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WASHINGTON D.C., 20460

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

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MEMORANDUM

SUBJECT: Registration Review: Preliminary Problem Formulation for Environmental Fate, Ecological Risk, Endangered Species, and Drinking Water Exposure Assessments for Mesosulfuron-methyl

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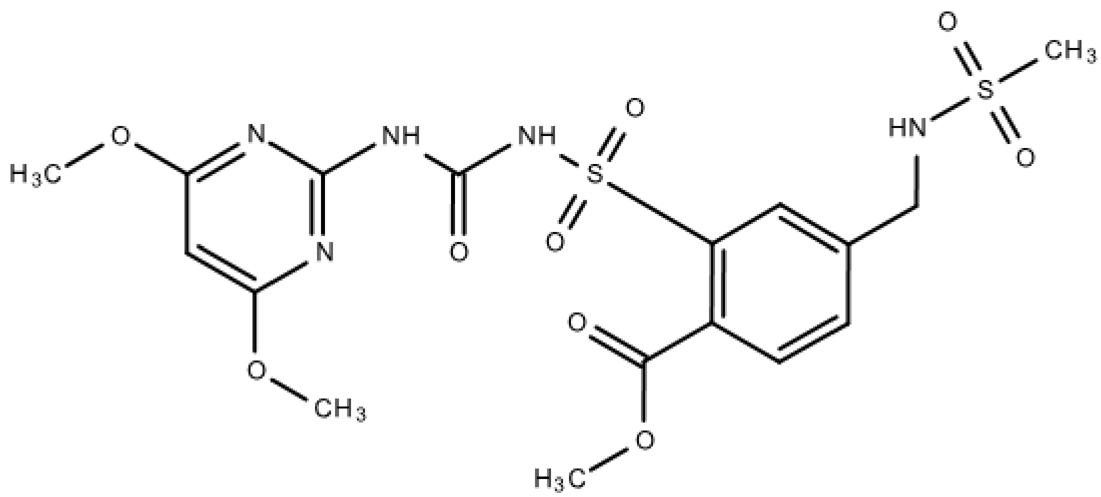
The Environmental Fate and Effects Division (EFED) has completed the preliminary problem formulation for the environmental fate, ecological risk, endangered species, and drinking water exposure assessments to be conducted as part of the Registration Review of mesosulfuron-methyl (CAS 208465-21-8), a sulfonylurea herbicide registered for use on wheat and triticale. Functioning as the first stage of the risk assessment process for Registration Review, this problem formulation provides an overview of what is currently known about the environmental fate and ecological effects associated with mesosulfuron-methyl and its degradation products. It also describes the preliminary ecological risk hypothesis and analysis plan for evaluating and characterizing risk to non-target species in support of the registration review of mesosulfuron-methyl. This document also recommends studies that should be included in a generic data call-in (DCI) to address uncertainties surrounding the environmental fate and potential ecological effects of mesosulfuron-methyl.

OFFICE OF CHEMICAL SAFETY AND
POLLUTION PREVENTION

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



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1. Purpose

The purpose of this problem formulation is to provide an understanding of what is known about the environmental fate, ecological effects, and currently registered uses of mesosulfuron-methyl. This document provides a plan for analyzing data relevant to mesosulfuron-methyl and for conducting environmental fate, ecological risk, endangered species, and drinking water exposure assessments for its registered uses. Additionally, this problem formulation identifies data gaps, uncertainties, and potential assumptions used to address those uncertainties relative to characterizing the potential ecological risk associated with the registered uses of mesosulfuron-methyl.

2. Problem Formulation

2.1. Nature of Regulatory Action

As part of the implementation of the new Registration Review program[1] pursuant to Section 3(g) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), the Agency is beginning its evaluation of mesosulfuron-methyl to determine whether it continues to meet the FIFRA standard for registration. This problem formulation in support of the registration review of mesosulfuron-methyl will be posted in the initial docket which will open the public phase of the review process.

2.2. Previous Assessments

2.2.1. Ecological Risk Assessments

Mesosulfuron-methyl (methyl-2-[3-(4,6-dimethoxypyrimidin-2-yl) ureido-sulfonyl]-4-methanesulfonamido-methylbenzoate), a sulfonylurea herbicide, was first registered in the US in 2004 for use as postemergent control and suppression of several types of weeds. Wheat and triticale are the only registered uses of mesosulfuron-methyl. EFED has conducted one ecological risk assessment (wheat use).

The previous risk assessment identified a risk concern for non-target terrestrial plants (listed and non-listed) and aquatic vascular plants (listed) (USEPA, 2004b).

2.2.2. Drinking Water Exposure Assessments

The drinking water assessment (DWA) for wheat use was conducted using the Tier 1 FQPA Index Reservoir Screening Tool (FIRST) and the Screening Concentration in Ground Water model (SCIGROW) (USEPA, 2004a). Three bridge-intact major degradates (AE F154851, AE F160459, and AE F160460) were modeled along with mesosulfuron-methyl per request of the Health Effect Division (HED) Metabolism Committee Meeting (MARC). The findings from the DWA are summarized in **Table 1**.

Table 1. Previous Estimated Drinking Water Concentrations

Product Use	Peak (µg/L, Acute)[1]		Annual Average (µg/L ,Chronic)[1]	
	Parent Only	Total Residues	Parent Only	Total Residues
Surface Water Sources using Tier I FIRST model				
OSPREY Winter Wheat	0.7	0.9	0.1	0.2

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

Product Use	Peak (µg/L, Acute)[1]		Annual Average (µg/L ,Chronic)[1]	
	Parent Only	Total Residues	Parent Only	Total Residues
SILVERADO Spring Wheat (including durum)	0.3	0.4	0.05	0.06
Ground Water Sources using Tier I SCIGROW model				
OSPREY Winter Wheat	0.01	0.02	0.01	0.02
SILVERADO Spring Wheat (including durum)	0.01	0.007	0.005	0.007

[1]A PCA of0.56 was used for the surface water EDWC

3. Stressor Source and Distribution

Mesosulfuron-methyl is a sulfonylurea herbicide used to control and suppress several types of weeds. The formulated water dispersible granules are applied as a post-emergence ground or aerial spray. Several mesosulfuron-methyl degradates were identified from the submitted studies; some are common to other sulfonylurea herbicides. The major (formed ≥ 10%) degradates are AE F154851, AE F160459, AE F160460, AE F140584, AE F147447, AE F099095, and AE F092944.

3.1. Mechanism of Action

Mesosulfuron-methyl belongs to the sulfonylurea herbicide family and more specifically to the pyrimidinylsulfonylurea group. Like all of the sulfonylurea herbicides, it is an acetolactate synthase inhibitor (ALS- inhibitor). Inhibition of this enzyme curtails the synthesis of branched-chain amino acids (valine, leucine, and isovaline), thus disrupting plant development and causing subsequent death. Valine, leucine, and isovaline are essential amino acids but they are not synthesized by higher animals. Sulfonylurea herbicides or other ALS-inhibitors are not expected to have any direct acute effects on animals because the ALS enzyme is not present in higher animals. Nevertheless, chronic effects cannot be ruled out.

3.2. Overview of Pesticide Use and Usage

There are currently eight registered end-use products containing mesosulfuron-methyl. All products are post-emergence herbicides formulated as water dispersible granules. About 6000 lb mesosulfuron-methyl is applied annually (Screening Level Usage Analysis, 1/18/2012) according to the Biological and Economic Analysis Division (BEAD). Uses and application rates are based on the most recent label use information system report (LUIS report), provided by BEAD (11/8/2012). The maximum application rates and application methods are listed in **Table 2,** although it should be noted that some labels do not indicate a maximum annual rate. To reduce uncertainty in the risk assessment, the Agency requests that the registrant provide additional label information where necessary on the number of applications per year, the total amount applied per year, and the application interval if applicable. The registration review risk assessment will be based on current label information at the time of assessment.

Table 2. Maximum Rates for Registered Uses of Mesosulfuron-methyl

Use	Method of Application	Single Maximum Application Rate (lb ai/A)	Maximum Number of Applications per Year[1]	Annual Maximum (lb ai/A)[1]
Winter Triticale	Ground/Air	0.0134	NS	NS
Winter Wheat	Ground/Air	0.0134	1	0.0134
Spring Wheat	Ground/Air	0.0036	1	0.003

[1] Assumes one season/crop of winter or spring wheat per acre per year
NS – not stated on label

3.3. Environmental Fate and Transport

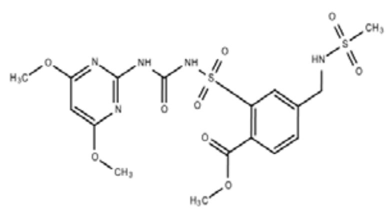
The physical, chemical, and environmental fate properties of mesosulfuron-methyl and its degradation products are summarized in **Table 3**. Mesosulfuron-methyl, like other sulfonylurea herbicides, has pH-dependent water solubility (e.g., medium (483 ppm) at pH 7 to very high (15,390 ppm) at pH 9) and exhibits weak binding to soils (Koc = 26-345). Mesosulfuron-methyl has the potential to reach surface water by runoff and leaching to ground water but has low potential to bioaccumulate in fish or volatilize from soil and water.

Mesosulfuron-methyl will enter the environment through direct application onto soil and foliage. It may move off-site via spray drift, runoff, and leaching. Biotransformation is the major route of degradation in the environment (e.g., aerobic soil metabolism $t_{1/2}$ = 20-199 days; anaerobic aquatic metabolism $t_{1/2}$ = 6-36 days, and aerobic aquatic metabolism $t_{1/2}$ = 25-100 days). Mesosulfuron-methyl breaks down to unique degradates and degradates common to other sulfonylurea herbicides. Bridge-intact degradates (AE F154851, AE F160459, and AE F160460) were found more frequently than bridge-cleavage degradates (AE F140584, AE F147477, AE F099095, AE F119094, and AE F092944) although the relative ratios among degradates appear to vary. There is no evidence from the environmental fate studies that the 4-methanesulfonamide group in the phenyl ring undergoes transformation for bridge-intact metabolites and phenyl ring bridge-cleavage metabolites.

Terrestrial field dissipation of mesosulfuron-methyl was conducted using the highest labeled application rate in bare plots in Florida, Illinois, and California (MRID 45386501). Rainfall was supplemented with irrigation to exceed the 10-year average rainfall at the Florida and California test sites; total water input during the study period was approximately 83% of the 10-year average at the Illinois test site. Under the field conditions, mesosulfuron-methyl exhibited a biphasic dissipation pattern, with an initial rapid dissipation phase occurring through approximately 30-50 days post treatment. The calculated half-life values of mesosulfuron-methyl were 58 days (r^2 = 0.62), 136 days (r^2 = 0.59), and 80 days (r^2 = 0.75) at the Florida, Illinois, and California sites, respectively. In the study, soil samples were not analyzed for transformation products of mesosulfuron-methyl. However, in a laboratory aerobic soil metabolism study (MRID 45386425), three major and four minor nonvolatile transformation products of mesosulfuron-methyl were identified as AE F099095 (29.2%), AE F092944 (10.9%), AE F154851(16.2%), AE F160459 (8.9%), AE F160460 (8.6%), AE F147447 (7.2%), and AE F140584 (7.1%). Volatilized $^{14}CO_2$ totaled 49.2% of the applied mesosulfuron-methyl at termination; volatile [^{14}C] organic compounds were <0.1% at all intervals.

