present as the specified degradate is shown in **Appendix A**. Most structures are available in **Figure 2**, with additional information in **Appendix A**. Many minor degradates were not fully characterized and chemical names were only provided for a couple of compounds. Almost all of the identified degradates are similar to the parent (an anilide, **Figure 1**) except for a few changes in functional groups or the parent base structure present as a dimer or trimer. This includes the three major degradates:

- C-C Biphenyl Dimer,
- M4, and
- WAK 7004 (7-Chloro-2-(1-methylcyclohexyl)-1,3-benzoxazol-6-ol).

WAK 7004 was the only degradate analyzed for in the terrestrial field dissipation studies, and it was found at a maximum of 28 µg/kg-soil. WAK 7004 was a major degradate in aqueous photolysis studies, where it appeared as a major degradate in the first 5-hours and then was undetectable after 24 hours. M4 was also a major degradate observed in the aqueous photolysis studies, where it increased in amounts up to 26% applied radioactivity (AR) over 24 hours, and

then was detected at 4% AR at the next sampling point, seven days after application. The C-C biphenyl dimer was a major degradate in the soil photolysis study, where it reached 14% AR in the first day, decreased to 5% AR on day 7, and was 2.4% AR on the last sampling day (18 d).

In the aqueous photolysis study, degradates M1 and M2 were only characterized as a mixture of up to twelve compounds with the highest amount present as 7%[9]. Most of the characterized structures for M1 and M2 were similar to the parent (an anilide) with different functional groups. Succinic acid (CAS No. 110-15-6, butanedioic acid) was also identified as being present in the mixture. Maximum amounts of the M1 and M2 mixture were increasing at the end of the aqueous photolysis study. A mixture identified as M7 was identified in the anaerobic soil study. All of the M7s are also anilides, and are similar to the parent structure.

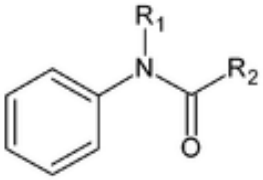

Figure 1. Structure of anilide

Formation of unextracted residues was the primary loss mechanism in the soil photolysis, aerobic soil, aerobic aquatic, and anaerobic soil studies (up to 40 to 80% of applied radioactivity). The extraction procedures were similar but slightly different in the various fate studies[10] and it is not clear whether these extraction procedures were exhaustive. Exhaustive extraction procedures use a range of polar and nonpolar solvents. A high percentage of carbon dioxide did form in the aerobic studies (18 to 40% of applied radioactivity), indicating that a significant portion of the parent (at least the portion associated with the phenyl ring) did mineralize. However, in some studies unextracted residues occurred prior to formation of the CO_2, suggesting that the unextracted residues were not mineralizing, and were not forming with degradation of the parent. Lower percentages of carbon dioxide were observed in the soil photolysis and aerobic aquatic studies (9 to 13% applied radioactivity). Finally, unextracted residues in some studies peaked in the middle of study and extraction recoveries at the beginning of the study were low (as low as 50%); these observations suggest that the extraction procedures were not exhaustive. Therefore, to account conservatively for the uncertainty in the calculated half-lives, unextracted residues will be considered as potential residues of concern. Additional information on the identity of unextracted residues and on the quality of the extraction procedure would reduce uncertainties in

[9] M1 and M2 were two separate peaks observed using high performance liquid chromatography (HPLC). Structures of compounds making up these two peaks (M1 and M2) were summarized as at least 12 different compounds with four representative structures provided (see page 32 of MRID 44346726).

[10] The extraction procedures involved shaking three times in acetone:water:1N HCl (94;5:1) (sometimes in full acetone and water for the second and third extraction). Subsamples were refluxed with boiling in methanol for six hours. Finally, some samples were subject to pyrophosphate extraction and fractionation. In the terrestrial field dissipation study, soils were soxhlet extracted with methanol:water (80:20 v:v) for eight hours, which yielded 77-91% recoveries of the parent. Solvent solubility studies indicated that fenhexamid was most soluble (>100 g/L) in acetone, polyethylene glycol, dimethylformamide, and dimethylsulfoxide (MRID 44346718). Methanol was not one of the solvents examined. Not enough information is available to evaluate whether the extractions were exhaustive extractions.

the fate of fenhexamid. Residues of concern for human health drinking water were identified by the Health Effects Division to be the parent only (Herndon, 1999). This determination may be re-visited in Registration Review. Residues of concern for ecological risk were determined by EFED in this problem formulation, to be the parent, identified residues that retain the anilide base structure of the parent, and unextracted residues.

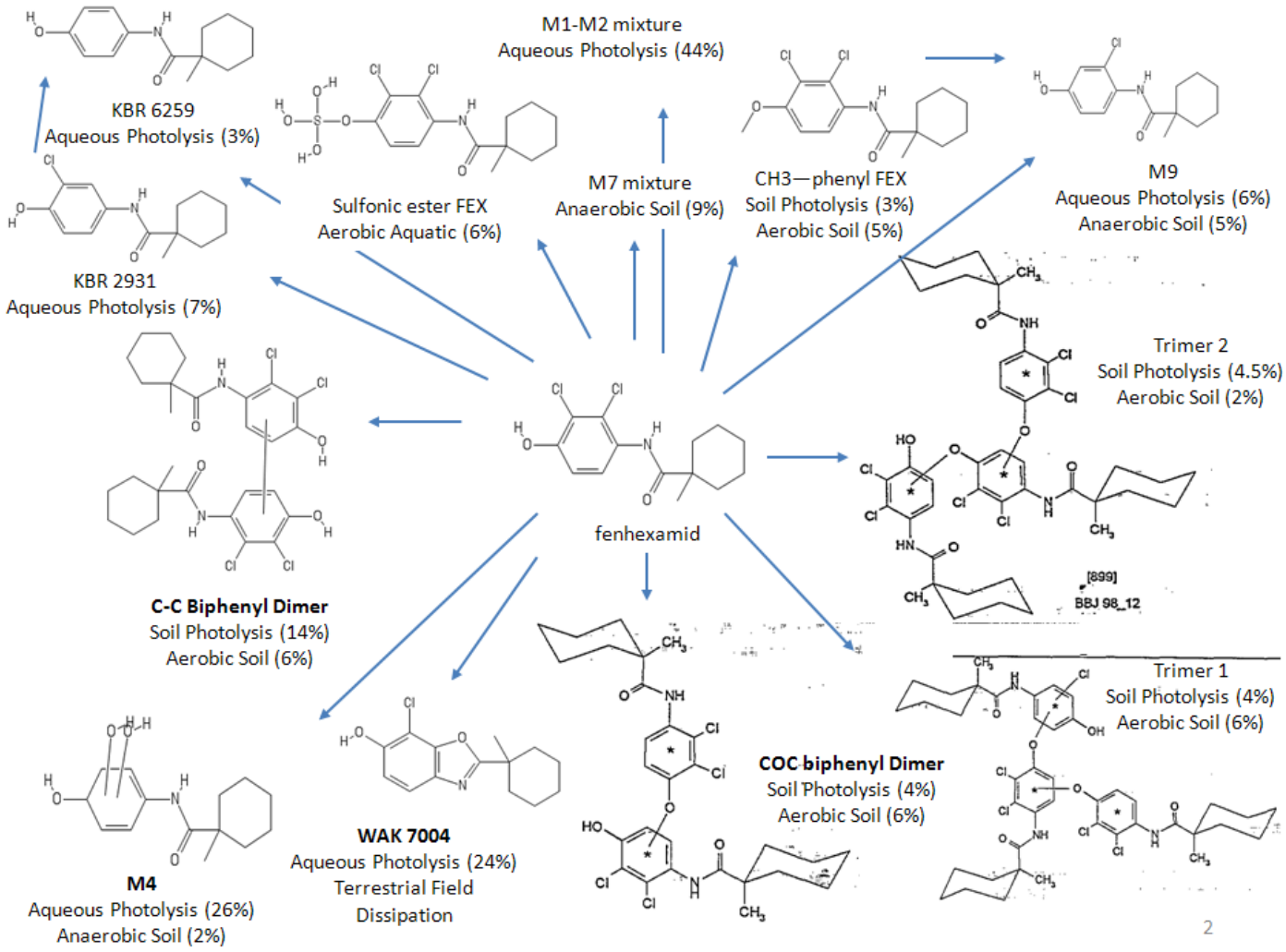

Figure 2. Potential Degradation Pathway for Fenhexamid. Bold degradates had greater than 10% applied radioactivity associated with the compound in at least one submitted fate study. The studies listed under the degradate name indicate the studies that the degradate was observed in and the maximum amount of the degradate observed in the study.

3.4. Field Dissipation

Four supplemental terrestrial field dissipation studies are available for fenhexamid. These studies only provide supplemental information as many did not monitor major degradates, none of the studies have environmental chemistry methods (ECM) with supporting independent laboratory validation (ILV), nor did they have the replication needed to fully characterize the variability in residues expected in the natural environment. Standard terrestrial field dissipation studies were completed for two bare ground sites in Canada, and one study examined a cropped strawberry plot and a bare plot. A lysimeter study was completed in Watsonville, CA. All four terrestrial field dissipation studies employed four applications at 0.75 kg a.i./ha each, with a 5-8 day interval between applications. This is similar to the highest registered use rates for agricultural uses, which is 0.75 lb a.i./acre with a maximum seasonal rate of 3 lb a.i./acre. When a minimum retreatment interval is provided, it is 7 days[11]. The field dissipation half-lives ranged from <1 to 3 days, which is similar to DT_{50} values observed in aerobic soil laboratory fate studies. A lysimeter study measured a much slower dissipation half-life of 44 days. Reasons for the higher DT_{50} in the lysimeter study are unknown; however, it may be noteworthy that extraction procedures were different than those used in other studies, and a typical end-use product was not used in the study.

Table 7. Summary of Terrestrial Field Dissipation Study Results For Fenhexamid

MRID (Year)	Study Site, Crop	DT50 (days)	DT90 (days)	Max. Depth	Max Conc in Soil (mg/kg-soil)		Comments
					Parent	WAK 7004	
44580303 (1998)	Branchon Ontario, bare soil (strawberries)	<1*	NR	15 cm	0.21	NA	Supplemental. Less than 5% recovery of field spiked samples. Did not characterize degradation pathway. No ILV. Paraquat applied to site. Storage stability had 70-110% recovery. Low recoveries observed with method.
44346724 (1996)	Watsonville, CA	44*	NR	15 cm	0.762		Supplemental. TEP not used in study. No replicates. Lysimeter study.3.05 lb/A, 4x, interval not reported in DER. Extracted with acetonitrile: 0.1% acetic acid (8:2) stirring for 1 hour.
45447501 (2000)	British Columbia, bare	3.19+	18.9+	15 cm	3.292	0.0280	Supplemental. Not enough samples to characterize variability on plot, no storage stability information, no ILV. Only 1 of 3 major degradates followed.
45447501 (2000)	Abbotsford, British Columbia, strawberries	3.05#	16.5#	15 cm	2.902	0.0206	

NA=not analyzed, NR=not reported; ILV=independent laboratory validation; TEP=typical end-use product
*The single first order equation was used to calculate degradation kinetics.
+ The DFOP equation was used to calculate degradation kinetics.
# The IORE equation was used to calculate degradation kinetics.
LOQ for parent=0.01 mg/kg-soil; LOQ for WAK 7004 =0.005 mg/kg-soil
MRID 44346734(soils not typical of those in U.S.) and 44580302 (time 0 concentrations near detection limit) are unacceptable.

[11] Some labels do not include a minimum retreatment interval.

3.5. Monitoring Data

The following databases and sources were searched on February 8, 2012 for monitoring information on fenhexamid:

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

Fenhexamid was looked for in 10 sediment samples (limit of quantitation (LOQ)=3.2 µg/kg) and two surface water samples (LOQ=7.6 ng/L) from three creeks in Georgia located in areas classified as agricultural, urban, and as "other" in the NAWQA program. Concentrations of fenhexamid were below LOQs. It is not known whether fenhexamid use occurred in the areas where these samples were collected.

4. Receptors

The most sensitive endpoint for each group of organisms will be used in the risk assessment. Assessment endpoints include direct toxic effects on the survival, reproduction, and growth of terrestrial and aquatic life, as well as indirect effects, such as reduction in prey base and/or modification of habitat. A summary of the available aquatic and terrestrial toxicity data for fenhexamid and its degradates is provided in Sections 4.1 and 4.2, respectively. In addition, a summary of ecological incidents associated with fenhexamid is provided in Section 4.3. Further discussion of potential degradate toxicity is provided in the description of the residues of concern for fenhexamid (Section 6.1).

Acute toxicity to fish and aquatic invertebrates is categorized using the system shown in **Table 8** (USEPA 2004). Acute toxicity to terrestrial fauna (birds and mammals) is categorized using the system shown in **Table 9**. Acute toxicity categories for plants have not been defined.

Table 8. Categories of acute toxicity for aquatic animals

LC_{50} (mg/L)[1]	Toxicity Category
< 0.1	Very highly toxic
> 0.1 - 1	Highly toxic
> 1 - 10	Moderately toxic
> 10 - 100	Slightly toxic
> 100	Practically nontoxic

[1] LC_{50} median lethal concentration to 50% of the organisms tested.

Table 9. Categories of acute toxicity for terrestrial animals

LD_{50} (mg/kg)[1]	LC_{50} (ppm)	Toxicity Category
<10	<50	Very highly toxic
10-50	50-500	Highly toxic
51-500	501 - 1000	Moderately toxic
501-2000	1001 - 5000	Slightly toxic
>2000	>5000	Practically nontoxic

[1]LD_{50} median lethal concentration to 50% of the organisms tested

4.1. Effects to Aquatic Organisms

Table 10 contains a summary of the most sensitive fenhexamid toxicity data for aquatic organisms.

Fenhexamid is moderately toxic to rainbow trout (*Oncorhynchus mykiss*; LC_{50} = 1.34 mg a.i./L; MRlD 44346742) and bluegill sunfish (LC_{50} = 3.42 mg a.i./L; MRID 44346741) on an acute exposure basis. Since freshwater fish serve as surrogates for aquatic-phase amphibians, the endpoints for fish apply to aquatic-phase amphibians as well. Acute toxicity testing using technical end-product (WG-50; 49% a.i.) on rainbow trout yielded roughly similar toxicity estimates (LC_{50} = 1.23 mg a.i./L; MRID 44523605). A chronic toxicity study of rainbow trout (early life-stage) produced a no observed adverse effect concentration (NOAEC) of 0.101 mg a.i./L (MRID 44346745) with the most sensitive endpoint being time to swim-up. Trout fry treated with as low as 0.391 mg a.i./L exhibited reduced survival.