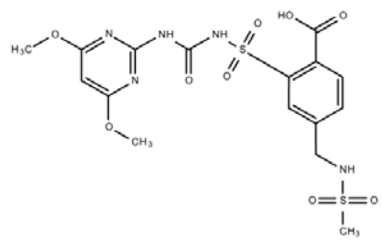
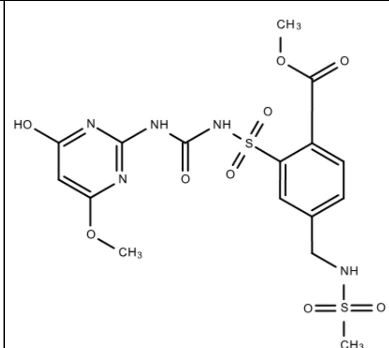
Aerobic aquatic biotransformation of mesosulfuron-methyl was studied in a gravel pit water-sand sediment system and a river water-silt loam sediment system. AE F160459 (21.6%) was a major transformation product in both systems. AE F147447 (16.1%) was a major product only in the water-sand sediment systems. Minor products (< 10%) were AE F160460, AE F154851, AE F092944, AE F140584, AE F099095, and AE F119094. In addition, there were two major unidentified products (A (Ul, 6.9-22%) and D (U3, 6.2-13.1%)) and three minor unidentified products (C (U2, ≤4.2%), E (U4, ≤1.9%), and G (U5, ≤1.9%)). In the anaerobic aquatic metabolism study, there were two major products (AE F160459 (25.9%) and AE F160460 (12.6%)) and six minor products (AE F140584, AE F147447, AE F154851, AE F099095, AE F092944, and AE F119772).

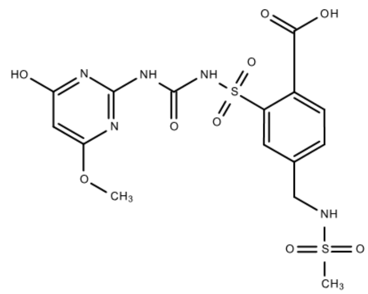
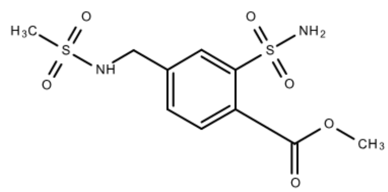
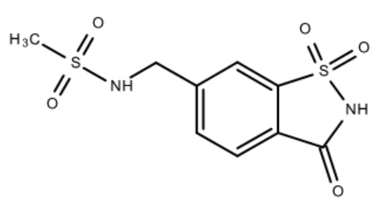
Table 3. Physical, Chemical, and Environmental Fate Properties of Mesosulfuron-methyl and Degradation Products

Parameter	Value	Reference	Comments
Chemical	Mesosulfuron-methyl (AE F130060)		
Chemical Name (IUPAC)	methyl-2-[3-(4,6-dimethoxypyrimidin-2-yl) ureido-sulfonyl]-4-methanesulfonamido-methylbenzoate	MRID 45386202	
Chemical Family	sulfonylurea herbicide		
Empirical Formula	$C_{17}H_{21}N_5O_9S_2$	MRID 45386202	Product Chemistry
SMILES	c1(ccc(cc1S(=O)(=O)NC(=O)Nc1nc(cc(OC)n1)OC)CNS(=O)(=O)C)C(=O)OC	EPI V4.10[1]	
CAS Number	208465-21-8	MRID 45386202	Product Chemistry
Structure		http://www.chemspider.com/StructureSearch.aspx	Product Chemistry
Select Physical/Chemical Parameters			
Molecular mass	503.55	MRID 45386202	Product Chemistry
Solubility (20ºC), mg/L	7.2 (pH 5) 483 (pH 7) 15,390 (pH 9)	MRID 45386215	Product Chemistry
Log Kow	1.39 (pH 5) -0.48 (pH 7) -2.06 (pH 9)	MRID 45386219	Product Chemistry
Vapor pressure in Pascals (Pa)	3.5×10^{-12} (20°C) 1.1×10^{-11} (25°C) 3.3×10^{-11} (30°C)	MRID 45386217	Product Chemistry
Henry's law constant (25°C, pH 7)	6.17×10^{-18} atm·m^3/mol	EPI 4.1	
Persistence			

Parameter	Value	Reference	Comments
Hydrolysis (25ºC) pH 4 pH 7 pH 9 Major Degradates: AE F092944 (38.4%, pH 4) AE F140584 (50.3%, pH 4) AE F092944 (37.4&32.1%, pH 7&9) AE F147447 (45.2&46.8%, pH 7&9) Minor Degradate: AE F154851 (3.8%, pH9)	3.5 days 253.1 days 318.5 days	MRID 45386418	Acceptable
Aqueous Photolysis (t ½) Minor Degradates (≤3.7%): AE F 147447 AE F 160459 AE F 140584	197 days 385 days	MRID 45386419 MRID 45386420	Supplemental Supplemental
Soil Photolysis (t ½)	Stable	MRID 45386421	Supplemental
Aerobic Soil Metabolism (t ½) Major Degradates: AE F092944(10.9%,MRID 45386425) AE F154851(16.2%,MRID 45386425) AE F099095(29.2%, MRID 45386425) Minor Degradates: AE F160459 (8.9%,MRID 45386424) AE F160460 (8.6%,MRID 45386424) AE F099095 (3.1%,MRID 45386422) AE F147447 (7.2%,MRID 45386423) AE F140584 (7.1%,MRID 45386423)	74 days (German loamy sand) 76 days (German loamy sand) 32 days (Illinois sandy loam) 86 days (German sandy loam) 100 days (German loamy sand) 20 days (German silt loam) 29 days (France loam) 82 days (UK loam) 199 days (North Dakota Clay)	MRID 45386422 MRID 45386423 MRID 45386424 MRID 45386425	Acceptable Acceptable Acceptable Acceptable
Anaerobic Aquatic Metabolism (t ½) Major Degradates: AE F160459(25.9%,MRID 45386427) AE F160460 (12.6%,MRID 45386429) Minor Degradates: AE F140584 (2.5%,MRID 45386427) AE F147447 (6.8%,MRID 45386427) AE F154851 (6.6%,MRID 45386429) AE F099095 (0.7%,MRID 45386427) AE F092944 (5.7%,MRID 45386429) AE F119772 (5.7%,MRID 45386429)	23-29 days (Water) 32-48 days (Sediment) 27-36 days (Total system) 5.4 days (Water) 8.0 days (Sediment) 6.2 days (Total system)	MRID 45386427 MRID 45386429	Supplemental Supplemental

Parameter	Value	Reference	Comments
Aerobic Aquatic Metabolism (t ½) <u>Major Degradates</u>: AE F160459 (21.6%) AE F147447 (16.1%) Unknown A (U1) (6.9-22%) Unknown D (U3) (6.2-13.1%) <u>Minor Degradates</u>: AE F160460 (8.4%) AE F154851 (4.9%) AE F092944 (4.4%) AE F140584 (1.9%) AE F099095 (≤ 0.9%) AE F119094 (1.5%) Unknown C (U2) (≤4.2%) Unknown E (U4) (≤1.9%) Unknown G (U5) (≤1.9%)	<u>Gravel pit water-sand sediment from Germany</u> [Phenyl-U-^{14}C]-label 97.2 days (Water) 108.7 days (Sediment) 99.8 days (Total system) [Pyrimidyl-2-^{14}C]-label 82.3 days (Water) 84.0 days (Sediment) 83.6 days (Total system) <u>River water-silt loam sediment from Germany</u> Phenyl-U-^{14}C]-label 26.2 days (Water) 70.0 days (Sediment) 35.7 days (Total system) [Pyrimidyl-2-^{14}C]-label 14.9 days (Water) 42.3 days (Sediment) 24.9 days (Total system)	MRID 45386430 MRID 45386431	Supplemental Supplemental (Kinetic Evaluation of MRID 45386430)
Bioconcentration/Depuration (t ½)	N/A	N/A	N/A
Mobility			
Koc (mL/g)	345 (Sand, pH 5.8) 137 (Sandy clay loam, pH7.9) 37 (Münster loamy sand, pH 6.3) 31 (Speyer loamy sand, pH 6.6) 92 (Millington sandy loam, pH 7.6) 26 (Schwanheim sandy loam, pH 7.1) 36 (Clay loam, pH 7.9) 85 (Loam, pH 8.0) 48 (Silt loam, pH 7.9)	MRID 45386432	Acceptable
Field Dissipation			
Terrestrial Field Dissipation (t ½)	58days (Florida) 136 days (Illinois) 80 days (California)	MRID 45386501	Supplemental
Mesosulfuron-methyl Degradates			
Parameter	**Value**	**Reference**	**Comments**
Bridge-intact Metabolites of Mesosulfuron-methyl (Unique to Mesosulfuron-methyl)			
Company Code	**AE F154851**	MRID 45386425	Mesosulfuron
Chemical Name	2-[3-(4,6-dimethoxypyrimidine-2-yl)ureidosulfonyl]-4-methanesulfonamidomethyl benzoic acid	MRID 45386425	
Empirical Formula	$C_{16}H_{19}N_5O_9S_2$	EPI 4.1	

Parameter	Value	Reference	Comments
SMILES	O=C(Nc1nc(OC)cc(OC)n1)NS(=O)(=O)c2cc(ccc2C(=O)O)CNS(=O)(=O)C	EPI 4.1	
CAS Number	400852-66-6		
Molecular mass	489.48	EPI 4.1	
Structure		http://www.chemspider.com/StructureSearch.aspx	
Koc (mL/g)	119 (Minnesota clay loam) 66 (Hattersheim silt loam) 50 (Münster sandy loam)	MRID 45386433 (Acceptable)	
Company Code	**AE F160459**	MRID 45386427 MRID 45386429	
Chemical Name	Methyl 2-[3-(4-hydroxy-6-methoxypyrimidine-2-yl)ureidosulfonyl]-4-methanesulfonamido-methyl benzoate	MRID 45386427 MRID 45386429	
Empirical Formula	$C_{16}H_{19}N_5O_9S_2$	EPI 4.1	
SMILES	C(=O)(c1c(S(=O)(=O)NC(=O)Nc2nc(O)cc(OC)n2)cc(CNS(C)(=O)=O)cc1)OC	EPI 4.1	
Molecular mass	489.48	EPI 4.1	
Structure		http://www.chemspider.com/StructureSearch.aspx	
Company Code	**AE F160460**	MRID 45386429	
Chemical Name	2-[3-(4-hydroxy-6-methoxypyrimidin-2-yl) ureidosulfonyl]-4-methanesulfonamidomethyl-benzoic acid	MRID 45386429	
Empirical Formula	$C_{15}H_{17}N_5O_9S_2$	EPI 4.1	
SMILES	C(=O)(O)c1c(S(=O)(=O)NC(=O)Nc2nc(O)cc(OC)n2)cc(CNS(C)(=O)=O)cc1	EPI 4.1	