Fenhexamid is slightly toxic to the freshwater invertebrate *Daphnia magna* (EC_{50} >18.8 mg a.i./L; MRID 44366507). In tests using technical end-product (WG 50; 49.6% a.i.), fenhexamid was practically non-toxic to daphnids (EC_{50} = 105 mg a.i./L; MRID 44523604). In a 21-day chronic toxicity test with daphnids, the NOAEC was 1.0 mg a.i./L (MRID 44346744) with growth (length) being the most sensitive endpoint.

In estuarine/marine animals, fenhexamid is moderately toxic to sheepshead minnow (*Cyprinodon variegatus*; LC_{50} = 11 mg a.i./L; MRD 44346743) and mysid shrimp (*Americamysis bahia*; EC_{50} = 4.6 mg a.i./L; MRID 4346740) on an acute exposure basis. No data were previously required for chronic toxicity to estuarine/marine fish or invertebrates.

Toxicity testing with both nonvascular aquatic green algae (*Pseudokirchneriella subcapitata*; EC_{50} = 4.15 mg a.i./L; MRID 44518706) and vascular aquatic plants duckweed (*Lemna gibba*; EC_{50} > 2.3 mg a.i./L; MRID 44731105) yielded similar estimates of toxicity. The percentage of duckweed fronds exhibiting necrosis and chlorosis was dependent on the concentration of fenhexamid. In studies with technical end-product (WG-50; 49.6% a.i.), green algae was the most sensitive aquatic plant species (EC_{50} = 1.37 mg a.i./L; MRlD 44518710).

Table 10. Most Sensitive Aquatic Toxicity Endpoints for Fenhexamid.

Group	Species (Common Name)	Study Type (Measured Effect)	Test Substance (% a.i.)	Endpoint (Test Duration)	Toxicity Value mg a.i./L (Acute Toxicity Category)	MRID (Study Classification)
Freshwater Fish[1]	*Oncorhynchus mykiss* (Rainbow trout)	Acute (Survival)	WG-50 (49%)	LC_{50} (96 hours)	1.23 (moderately toxic)	44523605 (Acceptable)
		Chronic: Early Life-Stage (Time to swim up)	Technical (95.9%)	NOAEC LOAEC	0.101 0.206	44346745 (Acceptable)
Estuarine/ Marine Fish	*Cyprinodon variegatus* (Sheepshead minnow)	Acute (Survival)	Technical (≥95%)	LC_{50} (96 hours)	11* (slightly toxic)	44346743 (Acceptable)
Freshwater Invertebrates	*Daphnia magna*	Acute (Immobilization)	Technical (95.7%)	EC_{50} (48 hours)	>18.8† (Slightly toxic to practically-non-toxic)	44366507 (Supplemental)
		Chronic life-cycle (growth [length]; larval survival)	Technical (95.9%)	NOAEC LOAEC	1.0 1.9	44346744 (Acceptable)
Estuarine/ Marine Invertebrates	*Americamysis bahia* (Mysid shrimp)	Acute (Survival)	Technical (95.8%)	LC_{50} (96 hours)	4.6 (moderately toxic)	44346740 (Acceptable)
Vascular Aquatic Plants	*Lemna gibba* (duckweed)	(Frond number, growth rate, biomass)	Technical (97.7%)	EC_{50} (14 days)	>2.3†	44731105 (Acceptable)
				NOAEC (14 days)	0.28	
Non-Vascular Aquatic Plants	*Pseudokirchneriella subcapitata* (green algae)	(Cell density)	WG-50 (49.6%)	EC_{50} (72 hours)	1.37	44523610 (Supplemental)
				NOAEC (72 hours)	0.558	

EC_{50} Effect concentration for 50% of the organisms tested; NOAEC no observed adverse effect concentration
† Non-definitive study endpoint; cannot be used to calculate RQs for risk estimation.
‡ Freshwater fish may be surrogates for aquatic-phase amphibians.

See **Appendix I** for a full list of available aquatic toxicity endpoints for fenhexamid.

4.2. Effects to Terrestrial Organisms

Table 11 contains a summary of the most sensitive fenhexamid toxicity data for terrestrial organisms.

An avian acute oral toxicity test with bobwhite quail (*Colinus virginianus*; MRID 44346750) resulted in no mortality at either of the two concentrations tested, resulting in a 14-day LD_{50} value of >2,000 mg a.i./kg-bw. Therefore, fenhexamid is classified as practically non-toxic to bobwhite quail on an acute oral exposure basis. No mortalities were observed in avian subacute dietary studies conducted with either bobwhite quail or mallard ducks (*Anas platyrhynchos*), resulting in 5-day LC_{50} values of >4,962 and >5,469 mg a.i./kg-diet, respectively (MRIDs 44346751 and 44346752). Therefore, fenhexamid is classified as practically non-toxic to bobwhite quail and mallard ducks on a subacute dietary exposure basis. However, feed consumption among bobwhite quail was dependent on the concentration of fenhexamid in the diet. In mallard ducks, there was a decline in average body weights with increasing treatment concentration groups during both the exposure and post-exposure periods; in addition, a decrease in body weight was observed in the post-exposure period (days 6-8) in mallard ducks treated with fenhexamid at 2,500 mg a.i./kg-diet relative to controls.

An avian reproduction study using bobwhite quail (MRID 44346753) did not result in any chronic growth or reproductive effects at the highest concentration tested (2074 mg a.i./kg-diet), but feed consumption was significantly ($P<0.05$) reduced at the 458 and 2,074 mg a.i./kg-diet levels, and was dependent on the concentration of fenhexamid in the diet. It is unclear if the decrease in food consumed was due to food palatability (repellency) or to fenhexamid-induced anorexia. Since reduced feed consumption was not associated with reduced body weight in treatment groups as compared to the control group, the NOAEC for this study is equal to the highest concentration tested (NOAEC: 2074 mg a.i./kg-diet)

Since birds serve as surrogates for reptiles and terrestrial-phase amphibians, and without data to the contrary, toxicity estimates for birds will apply to these other taxa as well.

Based on acute oral toxicity studies on rats, fenhexamid is categorized as practically non-toxic to rats (*Rattus norvegicus*; LD_{50} >5,000 mg/kg-bw; MRID 44346769). In chronic studies with rats (MRID 44346803), there were no compound-related effects on mortality, clinical signs, behavior, or reproductive parameters for adult animals; however, clinical chemistry and reduced organ weights resulted in a parental NOAEC and lowest observed adverse effect concentration (LOAEC) of 500 and 5,000 mg/kg-diet, respectively. The neonatal NOAEC and LOAEC were 5500 and 5,000 mg/kg-diet, respectively, based on decreased body weights on lactation days 7, 14 and 21 for first generation (F_1) pups (6-11 % less than controls) and on lactation days 7, 14, and 21 for second generation (F_2) pups (9-11% less than controls).

Fenhexamid is practically non-toxic to young adult honeybees (*Apis mellifera*) on acute contact and oral exposure bases (MRID 44346755). In the acute contact toxicity study, no mortalities occurred at either of the two concentrations tested (100 and 200 µg a.i./bee), resulting in a 48-hour LD_{50} of >200 µg a.i./bee. In the acute oral toxicity study with young adult honeybees, 0

and 13% mortality rates were observed at 100 and 201 µg a.i./bee levels, respectively, resulting in a 48-hour LC_{50} of >201 µg a.i./bee. No sublethal effects were noted.

No acceptable terrestrial plant toxicity data were identified for fenhexamid.

Table 11. Terrestrial toxicity profile for fenhexamid.

Group	Species	Study Type (Effect)	Test Substance (% a.i.)	Endpoint (Test Duration)	Toxicity Value (Acute Toxicity Category)	MRID (Study Classification)
Birds‡	*Anas platyrhynchos* (mallard duck)	Sub-acute dietary (Survival)	Technical (95.7%)	LC_{50} (5 days)	>4,962 mg a.i./kg-diet† (Practically non-toxic)	44346752 (Supplemental)
	Colinus virginianus (Northern Bobwhite Quail)	Acute oral (Survival)	Technical (95.7%)	LD_{50} (14 days)	>2,000 mg a.i./kg-bw† (Practically non-toxic)	44346750 (Supplemental)
		Reproductive toxicity (Feed consumption rate)	Technical (95.9%)	NOAEC/ LOAEC (23 weeks)	2,074/>2,074 mg a.i./kg-diet	44346753 (Acceptable)
Mammals	*Rattus norvegicus* (Norway rat)	Acute oral (Survival)	Technical (95.5%)	LD_{50} (Survival)	>5,000 mg a.i./kg-bw (Practically non-toxic)	44346769
		Rat 2-generation reproductive toxicity test (decreased body weights)	Technical (93.8-95.2%)	NOAEC/ LOAEC	500/5,000 mg a.i./kg-diet	44346803
Terrestrial Invertebrates	*Apis mellifera* (honeybee)	Acute Contact Toxicity (Survival)	Technical (95.7%)	LD_{50} (48 hours)	>200 µg a.i./bee	44346755 (Acceptable)
		Acute Oral Toxicity (Survival)	Technical (94%)	LD_{50} (48 hours)	>201 µg a.i./bee	44346755 (Supplemental)
Terrestrial Plants	No Toxicity Data Available					

LC_{50} lethal concentration for 50% of the animals tested; LD_{50} lethal dose for 50% of the animals tested; NOAEC no observed adverse effect concentration (mg/kg-diet); NOAEC no observed adverse effect concentration (mg/kg-diet)
† Non-definitive study endpoint; cannot be used to calculate RQs for risk estimation.
‡ Birds represent surrogates for terrestrial-phase amphibians and reptiles.

See **Appendix I** for a full list of available terrestrial toxicity endpoints for fenhexamid.

4.3. Ecological Incidents

A review of the Ecological Incident Information System (EIIS) for incidents involving fenhexamid was completed on January 31, 2013. Excluding incidents labeled as either unlikely or unrelated, only one incident (I013636-027) was identified in EIIS. This incident involved ornamental plants in Washington County, Oregon (IO13636-027) where unspecified damage to 6 acres of tulips was associated with a direct application of fenhexamid in 2002. Several other chemicals including isoxaben and glyphosate were included with fenhexamid in a tank mix around the time of the incident. Therefore, the likelihood that fenhexamid caused the incident was classified as "possible."

A search of OPP's aggregate incident report database on January 31, 2013 revealed no incidents related to fenhexamid. The Avian Incident Monitoring System of the American Bird Conservancy was also queried on January 31, 2013, and did not list any bird incidents associated with fenhexamid.[12]

5. Exposure Pathways of Concern and Risk Hypothesis

The environmental fate properties of fenhexamid and its transformation products indicate that direct application, spray drift, and runoff are transport mechanisms potentially relevant to ecological exposure. Potential risk to birds and mammals from drinking water exposure to fenhexamid was assessed using the screening program SIP (Screening Imbibition Program). When the highest available solubility level of fenhexamid (1000 mg/L; pH 9.3) is used in the program, there are potential drinking water risk concerns to mammals and birds on a chronic exposure basis (**Appendix C**). Since fenhexamid is classified as practically nontoxic to birds on both an acute oral and subacute dietary exposure basis, and to mammals on an acute oral exposure basis, the likelihood of adverse effects from acute drinking water exposures is considered low. When SIP is run with solubility values at a lower pH (200 mg/L at pH 8.5), there are still potential chronic drinking water exposure risks to mammals but not birds. The inhalation exposure pathway for birds and mammals was screened using the STIR (Screening Tool for Inhalation Risk) screening model, (**Appendix C**), and no potential risk concerns were found. These screening level models indicated that there was a potential exposure at high enough concentrations to result in a chronic risk concern for birds and mammals due to exposure to fenhexamid residues in drinking water. These models assume exposure occurs at the level of solubility and vapor pressure and are very conservative. SIP and STIR are described in detail at: http://www.epa.gov/oppefed1/models/terrestrial/index.htm.

Based on previous ecological risk assessments, fenhexamid has the potential to result in chronic risk to non-listed and listed terrestrial mammals. However, as the prior assessments did not include the minor anilide degradates as fenhexamid residues of concern, the following risk hypothesis will be used for this risk assessment:

Based on environmental fate parameters and potential transport pathways, fenhexamid total residues have the potential to reduce survival, reproduction, and/or growth in non-target terrestrial animals, aquatic vertebrates and invertebrates, and aquatic plants when used in

[12] http://www.abcbirds.org/abcprograms/policy/toxins/aims/aims/index.cfm

accordance with the current labels. These non-target organisms include listed as well as non-listed species.

Exposure pathways of concern for fenhexamid include spray drift, runoff, residues on foliage, residues in drinking water, bioconcentration/bioaccumulation, and residues in irrigation water. A risk assessment for sediment dwelling organisms will be performed when the risk assessment is completed. **Appendix G** summarizes the toxicity endpoints, exposure pathways, and models that will be used in the fenhexamid registration review risk assessment.

6. Analysis Plan

6.1. Residues of Concern

The stressors of ecological concern for aquatic and terrestrial organisms are fenhexamid and degradates that retain the anilide structure similar to the parent. Residues that retain the anilide structure include the following: WAK 7004, M4, BBJ98-8, M1, M2, M7, ZE056401, M9/KBR 5613, KBR3596, BBJ 98-9, BBJ 98-11, BBJ 98-12, KBR 2931, and KBR 6259.[13] M3 and M10 will also be considered residues of concern as their structures are unknown and most degradates observed are anilides. Additionally, since there is uncertainty in the identity of unextracted residues, they will conservatively be included in the half-life calculations. Because of their structural similarity to fenhexamid or uncertainty in the structure, and in the absence of data to the contrary, anilide degradates and unextracted residues are presumed to have toxicity similar to that of the parent and will therefore be included with fenhexamid as part of total toxic residues (TTR). In this approach, a single exposure concentration is estimated for total residues and compared to a representative toxicity endpoint (normally for the parent). To estimate exposure the amounts of the identified residues in fate studies are added and the sum of residues will be used to estimate a half-life that is in turn used in model inputs. Sorption coefficients used for model inputs are chosen from those for parent or a degradate (measured or estimated for degradates using Estimation Program Interface Suite (EPI Suite[14]) (USEPA, 2011) that is expected to be one of the more mobile residues. A TTR approach for the above degradates is the default option for risk assessment if suitable toxicity information on these degradates is not available. However, if suitable degradate toxicity data and environmental fate data are submitted or located through the ECOTOX database (USEPA, 2009a), there is the potential to derive exposure and risk values for these degradates independently.

Residues of concern for human health drinking water were identified by the Health Effects Division to be the parent only (Herndon, 1999). This determination may be re-visited in Registration Review.

Determinations on residues of concern may be revisited if new fate or toxicity becomes available.