Parameter	Value	Reference	Comments
Molecular mass	475.45	EPI 4.1	
Structure		http://www.chemspider.com/StructureSearch.aspx	
Phenyl Ring Bridge-cleavage Metabolites of Mesosulfuron-methyl (Unique to Mesosulfuron-methyl)			
Company Code	**AE F140584**	MRID 45386418	
Chemical Name	Methyl 4-methanesulfonamidomethyl-2-sulfamoylbenzoate	MRID 45386418	
Empirical Formula	C_{10} H_{14} N_2 O_6 S_2	EPI 4.1	
SMILES	C(=O)(c1c(S(N)(=O)=O)cc(CNS(C)(=O)=O)cc1)OC	EPI 4.1	
Molecular mass	322.35	EPI 4.1	
Structure		http://www.chemspider.com/StructureSearch.aspx	
Company Code	**AE F147447**	MRID 45386418	
Chemical Name	6-Methanesulfonamidomethyl- 1,2-benzisothiazol-3(2H)-one 1,l dioxide	MRID 45386418	
Empirical Formula	C_9 H_{10} N_2 O_5 S_2	EPI 4.1	
SMILES	C1(=O)c2c(cc(CNS(C)(=O)=O)cc2)S(=O)(=O)N1	EPI 4.1	
Molecular mass	290.31	EPI 4.1	
Structure		http://www.chemspider.com/StructureSearch.aspx	
Pyrimidine Ring Bridge-cleavage Metabolites of Mesosulfuron-methyl (Common to Other Sulfonylurea Herbicides)			
Company Code	**AE F099095**	MRID 45386434	
Chemical Name (CAS)	4,6-dimethoxypyrimidin-2-yl-urea	MRID 45386434	
Empirical Formula	C_7 H_{10} N_4 O_3	EPI 4.1	
SMILES	c1(OC)cc(OC)nc(NC(N)=O)n1	EPI 4.1	

Parameter	Value	Reference	Comments
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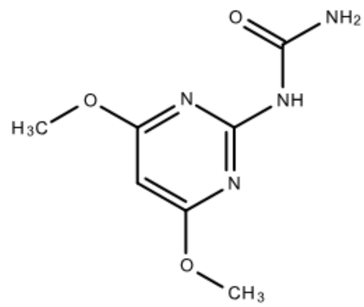
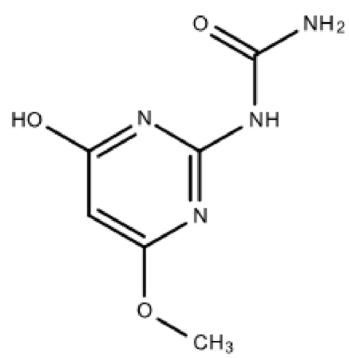
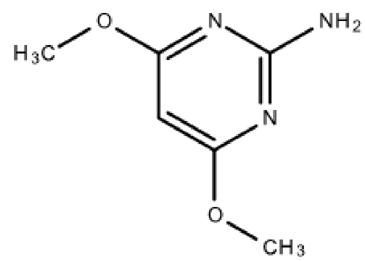
Structure		http://www.chemspider.com/StructureSearch.aspx	
Koc (mL/g)	3856 (Minnesota clay loam) 365 (Hattersheim silt loam) 206 (Münster sandy loam)	MRID 45386434 (Acceptable)	
Company Code	**AE F119094**		
Chemical Name (CAS)	4-Hydroxy-6-methoxypyrimidin-2-yl-urea		
Empirical Formula	$C_6\ H_8\ N_4\ O_3$	EPI 4.1	
SMILES	c1(O)cc(OC)nc(NC(N)=O)n1	EPI 4.1	
Molecular mass	184.16	EPI 4.1	
Structure		http://www.chemspider.com/StructureSearch.aspx	
Company Code	**AE F092944**	MRID 45386418 MRID 45386425	
Chemical Name (CAS)	2-Amino-4,6-dimethoxypyrimidine	MRID 45386418 MRID 45386425	
Empirical Formula	$C_6\ H_9\ N_3\ O_2$	EPI 4.1	
SMILES	c1(OC)cc(OC)nc(N)n1	EPI 4.1	
CAS Number	36315-01-2	CSID:106290	
Molecular mass	155.16	EPI 4.1	

Parameter	Value	Reference	Comments
Structure		http://www.chemspider.com/StructureSearch.aspx	

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

3.4. Clean Water Act

Mesosulfuron-methyl is not identified as a cause of impairment for any water bodies listed as impaired under section 303(d) of the Clean Water Act[2]. In addition, no Total Maximum Daily Loads (TMDL) have been developed[3]. The Impaired Waters and Total Maximum Daily Loads website can be consulted for more information[4]. The Agency invites submission of water quality data for mesosulfuron-methyl. To the extent possible, data should conform to the quality standards in the *OPP Standard Operating Procedure: Inclusion of Impaired Water Body and Other Water Quality Data in OPP's Registration Review Risk Assessment and Management Process*[5], in order to ensure they can be used quantitatively or qualitatively in pesticide risk assessments.

4. Receptors

Consistent with the process described in the Overview Document (USEPA, 2004c), the risk assessment for mesosulfuron-methyl relies on a surrogate species approach. Toxicological data generated from surrogate test species, which are intended to be representative of broad taxonomic groups, are used to extrapolate the potential effects on a variety of species (receptors) included under these taxonomic groupings.

Acute and chronic toxicity data from studies submitted by pesticide registrants along with the available open literature will be used to evaluate the potential direct and indirect effects of mesosulfuron-methyl to aquatic and terrestrial receptors. This includes toxicity on the technical grade active ingredient, degradates, and when available, formulated products (*e.g.*, "Six-Pack" studies). Open literature studies will be identified through EPA's ECOTOXicology (ECOTOX) database[6], which uses a literature search engine for locating chemical toxicity data.

A summary of data representing non-target organisms exposed to mesosulfuron-methyl and its degradation products in aquatic and terrestrial habitats is provided in **Sections 4.1** and **4.2**. A summary of ecological incidents associated with mesosulfuron-methyl is provided in **Section 4.3**. Studies submitted by the registrant are listed in **Appendix A**. The ECOTOX database will be searched when the risk assessment for mesosulfuron-methyl is prepared. At that time,

[2] http://iaspub.epa.gov/tmdl_waters10/attains_nation_cy.cause_detail_303d?p_cause_group_id=885
[3]http://iaspub.epa.gov/tmdl_waters10/attains_nation.tmdl_pollutant_detail?p_pollutant_group_id=885&p_pollutant_group_name=PESTICIDES
[4] http://www.epa.gov/owow/tmdl/
[5] http://www.epa.gov/oppfead1/cb/ppdc/2006/november06/session1-sop.pdf
[6] http://cfpub.epa.gov/ecotox/

endpoints more sensitive than available guideline studies will be reviewed from the open literature studies.

4.1. Effects to Aquatic Organisms

Table 4. Summary of Toxicity of Mesosulfuron-methyl (TGAI) to Aquatic Animals

Species	Exposure Scenario	% AI	Toxicity	MRID	Toxicity Category	Classification
Rainbow Trout (*Oncorhynchus mykiss*)	96 hr	94.6	LC_{50} > 91.5 mg total ai/L NOAEC ≥ 91.5 mg total ai/L	45386231	NA	Supplemental
Bluegill sunfish (*Lepomis macrochirus*)	96 hr	94.6	LC_{50} > 96.4 mg total ai/L NOAEC ≥ 96.4 mg total ai/L	45386230	NA	Supplemental
Rainbow Trout (*Oncorhynchus mykiss*)	28 day[1]	94.6	NOAEC ≥ 29.6 mg ai/L LOAEC > 29.6	45386232	NA	Supplemental
Waterflea *(Daphnia magna)*	48 hr	94.6	EC_{50} > 90.2 mg ai/L NOAEC ≥ 90.2 mg ai/L	45386233	NA	Acceptable (“Core”)
Waterflea *(Daphnia magna)*	Life-Cycle	94.6	NOAEC = 1.7 mg ai/L LOAEC = 3.0 mg ai/L based on dry weight	45386305	NA	Acceptable (“Core”)
Sheepshead minnow (*Cyprinodon variegatus*)	96 hr	95.7	LC_{50} > 105 mg ai/L NOAEC ≥ 105 mg ai/L	45386301	Practically non-toxic	Supplemental
Mysid shrimp (*Americamysis bahia*)	96 hr	95.7	LC_{50} > 111 mg ai/L NOAEC ≥ 111mg ai/L	45386303	Practically non-toxic	Acceptable (“Core”)
Eastern oyster (*Crassostrea virginica*)	96 hr	95.6	EC_{50} > 100 mg ai/L NOAEC ≥ 100mg ai/L	45386302	Practically non-toxic	Acceptable (“Core”)

[1] OECD 28-day sub-chronic study with 2 month old fish.
NA = not applicable

Table 5. Summary of Toxicity of Mesosulfuron-methyl Degradation Products (TGAI) to Aquatic Animals

Species	Exposure Scenario	% AI	Toxicity	MRID	Toxicity Category	Classification
Rainbow Trout (*Oncorhynchus mykiss*)	96 hr	Unknown AE F092944	LC_{50} = 97 mg ai/L	IUPAC footprint[1]	Slightly toxic	NA
Waterflea *(Daphnia magna)*	48 hr	Unknown AE F092944	EC_{50} > 100 mg ai/L	IUPAC footprint[1]	Practically non-toxic	NA

Species	Exposure Scenario	% AI	Toxicity	MRID	Toxicity Category	Classification
Waterflea *(Daphnia magna)*	21 day	Unknown AE F092944	NOAEC = 24 mg ai/L	IUPAC footprint[1]	NA	NA

[1] IUPAC footprint database studies are not reviewed by the Agency and the toxicity endpoints are used at face value. http://sitem.herts.ac.uk/aeru/iupac/441.htm
NA = not applicable

Table 6. Summary of Toxicity of Mesosulfuron-methyl (TGAI) to Aquatic Plants

Species	Exposure Scenario	% AI	Toxicity	MRID	Toxicity Category	Classification
Marine Diatom *(Skeletonema costatum)*	96 hr	95.7	IC_{50} = 98000 (91000-110000) [1] µg ai/L NOAEC = 37800 µg ai/L Based on reduced biomass (area under the growth curve)	45386314	NA	Acceptable ("Core")
Cyanobacteria *(Anabaena flosaquae*	96 hr	95.7	IC_{50} = 2400 (1700-3300) [1] µg ai/L NOAEC = 1100 µg ai/L Based on reduced cell density	45386315	NA	Acceptable ("Core")
Freshwater Diatom *(Navicula pelliculosa*)	96 hr	94.6	IC_{50} > 70800 µg ai/L NOAEC ≥ 70.8 µg ai/L	45386307	NA	Acceptable ("Core")
Duckweed *(Lemma gibba*)	7 day	95.3	IC_{50} = 0.64 (0.56-0.73) [1] µg ai/L NOAEC = 0.19 µg ai/L Based on reduced number of fronds	45386310	NA	Acceptable ("Core")