[13] Current modeling for terrestrial plants does not consider environmental fate data. Therefore, a total residue approach does not influence the plant risk assessment. In the model used to estimate exposure to terrestrial animals (TREX), the foliar dissipation rate could be influenced if a total residue approach is used in the risk assessment; however, if a 35-day default dissipation rate is used in TREX, fate data do not influence the risk assessment.
[14] http://www.epa.gov/opptintr/exposure/pubs/episuite.htm

Mixtures

Evaluation of pesticide environmental mixtures is beyond the scope of this assessment because of myriad factors that cannot be quantified based on the available data. Those factors include identification of other possible co-contaminants and their concentrations, differences in the pattern and duration of exposure among contaminants, and the differential effects of other physical/chemical characteristics of the receiving waters (*e.g.* organic matter present in sediment and suspended water). Evaluation of factors that could influence additivity/synergism is beyond the scope of this assessment and the capabilities of the available data to allow for an evaluation. However, it is acknowledged that not considering mixtures could over- or under-estimate risks depending on the type of interaction and factors discussed above. The assessment will, however, analyze the toxicity of formulated products (including formulations involving more than one active ingredient) and will determine whether formulated products are more toxic than the technical grade active ingredient data used for assessing both direct and indirect risks. One agricultural product contains both fenhexamid and captan (**Appendix F**). Captan, a phthalamide fungicide, is a non-specific thiol reactant and inhibits respiration of numerous fungi and bacteria (USEPA, 2000) and this acts as a fungicide in a different manner than fenhexamid. If use of any of these products result in spray drift to a water body, acute aquatic toxicity data on a representative typical end-use product should be available for that mixture of ingredients. Additionally, terrestrial plant toxicity data should be available for a typical end-use product containing the combination of active ingredients.

6.2. 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.**

Since the previous exposure assessments were completed, three main changes in standard procedures were made:

1) Transformation rates for fate studies were recalculated according to the North American Free Trade Agreement (NAFTA) *Guidance for Evaluating and Calculating Degradation Kinetics in Environmental Media* (Bohaty *et al.*, 2012; NAFTA, 2012). These updated results will be used in estimating model inputs for estimating aquatic exposure.
2) A new model for estimating concentrations in groundwater was developed called the Pesticide Root Zone Model – Groundwater (PRZM-GW) (Baris *et al.*, 2013). This model will be used along with SCI-GROW to estimate concentrations in ground water.
3) Residues of concern for ecological risk were updated. Estimated environmental concentrations will reflect exposure to total anilides.

The most up to date procedures and models will be used in the registration review exposure assessments.

6.3. Measures of Effect

Selected toxicity data presented in Section 4 of this problem formulation will be used to calculate RQ values. Any relevant additional information submitted by the registrant or found in the open

literature prior to conduct of the risk assessment will also be considered. The open literature studies are identified using EPA's ECOTOXicity (ECOTOX)[15] database, which employs a literature search engine for locating chemical toxicity data for aquatic life, terrestrial plants, and wildlife. The evaluation of both sources of data can also provide insight into the direct and indirect effects of pesticides on biotic communities from loss of species that are sensitive to the chemicals and from changes in structure and functional characteristics of the affected communities.

6.4. Endangered Species Assessments

Consistent with the Agency's responsibility under the Endangered Species Act (ESA), the Agency will evaluate risks to listed species from registered uses of pesticides in Registration Review. These assessments will be conducted in accordance with standard EPA procedures and good scientific judgment. The process for evaluating potential risks to listed species is further described in the Overview Document at http://www.epa.gov/oppfead1/endanger/litstatus/riskasses.htm.

6.5. Endocrine Disruptor Screening Program

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

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

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

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

7. Preliminary Identification of Data Gaps

7.1. Environmental Fate Data

Table 10 identifies environmental fate studies by MRID that provide data on fenhexamid for each guideline requirement, as well as study classifications and whether or not further data are needed in order to support risk assessment. Several fate studies are needed to better characterize and reduce significant uncertainties on the environmental fate and transport of fenhexamid. There are conditional registrations pending additional data on terrestrial field dissipation and fish bioconcentration[16]. The studies listed below will decrease the uncertainty in determining the potential exposure to the pesticide.

- Aerobic Soil Metabolism (OPPTS Guideline Number 835.4100[17]) for parent
- Aerobic Aquatic Metabolism (OPPTS Guideline Number 835.4300[18]) for parent
- Anaerobic Aquatic Metabolism (OPPTS Guideline Number 835.4400[19]) for parent
- Terrestrial Field Dissipation Study (OPPTS Guideline Number 835.6100[20]) using a typical end-use product with corresponding Environmental Chemistry Methods (ECM) for Soil (OCSPP Guideline 850.6100[21]) for parent and major degradates. The ECM should have an independent laboratory validation (ILV). If valid ECM with ILV and storage stability data are submitted for MRID 45447501 that may be used to fulfill this guideline. If additional terrestrial field dissipation studies are conducted, anilide degradates should be analyzed.
- Environmental Chemistry Methods for Water (OCSPP Guideline 850.6100) for parent and major degradates
- Fish Bioconcentration Study (OCSPP Guideline 850.1730[22]) for parent

[16] A waiver request for a fish bioconcentration study was submitted by the registrant in 2003. EFED did not concur with the waiver request (Sutton, 2003, D274862).
[17] USEPA. 2008. http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0152-0038
[18] USEPA. 2008. http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0152-0039
[19] USEPA. 2008. http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0152-0039
[20] USEPA. 2008. http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0152-0040
[21] USEPA. 2009. http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0154-0008
[22] USEPA. 1996. http://www.epa.gov/opptsmnt/pubs/frs/publications/OPPTS_Harmonized/850_Ecological_Effects_Test_Guidelines/Drafts/850-1730.pdf

Due to the uncertainty in the identity of the unextracted residues as described in Section 3.3 additional data are recommended (aerobic soil, aerobic aquatic metabolism, and anaerobic aquatic metabolism) to better understand whether these residues are of concern. EFED recommends that a range of solvents with different polarities be used in the studies to ensure that the extraction procedures are exhaustive for parent and transformation products. Once exhaustive extraction procedures are identified in preliminary experiments, studies should be completed using the exhaustive extraction procedures. It is recommended that studies be completed with both the phenyl and carboximide rings radiolabeled so that all potential degradates may be followed. This would reduce uncertainty in the potential that carboxamide degradates are forming that were not followed in fate studies. In lieu of additional data being submitted, EFED will assume that unextracted residues are potential residues of concern for the risk assessment. Characterization of uncertainty will be explored by also calculating risk quotients by assuming that unextracted residues are not residues of concern.

In addition to the studies recommended for data call in, the registrant is encouraged to submit the following information:

- WRB Soil Classifications for Foreign Soils: Many of the fate studies were conducted on foreign soils. Additional information on the World Resource Base (WRB) classifications for studies conducted on foreign soils would reduce uncertainty in determining whether the results apply to soils expected to occur in the United States.
- Batch Equilibrium Data on Degradates: Often when a TTR approach is used in risk assessment, additional data on sorption coefficients for other residues of concern are recommended. Most of the fenhexamid degradates were minor degradates in aerobic soil and aerobic aquatic metabolism studies. Therefore, it was determined that EFED would rely on the available sorption coefficients for WAK 7004 and fenhexamid. EPI Suite may also be used to estimate a sorption coefficient for some degradates. EFED encourages the registrant to submit any batch equilibrium data that may be available on degradates.
- Sensitive ECM: In addition to the ECM and ILV requests above, any other ECMs that the registrant has available may be useful for others to have available for monitoring. Having access to sensitive methods (and standards) using a variety of instruments would enable State Agencies and other interested third parties to investigate incidents or other impacts associated with fenhexamid use and could provide Agency with a better set of field data than we have at the present to assess the risk. These methods could be specific to fenhexamid and/or its transformation products, or multi-residue methods for multiple compounds that include fenhexamid and/or its degradates. These methods would add to the methods already available for monitoring.

Table 12. Submitted environmental fate data for fenhexamid

OCSPP Guideline	Data Requirement	Submitted Studies (Acc. No. or MRID)	Study Classification	Are data needed to conduct risk assessment?	Justification and Assumptions EPA will Make in Absence of Data
835.2120	Hydrolysis	44346725	Acceptable	No	
835.2240	Aqueous photolysis	44346726	Acceptable	No	
		44346732	Supplemental	No	
835.2410	Soil photolysis	44342728	Supplemental	No	

OCSPP Guideline	Data Requirement	Submitted Studies (Acc. No. or MRID)	Study Classification	Are data needed to conduct risk assessment?	Justification and Assumptions EPA will Make in Absence of Data
835.4100	Aerobic soil metabolism	44346729	Supplemental	Yes	High levels of unextracted residues were observed in available studies and there is uncertainty in whether the extraction procedures were exhaustive. Therefore, additional data are needed to better understand the uncertainty in the identity of the unextracted residues. In lieu of additional data, EFED will assume that unextracted residues are residues of concern in the risk assessment.
		44346730	Supplemental		
835.4200	Anaerobic soil metabolism	44346731	Acceptable	No	Data are typically required for four soils. Currently, data are only available on one anaerobic soil system. In lieu of additional data, EFED will characterize anaerobic metabolism based on the study available. While anaerobic soil metabolism data are required according the 40 CFR 158.1300, these data are not typically used in exposure modeling and exposure to humans in ground water is currently not a concern. Therefore, these data would likely have little impact on the risk conclusions.
835.4300	Aerobic aquatic metabolism	44518701	Acceptable	Yes	High levels of unextracted residues were observed in available studies and there is uncertainty in whether the extraction procedures were exhaustive. Therefore, additional data are needed to better understand the uncertainty in the identity of the unextracted residues. In lieu of additional data, EFED will assume that unextracted residues are residues of concern in the risk assessment.
835.4400	Anaerobic aquatic metabolism	No data submitted		Yes	Data are required for two water/sediments systems. In lieu of additional data, EFED will assume the anaerobic soil metabolism value is representative of anaerobic aquatic metabolism rates and will apply a 3-fold uncertainty factor (DT_{50}×3) to estimate a model input value. Additionally, there were high levels of unextracted residues in the anaerobic soil study. In lieu of additional data, EFED will assume that unextracted residues are residues of concern in the risk assessment.
835.1230	Adsorption/ desorption	44346722 (Parent)	Acceptable	No	Data are currently required for the parent on five soils and one sediment. Data are available for parent for six soils. Additional data are needed to characterize sorption of fenhexamid to one sediment. In lieu of additional data, EFED will use available sorption coefficients to estimate a mean sorption coefficient in modeling. Additional data were not requested as they are not expected to substantially impact the risk conclusions.
		44346732 (WAK 7004)	Supplemental		
835.6100	Terrestrial field dissipation	44580303	Supplemental	Yes	MRID 45447501 was submitted to fulfill this open data requirement. This study does not have an ILV, storage stability data, and only monitored 1 of 3 major degradates. Additionally, several of the minor
		44346724	Supplemental		
		45447501	Supplemental		
		44346734	Unacceptable		

OCSPP Guideline	Data Requirement	Submitted Studies (Acc. No. or MRID)	Study Classification	Are data needed to conduct risk assessment?	Justification and Assumptions EPA will Make in Absence of Data
		44580302	Unacceptable		degradates retain the anilide structure of the parent and are considered residues of concern. Therefore, additional information on terrestrial field dissipation is still needed. In lieu of additional data, there will be uncertainty in how well the laboratory fate studies reflect what occurs in the field. Submission of an ILV for the ECM used in MRID 45447501 and storage stability information may eliminate the need for additional information on this uncertainty.
850.6100	Analytical method in soil	44346734	Not classified	Yes	These studies are not standard environmental chemistry method studies. The studies examined degradation in soil and sediment. The environmental chemistry method components of the studies were reviewed. Methods are not the same methods used in the terrestrial field dissipation studies (*e.g.*, MRID 45447501). Additionally ECMs do not have a corresponding ILV. This is a standard data requirement to support terrestrial field dissipation studies.
	Analytical method in sediment	44346731	Not classified		
	Analytical method in freshwater	no data submitted			An ECM and ILV are needed with a limit of quantitation (LOQ) for the parent below 0.06 mg/L that may be used in monitoring.[1] All major degradates should be included in the method and have an associated LOQ and limit of detection (LOD) lower than levels that would result in a risk concern. Additionally, it would be very helpful for the method to be able to measure other anilide degradates.
	Analytical method in salt water	44346738	Not classified	No	--
	Analytical method in plant tissue	Not submitted to U.S.	Not reviewed	No	--
850.1730	Fish BCF	44346747	Supplemental	Yes	Radioactivity was not fully characterized in available studies. Fish BCF studies are still needed to fully understand the potential for bioconcentration of fenhexamid. In lieu of additional data, KABAM will be used to evaluate risk based on measured K_{ow} and K_{oc}.
		44346746	Supplemental		

ILV=independent laboratory validation; ECM=environmental chemistry method; BCF=bioconcentration factor

1 The LOQ is based on the 96-hour LC_{50} of 1.23 mg a.i./L for the rainbow trout and an LOC of 0.05 (MRID 44523605).

7.2. Effects Data

Table 13 identifies all available ecological effects studies for fenhexamid by MRID, as well as a description of whether further data are needed to support risk assessment.

Table 13. Submitted terrestrial and aquatic animal ecological effects data for fenhexamid

Guideline	Description—Test Substance	MRID	Study Classification	Are data Needed for Risk Assessment?	Comments (Justification and Assumptions EPA will Make in Absence of Data)
Avian and Mammalian Testing					
850.2100	Avian acute oral toxicity, waterfowl—TGAI	None	N/A	No	
	Avian acute oral toxicity, upland game bird species—TGAI	44346750	Supplemental	No	Only two dose levels tested (2000 mg a.i./kg-bw), but no mortality occurred at any test level. There were some indications of frank sublethal effects to body weight in birds treated with fenhexamid at 1050 mg a.i./kg-bw. According to the EFED Non-Definitive Endpoint Guidance Policy, additional study data would typically be recommended here because exposure levels were not tested up to 10x the EEC (e.g., peak short grass EEC for birds is 383.47 mg a.i./kg-bw based on 0.75 lbs a.i./A application rate of fenhexamid to ginseng at two applications per seasons with a retreatment interval of 7 days); However, since a passerine acute oral toxicity study (OCSPP 850.2100) is already being recommended, and since passerines tend to be more sensitive to feed consumption/body weight effects than upland game birds, additional toxicity testing is not being recommended at this time.