[1]Range is 95% confidence interval.
NA = not applicable

Table 7. Summary of Toxicity of Mesosulfuron-methyl Degradation Products (TGAI) to Aquatic Plants

Species	Exposure Scenario	% AI	Toxicity	MRID	Toxicity Category	Classification
Freshwater Green Algae *(Pseudokirchneriella subcapitata)*	96 hr	93.1 AE F147447	IC_{50} > 92000 µg ai/L NOAEC ≥ 92000 µg ai/L	45386308	NA	Acceptable ("Core")

Species	Exposure Scenario	% AI	Toxicity	MRID	Toxicity Category	Classification
Freshwater Green Algae *(Pseudokirchneriella subcapitata)*	96 hr	96.8 AE F160459	IC_{50} = 98000 µg ai/L NOAEC = 54600 µg ai/L Based on reduced biomass (area under the growth curve)	45386309	NA	Acceptable (“Core”)
Freshwater Green Algae *(Pseudokirchneriella subcapitata)*	72 hr	Unknown AE F092944	IC_{50} = 120000 µg ai/L	IUPAC footprint[2]	NA	NA
Duckweed *(Lemma gibba)*	7 day	93.1 AE F147447	IC_{50} > 90900 µg ai/L NOAEC ≥ 90900 µg ai/L	45386313	NA	Acceptable (“Core”)
Duckweed *(Lemma gibba)*	7 day	96.8 AE F160459	IC_{50} = 1500 (1100-2000)[1] µg ai/L NOAEC = 290 µg ai/L Based on reduced number of fronds	45386311	NA	Acceptable (“Core”)
Duckweed *(Lemma gibba)*	7 day	96.1 AE F160460	IC_{50} > 94710 µg ai/L NOAEC ≥ 94710 µg ai/L	45386312	NA	Acceptable (“Core”)
Duckweed *(Lemma gibba)*	7 day	Unknown AE F092944	IC_{50} > 100000 µg ai/L	IUPAC footprint[2]	NA	NA

[1]Range is 95% confidence interval.
[2] IUPAC footprint database studies are not reviewed by the Agency and the toxicity endpoints are used at face value. http://sitem.herts.ac.uk/aeru/iupac/441.htm
NA = not applicable

4.2. Effects to Terrestrial Organisms

Table 8. Summary of Toxicity of Mesosulfuron-methyl (TGAI) to Terrestrial Animals

Species	Exposure Scenario	% AI	Toxicity	MRID	Toxicity Category	Classification
Northern Bobwhite Quail (*Colinus virginianus*)	Single oral dose, birds observed for 14 days	94.6	LD_{50} >2000 mg/kg NOAEL < 2000 mg/kg LOAEL ≤ 2000 based on reduced consumption No mortality	45386224	Practically non-toxic	Acceptable (“Core”)

Species	Exposure Scenario	% AI	Toxicity	MRID	Toxicity Category	Classification
Mallard Duck (*Anas platyrhynchos*)	Single oral dose, birds observed for 14 days	94.6	LD_{50} >2000 mg/kg No mortality or sublethal effects observed	45386225	Practically non-toxic	Acceptable ("Core")
Northern Bobwhite Quail (*Colinus virginianus*)	8 days (5 days treatment and 3 days observation)	94.6	LC_{50} >4800 ppm ai NOAEC < 297 ppm ai LOAEC ≤ 297 based on reduced consumption No mortality	45386226	NA	Acceptable ("Core")
Mallard Duck (*Anas platyrhynchos*)	8 days (5 days treatment and 3 days observation)	94.6	LC_{50} >4750 ppm ai NOAEC < 309 ppm ai LOAEC ≤ 309 based on reduced consumption No mortality	45386227	NA	Acceptable ("Core")
Northern Bobwhite Quail (*Colinus virginianus*)	One-generation Reproduction Study	94.6	NOAEC ≥ 1000 ppm ai	45386228	NA	Supplemental
Mallard Duck (*Anas platyrhynchos*)	One-generation Reproduction Study	94.6	NOAEC ≥ 990 ppm ai	45386229	NA	Supplemental
Honeybee (*Apis mellifera*)	Acute contact	95.9	LD_{50} > 13 µg ai/bee	45386319	Practically nontoxic	Acceptable ("Core")
Rat	Acute Oral	95.6	LD_{50} > 5000 mg/kg	45386321	Practically nontoxic	Acceptable
Rat	2-year chronic	94.6	NOAEL ≥ 16,000 ppm (1175 mg/kg bw/day – males; 1388 mg/kg bw/day – females) Parental systemic, offspring, and reproductive	45430405	NA	Acceptable

NA = not applicable

Table 9. Summary of Toxicity of Mesosulfuron-methyl Degradation Products (TGAI) to Terrestrial Animals

Species	Exposure Scenario	% AI	Toxicity	MRID	Toxicity Category	Classification
Rat	Acute Oral	Unknown AE F099095	LD_{50} = 677 mg/kg (males)	47305223	Slightly toxic	NA
Rat	Acute Oral	Unknown AE F092944	LD_{50} = 737 mg/kg (males)	IUPAC footprint[1]	Slightly toxic	NA

[1] IUPAC footprint database studies are not reviewed by the Agency and the toxicity endpoints are used at face value. http://sitem.herts.ac.uk/aeru/iupac/441.htm
NA = not applicable

Table 10. Summary of Toxicity of Mesosulfuron-methyl Formulations to Terrestrial Animals

Species	Exposure Scenario	% AI	Toxicity	MRID	Toxicity Category	Classification
Rat	Acute Oral	2.26 Silverado Wild Oat Herbicide	LD_{50} > 2000 mg/kg	46034702	Practically nontoxic[1]	Acceptable
Rat	Acute Oral	4.84 Osprey	LD_{50} > 2000 mg/kg	46034602	Practically nontoxic[1]	Acceptable
Rat	Acute Oral	4.5 Olympus Flex (plus 6.8% propoxycarbazone -sodium)	LD_{50} > 2000 mg/kg	46038502	Practically nontoxic[1]	Acceptable
Rat	Acute Oral	3.08 (plus 0.61% iodosulfuron)	LD_{50} > 2000 mg/kg	47756302	Practically nontoxic[1]	Acceptable

[1] On a formulation basis

Table 11. Summary of Toxicity of Mesosulfuron-methyl Formulations to Terrestrial Plants

Species	Exposure Scenario	% AI	Toxicity	MRID	Toxicity Category	Classification
Terrestrial Plants	Vegetative Vigor, 21-day	4.81 Osprey 4.5 WG	Most sensitive monocot Oat (dry weight) IC_{25} = 0.42 (0.36-0.49)[1] g ai/ha NOAEC = 0.33 g ai/ha LOAEC = 1 g ai/ha Most sensitive dicot Soybean (dry weight) IC_{25} = 0.16 (0.14-0.19)[1] g ai/ha NOAEC = 0.04 g ai/ha LOAEC = 0.11 g ai/ha	46688201	NA	Under Review

Species	Exposure Scenario	% AI	Toxicity	MRID	Toxicity Category	Classification
	Seedling Emergence, 14-day	74.73 (TGAI plus adjuvant)	Most sensitive monocot Onion (shoot length) IC_{25} = 8.4 (5.4-13)[1] g ai/ha NOAEC = 7.5 g ai/ha LOAEC = 15 g ai/ha	45745702	NA	Supplemental
		50% (TGAI plus iodosulfuron and adjuvant)	Most sensitive dicot Lettuce (shoot length) IC_{25} = 0.92 (0.34-2.5)[1] g ai/ha NOAEC = 0.81 g ai/ha LOAEC = 1.63 g ai/ha	45386316		

[1]Range is 95% confidence interval.
NA = not applicable

Table 12. Summary of Toxicity of Mesosulfuron-methyl Degradation Products (TGAI) to Terrestrial Plants

Species	Exposure Scenario	% AI	Toxicity	MRID	Toxicity Category	Classification
Variable Flatsedge (*Cyperus difformis*) Barnyard Grass (*Echinochloa crus-galli*) Kidneyleaf Mudplantain (*Heteranthera reniformis*)	Vegetative Vigor, 21-day[1]	Unknown AE F099095	NOAEC ≥ 350 g ai/ha	46588504	NA	Unreviewed
Japonica Rice (*Oryza sativa*)		Unknown AE F099095	NOAEC ≥ 750 g ai/ha	46588501	NA	Unreviewed

[1] EPPO guideline n° 135 studies on rice and rice weeds
NA = not applicable

4.3. Incident Databases Review

Incidents involving mesosulfuron-methyl were reported in the Ecological Incident Information System (EIIS, v 2.1.1) and the Aggregate Incident Data System as of November 8, 2012. No incidents were reported in the Avian Incident Monitoring System (AIMS)[7].

All 29 reported incidents (2004-2011) reported in EIIS involved damage to wheat and all but one were considered possibly or probably caused by direct application of mesosulfuron-methyl. Thirty-seven incidents, all of minor plant-damage attributed to mesosulfuron-methyl products, were reported in the Aggregate Incident Data System.

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

The total number of actual incidents associated with the use of mesosulfuron-methyl may be higher than what is reported to the Agency. Incidents may go unreported since effects may not be immediately apparent or readily attributed to the use of a chemical. As such, the absence of incident reports cannot be construed as the absence of incidents.

5. Risk Hypothesis

Mesosulfuron-methyl, when used in accordance with current labels, can result in offsite movement of the compound via spray drift, runoff, and leaching to ground water, leading to exposure of non-target plants and animals. Application of mesosulfuron-methyl to wheat and triticale fields may serve as a major source of mesosulfuron-methyl exposure to wildlife. When used in accordance with the labels, mesosulfuron-methyl use will cause adverse effects upon the survival, growth, and reproduction of non-target terrestrial and aquatic organisms. These non-target organisms include federally-listed threatened and endangered species.

6. Analysis Plan

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

This analysis plan will be revisited and may be revised depending upon a full review of the data available in the open literature and the information submitted by the public in response to the opening of the Registration Review docket.

6.1. Stressors of Concern

The stressors of concern will be mesosulfuron-methyl and in some cases the major degradation products (**Table 13)**.

The Agency is seeking clarification on two unknown degradates from the submitted aerobic metabolism study (MRID 45386430 and 45386431) and requesting an ECM/ILV method that is capable of identifying the major degradates (*see* **Section 6.8**).