Guideline	Description—Test Substance	MRID	Study Classification	Are data Needed for Risk Assessment?	Comments (Justification and Assumptions EPA will Make in Absence of Data)
	Avian acute oral toxicity, passerine species—TGAI	None	N/A	**Yes**	Part of 40 CFR Part 158 data requirements as of December 2007; moreover, affects on feed consumption observed in other avian studies may impact passerines to a greater degree given their food intake requirements; in addition, only one avian acute toxicity study is available for fenhexamid, rather than the two species indicated in the guidelines (risk to passerine birds will be assumed in the absence of recommended data)
850.2200	Avian dietary toxicity, waterfowl species—TGAI	44346752	Supplemental	No	Non-definitive endpoint of >4,962 mg a.i./kg-diet is not greater than 10 times the dietary EEC for all uses and/or food items
	Avian dietary toxicity, upland game bird—TGAI	44346751	Supplemental	No	Non-definitive endpoint of >5,469 mg a.i./kg-diet is not greater than 10 times the dietary EEC for all uses and/or food items
850.2300	Avian reproduction, waterfowl species—TGAI	None	N/A	No	Study previously waived based on low acute oral and sub-acute dietary toxicity and lack of reproductive effects in the bobwhite quail chronic toxicity test (MRID 44346753).
850.2300	Avian reproduction, upland game bird species—TGAI	44346753	Acceptable	No	
850.2400	Wild mammal toxicity—TGAI	None	N/A	No	Not triggered based on ecotoxicity data, predicted EECs, fate properties, and use pattern criteria.
850.2500	Simulated or actual field testing—TEP	None	N/A	No	Not triggered based on ecotoxicity data, predicted EECs, fate properties, and use pattern criteria.
Aquatic Animal Testing					
850.1010	Freshwater invertebrate, acute toxicity—TGAI	44366507	Supplemental	No	
	Freshwater invertebrate, acute toxicity—TEP	44523604	Supplemental	No	

Guideline	Description—Test Substance	MRID	Study Classification	Are data Needed for Risk Assessment?	Comments (Justification and Assumptions EPA will Make in Absence of Data)
850.1025	Estuarine/Marine Mollusk acute toxicity—TGAI	None	N/A	**Yes**	EFED previously waived this study, given the slight to moderate toxicity of fenhexamid to aquatic organisms; however, in the two other anilide fungicides (boscalid; metalaxyl) for which Eastern oyster and mysid shrimp acute toxicity data are both available, the oyster was the more sensitive of the two species; in addition, oyster data would provide a firmer basis for informing risk estimates of the many (~123) listed freshwater mollusk species[23]
850.1035	Estuarine/Marine crustacean acute toxicity—TGAI	44346740	Acceptable	No	Precipitate observed at highest test level, but centrifugation performed prior to measurements
	Estuarine/Marine crustacean acute toxicity—TEP (Fenhexamid/ Captan Co-formulation; EPA Reg. No. 66330-48)	None	N/A	**Yes**	Acute toxicity data for this multi-a.i. product is recommended due to the potential for spray drift and uncertainty concerning how the two chemicals, together, would affect aquatic organisms; estuarine/marine organisms are recommended for testing since they are the most sensitive to fenhexamid TGAI on an acute exposure basis.
850.1075	Freshwater fish, acute toxicity, warm water species—TGAI	44346741	Acceptable	No	
	Freshwater fish, acute toxicity, cold water species—TGAI	44346742	Acceptable	No	
	Freshwater fish, acute toxicity, cold water species—TEP (WG-50)	44523605	Acceptable	No	

[23] Number of federally listed mollusks based on the US Fish And Wildlife Endangered Species Program website: http://www.fws.gov/endangered/species/us-species.html

Guideline	Description—Test Substance	MRID	Study Classification	Are data Needed for Risk Assessment?	Comments (Justification and Assumptions EPA will Make in Absence of Data)
	Estuarine/Marine fish acute toxicity—TGAI	44346743	Acceptable	No	Precipitate at two highest concentrations, but centrifugation performed prior to measurements; mean-measured concentrations did not appear to have been affected
850.1300	Freshwater invertebrate, reproduction test—TGAI	44346744	Acceptable	No	
850.1350	Estuarine/marine invertebrate, reproduction test—TGAI	None	N/A	**Yes**	Mysid shrimp (E/M invertebrate) are approximately 20 times more sensitive than *Daphnia magna* (FW invertebrate) on an acute exposure basis. Therefore, a chronic E/M invertebrate study is being recommended to account for this potential sensitivity. In addition, there is no available fate information to suggest that fenhexamid would not reach the estuarine or marine environments. (In the absence of this data, risk to estuarine/marine invertebrates will be assumed; an acute-to-chronic ratio cannot be used to derive a chronic toxicity value for the mysid shrimp since the freshwater acute toxicity value for daphnids is non-definitive)
850.1400	Freshwater fish, early life stage test—TGAI	44346745	Acceptable	No	
	Saltwater fish, early life stage test—TGAI	None	N/A	No	Based on acute toxicity data, E/M fish do not appear to be as sensitive to fenhexamid as FW fish; therefore, additional data is not expected to change the risk picture.

Guideline	Description—Test Substance	MRID	Study Classification	Are data Needed for Risk Assessment?	Comments (Justification and Assumptions EPA will Make in Absence of Data)
850.1500	Freshwater fish life cycle test	None	N/A	No	Aquatic EECs for some previous uses (e.g., ginseng; 60-day EEC 0.0136 mg/L) are > 0.1 of the FW fish early life-stage (ELS) NOAEC (0.1 mg a.i./L); however, since there were no chronic reproductive effects to birds at any fenhexamid concentration tested (MRID 44346753), and since the NOAEL values for pup and adults occurred at the same test level (5000 ppm) in the rat 2-generation reproduction study (MRID 44346803), there does not appear to be sufficient rationale for recommending a fish fully life cycle study.
	Estuarine/marine fish life cycle test	None	N/A	No	
850.1950	Simulated or actual field testing for aquatic organisms	None	N/A	No	Higher tier testing to address risk uncertainties have not been identified at this time
Sediment Testing					
850.1735	Whole sediment 10-d freshwater invertebrate—TGAI	None	N/A	**Yes**	Data requirement triggered since some K_{OC} and log K_{ow} values in submitted fate studies were above 1,000 and 3.0, respectively (see **Appendix J** and data justification below table for further details)
850.1740	Whole sediment 10-d estuarine/marine invertebrate—TGAI	None	N/A	**Yes**	Data requirement triggered since some K_{OC} and log K_{ow} values in submitted fate studies were above 1,000 and 3.0, respectively (see **Appendix J** and data justification below table for further details)
Agency-wide guideline	Whole sediment chronic freshwater and/or marine invertebrate—TGAI	None	N/A	**Yes**	Data are recommended pending the outcome of the 10-day sediment toxicity studies (850.1735; 850.1740) (see **Appendix J** and data justification below table for further details)

Guideline	Description—Test Substance	MRID	Study Classification	Are data Needed for Risk Assessment?	Comments (Justification and Assumptions EPA will Make in Absence of Data)
Insect Pollinator Testing					
850.3020	Honeybee acute contact toxicity—TGAI	44346755	Acceptable	No	
OECD 213	Honeybee acute oral toxicity study—TGAI	44346755	Supplemental	**Yes**	Submitted under EPPO Guideline No. 170[24]; two-concentration test; multiple mortalities at higher test level (201 µg/bee or 1,570 mg/kg); did not test high enough to preclude listed species risk for some uses (*e.g.*, LC_{50} of 1,570 is less than 20x the ginseng tall grass EEC of 271 mg/kg)
850.3030	Honeybee toxicity of residues on foliage—TEP	None	N/A	No	Data requirement not triggered
850.3040	Field testing for pollinators	None	N/A	No	Field testing to address risk uncertainties have not been identified at this time
Non-guideline	Larval Toxicity Test—TGAI	None	N/A	**Yes**	Recommended since data are only available on the toxicity of fenhexamid to young adult bees; no information is available on toxicity of fenhexamid to honeybee brood. A honeybee larval toxicity test is part of EFEDs current screening process for terrestrial invertebrates. It is recommended that a protocol be submitted before conducting this test. See **Appendix J** for further justification for recommending this study.
Terrestrial Plant Testing					
850.4100	Seedling emergence (10 species)—TEP (representative fenhexamid single a.i. formulation)	None	N/A	**Yes**	Submitted study should test up to highest currently registered application rate of fenhexamid. Terrestrial plant toxicity studies with the fenhexamid/captan co-formulated product are being

[24] https://secure.fera.defra.gov.uk/beebase/index.cfm?sectionid=64

Guideline	Description—Test Substance	MRID	Study Classification	Are data Needed for Risk Assessment?	Comments (Justification and Assumptions EPA will Make in Absence of Data)
	Seedling emergence (10 species)—TEP (Fenhexamid/ Captan Co-formulation; EPA Reg. No. 66330-48)	None	N/A	**Yes**	recommended since it represents a different typical end-use product than formulations containing fenhexamid only. In addition, both compounds are fungicides and may result in increased phytotoxic effects to non-target plants. If terrestrial plant toxicity studies are only submitted for the fenhexamid/captan formulation, then this data will be used to estimate risk of all fenhexamid formations (both single and multi-a.i.) to terrestrial plants during risk assessment. If terrestrial plant toxicity studies are only submitted for a single a.i. TEP (*i.e.*, fenhexamid only), risk to terrestrial plants will be assumed for the fenhexamid/captan formulation.
850.4150	Vegetative vigor (10 species)—TEP(representative fenhexamid single a.i. formulation)	None	N/A	**Yes**	
	Vegetative vigor (10 species)—TEP (Fenhexamid/ Captan Co-formulation; EPA Reg. No. 66330-48)	None	N/A	**Yes**	
Aquatic Plant Testing					
850.4400	Aquatic plant growth, vascular plant — TGAI	44731105	Acceptable	No	If uses result in peak EECs that are near or above 2.3 mg/L, then additional data would be needed. The most recent peak EECs for ginseng were 0.024 mg/L.
850.4500*	Aquatic Plant, freshwater green alga species—TGAI	44518706	Supplemental	No	
		44518705	Invalid	No	Additional data are not needed as there is an existing green algae study (MRID 44518706) that can be used for risk assessment
	Aquatic Plant, freshwater diatom—TEP	None	N/A	**Yes**	Study should test up to highest application rate and/or aquatic EECs as defined in this problem formulation or previous risk assessments
	Aquatic Plant, marine diatom — TEP	None	N/A	**Yes**	Study should test up to highest application rate and/or aquatic EECs as defined in this problem formulation or previous risk assessments

Guideline	Description— Test Substance	MRID	Study Classification	Are data Needed for Risk Assessment?	Comments (Justification and Assumptions EPA will Make in Absence of Data)
850.4550†	Aquatic Plant, cyanobacterium — TEP	None	N/A	**Yes**	Study should test up to highest application rate and/or aquatic EECs as defined in this problem formulation or previous risk assessments

TGAI = Technical Grade Active Ingredient
TEP = technical end product
* Algal toxicity tests are now under guideline OCSPP 850.4500 (formerly 850.5400)
† Cyanobacterium tests are now under guideline 850.4550 (formerly 850.5400)

Request for Sediment Toxicity Studies for Fenhexamid TGAI:

The use pattern, chemical properties, estimated exposure, and toxicity profile of fenhexamid indicate need for chronic (life cycle) sediment toxicity tests to fully evaluate potential risks to benthic invertebrates. These sediment toxicity studies include two freshwater species (the midge, *Chironomus dilutus* and the amphipod, *Hyalella azteca*) and one saltwater species (the amphipod, *Leptocheirus plumulosus*). Multiple species are being recommended in order to account for differential sensitivity and exposure potential of benthic invertebrates to fenhexamid. This recommendation is being made because some K_{OC} and log K_{ow} values in submitted fate studies were above the thresholds of 1,000 and 3.0, respectively.

As an alternative to the conduct of three chronic (life cycle) sediment toxicity tests, EFED would also consider a tiered testing approach for sediment toxicity testing. In this approach, sediment toxicity testing would first be conducted with the aforementioned species using the 10-d (subchronic) sediment toxicity test guidelines (OSCPP 850.1735[25] and 850.1740[26]). Then, pending a comparison of estimated environmental concentrations (EEC) in sediment and pore water with toxicity results from the 10-d sediment toxicity studies, the need for one or more chronic sediment toxicity studies would be determined. This tiered testing approach has the potential advantage of reducing the number of chronic (life cycle) studies that would be needed when results of the 10-d (subchronic) tests in conjunction with sediment EECs indicate chronic testing is not likely to alter risk assessment conclusions. In some cases, however, this tiered testing approach may result in the conduct of both a 10-d (subchronic) and a chronic (life cycle) study.

If the tiered test approach described above is not preferred, then chronic life-cycle sediment toxicity studies be carried out on the three preferred species, *C. dilutus*, *H. azteca*, and *L. plumulosus*.

[25] USEPA. 1996. http://www.epa.gov/opptsmnt/pubs/frs/publications/OPPTS_Harmonized/850_Ecological_Effects_Test_Guidelines/Drafts/850-1735.pdf
[26] USEPA. 1996. http://www.epa.gov/opptsmnt/pubs/frs/publications/OPPTS_Harmonized/850_Ecological_Effects_Test_Guidelines/Drafts/850-1740.pdf

8. Additional Information on Use

For risk assessment purposes, EFED will employ application scenarios that are expected to result in maximum exposure for each given use. Absence of information on the labels regarding maximum single application rates, application intervals, allowable annual maximum rates, or application methods will result in conservative assumptions as illustrated in the following examples:

- If a label does not specify an application interval, an application interval of 3 days will be assumed.

It would be helpful for the registrant to provide supporting information on the following label uncertainties:

- EPA registration number 66330-00035 states that for agricultural uses, applications may be made by ground only. Then in some sections of the label (almonds, pear, pistachios, stone fruit) it provides information for applications by air. EPA intends to engage the registrant to gain additional understanding on this label uncertainty.
- Maximum single application rates are provided on a crop cycle basis. The maximum number of crop cycles per year for each crop would help to understand the maximum yearly application rate for each crop.
- A maximum single application rate in lbs a.i./A for nursery and ornamentals, forest conifers, and non-bearing fruit trees and vines is not provided on some labels.

9. References

9.1. Literature Cited

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71-4 Avian Reproduction

44346753 Schmuck, R. (1997) Effects of a Subchronic Dietary Exposure of KBR 2738 (Technical) on Bobwhite Quail Including Effects on Reproduction and Health (Including Amendment): Lab Project Number: SXR/REP 06: TMN-001N: E 293 1027-9. Unpublished study prepared by Bayer Ag. 134 p.

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123-2 Aquatic plant growth

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141-1 Honey bee acute contact

44346755 Winkler, R. (1995) Testing Toxicity to Honeybee--Apis mellifera L. (Laboratory) According to EPPO Guideline No. 170: KBR 2738 (Technical): Lab Project Number: 95 10 48 058: TMN-017A: 0097201. Unpublished study prepared by Biochem Gmbh Karlsruhe. 23 p.

141-2 Honey bee residue on foliage

44346755 Winkler, R. (1995) Testing Toxicity to Honeybee--Apis mellifera L. (Laboratory) According to EPPO Guideline No. 170: KBR 2738 (Technical): Lab Project Number: 95 10 48 058: TMN-017A: 0097201. Unpublished study prepared by Biochem Gmbh Karlsruhe. 23 p.