Table 13. Summary of the Major and Minor Mesosulfuron-methyl Degradates

Company Code (Maximum % Formation)	Chemical Name	Mechanism of Formation	Comments
AE F154851 (16.2%) MRID 45386425	2-[3-(4,6-dimethoxypyrimidine-2-yl)ureidosulfonyl]-4-methanesulfonamidomethyl benzoic acid	Methyl ester hydrolysis	Bridge-intact degradates (unique to mesosulfuron-methyl)
AE F160459 (25.9%) MRID 45386427	Methyl 2-[3-(4-hydroxy-6-methoxypyrimidine-2-yl)ureidosulfonyl]-4-methanesulfonamido-methyl benzoate	Demethoxyfication at the 4-position of the pyrimidinyl group	

AE F160460 (12.6%) MRID 45386429	2-[3-(4-hydroxy-6-methoxypyrimidin-2-yl) ureidosulfonyl]-4-methanesulfonamidomethyl-benzoic acid	Demethoxyfication at the 4-position of the pyrimidinyl group, Methyl ester hydrolysis	
AE F140584 (50.3%, pH 4) MRID 45386418	Methyl 4-methanesulfonamidomethyl-2-sulfamoylbenzoate	Cleavage of the sulfonylurea bridge	Phenyl ring bridge-cleaved (unique to mesosulfuron-methyl)
AE F147447 (45.2 at pH 7, 46.8% at pH 9) MRID 45386418	6-Methanesulfonamidomethyl- 1,2-benzisothiazol-3(2H)-one 1,l dioxide	Cleavage of the sulfonylurea bridge, Methyl ester hydrolysis, Isothiazole ring formation	
AE F099095 (29.2%) MRID 45386425	4,6-dimethoxypyrimidin-2-yl-urea	Cleavage of the sulfonylurea bridge	Pyrimidine ring bridge-cleaved (common to other sulfonylurea herbicides)
AE F119094 (1.5%) MRID 45386430	4-Hydroxy-6-methoxypyrimdin-2-yl-urea	Cleavage of the sulfonylurea bridge, Demethoxyfication at the 4-position	
AE F092944 (38.4% at pH 4, 37.4% at pH 7, 32.1% at pH 9) MRID 45386418	2-Amino-4,6-dimethoxypyrimidine	Cleavage of the sulfonylurea bridge, Elimination of the –NH_2 CO- group	

Residues of Concern for Drinking Water Consumed by Humans

The only drinking water assessment for mesosulfuron-methyl was completed in 2004 (USEPA, 2004a). Mesosulfuron-methyl and three bridge-intact major degradates (AE F154851, AE F160459, and AE F160460) were modeled per request of the HED's MARC (01/28/2004 meeting). Residues of concern for human health drinking water may be revisited.

Residues of Concern for Ecological Risk Assessment

In the absence of degradate data, the major degradates will be considered stressors of concern when assessing risk to aquatic organisms; however, data are more likely to impact the assessment of aquatic vascular plants.

Limited aquatic toxicity data were available for the major degradation products; however, for most endpoints information was available from Ecological Structure Activity Relationship (ECOSAR) methods[8] or the IUPAC footprint database[9] (**Table 14**). The most toxic value was selected for this screening unless indicated otherwise. Some degradates may be more toxic than mesosulfuron-methyl to fish and invertebrates. For aquatic plants, available information suggests that some degradates are equal in toxicity to mesosulfuron-methyl and others are much less toxic.

Although some degradates may be more toxic than mesosulfuron-methyl to fish and invertebrates, preliminary estimates of exposure are much lower than would trigger a risk concern (**Table 15**). Exposure for this analysis was based on the highest application rate and mesosulfuron-methyl EECs assuming no degradation.

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[8] ECOSAR predictive software is available publically though the Epi Suite™ program. http://www.epa.gov/oppt/exposure/pubs/episuite.htm

[9] http://sitem.herts.ac.uk/aeru/iupac/577.htm

The lack of information on toxicity of two degradates (AE F154851 and AE F140584) to vascular plants could impact risk conclusions. Listed plants are anticipated to be a risk concern based on mesosulfuron-methyl alone. Non-listed plants may be a risk concern as well if a total toxic residue (TTR) approach is used (preliminary EEC = 2.69 µg/L, as reported in **Table 15)**; however, this may not be the case if all degradates are clearly less toxic than mesosulfuron-methyl and EECs are based on mesosulfuron-methyl alone (preliminary EEC = 0.31 µg/L as reported in USEPA, 2004b). One of the degradates, AE F154851, is a SU bridge-intact compound; thus it will be assumed equal in toxicity to mesosulfuron-methyl in the absence of data and a TTR approach will be used to estimate EECs. The other degradate, AE F140584, would only need to be slightly more toxic than mesosulfuron-methyl to trigger a risk concern (listed and non-listed species) based on its own preliminary EECs[10]. On the other hand, ECOSAR estimates suggest that AE F140584 is not more toxic than mesosulfuron-methyl to non-vascular plants which may or may not be representative of the potential toxicity to vascular plants (**Table 14**). AE F140584 toxicity will be assumed equal to mesosulfuron-methyl in the absence of data and a TTR approach will be used to estimate EECs.

[10] Preliminary EEC for AE F140584 (0.18 µg/L) was calculated by adjusting the maximum application rate of mesosulfuron-methyl (lb AE F140584/A = lb ai/A * maximum percent formation of AE F140584 in fate studies * (MW AE F140584/MW ai) and assuming that AE F140584 is stable to degradation.

Table 14. Comparative Aquatic Toxicity of Mesosulfuron-methyl and Major Degradation Products

Compound	FW fish 96-hr acute LC_{50} (mg/L)	FW fish chronic NOAEC (mg/L)[1]	FW invertebrate 48-hr acute EC_{50} (mg/L)	FW invertebrate chronic NOAEC (mg/L)[1]	ME fish 96-hr acute LC_{50} (mg/L)	ME invertebrate 96-hr acute LC_{50} (mg/L)	Vascular plant 7-day EC_{50} (µg/L)	Non-vascular plant 96-hr EC_{50} (µg/L)
Mesosulfuron-methyl	> 91.5	≥ 29.6[2]	> 90.2	1.7	> 105.0	> 111.0	0.64	**56.0**
AE F154851	**20367.7**[3]	**155.0**[4]	**7284.6**[3]	**96.0**[4,5]	-	-	-	**547.0**
AE F160459	**97.0**[4]	**0.02**	**5.5**	**6.8**[5]	**1314.1**[3]	**2739.4**[3]	1500.0	98000.0
AE F160460	**2023.2**[3]	**0.15**	**73.6**	**101.8**	**235000.0**[3]	-	> 94700.0	**532.0**
AE F140584	**731.0**[4]	**12.0**	**548.2**	**7.2**[5]	**1360.9**[4]	**3249.3**[4]	-	**2792.0**
AE F147447	**6.1**	**0.54**[5]	**7.6**	**0.7**[5]	**-**	**-**	> 90900.0	> 92000.0
AE F099095	**337.6**	**1.9**	**116.5**	**1.5**[5]	-	-	2.5-200.0[6]	**147.0**
AE F092944	***97.0***	**89.6**[7]	***> 100.0***	***24.0***	-	-	***>100000.0***	***120000.0***

[1] ECOSAR estimated chronic value is defined as the geometric mean of the no observed effect concentration (NOEC) and the lowest observed effect concentration (LOEC).
[2] OECD 28-day sub chronic study
[3] Endpoint exceeds predicted water solubility of compound by 10x – no effects at saturation are predicted if the compound is solid.
[4] Endpoint exceeds predicted water solubility of compound.
[5] Value is based on acute-to-chronic ratio. Other ECOSAR classes predict lower toxicity (i.e., higher values).
[6] AE F099095 is a urea-type compound. Urea herbicides (*e.g.*, linuron) are less toxic than mesosulfuron-methyl to vascular plants (EC_{50} = 2.5 - 200 µg/L). Data are reported in the problem formulation for orthosulfamuron (DP 390068).
[7] Neutral organic estimates are reported because N-substituted anilines are less toxic than estimated by the aniline ECOSAR class.
BOLD values are ECOSAR (v1.00) toxicity estimates (lowest toxicity value of multiple ECOSAR classes is shown, i.e., the most toxic). ***BOLD Italic*** values are from the footprint database (reported when toxicity value is lower than ECOSAR estimate). Non-bolded values are toxicity values from available studies.
FW = freshwater and ME = marine/estuarine

Table 15. Preliminary Aquatic RQs for Mesosulfuron-methyl and Major Degradation Products[1,2]

Compound	FW fish 96-hr acute LC_{50} (mg/l)	RQ	FW fish chronic NOAEC (mg/l)	RQ	FW invertebrate 48-hr acute EC_{50} (mg/l)	RQ	FW invertebrate chronic NOAEC (mg/l)	RQ
Mesosulfuron -methyl	91.5	0.000029	29.6	0.000091	90.2	0.000030	1.7	0.001582
AE F154851	20367.7	0.000000	155.0	0.000017	7284.6	0.000000	96.0	0.000028
AE F160459	97.0	0.000028	0.02	0.134000	5.5	0.000489	6.8	0.000396
AE F160460	2023.2	0.000001	0.15	0.017867	73.6	0.000037	101.8	0.000026
AE F140584	731.0	0.000004	12.0	0.000223	548.2	0.000005	7.2	0.000374
AE F147447	6.1	0.000441	0.54	0.004926	7.6	0.000354	0.7	0.003843
AE F099095	337.6	0.000008	1.9	0.001411	116.5	0.000023	1.5	0.001793
AE F092944	97	0.000028	89.6	0.000030	100.0	0.000027	24	0.000112

[1] Toxicity based on data in **Table 14** (marine-estuarine fish/invertebrates RQs are not presented because available toxicity data suggests that they are not more sensitive than freshwater fish/invertebrates). RQs are not typically calculated for non-definitive endpoints; however, they are presented here for comparative purposes only. RQs based on non-definitive endpoints are higher (overestimate risk) than if based on actual toxicity. RQs based on toxicity endpoints greater than the predicted solubility limit (i.e., ECOSAR estimates of some of the degradates) have limited meaning. Nonetheless, risk is low in these cases given that (1) the preliminary EECs are ≥ 11,000 X lower than the ECOSAR-estimated solubility limit(s) of the pertinent degradate(s) and (2) ECOSAR-estimated toxicity suggests that there is less than a 50% acute effect and no adverse chronic effect at the solubility limit(s) of the pertinent degradate(s).

[2] RQs calculated using mesosulfuron-methyl EECs based on the highest application rate and assuming no degradation (Peak, 21-day, and 60-day EEC = 2.69 µg/l).

Limited terrestrial toxicity data were available for the major degradation products (**Table 9 and 12**). However, the degradation products are not likely a risk concern for birds or mammals given that they would need to be at least two to three orders of magnitude more toxic than mesosulfuron-methyl to exceed levels of concern (LOC). Preliminary degradate EECs were calculated based on the highest acute (3.66 mg/kg bw) and subacute/chronic (3.22 mg/kg diet) mesosulfuron-methyl EEC calculated in T-REX. Each degradate EEC was calculated as follows:

EEC = mesosulfuron-methyl EEC * max % of degradate formed in fate studies * (MW degradate / MW mesosulfuron-methyl)

There are limited degradate toxicity data for terrestrial plants. SU bridge-intact degradates (AE F154851, AE F160459, and AE F160460) and mesosulfuron-methyl will be assumed equal in toxicity to terrestrial plants in the absence of data. AE F099095, a urea-type compound, is a potentially herbicidally-active non-SU degradate. Limited data for AE F099095 suggests that it is not more toxic than mesosulfuron-methyl. Furthermore, mesosulfuron-methyl is more toxic than urea herbicides (*see* orthosulfamuron problem formulation for toxicity comparison; DP 390068); thus, AE F099095 is likely not more toxic than mesosulfuron-methyl assuming its toxicity is similar to that of the urea herbicides.

6.2. Measures of Exposure

Mesosulfuron-methyl concentrations in aquatic and terrestrial environments will be modeled using the maximum labeled application rates and numbers of applications, the minimum application intervals, and application methods that have the greatest potential for off-site transport.

Spray Drift

The AgDRIFT spray drift model (v2.01; May, 2001) or AgDISP model[11] will be used to assess exposure of non-target organisms to mesosulfuron-methyl through off-site spray drift. The models also function as tools for evaluating potential buffer zones.

Aquatic Exposure

Tier II models PRZM (Pesticide Root Zone Model, v3.12.2; May, 2005) and EXAMS (EXposure Analysis Modeling System, version 2.98.04.06, April 2005) in the PE5 shell[12] will be used to estimate environmental concentrations (EECs) of mesosulfuron-methyl and degradation products (as appropriate) in surface waters.

If available, monitoring data will be evaluated and used for characterizing the distribution of mesosulfuron-methyl and degradation products.

Terrestrial Exposure

There is potential exposure to non-target organisms through consumption of contaminated food items (*e.g.*, insects or vegetation), drinking water, direct application, inhalation, runoff, and spray drift.

T-REX (v 1.5)[13] will be used to estimate exposure of birds and mammal to mesosulfuron-methyl. For input into T-REX, the default foliar dissipation half-life of 35 days will be used in the absence of acceptable foliar dissipation rate data (if labels allow multiple applications).

TerrPlant (v 1.2.2)[13] will be used to calculate EECs for characterizing exposure to terrestrial and semi-aquatic plants.

Screening Imbibition Program

The Screening Imbibition Program (SIP v.1.0)[13] was used to calculate an upper bound estimate of bird and mammal exposure to mesosulfuron-methyl in drinking water.

Although the model identifies a potential concern for birds (acute and chronic) and mammals (acute and chronic), the model prediction has limited meaning because toxicity was based on non-definitive endpoints from studies with no observed mortality (**Table 8**). That is, the potential concern is unquantifiable and less than suggested by the model.

Although conclusions about risk from drinking water exposure alone are uncertain, drinking water may contribute to a total exposure (dietary food sources, dermal, and inhalation) that has

[11] http://www.epa.gov/pesticides/science/models_pg.htm#atmospheric
[12] http://www.epa.gov/oppefed1/models/water
[13] http://www.epa.gov/oppefed1/models/terrestrial

potential for effects on non-target animals and should be explored further. **Appendix B** provides model results.

Screening Tool for Inhalation Risk

The Screening Tool for Inhalation Risk (STIR v. 1.0)[13] was used to provide an upper bound estimate of exposure of birds and mammals to pesticides through inhalation of spray drift or vapor.

The screening suggests that mesosulfuron-methyl exposure is not likely significant enough for an inhalation risk concern. **Appendix C** provides model results.

6.3. Measures of Effect

Toxicity effects data will be used as measures of direct and indirect effects to biological receptors (USEPA, 2004c). As discussed previously, data will be obtained from registrant-submitted studies and from literature studies identified in ECOTOX.

Quantitative assessment of risks will be based on study endpoints that can be directly linked to the Agency's assessment endpoints of impaired survival, growth, and reproduction. Sub-lethal effects (*e.g.*, lethargy and changes in coloration) will be evaluated qualitatively. Available incident data will be used to further characterize risk.

6.4. Integration of Exposure and Effects

The exposure and effects data will be integrated in order to evaluate potential adverse ecological effects on non-target species. The risk quotient (RQ) method will be used to compare exposure and measured toxicity values. EECs will be divided by acute and chronic toxicity values. The resulting RQs will be compared to the Agency's LOC (USEPA, 2004c).

6.5. Endangered Species Assessments

Consistent with the Agency's responsibility under the Endangered Species Act (ESA), the Agency will evaluate risks to Federally-listed threatened and endangered (listed) species from registered uses of mesosulfuron-methyl. This assessment will be conducted in accordance with the Overview Document (USEPA, 2004c), provisions of the ESA, and the Services' *Endangered Species Consultation Handbook* (USFWS and NMFS, 1998).

6.6. Endocrine Disruptor Screening

As required by Federal Food, Drug and Cosmetic Act (FFDCA) section 408(p), mesosulfuron-methyl is subject to the endocrine screening part of the Endocrine Disruptor Screening Program (EDSP)[14]. Mesosulfuron-methyl is not in the first or second group of pesticide active ingredients to be screened under the EDSP.

6.7. Drinking Water Assessment

A new DWA may be conducted for mesosulfuron-methyl based on new or revised label information at the time of risk assessment. Three bridge-intact major degradates (AE F154851, AE F160459, and AE F160460) will be included based on the past HED MARC meeting

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

(01/28/2004). Residues in surface waters will be estimated using PRZM/EXAMS and residues in ground water will be estimated using the Tier I SCI-GROW model and the Tier II PRZM/EXAM ground water model.[15] EECs will be adjusted by percent cropped area (PCA) factors to account for the maximum fractional area within a watershed that may be planted.[16]

6.8. Preliminary Identification of Data Gaps

Available studies submitted to fulfill environmental fate and ecological effects guideline requirements are presented in **Sections 6.8.1** and **6.8.2**, respectively. Data gaps are identified and discussed in regard to impacts on risk assessment.

6.8.1. Environmental Fate Data

Data gaps for mesosulfuron-methyl remain **(Table 16)**. The following data are recommended to reduce uncertainty in the ecological risk assessment.

- Aerobic Aquatic Metabolism (OPPTS Guideline 835.4300) – (mesosulfuron-methyl)
- Aquatic Field Dissipation Study (OPPTS Guideline 835.6200) – (mesosulfuron-methyl)
- Environmental Chemistry Methods for Soil and Plant Material (OCSPP Guideline 850.6100) - (mesosulfuron-methyl and major degradates AE F160459, AE F160460, AE F154851, AE F140458, AE F147447, AE F099095, and AE F092944)

Aerobic Aquatic Metabolism (mesosulfuron-methyl)

Two major metabolites ("unknown A and D") were not identified in the submitted studies (MRID 45386430 and 45385431). Data are needed that identifies all major transformation products (i.e., formed >10%).

Aquatic field dissipation (mesosulfuron-methyl)

No aquatic field dissipation data are available. Mesosulfuron-methyl is a very water soluble and persistent chemical in aquatic environments. It is very likely that the compound will be introduced into the aquatic environment via run-off and leaching.

ECM/ILV method for plant and soil (mesosulfuron-methyl and major degradates)

Studies are needed for mesosulfuron-methyl and major degradation products. Mesosulfuron-methyl, like most sulfonylureas, exhibits long term phytotoxicity. Whether this is due to sorption on soil or toxicity of degradates cannot be resolved with available information. It leaves open the possibility of soil mediated transport due to windborne dust or other pathways. The lack of analytical methods with a limit of quantitation (LOQ) at levels of ecological concern for plants will leave this question unresolved. ECM/ILV for soil will be used to confirm the submitted terrestrial field dissipation data. Therefore, the ECM/ILV methods are required for soil and plants to mediate the uncertainties.

[15] http://www.epa.gov/oppefed1/models/water
[16] http://www.epa.gov/oppefed1/models/water/pca_adjustment_dwa.html

Other data gaps, "Yes" without bold font in **Table 16**, are not likely to change risk conclusions; therefore, studies are not recommended at this time.

Table 16. Environmental Fate Data Gaps for Mesosulfuron-methyl

Guideline	Description	MRID	Classification	Data Gap	Comments
835.2120	Hydrolysis	45386418	Acceptable	No	[1] Data gaps exist for aquatic photolysis at pH 5 and 9; however, available data at pH 7 will be sufficient for modeling purposes. [2]Study is not required because of low vapor pressure. [3]Study can be substituted by Anaerobic Aquatic Metabolism (835.4400) [4]Addtional data are needed to identify two major unknown metabolites [5]Study waiver was granted DP Barcode(s): 297232, 12/08/03 [6]The terrestrial field dissipation study was not conducted with the typical end use products nor does it appear that attempts were made to identify degradates. [7] Additional data will not be needed if the available data are deemed acceptable.
835.2240	Photodegradation in Water	45386419 45386420	Supplemental Supplemental	Yes[1]	
835.2410	Soil Photolysis	45386421	Supplemental	No	
835.2370	Photodegradation in Air	--	--	Yes[2]	
835.4100	Aerobic Soil Metabolism	45386422 45386423 45386424 45386425	Acceptable Acceptable Acceptable Acceptable	No	
835.4200	Anaerobic Soil Metabolism	--	--	Yes[3]	
835.4300	Aerobic Aquatic Metabolism	45386430 45385431	Supplemental Supplemental	**Yes[4]**	
835.4400	Anaerobic Aquatic Metabolism	45386427 45386428	Supplemental Supplemental	No	
835.1230 835.1240	Leaching Adsorption/Desorption	45386432 45386433 45386434	Acceptable Acceptable Acceptable	No	
835.1410	Laboratory Volatility	--	--	Yes [5]	
835.8100	Field Volatility	--	--	No[2]	
835.6100	Terrestrial Field Dissipation	45386501 45386502 46948901	Supplemental In Review	Yes[6,7]	
835.6200	Aquatic Field Dissipation	--	--	**Yes**	
850.6100	ECM/ILV (Water)	45386522 45386523 46451701 46451702	In Review In Review In Review In Review	Yes[7]	
850.6100	ECM/ILV (Soil)	--	--	**Yes**	
850.1730	Bioaccumulation in Fish	--	--	Yes[5]	

6.8.2. Ecological Effects Data

Several data gaps for mesosulfuron-methyl remain (**Tables 17, 18, and 19**). After review, some studies have been reclassified and no longer meet a given data requirement. Studies are not recommended at this time for some data gaps ("Yes" without bold font in **Tables 17, 18, and 19**) because risk conclusions are unlikely to change.

The following studies are recommended:

- Aquatic plant growth (850.4500) - freshwater green alga (Mesosulfuron-methyl)
- Aquatic plant growth (850.4400) - vascular plant (AE F154851 and AE F140584)

Mesosulfuron-methyl

Acute freshwater fish toxicity

Available data for freshwater fish are supplemental in part because samples were not filtered or centrifuged prior to analysis given the presence of precipitate in the test chambers. The amount of mesosulfuron-methyl that was freely dissolved and bioavailable cannot be determined without centrifugation or filtration. As such, toxicity may be underestimated. However, uncertainty is minimal in regard to the risk conclusions. Effects were not observed (mortality or sublethal) and there is no risk concern as long as about 0.05% of the mesosulfuron-methyl was in solution (*i.e.*, dissolved)[17]. Furthermore, there is no risk concern based on the lowest ECOSAR estimate (LC_{50} = 332 mg ai/L). Repeat testing is unlikely to change risk conclusions unless aquatic EECs are substantially higher in the future (*e.g.*, higher application rates are requested).