143-1 Toxicity to Predator and Parasite Insects

44523608 Mead-Briggs, M. (1995) A Laboratory Evaluation of the Side-Effects of the Fungicide KBR 2738 WG 50 on the Parasitic Wasp Aphidius rhopalosiphi: Lab Project Number: BAY-95-1: TMN-017D. Unpublished study prepared by University of Southampton. 19 p.

870.1100 Acute oral toxicity

45829702 Mezin, L.; Kuhn, J. (2002) CaptEvate 68 WDG: Acute Oral and Dermal Toxicity in Rats and Dermal Irritation in Rabbits: Lab Project Number: TMN-0070: 7039-02: 7040-02. Unpublished study prepared by Stillmeadow, Inc. and Arvesta Corporation. 43 p.

870.1200 Acute dermal toxicity

45829702 Mezin, L.; Kuhn, J. (2002) CaptEvate 68 WDG: Acute Oral and Dermal Toxicity in Rats and Dermal Irritation in Rabbits: Lab Project Number: TMN-0070: 7039-02: 7040-02. Unpublished study prepared by Stillmeadow, Inc. and Arvesta Corporation. 43 p.

870.1300 Acute inhalation toxicity

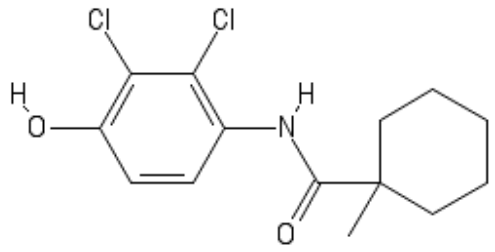
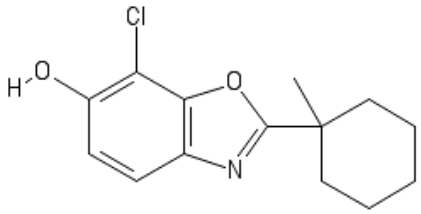
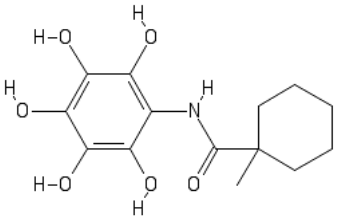
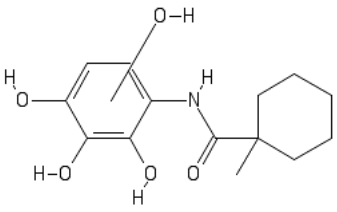
45829703 Carter, L. (2002) Acute Inhalation Toxicity Study in Rats: Captan 80 WP: Final Report: Lab Project Number: 7038-02. Unpublished study prepared by Stillmeadow, Inc. 27 p.

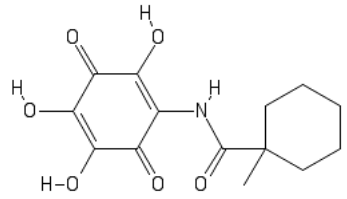
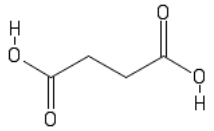
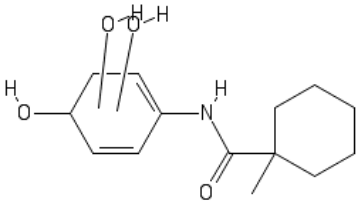
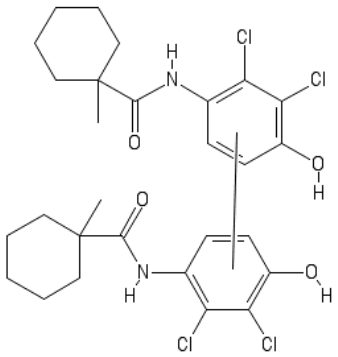
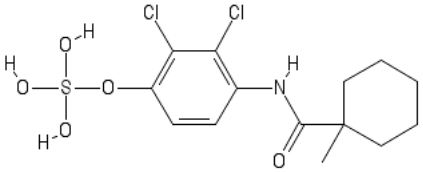
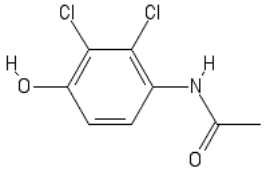
870.2500 Acute dermal irritation

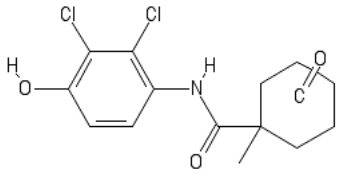
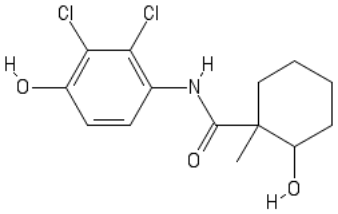
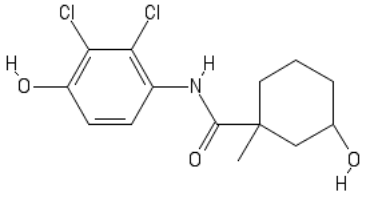
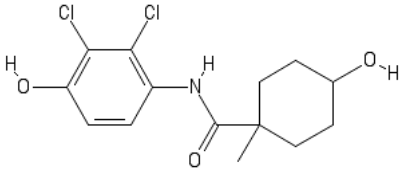
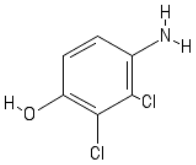
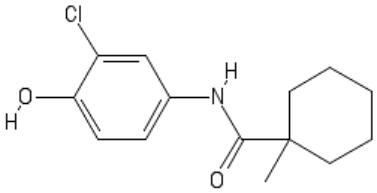
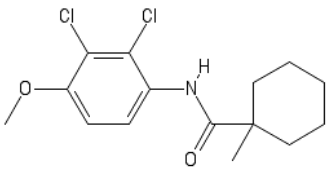
45829702 Mezin, L.; Kuhn, J. (2002) CaptEvate 68 WDG: Acute Oral and Dermal Toxicity in Rats and Dermal Irritation in Rabbits: Lab Project Number: TMN-0070: 7039-02: 7040-02. Unpublished study prepared by Stillmeadow, Inc. and Arvesta Corporation. 43 p.

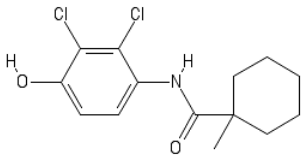
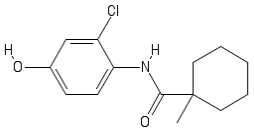
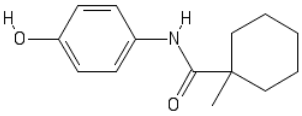
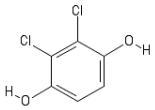
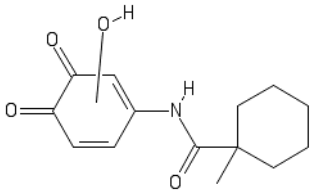
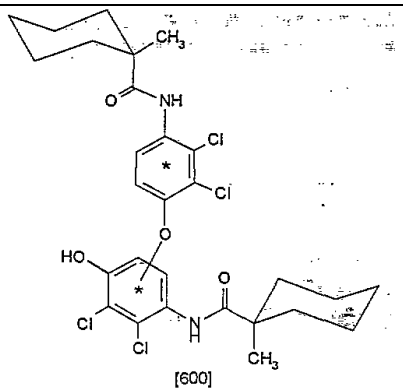
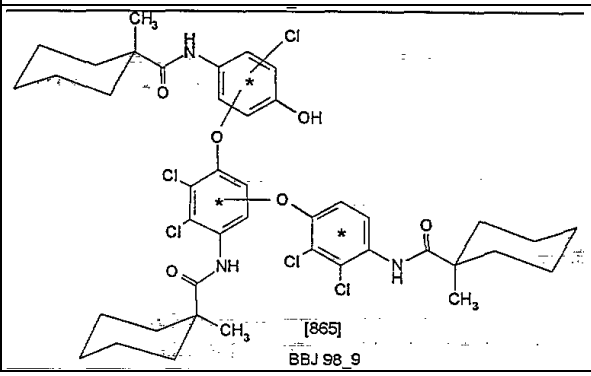
Appendix A. Supplemental Environmental Fate Information

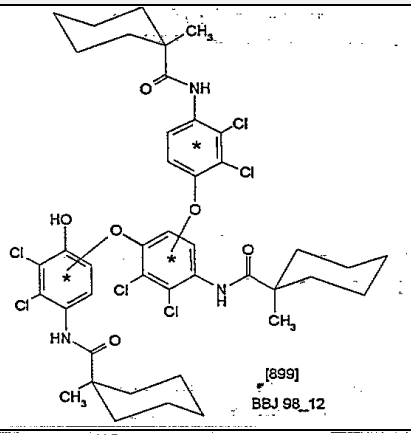
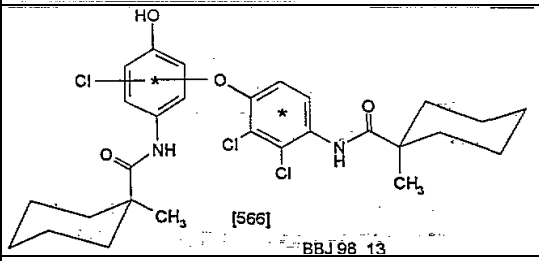
Table A1. Structures of Fenhexamid and Its Environmental Transformation Products.

Code Name/ Synonym/ Chemical Name/ Formula/MW/ SMILES	Chemical Structure
Fenhexamid, KBR 2738, TM-402, KBA 2738, FEX **IUPAC:** 2',3'-dichloro-4'-hydroxy-1-methylcyclohexanecarboxanilide **CAS:** N-(2,3-dichloro-4-hydroxyphenyl)-1-methylcyclohexanecarboxamide **CAS No.:** 126833-17-8 **Formula:** $C_{14}H_{17}Cl_2NO2$ **MW:** 302.2 g/mole **SMILES:** O=C(Nc1ccc(O)c(Cl)c1Cl)C2(C)CCCCC2	
WAK 7004, BB J 99-3 **IUPAC:** 7-Chloro-2-(1-methylcyclohexyl)-1,3-benzoxazol-6-ol **Formula:** $C_{14}H_{16}ClNO$ **MW:** 265.74 g/mol **SMILES:** C1=CC(=C(C3=C1N=C(C2(CCCCC2)C)O3)Cl)O[H] **Log K_{OC}**=3.9 to 4.9	
M1 and M2 **SMILES:** (a) O=C(NC1=C(C(=C(C(=C1O)O)O)O)O)C2(C)CCCCC2 (b) O=C(NC1=CC=C(C(=C1O)O)O)C2(C)CCCCC2.CO (c) O=C(NC1=C(C(C(=C(C1=O)O)O)=O)O)C2(C)CCCCC2 (d) succinic acid CAS Number 110-15-6 **SMILES:** C(CCC(O)=O)(O)=O	12 compounds not readily separated, see Page 33 of MRID 444346726, 4 structures for single components were provided (a)  (b)  (c)

Code Name/ Synonym/ Chemical Name/ Formula/MW/ SMILES	Chemical Structure
	 (d) 
M4, BBJ98-11, Trishydroxyl-KBR **SMILES:** O=C(N(C1=CCC(C=C1)O[H])[H])C2(C)CCCCC2.O.O	
C-C Biphenyl, BBJ98-8 **SMILES:**O=C(N(C1=C(C(=C(C=C1)O[H])Cl)Cl)[H])C2(C)CCCCC2.O=C(N(C3=C(C(=C(C=C3)O[H])Cl)Cl)[H])C4(C)CCCCC4.CC	
ZE056401, suflonic ester of parent, sulfonic ester Fex **SMILES:** O=C(NC1=C(C(=C(C=C1)O[S](O)(O)O)Cl)Cl)C2(C)CCCCCC2	
M7-B N-acetyl-2,3-dichloro-p-aminophenol (proposed) **SMILES:** O=C(N(C1=C(C(=C(C=C1)O[H])Cl)Cl)[H])C	

Code Name/ Synonym/ Chemical Name/ Formula/MW/ SMILES	Chemical Structure
Ketoisomers (proposed), M7-C, M7-F, M7-H-M7-K **SMILES:** O=C(N(C1=C(C(=C(C=C1)O[H])Cl)Cl)[H])C2(C)CCCCC2.=O	
KBR 7133, M7-I, OH-KBR **SMILES:** O=C(N(C1=C(C(=C(C=C1)O[H])Cl)Cl)[H])C2(C)C(CCCC2)O[H]	
KBR7115, M7-G, OH-KBR **SMILES:** O=C(N(C1=C(C(=C(C=C1)O[H])Cl)Cl)[H])C2(C)CC(CCC2)O	
KBR6720, KBR6798, M7-E **OH-KBR** **SMILES:** O=C(N(C1=C(C(=C(C=C1)O[H])Cl)Cl)[H])C2(C)CCC(CC2)O	
BNF 5537C **MW:** 178.02 g/mole **SMILES:** C1=CC(=C(C(=C1N)Cl)Cl)O Log K_{OW}=1.53 Water Solubility=2813.6 mg/L K_{OC}=246.7 (MCI method) and 82.53 (K_{OW} method)	
KBR 2931, WAK 6919 **MW:** g/mol **SMILES:** C1=C(C(=CC=C1N(C(C2(CCCCC2)C)=O)[H])O[H])Cl	
CH3-phenyl FEX, KBR 3596, BBJ 98-7 **SMILES:** C1(=C(C(=CC=C1N(C(C2(CCCCC2)C)=O)[H])OC)Cl)Cl	

Code Name/ Synonym/ Chemical Name/ Formula/MW/ SMILES	Chemical Structure
KBR3954 **SMILES:** C1(=C(C(=CC=C1N(C(C2(CCCCC2)C)=O)[H])O)Cl)Cl	
KBR5613, WAK6920, M9 **SMILES:** C1(=CC(=CC=C1N(C(C2(CCCCC2)C)=O)[H])O)Cl	
KBR6259, WAK 6918 **SMILES:** C1=CC(=CC=C1N(C(C2(CCCCC2)C)=O)[H])O[H]	
LSH 2344 **SMILES:** C1=C(C(=C(C(=C1)O)Cl)Cl)O	
M5, BBJ98-12 **SMILES:** O=C(N(C1=CC(C(C=C1)=O)=O)[H])C2(C)CCCCC2.O	
BBJ 98-11, deschloro-[C-O-C]biphenyl Dimer	 [600]
Trimer 1, BBJ 98-9	 [865] BBJ 98_9

Code Name/ Synonym/ Chemical Name/ Formula/MW/ SMILES	Chemical Structure
Trimer 2, BBJ 98-12	 [899] BBJ 98_12
BBJ 98-13 ***SMILES:** C1=CC(=C(C(=C1NC(C2(CCCCC2)C)=O)OC3=C(C(=C(C=C3)NC(C4(CCCCC4)C)=O)Cl)Cl)Cl)O	 [566] BBJ 98_13
M3	Structure not provided
M10	Structre not provided