Freshwater fish early life stage

Data are available for sub-chronic (28 day) toxicity to rainbow trout (two months of age) but not for early life stage (ELS) toxicity. No effects (mortality or growth) were observed in the 28-day study (NOAEC $\geq$ 29.6 mg ai/L). The potential for chronic effects on fish reproduction remains uncertain without an early life stage study. However, there is a large margin of safety based on the current application rates and available toxicity information. ELS toxicity would need to be $\geq$ four orders of magnitude more toxic than the sub-chronic NOAEC (29.6 mg ai/L) to have a risk concern. Additionally, ELS toxicity would need to be $\geq$ three orders of magnitude greater than the lowest ECOSAR estimate (most toxic, NOEC = 3.4 mg ai/L) to have a chronic risk concern. An ELS study is unlikely to change risk conclusions at this time given the margin of safety. However, additional data could be important in the future if aquatic EECs approach the ECOSAR estimate (*e.g.*, higher application rates are requested) or new information suggests reproductive effects at environmentally relevant concentrations of mesosulfuron-methyl.

Passerine acute oral toxicity

Data are not available for a passerine species, which are potentially more sensitive than larger birds due to their smaller size and higher metabolic rates. The available acute oral studies with

[17] Percentage not precise and would be lower because EECs were calculated using a TTR approach and toxicity endpoints are non-definitive.

bobwhite quail and mallard duck showed no mortality at a concentration of 2000 mg/kg. A passerine species (ca. 25 g) would need to be > 50 X more sensitive than the quail and duck to exceed the listed species LOC at the highest registered application rate. Additionally, no mortality was observed at 4800 ppm in the available avian acute dietary studies. At the current application rates, the value of a passerine study would be confirmatory in nature.

Avian reproduction

A non-definitive NOAEC was established in the available studies (MRID 45386228 and 45386229) based on no adverse effects at the highest dose tested. Requesting additional data to establish a definitive NOAEC has little value at this time because terrestrial EECs for currently registered uses are more than 300 X lower than the non-definitive NOAEC. However, additional data could be important in the future if terrestrial EECs approach the highest concentration tested in the available studies (*e.g.*, higher application rates are requested).

Terrestrial plants – seedling emergence

Available data are supplemental because the observation period was 14 days post-application instead of 21 days post-emergence of control plants. Additionally, the test material was TGAI plus adjuvant instead of a TEP (including inert materials) plus adjuvant. Available data suggest that repeat testing would likely result in minimal impact on risk conclusions.

Risk from spray drift is likely to be impacted more by foliar applications. Toxicity was greater for foliar application (vegetative vigor) than for application to seeds (seedling emergence) in studies conducted with the same test material and duration. The value of repeat testing would be confirmatory in this regard.

Seedling emergence data will have a greater impact on assessing risk from runoff. However, little may be gained from repeat testing considering the results of the available vegetative vigor studies. Vegetative vigor data show little difference in toxicity for studies conducted for 21 days using a TEP (MRID 46688201, under review) and 14 days using TGAI plus adjuvant (MRID 45386317 and 45745701). The general risk picture would change little if effects to seedling emergence, like vegetative vigor, are minimally impacted by extending the study duration and testing with a TEP.

Aquatic plant growth - freshwater green alga

Acceptable data are available for three of four recommended test species. Green alga data are needed to assess risk to non-vascular plants because different species are likely to show a range of sensitivity to mesosulfuron-methyl. The most sensitive species will be used to assess risk. Data are of value in reducing uncertainty of risk to non-vascular plants. Other means of addressing risk will be used to reduce uncertainty in the absence of a study. For instance, toxicity may be estimated based on the lowest ECOSAR estimate (IC_{50} = 56 µg ai/L) or data from other SU herbicides.

Non-Guideline – Special study for non-target plant reproductive toxicity with TEP

EFED's Plant Technical Team (PTT) conducted an analysis of available SU plant reproduction data from the open literature and the registrant-submitted data for chlorsulfuron and concluded that data from the 850.4150 vegetative vigor guideline study are sufficiently protective of potential impacts to plant reproduction. Acetolactate synthase (ALS) inhibitors primarily affect metabolically-active meristem tissues. When plants are exposed at a young, vigorously growing life-stage, effects are expressed primarily as inhibition of vegetative growth (*i.e.* biomass, shoot length). As plants mature these effects are less pronounced. However, as plants enter their reproductive life-stage, the metabolically-active tissue will include flower and seed production. Plants exposed to SU herbicides during the reproductive life stage are likely to exhibit adverse effects on reproduction, generally expressed as reduced seed number or reduced seed weight. Based on the latest data analysis, these effects are expected to occur at similar concentrations to those effects determined in the guideline vegetative vigor studies (850.4150). Therefore, fulfilling this DCI has a low potential to add value to the risk assessment and a study is not recommended.

<u>Degradation Products</u>

Fish and aquatic invertebrates (acute and chronic toxicity)

Data are not requested at this time because risk conclusions are unlikely to change based on the currently labeled rates (*see* **Section 6.1**). ECOSAR estimates suggest that some degradates may be more acutely or chronically toxic than mesosulfuron-methyl to fish and invertebrates. However, LOCs are not exceeded even when the lowest ECOSAR estimates (*i.e.*, most toxic for each degradate) are compared to preliminary mesosulfuron-methyl EECs (maximum application rate) calculated with the assumption of no degradation. EECs of individual degradates would be lower. Other means of addressing risk will be used to reduce uncertainty in the absence of studies. A TTR approach will be used to calculate EECs and toxicity may be based on ECOSAR estimates or analogous compounds. However, studies could be important in the future if aquatic EECs are expected to be higher (*e.g.*, higher application rates are requested).

Avian (acute and chronic toxicity)

Data are not requested at this time because risk conclusions are unlikely to change based on the currently labeled rates (*see* **Section 6.1**). Degradates would need to be at least two to three orders of magnitude more toxic than mesosulfuron-methyl to be a risk concern. However, data could be important in the future if EECs are expected to be higher (*e.g.*, higher application rates are requested).

Aquatic plant growth – vascular plant (AE F154851 and AE F140584)

Data are recommended to reduce potential uncertainty in risk conclusions for non-listed species (*see* **Section 6.1)**. AE F154851 (SU bridge-intact compound) and AE F140584 toxicity will be assumed equal to mesosulfuron-methyl in the absence of data and a TTR approach will be used to calculate EECs.

Aquatic plant growth – non-vascular plants

Data are not requested at this time because available information suggests that the degradation products are not more toxic than mesosulfuron-methyl (*see* **Section 6.1**). In the absence of submitted data, those degradates will be assumed as toxic as mesosulfuron-methyl and a TTR approach will be used to calculate EECs. However, as discussed above, an acceptable study is needed to establish mesosulfuron-methyl toxicity to green algae.

Terrestrial plants

Data are not requested at this time; however, SU bridge-intact degradates will be assumed equal in toxicity to mesosulfuron-methyl in the absence of data (*see* **Section 6.1**).

Table 17. Ecological Effects Data (TGAI) for Aquatic Animals Exposed to Mesosulfuron-methyl and Data Gaps

Guideline	Description	MRID	Classification	Data Gap?	Comments
850.1075	Acute freshwater fish toxicity (cold water species)	45386231	Supplemental	Yes[1,2]	[1]EFED does not recommend requesting a new study because little will be gained from submission of a new study. [2] See text above Table 17.
	Acute freshwater fish toxicity (warm water species)	45386230	Supplemental	Yes[1,2]	
	Acute estuarine/ marine fish toxicity	45386301	Supplemental	Yes[1]	
850.1010	Acute toxicity to freshwater invertebrates	45386233	Acceptable (“Core”)	No	
850.1025	Acute estuarine/ marine mollusk toxicity	45386302	Acceptable (“Core”)	No	
850.1035	Acute estuarine/ marine invertebrate toxicity	45386303	Acceptable (“Core”)	No	
850.1300	Freshwater invertebrate life cycle	45386305	Acceptable (“Core”)	No	
850.1400	Freshwater fish early life stage	45386232	Supplemental	Yes[1,2]	

Table 18. Ecological Effects Data (TGAI) for Terrestrial Animals Exposed to Mesosulfuron-methyl and Data Gaps

Guideline	Description	MRID	Classification	Data Gap?	Comments
850.2100	Avian acute oral toxicity (upland game or waterfowl species)	45386224 45386225	Acceptable ("Core")	No	[1]These data are required under 40 CFR part 158 for terrestrial outdoor uses. However, EFED does not recommend requesting a study at this time. [2] See text above Table 17 [3]EFED does not recommend requesting a new study because little will be gained from submission of a new study.
	Avian acute oral toxicity (passerine species)	None	Not applicable	Yes[1,2]	
850.2200	Avian dietary toxicity (upland game species)	45386226	Acceptable ("Core")	No	
	Avian dietary toxicity (waterfowl species)	45386227	Acceptable ("Core")	No	
850.2300	Avian reproduction (upland game species)	45386228	Supplemental	Yes[2,3]	
	Avian reproduction (waterfowl species)	45386229	Supplemental	Yes[2,3]	
850.3020	Honeybee acute contact toxicity	45386319	Acceptable ("Core")	No	

Table 19. Ecological Effects Data for Plants Exposed to Mesosulfuron-methyl and Data Gaps

Guideline	Description	MRID	Classification	Data Gap?	Comments
850.4100[A]	Terrestrial plant toxicity (Tier I&II seedling emergence)	45745702 45386316	Supplemental Supplemental	Yes[1,2]	[1]EFED does not recommend requesting a new study because little will be gained from submission of a new study. [2] See text above Table 17 [3] These data are required under 40 CFR part 158 for terrestrial outdoor uses. Data are of value in reducing uncertainty of risk to non-vascular plants. **[4] No data gap for mesosulfuron-methyl; however, data are recommended for two degradation products (AE F154851 and AE F140584).**
850.4150[B]	Terrestrial plant toxicity (Tier I&II vegetative vigor)	46688201	Under Review	TBD	
850.4500[C]	Aquatic plant growth (freshwater green alga)	45386306	Invalid	**Yes[3]**	
	Aquatic plant growth (freshwater diatom)	45386307	Acceptable ("Core")	No	
	Aquatic plant growth (saltwater diatom)	45386314	Acceptable ("Core")	No	
850.4550[C]	Aquatic plant growth (Cyanobacteria)	45386315	Acceptable ("Core")	No	
850.4400	Aquatic plant growth (vascular plants)	45386310	Acceptable ("Core")	**No[2,4]**	

[A] As of July 2012 the Final Guideline 850.4100 contains both Tier I and Tier II test guidance (formerly 850.4100 and 850.4225, respectively).
[B] As of July 2012 the Final Guideline 850.4150 contains both Tier I and Tier II test guidance (formerly 850.4150 and 850.4250, respectively).
[C] Formerly 850.5400

7. References

USEPA. 2004a. Drinking Water Assessment for Mesosulfuron-methyl and Its Major Metabolites New Chemical- Uses on Winter Wheat (OSPREY; 4.5% mesosulfuron-methyl) and Spring Wheat, Including Dumm (SILVERADO, 2.0% mesosulfuron-methyl). DP Barcode: D295662

USEPA. 2004b. Mesosulfuron Methyl Section 3 - Uses on Winter Wheat (OSPREY; 4.5% mesosulfuron-methyl) and Spring Wheat, Including Durum (SILVERADO, 2.0% mesosulfuron-methyl). DP Barcodes: D284053, D284719, D295614, D295656, D296 120, D297232

USEPA. 2004c. Overview of the Ecological Risk Assessment Process in the Office of Pesticide Programs. U.S. Environmental Protection Agency, Office of Prevention, Pesticides and Toxic Substances, Office of Pesticide Programs, Washington DC., January 23, 2004.