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

Table A2. Summary of Maximum Degradate Amounts in Environmental Fate Studies of Fenhexamid[b]

Compound[c]	Max Degradate % of AR Associated with Compound (Time of Peak) Amount Detected at Final Sampling Interval in Corresponding Study						Max Conc in TFD (µg/kg soil)
	Hydrolysis	Aqueous Photolysis	Soil Photolysis	Aerobic Soil	Anaerobic Soil	Aerobic Aquatic	
WAK 7004	--	24 (1 d) nd (15 d)	--	--	--	--	28.0
M4	--	26 (1 d) nd (15 d)	--	--	2.4 (360 d)a	NA	NA
C-C biphenyl dimer/ BBJ 98-8	--	--	14 (1 d) 2.4 (18 d)	6 (1 d) 1 (100 d)			NA
M1 Mixture	--	27 (15 d)a	--	--	--	--	NA
M2 Mixture	--	17 (15 d)a	--	--	--	--	NA
M7 Mixture	--	--	--	--	9 (120 d) 4 (360 d)	--	NA
M3	--	--	--	--	4.4 (120 d) <0.1 (360 d)	--	NA

Compound[c]	Max Degradate % of AR Associated with Compound (Time of Peak) Amount Detected at Final Sampling Interval in Corresponding Study						Max Conc in TFD (µg/kg soil)
	Hydrolysis	Aqueous Photolysis	Soil Photolysis	Aerobic Soil	Anaerobic Soil	Aerobic Aquatic	
Sulfonic Ester FEX/ ZE056401	--	--	--	--	--	7.4 (7 d) 0.15 (100 d)	NA
M9, KBR 5613	--	6 (5 h) nd (15 d)	--	--	5 (365 d)a	--	NA
KBR 2931	--	7 (0.5 h) nd (24 h)	--	--	--	--	NA
M10	--	--	--	--	3.2 (251 d) 2.3 (365 d)	--	NA
CH_3-phenyl FEX/ KBR 3596/ BBJ 98-7	--	--	3 (0.25 d) 2 (18 d)	5 (3 d) 0.3 (365 d)	--	--	NA
Trimer 1/ BBJ 98-9	--	--	4 (0.25 d) 1 (18 d)	--	--	--	NA
COC Biphenyl Dimer/ BBJ 98-11	--	--	6 (0 d) 0.5 (18 d)	4 (1 d) 0.5 (100 d)	--	--	NA
Trimer 2/ BBJ 98-12	--	--	5 (0.25 d) 1 (18 d)	2 (0 d) 1 (365 d)	--	--	NA
KBR 6259	--	3 (2 h) nd (24 hr)	--	--	--	--	NA

NA=not analyzed; h=hours; d=days; Max=maximum; Conc=concentration; TFD=terrestrial field dissipation study; nd=not detected. Degradate structures are available in **Appendix A** and Figure 2.

a Peak at final sampling interval in some studies

b See **Appendix A** for more information on source of information in this table.

c The structure of M3 and M10 are unknown.

Table A3. Maximum amount of applied radioactivity present as a specified compound in environmental fate studies submitted on fenhexamid.[1,2,3]

Compound	Study Type	Max %AR (Sampling Interval)	Final %AR (Sampling Interval)	Comment	MRID
Parent	Hydrolysis	Not Applicable	100.1 (35 d)	pH 5	44346725
			100.1 (35 d)	pH 7	44346725
			99.0 (35 d)	pH 9	44346725
	Aqueous Photolysis		nd (15 d)	sterile water, phe	44346726
			nd (24 h)	natural water, phe	44346732
	Soil Photolysis		1.1 (18 d)	sandy loam, phe	44346728
	Aerobic Soil		1.0 (365 d)	Howe soil U.S., phe	44346729
			1.0 (100 d)	BBA 2.1 soil, phe	44346729
			2.3 (100 d)	BBA 2.2 soil, phe	44346729

Compound	Study Type	Max %AR (Sampling Interval)	Final %AR (Sampling Interval)	Comment	MRID
			1.0 (100 d)	Laacher Hof Soil, phe	44346729
			0.6 (100 d)	Howe soil U.S., phe	44346730
			0.8 (100 d)	Laacher Hof Soil, carb	44346730
	Aerobic Aquatic		6.82 (100 d)	Lake Honniger, phe	44518701
			1.14 (100 d)	Lake Stanley, phe	44518701
	Anaerobic Soil		3.8 (360 d)	Howe soil, phe	44346731
	Terrestrial Field Dissipation	0.21 mg/kg-soil (0 d)	<0.01 mg/kg-soil (120 d)	Ontario, bare	44580303
		0.762 mg/kg-soil (0 d)	0.303 mg/kg-soil (120 d)	California, bare	44346724
		3.292 mg/kg-soil (0 d)	0.089 mg/kg-soil (63 d)	British Columbia, bare	45447501
		2.902 mg/kg-soil (0 d)	0.081 mg/kg-soil (63 d)	British Columbia, strawberrry	45447501
		0.03 mg/kg-soil (0 d)	<0.01 mg/kg-soil (60 d)	Ontario, bare	44580302
Major Degradates					
WAK 7004	Aqueous Photolysis	23.6 (1 h)	nd (15 d)	water, phe	44346726
		23.5 (0.5 h)	nd (24 h)	natural water, phe	44346732
	Terrestrial Field Dissipation	0.0280 mg/kg-soil	<LOQ	British Columbia, bare	45447501
		0.0206 mg/kg-soil	<LOQ	British Columbia, strawberrry	45447501
M4	Aqueous Photolysis	~26.3 (1 d)*	nd (15 d)	water, phe	44346726
	Anaerobic Soil	2.4 (360 d)	2.4 (360 d)	howe soil, phe	44346731
BBJ-98-8	Soil Photolysis	13.8 (0.25,1 d)	2.4 (18 d)	sandy loam, phe	44346728
	Aerobic Soil	4.7 (0 d)	0.5 (365 d)	Howe soil U.S., phe	44346729
		5.8 (1 d)	1.2 (100 d)	BBA 2.1 soil, phe	44346729
		1.5 (3 d)	0.6 (100 d)	BBA 2.2 soil, phe	44346729
		2.4 (1 d)	0.6 (100 d)	Laacher Hof Soil,	44346729
		2.9 (2 d)	0.6 (100 d)	Howe soil U.S., carb	44346730
		1.0 (2 d)	0.2 (100 d)	Laacher Hof Soil,	44346730
Minor Degradates					
M1(mixture)[4]	Aqueous Photolysis	27.3 (15 d)	27.3 (15 d)	water, phe	44346726
M2(mixture)[4]	Aqueous Photolysis	16.7 (15 d)	16.7 (15 d)	water, phe	44346726
M7 (mixture)	Anaerobic Soil	9.3 (120 d)	4.1 (360 d)	Howe soil, phe	44346731
M3	Anaerobic Soil	4.4 (120 d)	<0.1 (360 d)	Howe soil, phe	
ZE056401	Aerobic Aquatic	0.89 (14 d)	0.18 (100 d)	Lake Honniger, phe	44518701
		7.4 (7d)	0.15 (100 d)	Lake Stanley, phe	44518701
M9, KBR 5613	Anaerobic Soil	4.9 (365 d)	4.9 (365 d)	Howe soil, phe	44346731
	Aqueous Photolysis	5.9 (5 h)	nd (15 d)	sterile water, phe	44346726

Compound	Study Type	Max %AR (Sampling Interval)	Final %AR (Sampling Interval)	Comment	MRID
		4.4 (1 h)	nd (24 h)	natural water, phe	44346732
M10	Anaeroibic Soil	3.2 (251 d)	2.3 (365 d)	Howe soil, phe	44346731
KBR 3596, BBJ 98-7	Soil Photolysis	3.4 (0.25 days)	1.7 (18 days)	sandy loam, phe	44346728
	Aerobic Soil	2.8 (0 d)	0.3 (365 d)	Howe soil U.S., phe	44346729
		1.7 (1 d)	0.5 (100 d)	BBA 2.1 soil, phe	44346729
		5.1 (3 d)	1.0 (100 d)	BBA 2.2 soil, phe	44346729
		3.7 (1 d)	0.4 (100 d)	Laacher Hof Soil, phe	44346729
		2.2 (0 d)	0.5 (100 d)	Howe soil U.S., carb	44346730
		4.5 (2 d)	0.5 (100 d)	Laacher Hof Soil, carb	44346730
BBJ 98-9	Soil Photolysis	4.2 (0.25 days)	1.3 (18 days)	sandy loam, phe	44346728
	Aerobic Soil	3.8 (0 d)	1.6 (365 d)	Howe soil U.S., phe	44346729
		5.5 (1 d)	2.1 (100 d)	BBA 2.1 soil, phe	44346729
		1.2 (3 d)	0.7 (100 d)	BBA 2.2 soil, phe	44346729
		1.7 (1 d)	1.0 (100 d)	Laacher Hof Soil, phe	44346729
		3.4 (0 d)	1.1 (100 d)	Howe soil U.S., phe	44346730
		1.1 (8 d)	0.3 (100 d)	Laacher Hof Soil, carb	44346730
BBJ98-11	Soil Photolysis	5.5 (0 d)	0.5 (18 d)	sandy loam, phe	44346728
	Aerobic Soil	2.9 (0 d)	nd (365 d)	Howe soil U.S., phe	44346729
		3.7 (1 d)	0.5 (100 d)	BBA 2.1 soil, phe	44346729
		2.9 (3 d)	2.3 (100 d)	BBA 2.2 soil, phe	44346729
		2.7 (1 d)	0.3 (100 d)	Laacher Hof soil, phe	44346729
		2.2 (0 d)	0.1 (100 d)	Howe soil U.S., phe	44346730
		2.0 (2 d)	0.1 (100 d)	Laacher Hof soil, carb	44346730
BBJ 98-12	Soil Photolysis	4.5 (0.25 days)	0.9 (18 days)	sandy loam, phe	44346728
	Aerobic Soil	2.4 (0 d)	nd (365 d)	Howe soil U.S., phe	44346729
		2.0 (1 d)	nd (100 d)	BBA 2.1 soil, phe	44346729
		1.2 (3 d)	0.6 (100 d)	BBA 2.2 soil, phe	44346729
		1.2 (1 d)	0.6 (100 d)	Laacher Hof soil, phe	44346729
		1.7 (0 d)	0.5 (100 d)	Howe soil U.S., carb	44346730
		1.9 (2 d)	0.5 (100 d)	Laacher Hof Soil, carb	44346730
KBR 5613	Aqueous Photolysis	5.9 (5 h)	nd (15 d)	sterile water, phe	44346726
		4.4 (1 h)	nd (24 h)	natural water, phe	44346732
KBR 2931	Aqueous Photolysis	4.4 (3 h)	nd (15 d)	water, phe	44346726
		6.9 (0.5 h)	nd (24 hs)	natural water, phe	44346732
KBR 6259	Aqueous Photolysis	3.2 (2 h)	nd (24 h)	natural water, phe	44346732
Other Degradates					
CO_2	Aqueous Photolysis	39.3 (15 h)	39.3 (15 d)	sterile water, phe	44346726

Compound	Study Type	Max %AR (Sampling Interval)	Final %AR (Sampling Interval)	Comment	MRID
		28.2 (24 hr)	28.2 (24 h)	natural water, phe	44346732
	Soil Photolysis	8.7 (18 d)M1	8.7 (18 d)	sandy loam, phe	44346728
	Aerobic Soil	30 (365 d)	30 (365 d)	Howe soil U.S., phe	44346729
		20.6 (100 d)	20.6 (100 d)	BBA 2.1 soil, phe	44346729
		19.9 (100 d)	19.7 (100 d)	BBA 2.2 soil, phe	44346729
		17.8 (1 d)	17.8 (100 d)	Laacher Hof soil, phe	44346729
		36 (100 d)	36 (100 d)	Howe soil U.S., carb	44346730
		40 (100 d)	40 (100 d)	Laacher Hof soil, carb	44346730
	Aerobic Aquatic	4.7 (100 d)	4.7 (100 d)	Lake Honniger, phe	44518701
		12.8 (100 d)	12.8 (100 d)	Lake Stanley, phe	44518701
Unidentified Compound(s)[3]	Aqueous Photolysis	13.5 (5 h)+	nd (15 d)+	sterile water, phe	44346726
	Soil Photolysis	22 (0.25 d)	13 (18 d)	sandy loam, phe	44346728
Unextracted Residues	Soil Photolysis	47.3 (18 d)	47.3 (18 d)	sandy loam, phe	44346728
	Aerobic Soil	75 (14 d)	60.9 (365 d)	Howe soil U.S., phe	44346729
		58 (30 d)	50 (100 d)	BBA 2.1 soil, phe	44346729
		69 (100 d)	62 (100 d)	BBA 2.2 soil, phe	44346729
		81 (1 d)	77 (100 d)	Laacher Hof soil, carb	44346729
		60 (8 d)	50 (100 d)	Howe soil U.S., carb	44346730
		40 (100 d)	40 (100 d)	Laacher Hof Soil, carb	44346730
	Aerobic Aquatic	74.61 (100 d)	74.6 (100 d)	Lake Honniger, phe	44518701
		76.7 (60 d)	70.0 (100 d)	Lake Stanley, phe	44518701
	Anaerobic Soil	73.1 (360 d)	73.1 (360 d)	Howe soil U.S., phe	44346731

na=not analyzed; nd=not detected; AR=applied radioactivity; d=days; h=hours; phe=phenyl ring radiolabeled; carb=carbmoxide ring radiolabeled

[1] This Table was created from information in the data evaluation records (Cowles and Steeger, 1999, D244921) and the MRIDs. Many values reflect averaged data.

[2] Maximum amounts of organic volatiles were minimal.

[3] Many of the metabolism studies had multiple unidentified minor degradates that were not identified. They were not added together and placed under the unidentified compound(s) list as their presence was expected to have little impact on decision making.

[4] M1 and M2 structures were characterized together as the exact structures and radioactivity associated with each structure were uncertain. The maximum amount of a single compound (excluding succinic acid was reportedly 7%).

+Denotes that the value reflects radioactivity associated with multiple compounds, when considered alone made up less than 10% of applied radioactivity.

Mobility/Sorption Summary

Fenhexamid is classified as moderately mobile to slightly mobile with organic carbon normalized Freundlich soil-water distribution coefficients (K_{foc}) ranging from 446 to 1226 L/kg-organic carbon measured in six soils (MRID 44342722)[27]. Linear sorption coefficients were not

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

previously determined. Freundlich exponents ranged from 0.76 to 0.86 indicating that the equilibrium concentration in water influences sorption. The mean K_{foc} was 878 L/kg-organic carbon and the coefficient of variation for K_{foc} values (32%) is less than that for K_f values (39%) indicating that K_{foc} values will be better at predicting sorption across soils than K_f values. Additionally, K_fs tend to be higher as the percent organic carbon increases. Consistent with water solubility increasing with pH, K_{foc} values decrease with increasing pH. Based on the range of sorption coefficients, fenhexamid has the potential to reach ground water, especially in vulnerable sandy soils with low organic-carbon content and/or the presence of shallow ground water. Leaching may be mitigated by rapid formation of unextracted residues in soils. The maximum depth at which it was detected in terrestrial field dissipation studies was 15 cm. The mobility of the degradate WAK 7004 has higher K_{foc} values (2324 to 5037 L/kg in four soils) than fenhexamid.

Table A3. Freundlich Sorption Coefficients for Fenhexamid Measured at 19°C

Soil	K_f	K_{foc}	1/n	pH	%OC
Laacher Haf Germany loamy sand	8.02	446	0.83	7	1.8
Borstel German loamy sand	10.21	888	0.86	6.3	1.2
Stanley Kansas silty clay	10.75	1024	0.81	5.6	1.1
Howe Indiana sandy loam	7.69	1025	0.76	7.1	0.75
Vero Beach Florida sand	2.45	1226	0.85	5.1	0.2
Napa California clay loam	6.52	658	0.86	7.7	1.0

Table A4. Freundlich Sorption Coefficients for WAK7004

Soil	K_F	K_{foc}	1/n	pH	%OC
Stanley Kansas silty clay	24.4	2324	0.86	5.6	1.1
Howe Indiana sandy loam	26.4	2421	0.86	7.1	0.75
Vero Beach Florida sand	10.1	5037	0.89	5.1	0.2
Napa California clay loam	32.1	3212	0.9	7.7	1.0

Bioconcentration Summary

Bluegill sunfish (MRIDs 44346746) were exposed to ^{14}C-fenhexamid (phenyl label) for 28 days under flow through conditions at high and low concentrations (20 and 200 µg/L, pH 7.0 to 7.5; supplemental; 20-23^{o}C). The bioconcentration factor for total radioactivity was 132-185 L/kg-wet weight whole fish and 36.7 to 60.1 L/kg-wet weight in edible tissue, and 248 to 339 in viscera.Total ^{14}C residues in fish were measured via combustion. Tissue residues were further characterized via solvent extraction and HPLC and LC-MS. Transformation products observed include 4-hydroxy-KBR 2738, 3-hydroxy-KBR 2738 and KBR-glucuronide. Conjugation occurred at the aromatic hydroxyl group and with hydroxylation of the cyclohexyl ring. The depuration half-life was less than 1 day. As previously identified, there is still uncertainty in the BCF as concentrations of fenhexamid and degradates were not fully characterized.

Appendix B. Screening Level Usage Analysis

Fenhexamid (090209)
Screening Level Usage Analysis (SLUA)
Date: June 19, 2012

What is a Screening Level Usage Analysis (SLUA)?

- Available estimates of pesticide usage data for a particular active ingredient that is used on **agricultural** crops in the United States.
- Pesticide usage data obtained from various sources. The data are then merged, averaged, and rounded so that the presented information is not proprietary, business confidential, or trade secret.

What does it contain?

- Pesticide usage data for a **single** active ingredient only.
- Agricultural use sites (crops) that the pesticide is *reported* to be used on.
- Available pesticide usage information from U.S. states that produce 80% or more of a crop, in most cases, or less than 80%, in rare cases, depending on the scope of the survey and available resources.
- Annual percent of crop treated **(average & maximum)** for each agricultural crop.
- Average annual pounds of the pesticide applied for each agricultural crop (i.e., for the states surveyed, not for the entire United States).

What assumptions can I make about the reported data?

- **Average pounds of active ingredient applied** - Values are calculated by merging pesticide usage data sources together; averaging across all observations, then rounding. ***Note:*** *If the estimated value is less than 500, then that value is labeled <500. Estimated values between 500 & <1,000,000 are rounded to 1 significant digit. Estimated values of 1,000,000 or greater are rounded to 2 significant digits.)*
- **Average percent of crop treated** - Values are calculated by merging data sources together; averaging by year, averaging across all years, & rounding to the nearest multiple of 5. ***Note:*** *If the estimated value is less than 2.5, then the value is labeled <2.5. If the estimated value is less than 1, then the value is labeled <1.*
- **Maximum percent of crop treated** - Value is the single maximum value reported across all data sources, across all years, & rounded up to the nearest multiple of 5. ***Note:*** *If the estimated value is less than 2.5, then the value is labeled <2.5.*

What are the data sources used?

- **USDA-NASS** (United States Department of Agriculture's National Agricultural Statistics Service) – pesticide usage data from 2003 to 2010.
- **Private pesticide market research** – pesticide usage data from 2003 to 2010.
- **California Department of Pesticide Regulation (DPR) Pesticide Use Reporting (PUR)** data for 2003 to 2010.

What are the limitations to the data?

- Additional registered uses may exist but are not included because the available surveys do not report usage (e.g., small acreage crops).
- Lack of reported usage data for the pesticide on a crop **does not imply** zero usage.

- Usage data on a particular site may be noted in data sources, but **not quantified**. In these instances, the site would not be reported in the SLUA.
- Non-agricultural use sites (e.g., turf, post-harvest, mosquito control, etc.) are not reported in the SLUA. A separate request must be made to receive these estimates.
- Some sites show some use, even though they are not on the label. This usage could be due to various factors, including, but not limited to Section 18 requests, existing stocks of the chemical, data collection errors, and experimental use permits (EUPs).

June 19, 2012
Screening Level Estimates of Agricultural Uses of Fenhexamid (090209)
Sorted Alphabetically
Reporting Years: 2003-2010

			Percent Crop Ttd.	
	Crop	**Lbs. A.I.**	**Avg.**	**Max.**
1	Apricots	<500	10	10
2	Blueberries	2,000	5	15
3	Caneberries	4,000	20	40
4	Cherries	1,000	<2.5	10
5	Grapes	30,000	5	15
6	Peaches	<500	<1	<2.5
7	Pistachios*	2,000	NC	NC
8	Plums/Prunes	<500	<1	<2.5
9	Strawberries	40,000	50	65

All numbers are rounded.
<500: indicates less than 500 pounds of active ingredient.
<2.5: indicates less than 2.5 percent of crop is treated.
<1: indicates less than 1 percent of crop is treated.
* California data only.
NC: not calculated, only pounds a.i. is available.

SLUA data sources include:
USDA-NASS (United States Department of Agriculture's National Agricultural Statistics Service)
Private Pesticide Market Research
California DPR (Department of Pesticide Regulation)
These results reflect amalgamated data developed by the Agency and are releasable to the public.

Appendix C. SIP/STIR Model Results

(a) SIP Version 1.0 Model Output

Table 1. Inputs

Parameter	Value
Chemical name	Fenhexamid
Solubility (in water at 25°C; mg/L)	1000
Mammalian LD_{50} (mg/kg-bw)	5000
Mammalian test species	laboratory rat
Body weight (g) of "other" mammalian species	
Mammalian NOAEL (mg/kg-bw)	38.2
Mammalian test species	laboratory rat
Body weight (g) of "other" mammalian species	
Avian LD_{50} (mg/kg-bw)	2000
Avian test species	northern bobwhite quail
Body weight (g) of "other" avian species	
Mineau scaling factor	1.15
Mallard NOAEC (mg/kg-diet)	
Bobwhite quail NOAEC (mg/kg-diet)	2074
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)	172.0000	172.0000
Adjusted toxicity value (mg/kg-bw)	3845.8028	29.3819
Ratio of exposure to toxicity	0.0447	5.8539
Conclusion*	**Drinking water exposure alone is NOT a potential concern for mammals**	**Exposure through drinking water alone is a potential concern for mammals**

Table 3. Avian Results

Parameter	Acute	Chronic
Upper bound exposure (mg/kg-bw)	810.0000	810.0000
Adjusted toxicity value (mg/kg-bw)	1440.8590	220.4627
Ratio of exposure to acute toxicity	0.5622	3.6741
Conclusion*	**Exposure through drinking water alone is a potential concern for birds**	**Exposure through drinking water alone is a potential concern for birds**

(b) STIR Version 1.0 Model Output

Welcome to the EFED Screening Tool for Inhalation Risk

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

Input

Application and Chemical Information	
Enter Chemical Name	fenhexamid
Enter Chemical Use	Ginseng
Is the Application a Spray? (enter y or n)	y
If Spray What Type (enter ground or air)	air
Enter Chemical Molecular Weight (g/mole)	302.2
Enter Chemical Vapor Pressure (mmHg)	7.00E-09
Enter Application Rate (lb a.i./acre)	0.75
Toxicity Properties	
Bird	
Enter Lowest Bird Oral LD_{50} (mg/kg bw)	2000
Enter Mineau Scaling Factor	1.15
Enter Tested Bird Weight (kg)	0.178
Mammal	
Enter Lowest Rat Oral LD_{50} (mg/kg bw)	5000
Enter Lowest Rat Inhalation LC_{50} (mg/L)	5057
Duration of Rat Inhalation Study (hrs)	4
Enter Rat Weight (kg)	210

****NOTE**:** When entering values, press order to update linked cells.

Output

Results Avian (0.020 kg)		
Maximum Vapor Concentration in Air at Saturation (mg/m^3)	1.14E-04	
Maximum 1-hour Vapor Inhalation Dose (mg/kg)	1.43E-05	
Adjusted Inhalation LD_{50}	1.88E+01	
Ratio of Vapor Dose to Adjusted Inhalation LD_{50}	7.61E-07	**Exposure not Likely Significant**
Maximum Post-treatment Spray Inhalation Dose (mg/kg)	7.20E-02	
Ratio of Droplet Inhalation Dose to Adjusted Inhalation LD_{50}	3.83E-03	**Exposure not Likely Significant**

Results Mammalian (0.015 kg)		
Maximum Vapor Concentration in Air at Saturation (mg/m^3)	1.14E-04	
Maximum 1-hour Vapor Inhalation Dose (mg/kg)	1.80E-05	
Adjusted Inhalation LD_{50}	2.48E+03	
Ratio of Vapor Dose to Adjusted Inhalation LD_{50}	7.24E-09	**Exposure not Likely Significant**
Maximum Post-treatment Spray Inhalation Dose (mg/kg)	9.06E-02	
Ratio of Droplet Inhalation Dose to Adjusted Inhalation LD_{50}	3.65E-05	**Exposure not Likely Significant**

Appendix D. Reference List for OPPTS 835 Guidelines and 850 Guidelines Related to Fate

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

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

OPPTS or OCSPP Guideline	Citation
Terrestrial Field Dissipation 835.6100	USEPA. 2008. *Fate, Transport, and Transformation Guidelines. OPPTS 835.1230 Adsorption/Desorption (Batch Equilibrium)*. E. 712-C-08-009. October 2008. Office or Prevention, Pesticides, and Toxic Substances. United States Environmental Protection Agency. Available at http://www.epa.gov/ocspp/pubs/frs/publications/Test_Guidelines/series835.htm (Accessed May 5, 2012).
Aquatic Field Dissipation 835.6200	USEPA. 2008. *Fate, Transport, and Transformation Test Guidelines. OPPTS Aquatic (Sediment) Field Dissipation*. EPA 712-C-08-021. October 2008. Office of Prevention, Pesticides, and Toxic Substances. United States Environmental Available at http://www.epa.gov/ocspp/pubs/frs/publications/Test_Guidelines/series835.htm (Accessed May 15, 2012).
Bioconcentration Factor 850.1730	USEPA. 1996. *Ecological Effects Test Guidelines. OPPTS 850.1730 Fish BCF*. E. 712-C-96-129. April 1996. Environmental Fate and Effects Division. Office of Pesticide Programs. United States Environmental Protection Agency. Available at http://www.epa.gov/opptsmnt/pubs/frs/publications/OPPTS_Harmonized/850_Ecological_Effects_Test_Guidelines/Drafts/850-1730.pdf (Accessed May 14, 2012).
Environmental Chemistry Method 850.6100	USEPA. 2012. *Ecological Effects Test Guidelines. OCSPP 850.6100: Environmental Chemistry Methods*. EPA 712-C-001. January 2012. Office of Chemical Safety and Pollution Prevention. United States Environmental Protection Agency. Available at http://www.epa.gov/ocspp/pubs/frs/publications/Test_Guidelines/series850.htm (Accessed August 10, 2012).

Appendix E. AOPWIN V1.92 Output

SMILES : c1cc(c(CL)c(c1NC(=O)C2(CCCCC2)C)CL)O
CHEM :
MOL FOR: C14 H17 CL2 N1 O2
MOL WT : 302.20
---------- SUMMARY (AOP v1.92): HYDROXYL RADICALS (25 deg C) --------
Hydrogen Abstraction = 13.7303 E-12 cm3/molecule-sec
Reaction with N, S and -OH = 0.1400 E-12 cm3/molecule-sec
Addition to Triple Bonds = 0.0000 E-12 cm3/molecule-sec
Addition to Olefinic Bonds = 0.0000 E-12 cm3/molecule-sec
**Addition to Aromatic Rings = 3.5808 E-12 cm3/molecule-sec
Addition to Fused Rings = 0.0000 E-12 cm3/molecule-sec

OVERALL OH Rate Constant = 17.4511 E-12 cm3/molecule-sec
HALF-LIFE = 0.613 Days (12-hr day; 1.5E6 OH/cm3)
HALF-LIFE = 7.355 Hrs
..... ** Designates Estimation(s) Using ASSUMED Value(s)
---------- SUMMARY (AOP v1.91): OZONE REACTION (25 deg C) ----------

****** NO OZONE REACTION ESTIMATION ******
(ONLY Olefins and Acetylenes are Estimated)

NOTE: Reaction with Nitrate Radicals May Be Important!

Experimental Database: NO Structure Matches

Appendix F. Currently Registered Products Containing Fenhexamid

Table F1. Currently Registered Products Containing Fenhexamid

Registration Number	Product Name	**Registration Status**	Company Name	Percent Active Ingredient	Active Ingredient
264-780	FENHEXAMID 50 WDG	Conditionally Registered (16-Apr-2002)	BAYER CROPSCIENCE LP	50	Fenhexamid
264-785	FENHEXAMID TECHNICAL	Conditionally Registered (07-Jun-2002)	BAYER CROPSCIENCE LP	98.6	Fenhexamid
66330-35	ELEVATE 50 WDG FUNGICIDE	Conditionally Registered (21-May-1999)	ARYSTA LIFESCIENCE NORTH AMERICA, LLC	50	Fenhexamid
66330-36	FENHEXAMID TECHNICAL	Conditionally Registered (21-May-1999)	ARYSTA LIFESCIENCE NORTH AMERICA, LLC	98.6	Fenhexamid
66330-48	CAPTEVATE 68 WDG FUNGICIDE	Conditionally Registered (09-Jul-2003)	ARYSTA LIFESCIENCE NORTH AMERICA, LLC	14.3	Fenhexamid
				53.6	Captan

Appendix G. Summary of exposure pathways, endpoints, and models that will be used in the risk assessment.