USFWS and NMFS. 1998. Endangered Species Consultation Handbook: Procedures for Conducting Consultation and Conference Activities Under Section 7 of the Endangered Species Act. Final Draft. March 1998.

APPENDIX A. Submitted Environmental Fate and Effects Studies

MRID	Citation Reference
Fate Studies	
45386418	Burri, R. (2000) Hydrolysis of (Carbon 14)-AE F130060 at Different pH Values: Lab Project Number: 738090: C008110. Unpublished study prepared by RCC Ltd. 70 p. {OPPTS 835.2110 and 835.2130}
45386419	Schmidt, W.; Buerkle, W. (2000) Aqueous Photolysis Under Laboratory Conditions: (U-(Carbon 14)-AE F130060: Lab Project Number: CP97/040: C008008. Unpublished study prepared by Aventis CropScience. 58 p.
45386420	Buerkle, W. (2000) Real Half-Lives of the Aqueous Photolysis: AE F130060: Lab Project Number: C009998: OE00/118. Unpublished study prepared by Aventis CropScience. 6 p. {OPPTS 835.2210}
45386421	Burri, R. (2000) Photolysis of (Carbon 14)-AE F130060 on Soil Surface Under Laboratory Conditions: Lab Project Number: 738088: C006911. Unpublished study prepared by RCC Ltd. 51 p.
45386422	Tarara, G. (2000) Kinetics and Metabolism in Soil LS 2.2 at 10C and 20C Under Aerobic Conditions: (2-(Carbon 14)-Pyrimidyl)AE F130060: Lab Project Number: CB96/011: C009871. Unpublished study prepared by Aventis CropScience. 82 p.
45386423	Tarara, G. (2000) Kinetics and Metabolism in Soil LS 2.2 at 10C and 20C Under Aerobic Conditions: (2-(Carbon 14)-Phenyl)AE F130060: Lab Project Number: CB97/053: C009873. Unpublished study prepared by Aventis CropScience. 60 p.
45386424	Tarara, G. (2000) Degradation in Three Soils at 20C Under Aerobic Conditions: AE F130060: Lab Project Number: CB96/056: C009874. Unpublished study prepared by Aventis CropScience. 80 p.
45386425	Tarara, G. (2000) Degradation in Four Soils at 20C Under Aerobic Conditions: (2-(Carbon 14)-Pyrimidinyl)AE F130060: Lab Project Number: CB96/140: C009870. Unpublished study prepared by Aventis CropScience. 96 p.
45386426	Schafer, D. (2000) Kinetic Evaluation of AE F130060 Aerobic Soil Degradation Studies Using TopFit 2.0: Lab Project Number: C009951: OE00/105. Unpublished study prepared by Aventis CropScience GmbH. 121 p. {OPPTS 835.4100}
45386427	Tarara, G. (2000) Kinetics and Metabolism in Soil LS 2.2 at 20C Under Anaerobic Soil Conditions: (U-(Carbon 14)AE F130060 and (2-(Carbon 14)-Pryrimidinyl)AE F130060: Lab Project Number: CB98/136: C009872. Unpublished study prepared by Aventis CropScience GmbH. 71 p.
45386428	Schafer, D. (2000) Kinetic Evaluation of AE F130060 Anaerobic Soil Degradation Studies Using TopFit 2.0: Lab Project Number: C010057: OE00/122. Unpublished study prepared by Aventis CropScience GmbH. 33 p. {OPPTS 835.4200}
45386429	Gildemeister, H. (2001) Degradation in a Water/Sediment-System at Different Temperatures Under Anaerobic Conditions in the Laboratory (2-(Carbon 14)-Pyrimidinyl)-and (U-(Carbon 14)-Phenyl)-AE F130060: Lab Project Number: CB97/143: C011868. Unpublished study prepared by Aventis CropScience. 76 p.
45386430	Steinfuhrer, T.; Zumdick, A. (2000) Aerobic Degradation in Two Water/Sediment-System at 20C (Carbon 14)-AE F130060: Lab Project Number: CB97/082: C009416. Unpublished study prepared by Aventis CropScience. 218 p. {OPPTS 835.4300}
45386431	Schafer, D. (2000) Kinetic Evaluation of AE F130060 Aerobic Water/Sediment-System Using TopFit

2.0: Lab Project Number: C009952: OE00/115. Unpublished study prepared by Aventis CropScience GmbH. 97 p. {OPPTS 835.4300}

45386432 Allan, J.; Pate, M. (2000) The Adsorption/Desorption of (Carbon 14)-AE F130060 on Nine Soils: Lab Project Number: 500CK: C003710: CK96E500. Unpublished study prepared by Aventis CropScience. 84 p.

45386433 Rosenwald, J. (2000) AE F154851: Adsorption in Three Soils: Final Report: Lab Project Number: 1490-017: C007785. Unpublished study prepared by Covance Labs., GmbH. 79 p.

45386434 Rosenwald, J. (2000) AE F099095: Adsorption in Three Soils: Final Report: Lab Project Number: 1490-016: C007786. Unpublished study prepared by Covance Labs., GmbH. 79 p.

45386501 Cole, M. (2001) Dissipation of AE F115008 and AE F130060 in Soil Following Application of AE F115008 WDG and AE F122006 WDG or AE F130060 WDG and AE F107982 WDG to a Bare Plot at the Maximum Proposed Rates, USA, 1998: Lab Project Number: BY98R004: B003218. Unpublished study prepared by Aventis CropScience. 256 p.

46948901 Lenz, M. (2006) Terrestrial Field Dissipation of Mesosulfuron-methyl in North Dakota Soil, 2004. Project Number: MEMMY002. Unpublished study prepared by Agvise Inc and Bayer Corp. 109 p.

45386502 Wrede, A. (2000) Stability of AE F130060 in Soil During Deep Freeze Storage of 24 Months. Unpublished Study Performed and Submitted by Aventis CropScienceGmbH, Frankfurt, Federal Republic of Germany. Study ID. CR 97/037. Experiment Imitation August 12, 1997 and Completion August 12, 1999 p. 10. Final Report Issued August 21, 2000.

45386504 Frey, J.; Harrison, C.; Buerkle, L. (2000) Residues in Rotated Crops Sown 31 Days after Application to Bare Soil at a Rate of 15 g a.s./ha: (2-(Carbon-14)-Pyrimidyl)-AE F130060: Lab Project Number: CM97/044: C008238. Unpublished study prepared by Aventis CropScience. 32 p.

45386505 Frey, J.; Harrison, C.; Buerkle, L. (2000) Residues in Rotated Crops Sown 32 Days after Application to Bare Soil at a Rate of 15 g a.s./ha: (U-(Carbon-14)-Phenyl)-AE F130060: Lab Project Number: CM97/046: C008240. Unpublished study prepared by Aventis CropScience. 32 p.

45386506 Frey, J.; Harrison, C. (2000) Residues in Rotated Crops Sown 4 Months after Application to Bare Soil at a Rate of 15 g a.s./ha: (2-(Carbon-14)-Pyrimidyl)-AE F130060: Lab Project Number: CM97/163: C008242. Unpublished study prepared by Aventis CropScience. 26 p.

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APPENDIX B. SIP v.1.0 Inputs and Outputs

Table 1. Inputs

Parameter	**Value**
Chemical name	Mesosulfuron
Solubility (in water at 25^{o}C; mg/L)	15390
Mammalian LD_{50} (mg/kg-bw)	5000
Mammalian test species	laboratory rat
Body weight (g) of "other" mammalian species	
Mammalian NOAEL (mg/kg-bw)	1175
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)	990
Bobwhite quail NOAEC (mg/kg-diet)	1000
NOAEC (mg/kg-diet) for other bird species	0
Body weight (g) of other avian species	0
NOAEC (mg/kg-diet) for 2nd other bird species	0
Body weight (g) of 2nd other avian species	0

Table 2. Mammalian Results

Parameter	**Acute**	**Chronic**
Upper bound exposure (mg/kg-bw)	2647.0800	2647.0800
Adjusted toxicity value (mg/kg-bw)	3845.8028	903.7637
Ratio of exposure to toxicity	0.6883	2.9290
Conclusion*	**Exposure through drinking water alone is a potential concern for mammals**	**Exposure through drinking water alone is a potential concern for mammals**

Table 3. Avian Results

Parameter	**Acute**	**Chronic**
Upper bound exposure (mg/kg-bw)	12465.9000	12465.9000
Adjusted toxicity value (mg/kg-bw)	1440.8590	49.1164
Ratio of exposure to acute toxicity	8.6517	253.8030
Conclusion*	**Exposure through drinking water alone is a potential concern for birds**	**Exposure through drinking water alone is a potential concern for birds**

APPENDIX C. STIR v.1.0 Inputs and Outputs

Input		
Application and Chemical Information		
Enter Chemical Name	Mesosulfuron	
Enter Chemical Use	Outdoor	
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)	503.5	
Enter Chemical Vapor Pressure (mmHg)	8.25E-14	
Enter Application Rate (lb ai/acre)	0.013	
Toxicity Properties		
Bird		
Enter Lowest Bird Oral LD_{50} (mg/kg bw)	10	
Enter Mineau Scaling Factor	1.15	
Enter Tested Bird Weight (kg)	0.025	
Mammal		
Enter Lowest Rat Oral LD_{50} (mg/kg bw)	5000	
Enter Lowest Rat Inhalation LC_{50} (mg/L)	1.33	
Duration of Rat Inhalation Study (hrs)	4	
Enter Rat Weight (kg)	0.35	

Output		
Results Avian (0.020 kg)		
Maximum Vapor Concentration in Air at Saturation (mg/m^3)	2.24E-09	
Maximum 1-hour Vapor Inhalation Dose (mg/kg)	2.81E-10	
Adjusted Inhalation LD_{50}	1.99E-02	
Ratio of Vapor Dose to Adjusted Inhalation LD_{50}	1.41E-08	**Exposure not Likely Significant**
Maximum Post-treatment Spray Inhalation Dose (mg/kg)	1.25E-03	
Ratio of Droplet Inhalation Dose to Adjusted Inhalation LD_{50}	6.27E-02	**Exposure not Likely Significant**
Results Mammalian (0.015 kg)		
Maximum Vapor Concentration in Air at Saturation (mg/m^3)	2.24E-09	
Maximum 1-hour Vapor Inhalation Dose (mg/kg)	3.53E-10	
Adjusted Inhalation LD_{50}	7.92E+01	
Ratio of Vapor Dose to Adjusted Inhalation LD_{50}	4.46E-12	**Exposure not Likely Significant**
Maximum Post-treatment Spray Inhalation Dose (mg/kg)	1.57E-03	
Ratio of Droplet Inhalation Dose to Adjusted Inhalation LD_{50}	1.98E-05	**Exposure not Likely Significant**