Table G1. Summary of exposure pathways, endpoints, and models used in the registration review risk assessment for fenhexamid.

Assessed Group	Endpoints Evaluated	Transport and Exposure Pathway	Method of Estimating Exposure
Aquatic Vertebrates	Acute: 96-hr LC_{50} Chronic: NOAEC	Spray drift and runoff to water column and sediment	PRZM/EXAMS, AgDRIFT or AgDISP
Aquatic Invertebrates	Acute: 48-hr LC_{50}/EC_{50} Chronic: NOAEC		
Aquatic Plants	EC_{50}		Method to be determined
Terrestrial Vertebrates	Acute: Oral LD_{50}/ DietaryLC_{50} Chronic: NOAEC	Spray Drift and direct spray to Residues on foliage Residues in drinking water Inhalation Bioconcentration/Bioaccumulation	AgDRIFT or AgDISP TREX, AgDRIFT or AgDISP Method to be determined Method to be determined KABAM
Terrestrial Invertebrates	Method under development		
Terrestrial Plants	EC_{25}, EC_{05}, and NOAEC	Runoff (vegetative vigor and seedling emergence) and Spray Drift (vegetative vigor) Water used as irrigation water	TERRPLANT and AgDRIFT or AgDISP PRZM-GW, SCIGROW, and PRZM/EXAMs
Human Health Drinking Water	See Human Health Toxicity Assessment	Surface Water Ground Water	PRZM/EXAMs SCIGROW and PRZM-GW

Appendix H. Preliminary Rough Estimate of Exposure Assuming Unextracted Residues are a Residue of Concern.

This analysis does not account for potential exposure with anilides as residues of concern. It only considers parent and unextracted residues as residues of concern. Additionally, only one scenario was modeled. These are preliminary estimates of exposure only.

1 in 10 Year Estimated Environmental Concentrations of Fenhexamid and unextracted residues using PRZM/EXAMs

Residues	Fenhexamid Residue concentration in Surface Water (µg/L)							
	Ecological			Sediment Pore Water			Human Health Drinking Water	
	peak	21-day	60-day	peak	21-day	60-day	Peak	Annual Average
Fenhexamid + Unextracted Residues	69	45	23	15	14	12	165.2	6.9
Fenhexamid Alone	14	8.8	3.8	2.1	2.1	1.9	24	0.37

Table H1. PRZM/EXAMs Input Parameter Values for Fenhexamid (Parent and Unextracted Residues)[1]

Parameter	Value	Source	Comment
PRZM Scenario	FLcucumberSTD.txt	--	
EXAMs environment	pond298.exv (Eco) ir298.exv (DW)	--	
Field Size	EPA Pond (Eco) Reservoir (DW)	--	
Runoff flow	None	--	
Molecular Weight (g/mole)	302.2	--	
Henry's Law Constant (atm-m^3/mole)	6×10^{-11}	Calculated	
Vapor Pressure (Torr)	7×10^{-9}	MRID 44346720	
Solubility	20	MRID 44346719	pH 5-7
Soil-water distribution Coefficient (Kd; L/kg soil)	no input	--	
Organic-carbon normalized soil-water distribution coefficient (K_{OC}; L/kg OC)	878	MRID 44346722	Mean of six K_{FOC} values. K_{OC} values were not calculated.
CAM	2	--	
Incorporation Depth	0	--	
Application Efficiency	0.95	--	
Spray Drift Fraction	0.05 (Eco) 0.16 (DW)	--	
Application Date	16-10	--	Date of emergence in scenario

Parameter	Value	Source	Comment
Application Rate kg a.i./hectare (lbs a.i./A)[1]	0.84 (0.75)	EFED Table 1 LUIS Report	Application rates on ornamentals are uncertain and could be higher
Number of Applications	4		Assumed from the maximum single application rate and maximum annual application rate of 3 lbs a.i./A.
Interval between Applications (days)	3		The interval between application is not specified for all uses
IPSCND	3 (Left As is on foliage)	--	--
Hydrolysis (days)	0	MRID 44346725	--
Aquatic Photolysis Half-life at pH 7 (days)	0.1	MRID 44346732	--
Water Half-life (days)	Parent: 19 Parent+Unextracted: 1025	MRID 44518701	The 90th percentile upper confidence bound on the mean of four half-life values.
Benthic half-life (days)	Parent: 345 Parent+Unextracted: 3078	MRID 44346731	Anaerobic Soil Half-life x 3
Aerobic Soil Metabolism Half-life (days)	Parent: 2.6 Parent+Unextracted Residues: 700	MRID 45643802	The 90th percentile upper confidence bound on the mean of four half-life values. When a study on one soil was conducted with different rings labeled the values were averaged so that there was one value for each soil tested.

Eco=input value for ecological risk assessment; DW=input value for human health drinking water assessment
All input parameters were chosen consistent with **S***tandard Operating Procedure for Using the NAFTA Guidance to Calculate Representative Half-life Values and Characterizing Pesticide Degradation*. (Bohaty *et al.*, 2012; NAFTA, 2012) and *Guidance for Selecting Input Parameters in Modeling the Environmental Fate and Transport of Pesticides, Version 2.1* (USEPA, 2009b).

Appendix I. Toxicity Profile for Fenhexamid.

Table 1. Aquatic toxicity studies for fenhexamid.

Group	Species (Common Name)	Study Type (Measured Effect)	Test Substance (% a.i.)	Endpoint (Test Duration)	Toxicity Value mg a.i./L (Acute Toxicity Category)	MRID (Study Classification)
Freshwater Fish[1]	*Oncorhynchus mykiss* (Rainbow trout)	Acute (Survival)	Technical 92.7%	LC_{50} (96 hours)	1.34 (moderately toxic)	44346742 (Acceptable)
			WG-50 (49%)	LC_{50} (96 hours)	1.23* (moderately toxic)	44523605 (Acceptable)
		Chronic: Early Life-Stage (Time to swim up)	Technical (95.9%)	NOAEC LOAEC	0.101* 0.206	44346745 (Acceptable)
	Lepomis macrochirus (Bluegill sunfish)	Acute (Survival)	Technical (94.64%)	LC_{50} (96 hours)	3.42 (moderately toxic)	44346741 (Acceptable)
Estuarine/ Marine Fish	*Cyprinodon variegatus* (Sheepshead minnow)	Acute (Survival)	Technical (≥95%)	LC_{50} (96 hours)	11* (slightly toxic)	44346743 (Acceptable)
Freshwater Invertebrates	*Daphnia magna*	Acute (Immobilization)	Technical (95.7%)	EC_{50} (48 hours)	>18.8† (Slightly toxic to practically-non-toxic)	44366507 (Supplemental)
			WG-50 (49.6%)	EC_{50} (48 hours)	105 (Practically non-toxic)	44523604 (Supplemental)
		Chronic life-cycle (growth [length]; larval survival)	Technical (95.9%)	NOAEC LOAEC	1.0* 1.9	44346744 (Acceptable)
Estuarine/ Marine Invertebrates	*Americamysis bahia* (Mysid shrimp)	Acute (Survival)	Technical (95.8%)	LC_{50} (96 hours)	4.6* (moderately toxic)	44346740 (Acceptable)
Vascular Aquatic Plants	*Lemna gibba* (duckweed)	(Frond number, growth rate, biomass)	Technical (97.7%)	EC_{50} (14 days)	>2.3†	44731105 (Acceptable)
				NOAEC (14 days)	0.28*	
Non-Vascular Aquatic Plants	*Pseudokirchneriella subcapitata* (green algae)	(Cell density)	Technical (95.7%)	EC_{50} (120 hours)	4.82	44518706 (Supplemental)
				NOAEC (120 hours)	2.95	
			WG-50 (49.6%)	EC_{50} (72 hours)	1.37*	44523610 (Supplemental)
				NOAEC (72 hours)	0.558*	

EC_{50} Effect concentration for 50% of the organisms tested; NOAEC no observed adverse effect concentration

* Most sensitive endpoint and will be used for RQ calculations unless more sensitive data become available.
† Non-definitive study endpoint; cannot be used to calculate RQs for risk estimation.
‡ Freshwater fish may be surrogates for aquatic-phase amphibians.

Table 2. Terrestrial toxicity studies for fenhexamid.

Group	Species	Study Type (Effect)	Test Substance (% a.i.)	Endpoint (Test Duration)	Toxicity Value (Acute Toxicity Category)	MRID (Study Classification)
Birds‡	*Anas platyrhynchos* (mallard duck)	Sub-acute dietary (Survival)	Technical (95.7%)	LC_{50} (5 days)	>4,962 mg a.i./kg-diet† (Practically non-toxic)	44346752 (Supplemental)
	Colinus virginianus (Northern Bobwhite Quail)	Acute oral (Survival)	Technical (95.7%)	LD_{50} (14 days)	>2,000 mg a.i./kg-bw† (Practically non-toxic)	44346750 (Supplemental)
		Sub-acute dietary (Survival)	Technical (95.7%)	LC_{50} (5 days)	>5,469 mg a.i./kg-diet† (Practically non-toxic)	44346751 (Supplemental)
		Reproductive toxicity (Feed consumption rate)	Technical (95.9%)	NOAEC/ LOAEC (23 weeks)	2,074/>2,074 mg a.i./kg-diet*	44346753 (Acceptable)
Mammals	*Rattus norvegicus* (Norway rat)	Acute oral (Survival)	Technical (95.5%)	LD_{50} (Survival)	>5,000 mg a.i./kg-bw (Practically non-toxic)	44346769
		Rat 2-generation reproductive toxicity test (decreased body weights)	Technical (93.8-95.2%)	NOAEC/ LOAEC	500/5,000 mg a.i./kg-diet	44346803
Terrestrial Invertebrates	*Apis mellifera* (honeybee)	Acute Contact Toxicity (Survival)	Technical (95.7%)	LD_{50} (48 hours)	>200 µg a.i./bee	44346755 (Acceptable)
		Acute Oral Toxicity (Survival)	Technical (94%)	LD_{50} (48 hours)	>201 µg a.i./bee	44346755 (Supplemental)
Terrestrial Plants	No Toxicity Data Available					

Appendix J. Data Call-In Justification Tables for Non-guideline Studies

Study Title: Honeybee Larval Toxicity Study **Guideline Number: Non-guideline** **Test Substance: Fenhexamid—TGAI**
Rationale for Requiring the Data
Although fenhexamid is practically non-toxic to adult worker bees on an acute contact exposure basis, a larval toxicity study is needed to determine the toxicity of the compound to developing brood. This study is part of EFED's current screening level process for determining potential effects to terrestrial invertebrates. Therefore, a non-guideline honeybee larval toxicity study is recommended. The registrant should submit a proposed protocol for review and approval by EFED prior to initiation of the study.
Practical Utility of the Data
How will the data be used? Data will be used to assess risk to non-target listed and non-listed terrestrial invertebrate species. This study would allow the Agency to refine the screening-level hazard assessment for beneficial terrestrial invertebrates. The effects data will be used to determine the potential for adverse effects on beneficial terrestrial invertebrates through direct effects on larval bees. **How could the data impact the Agency's future decision-making?** EPA is required by section 7(a)(2) of the Endangered Species Act (ESA) to ensure that any action it authorizes or takes "*…is not likely to jeopardize the continued existence of any endangered or threatened species or result in the destruction or adverse modification of critical habitat*" and "*to use the best scientific data available*" in carrying out this obligation. The data EPA intends to call in are necessary to inform the determination required by ESA as to whether continued registration of a pesticide is or is not likely to jeopardize the species or its designated critical habitat. The lack of these data will limit the flexibility that the Agency has in coming into compliance with ESA and could result in use restrictions that are unnecessarily severe. In addition, the lack of these data may result in an uncertain assumed risk and potential mitigation of fenhexamid formulations under FIFRA.

Study Title: Whole sediment chronic freshwater and/or marine invertebrate (3 Studies) **Guideline Number: Agency-wide Guideline** **Test Substance: Fenhexamid—TGAI**
Rationale for Requiring the Data
The use pattern, chemical properties, estimated exposure, and toxicity profile of fenhexamid indicate need for chronic (life cycle) sediment toxicity tests to fully evaluate potential risks to benthic invertebrates. These sediment toxicity studies include two freshwater species (the midge, *Chironomus dilutus* and the amphipod, *Hyalella azteca*) and one saltwater species (the amphipod, *Leptocheirus plumulosus*). Multiple species are being recommended in order to account for differential sensitivity and exposure potential of benthic invertebrates to fenhexamid. This recommendation is being made because some K_{OC} and log K_{ow} values in submitted fate studies were above the thresholds of 1,000 and 3.0, respectively. The registrant should submit a proposed protocol for review and approval by EFED prior to initiation of the study. (Note: As an alternative to the conduct of three chronic (life cycle) sediment toxicity tests, EFED

would also consider a tiered testing approach for sediment toxicity testing. In this approach, sediment toxicity testing would first be conducted with the aforementioned species using the 10-d (subchronic) sediment toxicity test guidelines (OSCPP 850.1735[28] and 850.1740[29]). Then, pending a comparison of estimated environmental concentrations (EEC) in sediment and pore water with toxicity results from the 10-d sediment toxicity studies, the need for one or more chronic sediment toxicity studies would be determined. This tiered testing approach has the potential advantage of reducing the number of chronic (life cycle) studies that would be needed when results of the 10-d (subchronic) tests in conjunction with sediment EECs indicate chronic testing is not likely to alter risk assessment conclusions. In some cases, however, this tiered testing approach may result in the conduct of both a 10-d (subchronic) and a chronic (life cycle) study. If the tiered test approach described above is not preferred, then chronic life-cycle sediment toxicity studies be carried out on the three preferred species, *C. dilutus*, *H. azteca*, and *L. plumulosus*.)

Practical Utility of the Data

How will the data be used?

Data from sediment toxicity studies will be used to estimate potential risks to benthic organisms associated with uses of fenhexamid. The data will reduce uncertainties associated with the current risk assessment for benthic species and will improve our understanding of the potential effects of fenhexamid on aquatic ecosystems.

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

If the data indicates that registered fenhexamid uses may pose a risk of adverse effects to non-target benthic organisms above the Agency Level of Concern, the Agency may explore decision options to mitigate this risk. The lack of these data will limit the flexibility the Agency and registrants have in coming into compliance with the Endangered Species Act, and could result in use restrictions for fenhexamid which may otherwise be avoided, or which are unnecessarily severe.

[28] USEPA. 1996. http://www.epa.gov/opptsmnt/pubs/frs/publications/OPPTS_Harmonized/850_Ecological_Effects_Test_Guidelines/Drafts/850-1735.pdf

[29] USEPA. 1996. http://www.epa.gov/opptsmnt/pubs/frs/publications/OPPTS_Harmonized/850_Ecological_Effects_Test_Guidelines/Drafts/850-1740.pdf